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This abstract supplement unites the journal *SLEEP* and the science of the SLEEP 2008 22nd Annual Meeting of the Associated Professional Sleep Societies, LLC in a convenient format. This special issue includes all abstracts presented at SLEEP 2008 held June 7-12, 2008, in Baltimore, Maryland.

The abstract supplement provides all American Academy of Sleep Medicine and Sleep Research Society members, including those unable to attend the meeting, a glimpse into the new ideas and latest research taking place in the fields of sleep disorders medicine and sleep research.

Of the 1,159 abstracts accepted, 243 will be presented in a brief oral presentation format and the remainder will be presented in a poster format. Similar to prior meetings, the Program Committee elected to:

- 1) Group posters into thematic groups.
- 2) Display each poster on one of the three scheduled poster days (June 9, 10 and 11).

The poster sessions will continue to be two hours in length to allow attendees greater opportunity to view posters and interact with presenters. Each poster has a unique four-digit number and is assigned to one of the 19 categories listed below to facilitate identification and location.

- Category A – Neuroscience
- Category B – Physiology/Phylogeny/Ontogeny
- Category C – Pharmacology
- Category D – Circadian Rhythms
- Category E – Pediatrics
- Category F – Aging
- Category G – Sleep Deprivation
- Category H – Sleep Disorders – Breathing
- Category I – Sleep Disorders – Narcolepsy/Hypersomnia
- Category J – Sleep Disorders – Insomnia
- Category K – Sleep Disorders – Parasomnias
- Category L – Sleep Disorders – Movement Disorders
- Category M – Sleep Disorders – Neurologic Disorders
- Category N – Sleep in Medical Disorders
- Category O – Sleep in Psychiatric Disorders
- Category P – Instrumentation & Methodology
- Category Q – Healthcare Services, Research & Education
- Category R – Molecular Biology & Genetics
- Category S – Behavior, Cognition & Dreams

Attendees of the SLEEP 2008 meeting will experience a forum for the discussion of new ideas and key research in the fields of sleep medicine and sleep research. Our hope is that this experience fosters an environment in which members and attendees obtain education on the latest basic science, clinical science and technologies, which will further promote the continued growth of the field through the dissemination of new knowledge. We look forward to sharing in the success of this pivotal event.

David F. Dinges, PhD
Editor-in-Chief

WARNING: Central nervous system depressant with abuse potential. Should not be used with alcohol or other CNS depressants.

Sodium oxybate is GHB, a known drug of abuse. Abuse has been associated with some important central nervous system (CNS) adverse events (including death). Even at recommended doses, use has been associated with confusion, depression and other neuropsychiatric events. Reports of respiratory depression occurred in clinical trials. Almost all of the patients who received sodium oxybate during clinical trials were receiving CNS stimulants.

Important CNS adverse events associated with abuse of GHB include seizure, respiratory depression and profound decreases in level of consciousness, with instances of coma and death. For events that occurred outside of clinical trials, in people taking GHB for recreational purposes, the circumstances surrounding the events are often unclear (e.g., dose of GHB taken, the nature and amount of alcohol or any concomitant drugs).

Xyrem is available through the Xyrem Success Program, using a centralized pharmacy 1-866-XYREMS8* (1-866-997-3688). The Success Program provides educational materials to the prescriber and the patient explaining the risks and proper use of sodium oxybate, and the required prescription form. Once it is documented that the patient has read and/or understood the materials, the drug will be shipped to the patient. The Xyrem Success Program also recommends patient follow-up every 3 months. Physicians are expected to report all serious adverse events to the manufacturer. (See WARNINGS).

INDICATIONS AND USAGE

Xyrem (sodium oxybate) oral solution is indicated for the treatment of excessive daytime sleepiness and cataplexy in patients with narcolepsy.

In Xyrem clinical trials, approximately 80% of patients maintained concomitant stimulant use (see BLACK BOX WARNINGS).

CONTRAINDICATIONS

Sodium oxybate is contraindicated in patients being treated with sedative hypnotic agents.

Sodium oxybate is contraindicated in patients with succinic semialdehyde dehydrogenase deficiency. This rare disorder is an inborn error of metabolism variably characterized by mental retardation, hypotonia, and ataxia.

WARNINGS

SEE BOXED WARNING

Due to the rapid onset of its CNS depressant effects, sodium oxybate should only be ingested at bedtime, and while in bed. For at least 6 hours after ingesting sodium oxybate, patients must not engage in hazardous occupations or activities requiring complete mental alertness or motor coordination, such as operating machinery, driving a motor vehicle, or flying an airplane. When patients first start taking Xyrem or any other sleep medicine, until they know whether the medicine will still have some carryover effect on them the next day, they should use extreme care while performing any task that could be dangerous or requires full mental alertness.

The combined use of alcohol (ethanol) with sodium oxybate may result in potentiation of the central nervous system-depressant effects of sodium oxybate and alcohol. Therefore, patients should be warned strongly against the use of any alcoholic beverages in conjunction with sodium oxybate. Sodium oxybate should not be used in combination with sedative hypnotics or other CNS depressants.

Central Nervous System Depression/Respiratory Depression

Sodium oxybate is a CNS depressant with the potential to impair respiratory drive, especially in patients with already-compromised respiratory function. In overdoses, life-threatening respiratory depression has been reported (see OVERDOSAGE). In clinical trials two subjects had profound CNS depression. A 39-year-old woman, a healthy volunteer received a single 4.5 g dose of sodium oxybate after fasting for 10 hours. An hour later, while asleep, she developed decreased respiration and was treated with an oxygen mask. An hour later, this event recurred. She also vomited and had fecal incontinence. In another case, a 64-year-old narcoleptic man was found unresponsive on the floor on Day 170 of treatment with sodium oxybate at a total daily dose of 4.5 g/night. He was taken to an emergency room where he was intubated. He improved and was able to return home later the same day. Two other patients discontinued sodium oxybate because of severe difficulty breathing and an increase in obstructive sleep apnea.

The respiratory depressant effects of Xyrem, at recommended doses, were assessed in 21 patients with narcolepsy, and no dose-related changes in oxygen saturation were demonstrated in the group as a whole. One of the 21 patients had significant concomitant pulmonary illness, and 4 of the 21 had moderate-to-severe sleep apnea. One of the 4 patients with sleep apnea had significant worsening of the apnea/hypopnea index during treatment, but worsening did not increase at higher doses. Another patient discontinued treatment because of a perceived

increase in clinical apnea events. In the randomized controlled Trials 3 and 4, a total of 40 narcolepsy patients were included with a baseline apnea/hypopnea index of 16 to 67 events per hour indicative of mild to severe sleep disordered breathing. None of the 40 patients had a clinically significant worsening of their respiratory function as measured by apnea/hypopnea index and pulse oximetry while receiving sodium oxybate at dosages of 4.5 to 9 g/night in divided dosages. Nevertheless, caution should be observed if Xyrem is prescribed to patients with compromised respiratory function. Prescribers should be aware that sleep apnea has been reported with a high incidence (even 50%) in some cohorts of narcoleptic patients.

Confusion/Neuropsychiatric Adverse Events

During clinical trials, 2.6% of patients treated with sodium oxybate experienced confusion. Fewer than 1% of patients discontinued the drug because of confusion. Confusion was reported at all recommended doses from 6 to 9 g/night. In a controlled trial where patients were randomized to fixed total daily doses of 3, 6, and 9 g/night or placebo, a dose-response relationship for confusion was demonstrated with 17% of patients at 9 g/night experiencing confusion. In all cases in that controlled trial, the confusion resolved soon after termination of treatment. In Trial 3 where sodium oxybate was titrated from an initial 4.5 g/night dose, there was a single event of confusion in one patient at the 9 g/night dose. In the majority of cases in all clinical trials, confusion resolved either soon after termination of dosing or with continued treatment. However, patients treated with Xyrem who become confused should be evaluated fully, and appropriate intervention considered on an individual basis.

Other neuropsychiatric events included psychosis, paranoia, hallucinations, and agitation. The emergence of thought disorders and/or behavior abnormalities when patients are treated with sodium oxybate requires careful and immediate evaluation.

Depression

In clinical trials, 3.2% of patients treated with sodium oxybate reported depressive symptoms. In the majority of cases, no change in sodium oxybate treatment was required. Four patients (<1%) discontinued because of depressive symptoms. In the controlled clinical trial where patients were randomized to fixed doses of 3, 6, 9 g/night or placebo, there was a single event of depression at the 3 g/night dose. In Trial 3, where patients were titrated from an initial 4.5 g/night starting dose, the incidence of depression was 1 (1.7%), 1 (1.5%), 2 (3.2%), and 2 (3.6%) for the placebo, 4.5 g, 6 g, and 9 g/night doses respectively.

In the 717 patient dataset, there were two suicides and one attempted suicide recorded in patients with a previous history of depressive psychiatric disorder. Of the two suicides, one patient used sodium oxybate in conjunction with other drugs. Sodium oxybate was not involved in the second suicide. Sodium oxybate was the only drug involved in the attempted suicide. A fourth patient without a previous history of depression attempted suicide by taking an overdose of a drug other than sodium oxybate.

The emergence of depression when patients are treated with Xyrem requires careful and immediate evaluation. Patients with a previous history of a depressive illness and/or suicide attempt should be monitored especially carefully for the emergence of depressive symptoms while taking Xyrem.

Usage in the Elderly

There is very limited experience with sodium oxybate in the elderly. Therefore, elderly patients should be monitored closely for impaired motor and/or cognitive function when taking sodium oxybate.

PRECAUTIONS

Incontinence

During clinical trials, 7% of narcoleptic patients treated with sodium oxybate experienced either a single episode or sporadic nocturnal urinary incontinence and <1% experienced a single episode of nocturnal fecal incontinence. Less than 1% of patients discontinued as a result of incontinence. Incontinence has been reported at all doses tested.

In a controlled trial where patients were randomized to fixed total daily doses of 3, 6, and 9 g/night or placebo, a dose-response relationship for urinary incontinence was demonstrated with 14% of patients initiated at 9 g/night experiencing urinary incontinence. In the same trial, one patient experienced fecal incontinence when initiated at a dose of 9 g/night and discontinued treatment as a result.

If a patient experiences urinary or fecal incontinence during Xyrem therapy, the prescriber should consider pursuing investigations to rule out underlying etiologies, including worsening sleep apnea or nocturnal seizures, although there is no evidence to suggest that incontinence has been associated with seizures in patients being treated with Xyrem.

Sleepwalking

The term "sleepwalking" in this section refers to confused behavior occurring at night and, at times, associated with wandering. It is unclear if some or all of these episodes correspond to true somnambulism, which is a parasomnia occurring during non-REM sleep, or to any other specific medical disorder. Sleepwalking was reported in 4% of 717 patients treated in clinical trials with sodium oxybate. In sodium oxybate-treated patients <1% discontinued due to sleepwalking. In controlled trials of up to 4 weeks duration, the incidence of sleepwalking was 1% in both placebo and sodium

oxybate-treated patients. Sleepwalking was reported by 32% of patients treated with sodium oxybate for periods up to 16 years in one independent uncontrolled trial. Fewer than 1% of the patients in that trial discontinued due to sleepwalking. Five instances of significant injury or potential injury were associated with sleepwalking during a clinical trial of sodium oxybate including a fall, clothing set on fire while attempting to smoke, attempted ingestion of nail polish remover, and overdose of oxybate. Therefore, episodes of sleepwalking should be fully evaluated and appropriate interventions considered.

Sodium Intake

Daily sodium intake in patients taking sodium oxybate is provided below and should be considered in patients with heart failure, hypertension or compromised renal function.

Table 1 Sodium Content per Total Nightly Dose		
Xyrem Dose (g)	Xyrem (mL)	Sodium Content/Dose
3	6	546 mg
4.5	9	819 mg
6	12	1092 mg
7.5	15	1365 mg
9	18	1638 mg

Hepatic Insufficiency

Patients with compromised liver function will have an increased elimination half-life and systemic exposure to sodium oxybate. The starting dose should therefore be decreased by one-half in such patients, and response to dose increments monitored closely.

Renal Insufficiency

No studies have been conducted in patients with renal failure. Because less than 5% of sodium oxybate is excreted via the kidney, no dose adjustment should be necessary in patients with renal impairment. The sodium load associated with administration of sodium oxybate should be considered in patients with renal insufficiency.

Information for Patients

The Xyrem Patient Success Program* includes detailed information about the safe and proper use of sodium oxybate, as well as information to help the patient prevent accidental use or abuse of sodium oxybate by others. Patients must read and/or understand the materials before initiating therapy. Prescribers will discuss dosing (including the procedure for preparing the dose to be administered) prior to the initiation of treatment. Patients should also be informed that they should be seen by the prescriber frequently during the course of their treatment to review dose titration, symptom response and adverse reactions. Food significantly decreases the bioavailability of sodium oxybate. Whether sodium oxybate is taken in the fed or fasted state may affect both the efficacy and safety of sodium oxybate for a given patient. Patients should be made aware of this and try to take the first dose several hours after a meal. Patients should be informed that sodium oxybate is associated with urinary and, less frequently, fecal incontinence. As a safety precaution, patients should be instructed to lie down and sleep after each dose of sodium oxybate, and not to take sodium oxybate at any time other than at night, immediately before bedtime and again 2.5 to 4 hours later. Patients should be instructed that they should not take alcohol or other sedative hypnotics with sodium oxybate. For additional information, patients should see the Medication Guide for Xyrem.

Laboratory Tests

Laboratory tests are not required to monitor patient response or adverse events resulting from sodium oxybate administration.

In an open-label trial of long term exposure to sodium oxybate, which extended as long as 16 years for some patients, 30% (26/87) of patients tested had at least one positive anti-nuclear antibody (ANA) test. Of the 26, 17 patients had multiple positive ANA tests over time. The clinical course of these patients was not always clearly recorded, but one patient was clearly diagnosed with rheumatoid arthritis at the time of the first recorded positive ANA test. No instances of systemic lupus erythematosus have been reported in patients taking sodium oxybate.

Drug Interactions

Interactions between sodium oxybate and three drugs commonly used in patients with narcolepsy (zolpidem tartrate, protriptyline HCl, and modafinil) have been evaluated in formal studies. Sodium oxybate, in combination with these drugs, produced no significant pharmacokinetic changes for either drug. However, pharmacodynamic interactions cannot be ruled out. Nonetheless, sodium oxybate should not be used in combination with sedative hypnotics or other CNS depressants. Alteration of gastric pH with omeprazole produced no significant change in the oxybate kinetics.

Carcinogenicity, Mutagenicity, Impairment of Fertility

Sodium oxybate was not carcinogenic in rats administered oral doses of up to 1000 mg/kg/day (2 times the exposure in humans receiving the maximum recommended dose (MRHD) of 9 g/day, on an AUC basis) for 83 weeks in the male rats and for 104 weeks in female rats. The results of 2-year carcinogenicity studies in mouse and rat with gamma-butyrolactone, a compound that is metabolized to sodium oxybate *in vivo*, showed no clear evidence of carcinogenic activity. The plasma AUCs of sodium oxybate achieved at the

high doses in these studies were 1/2 (mice and female rats) and 1/10 (male rats) the plasma AUCs at the MRHD.

Sodium oxybate was negative in the Ames microbial mutagen test, an *in vitro* chromosomal aberration assay in CHO cells, and an *in vivo* rat micronucleus assay.

Sodium oxybate did not impair fertility in rats at doses up to 1000 mg/kg (approximately equal to the maximum recommended human daily dose on a mg/m² basis).

Pregnancy

Pregnancy Category B: Reproduction studies conducted in pregnant rats at doses up to 1000 mg/kg (approximately equal to the maximum recommended human daily dose on a mg/m² basis) and in pregnant rabbits at doses up to 1200 mg/kg (approximately 3 times the maximum recommended human daily dose on a mg/m² basis) revealed no evidence of teratogenicity. In a study in which rats were given sodium oxybate from Day 6 of gestation through Day 21 post-partum, slight decreases in pup and maternal weight gains were seen at 1000 mg/kg; there were no drug effects on other developmental parameters. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery

Sodium oxybate has not been studied in labor or delivery. In obstetric anesthesia using an injectable formulation of sodium oxybate newborns had stable cardiovascular and respiratory measures but were very sleepy, causing a slight decrease in Apgar scores. There was a fall in the rate of uterine contractions 20 minutes after injection. Placental transfer is rapid, but umbilical vein levels of sodium oxybate were no more than 25% of the maternal concentration. No sodium oxybate was detected in the infant's blood 30 minutes after delivery. Elimination curves of sodium oxybate between a 2-day old infant and a 15-year old patient were similar. Subsequent effects of sodium oxybate on later growth, development and maturation in humans are unknown.

Nursing Mothers

It is not known whether sodium oxybate is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when sodium oxybate is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in patients under 16 years of age have not been established.

Race and Gender Effects

There were too few non-Caucasian patients to permit evaluation of racial effects on safety or efficacy. More than 90% of the subjects in clinical trials were Caucasian. The database was 58% female. No important differences in safety or efficacy of Xyrem were noted between men and women. The overall percentage of patients with at least one adverse event was slightly higher in women (80%) than in men (69%). The incidence of serious adverse events and discontinuations due to adverse events were similar in both men and women.

ADVERSE REACTIONS

A total of 717 narcoleptic patients were exposed to sodium oxybate in clinical trials. The most commonly observed adverse events associated with the use of sodium oxybate were:

Headache (22%), nausea (17%), dizziness (17%), nasopharyngitis (8%), somnolence (8%), vomiting (8%), and urinary incontinence (7%).

Two deaths occurred in these clinical trials, both from drug overdoses. Both of these deaths resulted from ingestion of multiple drugs, including sodium oxybate in one patient.

In these clinical trials, 10% of patients discontinued because of adverse events. The most frequent reasons for discontinuation (>1%) were nausea (2%), dizziness (2%), and vomiting (1%).

Approximately 9% of patients receiving sodium oxybate in 5 placebo-controlled clinical trials (n=443) withdrew due to an adverse event, compared to 1% receiving placebo (n=79). The reasons for discontinuation that occurred more frequently in sodium oxybate-treated patients than placebo-treated patients were: nausea (2%), dizziness (2%), vomiting (1%), as well as urinary incontinence, confusional state, dyspnea, hyposthesia, paresthesia, somnolence, tremor, vertigo, and blurred vision, all occurring in <1% of patients.

Incidence in Controlled Clinical Trials

Most Commonly Reported Adverse Events in Controlled Clinical Trials

The most commonly reported adverse events (≥5%) in placebo controlled clinical trials associated with the use of sodium oxybate and occurring more frequently than seen in placebo-treated patients were: nausea (19%), dizziness (18%), headache (18%), vomiting (8%), somnolence (6%), urinary incontinence (6%), and nasopharyngitis (6%). These incidences are based on combined data from Trial 1, Trial 2, Trial 3, and two smaller randomized, double-blind, placebo-controlled, cross-over trials (n=655).

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from clinical trials

does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating incidence rates.

The data presented below come from two placebo-controlled clinical trials, Trial 1 and Trial 3.

Tables 2 and 3 list the incidence of treatment-emergent adverse events in Trials 1 and 3, respectively, for which there was an incidence of $\geq 5\%$ and the incidence in at least one dosage group on sodium oxybate was greater than placebo. The number of patients in each dosage group represents the total number of patients treated at each dose. Treatment was initiated at assigned doses of 3, 6, and 9 g in Trial 1.

Table 2

Incidence (%) of Treatment-Emergent Adverse Events in Trial 1				
System Organ Class	Placebo	Sodium Oxybate Dosage (g/night) at Onset		
		3	6	9
MedDRA Preferred Term	N = 34	N = 34	N = 33	N = 35
Ear and labyrinth disorders				
Tinnitus	0	2 (5.9%)	0	0
Eye disorders				
Vision blurred	1 (2.9%)	2 (5.9%)	0	0
Gastrointestinal disorders				
Abdominal Pain Upper	0	0	1 (3.0%)	4 (11.4%)
Diarrhea	0	0	2 (6.1%)	3 (8.6%)
Dyspepsia	2 (5.9%)	1 (2.9%)	3 (9.1%)	3 (8.6%)
Nausea	2 (5.9%)	3 (8.8%)	8 (24.2%)	14 (40.0%)
Vomiting	0	0	3 (9.1%)	8 (22.9%)
General disorders and administration site conditions				
Feeling Drunk	0	0	0	3 (8.6%)
Lethargy	0	2 (5.9%)	0	0
Pain	1 (2.9%)	1 (2.9%)	1 (3.0%)	2 (5.7%)
Infections and infestations				
Gastroenteritis viral	0	0	2 (6.1%)	0
Nasopharyngitis	1 (2.9%)	1 (2.9%)	2 (6.1%)	2 (5.7%)
Upper respiratory tract infection	1 (2.9%)	1 (2.9%)	2 (6.1%)	0
Injury, poisoning and procedural complications				
Post procedural pain	0	0	0	2 (5.7%)
Investigations				
Blood pressure increased	1 (2.9%)	0	2 (6.1%)	0
Musculoskeletal and connective tissue disorders				
Back Pain	2 (5.9%)	0	2 (6.1%)	2 (5.7%)
Cataplexy	0	0	0	3 (8.6%)
Muscular weakness	0	2 (5.9%)	1 (3.0%)	0
Nervous system disorders				
Disturbance in attention	0	1 (2.9%)	0	3 (8.6%)
Dizziness	2 (5.9%)	8 (23.5%)	10 (30.3%)	13 (37.1%)
Headache	8 (23.5%)	3 (8.8%)	7 (21.2%)	13 (37.1%)
Hypoesthesia	0	2 (5.9%)	0	0
Sleep Paralysis	1 (2.9%)	1 (2.9%)	2 (6.1%)	5 (14.3%)
Somnolence	3 (8.8%)	4 (11.8%)	4 (12.1%)	5 (14.3%)
Psychiatric disorders				
Confusional state	0	2 (5.9%)	1 (3.0%)	2 (5.7%)
Depression	0	2 (5.9%)	0	0
Disorientation	1 (2.9%)	1 (2.9%)	0	3 (8.6%)
Nightmare	0	1 (2.9%)	2 (6.1%)	0
Sleep disorder	0	0	2 (6.1%)	1 (2.9%)
Sleep walking	0	0	0	2 (5.7%)
Renal and urinary disorders				
Enuresis	0	0	1 (3.0%)	6 (17.1%)
Respiratory, thoracic and mediastinal disorders				
Pharyngolaryngeal pain	2 (5.9%)	0	3 (9.1%)	1 (2.9%)
Skin and subcutaneous tissue disorders				
Hyperhidrosis	0	1 (2.9%)	1 (3.0%)	2 (5.7%)

Table 3

Incidence (%) of Treatment-Emergent Adverse Events in Trial 3 where dose titration from 4.5 to 9 grams occurred in weekly intervals				
System Organ Class	Placebo	Sodium Oxybate Dosage (g/night) at Onset		
		4.5	6	9
MedDRA Preferred Term	N = 60	N = 185	N = 114	N = 46
Gastrointestinal disorders				
Nausea	2 (3.3%)	14 (7.6%)	12 (10.5%)	9 (19.6%)
Vomiting	1 (1.7%)	3 (1.6%)	4 (3.5%)	4 (8.7%)
Nervous system disorders				
Disturbance in Attention	0	2 (1.1%)	0	3 (6.5%)
Dizziness	1 (1.7%)	17 (9.2%)	9 (7.9%)	4 (8.7%)
Somnolence	0	2 (1.1%)	0	5 (10.9%)
Renal and urinary disorders				
Enuresis	1 (1.7%)	6 (3.2%)	4 (3.5%)	6 (13.0%)

Dose Response Information

Discontinuities of treatment due to adverse events were most common at the highest dose of sodium oxybate. A dose-response relationship was observed for nausea, vomiting, paresthesia, disorientation, irritability, disturbance in attention, feeling drunk, sleepwalking and enuresis. The

incidence of all these events was notably higher at 9 g/d. Dizziness was most common at 3 and 9 g/night.

Less Common Adverse Events

During clinical trials sodium oxybate was administered to 717 patients with narcolepsy, and 182 healthy volunteers. A total of 283 patients and 25 healthy volunteers received 9 g/night, the maximum recommended dose. A total of 334 patients received sodium oxybate for at least one year. To establish the rate of adverse events, data from all subjects receiving any dose of sodium oxybate were pooled. All adverse events reported by at least two people are included except for those already listed elsewhere in the labeling, terms too general to be informative, or events unlikely to be drug induced. Events are classified by body system and listed under the following definitions: frequent adverse events (those occurring in at least 1/100 people); infrequent events (those occurring in 1/100 to 1/1000 people). These events are not necessarily related to sodium oxybate treatment.

Blood and lymphatic system disorders

Frequent: none; **Infrequent:** leukopenia, lymphadenopathy.

Cardiac disorders

Frequent: none; **Infrequent:** tachycardia.

Ear and labyrinth disorders

Frequent: ear pain, vertigo; **Infrequent:** ear discomfort, tinnitus.

Eye disorders

Frequent: vision blurred; **Infrequent:** conjunctivitis, eye irritation, eye pain, eye redness, eye swelling, keratoconjunctivitis sicca, miosis.

Gastrointestinal disorders

Frequent: constipation, dyspepsia, toothache; **Infrequent:** abdominal distention, dysphagia, eructation, fecal incontinence, flatulence, gastroesophageal reflux disease, oral pain, retching, salivary hypersecretion, stomach discomfort.

General disorders and administration site conditions

Frequent: asthenia, chest pain, fatigue, influenza like illness, malaise, pyrexia; **Infrequent:** chest discomfort, discomfort, edema, feeling abnormal, feeling cold, feeling hot, feeling hot and cold, feeling jittery, gait abnormal, hangover, lethargy, sensation of foreign body, sluggishness.

Immune system disorders

Frequent: none; **Infrequent:** hypersensitivity, multiple allergies.

Infections and infestations

Frequent: bronchitis, gastroenteritis viral, influenza, nasopharyngitis, sinusitis, upper respiratory tract infection, urinary tract infection; **Infrequent:** bladder infection, bronchial infection, cellulitis, dental caries, ear infection, fungal infection, gastroenteritis, herpes simplex, herpes zoster, laryngitis, localized infection, otitis externa, pharyngitis, pneumonia, tinea pedis, tooth abscess, tooth infection, vaginal infection, vaginal mycosis.

Injury, poisoning and procedural complications

Frequent: contusion, fall, pain trauma activated; **Infrequent:** ankle fracture, back injury, concussion, head injury, joint sprain, limb injury, muscle strain, post procedural pain, road traffic accident, skin laceration, tooth injury.

Investigations

Frequent: weight decreased; **Infrequent:** alanine aminotransferase increased, blood alkaline phosphatase increased, blood calcium decreased, blood cholesterol increased, blood glucose increased, blood uric acid increased, blood urine, electrocardiogram abnormal, heart rate increased, liver function test abnormal, protein urine, respiratory rate increased, urine analysis abnormal.

Metabolism and nutrition disorders

Frequent: anorexia; **Infrequent:** decreased appetite, hypematremia, hypocalcemia, increased appetite.

Musculoskeletal and connective tissue disorders

Frequent: arthralgia, back pain, myalgia, neck pain; **Infrequent:** arthritis, chest wall pain, joint stiffness, joint swelling, muscle tightness, muscle twitching, muscular weakness, musculoskeletal discomfort, musculoskeletal stiffness, polyarthritis, sensation of heaviness, tendonitis.

Neoplasms benign, malignant and unspecified

Frequent: none; **Infrequent:** cyst.

Nervous system disorders

Frequent: balance disorder, headache, hypoesthesia, memory impairment; **Infrequent:** coordination abnormal, depressed level of consciousness, dizziness postural, dysarthria, dysgeusia, dyskinesia, dystasia, head discomfort, hyperaesthesia, mental impairment, migraine, myoclonus, paralysis, psychomotor hyperactivity, restless leg syndrome, sedation, sinus headache, sleep talking, sudden onset of sleep, syncope, tension headache.

Psychiatric disorders

Frequent: abnormal dreams, confusional state, depression, insomnia, nervousness, nightmare, sleep disorder; **Infrequent:** affect lability, crying, emotional disorder, euphoric mood, fear, hallucination-auditory, hypnagogic hallucination, initial insomnia, libido increased, middle insomnia, mood altered, panic disorder, paranoia, restlessness, sleep attacks, stress symptoms.

Renal and urinary disorders

Frequent: none; **Infrequent:** chromaturia, hematuria, incontinence, micturition urgency, nocturia, pollakiuria, proteinuria, urinary incontinence.

Reproductive system and breast disorders

Frequent: none; **Infrequent:** ovarian cyst, vaginal hemorrhage.

Respiratory, thoracic and mediastinal disorders

Frequent: cough, dyspnea, nasal congestion, pharyngolaryngeal pain, sinus congestion; **Infrequent:** allergic sinusitis, apnea, asthma, dry throat, hiccup, hyperventilation, nocturnal dyspnea, oropharyngeal swelling, respiratory disorder, rhinitis, rhinitis allergic, sinus disorder, snoring, throat secretion increased, upper respiratory tract congestion.

Skin and subcutaneous tissue disorders

Frequent: pruritis; **Infrequent:** acne, alopecia, cold sweat, dermatitis contact, night sweats, rosacea, skin irritation, urticaria.

Surgical and medical procedures

Frequent: none; **Infrequent:** endodontic procedure.

Vascular disorders

Frequent: hypertension; **Infrequent:** hypotension, peripheral coldness.

DRUG ABUSE AND DEPENDENCE

Controlled Substance Class

Xyrem is classified as a Schedule III controlled substance by Federal law. The active ingredient, sodium oxybate or gamma-hydroxybutyrate (GHB), is listed in the most restrictive schedule of the Controlled Substances Act (Schedule I). Thus, non-medical uses of sodium oxybate (Xyrem or GHB) are classified under Schedule I.

Abuse, Dependence, and Tolerance

Abuse

Although sodium oxybate (also known as GHB) has not been systematically studied in clinical trials for its potential for abuse, illicit use and abuse have been reported. Sodium oxybate is a psychoactive drug that produces a wide range of pharmacological effects. It is a sedative-hypnotic that produces dose and concentration dependent central nervous system effects in humans. The onset of effect is rapid, enhancing its desirability as a drug of abuse or misuse.

The rapid onset of sedation, coupled with the amnesic features of sodium oxybate, particularly when combined with alcohol, has proven to be dangerous for the voluntary and involuntary (assault victim) user.

GHB is abused in social settings primarily by young adults. GHB has some commonalities with ethanol over a limited dose range and some cross tolerance with ethanol has been reported as well. Cases of severe dependence and craving for GHB have been reported. Dependence is indicated by the use of increasingly large doses, increased frequency of use, and continued use despite adverse consequences. Some of the doses reported abused in the "rave" setting have been similar to the dose range studied for therapeutic treatment of cataplexy.

Hospital emergency department reports increased 100-fold from 1992 to 1999 (source: Substance Abuse Mental Health Services Administration, Drug Abuse Warning Network [DAWN]). Sixty percent of the ED reports involved individuals 25 years and younger. Numerous deaths had been reported over that period of time, typically involving GHB in combination with alcohol and other drugs, including five in the DAWN system in which GHB was the only drug that could be identified. However, the incidence of hospital emergency department reports of events involving GHB and GHB-related analogs has decreased by about 33% since 2000, and reports to the American Association of Poison Control Centers of GHB exposures has decreased from 1916 (involving 6 deaths) in 2001 to 800 (without any deaths) in 2003.

Dependence

There have been case reports of dependence after illicit use of GHB at frequent repeated doses (18 to 250 g/day), in excess of the therapeutic dose range. In these cases, the signs and symptoms of abrupt discontinuation included an abstinence syndrome consisting of insomnia, restlessness, anxiety, psychosis, lethargy, nausea, tremor, sweating, muscle cramps, and tachycardia. These symptoms generally abated in 3 to 14 days. The discontinuation effects of sodium oxybate have not been systematically evaluated in controlled clinical trials. An abstinence syndrome has not been reported in clinical investigations. Although the clinical trial experience with sodium oxybate in narcolepsy/cataplexy patients at therapeutic doses does not show clear evidence of a withdrawal syndrome, two patients reported anxiety and one reported insomnia following abrupt discontinuation at the termination of the clinical trial; in the two patients with anxiety, the frequency of cataplexy had increased markedly at the same time.

Tolerance

Tolerance to sodium oxybate has not been systematically studied in controlled clinical trials. Open-label, long-term (≥ 6 months) clinical trials did not demonstrate development of tolerance. There have been some case reports of symptoms of tolerance developing after illicit use at dosages far in excess of the recommended Xyrem dosage regimen. Clinical studies of sodium oxybate in the treatment of alcohol withdrawal suggest a potential cross-tolerance with alcohol. Because illicit use and abuse of GHB have been reported, physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely, observing them for signs of misuse or abuse of GHB (e.g. increase in size or frequency of dosing, drug-seeking behavior). Physicians should document the diagnosis and indication for Xyrem, being alert to drug-seeking behavior and/or feigned cataplexy.

OVERDOSAGE

Human Experience

Information regarding overdose with sodium oxybate is derived largely from reports in the medical literature that describe symptoms and signs in individuals who have ingested GHB illicitly. In these circumstances the co-ingestion of other drugs and alcohol is common, and may influence the presentation and severity of clinical manifestations of overdose. In addition, overdose with GHB may be indistinguishable from overdose with other drugs, or from several other medical conditions that result in similar symptoms.

In clinical trials two cases of overdose with Xyrem were reported. In the first case, an estimated dose of 150 g, more than 15 times the maximum recommended dose, caused a patient to be unresponsive with brief periods of apnea and to be incontinent of urine and feces. This individual recovered without sequelae. In the second case, death was reported following a multiple drug overdose consisting of Xyrem and numerous other drugs.

Signs and Symptoms

Information about signs and symptoms associated with overdose with sodium oxybate derives from reports of its illicit use. Patient presentation following overdose is influenced by the dose ingested, the time since ingestion, the co-ingestion of other drugs and alcohol, and the fed or fasted state. Patients have exhibited varying degrees of depressed consciousness that may fluctuate rapidly between a confusional, agitated combative state with ataxia and coma. Emesis (even when obtunded), diaphoresis, headache, and impaired psychomotor skills may be observed. No typical pupillary changes have been described to assist in diagnosis; pupillary reactivity to light is maintained. Blurred vision has been reported. An increasing depth of coma has been observed at higher doses. Myoclonus and tonic-clonic seizures have been reported. Respiration may be unaffected or compromised in rate and depth. Cheyne-Stokes respiration and apnea have been observed. Bradycardia and hypothermia may accompany unconsciousness, as well as muscular hypotonia, but tendon reflexes remain intact.

Recommended Treatment of Overdose

General symptomatic and supportive care should be instituted immediately, and gastric decontamination may be considered if co-ingestants are suspected. Because emesis may occur in the presence of obtundation, appropriate posture (left lateral recumbent position) and protection of the airway by intubation may be warranted. Although the gag reflex may be absent in deeply comatose patients, even unconscious patients may become combative to intubation, and rapid-sequence induction (without the use of sedative) should be considered. Vital signs and consciousness should be closely monitored. The bradycardia reported with GHB overdose has been responsive to atropine intravenous administration. No reversal of the central depressant effects of sodium oxybate can be expected from naloxone or flumazenil administration. The use of hemodialysis and other forms of extracorporeal drug removal have not been studied in GHB overdose. However, due to the rapid metabolism of sodium oxybate, these measures are not warranted.

Poison Control Center

As with the management of all cases of drug overdose, the possibility of multiple drug ingestion should be considered. The physician is encouraged to collect urine and blood samples for routine toxicologic screening, and to consult with a regional poison control center (1-800-222-1222) for current treatment recommendations.

Preparation and Administration Precautions

Care should be taken to prevent access to this medication by children and pets.

Rx only



CAUTION

Federal law prohibits the transfer of this drug to any person other than the patient for whom it was prescribed.

Distributed By: Jazz Pharmaceuticals, Inc., Palo Alto, CA 94304

For questions of a medical nature or to order Xyrem call the Xyrem Success Program® at 1-866-XYREM888 (1-866-997-3688).

Protected by US Patent Numbers 6780889, 6472431; Additional US Patents Pending

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0001

ROLE OF PROTEIN SYNTHESIS IN SLEEP-DEPENDENT CORTICAL PLASTICITY

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Introduction: Although it is admitted that sleep promotes memory formation, direct evidence that synaptic plasticity consolidation occurs during sleep is lacking. Our lab has shown that sleep consolidates a canonical model of in vivo cortical plasticity (ocular dominance plasticity, ODP) in cat visual cortex (V1) during development. De novo protein synthesis is a critical step in the consolidation of persistent forms of synaptic plasticity (e.g. late-long-term potentiation). Both local dendritic protein synthesis (mediated by the mTOR pathway) and global gene transcription and translation have been implicated in this process. Our study propose to determine if those protein synthesis mechanisms are involved in the consolidation of V1 plasticity during sleep.

Methods: This is achieved by a selective inhibition of local translation with rapamycin (mTOR pathway) and global cortical protein synthesis with cycloheximide. The drugs are infused in V1 during sleep and the effect on ODP is assessed with optical imaging of intrinsic cortical signals and single-unit electrophysiology. This study is completed by assessing the expression of candidate proteins known to be important in either local or global protein synthesis regulation in cortices derived from cats with normal vision, cats triggered to remodel (monocular deprivation, MD) without sleep and cats that are allowed to sleep after MD.

Results: Infusions of cycloheximide (6mM) or rapamycin (2 μ M) directly in the remodelling visual cortex during post-MD sleep impair the consolidation of ODP compare to vehicle infusion. Our preliminary results suggest that cycloheximide has a more pronounced effect compare to rapamycin on ODP. Our preliminary immunocytochemistry results show an increase of phospho-mTOR and phospho-CREB expression in remodelling visual cortices after sleep relative to control cortices.

Conclusion: Our results suggest that protein synthesis is required specifically during sleep to consolidate cortical plasticity. The relative contribution of local versus global protein synthesis pathways on sleep-dependent plasticity is currently being determined.

0002

EFFECTS OF SAPORIN-INDUCED LESIONS OF THREE AROUSAL POPULATIONS ON DAILY LEVELS OF SLEEP AND WAKE

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Introduction: Hypocretin (HCRT) neurons heavily innervate the cholinergic neurons in the basal forebrain (BF), histamine neurons in the tuberomammillary nucleus (TMN) and the noradrenergic locus coeruleus (LC) neurons; three neuronal populations that have traditionally been implicated in arousal. The most current model of sleep-wake regulation, the flip-flop model, proposes that HCRT neurons regulate arousal by exciting these downstream arousal neurons. We directly test this hypothesis by a simultaneous triple lesion of these neurons using saporin-conjugated neurotoxins.

Methods: Forty four adult male Sprague-Dawley rats were deeply anesthetized while three different saporin-conjugated neurotoxins were stereotactically delivered as follows: To lesion TMN neurons we injected HCRT2-saporin (250 ng/L in 0.25 μ L) while to destroy noradrenergic LC neurons we used anti-DBH-saporin (1 μ g/ μ L in 0.25 μ L). The BF cholinergic neurons were lesioned with 192-IgG-saporin (2 μ g/ μ L icv; 3 μ L). Control rats were injected with pyrogen-free saline solution. Then we recorded sleep continuously for three weeks. Sleep data from two consecutive 24h periods during the third post-injection week (19th and 20th days post-injection) was used to obtain the main sleep parameters. To assess lesions coronal brain sections were stained for ChAT, adenosine

deaminase (TMN), DBH or NeuN. Numbers of labeled cells were counted.

Results: Three weeks after lesion the daily levels of wake were not changed in rats with double or triple lesions, although rats with triple lesions were asleep more during the light to dark transition period. The double and triple lesioned rats also had more stable (fewer bouts) sleep architecture compared to non-lesioned rats.

Conclusion: These results suggest that the cholinergic BF, TMN and LC neurons jointly modulate arousal at a specific circadian time but they are not essential links in the circuitry responsible for daily levels of wake, as traditionally hypothesized.

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0003

EFFECT OF SLEEP DEPRIVATION ON SLEEP AND THE SLEEP EEG IN R192Q CA_v2.1 MIGRAINE MICEDeboer T¹, Oosterman JE¹, Ferrari MD², van den Maagdenberg AM^{2,3}, Meijer JH¹¹Molecular Cell Biology, Leiden University Medical Center, Leiden, Netherlands, ²Neurology, Leiden University Medical Center, Leiden, Netherlands, ³Human Genetics, Leiden University Medical Center, Leiden, Netherlands

Introduction: Mutation R192Q in Ca_v2.1 channels causes Familial Hemiplegic Migraine type 1. In a knock-in mouse model this mutation results in increased calcium influx and neurotransmitter release. Ca_v2.1 channels are common targets of G-protein linked neuromodulation. Therefore, mutation R192Q causes reduced susceptibility to G-protein inhibition. Adenosine and GABA act on G-protein coupled receptors and are both known to be involved in sleep regulation. A pilot study showed that R192Q mice sleep less than wildtype (WT) mice.

Methods: To investigate the influence of the channel mutation on sleep regulation, WT and R192Q mice were kept in 12:12 h LD cycles and EEG and EMG electrodes were implanted. After recovery and adaptation, a 24-h baseline day (both genotypes n=7) a 6-h SD and 18-h recovery (R192Q n=4, WT n=5) were recorded. Vigilance states were determined and EEG spectral analysis was performed.

Results: Over 24 h R192Q mice were 10% more awake than WT mice (p<0.01 t-test). This was attributable to a general reduction in NREM sleep. Waking episodes were longer and NREM sleep episodes were shorter in R192Q mice. REM sleep was not affected. The baseline time course of slow-wave activity (SWA, EEG power density between 0.75-4.0 Hz) did not differ between the genotypes. After SD both genotypes displayed an initial increase in SWA (p<0.05, paired t-test). This increase in SWA was significantly higher in WT compared to R192Q (p<0.05, t-test) and gradually declined during recovery in both genotypes.

Conclusion: R192Q mice show less NREM sleep during baseline and an attenuated increase in SWA after SD. These results are similar to those found in human short-sleepers who also display a smaller increase in SWA after SD. The data suggest that R192Q mice have a short sleeper phenotype.

0004

INTERLEUKIN-1 MICROINJECTION INTO THE RAT LATERODORSAL TEGMENTAL NUCLEUS INHIBITS REM SLEEP

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Introduction: Interleukin-1 (IL-1) increases NREM sleep and inhibits REM sleep. Although much information is available with respect to the

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mechanisms by which IL-1 enhances NREM sleep, little effort has been expended to determine mechanisms mediating IL-1-induced REM sleep suppression. Cholinergic neurons in the laterodorsal and pedunculopontine tegmental nuclei (LDT/PPT) are part of the neuronal circuitry responsible for REM sleep generation. Data indicate that IL-1 inhibits the cholinergic system. The aim of this study was to test the hypothesis that IL-1, directly microinjected into the rat LDT nucleus, will inhibit REM sleep.

Methods: Male Sprague-Dawley rats ($n=21$), maintained on a 12:12 h light:dark cycle at 22 °C, were instrumented for standard chronic polygraphic recordings. A stainless steel guide cannula aimed at the LDT nucleus was also stereotaxically implanted. IL-1 was dissolved in pyrogen-free saline (PFS; 100 nl) and given at the beginning of the light phase of the light-dark cycle. Each animal received both vehicle (PFS) and IL-1, thus serving as its own control. Animals were divided into two groups: rats in group 1 received IL-1 0.25 and 0.5 ng, whereas animals in group 2 received IL-1 1 and 4 ng. The order in which the doses were administered was randomized. At the end of the experiments, the location of injection sites was histologically verified.

Results: IL-1 (1 ng) microinjection into the LDT nucleus induced a significant and long lasting inhibition of REM sleep. In the first 12 post-injection hours REM sleep was reduced from 11.7 ± 0.9 % of recording time in control condition (vehicle microinjection) to 8.6 ± 0.9 % following IL-1 administration. REM sleep was not altered during post-injection hours 13-24.

Conclusion: Results of this study support the hypothesis that IL-1 can inhibit REM sleep by acting at the level of the LDT nucleus. In vitro data showing that IL-1 inhibits the firing rate of LDT cholinergic neurons suggest that REM sleep inhibition induced by IL-1 microinjection into the LDT may result from the IL-1-induced inhibition of cholinergic neurons.

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0005

DOPAMINERGIC MODULATION OF SOMATIC MOTONEURONS ACROSS THE SLEEP CYCLE IN BEHAVING RATS

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Introduction: Dysregulation of dopaminergic neurotransmission is implicated in a variety of sleep disorders that result from abnormal motor activity, including restless leg syndrome, periodic limb movement disorder and REM sleep behaviour disorder. Despite evidence linking dopamine transmission to motor disturbances in sleep, it is unknown whether dopamine directly modulates somatic motoneuron excitability and hence skeletal muscle tone. Evidence demonstrates that dopamine neurons in the A11 group innervate motoneurons, which also express dopamine receptors (i.e., D1- and D2-like receptors). Further, dopamine discharge patterns and release profiles within the CNS vary as a function of sleep-wake state. Therefore, we aimed to determine whether changes in dopamine neurotransmission within a somatic motor pool would affect muscle tone during different sleep-wake states. Based on recent evidence, we hypothesize that activation of D1-like receptors on motoneurons would facilitate their excitability to increase muscle tone.

Methods: We used reverse-microdialysis, electrophysiology, neuropharmacology and histology to determine if changes in dopamine neurotransmission within the trigeminal motor pool affect basal levels of masseter muscle tone in freely-behaving rats. We perfused 0.25, 0.5, 0.75 and 1mM of SKF38393 (D1-like receptor agonist) into the trigeminal motor pool while monitoring masseter muscle tone across the natural sleep-wake cycle in 8 male Sprague-Dawley rats.

Results: Activation of D1-like receptors on trigeminal motoneurons via SKF38393 perfusion dose-dependently facilitated masseter muscle tone (RM ANOVA, $p<0.05$). Perfusion of 1mM SKF38393 induced a robust increase in masseter EMG activity during all sleep-wake states

(RM ANOVA, $p<0.05$). Compared to baseline levels, activation of D1-like receptors increased masseter muscle tone during alert waking by 89%, during quiet waking by 274%, in NREM sleep by 265% and during REM sleep by 201%.

Conclusion: This study demonstrates that: 1) dopamine directly modulates somatic motoneuron activity and hence motor outflow via D1-like receptor activation; and, 2) exogenous dopamine can reverse sleep state-dependent suppression of muscle tone.

0006

THE ROLE OF KINASE AND PHOSPHATASE PATHWAYS IN SLEEP-DEPENDENT CONSOLIDATION OF CORTICAL PLASTICITY

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Introduction: Neural activity during sleep consolidates ocular dominance plasticity (ODP), a canonical form of in vivo synaptic remodeling in the visual cortex (V1) triggered by monocular deprivation (MD) during development. The effects of sleep on ODP are mediated by NMDA receptors (NMDARs), and may involve long-term potentiation (LTP) or long-term depression (LTD) of synapses within V1. V1 LTP and LTD are mediated by NMDAR-activated kinase and phosphatase pathways, respectively.

Methods: We investigated the role of LTP-like or LTD-like signaling pathways in sleep-dependent ODP consolidation by infusing specific kinase and phosphatase inhibitors (or vehicle) into V1 during post-MD sleep. ODP was assessed by intrinsic signal imaging and single-unit recording of responses in V1 to stimuli presented to the deprived and non-deprived eyes (DE and NDE, respectively).

Results: MD alone (without subsequent sleep) induced depression of DE responses, but did not significantly change NDE responses. Subsequent sleep resulted in NDE response potentiation, resulting in a large shift in neuronal responses in favor of the NDE. Either antagonizing NMDARs or inhibiting cAMP-dependent protein kinase (PKA) activity during post-MD sleep blocked consolidation of ODP, impaired sleep-dependent potentiation of NDE responses, and reversed depression of DE responses. These results are consistent with established roles for PKA in mediating both LTP and LTD in V1. In contrast, inhibition of extracellular signal-regulated kinase (ERK) did not impair consolidation of ODP during sleep. Inhibition of the protein phosphatase calcineurin during post-MD sleep resulted in an intermediate phenotype with moderately decreased ODP, suggesting a limited role for LTD-like signaling pathways in this form of plasticity.

Conclusion: These findings demonstrate that sleep consolidates synaptic remodeling primarily via PKA-dependent mechanisms, and suggest that both LTD-like and LTP-like synaptic changes may play a role in this process.

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0007

SEVERE IMPAIRMENT IN SLEEP AND THERMOREGULATORY RESPONSES TO METABOLIC CHALLENGES IN PREPROGHRELIN KNOCKOUT MICE

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Introduction: Mechanisms involved in the regulation of food intake, metabolism, thermoregulation and sleep show significant overlap in the hypothalamus. These mechanisms include neuropeptide Y, leptin, orexin

and ghrelin modulation of for example metabolic responses induced by fasting in cold environment. Here, we characterize sleep and thermoregulatory responses to metabolic challenges in mice lacking the preproghrelin (Ppg) gene.

Methods: Baseline body temperature (Tb) and sleep-wake activity were obtained for two days from Ppg knockout (KO, n = 8) and wild-type (WT, n = 7) mice kept at 30°C ambient temperature. On days 3 to 5, ambient temperature was reduced to 17°C. On day 6, cold exposure continued and food was removed for 24 hours. On day 7, food was returned and temperature was reset to 30°C.

Results: Cold exposure itself induced a significant suppression in non-rapid-eye movement sleep (NREMS) and rapid-eye movement sleep and a reduction in Tb in both groups. The changes were more pronounced and persisted during the entire cold exposure in KO mice but only during the dark periods in WT animals. On the fasting day, mice of both genotypes entered hypothermic bouts, during which WT mice had near normal amount of sleep while KO animals had about 50 % of NREMS observed in WTs. In the last 8 hours of the fasting day, Tb of WT mice gradually returned to normal while Tb of Ppg KO mice started to drop precipitously and reached near ambient temperature by the end of the day; the amplitude of the electroencephalographic waves greatly decreased during this period and normal sleep-wake cycles could not be determined.

Conclusion: Results indicate that the products of the preproghrelin gene are required for maintaining the normal sensitivity to metabolic challenges in mice. Present data provide further insight into the coordinated regulation of metabolism and sleep.

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0008

PERINATAL ALCOHOL EXPOSURE LEADS TO LONG-LASTING OVEREXPRESSION OF GABA(A) RECEPTORS IN THE RAT POSTERIOR HYPOTHALAMUS AND INCREASES BEHAVIORAL SENSITIVITY TO GABOXADOL

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Introduction: Prenatal alcohol exposure (AE) is associated with lasting sleep abnormalities, but the underlying mechanisms are unknown. We hypothesized that AE alters development of GABAergic signaling in hypothalamic regions important for the control of sleep and motor activity.

Methods: Alcohol (5.25 g/kg/day; in a milk formula) was administered via intragastric intubations to male rats on postnatal days (PD) 4-9, a period corresponding to the brain growth spurt equivalent to prenatal brain development during the third trimester in humans (AE group). Control pups (same litters) were sham-intubated (S group). On PD 29-30, total RNA and protein were bilaterally extracted from 700 µm tissue micro-punches from the perifornical (PF) region of the posterior hypothalamus and the ventrolateral preoptic (VLPO) region of the anterior hypothalamus. Samples from individual rats were subjected to quantitative assays to determine mRNA levels for $\alpha 1-5$, $\beta 1-3$, $\gamma 2$, δ , and ϵ GABA_A receptor subunits and protein levels for $\alpha 4$ and δ subunits using RT-PCR and immunoblotting, respectively (n=6-7 per group). In additional ~50-day old rats, movements were counted in a novel environment for 90 min following administration of GABA_A receptor agonist, gaboxadol (5 mg/kg s.c.; n=4 per group).

Results: In the PF region, mRNA levels for the $\alpha 4$, $\beta 3$, δ and $\gamma 2$ subunits were significantly higher in the AE group (p=0.01-0.04), and $\alpha 4$ and δ subunit immunoreactivity was also increased (p=0.04). In the VLPO region, only the δ subunit mRNA was increased (p=0.047). Following gaboxadol, motor activity was significantly more reduced, and the latency to a transient total loss of activity was shorter, in AE than S rats (p=0.02-0.004).

Conclusion: Perinatal AE may lead to prolonged overexpression of GABA_A receptors in the vigilance- and motor activity-controlling hypothalamic PF region. This may increase behavioral sensitivity to gaboxadol and contribute to long-lasting alterations in sleep-wake behavior in victims of prenatal AE.

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0009

AN INVERSE AGONIST OF THE HISTAMINE H3-RECEPTOR IMPROVES WAKEFULNESS IN NARCOLEPSY: STUDY IN OREXIN-/MICE AND PATIENTS

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Introduction: Narcolepsy is characterized by excessive daytime sleep, cataplexy, direct transitions from wakefulness (W) to REM sleep (DREMs) and deficiency of orexins (hypocretins), neuropeptides that promote W via activation of brain histamine (HA) pathways and other W-promoting systems. The hypothesis that the orexin defect can be circumvented by enhancing HA neuronal activity was explored in narcoleptic orexin-/mice and patients using tiprolisant, a potent/selective inverse agonist at H3-receptor controlling HA release/synthesis by autoregulation.

Methods: The turnover of brain HA and other monoamines was assessed by measuring their levels and those of their main metabolites in both wild type and orexin-/mice. Polygraphic recordings were used to examine the effects of oral dosing of tiprolisant and/or modafinil on cortical EEG, sleep and W in 12 orexin-/mice. A single-blind trial was performed on 22 patients receiving placebo followed by tiprolisant, both for one week using the Epworth Sleepiness Scale (ESS) score to evaluate daytime sleep/somnolence.

Results: We found that 1) in wild-type or orexin-/mice, tiprolisant was able to markedly enhance tele-methylhistamine levels, an index of HA turnover. This was accompanied by an enhanced 4-hydroxy-3-methoxyphenylglycol/noradrenaline ratio, indicating activation of two major W-promoting aminergic systems in spite of the genetic abrogation of their excitatory orexin inputs in the knockout mice; 2) tiprolisant (20 mg/kg) enhanced W like that of modafinil (64 mg/kg), a currently prescribed W-promoting drug. In contrast to modafinil, however, it also enhanced cortical EEG fast theta activity (7-10 Hz) and fast rhythms (20-60 Hz) and diminished the DREMs, the only characteristic narcoleptic phenotype identified so far in orexin-/mice using objective EEG/EMG recordings. All effects of tiprolisant were markedly amplified by co-administration with modafinil. 3) finally, in patients receiving a 40 mg oral dose, once a day for one week, after one week of placebo, the ESS score was reduced from 17.6 (baseline) to 11.7 (p<0.001) with tiprolisant vs 16.6 with placebo (p>0.05). Diurnal sleep and somnolence, unaffected under placebo, were nearly suppressed on the last days of tiprolisant treatment, whereas nocturnal sleep was not significantly affected.

Conclusion: From our preclinical/clinical data, H3-receptor inverse agonists appear to be novel effective and well tolerated treatment for excessive daytime sleep and DREMs associated with narcolepsy.

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0010

PROCESSING OF SOUNDS DURING SLEEP SPINDLES IN HUMANS: AN EEG/fMRI STUDY OF AUDITORY STIMULATION IN NON-REM SLEEP

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Introduction: Non-REM sleep (NREM) has classically been associated with isolation of the brain from the external world, due to the blockade of incoming stimuli at the thalamic level, in particular during sleep spindles. Although some data suggest that sounds are still processed during NREM, no neuroimaging study has assessed how spindles modulate the processing of auditory stimuli. Using simultaneous EEG / fMRI, this study aimed at describing the neural correlates of auditory information processing during NREM and spindles in humans.

Methods: In the experimental group (EG, n=13), non-sleep deprived healthy young subjects were scanned during the night in a 3T fMRI device, with a continuous EEG recording. During this session, pure tones were presented (400Hz, 300ms, 70% probability during each scan). In the control group (CG, n=14), subjects followed a similar protocol, but without sounds presentation. After artifacts removal, NREM (stages 2-3) and waking epochs, with corresponding fMRI images, were selected. Sleep spindles were automatically detected in NREM epochs. In the EG, tones were categorized in 3 types according to their occurrence during waking (TW), NREM but outside spindles (TN), or spindles (TS). We first assessed the brain responses to the 3 types of tones. Then we compared the brain responses to spindles between groups.

Results: TW were associated with activation of the thalamus and primary auditory cortex. TN induced activation of thalamus, primary auditory cortex, but also brainstem and posterior cingulate gyrus. TS were associated with activation of parahippocampal gyrus and brainstem. A higher activation of the hippocampus was found during spindles in the EG compared to the CG.

Conclusion: Sounds are processed in classical auditory circuits during NREM, but not during spindles. However, presentation of sounds during NREM affects the neural correlates of spindles, leading to increased activation of mesio-temporal areas in relation to spindles.

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0011

INTER-HEMISPHERIC CORRELATIONS IN SPONTANEOUS ACTIVITY OF HUMAN SENSORY CORTEX DURING WAKE AND SLEEP

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Introduction: Recent functional magnetic resonance imaging (fMRI) studies reveal the presence of spontaneous waves of activity in human cortex. These high amplitude fluctuations are puzzling since they emerge intrinsically, even in sensory cortex, in the complete absence of external stimuli or task. These fluctuations show remarkable network system selectivity and coherence across large cortical distances, and across hemi-

spheres, yet it is currently unknown what dynamics of neuronal activity underlie these waves. Spontaneous fMRI fluctuations also show inter-hemispheric correlations in anesthetized animals, raising the question whether they can be found also during natural human sleep.

Methods: Three patients underwent monitoring with multiple intracranial depth electrodes placed bilaterally for potential surgical treatment. Patients provided written informed consent, and the study conformed to the guidelines of the Medical IRB at UCLA. Simultaneous recordings of single unit and LFP activity from multiple electrodes in human auditory cortex were collected while 3 patients rested in a dimly-lit, silent room (N=9 sessions). Sound was recorded along with the neuronal data to verify quiet recording conditions. Electrophysiological signals were obtained during silent periods in wakeful rest, during sleep, and during auditory stimulation.

Results: We demonstrate the presence of spontaneous firing rate modulations which manifested a significant correlation across hemispheres ($r=0.32$, $p<0.0005$). These modulations were very slow ($< 0.1\text{Hz}$) and of low amplitude. LFP recorded by the same electrodes exhibited significant inter-hemispheric correlations predominantly for modulations in gamma (40-100Hz) power ($r=0.42$, $p<0.0005$), showing similar temporal dynamics to the firing rate modulations. Interestingly, data from one patient during REM and stage II sleep revealed a striking enhancement in correlations ($r=0.64$, $p<0.0005$), suggesting that these waves serve a role which is outside the domain of purposeful sensory tasks.

Conclusion: Our results point to slow, low amplitude, modulations in firing rate and gamma LFP power as the main mechanism underlying spontaneous fMRI fluctuations in human sensory cortex.

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0012

CLONAZEPAM REDUCES MYOCLONIC ACTIVITY DURING REM SLEEP IN A MOUSE MODEL OF REM SLEEP BEHAVIOR DISORDER

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Introduction: REM sleep behaviour disorder (RBD) is a neurological disorder of unknown cause that is characterized by excessive muscle activity in REM sleep. We previously showed that impaired GABA and glycine transmission in transgenic mice causes a motor phenotype in REM sleep (e.g. excessive myoclonic jerks) that mimics human RBD. Because RBD is effectively treated with clonazepam, we aimed to determine whether this drug would also alleviate the excessive motor behaviors that characterize our mouse model of RBD.

Methods: We used a transgenic mouse model in which both GABAergic and glycinergic neurotransmission is severely down-regulated. We characterized levels of skeletal muscle activity in these animals by recording EEG and EMG activity for 24 hours in transgenic (Tg; n=12) and wild-type (Wt; n=7) mice. We then gave a subset of mice (Tg; n=6; Wt; n=4) an i.p. injection of 0.3mg/kg clonazepam and measured motor activity for 6 hours to determine if this drug alleviated myoclonic activity in REM sleep.

Results: Compared to Wt mice, Tg animals had a 209% (2-way ANOVA; $P=0.007$) increase in muscle activity during REM sleep. In Tg mice, clonazepam administration reduced motor activity in REM sleep by 33% (paired t-test; $P=0.007$) without affecting sleep-wake architecture (2-way RM ANOVA; $P=0.886$). In Wt mice, clonazepam had no effect on either muscle activity (paired t-test; $P=0.407$) or sleep-wake architecture (2-way RM ANOVA; $P=0.360$).

Conclusion: We show that impaired GABA and glycine transmission induces a motor phenotype during REM sleep in transgenic mice and that clonazepam administration alleviates these symptoms. We suggest

that this mouse model is useful for studying the mechanisms of RBD and conclude that impaired inhibitory neurotransmission may underlie this disorder.

0013

HYPOCRETIN NEURON MORPHOLOGY AND NEUROTRANSMITTER IDENTITY IN ZEBRAFISH

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Introduction: The hypocretin/orexin (HCRT/ORX) system has been involved in the regulation of a large number of physiological functions, including sleep and wakefulness, feeding, cardiovascular function and nociception. In mammals, HCRT hypothalamic neurons are numerous, have widespread projections into the brain and spinal cord, and are likely heterogeneous, with potential differential effect reflecting functional diversity. In contrast to the complex mammalian situation where thousands of hypocretin neurons are present, we previously showed that the zebrafish offers a simpler situation with only 20 hypocretin neurons in larvae and 50 in adults. Here, we investigate the morphological characteristics and neurotransmitter phenotype of this small HCRT neuron population in zebrafish.

Methods: HCRT neuron morphology and projections were analyzed in a HCRT:EGFP line using a 2 photon microscopy imaging approach. Gene expression patterns and HCRT colocalization were determined using double in situ hybridization (ISH).

Results: The majority of projections were ipsilateral. Axon mainly extended towards the spinal cord whereas dendritic processes expended laterally, arborizing in the hypothalamus and diencephalic regions proximal to the eye. In addition, we analyzed the neurotransmitter phenotype of HCRT neurons using probes marking glutamatergic, GABAergic and dynorphinergic (pdyn) neurons. Double ISH experiments suggest that HCRT neurons express glutamatergic markers and a portion also express entpd3 and pdyn.

Conclusion: Similar to mammals, zebrafish HCRT neurons are likely glutamatergic. Heterogeneity is evident based on pdyn and entpd3 colocalization and projection patterns. Correlations between phenotype and function are needed.

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0014

DOPAMINERGIC MODULATION OF CATAPLEXY IN HYPOCRETIN-NULL MICE

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Introduction: Cataplexy is one of the most debilitating symptoms of narcolepsy. Previous studies demonstrate that changes in dopamine neurotransmission affect cataplexy in narcoleptic dogs. However, it is unknown whether dopamine also influences cataplexy in hypocretin-null mice. Therefore, we used neuro-pharmacology, electrophysiology and videography to determine if changes in dopaminergic neurotransmission affect cataplexy in narcoleptic mice.

Methods: Hypocretin-null (n=10) and wild-type mice (n=5) were given i.p. injections of saline, quinpirole (D2-like receptor agonist, 0.5mg/kg) or eticlopride (D2-like receptor antagonist, 1.0mg/kg) at lights-off (7pm). Cataplexy and sleep-wake states were determined by EEG, EMG and videography and were monitored for 3 hours following drug administration.

Results: Compared to baseline levels, quinpirole injection potently increased the total time spent in cataplexy by 99±40% (paired t-test, p=0.02). In contrast, eticlopride application markedly suppressed the total time spent in cataplexy by 84±12% (paired t-test, p=0.02). Neither quinpirole nor eticlopride administration affected the amount of waking, NREM or REM sleep in either hypocretin-null or wild-type mice (RM ANOVA, p>0.05).

Conclusion: We demonstrate that changes in dopaminergic neurotransmission, via D2-like receptor mechanisms, affect cataplexy without influencing REM sleep in hypocretin-null mice. We suggest that blockade of D2-like receptors could serve as an effective treatment for cataplexy in human narcoleptics.

0015

DIFFERENTIAL RESCUE OF LIGHT- AND FOOD-ENTRAINABLE CIRCADIAN RHYTHMS IN MICE LACKING THE BMAL1 CLOCK GENE

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Introduction: Mice with targeted disruption of the clock gene *Bmal1* lack molecular and neurobehavioral circadian rhythmicity in constant darkness. *Bmal1*^{-/-} mice also do not entrain to light-dark cycles nor, as we report here, do they entrain to temporally restricted windows of food availability. To test the role of the dorsomedial hypothalamic nucleus (DMH) as opposed to the suprachiasmatic nucleus (SCN) in entrainment of circadian rhythms, we attempted to rescue both light and food entrainment of circadian rhythms by selectively restoring clock function in the DMH or SCN in *Bmal1*^{-/-} mice.

Methods: We injected an adeno-associated viral vectors (AAV, serotype 8) containing the *Bmal1* gene (including both 5' and 3' promoter elements; AAV-*Bmal1*) into the brains of *Bmal1*^{-/-} mice. The circadian rhythms of body temperature (Tb) and locomotor activity were recorded during ad lib and restricted feeding conditions (under both 12:12 light-dark and constant darkness).

Results: The SCN functions as the master circadian pacemaker and restoration of clock function at this site alone by injection of AAV-*Bmal1* restores light- but not food-entrainable circadian rhythms. In contrast, restoration of the *Bmal1* gene only in the DMH had no effect on baseline or light entrainable circadian rhythms, but restored the ability of animals to entrain to food.

Conclusion: These results demonstrate the presence of a *Bmal1*-based oscillator in the DMH that is sufficient to drive food entrainment of circadian rhythms, and demonstrate the power of viral-based gene replacement in the CNS to dissect complex neural functions.

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0016

PROGRESSIVE DECREASE IN SLEEP DEPRIVATION-INDUCED EXTRACELLULAR ADENOSINE RELEASE AND RECOVERY NREM SLEEP FOLLOWING INTRACEREBROVENTRICULAR INJECTION OF 192 IGG-SAPORIN

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Introduction: The basal forebrain (BF) is an important site in the homeostatic sleep control mediated by adenosine (AD) release. The BF comprises different neuronal populations, including cholinergic, GABAergic and glutamatergic cells. Immunotoxin 192IgG-saporin has been used in several studies to investigate the role of BF cholinergic vs. non-cholinergic cells in the regulation of spontaneous sleep/recovery sleep after sleep deprivation (SD) but results of these studies are controversial. 2 weeks post local saporin injection into the caudal BF (horizontal diagonal band/magnocellular preoptic area/substantia innominata, HDB/MCPO/SI), recovery sleep was reduced; however, 2 weeks post ICV injection no changes in recovery sleep occurred. We hypothesized that this difference might be explained by a delayed lesion of cholinergic cells in HDB/MCPO/SI area after ICV injection. Consequently, in the

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same rats, we examined the time course of changes in SD-induced AD levels and homeostatic sleep response at 2 and 3 weeks post ICV injection.

Methods: Male rats were ICV injected with saporin (6 μ g, n=7) or saline (n=5) and implanted with EEG/EMG electrodes and guide cannulae for microdialysis probes targeting the HDB/MCPO/SI. Experimental schedule, performed 2 and 3 weeks post-injection, included spontaneous sleep-wake recording (8am-8am) and SD for 6h (10am-4pm) followed by recovery sleep at 4pm-8am. AD samples were collected at 30min intervals on SD day at 8am-8pm. Histology evaluated the extent of cholinergic cell loss and probe locations.

Results: 2 weeks post ICV saporin, SD induced significant increases in BF AD levels (+141%), NREM recovery sleep (+47%) and NREM delta power (+81%). However, 3 weeks post ICV saporin, AD increase and NREM recovery sleep were inhibited and NREM delta power was significantly attenuated. Histological control showed that 2 and 3 weeks post ICV injection 41% and 13% of BF cholinergic cells survived, respectively.

Conclusion: The changes observed 3 weeks post ICV saporin were quantitatively similar to those observed 2 weeks after local BF saporin injection (Kalinchuk et al., 2005), showing that the effect induced by ICV saporin injection follows a slower time course in reducing the SD-induced AD increase and recovery sleep. Taken together, our present and previous observations imply that cholinergic neurons in the BF play an important role in the regulation of SD-induced AD release and NREM recovery sleep.

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0017

MODAFINIL, IN CONTRAST TO CAFFEINE AND AMPHETAMINE, MAINTAINS WAKE ENHANCING EFFICACY AFTER 6 H OF SLEEP DEPRIVATION IN RATS

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Introduction: Several drugs, notably amphetamine, caffeine, and modafinil, maintain attention and vigilance in the presence of fatigue, such as that induced by sleep deprivation (SD). However, it is unclear whether these drugs maintain the same degree of wake promoting efficacy under such conditions. Therefore we evaluated these agents in normal and sleep-deprived rats.

Methods: Rats were implanted for chronic electroencephalographic and electromyographic recording. SD was produced by placing rats in rotating wheels (34 cm ID, 1 m/min rotation rate) at lights-on (8 AM) for 6 h, which limited their ability to sleep. They were then removed, administered caffeine (3-30 mg/kg ip), d-amphetamine sulfate (0.3-3 mg/kg ip), or modafinil (30-300 mg/kg ip), and recorded for 24 h. Non-sleep deprived (NSD) rats were maintained in their home cages during this period and injected with test compounds at the same time. Wake, slow-wave sleep (SWS), and rapid-eye-movement sleep (REMS) were scored from the polysomnographic records using standard criteria. Wake efficacy was measured using cumulative wake activity at 4 h post dosing (4h AUC). Statistical analysis consisted of ANOVA followed by Bonferroni t-test.

Results: Wake was reduced by ~44% in vehicle-treated SD versus NSD rats (53 vs. 95 min, respectively, 4h AUC, $p < 0.05$). In both NSD and SD rats, caffeine (15, 30 mg/kg), amphetamine (1, 3 mg/kg), and modafinil (150, 300 mg/kg) increased wake (4h AUC, $p < 0.05$ vs. vehicle). However, the magnitude of wake increase was significantly smaller in SD than in NSD rats for caffeine (124 vs. 200 min, 15 mg/kg) and amphetamine (148 vs. 192 min, 1 mg/kg) ($p < 0.05$). In contrast, modafinil produced comparable wake increases in SD and NSD rats (190 vs. 199 min respectively, 150 mg/kg; $p > 0.05$).

Conclusion: The wake promoting efficacy of modafinil, but not that of caffeine or amphetamine, is unaltered by sleep deprivation.

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0018

RESPONSE OF HUMAN GENIOGLOSSUS SINGLE MOTOR UNITS TO CHEMICAL AND PRESSURE STIMULATION

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Introduction: The human genioglossus, is an important upper airway dilator muscle, receiving respiratory and non-respiratory input (1). We wished to understand the effects of mechanical (continuous positive airway pressure, CPAP) and chemical (elevated CO₂) stimuli on upper airway motor control.

Methods: Single motor unit (SMU) activity was recorded in healthy subjects (n=5 to date) during CO₂ and CPAP stimulation. SMUs were recorded via three fine-wire electrodes inserted into the genioglossus based on prior ultrasound imaging. Subjects were studied during supine wakefulness breathing through a nose mask. During hypercapnic stimulation (10mmHg above eupnic), CPAP was applied in ~2cmH₂O increments each minute until 10cmH₂O was achieved at which point CPAP was terminated. SMUs were sorted and classified based on instantaneous discharge frequency plots according to respiratory activity for each SMU.

Results: Genioglossus motor unit activity with increased CO₂, shows a number of characteristic changes. Firstly there is an increase in the firing rate of inspiratory units already active with earlier pre-inspiratory activation, 4 units changed their pattern of discharge from a Phasic to a Tonic pattern and increased their discharge frequencies (5-15Hz increase). With further increases in CO₂ new SMUs in the genioglossus were recruited. With the application of sufficient CPAP (5.6 \pm 0.8 cmH₂O) SMU firing rates were reduced to near initial values or discharge ceased altogether.

Conclusion: This implies that while CO₂ can stimulate the activity of inspiratory units, CPAP can suppresses genioglossal motoneuron activity.

0019

EFFECTS OF CORTICAL SPREADING DEPRESSION (CSD) ON SLEEP

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Introduction: CSD is a slowly moving wave of tissue depolarization and decreased neuronal activity, resulting in a depression of amplitude of the electroencephalogram. CSD can be elicited unilaterally by local application of potassium chloride (KCl), and the affected hemisphere shows increased energy demands, transient hypoxia, as well as strong induction of plasticity-related genes such as BDNF, followed by morphological spine changes. Here we investigated the effects of unilateral CSD on sleep intensity as measured by slow wave activity (SWA).

Methods: Male WKY rats (7-8 week old; n=5) were implanted chronically for polysomnographic recordings and kept in a 12:12 light:dark cycle (lights on at 10am). Local field potentials (LFPs) were recorded from the left and right parietal cortical areas. Soon after lights on KCl was infused unilaterally either on the occipital intact dura (n=2) or in the frontal cerebral cortex (n=3).

Results: CSD effects on the EEG can be described in three phases: 1) Unilateral reduction in EEG power encompassing all frequencies during the infusion of KCl (first 62.4 + 18.5 min). 2) Unilateral increase in NREM SWA at the expenses of higher frequencies starting immediately after the end of CSD. During the first 2 hr after the end of CSD, SWA

at the affected hemisphere was $179.7\% + 15.7$ (mean + SEM) of the 24 hr baseline, while at the contralateral hemisphere it was $127.5 + 11.7$ ($p=0.043$ Wilcoxon Matched Pairs Test); 3) A recovery phase during which SWA returned to baseline levels (within ~ 12 hr from the onset of CSD).

Conclusion: NREM sleep following unilateral CSD is characterized by a large increase in SWA in the affected hemisphere compared to the contralateral one. Future studies are needed to clarify whether this increase is linked to the early increase in energy metabolism during CSD, or to the later synaptic and morphological changes.

Support (optional): Supported by NIH Director's Pioneer Award to GT.

0020

SIMULATION OF SLEEP HOMEOSTASIS IN THE DARK

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Introduction: Slow-wave activity (SWA) in the NREM sleep EEG is thought to reflect a sleep homeostatic process (S) and SWA has been simulated successfully on the basis of prior sleep and waking duration. However, in a simulation in the rat (Franken et al 1991) the decreasing time constant (Td) of S needed systematic adaptation depending on time of day and environmental lighting conditions. The question remained whether these daily changes in Td were caused by external (e.g. light) or endogenous factors.

Methods: To investigate this question, rats ($n=11$) were kept in 12:12 h LD cycles. EEG and EMG electrodes were implanted (Deboer et al 2003). After recovery, the animals adapted to the recording room in DD for at least a week. A baseline day was recorded, followed by a 6-h sleep deprivation (SD) and 18-h recovery period. Vigilance states were determined and EEG spectral analysis was performed. Simulations were performed as in Franken et al 1991. Mean r -values were calculated from Fisher- z transformed individual r -values of the correlation of hourly values of S and SWA ($n=39-42$).

Results: With a constant Td (3.2 h) the simulation was consistently lower than SWA during the rest phase and higher during the active phase ($r=0.555$ $p<0.01$). Introduction of a variable Td (3.9 h rest phase, 2.5 h active phase, Franken et al 1991) improved the correlation ($r=0.682$ $p<0.01$), but clear differences remained. Subsequent simulations showed that a variable Td of 4.8 h (rest) and 1.6 h (active phase) was the optimal solution ($r=0.748$ $p<0.01$).

Conclusion: In constant conditions simulation of S Td needs a correction for an apparent difference between the active and rest phase, although the animals spend at least a week in DD. This suggests that endogenous factors may influence sleep homeostatic processes.

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0021

SLEEP AND THE SLEEP EEG UNDER CONSTANT SLEEP PRESSURE

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Introduction: In mammals, slow-wave activity (SWA) in the NREM sleep EEG is a function of the previous amount of sleep and waking and reflects sleep homeostasis. In the rat, power density in the higher EEG frequencies (10-25 Hz, HFA) is thought to be under influence of circadian factors. We wanted to investigate whether daily changes in sleep and HFA are independent of changes in SWA and homeostatic sleep pressure.

Methods: To this purpose rats ($n=4$) were kept in 12h:12h LD cycles. EEG and EMG electrodes were implanted. After recovery the animals adapted to constant dark conditions (DD) for at least 1 week. A baseline

(BL) day was recorded followed by a "short-day protocol" of 2h sleep deprivation (SD) followed by 2 h rest (2h-2h) for 48 h. Vigilance states were determined and EEG spectral analysis between 0.1-25 Hz was performed. Comparisons were made between baseline and the second day in 2h-2h.

Results: The animals slept less over 24 h in 2h-2h ($43.3\pm 1.7\%$ SE) compared to baseline ($51.5 \pm 1.2\%$, $p<0.005$, t -test). Circadian changes in vigilance states were still present but the amplitude was markedly reduced (~25% of baseline, $p<0.05$, t -test). SWA (1.1-4.0 Hz) in NREM sleep did not show a significant modulation over 24 h ($p>0.5$, ANOVA 4-h intervals) during the 2h-2h protocol. At the same time the power density in the spindle range (11.1-15.0 Hz) and between 15.1-25.0 Hz still showed strong circadian modulation ($p<0.05$, ANOVA 4-h intervals) which virtually did not differ from baseline ($p>0.5$, ANOVA 4-h intervals).

Conclusion: Under the 2h-2h protocol, SWA in NREM sleep is constant and circadian modulation in vigilance states is markedly reduced. In contrast, HFA still displays significant circadian modulation, indistinguishable from baseline. The data show that circadian changes in HFA are endogenous and are not influenced by sleep homeostatic mechanisms.

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0022

EVOKED OPTICAL RESPONSES DIFFER BETWEEN QUIET SLEEP STAGES

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Introduction: In order to study the neural consequences of the different stages of quiet sleep, we recorded evoked cortical hemodynamic signals during auditory stimulation across sleep states in rats. We observe a larger electrical evoked response during quiet sleep 2 (QS2) compared to quiet sleep 4 (QS4). If the larger QS2 response is due to greater synchronous recruitment of cells, then we hypothesize the metabolic response would also be larger during QS2.

Methods: We implanted four Sprague-Dawley rats with two screw electrodes, an LED emitting 660 nm light, and a photodiode over the parietal cortex. A train of five speaker clicks (10 Hz) was delivered at random intervals from 2 to 13 seconds while recording the electrical and scattered light changes under different sleep states.

Results: As expected, QS2 exhibited a larger evoked response potential (ERP) over QS4. The evoked optical response during QS2 showed an initial dip at 0.5 s not observed in QS4, followed by a peak at 1 s that was much larger in QS4. A secondary dip at 2.4 s was significantly larger in QS2. Both quiet sleep states had a similar long lasting overshoot.

Conclusion: The ERP during QS2 was larger in amplitude compared to QS4 possibly due to greater synchronization of cellular activity. The evoked optical signal during QS2 exhibited a smaller increase but larger decrease in scattered light than QS4. Since 660 nm light is most tightly coupled with HbO₂ absorption, the QS2 changes may be due to a larger recruitment of blood to the activated area or a lower initial supply resulting in a larger change in blood volume.

Support (optional): This work was supported by NIH MH60263 and grants from the Beckman Young Investigators Fellowship Program, the Murdock Foundation, the Keck Foundation, and the Poncin Foundation.

0023

EFFECTS OF PRECEDING SLEEP/WAKE HISTORY ON ELECTRICALLY INDUCED CORTICAL LTP IN RATS

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Introduction: We have recently shown that in cortex and hippocampus molecular markers of long-term potentiation (LTP) and depression (LTD) prevail in waking and sleep, respectively. Moreover, we found that the slope of early cortical evoked potentials triggered by transcallosal stimulation increased after wakefulness and decreased after sleep. If indeed synaptic potentiation occurs during waking and shares the same mechanisms that mediate LTP, then it should be more difficult to induce LTP after wakefulness than after sleep.

Methods: Male adult WKY rats (n=7) were used. Intracortical local field potentials (LFP) recordings were obtained with bipolar concentric electrodes from the left frontal cortex while the right frontal cortex was stimulated (pulses duration = 0.1ms). LTP was induced according to an established protocol: sixty 24-ms trains of high-frequency (300 Hz) stimulation delivered at 0.1 Hz. Each rat was subjected to the LTP-inducing protocol twice, at light onset and after 4 hours of sleep, always in a standardized state of quiet wakefulness. LFPs and the EMG were continuously recorded to quantify vigilance states.

Results: In agreement with our previous results, the slope of the first negative component of the transcallosal evoked responses was high at light onset, after a spontaneous waking period, and decreased during ensuing sleep. LTP-inducing attempts at light onset did not result in consistent increases in the LFP slope relative to pre-stimulation values (12.7±6.6 %, n.s.). In contrast, LTP could easily be induced in all rats after a period of sleep (32.5±5.1%, p<0.01), and persisted for at least 1 hour (24.8±6.3%, p<0.01).

Conclusion: The induction of LTP is partially occluded after a period of spontaneous wakefulness and is restored after sleep, consistent with the idea that net synaptic strength is close to saturation after wakefulness and desaturates after sleep.

Support (optional): NIH Director's Pioneer award to GT, Swiss National Science Foundation grant PBZHB-106264 to VVV.

0024

MICRODIALYSIS DELIVERY OF THE ADENOSINE A1 RECEPTOR AGONIST N6-SULFYLPHENYLADENOSINE (SPA) TO THE PONTINE RETICULAR FORMATION (PRF) OF C57BL/6J (B6) MOUSE DECREASES PRF ACETYLCHOLINE (ACh) RELEASE AND DELAYS RECOVERY TIME FROM ISOFLURANE ANESTHESIA

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Introduction: Adenosine is a signaling molecule that modulates sleep and PRF ACh release (J Neurochem 96:1750, 2006). Laterodorsal and pedunculopontine tegmental (LDT/PPT) terminals release ACh in the PRF (J Neurosci 17:774, 1997) and adenosine inhibits LDT/PPT neurons (Science 263:689, 1994). This study is testing the hypothesis that microdialysis delivery of SPA to the PRF of B6 mouse decreases PRF ACh release and delays resumption of wakefulness after anesthesia.

Methods: Adult male B6 mice (n=7) were anesthetized with isoflurane. A CMA/7 dialysis probe was placed into the PRF and perfused with Ringer's (control) followed by Ringer's containing SPA (0.01, 0.1, or 1 mM). ACh release was quantified by HPLC/ECD. Mice were allowed to recover from anesthesia and time to resumption of righting was recorded. Dialysis probe placement in the PRF was confirmed histologically.

Results: Repeated measures one-way ANOVA and Tukey/Kramer post hoc test revealed that SPA caused a concentration-dependent decrease in ACh release (p<0.0001). Compared to control, ACh release was decreased 15.6%, 22.4%, and 40.2% by 0.01, 0.1, and 1 mM SPA, respectively. One way ANOVA showed that SPA also significantly increased

time to resumption of righting (p=0.0007). Average times for resumption of wakefulness were 20, 54, and 163 min following dialysis with 0.01, 0.1, 1 mM SPA, respectively.

Conclusion: Enhancing cholinergic neurotransmission in the PRF promotes cortical activation. The findings that SPA decreased PRF ACh release and delayed recovery from anesthesia support the interpretation that adenosine decreases arousal, in part, by decreasing PRF cholinergic neurotransmission.

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0025

GLUTAMATERGIC CELLS IN THE PARABRACHIAL NUCLEUS AND PRECOERULEUS COMPLEX REGULATE WAKEFULNESS AND CIRCADIAN RHYTHM OF SLEEP-WAKE BEHAVIOR

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Introduction: Cortical arousal is driven by the inputs from thalamus and basal forebrain, and both areas receive glutamatergic projections from the parabrachial nucleus (PB) and precoeruleus area (PC). We hypothesize that the PB-PC complex is critical to maintain wakefulness.

Methods: Adult male C57BL/6 mice containing loxP sequences flanking the second exon encoding vesicular glutamate transporter 2 (VGLUT2) were injected with an adeno-associated viral vector containing the gene for Cre recombinase (AAV-Cre) to selectively disrupt VGLUT2 expression in the PB and PC. Two weeks after surgery, EEG, EMG, temperature, and locomotor activity were monitored. VGLUT2 mRNA in situ hybridization and Cre immunohistochemistry were performed to assess the extent of the lesion.

Results: In four lox-Vglut2 mice receiving AAV-Cre injections into the PB and PC, the circadian pattern of sleep-wake behavior and locomotion was disrupted, revealing ultradian rhythms. Total amounts of wakefulness were decreased by 15-20% compared to wildtype mice or lox-VGLUT2 mice receiving AAV-GFP.

Conclusion: Wake-promoting glutamatergic neurons in the PB-PC are necessary for normal wakefulness and circadian control of sleep-wake behavior.

Support (optional): NIH/NHLBI T32 HL07901, NS051609, HL60292

0026

BLOCKAGE OF DOPAMINERGIC D2 RECEPTORS PRODUCES DECREASE OF REM BUT NOT OF SLOW WAVE SLEEP IN RATS AFTER REM SLEEP DEPRIVATION

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Introduction: Dopamine (DA) has, as of late, become singled out from the profusion of other neurotransmitters as what could be called a key substance, in the regulation of the sleep-wake states. We have hypothesized that dopaminergic D2 receptor blockage induced by haloperidol could generate a reduction or even an ablation of rapid eye movement (REM) sleep. Otherwise, the use of the selective D2 agonist, piribedil, could potentiate REM sleep.

Methods: Rats were paradoxically sleep deprived and distributed into saline, haloperidol or piribedil treatment. Sleep-wake pattern was recorded afterwards.

Results: Electrophysiological findings demonstrate that D2 blockage produced a dramatic reduction of REM sleep during the rebound (REB) period after 96 h of REM sleep deprivation (RSD). This reduction of REM sleep was accompanied by an increment in SWS, which is possibly accounted for the observed increase in the sleep efficiency. Conversely, our findings also demonstrate that the administration of piribedil

did not generate additional increase of REM sleep. Additionally, D2 receptors were found down-regulated, in the haloperidol group, after RSD, and subsequently up-regulated after REB group, contrasting to the D1 down-regulation at the same period. In this sense, the current data indicate a participation of the D2 receptor for REM sleep regulation and consequently in the REM sleep/SWS balance.

Conclusion: Herein, we propose that the mechanism underlying the striatal D2 up-regulation is due to an effect as consequence of RSD which originally produces selective D2 supersensitivity, and after its period probably generates a surge in D2 expression. In conclusion we report a particular action of the dopaminergic neurotransmission in REM sleep relying on D2 activation.

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0027

ROLE OF ADENOSINE IN ETHANOL INDUCED SLEEP

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Introduction: Acute intake of ethanol induces sleep. However, cellular mechanisms mediating the somnogenic effects of ethanol are unknown. *In vitro*, acute ethanol increases extracellular adenosine. Adenosine is involved in the homeostatic regulation of sleep. Is adenosine a mediator of the sleep following acute intake of ethanol? We designed a series of experiments to evaluate the role of adenosine in ethanol induced sleep, *in vivo*, in freely behaving rats.

Methods: Under standard surgical procedures, male Sprague Dawley rats (~300 g; 12:12 light:dark cycle; food/water ad lib) were implanted with sleep recording electrodes and bilateral guide cannulas targeted toward the wakefulness-promoting cholinergic basal forebrain (BF). After 7 days of post-operative recovery and habituation to the recording cables, the animals were habituated to a gavage tube by having it inserted once per day for 3 days. Following habituation the experiment was begun. Control day: 30 min before the onset of dark period, vehicle (500 nL of 10% DMSO in 0.9% saline) was microinjected locally and bilaterally into the BF. Subsequently, ethanol (3 gm/Kg) was administered intragastrically and sleep-wakefulness was recorded. The animals were allowed to rest for 3 days (no treatment). Experimental day: 30 min before the onset of dark period, DPCPX (50 pmol/500 nL), a selective A1 receptor antagonist was microinjected bilaterally into the BF. Subsequently, ethanol (3 gm/Kg) was administered intragastrically and sleep-wakefulness was recorded. On completion, the rats were sacrificed, brains removed and processed for choline acetyltransferase immunohistochemistry to localize the injection site.

Results: Initial results suggest that local infusion of A1R antagonist DPCPX into the BF attenuated the sleep inducing effects of ethanol in freely behaving rats (N=4; Statistical analysis pending). Histological localization of the injection site is in progress.

Conclusion: Our preliminary data implicates adenosine and its A1 receptor in mediating the somnogenic effects of ethanol.

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0028

GENDERS PRODUCE DISTINCT SLEEP PATTERNS IN AN EXPERIMENTAL MODEL OF TEMPOROMANDIBULAR JOINT PAIN

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Introduction: Studies show that hormonal factors influence the sleep pattern and sensibility to pain and also, that the tolerance threshold to pain in women varies according to their menstrual cycle. Despite these known facts, the literature offers little in the way of differing responses to pain within animal models, particularly in females. Painful conditions arising from the temporomandibular joint (TMJ) in male rats are detrimental to their sleep architecture and until the present moment, there are no investigations about the effects of orofacial pain in female rats. Objective: To assess the effect of orofacial pain in the sleep pattern of both genders in different phases of their estrous cycle.

Methods: Male and female rats were implanted electrodes that enabled the recording of their electrocorticogram (ECOG) and electromyogram (EMG). Males (n=8) and females (in diestrus n=8 and in proestrus n=8) were superficially anesthetized with halothane for bilateral injection of saline or Freund's adjuvant (AIA) into the TMJ and then connected to the polygraph. The sleep recordings were monitored for two light periods lasting 12h each. The electrophysiological signals were collected by a digital polygraph, and the recorded sleep stages were classified as wake, non-REM sleep, and REM sleep. Two-way variance (ANOVA) analysis was performed in the assessment of results, followed by the Tukey test.

Results: Subsequent to the administration of Freund's adjuvant the males presented a significant reduction in sleep efficiency, total non-REM sleep time, and in the percentage of REM sleep, as well as an increase of latency for the onset of sleep in comparison to their respective control group and to females.

Conclusion: Our results suggest that females and males present distinct responses to the model of orofacial pain adopted herein, males being more susceptible to alterations in the sleep pattern than females and control animals.

Support (optional): AFIP, FAPESP (CEPID 98/143033)

0029

TIME-FREQUENCY ANALYSIS OF THE SLEEP EEG: CHANGES ACROSS DEVELOPMENT

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Introduction: The sleep EEG undergoes dramatic changes during puberty. The most striking change is a substantial decrease in the EEG power. Furthermore, the amount of time spent in slow wave sleep (stage 3 and 4) decreases with age, while the amount of stage 2 sleep increases. The present analyses describe the sleep EEG frequency changes over the course of the night associated with pubertal development.

Methods: Longitudinal sleep EEG data were recorded from twelve healthy subjects (9 boys). Standard sleep recordings were run in lab for two nights (adaptation and baseline) when the subjects were 9- and 10-years-old and again 2-3 years later (mean = 2.4, SD = 0.28). During the initial recording session subjects were either Tanner 1 or 2 and had advanced at least one Tanner stage by the second recording session. EEG was recorded from two central (C3/A2 and C4/A1) and two occipital (O2/A1 and O1/A2) leads. Power spectra were calculated on 19-second epochs using a Fourier transform.

Results: Across the night, independent of state, all subjects showed greater spectral power in all frequency bands from all electrode sites when they were less mature. Power differences were largest in the delta

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band ($p < .01$), although large differences were also observed in the theta band. No significant power differences were seen for the alpha band; however, when more mature, the adolescents showed noticeably less power in the spindle range (11-14 Hz). Spindle range differences did not reach statistical significance, in part due to intersubject variability in the peak spindle frequency.

Conclusion: This longitudinal data analysis highlights the decline in power of the sleep EEG with adolescent maturation, particularly in the delta and sigma range. These data indicate that the pubertal amplitude changes in the sleep EEG are frequency specific and consistent across the night.

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0030

EFFECTS OF MODAFINIL (MOD) ON THE SLEEP STATE-DEPENDENT P13 POTENTIAL IN THE RAT

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Introduction: The stimulant MOD is an effective treatment for Narcolepsy. The pedunculopontine nucleus (PPN) is active during waking and REM sleep. The P13 auditory evoked potential is a measure of PPN output and the rodent equivalent of the human P50 potential. The P13 potential is sleep state-dependent, blocked by scopolamine, and habituates rapidly. We determined the dose-dependent effects of MOD injection into the PPN on the amplitude of the P13 potential. Since MOD may increase electrical coupling, we tested the ability of gap junction blockers to reduce the MOD-induced effects.

Methods: The P13 potential was recorded in adult male ($n=16$) Sprague-Dawley rats implanted with microinjection cannulae bilaterally as previously described. Following control recordings, saline or MOD (100, 200 or 300 μ M) was microinjected (0.1 μ l) into each PPN. Recordings were performed at 5, 10, 15, 25, 35, 45 and 55min postinjection. The gap junction blockers carbenoxolone (CBX, 300 μ M) or mefloquine (MEF, 25 μ M) were injected alone or 20min before MOD (300 μ M).

Results: Compared to control or saline, MOD (100 μ M) increased P13 potential amplitude at 35 and 45min postinjection (RMANOVA, $df=16$, $F=31.65$, $p<0.001$), at 200 μ M it increased it at 15, 25 and 55min ($df=16$, $F=3.81$, $P<0.001$), and at 300 μ M it increased it at 10, 25, 45 and 55min ($df=16$, $F=22.19$, $p<0.001$). Treatment with CBX (300 μ M) decreased P13 potential amplitude at 10, 25 and 55min ($df=16$, $F=16.12$, $p<0.001$), while MEF (25 μ M) decreased it at 5, 10, 15, 35, and 45min. Pretreatment with CBX (300 μ M) or MEF (25 μ M) followed by MOD (300 μ M) had no effect on P13 potential amplitude.

Conclusion: The amplitude of the P13 potential was increased in a dose-dependent manner by MOD injection into the PPN, effects neutralized by CBX and MEF. Results show that the P13 potential is a measure of arousal increased by MOD and neutralized by gap junction blockers.

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0031

CHOLINERGIC MODULATION OF FAST EXCITATORY AND INHIBITORY INPUT TO THE DORSAL SUBCOERULEUS

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Introduction: Injections of carbachol (CAR) into the rat dorsal Subcoeruleus (SubCD) have been shown to induce the generation of P-waves and the onset of REM sleep. In vitro studies have shown that SubCD neurons have differential excitatory and inhibitory responses to the application of CAR. We quantified changes in excitatory and inhibitory

post-synaptic currents during the application of CAR to determine the cholinergic modulation of fast glutamatergic and GABAergic activity.

Methods: Whole-cell recordings were conducted in brainstem slices from 7-20 day old rats, and analysis of the properties of evoked postsynaptic currents (PSCs), spontaneous PSCs, and miniature PSCs in different pharmacological conditions were conducted.

Results: Analysis of the properties of evoked PSCs, spontaneous PSCs, and miniature PSCs in different pharmacological conditions indicate that CAR exerts a predominantly inhibitory role on fast synaptic glutamatergic activity and a predominantly excitatory role on fast synaptic GABAergic activity in the SubCD. Additionally, power spectrum analyses revealed that oscillatory activity was principally generated in cells exhibiting an inward current following CAR application. This effect was blocked by either tetrodotoxin or gabazine and strychnine, but persisted during the application of the glutamate receptor antagonists, APV and CNQX.

Conclusion: Cholinergic projections to the SubCD may induce excitation of GABAergic neurons which could then lead to synchronized, rhythmic activity of SubCD projection neurons during REM sleep. Understanding the differential effects of CAR in the SubCD is an essential step towards determining how the onset and regulation of sleep-wake states are modulated.

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0032

POTENTIATING EFFECT OF ESZOPICLONE ON GABA_A RESPONSES OF PEDUNCULOPONTINE (PPN) NEURONS

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Introduction: The PPN is the cholinergic arm of the reticular activating system (RAS), which is most active during waking and REM sleep. GABAergic modulation of this area is known to be crucial for the regulation of sleep-wake cycles. Eszopiclone (ESZ), which is clinically used as a nonbenzodiazepine hypnotic agent, is known to modulate GABA_A receptors. Although the ESZ binding site and/or mechanism of action is still unresolved, our study tested the hypothesis that ESZ potentiates the effect of GABA_A receptors on PPN neurons.

Methods: Whole-cell voltage clamp recordings were performed on PPN neurons in 7-20 day rat brainstem slices, and the potentiating effect of ESZ on the responses to the selective GABA_A receptor agonist isoguvacine (IGV) were determined.

Results: In the presence of TTX, IGV induced an outward current in PPN neurons ($n=8$) with an amplitude of 15.9 ± 5.2 pA, 4.8 ± 0.3 min, and decreased input resistance (R_{in}) to $75\pm 4\%$ ($n=6$) compared to the resting state. Pretreatment with ESZ (10 μ M) a) increased the amplitude of the outward current induced by IGV to 30 ± 8 pA ($n=8$, $t=-3.85$, $p<0.01$), b) increased its duration to 7.9 ± 0.5 min ($n=8$, $t=-5.75$, $p<0.001$), and c) decreased R_{in} to $52.7\pm 0.1\%$ ($n=6$, $t=4.59$, $p<0.01$) compared to levels using IGV alone. ESZ potentiated the effects of IGV by 2.1 ± 0.25 times for amplitude, 1.5 ± 0.12 times for duration, and 1.4 ± 0.09 times for R_{in} decrease compared to the effects of IGV alone. ESZ alone did not activate any detectable currents in PPN cells or change R_{in} .

Conclusion: ESZ did not act directly on ionic conductances of PPN neurons, but significantly potentiated postsynaptic GABA_A inhibition of PPN neurons, which could be an important mechanism underlying the hypnotic effect of ESZ.

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0033

CORRELATION BETWEEN WHITE MATTER HYPERINTENSITIES AND NEUROPSYCHIATRIC INVENTORY SCORE IN PATIENTS WITH MEMORY DISTURBANCE

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Introduction: Currently we are investigating the association of behavioral and psychological symptoms of dementia (BPSD) in patients with memory disturbance including Alzheimer's disease (AD) and volumetric change of whole brain, hippocampus and white matter hyperintensity (WMH). The NPI includes questions on 11 different behavioral domains including night time behaviors indicating sleep status.

Methods: We retrospectively studied 37 subjects with probable AD who received the Neuropsychiatric Inventory (NPI), the Mini Mental Status Exam (MMSE), and an MRI scan (1.5T, T1 weighted, structural scan) as part of their clinical assessment at our memory clinic. 19 F and 18 M, mean age 77.6±8.5 (56 to 91 y.o.), mean MMSE score of 19.5 ±7.2. ANCOVA models using age as a covariate and the presence of specific BPSDs as independent variables were used to test for differences in normalized volume of whole brain, hippocampus, WMH and MMSE score.

Results: Existence of anxiety, aberrant motor behavior, and night time disturbance in NPI were significantly associated with increased WMH volume (ANCOVA, F(12,32)=3.03, p=0.014), while reduced WMH was found to be related to a symptom of disinhibition. No significant associations were found for hippocampal volumes and BPSD. MMSE score was not significantly associated with BPSD symptoms (ANCOVA, F(12,36)=1.43, p=0.220).

Conclusion: These findings suggest that white matter changes are associated with the presence of BPSD symptoms. Our finding that night time behaviors are not associated to MMSE score but are related to increased WHM volume might explain a possible cause of sleep changes due to neurodegeneration, although the pathological associations between the factors and observed volumetric changes are still unknown.

0034

DOPAMINERGIC MODULATION OF UPPER AIRWAY MOTONEURONS CONTROLLING TENSOR PALATINI MUSCLE TONE IN RATS

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Introduction: It is unknown whether dopamine directly modulates somatic motoneuron excitability and hence skeletal muscle tone. Our aim was to determine whether dopamine influences the trigeminal motoneurons that innervate the tensor palatini muscle, which plays a key role in maintaining upper airway patency. Evidence demonstrates that dopamine neurons in the A11 group innervate spinal motoneurons, which also express dopamine receptors (D1- and D2-like subtypes). Therefore, we hypothesize that changes in dopamine neurotransmission within the trigeminal motor pool would affect tensor palatini muscle tone.

Methods: We used neuro-pharmacological, electrophysiological and histological techniques to determine whether application of 1mM apomorphine (a nonspecific dopamine receptor agonist) into the trigeminal motor pool affected spontaneous tensor palatini muscle activity in anesthetized rats.

Results: Application of apomorphine into the trigeminal nucleus potently increased tensor palatini muscle EMG tone by 87% (n=20; signed rank test; p<0.001) above baseline values. Antagonism of D1-like receptors (by 1mM SCH23390) abolished this excitatory effect (n=11;

RM ANOVA; p=0.003); however, antagonism of D2-like receptors (by 20mM eticlopride) had no such effect (n=9; RM ANOVA; p=0.351).

Conclusion: We show that increased dopamine transmission within the trigeminal motor pool facilitates tensor palatini muscle tone and that this response is mediated by D1-like receptors. Whether endogenous dopamine release onto airway motoneurons influences their activity to regulate muscle tone in natural sleep-wake behaviours is unknown. This issue warrants investigation because loss of dopaminergic transmission in Parkinson's patients could lead to reduced airway tone and contribute to the increased prevalence of obstructive sleep apnea in this patient population.

0035

EFFECTS OF LEARNING TO REACH AND POST-LEARNING SLEEP ON FOS EXPRESSION IN THE RAT MOTOR CORTEX

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Introduction: We previously found in rats that learning a reaching task leads to a local increase of NREM SWA in the trained motor cortex relative to the untrained one, and that the SWA increase correlates with improved performance post-sleep. Here we tested how motor learning and post-learning sleep specifically affects the expression of Fos, a marker of neuronal activation, in the trained relative to the untrained motor cortex.

Methods: Male Long Evans rats implanted for polysomnographic recordings (parietal screw electrodes) were kept in a 12:12 light:dark cycle (lights on at 10am). Continuous video-recordings were performed to confirm behavioral states. Visual scoring of sleep stages and EEG power spectral analysis was based on 4-sec epochs. After surgery and habituation to sucrose pellets, animals were trained (10-11am) to reach with their preferred paw through a small hole in the front of the reaching chamber to retrieve a single sucrose pellet. After training, waking rats (W, n=4) were immediately sacrificed, while other rats slept ~1h and were sacrificed immediately after either an episode of NREM (n=3) or REM sleep (n=4). Fos expression was measured by immunocytochemistry.

Results: As expected, the number of Fos-positive cells in the motor cortex of both sides was higher in W (2563.2 ± 313) than in N (1093.9 ± 79) and R (1158.5 ± 150) rats, with no significant difference between the last 2 groups. Fos expression in layers II-III was higher in the trained relative to the untrained motor cortex in W rats (+32 ± 10.63, p = 0.05), but not in N and R rats.

Conclusion: Motor learning in rats produces a local and reversible increase in SWA, as well as an increase in Fos expression in the trained motor cortex relative to the untrained one. One hour of sleep is sufficient to reverse both the increase in SWA and the learning-induced asymmetry in Fos expression.

Support (optional): Supported by National Sleep Foundation Pickwick Postdoctoral Research Fellowship to ECH.

0036

SLEEP EEG IN AUTISM AND PERFORMANCE ON THE EMBEDDED FIGURE TEST

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Introduction: Neuropsychological, EEG and brain imaging studies point toward enhanced low-level visual perception in autism, leading to a more local bias and increased performance in low-level visual stimuli

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than typically developing participants (TDP). Our group has recently reported a decreased contrast between primary and non-primary visual areas for EEG Beta activity during REM sleep in autism in comparison to TDP (Bolduc et al., APSS 2005). The present study aimed at verifying if EEG Beta activity during REM sleep correlates with performance in the Embedded Figure Test (EFT), a task that relies on visual search and local perception, and consistently performed at a superior level in autism.

Methods: Eight autistic (21.9 ± 4.3 years) and 11 comparison participants (19.9 ± 4.4 years) were recorded for two consecutive nights. Spectral analysis of REM sleep Beta EEG activity (13.0 to 19.75 Hz) was performed on primary (O1, O2) and non-primary (P7, P8) visual areas. In the morning of night two, participants were tested with the Embedded Figure Test. Group performance on the EFT task was compared with Mann-Whitney U-tests. The correlation between performance and EEG spectral power was estimated with Spearman's rho coefficients.

Results: HFA participants performed better than comparison participants on the EFT task ($p < .03$). There was a negative correlation between REM sleep EEG Beta activity and time to complete the EFT task in controls only ($\rho = -0.66$; $p = 0.025$), not in the HFA group (-0.19 ; $p = 0.63$).

Conclusion: These results suggest that autistic individuals use an atypical visual cortical network in association with enhanced performance in local perceptions tasks. Once again REM sleep EEG Beta activity, thought to reflect the REM sleep control mechanisms, is shown to correlate with visual cognition and discriminate persons with autism from comparison groups.

Support (optional): Supported by the Canadian Institutes of Health Research

0037

BRAIN MICRO-CHANGES DURING THE TRANSITION TO SLEEP: EVIDENCE FROM MAGNETOENCEPHALOGRAPHIC (MEG) LOCALIZATION OF DIFFERENCES BETWEEN 8-11HZ AND 12-15HZ FREQUENCY

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Introduction: During the sleep onset process the multisource alpha rhythm changes rapidly. In order to begin to understand the functional role of alpha during this important transition, the spatial and temporal changes in low(8-11 HZ) and high alpha(12-15 HZ) were investigated. The aim of this study was to determine uncorrelated(unique) magnetic neural sources associated with low and high alpha activity during the transition to sleep in normal subjects.

Methods: Three healthy normal sleepers participated. Both the MEG(148 sensors) and standard EEG activity of sleep were recorded simultaneously(0730-0830) during a 1 hour period beginning in wake and ending in NREM sleep. MEG images of the difference between low and high alpha activity were computed using a constrained minimum-variance beamformer. The results of subtraction (8-11 Hz minus 12-15 Hz) were mapped for each subject in 1 minute intervals.

Results: Preliminary data indicate a similar pattern of topographical changes in brain organization for magnetic sources of low and high alpha activity across all the subjects during the sleep onset process. As expected the uncorrelated magnetic sources for 8-11 Hz were dominant in the occipital and temporal lobe. However, the 12-15 Hz sources localized more predominantly in the frontal lobe during the transition to sleep. Changes from low alpha with posterior predominance to high alpha with anterior predominance coincided with sleep onset. Changes in low alpha were easily seen in both the MEG and EEG whereas the pattern of increased frontal predominance in high alpha during sleep onset was observed with MEG brain mapping but was not visually apparent in the EEG data.

Conclusion: Brain micro-changes in MEG alpha activity during transition to sleep reflect spatial(posterior to anterior) and temporal(low to high frequency) changes. The functional significance of this initial MEG alpha activity speeding in the frontal region warrants further investigation.

Support (optional): NIH grant MH068372

0038

WHISKER-STIMULATION INCREASES THE NUMBER OF DOUBLE LABELED IMMUNOREACTIVE CELLS FOR NERVE GROWTH FACTOR AND INTERLEUKIN-1 BETA IN THE SOMATOSENSORY CORTEX IN RATS

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Introduction: Sleep is posited to be dependent upon prior neuronal activity. Sleep regulatory substances such as interleukin-1 beta (IL1) and tumor necrosis factor alpha (TNF) are examples of activity-dependent sleep regulatory substances. Unilateral manual brushing of the rats' mystacial vibrissae for 2 h increases the number of TNF- and IL1-immunoreactive (IR) cells in the somatosensory cortex (Sctx) (Fix et al., Sleep 29, 2006; Guan et al., Sleep 30, 2007). Previously nerve growth factor expression was shown to be sleep- and whisker-dependent in the Sctx. We now determine if IL1-IR colocalizes with NGF-IR in cells in layer V of the somatosensory cortex.

Methods: Animals were gradually habituated to being placed on inverted flower pots (to avoid rat self-stimulation of whiskers) and having the whiskers on one side of the face manually stimulated by hand for 8 days. On the ninth day, rats received 2 h of stimulation while on the inverted flower pot. Double labeling fluorescent immunohistochemistry was performed using antibodies to NGF & IL1. An individual blind to the experimental conditions counted double-labeled-positive cells in 3 adjacent sections from each rat that had activated columns as evident by Fos-IR cells on the side receiving input from the stimulated whiskers. IL1 & NGF-positive cell number from the control side was compared to the number on the side receiving whisker-stimulated afferent input. A paired Students' t-test was used to compare the cell counts from control sides to stimulated sides in the 6 rats.

Results: IL1 beta and NGF colocalized. When whiskers were stimulated for 2 h, the number of double-labeled NGF & IL1 beta-IR cells increased significantly in layer V of the Fos-activated region when compared with the unstimulated side.

Conclusion: Collectively, these data support the hypothesis that NGF and IL1 are dependent, in part, on neuronal activation.

Support (optional): NIH (USA) NS 25378 and NS 31453

0039

TUMOR NECROSIS FACTOR ALPHA-, NERVE GROWTH FACTOR- AND THE NEURONAL NUCLEAR PROTEIN- IMMUNOREACTIVITY ARE ALTERED DIFFERENTIALLY IN TWO AREAS OF CORTEX DEPENDING ON PRIOR ACTIVITY

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Introduction: Sleep is posited to be regulated in part by substances produced in response to neuron use, such as tumor necrosis factor alpha (TNF). Nerve growth factor (NGF) expression is activity-dependent and can also affect sleep. Under a 12:12 light-dark (LD) cycle, electroencephalographic (EEG) slow wave activity (SWA) differentially increased in the visual cortex (Vctx) during light hours and in the somatosensory cortex (Sctx) during the dark (Yasuda et al., Amer. J. Physiol., 289:R1083, 2005). We hypothesize that neural activity in the Sctx activated by whisker stimulation during the dark or in the Vctx activated by light enhances expression of sleep regulatory substances locally and

thereby provides a mechanism by which the brain keeps track of prior activity.

Methods: Six rats were killed in 10 min intervals 1 h before dark onset (light) or in the hour before light onset (dark). Immunohistochemistry was performed using antibodies to NGF, TNF or a neuronal nuclear protein (NeuN). TNF colocalized in neurons in all layers as evidenced by NeuN. Two individuals blind to the conditions counted cells.

Results: During the dark, the number of TNF-immunoreactive (IR) cells in the Sctx increased 2-3-fold in layers II-VI, when compared to the light ($p=0.002-0.02$). If the rats were killed in the light, the number of NGF-IR cells increased 1.1-1.2-fold in layer II-III & IV of the Vctx ($p=0.007-0.04$). The number of NeuN-IR cells in the Sctx increased 1.2-1.3 fold in the dark for layers II-III, V & VI ($p=0.01-0.04$) and in the light 1.1 fold for layer IV of the Vctx ($p=0.04$).

Conclusion: These data support in part our hypothesis that sleep is dependent upon the activity-induced production/release of sleep regulatory substances; however, different sleep regulatory substances have a unique pattern in the Sctx and Vctx. Also NeuN shows activity dependent increases.

Support (optional): NIH (USA) NS 25378 and NS 31453

0040

PRENATAL ALCOHOL EXPOSURE INCREASES THE NUMBER OF TUMOR NECROSIS FACTOR ALPHA-IMMUNOREACTIVE CELLS IN THE SOMATOSENSORY CORTEX OF ADULT FEMALE RATS

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Introduction: Prenatal alcohol exposure causes abnormal sleep patterns in human infants. Rats also have deficits in sleep patterns after prenatal alcohol exposure (PAE). PAE alters somatosensory-motor functions in both human and animal studies. Tumor necrosis factor α (TNF α) is a sleep regulatory substance and plays a role in brain development. Previously we showed that the sleep-inducing effect of TNF α was reduced in mature female rats after PAE. Chronic alcohol exposure increases cytokine levels in rat cortex and cultured astrocytes; therefore we hypothesize that PAE-induced sleep pathologies are related to changes in TNF α expression in the somatosensory cortex (Sctx) of adult female rats.

Methods: Pregnant female Sprague-Dawley rats on gestational day 8 were randomly assigned to two groups: Group A (alcohol treated) had free access to a liquid diet (BioServ, NJ) with 6% alcohol added, Group B (pair-fed control) were pair-fed to the first group in a weight-matched manner. Thirty-five percent of the caloric content of this diet is provided by ethanol. Liquid diets were fed from gestational days 8-20. At birth, offspring were counted, weighed, randomly culled to 8 per litter, and returned to the dams. Offspring were weaned at 21 days of age, separated by gender, and group housed (3-4 per cage) until 3 months. The female rats were sacrificed on the day of estrus and the brains were frozen for immunohistochemistry.

Results: PAE significantly increased the number of TNF α -immunoreactive cells in layer V of the Sctx in comparison to the pair-fed control group. TNF α -immunoreactive cells were neurons as determined by cell shape and colocalization with NeuN immunoreactivity.

Conclusion: This data supports our hypothesis that sleep changes after PAE are related to the increased expression of TNF α in the Sctx possibly by down regulating TNF α receptors.

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0041

TIME COURSE OF WHISKER-STIMULATION INDUCED INCREASES IN TUMOR NECROSIS FACTOR ALPHA-IMMUNOREACTIVE CELLS IN THE SOMATOSENSORY CORTEX IN RATS

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Introduction: Sleep is posited to be a local process dependent upon prior neuronal activity. Tumor necrosis factor alpha (TNF) is an example of an activity-dependent sleep regulatory substance. Unilateral manual brushing of the rats' mystacial vibrissae for 2 h increases the number of TNF-immunoreactive (IR) cells in the somatosensory cortex (Sctx) (Fix et al., Sleep 29, A11, 2006). We now determine the time course of whisker stimulation-induced increases in TNF-IR cells.

Methods: Animals were gradually habituated to being placed on inverted flower pots (to avoid rat self-stimulation of whiskers) and having the whiskers on one side of the face manually stimulated by hand for 8 days. On the ninth day, rats received either 20 min, 1 h or 2 h of stimulation while on the inverted flower pot. Immunohistochemistry was performed using antibodies to Fos or TNF. Two individuals blind to the experimental conditions counted TNF-positive cells in 3 adjacent sections from each rat that had activated columns as evident by Fos-IR cells on the side receiving afferent input from the stimulated whiskers. TNF-positive cell number from the control side was compared to the number on the side receiving whisker-stimulated afferent input. A paired Students' t-test was used to compare the cell counts from control sides to stimulated sides in the 6 rats.

Results: When whiskers were stimulated for 2 h, the number of TNF-IR cells increased significantly in layer IV of the Fos-activated region when compared with the unstimulated side. A significant increase in the number of TNF-IR cells occurred between 1 and 2 h but not between 20 min and the other times.

Conclusion: Collectively, these data support our hypothesis that TNF expression is dependent, in part, on neuronal activation.

Support (optional): NIH (USA) NS 25378 and NS 31453

0042

SOMNOGENIC CYTOKINES INTERLEUKIN-1B AND TUMOR NECROSIS FACTOR- α INCREASE IN THE PIRIFORM CORTEX AND THE HYPOTHALAMIC ARCUATE NUCLEUS FOLLOWING INTRANASAL INOCULATION WITH INFLUENZA A VIRUS

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Introduction: Many viral infections are associated with characteristic systemic symptoms such as fever, somnolence and fatigue. These symptoms are considered part of the acute phase response and are regulated in part by host cytokines. Viral RNA and antigens are detected and tumor necrosis factor α (TNF α and interleukin-1 β (IL-1 β). mRNAs are elevated in the olfactory bulb (OB) of influenza-infected mice at the onset of hypothermia [15h after intranasal inoculation (Majde et al., J Neurovirology, 2007)]. Additionally, the number of cells immunoreactive (IR) for TNF α and IL-1 β increases in the OB of such mice at the onset of hypothermia. We hypothesized that because sleep and fever are in part regulated by the hypothalamus (HT), that increases in cytokine-IR cells in different regions of the olfactory projection pathway to the HT would occur at the time when fever and sleep responses are induced by virus challenge.

Methods: Mature C57BL/6 male mice were inoculated intranasally with the PR8 H1N1 strain of live ($n=6$) or boiled ($n=6$) human influenza virus. Mice were anesthetized and perfused with 4% paraformaldehyde at 15 h post-infection and whole brains were collected. Midbrain sections

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(30 μm) were processed for immunohistochemistry using TNF α and IL-1 β antibodies. Stained sections were examined and photographed using light microscopy; and IR cells were counted on printed pictures by two blinded observers.

Results: There was a significant increase in the number of IL-1 β -IR cells in the piriform cortex (Pir) and the arcuate nucleus (Arc). The number of TNF- α IR cells was significantly increased in the Pir but not in the Arc after viral challenge.

Conclusion: After intranasal inoculation, influenza virus activates specific regions within the olfactory projection pathway and the hypothalamus to increase the production of somnogenic cytokines such as IL-1 β and TNF- α .

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0043

SLEEP EEG SPECTRA AFTER EXPOSURE TO MOBILE PHONE 'TALK' AND 'LISTEN' MODE SIGNALS: PULSE-MODULATION FREQUENCY DEPENDENT EFFECTS

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Introduction: Mobile phone 'talk' and 'listen' mode signals share the same pulse modulation frequency at 8 and 217 Hz while listen mode has an extra 2-Hz modulation. Our previous study showed talk-mode to delay sleep onset (Hung et al., 2007). Here we reported an extended analysis of the same study with EEG spectra during stage 2 (S2) and slow-wave sleep (SWS).

Methods: 90-min sleep EEGs, early afternoon, were obtained from 10 right-handed healthy young men (sleep restricted to 6h), after a 30-min exposure to a standard GSM 900 MHz mobile phone emissions at talk, listen and sham (nil signal) modes during prior waking, given weekly. Mean S2 and SWS EEG power (log-transformed values) across 1-16 Hz range per recording were calculated in 1-Hz bins at bipolar derivations (F3-C3, C3-P3, P3-O1, F4-C4, C4-P4, P4-O2), by averaging individual time series, aligned with respect to the onset of S2 and SWS. Condition effects on: (i) S2 and SWS EEG power at single Hz and (ii) SWS EEG combined 1-4 Hz power were assessed by one-way ANOVAs for repeated measurements. We also investigated effects on the modulation of EEG spindles (14-16 Hz power) by 2-4 Hz power during SWS, using linear regression coefficients between these two EEG dynamics and compared three modes.

Results: Compared with sham, both talk and listen modes reduced S2 EEG spindles (talk: 12-15 Hz, listen: 13-16 Hz) power but this effect of listen-mode was less distributed (only seen at C4-P4). During SWS, EEG 1-4 Hz power was not different from sham mode in either condition. However, listen mode significantly enhanced: SWS EEG 11-13 Hz power at F4-C4; 12-14 Hz power at C3-P3, compared with sham mode. Talk mode showed no effect on SWS EEG spectra. Regression coefficients between EEG power at 2-4 Hz and 14-16 Hz during SWS over the central/parietal/occipital regions showed significantly higher values after listen-mode exposure.

Conclusion: Compared with talk mode, listen mode increased S2 and SWS EEG spindle frequency activities, without significant changes in sleep propensity and SWS intensity. It suggests the extra 2-Hz modulation has different sleep effects from 8 and 217-Hz modulation.

0044

THE PUTATIVE SLEEP HOMEOSTATIC FACTOR ADENOSINE SELECTIVELY INHIBITS ONE TYPE OF BASAL FOREBRAIN GABA NEURONS

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Introduction: The basal forebrain (BF) constitutes the ventral extrathalamic relay from the brainstem activating system to the cortex and is a crucial site for biochemical processes related to sleep homeostasis. Here we characterized the effects of the putative sleep homeostatic factor, adenosine, on GABAergic BF neurons.

Methods: Coronal brain slices were prepared from young (14-22 d) heterozygous GAD67-GFP knock-in animals. GABAergic BF neurons (0.50 to -0.10 caudal to Bregma) were identified prior to recording based on their expression of green fluorescent protein (GFP). Whole-cell patch-clamp recordings were made using a Multiclamp 700B amplifier. Drugs were bath-applied.

Results: Adenosine (100 μM) selectively hyperpolarized (-3.1 ± 0.4 mV, $n=14$) one group of GABAergic BF neurons characterized by a prominent depolarizing sag during hyperpolarizing current pulses. Application of the A1 receptor antagonist cyclopentyltheophylline (CPT) to the same type of neuron caused a depolarization of 3.4 ± 0.7 mV ($n=8$) and blocked the effect of adenosine ($n=4$). Application of the nitric oxide donor DEA NONOate (100 μM , $n=14$) also caused a hyperpolarization which was blocked by CPT ($n=6$), suggesting mediation by adenosine. These neurons were excited by noradrenaline ($n=8$), suggesting they are wake-active. Since it was reported (Arrigoni et al., 2006) that adenosine inhibits unidentified BF non-cholinergic neurons via inhibition of I_h we examined the effect of AD on the depolarizing sag mediated by I_h and confirmed that it was reduced by adenosine ($n=4$). Similar to the effect of adenosine, the selective H-current blocker ZD7288 (100 μM) caused a hyperpolarization of -2.4 ± 0.7 mV ($n=4$). Other BF GABA neurons were unaffected by adenosine.

Conclusion: In addition to its inhibitory action on basal forebrain cholinergic neurons adenosine is likely to exert its somnogenic effects by inhibition of one type of BF GABA neurons via an action on A1 receptors and subsequent block of I_h.

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0045

HYPOGLOSSAL PREMOTOR NEURONS OF THE INTERMEDIATE MEDULLARY RETICULAR REGION EXPRESS MRNA MARKERS OF CHOLINERGIC CELLS

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Introduction: In obstructive sleep apnea patients, upper airway muscle tone is inspiratory-modulated; this helps protect the airway from collapse. Inspiratory neurons of the intermediate medullary reticular region (IRt) are the main source of respiratory input to hypoglossal (XII) motoneurons that innervate the genioglossus, a major upper airway dilator. The neurochemical mechanisms of modulation and transmission of inspiratory drive to XII motoneurons may involve transmitters that have state-dependent release, such as acetylcholine. Here, we assessed the expression of cholinergic mRNA markers in IRt neurons with projections to the XII nucleus.

Methods: Fluorescein (FITC)-labeled latex microspheres (20-50 nl) were microinjected into the left XII nucleus in four pentobarbital-anesthetized, young rats. After 5-7 days, the rats were sacrificed and a coronal 400 μm slice was obtained from the XII nucleus level. Following

enzymatic digestion, 700 μm tissue micropunches were cut out from the right IRT, cells were mechanically dispersed and plated. Individual FITC-containing (FITC(+)) and FITC-free (FITC(-)) cells were collected, their DNA digested, and the remaining material subjected to reverse transcription and semi-nested PCR with primers for choline acetyltransferase (CHAT), M1-M5 muscarinic receptors, and $\alpha 4$ subunit of nicotinic receptor (Na4).

Results: Out of 25 FITC(+) cells, 12 (48% \pm 10(SE)) were positive for CHAT, 10 for M2 receptor (40% \pm 10), and 5 co-expressed both (20% \pm 8). These proportions were significantly higher than for 13 FITC(-) cells (2 positive for CHAT and none for M2). FITC(+) cells also expressed M1 (12% \pm 7), M3 (28% \pm 9), M4 (12% \pm 7), M5 (20% \pm 8), and Na4 (60% \pm 10) mRNA; not different from FITC(-) cells.

Conclusion: Some IRT XII premotor neurons may be cholinergic because they express mRNA for both CHAT and M2 receptors that frequently act as autoreceptors. The presence of multiple cholinergic receptor mRNAs in XII premotor neurons also suggests that acetylcholine postsynaptically controls these neurons or presynaptically regulates transmitters release from their terminals.

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0046

CORTICOTROPIN RELEASING HORMONE (CRH) MODULATES FEAR-INDUCED ALTERATIONS IN SLEEP IN MICE

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Introduction: Contextual fear (CF) significantly reduces rapid eye movement sleep (REM) during post-exposure sleep in mice and rats. Mice that are more reactive in behavioral tests of anxiety (e.g., BALB/c mice) exhibit greater reductions in REM after conditioned fear. CRH plays a major role in CNS responses to stressors. Central administration of CRH increases whereas CRH antagonism generally reduces anxiety-like behaviors. We examined the influence of CRH and astressin (AST), a non-specific CRH antagonist, on sleep after CF in the reactive BALB/c mouse strain.

Methods: Three groups of BALB/c male mice (n=5 per group) were implanted with transmitters for recording sleep and activity via telemetry and with a guide cannula aimed into the lateral ventricle. Recordings for vehicle and handling control were obtained after ICV microinjection of saline (SAL) followed by exposure to a novel chamber. Afterwards, the mice were subjected to shock training (20 trials, 0.5 mA, 0.5 s duration) for 2 sessions. After training, the three groups of mice received ICV microinjections of SAL (0.2 μl), CRH (4.0 μg), or AST (10.0 μg) prior to induction of CF by exposure to the shock context alone. Sleep was recorded for 20 hours (8-hour light and 12-hour dark period) following CF. Comparisons of sleep parameters were conducted with paired t-tests.

Results: Compared to handling control, CF significantly decreased REM in mice receiving SAL (-17%, $p < 0.037$) and in mice receiving CRH (-33.7%, $p < 0.001$), but not in the mice receiving AST (-9.0%, ns). Mice receiving CRH also exhibited further reductions in REM during the 12-h dark period after CF (-12.7%, $p < 0.04$), but mice receiving SAL (-7.7%) or AST (7.0%) did not. No significant alterations were found in NREM.

Conclusion: These findings demonstrate a role for the central CRH system in regulating alterations in sleep induced by CF.

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0047

CORE BODY TEMPERATURE (BT) DURING 24-HOUR SLEEP-WAKEFULNESS CYCLE IN TREE SHREWS, RATS AND MICE

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Introduction: Tree shrews are small, squirrel-like, arboreal mammals native to Southeast Asia. They are highly active during the light period and are extremely inactive during the dark period. Their daily temperature variations have been reported to be large and synchronized to locomotor activity, but have not been characterized with respect to sleep. We compared the relationship of BT to sleep and wakefulness in tree shrews to that in laboratory rats and mice.

Methods: Six adult male tree shrews (*Tupaia belangeri*, weight 120-140 gram) were intraperitoneally implanted with transmitters (DataSciences TL11M2-ETA-F20) for recording EEG, EMG, activity and core BT. Data also were collected via telemetry in rats (Sprague-Dawley, n=4) and mice (C57BL/6J, n=7). All animals were maintained on a 12-12 light-dark cycle. Core BT was analyzed in active waking (AW), quiet waking (QW), non-rapid eye movement sleep (NREM), and rapid eye movement sleep (REM).

Results: Rankings ($p < 0.001$) for overall BT (M \pm SEM, $^{\circ}\text{C}$) were tree shrews (39.1 \pm 0.1) > rats (37.9 \pm 0.1) > mice (37.2 \pm 0.1) during the 12-h active phase (light period for tree shrews and dark period for rats and mice), and rats (37.0 \pm 0.1) = tree shrews (36.8 \pm 0.1) > mice (36.1 \pm 0.1) during the 12-h inactive phase. Differences in mean BT between active and inactive periods were tree shrews (2.3 \pm 0.1) > rats (0.9 \pm 0.1) = mice (1.1 \pm 0.1). All three species showed greater BT during wakefulness than during sleep. Differences in BT between AW (higher) and QW were significant during the inactive phase for all three species and during the active phase for tree shrews and mice. All three species showed higher BT in NREM than in REM during the active phase, but not during the inactive phase.

Conclusion: Tree shrews exhibited the largest variation in overall mean BT across active and inactive phases. Differences in BT in AW and QW during the active phase may be associated with differences in locomotion across species.

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0048

THE CENTRAL NUCLEUS OF THE AMYGDALA (CNA) REGULATES CHANGES IN RAPID EYE MOVEMENT SLEEP (REM) AFTER ESCAPABLE SHOCK IN RATS

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Introduction: Training with inescapable shock (uncontrollable stressor) is followed by significant reductions in REM. However, controllability is a significant factor in the effects of stress. We examined the effects of escapable shock (controllable stressor) on subsequent sleep and the potential role of the CNA, a region involved in the stress response and the control of arousal, in regulating these effects.

Methods: Wistar rats (n=7) were implanted with electrodes for recording sleep and with cannulae aimed bilaterally into CNA. After recovery from surgery and habituation to the injection procedure, baseline sleep was recorded. On experimental day 1 and 2, the rats underwent escapable shock training (ST1 & ST2) in a shuttlebox (20 footshocks, 0.5mA, maximum 5s duration) presented over 30 minutes. The animals could learn to terminate shock by moving into the opposite chamber. On day 7 (context alone), the animals were placed back in the chamber without shock for 30 minutes. On days 11 and 17, the animals were injected with

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either the GABAA agonist, muscimol (1.0 mM, MUS-ST) to inactivate CNA or saline (0.2 µl, SAL-ST) prior to escapable shock sessions (as described above). Sleep was recorded for 20 h post-session and scored for NREM, REM, and wakefulness.

Results: Following ST1, but not ST2, the rats exhibited significant reductions in REM in the first 2h of recording compared to baseline levels. In the 5th and 6th h of recording, REM was significantly increased compared to baseline levels on both ST1 & ST2. Following context alone, rats showed no significant differences in sleep compared to baseline. SAL-ST showed changes in REM similar to those found in ST1 in REM whereas MUS-ST showed significant reductions in REM in the first 2h of recording and did not show the later increase in REM.

Conclusion: Controllable stress in the form of escapable shock is followed by increased REM that involves regulation by CNA.

Support (optional): Supported by NIH research grants MH64827 and MH61716

0049

ANTAGONIZING CORTICOTROPIN RELEASING HORMONE (CRH) 1 RECEPTORS IN THE CENTRAL NUCLEUS OF THE AMYGDALA (CNA) ATTENUATES FEAR-INDUCED REDUCTIONS IN SLEEP

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Introduction: Contextual fear produces alterations in sleep including significant reductions in rapid eye movement sleep (REM) and/or non-REM (NREM). The neuropeptide CRH plays a major role in regulating central aspects of the stress response as well as playing a role in the regulation of arousal. CNA is critical for behavioral and physiological signs of contextual fear and it plays a role in regulating arousal and sleep. CRH in CNA has been implicated in stress-related behavior. In this study, we examined the effects of microinjections of the CRH1 antagonist, antalarmin (ANT) into CNA on fear-induced alterations in sleep.

Methods: Wistar rats (n=16) were implanted with electrodes for recording EEG and EMG and with cannulae aimed into CNA for administration of drug. On separate days, the rats were subjected to handling control and two shock training sessions (ST1 and ST2) with 20 foot-shocks (0.5 s, 0.8 mA) at 1 min intervals. Afterwards, the rats received microinjections (0.2 µl) of ANT (4.8 mM; n=8) or vehicle alone (n=8) prior to exposure to the fearful context alone. Sleep was recorded for 20 h (8 h light, 12 h in dark period) after each condition and scored in 10 sec epochs.

Results: Compared to handling control, S1 and S2 significantly reduced both NREM and REM during the first 4 h of recording. Vehicle treated rats exposed to the fearful context alone showed reductions in NREM and REM that did not significantly differ from those after S1 and S2. By comparison, ANT treated rats exposed to the fearful context alone showed levels of NREM and REM that did not differ from handling controls, and that were significantly greater than levels exhibited during S1 and S2.

Conclusion: The results demonstrate a significant role for CRH1 receptors in CNA in regulating fear-induced changes in sleep.

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0050

EFFECTS OF UNPREDICTABLE CHRONIC MILD STRESS (UCMS) AND PARTIAL SLEEP DEPRIVATION (PSD) ON 5-HT AND ADENOSINE IN RAT BRAIN

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Introduction: The 5-HT and adenosine systems play roles in the regulation of sleep and emotion. UCMS is a model of depression associated with significant alterations in levels of 5-HT and adenosine in the brain, especially in the hippocampus, whereas PSD may improve mood in patients with depression. We examined the influence of UCMS and PSD on concentrations of 5-HT, 5-HT1A and adenosine A1 receptors in the rat brain.

Methods: Thirty adult male Sprague-Dawley rats were exposed to UCMS (e.g., variations of footshock, dirty cage exposure and food deprivation) for 21 days. Afterwards, 10 rats were euthanized immediately to determine the effects of UCMS, 10 rats received PSD via small platform over water and 10 rats served as platform controls (PC) by exposure to a large platform over water. PSD and PC were conducted for 72 h. An additional group of 10 rats served as home cage controls (HCC). Concentrations of 5-HT and mRNA levels of 5-HT1A receptors and adenosine A1 receptors were examined via HPLC or RT-PCR in hippocampus, frontal cortex, hypothalamus and brainstem in each group.

Results: The most dramatic differences between groups were found in the hippocampus. Compared to HCC, UCMS rats had a decrease in 5-HT and an increase in mRNA levels of adenosine A1 receptors and no change in mRNA levels of 5-HT1A receptors. Compared to UCMS and PC, 5-HT concentrations and mRNA levels of 5-HT1A receptors were increased and mRNA levels of adenosine A1 receptors were decreased in the hippocampus of PSD rats.

Conclusion: In agreement with previous reports, the findings demonstrate that UCMS can result in pathological changes in hippocampus. This work suggests that PSD may reverse changes in hippocampus produced by UCMS. These changes by PSD may be involved in its effects on mood in patients with depression.

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0051

INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-3 REDUCES HYPOCRETIN/OREXIN TRANSMISSION

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Introduction: Microarray analysis of humans and mouse models of narcolepsy have revealed a cellular colocalization of insulin-like growth factor binding protein 3 (IGFBP-3) and hypocretin/orexin neuropeptides in the lateral hypothalamus. We investigated the effect of IGFBP-3 on hypocretin expression. Further, we studied the effect of IGFBP-3 overexpression on sleep/wake behaviors in a transgenic model and examined the relationship between cerebrospinal fluid (CSF) hypocretin level and an IGFBP-3-regulating single nucleotide polymorphism (SNP) known to affect circulating IGFBP-3 in human subjects.

Methods: Mice (8 weeks old) overexpressing human IGFBP-3 (TG, CD-1 background) and IGFBP-3 knockout animals (KO, C57Bl/6 background) were euthanized, and brains dissected for real-time PCR and hypocretin-1 radioimmunoassays. TG mice of 4-5 months old were implanted with transmitters and monitored for locomotion, core temperature and electroencephalography. DNAs of human subjects with normal

CSF hypocretin levels (controls and with sleep disorders) were subject to IGFBP-3 promotor SNP genotyping by PCR-RFLP.

Results: Hypothalamic hypocretin mRNA level in TG mice overexpressing IGFBP-3 was significantly lower than in the wild type (WT) littermates, while MCH expression was similar in both genotypes. Hypocretin-1 contents in the hypothalamus and brain stem were also significantly lower in TG mice. Both genotypes displayed comparable levels of locomotion and core temperature, and overall sleep/wake patterns were similar. However, at the end of the dark period (zeitgeber time 20-24 h) when the hypocretin release is highest, TG mice displayed more sleep and less wake than WT mice. KO mice did not show any appreciable changes in these measurements, possibly due to functional compensation by other IGFBPs. In Caucasians, a significant correlation between the IGFBP-3 SNP and CSF hypocretin levels was found. Most notably, in subjects with the CC genotype that has been known to contribute to lower circulating IGFBP-3, hypocretin levels were significantly higher than in subjects with the AA and AC genotypes. These results, together with *in vitro* hypocretin promoter studies, suggest modulation by IGFBP-3 and the IGF axis of hypocretin transmission.

Conclusion: These studies demonstrate that IGFBP-3 negatively regulates hypocretin transmission. This may result in reduced wakefulness when the hypocretins are most needed to sustain vigilance at the end of the active period.

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0052

THE RELATIONSHIP BETWEEN PRIOR SLEEP AND NAP ARCHITECTURE

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Introduction: Most literature examining the effects of sleep duration on subsequent sleep is derived from sleep deprivation (SD) and restriction (SR) studies. Research examining the influence of “normal” (7+hrs) nocturnal sleep on subsequent daytime sleep focuses primarily on MSLT-based sleep latency. Here, we examine how prior, normal amounts of nocturnal sleep influence the architecture of a single afternoon nap.

Methods: 24 healthy subjects (age:25±4.9,17F) wore an actigraph for 7 nights while adhering to a regular sleep-wake schedule followed by a 90-minute, PSG-recorded nap. We examined the influence of 2-night and 7-night averages of total sleep time (TST) immediately prior to the nap on nap architecture (i.e., TST, %Stg1, %Stg2, %SWS, %REM). To control for the effects of early or late bed/wake times, we performed hierarchical regressions, first using bed and wake time as the independent variable (Model1), then adding average TST (Model2) and testing R²-change values.

Results: Mean %REM of all naps = 9.8±13.8. Less prior nocturnal TST increased the %REM during the nap (2 nights: Model1: R²=0.26, p=0.06, Model2: R²=0.35, p=0.047, R²-change=0.09; 7 nights: Model1: R²=0.12, p=0.25, Model2: R²=0.35, p=0.03, R²-change=0.23). Average TST did not affect any other architecture variable of the nap. Bed and wake time appear to influence %REM only in the short-term (i.e., 2-night average).

Conclusion: Decreased nocturnal TST, even within the normal range, is associated with increased %REM during subsequent naps. Studies of recovery sleep after SD and SR show a rebound of SWS and REM on sequential nights. The present study indicates that, in the context of an afternoon nap, small variations in prior healthy sleep impact REM exclusively. Quantitatively, 10-min less TST led to 1.3% more REM. These fluctuations in sleep architecture reveal possible homeostatic regulations

of REM sleep, in which shorter TST leads to subtle REM debt that can be recovered in an afternoon nap.

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0053

ANTAGONISM OF α 1-ADRENERGIC AND SEROTONERGIC RECEPTORS IN THE HYPOGLOSSAL (XII) NUCLEUS DOES NOT ABOLISH ACTIVATION OF XII MOTONEURONS ELICITED FROM THE POSTERIOR LATERAL HYPOTHALAMUS

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Introduction: In anesthetized rats, antagonism of GABAA receptors located in the perifornical (PF) region of the posterior hypothalamus with bicuculline activates many local cells, including the wake-promoting orexin neurons, activates brainstem noradrenergic neurons, desynchronizes cortical EEG and increases XII nerve activity (Lu et al., *J. Physiol.*, 2007). Since orexin cells project to, and activate, noradrenergic and serotonergic neurons, and aminergic projections to XII motoneurons are an important source of their wake-related activation, we hypothesized that the excitatory effect of PF bicuculline on XII nerve activity is mediated by aminergic neurons. To test this, we assessed the effects of PF bicuculline on XII nerve activity following local antagonism of α 1-adrenergic and serotonergic receptors using a previously validated methodology (Fenik et al., *Am. J. Resp. Crit. Care Med.*, 2005).

Methods: In 6 urethane-anesthetized, paralyzed, vagotomized and artificially ventilated rats, we recorded XII nerve activity, cortical EEG and hippocampal activity. Three 40 nl injections of 0.2 mM prazosin and 1 mM methysergide combined were made into the XII nucleus followed 30 min later by PF injections of 1 mM bicuculline (20 nl).

Results: In 4 animals, prazosin and methysergide injections decreased spontaneous XII nerve activity to 29.7±4.3(SE)% (p<0.01) of baseline and abolished it in the remaining 2 animals. The subsequent PF injection of bicuculline activated the cortical EEG and hippocampus and increased (n=4) or made re-appear (n=2) XII nerve activity, bringing it to 96±17% of the pre-antagonist level (n=6).

Conclusion: Since the bicuculline-induced increase of XII nerve activity was of a comparable magnitude to that evoked without antagonism of aminergic receptors in the XII nucleus (cf., Lu et al., 2007), the activating effects of PF bicuculline on XII motoneurons must be largely mediated by pathways other than the wake-related aminergic projections to the XII nucleus.

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0054

SLEEP AND SLEEP REGULATION IN MICE LACKING THE GABA-A RECEPTOR α 3-SUBUNIT

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Introduction: The inhibitory transmitter gamma-aminobutyric acid (GABA) and its receptors play an important role in the neuronal systems regulating sleep. GABA-A receptors containing the α 3-subunit are markedly expressed in several neuronal circuitries involved in sleep regulation. The thalamic reticular nucleus (nRT), which modulates thalamo-cortical network rhythmic activities, exclusively expresses GABA-A α 3-containing receptors. To determine whether the loss of these receptors may alter sleep and sleep regulation, we investigated sleep in mice lacking the alpha3-subunit (α 3KO mice).

Methods: We performed EEG recordings under baseline conditions in wild-type and α 3KO mice for 24 h and further, studied the response to 6 h sleep deprivation (SD), a well-established method to enhance sleep

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pressure and thereby uncover differences in sleep regulation (α 3KO, $n=12$; wild-type, $n=11$).

Results: The genotypes did not differ in their vigilance states or 24-h sleep patterns. Spectral analysis of the baseline EEG showed no difference between the genotypes in the NREM sleep EEG spectrum or at the waking-NREM sleep transition. A difference occurred in the last 4-s epoch of the NREM-REM sleep transition. Thus, EEG power in the spindle frequency range (10-15 Hz) was significantly lower in α 3KO mice than in wild-type. Enhancement of sleep pressure by 6 h SD did not reveal differences in the NREM sleep spectra or at transitions between α 3KO mice and wild-type. Finally, analysis of the wake EEG showed slightly larger power in the 11-13-Hz band in α 3KO mice vs wild-type. Behavior and the waking EEG failed to reveal any alterations suggestive of absence seizures in α 3KO mice.

Conclusion: Overall, sleep regulation and cortical NREM sleep EEG activity was unaltered in α 3KO mice. Further studies are required to determine how functions of nRT neurons are preserved in the absence of GABA-A α 3-containing receptors in the nRT and neocortex.

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0055

COGNITIVE IMPAIRMENT IN FATIGUE AND SLEEPINESS ASSOCIATED CONDITIONS

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Introduction: Cognitive impairment has previously been associated to fatigue related conditions and to the chronic fatigue syndrome (CFS) in particular. Sleepiness associated daytime conditions as the sleep apnea-hypopnea syndrome (SAHS) also reported lowered attention, concentration and memory performances. The objective of the study was to qualify discriminating differences on classical neuro-cognitive and behavioural testing between these two clinical conditions.

Methods: 16 pure CFS patients (mean age 34.2, all females), without primary sleep disorders (PSD), mental disorder nor clinically relevant sleepiness, were compared to matched healthy controls (mean age 31.9, all females) and to 13 untreated SAHS patients (mean age 49, all females). All subjects were right handed. Auditory verbal learning test (AVLT), digit-span, digit symbol and finger tapping test (FTT) were used as cognitive and behavioural testing. Fatigue and sleepiness were measured with the Fatigue Severity Scale and the Epworth Sleepiness Scale respectively.

Results: With exception for the digit span, which did not show significant difference between CFS and HC, all tests of the administered battery showed lower cognitive performance in patient groups. Globally, memory dysfunction on the AVLT did not differ between the two patient groups, but the digit and symbol span showed more severe impairment in SAHS ($p<0.003$). Psychomotor performance on the FTT also showed significantly slower hit rates (HR) in SAHS than in CFS patients (mean HR on the dominant hand, $p<0.0001$).

Conclusion: Fatigue and sleepiness associated daytime conditions can show significant and objective impairment of cognitive functioning. Discrimination between sleepiness and fatigue, based on neuropsychological testing, remains difficult. A specific cognitive impairment type is still to be described. However lowered vigilance and lower psychomotor performance, associated to SAHS, showed the FTT to discriminate between fatigue and sleepiness in this exploratory study. In our sample cognitive impairment and psychomotor performance were worse when associated to sleepiness than to fatigue alone.

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0056

ANATOMICAL RELATIONSHIPS BETWEEN MESOPONTINE TANCYTES AND SEROTONERGIC NEURONS

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Introduction: Tancytes are specialized cells that are located in the ependyma of the ventricular system. These cells are capable of absorbing substances from the cerebrospinal fluid (CSF) at their apical pole, and release these substances by a process of transcytosis, via their radially-oriented, unbranched basal processes that extend into the neuropil. In the present study, we determined the relationships between mesopontine tancytes and serotonergic neurons of the raphe nuclei.

Methods: Adult cats were euthanized and the brainstem was removed in order to carry out single/double immunohistochemical procedures to identify tancytes and serotonergic neurons. The presence of tancytes was determined using primary antibodies against vimentin, which is a marker for tancytes; serotonergic neurons were identified with the appropriate antibodies. The data were analyzed by standard methodologies.

Results: Tancytes in the ependyma of the fourth ventricle were concentrated at the level of the mesopontine raphe nuclei. Basal processes from these tancytes projected into the neuropil, where they were juxtaposed to serotonergic neurons in the dorsal and medial raphe nuclei.

Conclusion: Ependymal tancytes in the fourth ventricle were found to closely relate, via their basal processes with serotonergic processes. These data provide an anatomical substrate for the transmission of neurotransmitters from the CSF to serotonergic cells of the raphe nuclei. Consequently, we suggest that serotonergic cells are controlled not only by neurally delivered neurotransmitters, but also by the actions of neurotransmitters that are transported from the CSF. Functionally, this CSF-tancyte pathway may provide for the sustained activation/inhibition of serotonergic neurons, which play a role in the regulation of various sleep and waking behaviors and processes such as mood, body temperature and feeding.

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0057

USING ELECTROPHYSIOLOGY TO BETTER PREDICT MINOR SLEEP LOSS IN CHILDREN

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Introduction: The purpose of the study was to use electrophysiological data to examine the validity of parental reports and actigraphy devices to measure sleep in children.

Methods: 24 children (females=8) ranging from five to eight years wore actigraphs, while parents recorded nightly sleep logs for two consecutive weeks. During week two of participation, children were placed in a control (CO) or one-hour sleep restriction (SR) group. The current analysis compares sleep groups based on parental reports and groups based on

the actigraphy analyses. Electrophysiological recordings using event-related potentials (ERPs) measured attention during a tone discrimination task at the end of week one (baseline) and the end of the week two (sleep condition). During ERP recordings, children listened to two randomly presented tones and were told to discriminate frequent (probability 70%) from infrequent (probability 30%) tones using a button-response.

Results: Using a temporal principal components analysis (PCA), three regions of the ERP were identified that accounted for approximately 87% of the total variance. In week two, factor one produced a significant condition X hemisphere X group interaction, $F(3,20) = 3.938$, $p=0.023$. The effect indicated that controls processed targets differently over both the left and right hemispheres from 328-720 ms (left: $F(1,22) = 6.850$, $p=0.016$; right: $F(1,22) = 7.461$, $p=0.012$). Discriminate function analysis used the brain response to infrequent tones over both hemispheres to identify the accuracy of assignments to the CO and SR groups. ERP data using parental reports to group children correctly classified 75% of the children while only 62.5% of the children were correctly classified using the actigraphy data.

Conclusion: Results indicate processing infrequent tones is influenced by the amount of sleep a child receives. Classifying children into restricted or control groups based on ERP response was slightly more accurate based on parental reports compared to actigraphy analysis.

0058

CONSISTENT SLEEP AIDS CHILDREN'S PERFORMANCE ON AUDITORY ATTENTION TASK

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Introduction: Children are particularly sensitive to the amount of sleep they receive. Little research has investigated the role of consistent sleep/wake cycles in children, but adult research suggests that irregular sleep patterns can negatively impact learning and attention. The purpose of this study was to examine whether irregular sleep periods affected children's performance on an auditory attention task.

Methods: Twenty-nine children (14 males) aged four to eight years participated in this study. Children underwent a one-night polysomnographic screening to rule out pre-existing sleep abnormalities. Subsequently, for one week, all children maintained their normal sleep schedule. Mean sleep times and standard deviations were calculated for each participant based on parent logs and child wrist actigraphs. Children with the least variability in sleep time ($SD \leq .21$ hours) were assigned to one group while those with the most variability ($SD \geq 1.10$ hours) were placed in a second group for analysis purposes. Event-related potentials (ERPs) were recorded using a Geodesic Sensor Net of 128 Ag/AgCl electrodes. During an auditory oddball paradigm task, children were asked to attend to frequently and infrequently occurring (30%) tones.

Results: ERPs were entered into a Principal Component Analysis (PCA) - Analysis of Variance sequence. PCA identified five ERP regions that accounted for 88.376% of the total variance. A five way repeated measures ANOVA was utilized with a Greenhouse-Geiser correction. Analyses identified a significant Condition (Infrequent vs Frequent tone) by Electrode by Group interaction. Follow up paired t-tests indicated that the brain responses recorded over the frontal and parietal lobes of children with low sleep variability were better able to discriminate between frequent and infrequent tones.

Conclusion: These results suggest a difference in brain organization for those children who get a consistent amount of sleep during a week compared to those who fluctuate in the amount of sleep they receive.

0059

EFFECTS OF ISOFLURANE ANESTHESIA ON THE RESPONSE TO SLEEP DEPRIVATION (SD)

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Introduction: Slow wave activity (SWA, NREM EEG power between 0.5-4Hz) is thought to reflect the accumulation of sleep need during wakefulness, because it increases in proportion to the time spent awake and decreases during sleep. NREM sleep and anesthesia are both characterized by high-voltage, low frequency EEG activity, but the effect of anesthesia on the response to SD remains unclear. In rats, Tung et al. (2004) found that 6h of propofol anesthesia following 24h SD reduced the post-SD increase in NREM and REM duration, and abolished the rebound of high-range (2-4Hz) SWA. To extend those findings, we studied the effects of 1h of isoflurane (ISO) anesthesia after 4h SD.

Methods: In male WKY rats ($n=12$; 12light:12dark cycle) local field potentials were recorded from frontal and parietal cortices of both hemispheres using bipolar electrodes. A 4hr SD by exposure to novel objects started at lights on and was followed, in a counterbalanced design, by either 1h of ISO anesthesia (SD-ISO) or by a brief (3-5min) anesthesia induction (SD-MOCK). ISO concentration (0.5-1.5%) was modulated to maintain an EEG tracing that best resembled NREM slow waves. Sleep stages were scored visually (4-sec epochs). EEG power spectra (0.25-20 Hz) were computed and normalized to baseline.

Results: After SD-Mock rats had a significant increase in SWA in all derivations compared to baseline (Frontal $p<.01$ Parietal $p=.012$) but following SD-ISO, NREM SWA was not significantly increased relative to baseline. NREM slow wave energy (SWE, cumulative sum of NREM SWA) after SD-ISO was significantly lower than the SWE after SD-MOCK (Frontal $p=.03$, Parietal $p=.02$) but if the SWA occurring during the anesthesia is included in the SWE computation, the difference is no longer significant. The difference in consolidated sleep onset between conditions was 3.3 ± 3.4 min.

Conclusion: A brief period of anesthesia dominated by slow waves abolishes the SWA rebound normally seen after SD.

0060

ANATOMY OF THE MELANIN-CONCENTRATING HORMONE (MCH) SYSTEM IN ZEBRAFISH

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Introduction: In mammals, neurons expressing melanin-concentrating hormone (MCH) and hypocretin/orexin (HCRT/ORX) are intermingled in the hypothalamus and project diffusely throughout the central nervous system. The MCH and HCRT systems are both involved in the control of food intake and sleep. Prior studies have shown that the zebrafish HCRT system is present in this species and is involved in sleep regulation. Zebrafish is a powerful genetic model that shares similar central nervous system organization with mammals. In order to pursue our fine analysis of networks putatively involved in sleep control, we have initiated a neuroanatomical study of the zebrafish MCH system.

Methods: HCRT, MCH and receptors expression patterns were determined by colorimetric and fluorescent in situ hybridization (ISH) in larvae and adults.

Results: Zebrafish MCH sequences were identified and expression characterized during development and adulthood. We also describe the distribution of 3 MCH receptors mRNAs. Similar to mammals, zebrafish MCH expressing neurons are located in the hypothalamus. Interestingly however, unlike HCRT, the MCH cell cluster is present in the posterior and not anterior region of the hypothalamus. As a consequence, HCRT and MCH neurons are not intermingled in zebrafish in contrast to mammals. MCH receptors were broadly distributed in the brainstem, hypothalamus, and forebrain as reported in mammals.

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Conclusion: Although there is strong conservation of various neurotransmitter systems between vertebrates, mammalian and teleost brain organization may differ. Most notably, anatomical proximity between cell clusters may vary substantially, a phenomenon already observed across mammals. These results further suggest that as suggested in mammals, HCRT and MCH cells differ significantly in their developmental origin. A better understanding of zebrafish brain neuroanatomy is a prerequisite to analyze networks putatively involved in sleep and wakefulness in this species, and to reinforce the status of zebrafish as a model for sleep neurobiology.

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0061

A NOVEL INHIBITORY AFFERENCE TO THE PONTINE REM SLEEP INDUCTION ZONE

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Introduction: Pharmacological manipulations of GABA_A receptors in the caudal, nucleus pontis oralis (PnOc) of the rat produce alterations in sleep/wake behavior. Local applications of agonists increase wakefulness and antagonists increase REM sleep. These findings support a role for GABA mechanisms of the PnOc in the control of arousal state. We have been investigating sources of GABA innervation of the PnOc that may interact with local GABA_A receptors in the control of state. Reported here for the first time is the immunohistochemical identification of an extensive network of GABAergic neurons with contralateral axonal projections to PnOc.

Methods: Long-Evans Hooded rats were unilaterally injected in the PnOc with 9.2 nl of a 0.5% solution of cholera toxin subunit B (CTb) and sacrificed 10 days later. Coronal sections were studied from the caudal border of the pontine reticular formation to the midbrain at the level of the substantia nigra. Sections were doubly labeled with antibodies to CTb (List) and GAD67 (Chemicon). Double-labeled neuronal somata were identified as retrogradely transporting CTb from the injection site and GABAergic, containing the GABA synthetic enzyme, GAD67.

Results: With injections confined to the PnOc, neuronal perikarya labeled with CTb had a widespread, bilateral distribution along the neuraxis. Some of these neurons were GABAergic. One double labeled population with relatively high density was found contralateral to the injection site. These cells are located in a column extending over 3.5 mm starting rostral, in close proximity to the rostral pole of the pedunculo-pontine tegmental nucleus and extending caudal, through the reticular formation, ending in the caudal pontine reticular formation, nucleus pontis caudalis.

Conclusion: Inasmuch as GABAergic mechanisms operate in the PnOc in control of state, this new found system may play a critical role in this behavior. The hypothesis is currently under test.

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0062

HYPOCRETIN RELEASE DURING WAKE AND SLEEP IN THE HUMAN BRAIN

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Introduction: Hypocretin (Hcrt, also known as orexin) is a hypothalamic peptide whose loss causes narcolepsy, a disorder characterized by sleep attacks and sudden losses of muscle tone triggered by certain, generally positive, emotions. We investigated Hcrt release in the human brain during waking and sleep.

Methods: Depth EEG electrodes with microdialysis membranes (12.5 kDa cut-off) attached were implanted into the brain of patients with

pharmacologically resistant temporal lobe epilepsy for localization of seizure foci for subsequent surgical removal. Microdialysis samples were collected continuously at 15 minute intervals for a period of 2-4 days. Samples were analyzed by radioimmunoassay (RIA).

Results: In the six patients studied, Hcrt levels in the amygdala during sleep were significantly lower than average waking levels. Melanin-concentrating hormone (MCH) levels were also investigated as cells containing MCH are located in close proximity and with reciprocal connections to the Hcrt cells. Average MCH levels during sleep showed a tendency to increase above waking levels, although this was not significant. Interestingly, increases in Hcrt were associated with sleep-wake transitions, and increases in MCH were associated with wake-sleep transitions. In addition, Hcrt levels were high during social interaction and low after eating. Finally, Hcrt was negatively correlated with distal to proximal skin temperature gradient.

Conclusion: This pattern of Hcrt release is consistent with the sleepiness and cataplexy seen when the Hcrt system is nonfunctional, as in narcolepsy.

0063

INTERLEUKIN-1B RECEPTOR 1 AND TUMOR NECROSIS FACTOR-A RECEPTOR 1 DOUBLE KNOCKOUT MICE SHOW REDUCED SLEEP ALTERATIONS IN RESPONSE TO LIPOPOLYSACCHARIDE ADMINISTRATION AT LIGHT ONSET

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Introduction: The pro-inflammatory cytokines Interleukin (IL)-1 β and Tumor Necrosis Factor- α (TNF α) are well characterized sleep regulatory substances. In general, manipulations that increase endogenous IL-1 β or TNF α increase NREMS and reduce REMS. Data demonstrate that the effects on sleep of IL-1 β and TNF- α are mediated by IL-1 type 1 receptor (IL-1R1) and TNF kDa55 receptor (TNFR1), respectively. Mice lacking both IL-1 β type 1 and TNF- α type 1 receptors spend less time in spontaneous NREMS during the dark period and less time in REMS during the light period. The aim of this study was to determine a role for these two cytokine receptors in mediating alterations in sleep that occur during immune challenge. To that end, we evaluated the impact of an immune challenge on sleep-wake behavior and brain temperature of IL-1 β receptor 1 / TNF- α receptor 1 double-KO mice (IL-1R1/TNFR1-KO) and B6129SF2/J control mice.

Methods: Male mice (30-40g, n=4 each strain) were surgically implanted with EEG electrodes and a thermistor to record brain temperature. After recovery, 48h undisturbed baseline recordings were obtained. Then, mice were injected intraperitoneally at light onset with vehicle (pyrogen free saline-PFS) and on a subsequent day with 10 μ g of lipopolysaccharide (LPS; Escherichia coli serotype O111:B4).

Results: LPS injection increased NREMS in both IL-1R1/TNFR1-KO and B6129SF2/J mice. However, the increase in NREMS of the double KO mice was significantly less than that of control mice during the light period following injection (13.50 \pm 1.1 vs 25.43 \pm 4.0, mean \pm SEM, % difference PFS values) and during the subsequent dark period (13.79 \pm 3.7 vs 31.47 \pm 3.8). Delta power during NREMS tended to be reduced by LPS in the B6129SF2/J control mice and tended to increase in IL-1R1/TNFR1-KO mice, resulting in a statistically significant difference between the two strains (10.94 \pm 5.7 vs -23.00 \pm 10.9, % difference PFS values). LPS suppressed REMS of the B6129SF2/J control mice for 12h, whereas the reduction in REMS of the double KO mice was limited to 6h.

Conclusion: These data demonstrate that the lack of both IL-1R1 and TNFR1 reduces the effects of LPS on sleep-wake behavior when administered prior to light onset. These results further implicate IL-1 and TNF in the alterations in sleep that occur after immune challenge.

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0064

MODULATION OF THE SPINAL CORD PROJECTING NEURONS OF THE SUBLATERODORSAL NUCLEUS

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Introduction: The sublateralodorsal nucleus (SLD), also known as the SubCoeruleus, is a region of the pontine reticular formation that contains REM-on neurons and is critical for the generation of REM sleep. These REM-on neurons project caudally, some directly to the spinal cord (Lu et al., 2006), to generate muscle atonia. SLD neurons that project to the spinal cord (SLDsp) are glutamatergic and project to GABA/glycinergic spinal interneurons. Here we study the responses of SLDsp neurons to carbachol, noradrenaline, dopamine and orexin.

Methods: We performed patch-clamp recordings on SLDsp neurons in brain slices prepared from mice. SLDsp neurons were prelabeled by injecting fluorescent beads in the ventral horn of the spinal cord (C8-T1 level). Three days after surgery, under a fluorescent microscope, SLDsp neurons appeared red and were targeted for recordings.

Results: SLDsp neurons were spontaneously active. They were characterized by short action potentials, no Ih, no burst activity, small or no IK(A), and by an inwardly rectifying IK. Carbachol depolarized SLDsp neurons and this effect was maintained in TTX and blocked by atropine. Carbachol also increased spontaneous and miniature glutamatergic EPSCs. We found that noradrenaline and dopamine inhibited the spontaneous firing of SLDsp neurons and both induced membrane hyperpolarization. In addition, we found that orexin-A increased the frequency of spontaneous and miniature IPSPs in SLDsp neurons, without affecting their spontaneous firing rate. All these neurons were negative for ChAT and TH immunoreactivities.

Conclusion: Carbachol directly excites SLDsp neurons and presynaptically increases glutamatergic synaptic input to the SLDsp neurons. These effects may be responsible for generating the muscle atonia during carbachol-induced REM. We also found that noradrenaline inhibits the SLDsp neurons supporting the view that the locus coeruleus may provide the inhibition of REM-on neurons during waking.

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0065

STRESS AND SLEEP IN HYPOPHYSECTOMIZED RATS

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Introduction: It has been reported that a number of stressful conditions have an influence on the sleep pattern of several species. In rats, it has been repeatedly shown that stress by immobilization induces a clear increase in the percentage of REM sleep. On the other hand, it is well known that stress response includes the activation of the hypothalamus-hypophysis-adrenal axis. However, reports on sleep recordings in hypophysectomized subjects have controversial results, with no clear effects on the sleep pattern. In the present study, sleep and sleep after immobilization stress was analyzed in hypophysectomized rats.

Methods: Adult male Wistar rats (N = 10) were chronically implanted for sleep recordings. After a recovery period, rats were polygraphically recorded for 8 hours for basal sleep parameters. Thereafter, rats were hypophysectomized. After a new recovery period, the rats were again polygraphically recorded for 8 hours. Finally, rats were stressed by immobilization in a small cylinder for 2 hours and immediately recorded for 8 hours.

Results: Results showed that there were no differences in any of the sleep parameters recorded after hypophysectomy. However, the increase

in REM sleep normally observed after immobilization stress was not observed in hypophysectomized animals.

Conclusion: These data suggest that the normal sleep pattern can be present despite the absence of the hypophysis. However, our results suggest that the increase in REM sleep after immobilization stress depends on the integrity of the HHA axis.

Support (optional): CONACYT GRANT (JARZ 193082)

0066

MICRODIALYSIS PERFUSION OF ESZOPICLONE INTO THE RAT PERIFORNICAL-LATERAL HYPOTHALAMUS SUPPRESSES WAKING C-FOS EXPRESSION IN HYPOCRETIN NEURONS

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Introduction: Hypocretin (HCRT) neurons in the perifornical-lateral hypothalamus (PF-LH) participate in the regulation of arousal. HCRT neurons are active during waking and quiescent during sleep. We have shown that sleep evoked by systemic administration of eszopiclone (ESZ) in rats is accompanied by suppression of c-Fos protein immunoreactivity (IR) in HCRT neurons. However, in that study it could not be determined if ESZ directly inhibited HCRT neurons or if effects were secondary to increased sleep. To determine if ESZ can evoke state-independent inhibition of HCRT neurons, we quantified neuronal Fos-IR after unilateral perfusion of ESZ directly into the PF-LH of awake rats.

Methods: Fifteen male Sprague-Dawley rats were surgically prepared for unilateral microdialysis perfusion of vehicle (VEH) or drug. Groups of 5 rats were perfused with ESZ (concentrations of 50µM or 500µM) or VEH for 2 hrs during the dark phase. Animals were kept awake to prevent sleep-dependent suppression of Fos-IR. Following perfusions, rats were sacrificed and brain tissue was processed for HCRT-1 and c-Fos protein IR.

Results: In the presence of 50µM ESZ, the percentage HCRT neurons adjacent to the dialysis probe (within 250 µm) that were also Fos+ decreased significantly compared to VEH (31 ± 7% vs. 53 ± 4%, p<0.05). Numbers of single Fos+ neurons adjacent to the probe did not differ between ESZ- and VEH-treated rats (477 ± 57 vs. 599 ± 62, p=0.18). Percentages of HCRT neurons that were Fos+ also decreased significantly with 500µM ESZ (28 ± 5% vs. 53 ± 4%, p<0.01), but numbers of single Fos+ neurons were reduced as well (282 ± 31 vs. 599 ± 62, p<.01).

Conclusion: Local perfusion of 50µM ESZ into the PF-LHA evoked selective suppression of waking-related Fos-IR in HCRT neurons. The findings support the hypothesis that sleep-enhancing effects of ESZ are due, in part, to inhibition of HCRT neurons.

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0067

GROWTH HORMONE RELEASING HORMONE (GHRH) ACTIVATES GABAERGIC NEURONS IN THE RAT PREOPTIC HYPOTHALAMUS

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Introduction: Microinjection studies have identified the preoptic area (POA) of the hypothalamus as a potential site of the non-REM sleep promoting actions of growth hormone releasing hormone (GHRH). Specific POA cell types targeted by GHRH are unknown. We provide the first evidence that GHRH promotes non-REM sleep by activating GABAergic neurons in the median preoptic nucleus (MnPN) and the ventrolateral preoptic area (VLPO).

Methods: Male Sprague-Dawley rats were implanted with EEG, EMG electrodes and unilateral intracerebroventricular (icv) cannula. Rats

Category A—Neuroscience

(n=10) received icv injections (3µl) of GHRH (0.01 nmol/100 g) or equal volume of saline (n=10) at the onset of the dark period. Other groups of rats received 1) octreotide (n=8), a long lasting somatostatin analog (OCT, 0.1 µg/µl), 2) a competitive GHRH antagonist (0.5 nmol/kg, n=8 or 15 nmol/kg, n=8) or 3) saline (n=14) injection at the onset of the light period. After 90 min of undisturbed sleep/waking, animals were deeply anesthetized and brain tissue processed for immunohistochemistry for c-Fos protein and GAD67. States of vigilance were determined for 10-s intervals. Cell counts were analyzed in the MnPN and in the VLPO.

Results: GHRH elicited significant increases in non-REM sleep time. Double-labeled Fos+GAD cell counts were significantly ($p<0.001$) elevated after GHRH injection in both MnPN (GHRH 30.69 ± 3.90 ; Saline 6.52 ± 0.91) and VLPO (GHRH 34.12 ± 2.67 ; Saline 7.08 ± 1.22). OCT and both doses of GHRH antagonist significantly decreased ($p<0.05$) non-REM sleep time, compared to saline. Double-labeled cell counts were significantly ($p<0.01$) reduced after OCT and GHRH antagonist (15 nmol/kg) in the MnPN (OCT 7.96 ± 1.38 ; GHRH-A 5.07 ± 1.18 ; Saline 23.42 ± 1.20) and VLPO (OCT 8.16 ± 0.78 ; GHRH-A 12.44 ± 1.48 ; Saline 37.98 ± 2.80).

Conclusion: These findings identify GABAergic neurons in the MnPN and VLPO as potential targets of the sleep regulatory actions of GHRH.
Support (optional): Supported by the Department of Veterans Affairs, MH63323 and HL60296.

0068

AN INVESTIGATION OF THE ASSOCIATION BETWEEN SLOW-WAVE OSCILLATIONS AND SLEEP SPINDLES USING 256-CHANNEL EEG

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Introduction: Sleep spindles and slow-wave oscillations (SWO) are characteristic EEG patterns observed during non-REM sleep (NREM). Sleep spindles (7-14 Hz) reflect activity of thalamocortical neurons, which are regulated by cells of the reticular nucleus. In contrast, slow-wave oscillations (<1Hz) are believed to be generated by the cortex. Previous research has shown that SWO serve to organize sleep spindles and delta oscillations, which are also of thalamocortical origin. In this paper, we investigate the relation between slow-wave oscillations and sleep spindles recorded in humans using dense-array EEG technology.

Methods: Sleep EEG was acquired from 10 subjects using a 256-channel sensor array. Non-REM sleep stages were identified and sleep spindles and SWO were scored. To evaluate the association between the two sleep events, we grouped spindles that occurred in the presence (within +/- 1 sec) and absence of SWO and performed statistical analysis of this distribution. We also compared the amplitude of the spindles that occurred with or without SWO activity. Source distribution of these two spindle types and their overlap with SWO sources were also compared by transforming the scalp data to source space using a realistic head model and linear-inverse method.

Results: Although spindles do occur in the absence of SWO, they are more often than not found immediately after the negative cycle of SWOs. Preceding each SWO, we found very little power at the spindle frequency. However, following SWOs, there is an increase in power between 7-14 Hz. Source estimates show that the SWOs and spindles overlap but are not necessarily identical.

Conclusion: The association between SWO and sleep spindles provides intriguing clues for understanding the neurophysiological mechanisms of thalamocortical organization by cortical activity during sleep.

0069

THE EFFECT OF MINOR SLEEP RESTRICTION AND MICROGRAVITY ON CIRCADIAN RHYTHM TYPE

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Introduction: Adults are susceptible to sleep deprivation and microgravity conditions. Event-related potentials (ERPs) provide a useful tool to explore these vulnerabilities by elucidating neural responses to events in an individual's internal and external environment. This study examined the relationship between minor sleep restriction, cognitive processing and Circadian rhythm type.

Methods: Adults aged 30-45 with doctoral degrees (n=30, 15 females) were recruited for participation. All were screened for hearing, vision, neuropsychological history, and sleep abnormalities. Participants were tested at the end of each week for two weeks. Participants' sleep was monitored through actigraph and sleep log recordings throughout the study. During week two, participants were assigned a sleep condition of no change, one-hour restriction, or three-hour restriction per night of sleep. ERPs were recorded using a 256-electrode Geodesic Sensor Net while participants attended to two randomly ordered tones, one of which occurred infrequently (30%). Participants completed the task in both upright and 6-degree head-down tilt positions. Each participant completed the Automated Morning/Eveningness questionnaire. Scores obtained classified participants as morning, intermediate, or evening types.

Results: A principal components analysis (PCA) identified four regions of the brain response accounting for 90% of total variance. A stepwise regression analysis was performed for one peak at 124 ms and a second at 388 ms to predict circadian rhythm type and identified 2 significant models. Model 1 indicated that ERP responses over left temporal and right inferior frontal sites during the head-down tilt position predicted circadian rhythm type (adjusted R²= .252). Model 2 utilized ERP responses over right inferior frontal sites during the head down-tilt position to predict circadian rhythm type (adjusted R²= .102).

Conclusion: Physiological processing identified regions of variability among circadian rhythm type in association with sleep loss and microgravity effects.

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0070

THE EFFECTS OF SLEEP RESTRICTION AND SIMULATED MICROGRAVITY IN ADULTS USING A ROCK-PAPER-SCISSORS PARADIGM

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Introduction: It is well documented that chronic partial sleep restriction is associated with decreases in attention and cognitive efficiency during working memory tasks. In addition, microgravity experienced by astronauts also contributes to the adverse effects of sleep loss on cognitive functioning. The present study examined the combined effects of simulated microgravity and sleep restriction using a Rock-Paper-Scissors paradigm.

Methods: Ten native English-speaking adults (7 male) between the ages of 30 and 45yr (M = 37, SD = 5.1) were recruited and paid \$1000 for participation and completion of the study. Participants played a computer version of the Rock-Paper-Scissors game using a 4-button response pad. Visual event-related potentials (ERPs) were recorded during a prompt screen and stimulus presentations for "win" "draw" and "lose" conditions over 108 trials using a 256 electrode high density Geodesic Sensor

Net (EGI Inc.). Participants were randomly assigned to a one-hour sleep restriction group (requiring them to reduce their sleep by one hour for seven consecutive nights prior to testing) or a control group (no change in sleep duration). Counterbalanced across all participants, testing occurred in both a normal upright, sitting position and in a head-down-tilt (HDT) position. In the HDT position, participants reclined on a bed with a -60 tilt designed to simulate the effects of microgravity.

Results: Results indicated a significant Week x Stimulus x Hemisphere x Sleep interaction, $F(7.496, 1.392, 11.137) p < 0.013$, power = .784, and significant Week x Position x Stimulus x Hemisphere x Sleep interaction, $F(7.551, 2.290, 18.324) p < .003$, power = .925). Post hoc t-Tests indicated that participants in the sleep condition process information concerning losses differently than controls, $t(7.644) = 2.986$, $p < .018$; $t(7.980) = -4.357$, $p < .002$.

Conclusion: Given peak latencies, the losses are processed with less efficiency, accounting for the lower mean activity early in processing, requiring a greater recruitment of cortical resources in later stages of processing accounting for the increase in late slow-wave activity.

0071

GENERALIZABILITY OF THE RELATIONSHIP BETWEEN FOLLICLE STIMULATING HORMONE AND SLEEP DISCONTINUITY IN HEALTHY ADULTS

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Introduction: In a recent study (Tompkins et al., 2007) we found that in both women and men the level of follicle stimulating hormone (FSH) was positively related to trait inter-individual differences in sleep discontinuity, where sleep discontinuity was characterized by increased stage 1 sleep, increased movement time, more sleep stage transitions, and less REM sleep. Here we assess the generalizability of our finding by including a sample of an additional study in our analysis.

Methods: Data from two different studies were considered, each with three sessions involving 36h sleep deprivation preceded by baseline sleep and followed by recovery sleep. In study A, 21 healthy young adults (ages 22-40y; 11 pre-menopausal women, 10 men) spent 11 consecutive days in a sleep laboratory and experienced the three sleep deprivation sessions back to back. This study included eight nights of nocturnal PSG (12h TIB, 22:00-10:00). In study B, another 21 healthy young adults (ages 21-37y; 8 pre-menopausal women, 1 perimenopausal woman, 12 men) experienced the sleep deprivation sessions in separate sleep laboratory visits intervened by 2-week periods at home. For this study, four nights of nocturnal PSG (12h TIB, 22:00-10:00) were available for analysis. All PSG records were scored according to the criteria of Rechtschaffen and Kales. Sleep discontinuity was assessed from the sleep variables using the method applied in our original study (Tompkins et al., 2007). Prior to the studies during medical screening, FSH levels were measured from blood serum in all subjects. The relationship between pre-study FSH and trait sleep discontinuity as observed across the PSG recordings was analyzed using mixed-effects analysis of covariance, leaving out the one perimenopausal subject because of outlying FSH level.

Results: FSH was positively related to sleep discontinuity ($F[1,106]=6.24$, $P=0.014$). This finding persisted after gender was added as a covariate ($F[1,106]=6.02$, $P=0.015$), indicating that the relationship existed independently of gender ($F[1,106]=0.18$, $P=0.67$).

Conclusion: Our results show that the relationship we found between FSH and sleep discontinuity is generalizable across study samples. Our results are also in agreement with a recent study reporting a relationship between daily FSH measurements and self-reported sleep quality in the previous night. These findings add to mounting evidence of the influence of sex hormones on sleep regulation.

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0072

NEURAL MECHANISMS OF APNEA-INDUCED RESPIRATORY LONG-TERM FACILITATION OF GENIOGLOSSUS MOTOR OUTFLOW

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Introduction: Respiratory long-term facilitation (LTF) is a persistent increase in respiratory motor outflow in response to intermittent hypoxia. Previously, we showed that LTF of genioglossus motor outflow can be induced by repeated obstructive apneas in spontaneously breathing anesthetized rats and that vagotomy prevented apnea-induced-LTF. The aim of this study was to determine the neural mechanisms that mediate apnea-induced LTF.

Methods: Experiments were performed on anesthetized and tracheostomized spontaneously breathing adult rats. Diaphragm and genioglossus muscle EMG activity served as an index of respiratory motor outflow. Apneas (10, 15-sec apneas, separated by 1 min) were induced by obstructing tracheal airflow using a specially-constructed device. After a 45-min stabilization period, one of 4 experimental protocols was executed. After each protocol, activities were further recorded for at least another 60 minutes. 1) To determine whether apnea-induced LTF involves serotonin-dependent processes, methysergide (serotonin receptor antagonist; 4mg/kg; i.v.) was administered 20 min prior to apneas (n=5). 2) The effect of methysergide alone on respiratory motor outflow was determined under time matched control conditions (120-min; n=5). 3) To determine the role for vagal feedback in apnea-induced LTF, cervical vagus nerves were bilaterally cooled (13-min in duration) while animals were concomitantly exposed to apneas (n=8). 4) Effect of vagal cooling alone on respiratory motor outflow was determined in time matched control animals (120-min; n=7).

Results: Repeated apneas induced LTF of genioglossus respiratory motor outflow without enhancing diaphragm EMG activity; vagotomy abolished LTF. Methysergide treatment before apneas prevented LTF and respiratory motor outflow under remained stable under control drug conditions ($p > 0.05$). Bilateral vagus nerve cooling alone had no long-term affect on genioglossus EMG activity ($p > 0.05$), but completely abolished apnea-induced LTF of genioglossus respiratory motor outflow.

Conclusion: LTF of genioglossus motor outflow is evoked by obstructive apneas. Apnea-induced LTF requires both serotonin receptor activation and intermittent cessation of vagus nerve activity. We suggest that LTF of upper airway motor outflow may be a protective mechanism for maintaining airway patency in response to repeated airway obstructions as in obstructive sleep apnea.

0073

STUDY OF SLEEP IN A WALRUS

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Introduction: Sleep has been extensively investigated in Pinnipeds, including Otariidae and Phocidae seals. In this study we examined sleep in a walrus, the only representative of the family Odobenidae.

Methods: Polygraphic recording of electroencephalogram, electromyogram, electrooculogram and electrocardiogram was performed in a 2-year old walrus using the conventional direct cable connection or a digital recorder placed on the animal.

Results: During 3 continuous days on land, slow wave sleep (SWS) averaged 21.1±3.1% and rapid eye movement (REM) sleep 4.6±1.0% of 24-h. Average SWS and REM sleep episodes lasted 16.2±1.3 (n=52) and 8.8±1.1 (n=18) min, respectively, with some REM sleep episodes lasting up to 16 min. Breathing was regular during quiet waking and SWS (98% of all pauses ranged between 8-20 sec). REM sleep was accompanied by head, vibrissae and eye jerks and apneas up to 1 min. In water, sleep occurred while the walrus was floating motionless at the surface, standing in a shallow area with its head above water or lying on the bottom of the pool. The breathing pattern during SWS in water was characterized by an alternation of apneas (<4 min) and eupneas (3-12 breaths with an inter-breath interval <20 sec). While on the bottom, SWS episodes varied between 0.8-4.4 min (on average 3.3±0.1 min, n=55) and were marked by pronounced bradycardia (16-50 beats/min during apnea compared to 70-105 beats/min during eupnea). The walrus usually woke up briefly before surfacing to breathe. All REM sleep episodes in water occurred during one apnea and lasted <2 min. Episodes of interhemispheric elec-

troencephalogram asymmetry were recorded occasionally while the walrus slept on land and resembled those recorded in Otariidae seals.

Conclusion: Long apneas (similar to that shown by Phocidae seals) appear to be a distinctive feature of sleep in the walrus, allowing them to sleep in water under ice and survive in Arctic conditions.

Support (optional): The research was supported by Utrish Dolphinarium Ltd. and The VA Medical Research Service.

0074

INFLUENCES OF POSTURAL TILT STRESS AND THE CIRCADIAN SYSTEM ON CARDIOVASCULAR RISK FACTORS

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Introduction: Adverse cardiovascular events exhibit a 24-h pattern with a primary peak in the early morning hours, around 9 AM. This daily pattern may be influenced by postural stress associated with sleep/wake transition and/or endogenous circadian influences. Here we test the effects of passive tilt stress, human circadian system, and the interaction between the postural stress and circadian system on cardiovascular function.

Methods: 12 healthy adults (6 female) underwent a 13 day protocol in dim light, wherein subjects underwent 12 tilt-table tests at all phases of the circadian cycle—achieved by scheduling 12 recurring 20-hour 'days'. During each 20-hour day, subjects performed a 15-minute passive head-up tilt test at the same time (~4 h) after wakeup. Each test was preceded by a 20-minute baseline. Cardiovascular risk factors such as heart rate (HR), blood pressure (BP), and baroreflex sensitivity (BRS) were studied. BRS was estimated from SBP and inter-beat interval (IBI) using cross-correlation BRS and sequential methods. Body temperature was used to assess circadian phase (the fitted minimum was assigned 0°). Data was binned according to 60°-bins and analyzed with Mixed Model AVOVA.

Results: For the independent effects of tilt, there were significant average increases in HR (50% increase; $p=0.005$) and diastolic BP ($p<0.0001$) but no significant change in average systolic BP, compared to baseline. For circadian rhythms during tilt, the maximum decreases in systolic BP (mean±SE: 21.4±1.5mmHg) was negatively correlated with baroreflex sensitivity indices (Cross-correlation BRS $p=0.0001$; sequential BRS $p=0.001$); there were significant circadian rhythms in systolic BP with a peak at ~240° (22:30), and in HR with a maximum at ~180° (16:30); and no circadian rhythms in diastolic BP and BRS. No interactions were found between the circadian system and influences of tilt stress on BP and HR. 16 aborted tests occurred in 5 of the 12 subjects due to presyncope. There was a large and significant circadian rhythm in the frequency distribution of presyncope with a peak during the biological night ($P<0.008$ Friedman ANOVA). In addition, the maximum score of subjective nausea during tilt had a significant circadian rhythm with a maximum at ~0° (4:30).

Conclusion: There exists a significant circadian rhythm in the cardiovascular effect of postural stress.

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0075

THE ASSOCIATION BETWEEN SERUM CALCIUM, MAGNESIUM, AND ZINC LEVELS WITH SLEEP HOURS IN ADULT WOMEN

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Introduction: Minerals are known to be involved in the neurotransmitter system, including the NMDA receptor system, thus affecting neuropsychiatric functions such as depression, anxiety, cognitive function, and sleep hours. We investigated the relationship between the serum levels of main minerals such as calcium, magnesium, and zinc with sleep hours.

Methods: The participants were healthy adult women who visited one of our university hospitals located in the Seoul area from March to August in 2004. Hospital Depression-Anxiety Scale and Stanford Sleepiness Score were administered to evaluate depression, anxiety, and sleep hours. Serum calcium, magnesium, and zinc levels were measured by Automatic Analyser after fasting 6 hours. The relationship between serum mineral levels, calcium/magnesium ratio, and calcium/zinc ratio with sleep hours were evaluated using multiple regression analysis after correction for covariables.

Results: Serum calcium level showed negative association, while magnesium and zinc showed positive association with sleep, but they were not statistically significant. Calcium/magnesium and calcium/zinc ratios were negatively associated with sleep hours, but only the latter was statistically significant ($\beta=-8.745$, $p=0.013$).

Conclusion: Negative association between serum calcium/zinc ratio with sleep hours in our study suggests that the balance between minerals is more important in sleep hours than those of each particular mineral.

0076

EFFECTIVE AND INEFFECTIVE SLEEP HOMEOSTASIS - MODELING SLEEP PHYSIOLOGY BEYOND DELTA POWER

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Introduction: Models based on delta power do not adequately explain phenomena observed in the clinic. Stable and unstable sleep states, Effective and Ineffective Sleep Homeostasis respectively, are proposed as a complementary dimension that can inform sleep physiology and pathology in unique ways.

Methods: The data summarizes the results of a large body of work over 4 years in humans (over 12,000 polysomnograms), rats and mice. The technique uses the ECG to generate sleep spectrograms, by mathematically combining heart rate variability and respiratory modulation of R-wave amplitude. Proportions of high and low frequency cardiopulmonary coupling, state transition indices, state oscillation indices, and spectral dispersion were computed. Correlations with conventional polysomnographic measures and delta power were evaluated.

Results: Sleep is readily characterized as stable or unstable. Effective sleep homeostasis (stable sleep state) is not invariably related to increased delta power, and occurs throughout the night. It is characterized by high frequency cardiopulmonary coupling, blood pressure dipping, strong sinus arrhythmia, temporal stability of respiration, and a mode of the < 1 Hz slow oscillation that is best described as "continuous". Ineffective Sleep Homeostasis (unstable sleep state) shows strikingly opposite characteristics, is non-restorative, and the two states are clearly separated (no overlap). Stable and unstable REM sleep are also identifiable states. Weak or strong chemoreflex modulation of sleep-respiration can be readily identified; presence of the latter predicts acute positive

Category B—Physiology/Phylogeny/Ontogeny

airway pressure therapy failure. There is a cross-sectional correlation between spectrographically defined sleep states and risk of hypertension at the population level. Rats and mice have cardiopulmonary coupling profiles nearly identical to humans. Benzodiazepines reduce delta power but increase high frequency coupling as a proportion of state.

Conclusion: Sleep physiology has strong bistable characteristics that seem conserved across mammalian species. Pathology sculpts this bimodal characteristic in predictable ways.

0077

PREDATOR-INDUCED PLASTICITY IN SLEEP ARCHITECTURE IN WILD-CAUGHT NORWAY RATS (*RATTUS NORVEGICUS*)

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Introduction: Sleep is a prominent behaviour in the lives of animals, but the unresponsiveness that characterizes sleep makes it dangerous. However, the vulnerability associated with sleep may depend upon the state involved, as the intensity of stimuli required to induce an arousal to wakefulness is highest during deep slow-wave sleep (SWS) or rapid-eye-movement (REM) sleep. Thus, we predicted that animals should selectively reduce deep SWS and REM sleep following an increase in the risk of predation.

Methods: To test this prediction, we simulated a predatory encounter with wild-caught Norway rats (*Rattus norvegicus*). To record the EEG, two electrodes were implanted over each cerebral hemisphere. EEG and video were recorded during two 12 hr days (i.e., the normal sleeping phase for Norway rats). The first 12 hr day served as a baseline; just prior to lights-on on the second 12 hr day, the rats were chased around their cages by a gloved hand. The state of the rats (wakefulness, SWS, transition sleep, and REM sleep) was scored for each 30 sec epoch of the baseline and post-encounter days.

Results: Immediately following a simulated predatory encounter, rats spent more time awake and less time in SWS and REM sleep. However, the reduction of REM sleep was disproportionately large during the first quarter of the sleep phase, and slow-wave activity (SWA) (0.5 - 4.5 Hz power density) was lower during the first 10 min of SWS post-encounter. The reduction of SWS was due to the shorter duration of SWS episodes, whereas the reduction of REM sleep was due to a lower number of REM sleep episodes. The onset of SWS and REM sleep was delayed post-encounter by about 20 min and 100 min, respectively. An increase in SWA and REM sleep was observed later in the sleep phase, which may reflect sleep homeostasis.

Conclusion: Rats altered their sleep and waking behaviour after being chased by a simulated predator. During the first 3 hrs of the baseline day, rats spent the majority of their time sleeping, but post-encounter, the rats passed most of this time awake. As predicted, REM sleep was particularly sensitive to the increase in predation risk and may be a relatively dangerous sleep state. Slow-wave activity was also reduced after the predatory encounter, but was elevated during much of the post-encounter day. These results suggest that sleep architecture can be adjusted to the prevailing risk of predation.

0078

NEU-P11, A NOVEL MELATONIN AGONIST: EFFECT ON GLUCOSE TRANSPORT IN A CELLULAR MODEL OF INSULIN RESISTANCE

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Introduction: Insulin action in the brain is part of the multifaceted circuit involved in the central regulation of energy and glucose homeostasis. Recent evidence suggests that sleep disorders have a role in the induction of metabolic disturbances, obesity and insulin resistance. The later has also been implicated in the disruption of circadian rhythms and early Alzheimer disease pathology. There is a significant need for new drugs that effectively manage both insomnia and insulin resistance while minimizing the risk of significant adverse effects. The aim of the present study was to characterize the actions of Neu-P11 a novel GABA enhancing melatonin agonist, on insulin-resistant mouse adipocytes in-vitro.

Methods: Glucose-starved 3T3-L1 adipocytes were incubated with Free Fatty Acids (FFA) containing buffer and with melatonin or Neu-P11. The cells were then stimulated with insulin in 2-[3H]-deoxy-d-glucose containing buffer, washed and solubilized in NaOH. The amount of 2-[3H]-deoxy-d-glucose taken up by the cells was determined. In addition the cells were solubilized and the whole cell lysate was homogenized and centrifuged to harvest sample fluid. Insulin receptor substrate-1 (IRS-1) and phospho-IRS-1 (pIRS1) were subjected to western blot and detected immunologically by rabbit anti-IRS-1 or anti-pIRS-1(Ser307) polyclonal antibodies.

Results: FFA pretreatment reduced by 55% insulin-induced 2-deoxy-d-glucose uptake by adipocytes. Neu-P11 significantly decreased the FFA-induced inhibition of insulin-stimulated glucose transport by 70% in the same way as melatonin (10nM). Neu-P11 induced IRS-1 protein expression and reduced its Ser307 phosphorylation in a dose-dependent manner and was shown to be more potent than melatonin.

Conclusion: Neu-P11 improved glucose transport assessed by an in-vitro model of insulin resistance of mouse adipocytes in-vitro in the same way as melatonin. Neu-P11 partially restored both FFA impaired IRS-1 levels and its over-elevated phosphorylation. These results suggest that Neu-P11 treatment can lead to improvements in insulin resistance.

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0079

RELATIVE DECREASE IN ENDOTHELIAL FUNCTIONING AFTER AWAKENING FROM REM SLEEP IN COMPARISON WITH AWAKENING FROM NONREM SLEEP

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Introduction: Rapid-eye-movement (REM) sleep is associated with intense sympathetic activation and peripheral vasoconstriction. These, and the preponderance of REM in the early morning, have led to the suggestion that REM sleep may be associated with the early morning peak in the occurrence of cardiovascular events. The present study investigated if awakenings from REM and nonREM sleep are associated with different vascular tones.

Methods: Endothelial functioning was tested with the peripheral arterial tonometry (PAT) technique. The test comprises: 5-min baseline, 5-min blood occlusion, and 5-min post-occlusion recording. The reactive hyperemia PAT index is a ratio calculated as the average amplitude of the PAT signal 90-150 seconds after occlusion divided by the average amplitude before occlusion, normalized to the concurrent signal from the non-occluded hand. Fourteen healthy young adults were tested during two non-consecutive nights. On each of the nights they were tested

twice, once before sleep, and then in a balanced order after awakening from either the second or third REM period (mean time of awakening: 3:34 AM), or from the second or third nonREM sleep (mean time of awakening: 3:24 AM).

Results: Subjects had comparable sleep data on the two experimental nights. There were no significant differences in sleep latency (REM awakening: 25.7±9.3 min; nonREM awakening: 23.1±9.3 min), and percentages of sleep stages 1+2, 3-4 and REM until the awakenings (REM awakening: 54.0±9.9%; 34.3±11.4%; 11.8±4.8%; nonREM awakening: 53.3±12.7%; 33.5±12.7% 13.1±3.8%, respectively). Awakening from REM sleep was associated with significantly lower reactive hyperemic PAT index than awakening from nonREM sleep (1.76±0.32 vs. 2.11±0.53; $p < .02$, paired t-test).

Conclusion: The relative impairment in endothelial functioning after waking from REM sleep may predispose patients with compromised coronary arteries to ischemic events. These may contribute to the increased vulnerability to cardiac events during the early morning hours.

0080

RELATIONSHIP BETWEEN NASAL RESISTANCE AND DELIVERED POSITIVE AIRWAY PRESSURE

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Introduction: Despite the marked benefits of CPAP, compliance with therapy has been disappointingly low. Many patient using CPAP have nasal pathology and CPAP complaints often include nasal symptoms. For a constant mask pressure, nasal resistance should have a directional effect on CPAP pressure within the oropharynx and these pressure effects could affect patient comfort. The goal of this study was to examine pressure fluctuations within breaths in the collapsible part of the upper airway (UA) and relate these to nasal resistance.

Methods: To date, we have studied 6 subjects (5M/1F; mean BMI 36±4kg/m²; mean age 50±7) with obstructive sleep apnea requiring CPAP. During therapeutic CPAP (no flow limitation) peak supraglottic (Millar catheter) and mask (Braebon transducer) pressure were recorded during stage N2 sleep. Mask flow was recorded using the output of the Resprionics Bipap Auto M Series device in CPAP mode. Peak pressures during inspiration and expiration were determined separately and averaged over three stable breaths and used to calculate inspiratory and expiratory UA resistance. Nasal resistance (rhinomanometry) and nasal cross sectional area (acoustic rhinometry) were obtained in the sitting position in a separate daytime session.

Results: Whereas pressure in the mask remained within 0.5 cmH2O of set pressure with this CPAP device, mean supraglottic pressure varied from set CPAP during inspiration or expiration by 0.8-8.3 cmH2O across subjects. Similarly, mean inspiratory and expiratory UA resistances varied from 0.5 to 8.0 cmH2O/l/sec. In 4/6 subjects, inspiratory UA resistance was similar to expiratory UA resistance. However in two subjects inspiratory UA resistance was much higher than expiratory UA resistance, suggesting suboptimal CPAP may have been present. No relationship was found between inspiratory, expiratory or average UA resistance on CPAP and daytime awake measurements of nasal resistance or cross sectional area.

Conclusion: During conventional CPAP (near-constant mask pressure) supraglottic pressure swings and resistance vary widely across subjects. The clinical implication is that, as mask pressure alone is a poor predictor of supraglottic pressure variations (even at therapeutic CPAP), mask pressure may not predict either patient inspiratory effort or expiratory discomfort. While expiratory UA resistance on CPAP may be independent of collapse in the upper airway, we have not to date shown a correlation between UA resistance and daytime measures of nasal patency.

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0081

THE RANGE OF TRAIT INDIVIDUAL DIFFERENCES EXCEEDS THE AVERAGE EFFECT OF 36 HOURS OF TOTAL SLEEP DEPRIVATION ON TOTAL SLEEP TIME

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Introduction: It is well established that relative to baseline, total sleep time (TST) is increased in recovery sleep following total sleep deprivation. However, there are also considerable trait individual differences in TST. In a recent laboratory study conducted at the University of Pennsylvania, Philadelphia, PA we found that the range of individual differences in TST exceeded the group-average change from baseline induced by 36 hours of prior total sleep deprivation (Tucker et al., 2007). To investigate the replicability of this finding, we repeated the study in a different sample, in the sleep laboratory of Washington State University, Spokane, WA.

Methods: Ten healthy volunteers (ages 22-40; 7 females) spent eleven consecutive days and nights in the laboratory. They underwent three 36h periods of total sleep deprivation. Each sleep deprivation period was preceded by a night of baseline sleep and followed by a night of recovery sleep. The experiment began with an adaptation night and ended with an additional recovery night. All eight sleep periods involved 12h TIB. These sleep periods were recorded polysomnographically and scored visually using the criteria of Rechtschaffen and Kales. Results for TST were analyzed with mixed-effects ANOVA to assess the effect of sleep deprivation on TST, and to quantify systematic individual differences using the intraclass correlation coefficient (ICC).

Results: Baseline TST was 10.4h ± 0.2h (mean ± s.e.). TST in the recovery nights following 36h sleep deprivation was 11.5h ± 0.2h; the difference from baseline was 1.1h ± 0.2h ($t[58]=4.7$; $P < 0.001$). An ICC of 0.42 showed that there were systematic individual differences in TST across the eight study nights. These trait individual differences spanned a range of 1.6h in this sample.

Conclusion: The magnitude of trait individual differences in TST exceeded the group-average effect of 36h of total sleep deprivation on TST in the present sample of healthy young adults studied in Spokane. The results were similar to those obtained in a different sample of healthy young adults studied previously in Philadelphia. This demonstrates that trait individual differences in TST are a robust finding. Although the magnitude of these individual differences is considerable, their functional significance remains to be elucidated.

Support (optional): NIH grants HL70154 and RR00040 and DURIP grant FA9550-06-1-0281.

0082

RATS BRED FOR LOW INTRINSIC AEROBIC RUNNING CAPACITY EXHIBIT DECREASED AND MORE DISRUPTED SLEEP COMPARED TO THOSE BRED FOR HIGH INTRINSIC AEROBIC RUNNING CAPACITY

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Introduction: Human data demonstrate a linkage between disordered sleep and indices of the metabolic syndrome (J Sleep Res 16:66, 2007). Defining the mechanism of this linkage has been limited by the difficulties of human research. To circumvent these limitations we are using two rat strains that differ for both intrinsic aerobic fitness and features of the metabolic syndrome (Science 307:418, 2005). The strains were developed by two-way artificial selection for intrinsic low capacity running (LCR) and high capacity running (HCR) on a treadmill. If low aerobic capacity and the accompanying features of the metabolic syndrome con-

Category B—Physiology/Phylogeny/Ontogeny

tribute to disordered sleep, then the LCR rats should have more sleep problems relative to the HCR rats.

Methods: Six HCR and six LCR rats (males, generation 20) were implanted with electromyogram and electroencephalogram electrodes for recording states of sleep and wakefulness. Rats were conditioned to a 12-h light-dark cycle for two weeks in a chamber that allows free movement during 24-h recordings of sleep and wakefulness. Every 10 seconds of each 24-h recording was scored as rapid eye movement (REM) sleep, non-REM (NREM) sleep, or wakefulness.

Results: LCRs experienced 16.4% more time awake ($p < 0.05$) and 22.9% less time in NREM ($p < 0.05$) than the HCRs during the 24-hr recording. LCRs also had 42% more state transitions ($p < 0.05$) and an average duration of NREM that was 33% ($p < 0.05$) shorter than HCRs. All aforementioned findings were similar in both the light and dark cycle.

Conclusion: These results are consistent with the hypothesis that low aerobic capacity and associated flaws in metabolism contribute to disordered sleep. The LCR and HCR rats provide a novel model for mechanistic studies of sleep dysfunction.

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0083

GENDER DIFFERENCES IN POLYSOMNOGRAPHIES FINDINGS AND SLEEP COMPLAINTS IN CLINIC POPULATION

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Introduction: The purpose was to examine the influence of gender on the sleep pattern in a clinic population samples database of 2006 do Instituto do Sono, AFIP, São Paulo, Brazil.

Methods: The data obtained by questionnaires and polysomnographic recordings was collected from a total of 2.365 patients (1.550 men and 815 women) sought our practice because of some sleep complaint in 2006.

Results: After analyses of the data, it was found that men presented a statistical higher body mass index than that of women. The same occurred in the Epworth Sleepiness Scale, which produced a significantly higher score for men than women, suggesting daytime sleepiness. As for the polysomnographic parameters, women presented significantly higher sleep latency as well as rapid eye movement (REM) latency than men. And the sleep stages revealed that men spent more time in superficial stages (1 and 2) than women, whereas women spent significantly more time in deep sleep stages (3 and 4) when compared to men. In regards to sleep disturbance parameters the apnea/hypoapnea and arousal indexes were significantly higher and more frequent in men than in women, respectively.

Conclusion: We did not encounter meaningful differences between genders in the percentage of REM sleep, sleep efficiency, and the rate of periodical leg movement. Sleep disturbances that generally causes sleep loss might produce coping resources that are distinct to gender.

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0084

INFLUENCE OF CALORIC INTAKE ON SLEEP PATTERN IN HEALTHY ADULTS

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Introduction: Previous studies have demonstrated that circadian distribution of food intake is capable of modifying endocrine and metabolic

patterns during sleep. However, studies of the influence of food intake distribution on sleep pattern are scarce. The aim of this study was to analyze the influence of energy intake on sleep pattern of healthy subjects.

Methods: Fifty-two healthy volunteers (20-45 years) participated in the study. Food intake was analyzed by a three-day food record. An overnight polysomnographic examination (PSG) was performed to determine sleep pattern according to Rechtschaffen and Kales' international standard scoring criteria.

Results: Positive and statistically significant correlations were found between total energy intake and late-night snack energy intake and awakenings during sleep ($r = 0.33$ and $r = 0.70$; $p < 0.05$, respectively). Similarly, total energy intake and late-night snack energy intake were significantly correlated with apnea-hypopnea index (AHI) ($r = 0.40$ and $r = 0.65$; $p < 0.05$, respectively).

Conclusion: we concluded that total energy intake and late-night snack energy intake influence sleep pattern in healthy subjects and may increase sleep fragmentation. New studies on this area are needed to better understand these associations.

Support (optional): AFIP, FAPESP (CEPID 98/14303-3), CNPQ, FADA/UNIFESP

0085

DOES FAT INTAKE INFLUENCE THE SLEEP PATTERN IN HEALTHY ADULTS?

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Introduction: Increased fat intake has been associated with a number of health problems. However, the relationship between fat intake and sleep pattern is little explored. The aim of this study was to analyze the correlation between fat intake and sleep pattern in healthy adults.

Methods: Fifty-two healthy volunteers (20-45 years) participated in the study. Food intake was analyzed by a three-day food record. Sleep pattern was evaluated by a polysomnographic recording, after an adaptation night. Pearson's correlation coefficient was used and $p < 0.05$ was considered as statistically significant.

Results: It was found a significant correlation between total fat intake and percentage of stage 2 sleep ($r = 0.31$; $p < 0.05$); percentage of REM sleep ($r = -0.33$; $p < 0.05$); arousal index ($r = 0.33$; $p < 0.05$) and apnea-hypopnea index ($r = -0.30$; $p < 0.05$). Indeed, it was found a significant correlation between fat intake at dinner and sleep efficiency ($r = -0.33$; $p < 0.05$) and REM percentage and REM latency ($r = -0.47$ e $r = 0.38$, respectively, $p < 0.05$).

Conclusion: Total fat intake and dinner fat intake seem to influence negatively the sleep pattern. However, researches in the nutrition and sleep area should be carried out to better understand these associations.

Support (optional): AFIP, FAPESP (CEPID 98/14303-3), FADA/UNIFESP, CEMSA, CNPQ.

0086

EFFECTS OF ESZOPICLONE ON SLEEP AND WAKING STATES IN AGED GUINEA PIGS: COMPARISON WITH ADULT ANIMALS

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Introduction: The present experiment was designed to determine the effects on sleep and waking states induced by eszopiclone in aged guinea pigs. In addition, we compared the hypnotic effects of eszopiclone in aged guinea pigs with the responses produced in adult animals.

Methods: Aged (24-36 months old) and adult (3-8 months old) guinea pigs were implanted with EEG, EOG and EMG electrodes to record sleep and waking states and to perform a frequency analysis of the EEG.

Eszopiclone (1 and 3 mg/kg) and a control vehicle (50 mM acetate buffer, 0.5 ml) were injected intraperitoneally.

Results: In aged guinea pigs, compared to control injections, the administration of eszopiclone at 1 and 3 mg/kg resulted in significant increases in NREM sleep (33.8% and 60.8%, respectively), and decreases in wakefulness (12.0% and 21.5%, respectively). The same effects, but of greater magnitude, were observed in adult animals. In aged and adult animals, eszopiclone at 3 mg/kg produced a significant increase in EEG power in the delta band (9.9% and 12.5%, respectively) and a decrease in EEG power in the theta band (5.7% and 7.9%, respectively) during NREM sleep. However, in adult animals, eszopiclone only at 1 mg/kg produced a significant increase in EEG delta power (10.2%).

Conclusion: In aged as well as adult guinea pigs, administration of eszopiclone resulted in an increase in NREM sleep and enhanced EEG delta power; these effects were greater in adult animals. Previous studies have shown a reduction in the expression of $\alpha 3$ subunit of GABA_A receptors in aged animals compared with adult animals. Since $\alpha 3$ subunits are one of the principal GABAergic subunits that are targeted by eszopiclone, we suggest that the effects of eszopiclone in aged guinea pigs compared with adult animals may be a reflection of the decrease in $\alpha 3$ subunit activity in old age.

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0087

CONTINUOUS RECORDING OF WEIGHT CHANGES DURING SLEEP: WEIGHT LOSS RATE IS SLEEP STAGE-DEPENDENT

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Introduction: Weight loss rate change during day and night with changes in activity and environment. This study evaluates if weight loss rate due to insensible losses is variable during sleep stages.

Methods: Six normal volunteers 21-30 yrs old, 2 males, 4 females underwent full polysomnography with accurate continuous weight recording. They received a diet proportional to weight the day before polysomnography, and had no solid or liquid losses during sleep. Polysomnograms were scored and weight loss rate was calculated for each sleep stage. Chi square statistic was used to determine if weight loss differed for each stage.

Results: Weight loss rate during sleep stages was dissimilar ($p < 0.01$). Weight loss rate was highest during slow wave sleep followed by REM sleep, stage 2 and stage 1.

Conclusion: Weight loss rate distribution is different through sleep stages, being higher during slow wave sleep.

Support (optional): FAPESP AFIP

0088

WOMEN WITH DIFFICULTIES INITIATING SLEEP AND VASOSPASTIC SYNDROME EXHIBIT LOWER HEART RATE VARIABILITY IN THE HIGH FREQUENCY BAND

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Introduction: Women with primary vasospastic syndrome (VS), a functional disorder of vascular regulation in otherwise healthy subjects (main symptom: cold hands and feet), often suffer from difficulties initiating sleep (DIS) without any other sleep complaints. DIS belongs to the DSM-IV criteria for primary insomnia, but also occurs secondarily during other sleep disorders e.g. Delayed Sleep Phase Syndrome. Chronic primary insomnia has been characterized as a state of hyperarousal seen for example in higher sympathetic nervous activity as measured by

spectral analysis of heart rate variability (HRV). The low frequency band (LF=0.04-0.15Hz) of the HRV-spectrum mirrors the influence of both sympathetic and parasympathetic nerve activity, whereas the high frequency band (HF=0.15-0.4Hz) is associated with pure parasympathetic nerve activity. In a controlled laboratory study we aimed to compare women having both VS and DIS (WVD) with controls (CON) to test the hypothesis whether WVD exhibit a sympathetic dominance in the HRV spectrum similar to primary insomniacs.

Methods: 9 CON and 8 WVD (luteal phase; 20-33yr) completed two protocols, either carried out with paced (0.2Hz) or unpaced (spontaneous) 3min breathing episodes at hourly intervals distributed throughout a 40h constant routine (CR). Power spectral analysis of log-transformed purified inter-beat interval data was carried out by FFT.

Results: In comparison to CON, WVD showed significantly ($p < 0.05$) lower power values in both LF and HF from spectral analysis of 'spontaneous breathing'-data (main effect). Spectral analysis of 'paced breathing'-data revealed significantly ($p < 0.05$) lower power values predominantly in HF but not in LF, leading to a significantly ($p < 0.05$) reduced HF/LF-ratio.

Conclusion: This finding indicates a sympathetic predominance in WVD compared with CON which could represent a pathophysiological correlate for the syndrome of combined VS and DIS.

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0089

HEART RATE VARIABILITY DURING SLEEP IN WOMEN WITH SEVERE PREMENSTRUAL SYNDROME

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Introduction: Severe premenstrual syndrome (PMS) is a common, distressing disorder characterized by significant mood, behavioral, and somatic symptoms that occur exclusively during the premenstrual (late-luteal) phase of the ovulatory menstrual cycle. While rarely studied, altered autonomic function may be an important component of PMS. We investigated autonomic activity in women with severe PMS using heart rate variability (HRV) analysis, a sensitive marker of autonomic activity.

Methods: We investigated time and frequency domain HRV measures derived from the ECG recorded during sleep in nine women with severe PMS (28 ± 6 years) and twelve controls (31 ± 5 years) during the mid-follicular and late-luteal phases of their menstrual cycles.

Results: The normal-to-normal (NN) RR-interval was shorter ($p = 0.04$) during the sleep period in women with PMS than controls in both the follicular and late-luteal phases of the menstrual cycle. The standard deviation of all NN intervals (SDNN), a measure of total variability in the inter-beat interval, and the square root of the mean of the sum of the squares of differences between adjacent NN intervals (rMSSD), a measure reflecting high frequency activity, were lower ($p < 0.05$) during the sleep period in the late-luteal phase than in the follicular phase in women with PMS. Also, high frequency power, a marker of parasympathetic activity, was lower ($p < 0.05$) during non-rapid eye movement (non-REM) and REM sleep in the late-luteal phase than in the follicular phase in women with severe PMS. Controls had a shorter NN-interval, but similar HRV measures, in the late-luteal phase compared with the follicular phase. As expected, high frequency power was lower ($p = 0.001$) during REM sleep than non-REM sleep in all subjects.

Conclusion: Our results suggest that women with severe PMS have decreased parasympathetic activity during sleep when they are experiencing premenstrual symptoms compared to when they are symptom-free.

Category B—Physiology/Phylogeny/Ontogeny

Support (optional): Developmental grant from SRI International (FC Baker).

0090

SLOW-WAVE ACTIVITY SELF-DISSIPATION EFFICIENCY ESTIMATES SUGGEST SLEEP HOMEOSTASIS RESTRICTED TO FRONTAL CORTEX

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Introduction: In the two-process model of sleep regulation, Process S is an exponentially decaying function to which empirical SWA is approximated. By estimating the decay rate of S, a measure of sleep homeostatic efficiency is obtained. We propose an advanced method based on previous work of Achermann, introducing a new parameter, ‘gain constant’ (GC), to supersede the decay rate of S. Here, S is not exponential but free-form, with GC relating current SWA to instantaneous rate of change of S, thus: $dS/dt \sim -GC \times SWA$. Otherwise S follows the classical interpretation in that it dynamically projects the course of SWA; the latter is fitted to empirical SWA yielding estimation of the gain constant.

Methods: EEGs at 26 derivations taken from 9 normal subjects sleeping for 8 h at habitual time were FFT-transformed, and gain constants obtained from 1-Hz bins of resulting power spectra in 1-7 Hz range. Topographic ANOVAs were performed on gain constant scalp maps, both raw and normalized to map average.

Results: The 1-2 Hz map showed no significant deviation from map average (TANOVA $p=0.16$) while maps of all higher bins did, each presenting a similar antero-posterior cline ($p<0.01$). The Fz-Oz gradient was most pronounced in the 2-3 Hz map.

Conclusion: Gain constant is a valid sleep homeostat parameter, confirming well previous findings of “frontal predominance”. Using it, we show that 1-2 Hz range conforms poorly to the homeostatic proposition, exhibiting low, uniform gain constants. So also do occipital areas, suggesting the discharge of sleep homeostatic function is restricted to frontal cortex.

0091

ARE THE N350 AND N550 OF THE NREM EVENT-RELATED POTENTIAL ATTENTION DEPENDENT?

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Introduction: Event-related potential (ERP) waveforms are useful for examinations of information processing in drowsy and sleeping individuals. The functional significance of N350 and N550, which appear during the wake-to-sleep transition, are unclear. Both may reflect inhibitory processes facilitating the transition to and maintenance of sleep. Finding that changes in these waveforms are attention dependent would indicate that they reflect cognitive experience rather than simple sensory processing and provide insight into their relationship with inhibitory processes.

Methods: ERPs were recorded from 8 participants using a modified oddball-omitted stimulus paradigm (target tones, $p=.1$; target omissions, $p=.1$; and nontarget tones, $p=.8$; interstimulus interval of 1 second). Participants fell asleep 1) while ignoring the stimulus series and 2) while attending and responding to targets. Averages of baseline-to-peak amplitude N550 at Fz and N350 at Cz from each participant during four wake/sleep stages (Awake/Alpha, Awake/Mixed, Stage 1, Stage 2) were analyzed.

Results: 3-way repeated measures ANOVA (attention X state X stimulus) showed significant attention effects for N550 but not N350. For N350, no significant interactions or main effects involving attention were found. A significant state by stimulus interaction ($F(6,42)=5.18$;

$p<.05$) showed expected amplitude increases as participants fell sleep for tones but not omissions. For N550, simple effects analyses following a significant 3-way interaction ($F(6,42)=3.90$; $p<.05$) showed significantly larger amplitude N550s following target tones during stage 2 ignore ($M=7.9$ microV, $SD=6.6$) than during the attend condition ($M=2.9$ microV, $SD=4.8$).

Conclusion: It is possible that the transition to sleep must be protected against potential disturbances regardless of sleeper attention (reflected in N350’s attention independence); however, once sleep is established, only the voluntarily invoked inhibition of ignored stimuli amplifies the magnitude of protective processes (reflected in N550’s attention dependence).

0092

EEG CORRELATES OF BEHAVIORAL SLEEP IN THE HOUSE SPARROW, *PASSER DOMESTICUS*

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Introduction: Sleep studies in birds are rare compared to those in mammals. The House Sparrow, *Passer domesticus*, is perhaps the most frequently studied wild avian species. We examined the relationship between behavior, EEG, and respiration during sleep in order to establish the validity of studying behavioral sleep in wild birds.

Methods: We simultaneously recorded infrared video, EEG, and respiration rate over a 24-hour period (L:D 10:14) in eight male birds, and analyzed their correspondence in one-minute intervals. Behavioral sleep was defined as eyes closed with beak facing forward or backward, and “drowsiness” was coded when eyes were blinking and not closed continuously for more than one minute.

Results: Behavioral and EEG-defined sleep occurred primarily at night (98.2% and 90.3% of 24 hours, respectively). Behaviorally, we found sleep latency from lights out to be 58.6 minutes and total nighttime sleep duration to be 10.6 hours. Birds spent 37.4% of the night in beak-forward sleep, 44.1% in beak-backward sleep, and 11% in drowsiness. EEG-defined nighttime sleep comprised 10.7 hours, 18.8% in REM. There was a significant decline in SWS and an increase in REM activity across the night ($p<.05$). Birds that spent a greater proportion of sleep with beak-forward showed less EEG-denoted sleep, suggesting the occurrence of “deeper” sleep in the beak-backward posture ($p<.05$). Average respiration rate (bpm) was highest in waking (64.7), lower in SWS (45.1) and lowest during REM (42.1). Birds averaged 79 arousals, approximately 50 seconds in duration. Overall coding accuracy between behavioral and EEG-denoted sleep and wakefulness was 95.8%; 99.4% when birds were in the backward sleep posture.

Conclusion: Behavioral coding of *P. domesticus* sleep is effective for distinguishing sleep versus wakefulness. Further, sleep posture in a thermoneutral environment appears to be indicative of sleep depth. Through the use of specially-designed nestboxes, future work will obtain video-recordings of sleep in wild birds.

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0093

SLEEPING OUTSIDE THE BOX: EEG DEFINED SLEEP AND WAKEFULNESS IN WILD THREE-TOED SLOTHS (*BRADYPUS VARIEGATES*) INHABITING A RAINFOREST

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Introduction: Insight into the functions of sleep may be obtained by comparing sleep in different types of animals. Historically, technological limitations restricted electrophysiological recordings of sleep to the unnatural laboratory environment. Herein we demonstrate the feasibility of performing minimally invasive surgeries and subsequent electrophysiological recordings of sleep in animals in the wild.

Methods: Three adult female sloths were studied at the Smithsonian Tropical Research Institute in Panama. The sloths were caught in the rainforest canopy. Silver-silver/chloride wire electrodes were inserted under the skin overlying the cranium to record EEG activity from the anterior and posterior cortex of each hemisphere. The wires were connected to an EEG data logger (developed by A. Vyssotski) that recorded four channels at 100 samples per second for up to 5 days. The logger was glued on top of the head. This procedure did not require general anesthesia and took only 1 hr to complete. After attaching a radio collar and activity data logger, the sloths were released back into the rainforest. Sloths were recaptured 3 or 5 (N=2) days later. For each sloth, one 24-hr period starting 48-hrs after release was scored for wakefulness, slow-wave sleep and REM sleep in 10 s epochs. Reported values are mean \pm s.e.m.

Results: The quality of the EEG signals remained high throughout all recordings, and each state was readily identifiable. The sloths spent $64.75 \pm 3.40\%$ (15.53 ± 0.82 hrs) of the time awake, $29.41 \pm 2.78\%$ (7.06 ± 0.67 hrs) in slow-wave sleep and $5.84 \pm 1.36\%$ (1.40 ± 0.33 hrs) in REM sleep. REM sleep encompassed $16.48 \pm 3.03\%$ of total sleep time.

Conclusion: Sloths in the wild slept only 8.5 hrs during a 24-hr day. In contrast, an EEG study of captive sloths of the same species reported 15.8 hrs of sleep per day. Our preliminary study demonstrates the feasibility of recording sleep in wild animals living in their natural habitat, and questions whether data obtained from laboratory studies reflects the expression of niche-adapted sleep.

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0094

PARTIAL AIRWAY OCCLUSION AUGMENTS THE CARDIO-RESPIRATORY ACTIVATION RESPONSE AT AROUSAL FROM SLEEP

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Introduction: It has been hypothesized that the cardio-respiratory activation response at an arousal from sleep is due to a reflex response elicited by the arousal. However, this mechanism does not explain the heightened activation response that occurs in OSA patients. We tested the hypothesis that the reflex response is augmented by the presence of partial airway occlusion at the time of the arousal.

Methods: The magnitude of the changes in minute ventilation (V), heart rate (HR) and blood pressure (BP) were assessed as a function of arousals from sleep. Subjects were 15 young (18-25 years) healthy males. 8 subjects showed intermittent flow limitation during sleep (FL group), while 7 had completely normal ventilation (NFL group). Spontaneous and elicited arousals from sleep were identified. In the FL group arous-

als were divided into flow limited arousals (FL arousals) and non-flow limited arousals (NFL arousals), while all arousals in the NFL group were NFL arousals. PetCO₂ at the time of arousals was also manipulated (eucapnic, +3 mmHg and +6 mmHg).

Results: In the FL group the maximum post arousal V was significantly higher in FL (15.1 l/min) than NFL (13.4 l/min) arousals ($p < .05$), but the changes in HR and BP were not significantly different ($p > .05$). In contrast, the FL group had significantly larger cardiovascular responses on NFL arousals (HR=18.9, SBP=22.3) than the NFL group (HR=11.4, SBP=17.4; $p < .05$ for both), but did not differ on the ventilatory response ($p > .05$). PetCO₂ had no effect on the magnitude of the activation response in any group or arousal condition.

Conclusion: Partial airway occlusion augments the magnitude of the cardio-respiratory activation response at an arousal from sleep, acutely for ventilation and chronically for cardiovascular activity.

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0095

INSTANTANEOUS BREATHING RATE AND 2-MIN-AVERAGED BREATHING RATE FOR ANALYSIS AND SCORING OF REM SLEEP STAGE

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Introduction: Breathing rate (BR) during REM sleep is known to fluctuate with a slight increase (Aserinsky E. 1965). However, we previously found that a rapid, momentary increase of over 2 fold in BR (MIBR) appears during REM sleep and stage 1, 2. Furthermore, we recently found that averaged BR can be a good index for scoring of REM sleep stage.

Methods: Standard polysomnographic recordings and scoring of sleep stages of eleven healthy volunteers (age: 22.3 ± 2.8) were performed including measurement of BR by nasal/oral airflow and belt sensors. Instantaneous BR was calculated after peak-detection process and the BR was averaged over every 1 (BRA1) and 2 (BRA2) min. Changes in BRA1 and BRA2 at each sleep stages were then compared and analysed after excluding artifacts of body movement.

Results: Number of REM episodes during a sleep was 3.7 ± 1.0 (n = 11); REM sleep duration and REM sleep cycle was 31 ± 18 and 94 ± 55 min, respectively. MIBRs were observed 1 to 8 times during total REM sleep period in 9 volunteers with accompanying a large REM and atonia. BRA2 reduced fluctuation and made it easy to discriminate the increase in BR during REM sleep than BRA1 did. Averaged maximum BRA2 over all REM sleep episodes was significantly higher than that at stage 1, 2 in three subjects. While, 89% of increases in BRA2 during REM sleep of all subjects were over 2 breaths/min larger than those during preceded stage 1, 2 (5.4 ± 2.6 v/s 1.3 ± 0.7 breaths/min, $P = 0.0001$). Changes in BRA2 during REM sleep were tentatively classified into 3 patterns as (1): increased for a duration, (2): decreased before and/or after (1), and (3): slightly decreased or unchanged; they were 60, 38 and 2 % in total, respectively.

Conclusion: Analysis of MIBR may be important to study the central nervous system activity during REM sleep, and BRA2 may provide us a new index for scoring the REM sleep stage.

0096

MAPPING SLEEP ACROSS A SOCIETY: SPATIAL AND TEMPORAL ANALYSIS OF WORKER HONEY BEE SLEEP

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Introduction: If situated in a perpetually bustling society, where and when do individuals sleep? Honey bee societies are composed primar-

Category B—Physiology/Phylogeny/Ontogeny

ily of worker bees, which change tasks as they age. Known to exhibit sleep behavior (Kaiser 1988), honey bees (*Apis mellifera*) are faced with variables that may impact their sleep schedule, both spatially and temporally. We mapped sleep patterns of worker honey bees with respect to these variables during different stages of their adult lives.

Methods: We introduced individually marked, recently eclosed worker honey bees into an observation hive consisting of 1500 bees belonging to a single colony. We recorded bees' behavior and temperature as the bees aged and changed tasks (callows, hive bees, foragers, in chronological order). We also produced maps of the hive's comb contents as the colony grew and the contents changed. All work was conducted with Carniolan bees at the Bienenforschungsstation in Würzburg, Germany in June 2006.

Results: Bees exhibited a state of relative immobility while discontinuously ventilating (correlated with highest arousal threshold, Kaiser 1988) during each stage of adult life, although callows exclusively did so inside cells and hive bees did so rarely. Callows' sleep depended only on the behavior's interaction with distance from hive edge ($F_{1,358} = 4.53$, $P = .034$), callows preferring to sleep in areas closer to hive edge and in the vicinity of uncapped brood. Foragers' average body temperature (T_{avg} ; specifically of alitrunk) was higher when bees were in a wakeful state than when in a sleep state ($F_{1,128} = 28.75$, $P < .0001$) and a sleeping forager's T_{avg} did not differ between day and night. Foragers primarily slept on capped brood comb or the edge of the hive devoid of comb.

Conclusion: Producing sleep "maps" of the temporal and spatial patterns of societies may contribute to our understanding of societal functioning, and criteria shaping individuals' sleep patterns. Thermal and behavioral maps of honey bees may serve as a new means of scientifically visualizing sleep within a society. [Kaiser, W. 1988. *J. Comp. Phys. A.* 163:565-584.]

0097

A STUDY OF OSA, FAT DISTRIBUTION AND RESPIRATORY MUSCLE STRENGTH

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Withdrawn

0098

REMS DEPRIVATION MAY REDUCE INHIBITORY TONE IN LAYER IV TO DELAY MATURATION OF VISUAL CORTEX

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Introduction: Relative inhibitory tone in layer IV of visual cortex in early life is thought to underlie a functional "plasticity gate" that mediates production (or not) of a developmentally regulated form of long-term potentiation (LTP) in the upper layers after white matter stimulation (LTP_{wm-III}). Because REMS deprivation (REMSD) extends the age until which this form of LTP can be elicited, we wondered whether REMSD affects this "plasticity gate". Here, we assessed inhibitory tone in visual cortical layer IV utilizing a paired-pulse stimulation (PPS) protocol in REMS-deprived and age-matched normal rats.

Methods: Twelve, 35 day old rats were REMS deprived for 24-76 hrs by a computer-controlled cage-shaking system. Age-matched control animals were maintained undisturbed in their home cages. Visual cortical slices were prepared from both groups for *in vitro* PPS experiments. A stimulating electrode was set in the WM below layer IV and a recording electrode was placed above it, in layer II-III. In the REMSD animals, LTP_{wm-III} was obtained before PPS was attempted after moving the electrodes to a new placement 1-2 mm away. One to five series of PPSs, at four inter-pulse intervals (IPI; 20-, 40-, 60- and 80-ms), were presented, every 30-s. Degree of inhibition was expressed as a ratio of

the average field response (fEPSP) to the second test-pulse to that of the first ($\times 100$). Group differences at each IPI were assessed with a repeated measures ANOVA.

Results: The normal control animals on average exhibited inhibition at all four IPIs, while REMS-deprived animals showed inhibition at the shortest IPI (20ms), but facilitation at the remaining three longer IPIs. Although the mean differences were not significant, there were trends for REMS-deprived animals to exhibit more facilitation than control animals at the 60-ms ($p = 0.082$) and 80-ms ($p = 0.092$) IPIs.

Conclusion: Inasmuch as PPS-facilitation is usually observed solely in rats less than 35-days, maturation of the inhibitory response to PPS in visual cortex tended to be delayed in the REMSD animals. Given the low number of animals, these data are only preliminary support for the possibility of REMSD delaying visual cortical maturation by reducing inhibitory tone in layer IV. Additional studies are ongoing.

0099

ENRICHED DIET INFLUENCES SLEEP/WAKE CYCLE IN MIGRATING BIRDS

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Introduction: Nocturnally migrating birds experience disrupted sleep/wake cycles in spring. Daytime activity decreases and nighttime activity and arousals increase compared to winter. They exhibit migratory restlessness or Zugunruhe when exposed to a longer photoperiod. Migratory birds increase in weight and fat before migration depending on the species. The Harris sparrow is a long distance migrant and increases in weight by at least 30% before vernal migration. Along the way, sparrows make stopovers to refuel and rest. This suggests that the Harris' sparrow sleep/wake cycle may be variable and closely associated to metabolic hormones or neuropeptides. We hypothesized that decreasing the diet will suppress nocturnal activity and temporarily restore a nearly normal sleep/wake cycle.

Methods: Harris' sparrows were exposed to a long photoperiod (16L:8D) to elicit migratory activity. We videotaped to confirm Zugunruhe and recorded weights and fat scores. Birds were divided into an enriched diet (spring diet) group or a lower protein diet (winter diet) group. We videotaped day and night, scoring migratory activity, sleep postures and daytime activity. We compared activity levels between groups as well as day vs. night.

Results: The intensity of migratory activity exhibited by the enriched diet group did not change. Birds receiving a winter diet did show a decrease in nocturnal activity and an increase in daytime activity (trend, $P = 0.09$; $P = 0.07$) though not significant. In addition, there was an increase in sleep postures and immobility observed during the night.

Conclusion: Decreasing nutritional content in the migratory bird diet may temporarily stabilize the sleep/wake cycle. Stopovers allow birds to eat and rest before migrating again and the metabolic signals initiating this flight may also help adjust sleep/wake cycles accordingly.

0100**CODEINE EFFECTS IN SLEEPY VERSUS ALERT HEALTHY NORMALS**Roehrs T^{1,2}, Harris E¹, Hyde M¹, Roth T^{1,2}¹Internal Medicine, Sleep Disorders & Research Center, Henry Ford Health System, Detroit, MI, USA, ²Psychiatry & Behavioral Neurosciences, School of Medicine, Wayne State University, Detroit, MI, USA

Introduction: Basal sleepiness-alertness modulates sedating drug effects. Sleepiness produced by severe acute or mild chronic sleep restriction is hyperalgesic, suggesting analgesic effects may also be modulated by sleepiness-alertness. This study was done to compare pain sensitivity in sleepy versus alert healthy normals after codeine 60 mg or placebo.

Methods: Twelve healthy adults, 18-35 yrs, participated. Each had a 8-hr sleep recording (NPSG) and alertness assessment (MSLT) the following day. All had sleep efficiencies >85% on their NPSG and 6 had MSLT > 8min and 6 had MSLT < 7 min. All served in experiments assessing pain threshold under conditions that included a 8-hr time-in-bed condition with a standard MSLT and pain assessment conducted the following day with codeine 60 mg or placebo administered at 900 and 1300 hrs. Pain threshold was assessed (AM 1030 and PM 1430 hrs) using a novel radiant heat stimulation method. Finger withdrawal latency (FWL) in sec was measured to 5 randomly presented radiant heat intensities directed to the index finger pad of each hand.

Results: Daily sleep latency (MSLT) in the sleepy group was 4.72 + 1.83 min and 13.04 + 4.90 min in the alert group. As hypothesized, decreasing heat intensity (AM: F=16.63, p<.001; PM: F=16.85, p<.001), codeine 60 mg (AM: F=7.05, p<.02; PM: F=10.21, p<.01), and decreased sleepiness (AM: F=12.23, p<.01; PM: F=6.05, p<.03) produced increased FWL. Importantly, there was a group by drug interaction (AM: F=10.37, p<.01; PM: F=7.51, p<.02) with codeine increasing latency in the alert group, but not the sleepy group. There were no significant intensity by group or drug interactions.

Conclusion: These data show the analgesic effects of codeine are diminished by mild chronic sleep restriction. It suggests that clinical differences in response to analgesics are in part explained by basal state of sleepiness-alertness.

Support (optional): The Fund for Henry Ford Hospital, B10914 awarded to Dr Roehrs

0101**SLEEP-INDUCING EFFECTS MEDIATED BY SELECTIVE BLOCKADE OF OREXIN OX2 RECEPTORS DURING THE LIGHT PHASE IN THE RAT**

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Introduction: The neuropeptides orexins (hypocretins) produced by lateral hypothalamic neurons exert a prominent role in the maintenance of wakefulness. A recent study in animals and humans with the dual orexin OX1/OX2 receptor antagonist ACT-078573 has provided evidence of its hypnotic activity during the active period. Using selective orexin receptor antagonists the present study investigated the specific role of selective blockade of OX1 and OX2 receptors in sleep modulation.

Methods: Pharmacological treatments were performed in adult male Sprague-Dawley rats implanted with telemetric devices for recording of EEG/EMG sleep, locomotor activity and body temperature. Separate groups of animals received selective antagonists at OX1 (SB-334867 and SB-408124, 30 mg/kg sc) or OX2 (JNJ-10397049, 0.3-30 mg/kg sc and 50-100 mg/kg po) receptors, or the dual OX1/OX2 receptor antagonist ACT-078573 (100-300 mg/kg po) and their corresponding vehicles either at two hours into the light phase or at dark onset.

Results: As expected, ACT-078573 (100 mg/kg po) given at dark onset was effective in promoting NREM and REM sleep. Neither SB-334867

nor SB-408124 demonstrated any sleep-promoting effect after treatment during the light or dark phase. When administered either during the light or the dark phase, JNJ-10397049 showed efficacy at 3 mg/kg sc and 100 mg/kg po in both sleep induction (decreased NREM and REM sleep latencies) and sleep promotion (increased NREM and REM sleep time due to an increase in the number of sleep bouts). Power spectral densities in NREM and REM sleep were not altered. These effects lasted for 2 hours following the treatment in the light phase and were associated with a decrease in locomotor activity and body temperature, and about 6 hours in rats treated at dark onset.

Conclusion: These data indicate that the sleep-inducing and promoting effects of orexin receptor antagonists can be revealed during the light/sleep period and are mediated through the OX2 receptor. These promising candidates for the treatment of insomnia might be a novel non-scheduled class of hypnotics as opposed to classical GABA modulating agents.

0102**EFFECT OF TWO DOSE REGIMENS OF EPLIVANSERIN, A NEW SLEEP AGENT, ON SLEEP AND PSYCHOMOTOR PERFORMANCE OF HEALTHY SUBJECTS**Hindmarch I¹, Cattelin F²¹HPRU, Guilford, United Kingdom, ²sanofi-aventis, Gently, France

Introduction: Eplivanserin is an Antagonist of Serotonin Two A Receptors (ASTAR) developed at a 5mg dose in insomnia characterized by nocturnal awakenings. In contrast to benzodiazepines, eplivanserin does not bind to GABA receptors. The effect of time of administration (morning or evening) and of various doses of eplivanserin were assessed on sleep, motor activity, attention, short-term memory, alertness and mood in healthy subjects.

Methods: Double-blind, double-randomized, placebo-controlled, cross-over study. 16 young healthy male subjects were randomized to receive eplivanserin in the morning (8) or evening (8) and then randomized again to a sequence of treatment with an oral single dose of eplivanserin (1, 10 and 40 mg) and placebo, with a 1-2 week washout between the 4 periods. Activity parameters included EEG parameters, psychomotor tests [Critical Flicker Fusion (CFF), Choice Reaction Time (CRT), Compensatory Tracking Test (CTT) and Sternberg Memory Scanning Task (STM)] and subjective ratings of sleep.

Results: All 3 doses of eplivanserin, given in the morning or in the evening, doubled SWS time, in correlation with a decrease in stage 2. An improvement of sleep efficiency and a decrease in episodes of wake after sleep onset (WASO) longer than 120 seconds were observed with all 3 doses. No effect on sleep latency and sleep duration was observed. No dose regimen effect was observed: whatever the administration time, eplivanserin did not affect performance of attentional or psychomotor tasks (CRT, CTT) or short-term memory (STM). A slight decrease in CFF threshold detection was observed at all doses, likely related to a direct effect on pupillary response (myosis) as described with other 5HT2 antagonists. No subjective CNS impairment was reported. Eplivanserin was generally well tolerated.

Conclusion: Single oral doses of eplivanserin 1, 10 and 40 mg, doubled the time spent in SWS without any dose-dependent effect in healthy subjects. Whatever the timing of drug administration - morning or evening - eplivanserin did not impair attentional or psychomotor tasks.

0103

ADMINISTRATION OF A CERAMIDE SYNTHASE INHIBITOR, FUMONISIN-B1, INTO THE PREOPTIC AREA SUPPRESSES SLEEP IN FREELY BEHAVING RATS

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Introduction: The Preoptic anterior hypothalamic area (POAH) has been implicated in many physiological functions including the regulation of sleep-wakefulness and body temperature. Recent studies suggest that in the POAH, ceramide may be the second messenger mediating the rapid febrile responses of interleukin-1b. However, the contribution/role of endogenous ceramide in the POAH on sleep-wakefulness is not known. We examined the effects of perfusion of fumonisin-B1, a specific inhibitor of ceramide synthase, into the POAH using reverse microdialysis on sleep-wakefulness.

Methods: Three male Sprague-Dawley rats were stereotaxically implanted with EEG and EMG electrodes, and a guide cannula directed at the POAH (AP, -0.4 to -0.5; L, 0.8; H, -8.5 to -9.0). Experiments were conducted after at least 7 days of recovery from surgery, and during the lights-on period (ZT 2.00 - ZT 8.00). Each rat was subjected to six hrs of EEG and EMG recording with microdialytic perfusion of artificial cerebrospinal fluid (aCSF) or either of two doses of fumonisin-B1 (500µM and 100µM) for 2 hrs followed by 4 hrs of aCSF perfusion in a random order.

Results: As compared to aCSF during the first 2 hr, rats microdialysed with 500µM of fumonisin-B1 into the POAH tended to spent more time in waking (54.91 ± 11.7% vs. 33.88 ± 3.8) and less time in nonREM (37.12 ± 9.1% vs. 54.58 ± 3.5%) and REM sleep (7.96 ± 2.7% vs. 11.52 ± 2.4). 100µM of fumonisin-B1 produced only marginal effects.

Conclusion: These preliminary results suggest that ceramide signaling in the POAH may play a role in the regulation of sleep-wakefulness, and could mediate rapid responses to IL-1b

Support (optional): NS-050939, MH-47489, HL-60296, and MH-63323

0104

EVT 201: A HIGH AFFINITY, PARTIAL POSITIVE ALLOSTERIC MODULATOR OF GABA_A RECEPTORS WITH PREFERENCE FOR THE α 1-SUBTYPE

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Introduction: EVT 201 has recently completed two Phase II trials in primary insomniacs and has demonstrated robust effects on sleep onset together with sleep maintenance activity throughout the night. This study explored the molecular pharmacology of EVT 201 and its active metabolite, M1, at recombinant GABA_A receptor subtypes in comparison with zolpidem.

Methods: Effects of EVT 201, M1 and zolpidem on GABA (EC₃₋₅) stimulated currents were examined in *Xenopus* oocytes expressing recombinant GABA_A receptor α 1, α 2, α 3 or α 5 in conjunction with β 2 γ 2 subunits. The stimulation produced by each compound was standardized to that produced by 1 µM diazepam (=100 %).

Results: Both EVT 201, and its active metabolite, M1, exhibited EC₅₀s in the range 18-84 nM, with both compounds showing highest potency at α 1 containing subtypes. Zolpidem exhibited approximately 10-fold selectivity for α 1 containing receptors where its EC₅₀ was 191 nM. The maximum potentiation produced by EVT 201 at each GABA_A receptor subtype ranged from 31-69% of that produced by diazepam (1 µM) whereas M1 produced a maximum potentiation of approximately half that produced by EVT 201. In contrast, zolpidem produced a maxi-

mum potentiation much greater (166-215%) than that of diazepam at all GABA_A receptor subtypes except those containing α 5.

Conclusion: These data demonstrate that EVT 201, and its active metabolite M1, act as α 1-preferring high affinity, partial agonists at GABA_A receptor subtypes. In contrast, while showing lower potency, Zolpidem acts a 'super' agonist compared to diazepam since it produces a much greater maximum potentiation of the GABA response. This pharmacological profile may contribute to the advantageous clinical profile of EVT 201 seen to date, since it avoids excessive potentiation of GABA_A receptors produced by 'full' or 'super' agonists that may underlie some of the unwanted effects produced by these agents.

Support (optional): The study was sponsored by Evotec.

0105

A PHARMACOKINETIC STUDY OF THE CO-ADMINISTRATION OF A HIGH FAT MEAL WITH A LOW DOSE, SUBLINGUAL FORMULATION OF ZOLPIDEM TARTRATE

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Introduction: Clinically relevant reductions in rate and extent of bioavailability of zolpidem tartrate due to the presence of a high fat meal have been previously demonstrated in immediate- and controlled-release formulations. However, a drug formulation with partial buccal absorption may show a reduced propensity for the rate of absorption to be affected by food. This study assessed the effects of co-administration of a high fat meal on the pharmacokinetics of Intermezzo® 3.5mg, a low dose, buffered, sublingual formulation of zolpidem tartrate (SZT) for the *prn* treatment of MOTN insomnia.

Methods: Healthy adults (N=36) participated in a randomized, open label crossover study of morning dosing with 3.5 mg sublingual zolpidem tartrate (SZT) lozenges in the fed state (following a standard high fat meal) and 10-hour fasted state. PK assessments began prior to dosing and continued for 8 hours post-dose.

Results: The early SZT mean plasma concentration at 15 minutes post-dosing (C_{15 min}) was similar for both conditions at 19.85 ng/ml in the fasted state and 15.92 ng/ml in the fed state. However overall C_{max} and AUC were both reduced in the fed state relative to the fasted state: fasted C_{max} and fasted AUC were 57.18 ng/ml and 201.4 ng*hr/ml respectively, while fed C_{max} and fed AUC were 35.63 ng/ml and 160.77 ng*hr/ml, respectively.

Conclusion: The optimal pharmacokinetic profile of SZT occurs in the fasted state, however this data indicates in both the fasted and the fed state the attainment of serum concentrations likely to be sufficient to produce a pharmacodynamic effect within the first 15 minutes. Although a high fat-meal reduces the total bioavailability of SZT by 20.2%, and reduces C_{max} by 37.7% these respective changes may be insufficient to significantly impact efficacy of MOTN dosing.

Support (optional): This study was fully funded and supported by Transcept Pharmaceuticals, Inc., Richmond CA.

0106

NEU-P11, A NOVEL MELATONIN AGONIST: EFFECTS ON SLEEP AND EEG POWER SPECTRA IN RATS

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Introduction: Neu-P11 is a novel melatonin agonist with GABA enhancing properties currently in development for the treatment of insomnia. It binds with high affinity to melatonin receptors and enhances GABA activity without interaction with GABA receptors. The aim of

the present study was to characterize the actions of Neu-P11 on the sleep structure and EEG power spectra in rats.

Methods: Adult male rats (5/group) were implanted with permanent electrodes for electroencephalogram (EEG) and electromyogram (EMG) recordings. Neu-P11 (50 and 100 mg/kg, i.p.) or Vehicle were administered at 22:00. EEG and EMG signals were scored using SLEEPSIGN. Changes in the sleep-wake profiles were compared using Student's *t*-tests and one-way, repeated measures analysis of variance (ANOVA).

Results: At a dose of 50 mg/kg, the profiles of wakefulness and NREM sleep were almost identical before and after drug injection. During the second four hour interval after drug injection, Neu-P11 (100 mg/kg) significantly decreased wakefulness by 23% and increased both NREM and REM sleep by 1.7-fold, as compared with control. At both doses, Neu-P11 significantly increased the power density of NREM sleep in the delta band while significantly decreasing the beta band during the first four hour period after drug administration. This effect lessened during the second four hour period after dosing.

Conclusion: Neu-P11 demonstrated significant hypnotic effects when administered at the early dark phase in rats and it was also able to significantly increase the delta band while decreasing the beta band. These effects of Neu-P11 resemble those of recovery sleep after sleep deprivation unlike benzodiazepines and zolpidem which suppress delta sleep. The present findings underline a unique hypnotic profile of Neu-P11.

Support (optional): Pharmaceuticals Research Grant (to UY and HZL).

0107

NEU-P11, A NOVEL GABA-ENHANCING MELATONIN AGONIST: ANTIDEPRESSANT EFFECTS IN THE LEARNED HELPLESSNESS MODEL IN RATS

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Introduction: Neu-P11 is a novel melatonin agonist with GABA enhancing properties currently in development for the treatment of insomnia. In animal studies, Neu-P11 demonstrated hypnotic effects suggesting an induction of a high quality, restorative sleep. It has been documented that depression can lead to insomnia and that conversely long-standing insomnia can often lead to depression. The aim of the present analysis was to characterize the potential antidepressant activity of Neu-P11 and melatonin in the learned helplessness model in rats.

Methods: The behavioral procedure involved two phases (shock pre-training and avoidance-escape training/testing). Forty-eight hours after pretraining (i.e., day 3), all the rats (adult male Sprague-Dawley) were exposed to an avoidance-escape task in the automated two-way shuttle-boxes. The shuttle-box test was repeated on day 4 and day 5. Neu-P11 and melatonin (25, 50 and 100mg/kg/day IP) were administered 2h before the beginning of the dark phase once a day for 5 days and their effects were compared with those of imipramine (32 mg/kg/day, IP). The numbers of escape failures were recorded over the three days of testing.

Results: Compared with helpless control animals, animals treated with Neu-P11 at 50 mg/kg/day showed a significant decrease of escape failures over the 3 days of testing ($p < 0.01$, $p < 0.001$ and $p < 0.001$, respectively). A similar effect was seen with imipramine (all $p < 0.001$). The level of escape failures did not differ in animals treated with melatonin (all doses, $p > 0.05$).

Conclusion: Neu-P11, Like imipramine, reversed the escape deficit induced by uncontrollable shock in the learned helplessness model in rats. The results suggest that Neu-P11, a potent sedative-hypnotic melatonin agonist, exerts antidepressant-like properties.

Support (optional): Neurim Pharmaceuticals Research Grant (to S.T).

0108

EFFECT OF A TRANSDERMAL NICOTINE PATCH ON EEG AND EKG POWER SPECTRA DURING SLEEP OF HEALTHY MALE ADULTS

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Introduction: Transdermal nicotine patch has been widely used as an aid to smoking cessation. Nevertheless, its effects on sleep physiology are not well characterized, despite the well-known fact that the administration of nicotine patch could influence the sleep architecture. Moreover, previous reports were based on visual sleep scoring method. While visual sleep scoring is useful for characterization of sleep architecture and continuity, it is insufficient for more refined, quantitative analysis of sleep electroencephalogram (EEG). This study, therefore aimed to measure the influence of transdermal nicotine patch on sleep EEG and EKG power spectra in order to examine whether it effects homeostatic sleep propensity and autonomic nervous system.

Methods: We studied sixteen nonsmoking young healthy volunteers polysomnographically for three nights including one adaptation night in a double blind crossover design and compared all-night sleep variables, sleep EEG and EKG power spectra between sleeps with and without nicotine patch of 14 mg. Digital polysomnography used in this study was intelligent polysomnography system (IPSS), which was developed through the joint action of division of sleep studies in Seoul national university hospital and institute of biomedical engineering in Seoul national university.

Results: Visual sleep scoring showed that transdermal nicotine increase sleep latency, wake after sleep onset (WASO), stage 1 sleep time percent, and decrease total sleep time (TST), sleep efficiency, REM sleep time percent. Spectral analysis of the sleep EEG revealed important changes as follows. Decreased Slow wave activity (SWA) was seen in stage 2 sleep of the first non-rapid eye movement cycle after administration of nicotine patch. Decreased slow wave activity (SWA) accompanied by increased alpha activity were seen in the first cycle of REM sleep after administration of transdermal nicotine patch. We found no differences in spectral analysis of EKG between sleeps with and without nicotine patch, except low to high ratio (indicating sympathetic nervous system activity) was correlated positively with WASO after administration of transdermal nicotine patch.

Conclusion: These results suggest that transdermal nicotine patch significantly disrupts sleep continuity, sleep architecture and homeostatic sleep propensity. These effects of transdermal nicotine patch appears to be associated with the activation of sympathetic nervous system.

0109

DISRUPTED SLEEP IN MARIJUANA USERS DURING TWO WEEKS OF ABSTINENCE

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Introduction: Marijuana (MJ) is the most widely used illicit drug in the United States. In withdrawing MJ users, 76% report sleep disturbance. Few studies have used polysomnography (PSG) to characterize self-reported sleep problems in withdrawing MJ users.

Methods: We studied 16 heavy MJ users and 16 drug-free controls during 14-days of abstinence from heavy MJ use. The MJ group (18 - 25 yrs old; MJ use was 63-210 joints/wk) resided on an inpatient research unit for 14 days. PSG measurements were recorded on Nights 1, 2, 7, 8, and 13 of withdrawal. The drug-free control group stayed for 3 inpatient nights and PSG studies were recorded on Nights 1 and 2.

Category C—Pharmacology

Results: The between group comparison showed that the MJ users had lower total sleep time (TST) and less slow wave sleep (SWS) than the drug-free control group on Nights 1 and 2 and worse sleep efficiency (SE), longer initial sleep latency (ISL) and reduction in REM latency on Night 2 compared to Night 1. Paired t-tests were used to determine within-group differences and showed that sleep parameters changed significantly ($p < 0.05$) from Night 2 to Night 13 in the direction of less REM %TST, more period leg movements, and more wake after sleep onset (WASO) episodes. Trends indicating more impaired sleep were found for TST, SE, and longer ISL. SWS increased slightly over nights. Withdrawal symptoms, craving, and depression did not appear to influence these findings.

Conclusion: During withdrawal from heavy MJ use, MJ users showed PSG findings consistent with sleep disturbance that worsened during the 14-days of the study. Since sleep is essential for good quality of life, we believe that sleep disturbance may significantly hinder treatment of cannabis abuse disorders and could help explain why 93% of treatment seekers report that they are unable to stop smoking MJ.

0110

POOR SLEEP QUALITY INCREASES VULNERABILITY FOR DEPRESSION AND IRRITABILITY FOLLOWING INTERFERON TREATMENT

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Introduction: Neuropsychiatric sequelae, including major depressive disorder (MDD) and severe irritability, can be frequent consequences of interferon-alpha (IFN- α) treatment. We examined whether pre-treatment Pittsburgh Sleep Quality Index (PSQI) global scores predicted time to develop depression or severe irritability during combination IFN- α 2 and ribavirin treatment for Hepatitis C.

Methods: Forty-six euthymic adults with Hepatitis C were evaluated prior to IFN- α treatment and prospectively monitored for up to 16 weeks of treatment. Self-report measures of sleep quality, depression and irritability severity, and history of MDD were collected at baseline. The outcome assessed was time to develop MDD or severe irritability requiring psychiatric intervention. Survival analyses were conducted using Kaplan-Meier survival plots and Cox proportional hazards models to examine sleep quality (pre-treatment PSQI global scores ≥ 10) as a predictor of MDD or severe irritability, controlling for baseline depression/irritability symptoms or past history of MDD.

Results: During IFN- α treatment, 17% developed MDD and 28% developed severe irritability. These conditions developed significantly faster in patients with worse pre-treatment sleep quality (log-rank chi-square=7.58, $p=.006$). In Cox models controlling for baseline depression severity and history of MDD, poor sleep at baseline had a hazard ratio of greater than 6.0 ($p's < .035$) for developing MDD during IFN- α treatment. Similarly, poor sleep had a hazard ratio of 4.4 ($p=.012$) for developing severe irritability.

Conclusion: Participants reporting worse sleep quality prior to IFN- α treatment were over six times more likely to develop MDD and over four times more likely to develop severe irritability even after accounting for baseline depression/irritability severity or history of MDD. Poor sleep may be a critical modifiable risk factor prior to IFN- α treatment. These findings may have important implications for predicting and possibly preventing depression and irritability in individuals treated with IFN- α .

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0111

SEDATION RELATED RESPIRATORY EVENTS IN PATIENTS WITH OSA

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Introduction: Upper airway collapse during sedation is likely mediated by an interplay of anatomic and neurologic factors that are similar to those thought to be responsible for OSA. This, along with the occurrence of sleep during sedation, makes it likely that: 1) patients with OSA are at increased risk for upper airway events during sedation, and 2) this risk may vary by type of sedative. In the present study, two compounds were assessed in patients with OSA for their propensity to produce sedation related respiratory events.

Methods: Adult subjects with moderate to severe OSA were recruited to undergo a two way crossover PSG assessment during intravenous propofol (prop) or dexmedetomidine (dex). Computerized drug delivery was utilized to obtain constant predicted plasma levels of each drug. Depth of sedation was quantified using the modified Observer's Assessment of Alertness/Sedation Scale (OAAS) and the Bispectral Index Monitor (BIS). A sedated apnea hypopnea index (S-AHI) was calculated for each individual for each medication condition (each 1-2 hours in duration).

Results: Six subjects (4 male; age=51 \pm 11; BMI=38 \pm 9; AHI=61 \pm 34) completed the protocol but S-AHI data was only available for 5 subjects. There was no difference between medications for the occurrence of sleep (TST) or type of sleep (Stages 1 & 2). Dex showed a tendency for a lower S-AHI, 36 \pm 27 vs 49 \pm 41, NS. Most events were hypopneas (31 \pm 23 for dex vs. 36 \pm 39 for prop, NS) but there was a trend to a differential occurrence of obstructive apneas (0.8 \pm 0.8 dex vs. 5.6 \pm 4.4 prop, $p=0.07$).

Conclusion: The data from this pilot study suggest that, in individuals with OSA, respiratory events occur during sedation and that the type and frequency of the events tend to vary with the type of sedative used. Both prop and dex appeared to produce sleep during sedation and of comparable types. Research in a larger study may help determine the best sedative to use in patients with OSA.

0112

AMYGDALOID SEROTONERGIC SYSTEM MEDIATES CANNABIDIOL-INDUCED SLEEP ALTERATION IN RATS

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Introduction: Cannabidiol (CBD) is one of the major constituents of marijuana. The pharmacological properties of CBD, especially the anxiolytic effect, are more significant in therapeutic purpose because of its psycho-inactivity. The central nucleus of amygdala (CeA) plays a key role in emotion and anxiety-related behavioral responses (e.g. arousal), and serotonin is one of the major mediators. However, the sleep-wake effect of CBD in the CeA remains unclear. This study was designed to elucidate the effects of CBD on sleep-wake alteration and the involvement of serotonin in the CeA.

Methods: Male Wistar rats were implanted with EEG electrodes and a microinjection cannulae directly into the CeA. A 24-h sleep was recorded from undisturbed and pyrogen-free saline (PFS)-treated rats after recovery. Administration of 5-hydroxytryptamine (5-HT), 5-HT1A receptor agonist (buspirone), 5-HT2 antagonist (ritanserin), cannabinoid CB1 receptor agonist (ACEA) or antagonist (AM-251) was employed to

elucidate the involvement of the presynaptic CB1 receptors and serotonergic activity of the CeA.

Results: Microinjection of CBD into the CeA decreased slow wave sleep (SWS) with limited effect on rapid eye movement sleep (REMS) during the light period. Sleep was not altered when administration of CBD prior to the dark period. CBD-induced SWS suppression during the light period could be mimicked by direct administration of serotonin. Both buspirone and ritanserin blocked the CBD-induced decrease of SWS during the light period. Furthermore, administration of AM-251 alone exhibits similar effect as that of CBD, and the CBD-induced sleep alteration was partially blocked by ACEA.

Conclusion: These observations demonstrated that CBD acting on the CeA neurons decreases SWS and increases wakefulness during the light phase. The mechanism of CBD on sleep-wake activity may be partly mediated by antagonizing presynaptic CB1 receptors, enhancing serotonin release from the presynaptic terminal and the subsequent action on the postsynaptic 5-HT₂ receptors.

0113

PRE-SLEEP SALIVARY CORTISOL LEVELS IN INSOMNIACS USING ZOLPIDEM LONG-TERM

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Introduction: Primary insomnia is hypothesized to reflect a state of 'hyperarousal', as shown in an activated HPA axis with elevated levels of cortisol, particularly before sleep. However, not all short-term studies have shown elevations compared to controls. This ongoing long-term study sought to compare pre-sleep salivary cortisol levels among primary insomniacs randomized to zolpidem or placebo taken nightly for 4 months.

Methods: Primary insomniacs, ages 23-70, meeting DSM-IV criteria and in good general health were recruited. Participants had a sleep efficiency of <85% on a screening NPSG with no other primary sleep disorders. Pre-sleep saliva samples were collected (45 min. prior to bedtime) on nights 1, 2, 7-9, and 14 of month 1 and nights 1, 2 and 7 of month 4. Samples were collected prior to nightly administration of zolpidem or placebo (30 min prior to bedtime) in a single blind study. Zolpidem 10 mg was administered nightly for four months except on nights 8-9 & 14 of month 1 and nights 1-7 of month 4.

Results: No significant baseline differences were found among the placebo and zolpidem groups on any outcome measures. Zolpidem 10 mg produced a significant increase in sleep efficiency [F(1, 9)=12.933; p=0.002] in month 1 and decreased the latency to persistent sleep in comparison to the placebo group [F(1, 19)= 12.69; p=0.002]. There was a significant reduction in pre-sleep and pre-drug salivary cortisol levels across the months in the zolpidem group [F(8, 64)=5.569; p=0.046] with no nights x drug interaction.

Conclusion: Use of zolpidem, in these preliminary data, was associated with decreased pre-sleep and pre-drug salivary cortisol levels in comparison to the placebo group. The decreased pre-sleep salivary cortisol levels might reflect reduced hyperarousal, possibly mediated by the faster sleep onset and increased sleep efficiency seen with zolpidem.

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0114

EFFECTS OF MODAFINIL ON EEG OF HEALTHY ADULTS: USING DETRENDED FLUCTUATION ANALYSIS

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Introduction: Effects of Modafinil on EEG of healthy adults was not fully understood. In this study, we analyzed EEG of healthy young adults with detrended fluctuation analysis (DFA) and compared their linear and nonlinear characteristic at baseline and after modafinil medication.

Methods: Twelve healthy subjects (7 men / 5 women; 23.8 ± 2.5 year old) were participated. All of them had done polysomnography (PSG), multiple sleep latency test (MSLT) and have repeated same procedure after taking 200 mg of modafinil. Detrended fluctuation analysis and spectral analysis have been done on the EEG from nPSG and MSLT. We evaluated scaling exponents in terms of sleep stages, relative spectral powers.

Results: In the analysis of nPSG data, scaling exponent of C3 EEG was higher than that of O1 (Linear mixed model analysis (LMM); F= 6.9, p=0.002). Scaling exponents were different with sleep stages and showed negative correlation with alpha, theta relative powers. In the analysis of scaling exponents from MSLT, medication decrease scaling exponents (LMM; F= 20.1, Num df=1, Den df=11, p=0.001) in healthy adults. In addition, scaling exponents of C3 has increased after sleep onset.

Conclusion: Scaling exponents in terms of sleep stage were consistent with traditional liner indexes. Scaling exponents reflect effects of medication effectively.

0115

DOPAMINE D2/D3 AGONISTS AND DAYTIME SLEEPINESS: SLEEP PROMOTION BY LOW DOSE OF QUINPIROLE IN RATS IN ACTIVE PERIOD

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Introduction: Although several pharmacological and physiological studies showed that dopaminergic neurotransmission plays an important role in the sleep-wake regulation, the detailed mechanisms in the regulation of arousal are still controversial. Recent reports suggest that D2/D3 dopamine agonists, such as pramipexole and ropinirole, frequently cause excessive daytime sleepiness and sudden sleep attacks in patients with Parkinson's disease (PD), although these sleep problems are also observed in some unmediated PD subjects. These compounds enhance dopaminergic neurotransmission by stimulating the postsynaptic dopamine (DA) receptors, and this is a proposed pharmacological property for the treatments of the main symptoms of the PD. However, the lower doses of these compounds may act dominantly on presynaptic dopaminergic autoreceptors. Consequently, dopaminergic neurotransmission is suppressed. In this study, we investigated the effect of D2/D3 agonist, quinpirole, on the sleep-wake parameters in the active (dark) period of rats.

Methods: Male Sprague-Dawley rats underwent surgery for implantation of electrodes for EEG and EMG. After recovery and acclimation period for recording chamber, vehicle was injected (i.p.) at five minute before the beginning of lights-off period (20:00) on day 1, then EEG and EMG were recorded for 12-hour. On day 2, quinpirole (30ug or 1000ug/kg) was injected at the same time of day and polygraph recording was also performed. The amount of each sleep parameters (SWS, REM sleep, and wakefulness) for 12-hour in vehicle days was compared to that in quinpirole days.

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Results: A low dose of quinpirole significantly increased the amount of SWS and REM sleep, and decreased the amount of wakefulness. On the contrary, the amount of wakefulness significantly increased by injecting high dose of quinpirole.

Conclusion: These results suggest that sleep enhancement by quinpirole is related to stimulation of dopaminergic autoreceptors in normal animals. It is important to evaluate if DA autoreceptor functions are altered and responsible for sleepiness in PD patients.

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0116

MULTIPLE-DOSE PHARMACOKINETICS, PHARMACODYNAMICS, SAFETY, AND TOLERABILITY OF THE OREXIN RECEPTOR ANTAGONIST ALMOREXANT IN HEALTHY SUBJECTS

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Introduction: The orexin system plays a central role in the regulation of sleep-wake balance. Almorexant, a first-in-class orexin receptor antagonist, decreased alertness and promoted sleep following single-dose administration in healthy subjects, and improved both objective and subjective sleep variables in patients with primary insomnia.

Methods: Almorexant was given orally at multiple ascending doses of 100, 200, 400, and 1000 mg in the morning (Days 1 - 4) and in the evening (Days 5 and 6) in a double-blind, placebo-controlled, parallel design. At each dose level a new group of 10 healthy subjects was randomized to almorexant (8) or placebo (2). Main objectives were pharmacokinetics (PK), pharmacodynamics (PD), safety, and tolerability. Safety assessments and validated PD tests (saccadic peak velocity [SPV], adaptive tracking, body sway, and subjective alertness) were conducted at regular time points.

Results: The drug was well tolerated and no serious adverse events were reported. PK showed rapid absorption (T_{max} = 1.0-1.5 h) and marked distribution after attainment of C_{max}. Plasma concentrations decreased approximately 80% within 8 hours with a terminal elimination half-life of 24 h. No relevant accumulation was observed on Day 4. Evening administration showed a similar exposure with slower absorption. PD results of 100 mg were similar to placebo; doses of 200 to 1000 mg showed dose-dependent effects on vigilance and alertness with onset of effects within 0.5-1 h, maximum effect around 2 h, and return to baseline within 4-8 h. The PD effects (reduced SPV, adaptive tracking, and alertness, and increased body sway) were not more pronounced on Day 4 as compared to Day 1.

Conclusion: Multiple-dose administration of almorexant was well tolerated in healthy subjects. Neither PK accumulation nor increased PD effects were observed following repeated administration. These results support the initiation of multiple-dose studies in insomnia patients.

Support (optional): This study was financially supported by Actelion Pharmaceuticals Ltd., Allschwil, Switzerland.

0117

MODAFINIL INDUCES PLACE PREFERENCE AND ATTENUATES COCAINE-INDUCED PLACE PREFERENCE IN MICE

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Introduction: Modafinil is a wake promoting drug approved for the treatment of narcolepsy, shift work sleep disorder, and obstructive sleep apnea. The drug is also widely prescribed off-label to enhance alertness,

attention, or memory for dementia, attention deficit hyperactivity disorder, excessive daytime sleepiness, and depression. Recently, modafinil has emerged as a candidate for the pharmacological treatment of cocaine addiction.

Methods: Conditioned place preference was tested by pairing injections of drug (modafinil, cocaine, or cocaine plus modafinil) with one side of a chamber and saline with the other side. Training lasted seven days and locomotor activity was measured. On testing, mice were allowed to explore both sides of the chamber and percent time spent in each chamber was measured. Testing was performed with pre-training injections of saline, a low dose of modafinil (0.75mg/kg), and a high dose of modafinil (75mg/kg).

Results: Cocaine (15mg/kg) and cocaine+modafinil (15mg/kg and 75mg/kg, respectively) induced sensitization of locomotor activity; modafinil (75mg/kg) alone did not. Modafinil, cocaine, and the combination of modafinil+cocaine each induced a strong preference for the drug paired side. A low dose of modafinil, but not a high dose, decreased the conditioned place preference of cocaine-trained mice.

Conclusion: Similar to previous studies, modafinil did not induce locomotor sensitization. However, contrary to prior reports, we found that modafinil does induce conditioned place preference equal to that of cocaine. Also, a low dose of modafinil may attenuate drug seeking behavior in cocaine addicts.

Support (optional): DA020041 National Institute on Drug Abuse (SGA)

0118

EFFECTS OF REPEATED ORAL ADMINISTRATION OF THE OREXIN RECEPTOR ANTAGONIST ALMOREXANT IN MALE RATS AND DOGS

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Introduction: Almorexant decreases alertness and promotes sleep when given during the active period of the circadian cycle in healthy male rat, dog and human subjects. Almorexant is an orexin receptor antagonist that readily crosses the blood-brain barrier and is capable of inducing a transient, reversible and selective blockade of both OX1 and OX2 receptors. Safety and efficacy were assessed in laboratory animals following repeated administration of almorexant.

Methods: Three studies were conducted. In an EEG-sleep study in rats aimed at evaluating short-term treatment effects, oral almorexant, versus zolpidem, was given repeatedly for 5 days at pharmacological dose. In two additional rat and dog studies, animals were exposed to oral almorexant administered versus vehicle for four weeks and observations made on a daily basis.

Results: Five days of repeated dosing with almorexant did not induce different responses from single dosing on behavioral and electrophysiological measures of sleep in rats. Tachyphylaxis developed following zolpidem administered under the same regimen. Discontinuation of almorexant or zolpidem after 5 days did not lead to residual effects, rebound or signs of acute withdrawal. Abrupt discontinuation of almorexant treatment after one month did not lead to reports of withdrawal in rats nor dogs. No episodes of cataplexy were reported in rats nor dogs during or after a one-month treatment. Concentrations of almorexant were quantified in plasma samples collected on day1 and day28, confirming high systemic exposure to almorexant. C_{max} and AUC 0-24h values were slightly lower in rats and slightly higher in dogs on day 28 when compared to values of day1.

Conclusion: In contrast to zolpidem, almorexant-induced effects remained constant during 5 days of administration. Daily treatment with almorexant for one month did not lead to drug accumulation and no withdrawal symptoms were observed at discontinuation. There were no behavioral disturbances noted in rats and dogs during four weeks of repeated treatment.

0119

THE EFFECTS OF FEXOFENADINE AT STEADY-STATE ON SLEEP ARCHITECTURE

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Introduction: Fexofenadine is a nonsedating, selective histamine H1 receptor antagonist that does not cross the blood brain barrier. The aim of this study was to compare the effects of a first-generation antihistamine, chlorpheniramine and a second-generation antihistamine, fexofenadine, at steady-state, on nocturnal sleep architecture using polysomnography (PSG).

Methods: A single-site, randomized, double-blind, 2-treatment, 2-way crossover study of fexofenadine and chlorpheniramine in ten healthy male volunteers. Each subject was randomized to receive one capsule of fexofenadine HCl (Allegra[®]R) 180mg once each morning or chlorpheniramine 6mg (2mg in the morning and 4mg after 12 hours) for 2 days. Each treatment period was separated by a washout period of 7 days.

Results: There was no significant difference in total sleep time among baseline, Chlorpheniramine and fexofenadine. Chlorpheniramine and fexofenadine increased the sleep efficiency compared with baseline, but showed no significant differences. Chlorpheniramine and fexofenadine decreased the sleep latency compared with baseline, but showed no significant differences. In addition, chlorpheniramine reduced the percentage of REM sleep compared with baseline, but there was no significant change in percentage of stage REM sleep after dosing with chlorpheniramine and fexofenadine compared with baseline. And there also was no significant change in percentage of stage 1,2,3 and 4 sleep after dosing with chlorpheniramine and fexofenadine compared with baseline. Chlorpheniramine and fexofenadine increased arousal index compared with baseline, but showed no significant differences. Chlorpheniramine and fexofenadine increased apnea-hypopnea index compared with baseline, but showed no significant differences.

Conclusion: Our study suggests that both fexofenadine and chlorpheniramine have little adverse effect on sleep at steady-state, and more reduced psychomotor or cognitive function in chlorpheniramine was not associated with disturbed sleep, and that they did not affect upper airway function during sleep, so they could safely be prescribed patients with snoring or OSA. Although additional and controlled studies evaluating the usefulness of PSG as a tool for screening adverse effects on sleep in clinical settings are needed to confirm these preliminary results, we thought that PSG could be one of the methods for assessing CNS side effects of newly developed drug during sleep.

0120

EVALUATION OF POTENTIAL FOOD EFFECT ON PHARMACOKINETIC PARAMETERS OF A SINGLE DOSE OF 5 MG EPLIVANSERIN, A NEW SLEEP AGENT, ADMINISTERED ORALLY TO HEALTHY SUBJECTS

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Introduction: Eplivanserin is an Antagonist of Serotonin Two A Receptors (ASTAR) developed at a 5mg dose in insomnia characterized by nocturnal awakenings. Unlike benzodiazepines, eplivanserin does not bind to GABA receptors and increases slow wave sleep (SWS). The objective of this study was to assess the effect of food on the bioavailability of a single oral dose of 5 mg eplivanserin and evaluate its safety and tolerability in healthy subjects.

Methods: Single centre, open-label, randomized, two-period cross-over study. 20 healthy male and female subjects received a single oral dose of eplivanserin 5mg in fasted conditions and at the end of a high-fat breakfast. Blood samples for eplivanserin and its active N-demethyl metabolite, SR141342, were collected over a 240 h period after administration. Eplivanserin and SR141342 plasma concentrations were determined

by a validated LC-MS/MS method. Pharmacokinetic parameters were calculated using non-compartmental analysis. Safety was evaluated through monitoring of Treatment Emergent Adverse Events, laboratory tests, vital signs and ECG parameters.

Results: Eplivanserin and SR141342 pharmacokinetic parameters (C_{max} and AUCs) were not modified by food intake. Estimated ratios (fed/fasting) ranging from 0.96 to 1.07 and 90% CIs were within the [0.8 - 1.25] bioequivalence interval, whatever the parameters (C_{max} or AUCs). Eplivanserin 5 mg showed a good clinical and biological safety and tolerability in the fed and fasted states.

Conclusion: The administration of food (high-fat meal) does not affect the pharmacokinetics of eplivanserin or SR141342 following single-dose administration in healthy subjects. Therefore, eplivanserin can be administered regardless of food intake.

0121

REPEATED DOSES OF PANTOPRAZOLE HAVE NO INFLUENCE ON THE PHARMACOKINETIC PROFILE OF EPLIVANSERIN, A NEW SLEEP AGENT, IN HEALTHY MALE SUBJECTS

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Introduction: Eplivanserin is an Antagonist of Serotonin Two A Receptors (ASTAR) developed at a 5mg dose in insomnia characterized by nocturnal awakenings. Unlike benzodiazepines, eplivanserin does not bind to GABA receptors and increases slow wave sleep (SWS). Because eplivanserin exhibits pH-dependent solubility, the effect of pantoprazole, a gastric acid-reducing agent with a minimized potential of interaction with the cytochrome P450 system, was evaluated

Methods: Single centre, open-label, non-randomized, uncontrolled single-group study. Twelve healthy male subjects received a single oral dose of eplivanserin 5 mg alone followed by oral repeated doses of pantoprazole 40 mg OD for 8 days co-administered with eplivanserin on the 8th day. A wash-out of at least 13 days separated the two periods. Blood samples for assay of eplivanserin and its active N-demethyl metabolite, SR141342, were collected over a 96 h period after eplivanserin administration. Blood samples for pantoprazole assay were collected over a 24-h period after the last dose of pantoprazole. Eplivanserin, SR141342 and pantoprazole plasma concentrations were determined by validated LC-MS/MS methods. Pharmacokinetic parameters were calculated using non-compartmental analysis. Safety assessments included monitoring of Treatment Emergent Adverse Events (TEAEs), laboratory tests, vital signs and ECG parameters.

Results: Repeated oral administration of pantoprazole 40 mg did not affect the pharmacokinetic profile of eplivanserin and SR141342. Estimated ratios (co-administration/ alone) for C_{max} and AUCs ranged from 0.91 to 0.97 and 90% CIs were within the [0.8 - 1.25] bioequivalence interval. Overall, eplivanserin was well tolerated both alone and in combination with pantoprazole.

Conclusion: Co-administration of multiple daily oral doses of pantoprazole did not alter the pharmacokinetics of eplivanserin and its active metabolite SR141342. Therefore no dose adjustment is required when eplivanserin is co-administered with a drug that increases gastric pH

0122

REPEATED DOSES OF EPLIVANSERIN, A NEW SLEEP AGENT, DO NOT ALTER THE PHARMACOKINETICS OF AN ORAL CONTRACEPTIVE IN HEALTHY WOMEN

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Introduction: Eplivanserin is an Antagonist of Serotonin Two A Receptors (ASTAR) developed at a 5mg dose in insomnia characterized by

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nocturnal awakenings. Unlike benzodiazepines, eplivanserin does not bind to GABA receptors and increases slow wave sleep (SWS). In vitro data showed that eplivanserin has no potential to induce CYP1A, 2A and 3A. The effect of repeated doses of eplivanserin on the pharmacokinetic profile of oral contraceptive steroids was evaluated in vivo.

Methods: Single centre, open-label, non-randomized, uncontrolled single-group study. Eighteen healthy young female subjects received a repeated oral dose of MinidrilR (ethinylloestradiol and levonorgestrel) for 21 days, co-administered with eplivanserin 60 mg from Day 15 to Day 21. Blood samples were collected over a 24 h period after dosing, on Day 10, 13 and 21 for ethinylloestradiol and levonorgestrel assays, and on Day 21 for eplivanserin and SR141342, its active N-demethyl metabolite, assays. Ethinylloestradiol and levonorgestrel were assayed by a validated gas chromatography/mass spectrometry method after liquid-liquid extraction, and eplivanserin and SR141342 by a validated LC-MS/MS method. Pharmacokinetic parameters were calculated using non-compartmental analysis. Safety assessments included monitoring of Treatment Emergent Adverse Events (TEAEs), laboratory tests, vital signs, ECG parameters.

Results: Repeated oral administration of eplivanserin 60 mg did not affect the pharmacokinetic profile of ethinylloestradiol or levonorgestrel. 90% confidence intervals of estimated ratios (co-administration/ alone) for C_{max}, C_{min} and AUC₀₋₂₄ were within the [0.8 - 1.25] bioequivalence interval, for both ethinylloestradiol and levonorgestrel. Overall, the combination of eplivanserin and MinidrilR was well tolerated.

Conclusion: Co-administration of repeated daily doses of eplivanserin did not alter the pharmacokinetics of an oral contraceptive containing ethinylloestradiol and levonorgestrel, and therefore should not affect the contraceptive efficacy.

0123

INFLUENCE OF REPEATED DOSES OF KETOCONAZOLE, A POTENT CYP 3A4 INHIBITOR, ON THE PHARMACOKINETIC PROFILE OF EPLIVANSERIN, A NEW SLEEP AGENT, IN HEALTHY MALE SUBJECTS

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Introduction: Eplivanserin is an Antagonist of Serotonin Two A Receptors (ASTAR) developed at a 5mg dose in insomnia characterized by nocturnal awakenings. Unlike benzodiazepines, eplivanserin does not bind to GABA receptors and increases slow wave sleep. In vitro data showed that eplivanserin is slightly metabolized by CYP3A4 (fm=15%). The effect of repeated doses of ketoconazole, a potent CYP3A4 inhibitor, on the pharmacokinetic profile of eplivanserin was thus evaluated.

Methods: Single centre, open-label, non-randomized, uncontrolled single-group study. 12 healthy male subjects received a single oral dose of eplivanserin 5 mg alone followed by a repeated doses of ketoconazole 200 mg OD for 8 days coadministered with eplivanserin 5mg on the 8th day. A wash-out of at least 13 days separated the two periods. Blood samples for eplivanserin and its active N-demethyl metabolite, SR141342, were collected over a 96 h period after eplivanserin administration. Blood samples for ketoconazole assay were collected over a 24 h period after the last dose of ketoconazole. Eplivanserin and SR141342 plasma concentrations were determined by a validated LC-MS/MS method and ketoconazole by a validated HPLC method using fluorescence detection. Pharmacokinetic parameters were calculated using non-compartmental analysis. Safety assessments included monitoring of Treatment Emergent Adverse Events (TEAEs), laboratory tests, vital signs, ECG parameters.

Results: Ketoconazole did not affect the pharmacokinetic profile of eplivanserin or SR141342. Estimated ratios (co-administration/ alone) for C_{max} and AUCs ranged from 0.88 to 1.05 and 90% CIs were within the bioequivalence interval, except for eplivanserin C_{max} with a ratio

estimate [90 CI] of 1.15 [1.03 - 1.29]. Overall, eplivanserin was well tolerated both alone and in combination with ketoconazole.

Conclusion: Co-administration of multiple daily doses of ketoconazole did not meaningfully alter the pharmacokinetics of eplivanserin or SR141342.

0124

CHLORPHENIRAMINE EFFECTS ON REM SLEEP IN RATS SUBMITTED TO STRESS BY IMMOBILIZATION

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Introduction: Chlorpheniramine is a selective antagonist of the H1 histaminergic receptor subtype and is widely used as an antiallergenic agent. However, the effects in humans include somnolence. Previous reports in rats indicate that chlorpheniramine affects sleep in rats, mainly by decreasing REM sleep. On the other hand, stress by immobilization induces an important increase in the percentage of REM sleep. As the central histaminergic system has been involved in stress response, in the present study we analyzed the effects of blocking histaminergic receptors in REM sleep induced by immobilization stress.

Methods: Adult male Wistar rats were chronically implanted for sleep recording. After a recovery period, rats were habituated to the recording conditions. Immobilization stress was induced by placing the rat in a small cylinder for 2 hours. Experimental conditions were: A. Control; B. Stress; C. Stress plus vehicle and D.- Stress plus chlorpheniramine.

Results: Results showed that the increase of REM sleep observed after immobilization stress was completely abolished in the group that received chlorpheniramine. Furthermore, the decrease of REM sleep was significant compared to the non stressed control rats. REM sleep latency was also significantly larger than that observed in the control group. The present results suggest that REM sleep is quite sensitive to histaminergic blockage.

Conclusion: It seems that Chlorpheniramine is mainly acting on the mechanisms generating REM and not only in the response to stress.

0125

SLEEP ONSET AND MAINTENANCE IN PATIENTS WITH CHRONIC INSOMNIA TREATED WITH ADIPIPLON IN A CROSS-OVER STUDY

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Introduction: Adipiplon, a GABA_A partial agonist with preference for $\alpha 3$ subunit receptors, has been shown to induce onset of sleep as assessed by Latency to Persistent Sleep (LPS). This study evaluated the efficacy of different doses and formulations of the drug in sleep maintenance.

Methods: This randomized, double-blind, placebo-controlled, cross-over study evaluated adipiplon compared to placebo on sleep maintenance as assessed by Wake After Sleep Onset (WASO) in 36 patients with chronic insomnia, aged 25 - 64. Sleep maintenance difficulty was confirmed with a two night baseline polysomnography (PSG). Using a balanced incomplete block design, each patient was assigned to five treatment periods of three nights each where they received placebo or one of eight possible treatments. These treatments contained three different controlled release ("A", "B" or "C") and/or immediate release formulations spanning total doses of 3 to 12mg of adipiplon. PSGs occurred on the first 2 and pharmacokinetics on the third night of each treatment period.

Results: Adipiplon demonstrated statistically significant improvement over placebo for reducing WASO with all doses and formulations tested

(WASO was 73.4 minutes for placebo and 41.7 - 62.7 minutes for the 8 adiplon treatments). Statistically significant improvements were also noted for all doses of formulation "A" for Total Sleep Time, Sleep Efficiency, Number of Arousals, LPS, and quality of sleep. No next day effects, measured by Digit Symbol Substitution Test (DSST) and Visual Analog Scales of sedation, occurred with formulation "A" at any dose (3-10mg). Adiplon was generally well tolerated with headache and somnolence reported most commonly. There were no deaths, serious AEs or discontinuations due to drug-related AEs during the study.

Conclusion: In patients with chronic insomnia, adiplon was a well-tolerated, sedative hypnotic effective in inducing sleep onset and maintenance without residual next day sedative effects using formulation "A" at doses between 3 and 10mg.

0126

SEX DIFFERENCES IN SLOW WAVE ACTIVITY AND THETA SPECTRAL POWER DENSITY WITH TIAGABINE

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Introduction: The GABA reuptake-inhibitor tiagabine increases EEG spectral power density in SWA and theta frequencies. We examined whether sex affects spectral power response to tiagabine.

Methods: Power density was calculated for NREM (stages 1, 2, 3, and 4) during a baseline night (14m, age=28.7 +/- 12.1; 14f, age=27.6 +/- 8.5), a night with 8mg tiagabine (7m, age=25.0 +/- 5.71; 7f, age=30.14 +/- 10.96), and during the fourth night of sleep restriction to 5 hours (7m, Age=28.14 +/- 7.27; 7f, Age=25.0 +/- 4.76). Power density was calculated for each 1-Hz band up to 16 Hz, as well as for slow wave activity (SWA; 0.75-4.5 Hz) and theta (4.75-7.75 Hz) bands. ANCOVAs, covarying for age, compared males vs. females for 1) absolute spectral power at baseline, 2) relative (to baseline) spectral power with tiagabine, and 3) relative spectral power during sleep restriction.

Results: Baseline absolute spectral power from 1-4 Hz and for SWA was greater for females than males ($p < 0.05$ for all). With tiagabine, females had greater relative spectral power than males from 1-8 Hz and for SWA and theta ($p < 0.05$ for all). After sleep restriction, relative spectral power from 3-6 Hz was greater for females compared to males ($p < 0.05$ for all).

Conclusion: Relative spectral power density in SWA and theta frequencies with tiagabine is greater in females than males. Differences in body weight may contribute to the sex difference in drug response. However, the consistent observation that females have more slow wave activity at baseline and have a larger increase in SWA with sleep loss as well as with tiagabine suggests that heightened EEG synchrony in females may be related to biological sex differences such as GABA-A receptor density or sex specific neurosteroids.

Support (optional): Cephalon, Inc.

0127

MODAFINIL AMELIORATES SLEEP-DEPRIVATION IMPAIRMENTS ON PAVLOVIAN FEAR CONDITIONING

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Introduction: Inadequate sleep, both acute and chronic, is becoming increasingly common in our 24-hour society. Recent studies suggest sleep is critical to consolidation of hippocampal-dependent memories (i.e. verbal learning) in human subjects. This current study aims to use a mouse model in assessing 1) the impact of sleep deprivation for Pavlovian fear conditioning and 2) the efficacy of modafinil, a novel wake-promoting drug, to ameliorate memory impairments caused by sleep deprivation.

Methods: A low dose of modafinil (0.75mg/kg, i.p.) or vehicle was administered 15 minutes prior to fear conditioning training, consisting of a paired tone and footshock. During the first light phase (12 hours) after training, half of the mice were sleep deprived by gentle poking with a wooden dowel. The control group was allowed to sleep during the light phase and was gently poked during the dark phase to control for non-sleep related consequences of poking across groups. Following 72 hours after training, all mice were tested for contextual and cued fear.

Results: Sleep deprivation disrupted contextual memory. Modafinil rescued the effects of sleep deprivation, restoring contextual memory to the level of non-deprived controls.

Conclusion: This provides further evidence that sleep plays an important role for memory and the lack of sleep may cause detriments for consolidation processes. In addition to modafinil's use as a wake-promoting agent, it may also be used to ameliorate sleep-deprivation-related memory impairments.

0128

ANALYZING THE TIME COURSE OF PERFORMANCE EFFECTS OF A HYPNOTIC DRUG

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Introduction: Studies of performance effects of GABA-A agonist hypnotics have produced inconsistent findings. We hypothesized that a consistent profile could emerge from systematic hourly tabulation of double-blind placebo-controlled studies of cognitive and psychomotor data. Using racemic zopiclone, a GABA-A agonist hypnotic only available in Europe, effects were sought in separate analyses of coordination, arousal, attention, sway, memory, sleep latency and driving ability.

Methods: Searches of the MEDLINE and SearchLight databases were used to find experimental studies on cognitive or performance effects, which were tabulated into hourly reports where similar tests were clustered into specific domains of cognitive and psychomotor function.

Results: Thirty-two racemic zopiclone studies were chosen for review. Racemic zopiclone showed statistically significant decrements compared to placebo across a broad range of measures for up to 8 hours. Beyond 8 hours the behavior most consistently affected was driving (simulator driving and road driving), with impairments in lateral tracking demonstrated in 4 of the five studies 9 or 10 hours after dosing. Visual saccade measures also showed a persistent effect: three of the six studies found impairments 10 hours after dosing. A significant effect was seen on sleep latency 9 and 12 hours after dosing, but not from 14 to 22 hours. Impairments appeared in other measures less consistently.

Conclusion: Systematic tabulations of cognitive and performance measures across studies may help to determine the most appropriate measures for assessing effects of hypnotics at different time points. More statistically significant impairments presented in tests of driving performance, visual saccades, and sleep latency than in other tasks tested eight or more hours after dosing with racemic zopiclone. Whether a similar pattern will emerge with other hypnotics is not known at present. Qualifications to the method will be discussed.

0129

IN WHICH TESTS DO ZOLPIDEM RESIDUAL EFFECTS PERSIST LONGEST?

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Introduction: Many tests been administered to assess the cognitive and motor impairments produced by zolpidem, but their results are often inconsistent or contradictory. To resolve these, we reviewed the hourly findings from the double-blind placebo-controlled studies that quantified the cognitive and psychomotor effects of ingesting zolpidem. Differen-

Category C—Pharmacology

tial effects were sought in separate analyses of coordination, arousal, attention, sleep latency and driving ability.

Methods: Searches of the MEDLINE and SearchLight databases located 28 experimental studies of the effects of zolpidem on cognition or performance. The findings in these studies were tabulated and mapped into hourly reports of test results.

Results: Most studies reported significant impairments extending for at least 3 hours after dosing with 10mg of zolpidem. Tests of digit symbol substitution, night-time postural sway, delayed free recall, and sleep latency continued to show statistically significant effects for five or more hours after dosing. On tests of simple reaction time, choice reaction time, divided attention, Sternberg numeric working memory, immediate free recall and driving, statistically significant impairments were not present five or more hours after dosing.

Conclusion: In an hour-by-hour tabulation of cognitive and performance measures after ingesting zolpidem, significant medication effects continued for five or more hours in tests of some -but not all - domains. When adjusted for confounding factors, differences in the persistence of significant impairments may reflect differences in the sensitivity of the tests to the effects of zolpidem.

0130

INFLUENCE OF SLEEP EXTENSION ON CIRCADIAN TIMING OF SLEEP

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Introduction: More than one-third of adults in the USA obtain <6.5h sleep per night, a sleep duration that is considered inadequate. When adults maintain ~8h adequate sleep schedules, sleep is initiated on average ~2h after the dim light melatonin onset (DLMO). The aim of the current study was to determine the influence of short sleep schedules and of sleep extension on circadian phase and the phase angle of entrainment.

Methods: Twenty-two subjects (10 women, 12 men) aged 22.7±4.2 with habitual short sleep schedules participated. After 2-weeks of maintaining their habitual ~6h sleep schedules at home, participants completed a 24h laboratory visit to assess circadian phase. Twelve subjects were then randomly assigned to extend their sleep by ~2h per night and the remaining ten were assigned to maintain their habitual short sleep schedule for another 2-weeks. Circadian phase was then reassessed. Phase angle of entrainment was defined as the time between DLMO and habitual bedtime. Sleep schedules were verified with actigraphy.

Results: Bedtime occurred ~4h after DLMO in subjects who maintained ~6h sleep schedules. A significant change in phase angle of entrainment was found for subjects who extended their sleep ($p < 0.05$) such that bedtime occurred ~2.7h after DLMO. This change in phase angle of entrainment was mainly due to the change in bedtime and not a change in the clock hour of the DLMO.

Conclusion: Short sleep schedules of ~6h per night resulted in subjects initiating sleep at a later internal biological time than previously reported for adults with ~8h adequate sleep schedules. Sleep extension altered the phase angle of entrainment such that sleep occurred at an earlier biological time more similar to habitual ~8h sleepers. Thus, alterations in the phase angle of entrainment may contribute to the physiological and behavioral changes reported to be caused by short sleep schedules.

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0131

ACHIEVING A COMPROMISE PHASE POSITION FOR PERMANENT NIGHT SHIFT WORK USING SCHEDULED BRIGHT LIGHT AND DARKNESS

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Introduction: This is the third in a series of studies designed to produce and maintain a compromise phase position for permanent night work, in which the sleepest time of the circadian cycle is delayed out of the night work period and into the first half of daytime sleep, improving night shift alertness and subsequent daytime sleep, but not precluding late nighttime sleep on days off.

Methods: Subjects underwent 3 night shifts (23:00-7:00), had two days off, and then completed 4 more night shifts. During night shifts, an experimental group (n=12) received five 15-minute light pulses (~ 3,200 lux, ~1,100 μ W), interspersed by 45 minutes of room light. The first pulse began at 00:45 and the last pulse ended at 5:00. They wore dark sunglasses (~ 15% transmission) when outside. Home sleep episodes in darkened bedrooms occurred from 8:30-15:30 after night shifts, except for sleep before days off which was 8:30-13:30. Sleep episodes were from 3:00-12:00 on days off. Subjects went outside for ≥ 15 minutes after awakening to receive a "light brake" to keep them from delaying past the compromise phase position, defined as a dim light melatonin onset

(DLMO) of 3:00. A control group (n=12) remained in room light during night shifts, wore lighter sunglasses (~ 36% transmission), and had unrestricted sleep and outside light exposure.

Results: The final DLMO for the experimental group was significantly later than the control group (4:34 ± 1.5 vs. 00:39 ± 2.9 h, $p < 0.001$). Experimental subjects had faster and less variable reaction times during night shifts.

Conclusion: Circadian phase for the experimental group was close to the target compromise phase position, with concomitant improvements in nighttime performance, relative to a control group.

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0132

SYSTEMATIC INDIVIDUAL DIFFERENCES IN CIRCADIAN CONTRIBUTION TO NEUROBEHAVIORAL IMPAIRMENT DURING SLEEP DEPRIVATION

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Introduction: Neurobehavioral impairment due to sleep deprivation exhibits substantial, replicable individual variability. Per the two-process model, neurobehavioral impairment reflects sleep homeostasis and circadian rhythm. We examined whether individual differences in these distinct processes are also replicable, considering two different implementations of the model. Model 1: $Y \sim (S_0 - 1) * \exp(\text{RATE} * (\text{TW} - \text{T})) + \text{AMP} * \sin(2\pi * (\text{T} - \text{PH}) / 24) + \text{BL}$. Model 2: $Y \sim S_0 * \exp(\text{RATE} * (\text{TW} - \text{T})) + \text{AMP} * \sin(2\pi * (\text{T} - \text{PH}) / 24) + \text{BL}$. Here T is clock time, TW awakening time, PH circadian phase, and S0 two different representations of initial homeostatic level. Model parameters are RATE for homeostatic build-up rate, AMP for amplitude of circadian rhythm, and BL for baseline performance capability.

Methods: As part of a larger study, 10 healthy young adults (7 females; age 22-40; intermediate circadian phase preference) underwent two 36h total sleep deprivation sessions, each preceded by two 12h baseline nights (22:00-10:00) to satiate sleep need. Neurobehavioral performance was tested every 2h on the psychomotor vigilance task (PVT). For each sleep deprivation session, models 1 and 2 were fitted to PVT lapses (reaction times > 500ms) using nonlinear mixed-effects regression. Random effects were included for parameters expected to vary among individuals: RATE, AMP, BL. Subject-specific empirical Bayes estimates of these parameters were subjected to random-effects ANOVA to estimate replicability of the individual differences, as quantified with the intraclass correlation coefficient (ICC).

Results: For model 1, replicability was 30% for RATE, 59% for AMP, and 69% for BL. For model 2, replicability was 72% for RATE, 60% for AMP, and 69% for BL. In both models, RATE and BL parameter estimates were highly correlated ($r > 0.94$).

Conclusion: Two components of the replicable individual differences in neurobehavioral impairment from sleep deprivation, homeostatic build-up rate and circadian amplitude, each separately showed fairly high within-subject replicability depending on model parameterization. Here homeostatic build-up rate could not be estimated independently of baseline performance. Systematic individual differences were shown reliably, however, for the contribution of circadian amplitude to PVT performance impairment during sleep deprivation.

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0133

ASSOCIATION BETWEEN REST/ACTIVITY RHYTHMS AND MORTALITY IN COMMUNITY-DWELLING OLDER MEN

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Introduction: Prior research has suggested that disruptions in biological rhythms (including rest/activity) occur with advancing age. However, the association between rest/activity rhythms and mortality rates in older adults is uncertain.

Methods: To test the hypothesis that disturbed rest/activity rhythms are associated with increased mortality rates, we measured activity patterns using wrist actigraphy for an average of 5.2 nights (range 1-13) in a cohort of 3053 community-dwelling men aged 67 and older. Rest/activity rhythm parameters were obtained through cosinar analysis. Parameters of interest included acrophase (time of peak activity), amplitude (height of peak), mesor (mean activity) and F-value (robustness), and were expressed as quintiles. Vital status, with cause of death verified through death certificates, was ascertained during an average of 5.9+0.6 years of follow-up.

Results: After controlling for multiple potential confounders including age, race, alcohol, health status, IADL impairments, cardiovascular disease, diabetes, cognitive impairment, depressive symptoms and renal function, there was a graded inverse association between amplitude and mortality rates (p-trend<.001) with higher mortality rates observed in the lowest quintile of amplitude (Hazard ratio [HR]=2.34, 95%CI, 1.23-4.43) compared with the highest quintile. A similar association was observed between decreasing F-value and higher rates of mortality (p-trend=0.002). Mortality rates were greatest for the lowest quintile of F-value (HR=1.88, 95%CI, 1.08-3.25), compared with the highest quintile. There was a u-shaped association between mortality rates and acrophase quintiles, with mortality rates greatest in the highest and lowest quintiles (HR=1.85, 95%CI, 1.08-3.18) and (HR=1.91, 95%CI, 1.12-3.24) respectively, compared with the third quintile. There was no association between quintiles of mesor and increased mortality rates (p-trend=0.442).

Conclusion: Disrupted rest/activity rhythms, especially deviance in time of peak activity (acrophase), lower peak activity level (amplitude) and robustness (F-value) are predictors of increased mortality rates in older community-dwelling men. Further research should examine potential biological mechanisms underlying this association.

0134

PHASE DELAY SHIFTS TO BLUE-ENRICHED VS. STANDARD POLYCHROMATIC WHITE LIGHT IN HEALTHY OLDER PEOPLE IN A SEMI-AMBULATORY SETTING

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Introduction: Light exposure in the late subjective day/ early subjective night produces phase delays of the human circadian system. This effect of light is wavelength-dependent, with blue (~460nm) monochromatic light of 12.1µW/cm2 or 2.8.E+13 photons/cm2/s (equivalent to only ~5 photopic lux) achieving the same phase delays as ~10,000 photopic lux

of polychromatic light in young subjects. One treatment of age-related sleep disruption has involved giving evening light exposure to re-align the timing of the sleep-wake cycle and circadian rhythms, although up to now only polychromatic white light has been used. The present study compared the phase delay shift produced by two different fluorescent lamps, standard polychromatic white vs. blue-enriched polychromatic white light.

Methods: We recruited older adults free from medical, psychological, ophthalmologic or sleep disorders for a 13-day semi-ambulatory study. Subjects remained in the laboratory each evening and night, but were free to leave during the day. Each was randomized to receive either blue-enriched or standard white light at the same illuminance level. After 3 baseline days, on Day 4 they underwent a 24h constant posture in dim light (CP) to assess their melatonin rhythm. On days 5 to 8, they received evening light exposure for 2h starting 3h before bedtime. On day 9, they underwent a second CP to reassess their melatonin rhythm. Dim light melatonin onset from plasma or saliva (assayed using a direct RIA, ALPCO Diagnostics) was used as a marker of circadian phase. Between-group comparisons were made using a t-test.

Results: We studied 10 subjects (mean age=63.3 [57-79], 4M). We were able to assess the phase shift for only 4 of the 5 subjects in the blue-enriched group because one subject's melatonin was completely suppressed during the second CP. Mean illuminance (±SD) in the blue-enriched and standard white light groups was 1.07.E+15 ± 0.07.E+15 photons/cm2/s and 1.025.E+15 ± 0.12.E+15 photons/cm2/s, respectively (p=0.6). Mean phase delays (±SD) of 116±48min and 101±32min were obtained in the blue-enriched and standard white light groups, respectively (p=0.5).

Conclusion: At the same illuminance levels, both light sources produced phase delays of similar magnitude in these healthy older people. Additional studies will be needed to determine whether differences between these light sources would be produced using light of a lower illuminance or with shorter duration light exposures.

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0135

ALTERED CIRCADIAN PROFILES OF ENDOGENOUS MELATONIN IN PATIENTS WITH RETINITIS PIGMENTOSA

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Introduction: Light is the main synchronizer of circadian rhythms via the pineal hormone, melatonin. We and others have shown that visually impaired individuals with retinitis pigmentosa (RP) have a higher incidence of sleep disturbances. To investigate this phenomenon further, we assessed the circadian patterns of melatonin secretion, daytime sleepiness and alertness in blind RP patients.

Methods: Twelve RP patients with non-recordable electroretinogram responses and less than 20 degrees of central visual field were compared to 12 controls with normal vision, matched for age and body mass index. Salivary melatonin levels were obtained for 44 hours, at two-hourly interval from 07:00 to 23:00. Alertness and daytime sleepiness were measured using the maintenance of wakefulness test (MWT) and multiple sleep latency test (MSLT), respectively.

Results: The expected nocturnal melatonin rise seen in controls was absent in the RP patients who exhibited consistently significantly higher

melatonin values during the day. Peak melatonin levels at 11:00 in the RP patients were higher than in the control group ($p=0.002$). At 11:00 the RP patients also had more daytime sleepiness and more difficulty staying awake, with a mean sleep onset latency of 7 ± 5 min versus 19 ± 1 min for the controls on the MSLT ($p=0.001$), and 21 ± 9 min versus 29 ± 1 for the controls on the MWT ($p=0.006$).

Conclusion: The circadian rhythm of melatonin secretion in blind RP individuals was significantly different to that of normally sighted controls, suggesting that the photic input to the suprachiasmatic nucleus may be altered by photoreceptor degeneration. Higher daytime melatonin levels were associated with daytime sleepiness in the RP patients, indicating that abnormally timed melatonin may induce sleepiness in this population.

0136

NEUROBEHAVIORAL PERFORMANCE IN OLDER ADULTS LIVING ON A 20H DAY

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Introduction: Performance has been shown previously to be affected by both homeostatic and circadian processes. Forced-desynchrony studies have quantified the magnitude of the effect of these processes, although primarily in young adults. The present analysis aims to assess how time awake and circadian phase affect performance on two different tasks in a group of older adults living on a 20h day.

Methods: Ten healthy subjects (age 64.00 ± 5.98 , 5f) participated in a study consisting of 3 baseline days followed by 18, 20h forced-desynchrony "days" (13.33h wake). A 4-min addition test (ADD) and a 10-min psychomotor vigilance test (PVT) were administered every 2h beginning 2h after scheduled waketime. Core body temperature (CBT) data were collected throughout the study to assess circadian phase. Performance data from each subject were binned into 2h "time awake" bins and 60 degree "circadian phase" bins. Within-subject averages for correct additions, PVT median reaction time (RT) and number of lapses ($RT>500$ msec) were analyzed via mixed model analysis for factors TIME AWAKE and CIRCADIAN PHASE.

Results: Performance degraded as time awake increased, with a significant main effect of TIME AWAKE on all measures ($p<0.01$). There was also a significant main effect of CIRCADIAN PHASE on all measures ($p<0.01$), with worst performance surrounding the CBT minimum, between 300 and 60 degrees. There was a significant interaction between TIME AWAKE and CIRCADIAN PHASE on PVT lapses ($p<0.05$).

Conclusion: In these older subjects, we observed a significant effect of TIME AWAKE and CIRCADIAN PHASE on two different performance tasks. In PVT lapses, where there was a significant interaction of main effects, circadian phase had an increasing effect on performance as time awake increased. Future studies which include additional measures of performance and comparisons between young and older subjects are needed to determine if these effects are of similar magnitude.

Support (optional): NIH-AG06072; NIH-AG09975; NIH-RR02635

0137

LINEAR DISSIPATION OF HOMEOSTATIC SLEEP PRESSURE ACROSS THE NIGHT BETWEEN THE TWENTIES AND THE SIXTIES

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Introduction: The decline in slow-wave activity (SWA) across the night is thought to reflect the dissipation of homeostatic sleep drive. Studies suggested age-related changes in the function (linear vs. exponential)

and in the slope underlying this decline. We evaluated if SWA in men and women dissipates differently with increasing age across topographical locations.

Methods: The sleep of 87 healthy volunteers (48 young, 20-30y and 39 middle-aged, 40-60y) was analyzed. Spectral analysis in SWA (1.00-5.00Hz) was performed per N-REM periods for Fp1, F3, C3, P3, and O1 (expressed as % of the night). Linear and exponential decay functions were applied on individual datasets for each derivation. ANOVAs (2 age groups*2 genders*5 derivations) were performed on goodness of fit coefficient (R2), slope, and intercept calculated individually for each derivation.

Results: For 77% young (18F-19M; $23.7y\pm 2.4$) and 87% middle-aged subjects (20F-14M; $53.8y\pm 3.7$; χ^2 , n.s.), R2 of exponential fit was not significantly higher than of linear. Subsequent analyses were performed with this subsample of subjects using linear fit. Anterior derivations (FP1+F3) showed better fits than in posterior derivations (P3+O1). Slopes differed between age groups and across derivations: middle-aged subjects had a smaller SWA decay rate ($p<0.004$) and anterior regions showed a steeper SWA decay ($p<0.001$). SWA intercept was higher in young subjects ($p<0.001$), in anterior derivations ($p<0.000$) and tended to be higher in women ($p<0.07$).

Conclusion: For 80% of subjects between their twenties and sixties, linear function adequately explained SWA decline across the night with no significant impact of age on this proportion. In these subjects, anterior derivations better fitted linear model and had a steeper decline of SWA than posterior derivations. The dynamic of homeostatic dissipation was similar in men and women. Our results support the notion that age-related shallower dissipation of sleep homeostatic drive is similar across scalp topography and between genders.

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0138

ADAPTATION OF THE HUMAN CIRCADIAN SYSTEM BY PRIOR LIGHT HISTORY

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Introduction: Light is the most potent stimulus to suppress melatonin secretion and shift the phase of the endogenous circadian timing system. However, the effects of the preceding light history on the sensitivity of the circadian system to subsequent light exposure are less well understood. Therefore, we tested the hypothesis that prior light history modulates the sensitivity of the human circadian timing system to submaximal light stimuli, as assessed by: a) the magnitude of melatonin suppression; and b) the phase delay of the melatonin rhythm.

Methods: Thirteen healthy young adults (6 females; 18-30 years of age) completed a 32-day inpatient protocol and were included in this analysis. Each subject was exposed to four 6.5-h light stimuli: two control dim-light exposures ($0.16\mu\text{W}/\text{cm}^2$; ~ 0.5 lux) and two experimental bright light exposures ($23\mu\text{W}/\text{cm}^2$; ~ 90 lux). Each control and experimental light exposure was preceded by 3 days of either very dim light (~ 0.5 lux) or typical indoor light level (~ 90 lux) throughout the waking episode, in counter-balanced order. Plasma melatonin was sampled hourly during constant posture conditions in dim light prior to, during, and following the 4 light exposures. Melatonin suppression was calculated as the relative change in area under the curve comparing each 6.5-h light exposure with the 6.5-h time window, 24 hours earlier. Phase shifts were calculated by comparing the midpoint of the melatonin profile on the day following the light exposure with that on the day preceding the light exposure. T-tests were used to compare the melatonin suppression and phase shift results between very dim and brighter prior light conditions. Results are reported as mean \pm SEM with significance of $p\leq 0.05$.

Results: Melatonin suppression in the very dim and brighter prior light conditions were $85.05\% \pm 4.13$ and $53.80\% \pm 7.21$, respectively

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($p=0.001$). Phase delays in the dim and brighter prior light conditions were $1.67 \text{ h} \pm 0.12$ and $0.98 \text{ h} \pm 0.12$, respectively ($p=0.004$). We found significant adaptation (sensitization) of both melatonin suppression (58% increase) and phase shifts (70% increase) when the experimental light exposures followed the very dim background light level than the brighter light level.

Conclusion: The light intensity preceding a light exposure modulates the sensitivity of the human circadian timing system to that light exposure.

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0139

INFLUENCE OF ENDOGENOUS CIRCADIAN SYSTEM, PHYSICAL EXERCISE, AND THEIR INTERACTION ON CARDIOVASCULAR RISK FACTORS

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Introduction: The risk of adverse cardiovascular events has a day/night pattern peaking in the morning (~9AM), possibly related to a day/night pattern of behavioral triggers, circadian factors, and/or their interaction. Irregular physical exertion can be a trigger for myocardial infarction in vulnerable people. We tested the effect of 1) the circadian system; 2) physical exercise; and 3) their interaction, on hemodynamic, autonomic, and hemostatic markers of cardiovascular risk.

Methods: 12 healthy adults (6 female) underwent a 13 day protocol in dim light, wherein subjects performed exercise at all phases of the circadian cycle. This was achieved by scheduling 12 recurring 20-hour 'days'. On each 'day' subjects performed a 15-min exercise test (cycling 60% HRmax), preceded and followed by 20-min rest periods. Body temperature was used to assess circadian phase (the fitted minimum was assigned 0°). Data were binned in 60°-bins and analyzed with Mixed Model ANOVA.

Results: There were significant circadian rhythms in systolic blood pressure (peak 240°; equivalent to ~9 PM in these subjects), heart rate (peak 180°-240°), plasma epinephrine (peak 120°), plasma norepinephrine (peak 180°-240°) and cardiac vagal markers (trough at 180°). The most rapid increase in epinephrine occurred at ~60° (equivalent to ~9AM). The impact of the circadian system on plasma epinephrine (peak-trough change: 115% during baseline and 78% during exercise) was similar to the impact of exercise itself (83% increase from rest). There were no significant circadian rhythms in diastolic blood pressure or whole blood platelet aggregation. There was no statistical interaction between circadian and exercise effects except for vagal markers, where the circadian rhythm disappeared during exercise.

Conclusion: These data demonstrate significant effects of the circadian system on hemodynamic and autonomic function, but not on hemostatic function. These potential risk factors did not peak at the vulnerable circadian phase equivalent to 9 AM. These data suggest that circadian rhythms in cardiovascular function in young healthy subjects may actually be cardioprotective. Alternatively, the rate of change of cardiovascular risk markers—rather than the absolute value—may be more relevant to the timing of cardiovascular events. Finally, the day/night distribution of potential behavioral triggers are likely to interact to affect the pattern in overall risk.

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0140

ENDOGENOUS CIRCADIAN RHYTHM OF ACTIVITY IN HUMANS

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Introduction: Day/night activity patterns that persist in constant darkness have been found in many species. Such 'free-running' activity patterns have been used as circadian phase markers, but in animal studies the endogenous circadian cycle is often not uncoupled from the sleep/wake cycle. It is possible in humans to uncouple circadian rhythms from the sleep/wake cycle by use of a forced desynchrony (FD) protocol, and thereby uncover any true endogenous circadian pattern of activity.

Methods: 10 healthy adults underwent activity recording each minute using Actigraphy for 2 weeks of a regular sleep/wake schedule at home, followed by a 13 day FD protocol in dim light in a laboratory. In the FD subjects were scheduled to 12 recurring 20-h 'days', involving 13.33 h scheduled wakefulness and 6.67 h scheduled sleep each 'day'. On each wake period subjects performed a test battery, and thereafter remained awake and free to perform spontaneous activities, excluding exercise and sleep. Body temperature was used to assess circadian phase (the fitted minimum was assigned 0°). Activity data were binned in 60°-bins and subject to cosinor analysis.

Results: As expected, there was a clear day/night pattern of mean activity in the home environment (mean activity: 234 arb units/min; ratio of activity during scheduled sleep to wakefulness was 1:15). Average activity was significantly reduced in the FD (mean: 97 arb units/min; with a less pronounced scheduled sleep/wake ratio of 1:8). Analyzing the free-times during wakefulness in the FD, despite constraints on activity imposed by being confined to a laboratory, the subjects exhibited a significant circadian rhythm in activity ($p = 0.008$) with a minimum at 0° circadian phase (~5 AM in this group), a peak at 180° (~5 PM), and a peak-to-trough change of 30% of the daily average. The standard deviation of activity fluctuations also exhibited similarly significant circadian rhythmicity with identical phases of the peak and trough.

Conclusion: In the FD protocol, mean and variability of activity are driven by the endogenous circadian system to lower values in the middle of the biological night and higher values in the biological day. We speculate that if preferred times to be more active in unconstrained conditions coincide with the endogenous circadian rhythm of activity this would have implications for the optimal time to perform work or volitional exercise, and deserves further study.

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0141

REDUCTION OF SCALE-INVARIANT ACTIVITY CONTROL WITH AGING AND ALZHEIMER'S DISEASE: POSSIBLE INVOLVEMENT OF THE CIRCADIAN PACEMAKER IN MULTISCALE REGULATION OF HUMAN ACTIVITY

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Introduction: Activity fluctuations in humans and other animals display an intrinsic scale-invariant, or fractal, pattern that persists over a wide range of time scales from minutes to at least ~24 h. The scale-invariant pattern can be characterized by a specific power-law increase in the fluctuation amplitude as a function of the time scale. In experimental animals, lesioning the suprachiasmatic nucleus (SCN) abolishes the scale-invariant behaviors at time scales $> \sim 3.6$ hours, indicating that the SCN influences activity regulation at multiple time scales. Since the SCN's function has been reported to degrade with aging and in Alzheim-

er's disease (AD), we hypothesize that there could be an SCN-related disturbance in the scale-invariant activity regulation in these groups.

Methods: We studied (1) 13 young control subjects; (2) 13 elderly control subjects; (3) 13 elderly diagnosed with early AD; and (4) 14 elderly diagnosed with advanced AD. Activity was continuously recorded using wrist-actigraphy over one week, while subjects maintained regular sleep/wake schedules. Detrended fluctuation analysis (DFA) was used for assessment of scale-invariant patterns in activity fluctuations during scheduled wakeful periods.

Results: Activity in healthy young controls during wakefulness exhibited robust scale-invariant patterns at time scales from minutes to 10 h, characterized by a DFA scaling exponent, $\alpha=0.93\pm 0.02$ (mean \pm SD). Compared to this control group, the scale-invariant patterns were significantly altered at time scales >2 h in elderly controls ($\alpha=0.82\pm 0.03$; $p=0.0018$), and were progressively altered further in early AD ($\alpha=0.80\pm 0.03$; $p=0.0003$) and advanced AD groups ($\alpha=0.68\pm 0.02$; $p<0.0001$). The reduction in scale invariance in the advanced AD group resembled the loss of scale invariance at large time scales previously observed after lesioning of the SCN in experimental animals.

Conclusion: AD has a significant influence on scale-invariant activity control in humans during wakefulness over time scales from ~ 2 up to 10 hours. The reduction in scale-invariant activity regulation with AD may be a reflection of disturbances within the SCN.

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0142

CHRONIC ETHANOL DISRUPTS CIRCADIAN SLEEP AND ACTIVITY RHYTHMS IN THE SYRIAN HAMSTER

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Introduction: Alcoholism is associated with various sleep pathologies, including sleep fragmentation. To study this, we assessed circadian activity patterns in Syrian hamsters undergoing chronic, long-term alcohol administration.

Methods: Male Syrian hamsters maintained under a 14L:10D photoperiod received water ($n=5$) or 20% ethanol ($n=5$) as their sole fluids throughout the study. General circadian locomotor activity was measured using motion detectors interfaced with a computerized data acquisition system. Activity measurements were averaged over a 2 wk period beginning 2 wks after ethanol introduction.

Results: There were no differences in total activity bouts averaged over the 24 h circadian day between the ethanol and water drinkers (16.8 \pm 1.54 vs. 17.5 \pm 1.58, respectively; $p<0.26$). However, there were significant differences in the distribution of bouts during the light and dark phases. Activity bouts during the light phase for the ethanol and water drinkers averaged 10.58 \pm 0.97 vs. 8.50 \pm 0.87, respectively ($p<0.001$), and activity bouts during the dark phase for ethanol and water drinkers averaged 6.30 \pm 0.58 vs. 8.88 \pm 0.81, respectively ($p<0.001$). Total duration of dark phase activity (alpha) did not differ between groups (10.64 \pm 0.09 vs. 10.56 \pm 0.08, respectively; $p=0.78$).

Conclusion: Fragmented sleep is problematic with alcoholism. This analysis revealed an increased incidence of sporadic activity during the light phase (sleep period) in the ethanol group. Although sleep per se was not measured, these results are evidence that in this animal model, the patterns of sleep and activity are significantly altered by chronic alcohol consumption

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0143

TREATMENT RESPONSE OF PATIENTS WITH DELAYED SLEEP PHASE WITH CO-EXISTENT SLEEP-DISORDERED BREATHING AND PSYCHIATRIC DISORDERS

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Introduction: Patients with delayed sleep phase syndrome (DSPS) frequently have co-morbid psychiatric conditions, but their effects on treatment response is less well known. DSPS patients frequently have obstructive sleep apnea (OSA) and in our experience, this affects response to treatment. We report the incidence of psychiatric conditions and sleep disordered breathing in this population of patients and how these factors influence treatment response.

Methods: We retrospectively analyzed 100 patients diagnosed with DSPS (sleep onset after 1AM and delayed arousal time) who presented to the sleep disorders clinic. We evaluated the subjective response of patients after treatment including phototherapy, behavioral therapy, melatonin, and CPAP.

Results: The chief presenting complaints included 46 patients with excessive daytime sleepiness, 61 with sleep-onset insomnia, 31 with sleep-maintenance insomnia, and 5 with cognitive symptoms. Sixty-eight patients carried a psychiatric diagnosis of which 50 patients had a history of depression. Forty-three were diagnosed with OSA with an average Medicare AHI of 9.1 and RDI of 49.1. Data regarding overall improvement was known in 59 patients (41 improved). 63% of 43 patients with a psychiatric diagnosis improved, while 88% of 16 patients without psychiatric history improved ($p=.025$). 44% of 9 patients with bipolar improved and 74% of 50 patients without bipolar improved ($p=.060$). In 43 patients with OSA, 65% of patients improved with treatment, which was not significantly different from patients without OSA. There was no significant difference in the number of patients with improvement based on presenting symptom, depression, severity of OSA, or timing of sleep onset.

Conclusion: This preliminary analysis suggests that the presence of a psychiatric disorder with DSP may predispose patients to an unfavorable treatment outcome. We did not find a difference between response in patients with and without OSA. We plan to evaluate additional patients with DSPS and compare treatment response to patients without DSPS.

0144

FREE-RUNNING, BUT NOT ENTRAINED, BLIND INDIVIDUALS HAVE THE SAME PERIOD UNDER FORCED-DESYNCHRONY AS IN THE FIELD

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Introduction: In the majority of blind individuals without light perception, the lack of photic input to the circadian pacemaker results in rhythms that free-run, usually with a period > 24 h. Such blind free-runners (BFRs) suffer from recurrent sleep disruption. We have demonstrated that the circadian rhythms of BFRs are affected by unknown weak time cues (zeitgebers) causing relative coordination. It has been hypothesized that such weak zeitgebers may lengthen the overall observed period in BFRs. We compared the observed field period in these BFRs to the intrinsic period measured using forced desynchrony (FD). We also compared the FD period in entrained and free-running blind individuals.

Methods: Subjects (2 F, 3 M; 25-60 y.o.) were totally blind adults in good health. Three were free-running and two were entrained. For ambulatory studies, saliva samples were collected every 1-2 hours for 17-25 hours at the Oregon Health & Science University Clinical and Translational Research Center (CTRC) or at home every 3-18 days. Salivary melatonin concentrations were measured by radioimmunoassay (ALPCO, Windham, N.H.) and the melatonin onset (MO) was assessed

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using a 0.7 pg/ml threshold. Circadian period was calculated by linear regression through a series of MOs. Free-running periods were calculated using MOs that traversed a whole number of circadian beat cycles. The FD studies were conducted on the CTSC using an imposed 20-h day (6:40 h sleep, 13:20 h wakefulness) for 120 hours in dim light (< 10 lux). Subjects were in temporal isolation throughout. Saliva samples were collected every hour for 25 h before and after FD. FD period was calculated using the difference in MO before and after FD.

Results: The average (\pm SD) field period in the BFRs (24.47 ± 0.07 h) was the same as the period measured using FD (24.44 ± 0.15 h, $p = 0.79$). The FD period in the entrained blind individuals (24.10 ± 0.01 h) was longer than the field period (24.00 ± 0.01 h, $p = 0.03$) and shorter than the FD period in the BFRs ($p = 0.03$).

Conclusion: Although weak zeitgebers do modulate circadian period, they do not significantly distort the overall field period in BFRs. Despite the small sample size, we found that intrinsic period is shorter in entrained vs. free-running blind individuals. This may be because blind individuals with intrinsic periods close to 24-hours are more likely to entrain or because long term entrainment to the 24-hour day shortens period via after-effects.

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0145

ASSOCIATION OF A -1420 G POLYMORPHISM IN A PUTATIVE BMAL1 PROMOTER REGION WITH CHRONOTYPE IN BRAZILIAN POPULATION SUBSET

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Introduction: Chronotype refers to the individual preference in the timing for activity and sleep and is influenced by a number of factors, including the internal circadian clock. The molecular basis of the circadian clock relies on interactive feedback loops that comprise diverse clock genes. Expression of these genes is controlled by a key component, the heterodimer CLOCK/BMAL1. An auxiliary loop is driven by REV-ERB α and ROR α which suppress or activate the BMAL1 transcription by binding to the RORE sequences in BMAL1 promoter. In this study we analyzed the influence of polymorphisms located in selected regions of BMAL1 gene including UTR putative promoters sites and exons correlate of well established functional BMAL1 protein domains in diurnal preference.

Methods: Based on HO questionnaire, 154 samples were classified in three groups: extreme for morning or evening preference and intermediates. Polymorphisms in the human BMAL1 gene were identified in Ensemble data bank and TFSEARCH software was used for searching of RORE transcription factor binding sites. DNA from blood was subjected to PCR and polymorphisms were screened using the DHPLC system. The variants were confirmed by direct sequencing in both directions. Statistical analysis was performed using Software Prism 5.

Results: A polymorphism A -1420 G (rs4757138) in a putative Bmal1 promoter region revealed statistically significant difference between extreme eveningness and morningness sample ($X^2 = 7.864$, $p = 0.0024$).

Conclusion: This study demonstrate that the frequency of A -1420 G was higher in the extreme morning group, so the polymorphism rs4757138 can contribute to interindividual differences in chronotype.

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0146

ASSESSMENT OF SALIVARY DIM LIGHT MELATONIN ONSET (DLMO) AND REPORTED SLEEP IN PRESCHOOL CHILDREN

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Introduction: Circadian rhythms are endogenous cycles approximating 24-hrs that influence the timing of physiological processes and behavior (e.g., sleep, hormones, attention, performance). Developmental changes in the circadian system might affect early brain and behavior interactions; however, no data exist for preschoolers. This study reports DLMO phase in association with parental reported sleep variables for a group of normally developing preschool children.

Methods: Fourteen healthy preschoolers (6 males; 12 Caucasians; 30-36 months) with no reported sleep problems were studied during a 5-day typical sleep-wake schedule measured from daily parental reports and verified with actigraphy. On day 6, children did not nap and provided saliva samples by chewing on a dry dental cotton roll for 1-2 minutes. Saliva was collected under dim light conditions (<40 lux) in the home environment every 30min for 6hrs (12 samples total) up to an hour past their average bedtime. Saliva was assayed for melatonin (DLMO determined with a 4pg/mL threshold). Phase angles were computed between DLMO and average bedtime, mid sleep time, and rise time as calculated from days 1-5.

Results: Average DLMO phase was 7:30pm (± 42 min). Average bedtime was 20:12pm (± 42 min), mid sleep time 1:37am (± 28 min), rise time 7:03am (± 29 min), and time in bed 10hr51min (± 45 min). Phase angles between DLMO and bedtime, mid sleep time, and rise time were 41min (± 42 min), 6hr7min (± 37 min), and 11hr33min (± 45 min), respectively.

Conclusion: In this group of healthy preschoolers, individual variability in DLMO and phase angles was substantial. As expected, DLMO phase in preschoolers occurs earlier than in adolescents and adults. Additional normative and longitudinal data are needed to describe developmental changes in the circadian system. Future studies should (a) examine stability of DLMO in preschoolers; (b) examine DLMO and phase angles in young children with sleep problems (e.g., sleep onset insomnia); and (c) explore early evidence of relationships between circadian phase and chronotype preference.

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0147

ARE THREE 24-HOUR CONSECUTIVE DAYS OF ACTIGRAPHIC RECORDING SUFFICIENT TO ASSESS THE SLEEP-WAKE CYCLE CHANGES ASSOCIATED WITH PREGNANCY AND POSTPARTUM? -PRELIMINARY RESULTS

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Introduction: Changes of the sleep-wake cycle have been observed from late pregnancy to postpartum using long term actiwatch registration. The aim of the present study was to investigate if actiwatch data of 3-4 days activity monitoring were satisfactory to assess the sleep-wake cycle changes associated with late pregnancy and postpartum.

Methods: Fifty-six pregnant women who were in their last trimester of pregnancy participated in the study. Seventeen mothers were followed up at 3 months postpartum and 10 mothers at 6 months postpartum. In all these occasions women were asked to strap an actiwatch on their non-dominant wrist for a period of at least three consecutive 24-hour days. Twenty one non-pregnant women, who were not recently mothers, were

used as a control group. To analyse the actimetry data the Wake Activity Index (WAI) and the Sleep Inactive Index (SII) were calculated. Mann Whitney U statistical tests were applied.

Results: WAI was significantly lower at 3 months postpartum (Md= 86.6%; $p < .001$) and during late pregnancy (Md= 91.0%; $p < .001$) than normal (Md= 94.4%). Similar results were obtained when the SII was considered. The SII at 3 months postpartum (Md= 97.4%) and in late pregnancy (Md= 97.6%) was significantly lower ($p = .029$, $p = .001$, respectively) than normal (Md= 98.7%). At six months postpartum the WAI and SII values were not significantly different from normal values (WAI, Md= 93.1%; SII, Md= 98.6%; p values $> .05$).

Conclusion: The sleep-wake cycle was less robust in late pregnancy and particularly at 3 months postpartum. Short periods of actiwatch recording (at least three 24-hour consecutive days) enabled valuable assessments of the sleep-wake cycle

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0148

THE SCHEDULE OF DAY-NIGHT HABITS (SDNH): AN OBJECTIVE QUESTIONNAIRE TO MEASURE DELAYED AND ADVANCED SLEEP PHASE DISORDERS

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Introduction: This is a report on the Schedule of Day-Night Habits (SDNH), an objective questionnaire designed to provide a reliable assessment of delayed versus advanced sleep phase syndromes (DSPS versus ASPS). The SDNH consists of 125 true-false items and can be machine scored. There are four subscales: (1) DSPS - 40 items, (scoring reversed for ASPS); (2) Consequences - 49 items (e.g., sleep debt behaviors); (3) Cognitions - 23 items (e.g., night people enjoy socializing more); and (4) Parasomnias, 13 items.

Methods: Subjects were 1245 students in introductory psychology classes at a large Midwestern university who volunteered to complete the SDNH anonymously for course credit, 580 males and 665 females, 90+% of whom were aged 18-20.

Results: On Scale 1, a strong majority (60-95%) endorsed late night DSPS lifestyle items, or strongly disagreed with early morning ASPS choices. There were significant gender differences ($p < .001$) on 14 of the 40 items, with males scoring more in the DSPS direction in every case but one (after hours use of cell phones). On Scale 2, a strong majority (80-95%) answered false to early morning (ASPS) items. On Scale 3, a strong majority (60-97%) classified themselves as night people, most alert at night, and preferring a "late to bed and late to rise" lifestyle. On Scale 4, the most frequently reported parasomnias were: sleep walking (62%), leg stretching (60%), sleep talking (51%), night sweats (24%), sleep paralysis (12%), loud snoring (12%), bruxism (11%), and breathing difficulties (7%). Significantly more males than females reported snoring and sleep walking.

Conclusion: Based on this preliminary analysis we plan additional data collection (especially with an elderly sample) ultimately to determine norms for (1) both DSPS and ASPS behaviors by gender, (2) sleep debt consequences of DSPS, and (3) incidence of various sleep cognitions and parasomnias in these samples.

0149

DIURNAL VARIATIONS OF AMBIENT LIGHT IN A CRITICAL CARE UNIT

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Introduction: Light variation is the most important regulator of diurnal biologic processes. In a medical intensive care unit (MICU), light variation may be asynchronous with clock time, or even absent. Absent circadian variation could affect clinical outcomes.

Methods: We measured ambient light for 48 hours at eye level in various locations of our MICU including; 1) four patient rooms with different directional orientation (South, West, North, East); 2) at each of two nursing stations (NS), and 3) outside light through a window. Measurements were collected at 30 second intervals, and divided into periods of six hours. Levels were plotted across time to determine synchronization with clock time. The light levels were averaged per period, and ranges determined. MICU room and nursing station light levels were compared to outside light.

Results: Ambient light levels were: MICU rm 1 (southward): 0 - 674 lux; MICU rm 2 (westward): 0 - 170 lux; MICU rm 3 (northward): 0 - 48 lux; MICU rm 4 (eastward): 0 - 86 lux; NS A : 0 - 57 lux ; NS B : 0 - 70 lux. Outdoors 0 - 730 lux. Light peaks occurred at the appropriate time of day (9 AM - 3 PM). For each area, the difference between daylight hours and other time periods was statistically significant.

Conclusion: Peak diurnal light levels vary between rooms in the MICU. Although light levels in our MICU demonstrate variability consistent with clock time, the overall peak and mean light levels are dismally low when compared to outdoor light. Only one room had light comparable to that of the outdoors. The low levels of light, coupled with the dearth of external stimuli in the MICU may prove inadequate in maintaining circadian rhythms, and may potentially impact clinical outcomes.

0150

DAYTIME LIGHT EXPOSURE AND WELL-BEING AMONG MOTHERS OF LOW BIRTH WEIGHT INFANTS: A PRELIMINARY REPORT

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Introduction: Circadian rhythms (CR) influence sleep and wakefulness. Lights have been identified as the most powerful external cue in regulating the CR. The dim lights of the neonatal intensive care unit (ICU) are designed to promote the premature baby's development. However, this environment does not promote sleep for adults and may lead to circadian phase desynchronization. The purpose of this study was to describe light exposure level and its relationship to well-being among mothers of hospitalized low birth weight (LBW) infants.

Methods: Eighteen first-time postpartum mothers of LBW infants hospitalized in the ICU participated in this cross-sectional descriptive study. Objective light exposure and nocturnal total sleep time (TST) data were collected for 2 consecutive days and nights using wrist actigraphy with a light sensor 40,000 lux (Mini Motionlogger Actigraphy, octagonal motionlogger, Ambulatory Monitoring In., Ardsley, N.Y.). Self-report data were collected with the General Sleep Disturbance Scale (GSDS) and the Medical Outcomes Short Form-36version 2 (SF36v2), along with maternal perception of infant's vulnerability (MPV).

Results: The average 12-hour light exposure levels after the mothers' waking time was 101 lux (SE= 2.8) and TST was less than 7 hours (400 minutes, SE= 22.3). The mean amplitude of actigraph counts was 87.5 (SE= 4.6), acrophase (clock time) was 16:42 (SE= 0:16). The levels of light exposure were negatively correlated with sleep quantity ($r = -.56$, $p < .03$) and TST ($r = -.27$), and positively correlated with aggregated physical health from SF36v2 ($r = .52$, $p = .03$). Light exposure levels were negatively correlated with MPV ($r = -.59$, $p < .05$).

Category D—Circadian Rhythms

Conclusion: Mothers' light exposure levels were lower than normal and consistent with our hypothesis that because of the severity of their infants' medical condition they may be spending substantial amounts of time in the ICU. Results suggest the need for developing and testing interventions which help support the normal circadian pattern of light and potentially improve the circadian patterns of sleep and activity in mothers of LBW infants.

Support (optional): This study was supported by Georgia State University and the Association of Women's Health, Obstetric and Neonatal Nurses (AWHONN).

0151

DEVELOPING MATURE STRESS SYSTEMS IN 30 TO 72 MONTH OLDS: RELATIONS WITH SLEEP AND ATTENTION

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Introduction: A growing body of research suggests reciprocal associations between sleep and the hypothalamic-pituitary-adrenal axis. As a developing set of bioregulatory processes, these systems are not well understood across early childhood; however, their individual contributions for physical and psychological risks are more fully established. Research with adults suggests that learning, memory, and attention are compromised by sleep dysregulation. This analysis extends prior findings by examining relations between actigraphic estimations of sleep, salivary cortisol, and laboratory assessments of attention in young children.

Methods: A sample of 197 children (30-72 months) completed an auditory stroop task consisting of practice trials and 2 blocks of congruent and incongruent trials and wore an actigraph for 7-9 days. Home saliva samples were collected at wake-up, 10am, 4pm, and bedtime on two weekend days.

Results: Findings revealed a developmental trend in sleep patterns; increasing age was associated with increased nighttime sleep duration ($r = .38, p < .01$) and decreased days napping ($r = -.71, p < .01$). Controlling for age, this more mature sleep pattern predicted performance on the attention task in the following ways: (a) longer nighttime sleep duration ($r = -.21, p < .05$) and fewer days napping ($r = .21, p < .05$) predicted passing the "practice" stroop task (b) longer nighttime sleep duration was associated with decreased error rate on incongruent trials (block 1: $r = -.26, p < .01$; block 2: $r = -.21, p < .05$); and (c) nighttime sleep duration was related to reaction time in block 2 on congruent ($r = -.21, p < .05$) and incongruent trials ($r = -.18, p < .05$). Afternoon cortisol levels predicted error rate on incongruent trials (block 1: $r = .17, p < .05$; block 2: $r = .27, p < .01$), with higher levels associated with more errors.

Conclusion: Together, these findings suggest that attention and inhibition may be compromised by sleep dysregulation and increased cortisol as early as 2.5 years of age.

0152

HISTAMINE H3 RECEPTOR BLOCKADE ENHANCES THE LIGHT-INDUCED PHASE DELAY OF THE CIRCADIAN RHYTHM OF LOCOMOTOR ACTIVITY IN MICE

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Introduction: A number of in vitro and in vivo studies indicate that histamine is involved in mediating the entraining effects of light on the circadian clock of mammals. In rodents, histamine-induced phase shifts of the locomotor activity rhythm are similar to those elicited by light pulses, and the photic responses are attenuated by histamine synthesis inhibition. Since histamine H3 receptor antagonists can stimulate the re-

lease of histamine, we hypothesized that they could mimic and modulate the light-induced phase shifts of the mouse locomotor activity rhythm.

Methods: Male adult C57BL/6J mice were housed in a cage with a running wheel for the recording of locomotor activity under free running conditions in constant darkness. Animals (N=11-12 per group) received an injection of the H3 receptor antagonist JNJ-10181457 (10 mg/kg ip) or vehicle, in combination with either no light pulse (NL) or a 15-min pulse of light at low intensity (200-300 lux) (LP) at two circadian times, CT16 and CT23, known to induce phase delays and phase advances, respectively.

Results: The treatment with JNJ-10181457 or vehicle alone without a light pulse at CT16 or CT23 had no significant effect on the phase of locomotor activity. When the vehicle injection was followed by a LP, the animals exhibited a significant phase delay at CT16 (-74 min, $p < 0.001$) or phase advance at CT23 (+26 min, $p < 0.05$) in the activity rhythm compared to the respective vehicle-NL groups. The administration of JNJ-10181457 prior to the LP enhanced the phase delaying effect of the LP at CT16 (-124 min, $p < 0.01$), but not the phase advancing effect of the LP at CT23 (+13 min) compared to the vehicle-LP groups.

Conclusion: These data indicate that JNJ-10181457 is selective for augmenting the effects of light on the clock that are dependent on the direction of the phase shift. This light dependent selectivity is of particular interest in the potential therapeutic indications for H3 receptor antagonists on circadian rhythm disorders.

0153

NEUROCOGNITIVE FUNCTION RELATED WITH THE SLEEP-WAKE RHYTHM IN MILD COGNITIVE IMPAIRMENT (MCI) PATIENTS

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Introduction: In the elderly, circadian rhythm changes such as decreased amplitude and phase advance would result in various sleep disturbances. Particularly, the excessive daytime sleepiness is usually associated with circadian rhythm disruption, and could cause neurocognitive dysfunction. The decline of certain neurocognitive domain has been suggested as a predicting factor for the progression to dementia. Our study aimed to examine the relationship of circadian rhythm parameters with each domain of neurocognitive function in MCI patients

Methods: Among the elderly subjects above 60 years, MCI was diagnosed according to the Petersen's criteria. Nine MCI patients (Age \pm SD=69.11 \pm 4.34) and 9 age- and sex-matched normal control subjects (Age \pm SD=69.44 \pm 4.39) were selected. Eight tests from the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD-K) Assessment Packet: Neuropsychological Battery, and Stroop Color and Word Test were administered. Actiwatch-16 (Actiware version 5.0: Mini-Mitter Co. Oregon, USA) was applied to each subject for 96 hours.

Results: (1) The sleep efficiency was smaller, and wake time after sleep onset and fragmentation index were greater in the MCI group, compared to those of the normal group. (2) There was no difference in the mean acrophase of the sleep-wake rhythm between the two groups, and the mean amplitude in the MCI group tended to be lower compared to the normal group ($p = 0.071$). (3) In the combined group, there were significant correlations of acrophases with the Word List Recall scores ($r = 0.494$), and amplitudes with the scores of Verbal Fluency and Constructional Praxis ($r = 0.591, r = 0.588$).

Conclusion: The difficulty in maintaining sleep and the tendency of lower amplitude of the sleep-wake rhythm were found in the MCI group, when compared to the normal group. In MCI patients and normal subjects, the earlier acrophase was related with memory impairment, and the lower amplitude with impaired language and visuospatial functions.

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0154

CIRCADIAN EVENINGNESS IS ASSOCIATED WITH INSOMNIA AND DEPRESSIVE SYMPTOMS IN A POPULATION BASED SAMPLE OF US TWINS

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Introduction: Genetics contributes to expression of circadian rhythms, insomnia, and depression in humans. We investigated these phenotypes in twins to better understand their familial interrelationships.

Methods: A Health Survey was mailed to >4400 members of the University of Washington Twin Registry evaluating circadian rhythms, depressive symptoms, and insomnia. Circadian rhythms were ascertained using a reduced 5-item Horne-Östberg Morningness-Eveningness questionnaire (MEQ). Depressive symptoms were determined using the Patient Health Questionnaire-2 (PHQ-2). Insomnia was assessed by asking "How often do you have difficulty falling asleep or staying asleep?" A response of "always" or "often" was considered insomnia while a response of "never" or "sometimes" was considered no insomnia. Logistic regression provided odds ratios of associations with adjustment for age and gender in the overall analysis.

Results: Of the >4400 surveyed, 1634 twins from same-sex pairs completed the insomnia measure and MEQ while 1618 twins from same-sex pairs completed the PHQ-2 and MEQ. For the total sample, the mean age was 37 (SD=15), 68% were female, 17% endorsed insomnia, and 29% scored ≥ 2 on the PHQ-2. The overall comparison revealed a greater odds of insomnia among circadian eveningness twins compared to morningness twins (OR=3.4; 2.0-6.0; $p<0.01$). This was true for both monozygotic (OR=3.3; 1.6-6.8; $p<0.01$) and dizygotic (OR=4.0; 1.8-8.8; $p<0.01$) twins. The within-pair analysis revealed no similar associations. Similarly, the overall comparison revealed a greater odds of depressive symptoms among circadian eveningness twins compared to morningness twins (OR=2.3; 1.5-3.7; $p<0.01$). This was true for both monozygotic (OR=2.2; 1.2-3.9; $p=0.01$) and dizygotic (OR=2.8; 1.3-6.1; $p=0.01$) twins. Again, the within-pair analysis revealed no similar associations.

Conclusion: Circadian eveningness is associated with insomnia and depressive symptoms in twins. Within-pair analyses reveal no associations suggesting that familial factors (i.e., genetics and common environment) confound these associations or the sample size was too small. This may also suggest shared genetic influences between circadian rhythms and insomnia and depression.

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0155

EFFECTS OF SHIFT WORK INCONGRUENCE AND AGE ON NEGATIVE SLEEP AND HEALTH OUTCOMES IN POLYSOMNOGRAPHIC TECHNICIANS

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Introduction: Previous research has linked shift work with negative health outcomes including sleep disruption, gastrointestinal disease, and fatigue. The majority of research on shift work has focused on employees in the healthcare profession, especially nurses. However, this research aims to understand the impact of shift work on polysomnographic (PSG) technicians.

Methods: A total of 36 PSG technicians working at various sleep labs in a Midwestern metropolitan region ($n=21$), and a Northeast metropolitan

region ($n=15$), who have worked night shifts for a least six months, completed a modified version of the Standard Shiftwork Index. This questionnaire assesses various modalities affected by shift work specifically, circadian rhythms and physical health. The Pittsburgh Sleep Quality Index was integrated to assess sleep quality before, during, and after shift work each week. Shift incongruence with circadian rhythm preference (morningness/ eveningness) was calculated by comparing the score of circadian rhythm preference with their answer to preference for day or night shift.

Results: One-way ANOVAs were conducted to evaluate the relationship between age, sleep quality, and sleep habits. Younger technicians (less than 35 years of age) reported poorer sleep quality day before their shift when compared to older technicians, $F(1,33)=6.90$, $p=.013$. Older technicians (35 years of age or older) reported being more rigid with their sleep habits than younger technicians, $F(1, 32)=7.49$, $p=.010$. Additional one-way ANOVAs were conducted to evaluate the relationship between shift incongruence with circadian rhythm preference, fatigue, and digestive health. PSG technicians who expressed shift incongruence reported more fatigue, $F(1,33)=6.39$, $p=.017$ and poorer digestive health, $F(1, 34)=4.30$, $p=.046$.

Conclusion: This data suggests that age and shift incongruence with circadian rhythm may have an impact on sleep quality, sleep habits, and physical health in shift workers. Older technicians reported better sleep quality, perhaps due to their rigidity of sleep habits. In addition, night shift technicians who preferred to work day shifts experienced more negative health outcomes than those who preferred working night shifts.

0156

ADDITIVE INFLUENCES OF THE ENDOGENOUS CIRCADIAN SYSTEM AND MENTAL STRESS ON CARDIOVASCULAR RISK FACTORS

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Introduction: The risk of adverse cardiovascular events has a day/night pattern with a peak in the morning (~9AM), possibly related to a day/night pattern in behavioral triggers, internal circadian factors, and/or their interaction. Mental stress can be a trigger for myocardial infarction in vulnerable people. We tested the effect of 1) the circadian system; 2) mental stress; and 3) the interaction between the circadian system and stress on hemodynamic, autonomic, and hemostatic markers of cardiovascular risk.

Methods: 12 healthy adults (6 female) underwent a 13 day protocol in dim light, wherein subjects performed a mental arithmetic challenge at all phases of the circadian cycle. This was achieved by scheduling 12 recurring 20-hour 'days'. On each 'day', subjects performed a 10-min mental stress test (serial addition test, e.g., $45 + 32 = \dots$). Each test was preceded and followed by a 20-minute baseline period. Body temperature was used to assess circadian phase (the fitted minimum was assigned 0°). Data was binned in 60°-bins and analyzed with Mixed Model ANOVA.

Results: Mental stress significantly increased diastolic blood pressure (DBP; $P=0.01$), heart rate (HR; $P<0.0001$), and platelet aggregability ($P<0.001$), and decreased cardiac vagal markers (e.g., PNN50; $P=0.0006$), without significantly affecting systolic blood pressure (SBP), plasma epinephrine or plasma norepinephrine. There were significant circadian rhythms in HR ($P<0.0001$) and epinephrine ($P=0.03$), both with a peak in the biological day (120°-180°), and in cardiac vagal markers ($P=0.004$) with a trough in the biological day (120°-180°). There were no significant circadian effects on SBP, DBP, norepinephrine or platelet aggregability. The most rapid increase in HR and epinephrine, and the steepest decline in vagal markers occurred at ~60° (equivalent to ~9AM in these subjects). There was no statistical interaction between

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the effects of circadian phase and mental stress on cardiovascular risk factors, suggesting that these are additive effects.

Conclusion: There was a significant circadian rhythm in autonomic function and HR, but these potential risk factors did not peak at the vulnerable circadian phase equivalent to 9AM. The fact that the rate of change of cardiovascular risk markers peaked at 60° raises the possibility that the rate of change of cardiovascular risk markers—rather than the absolute value—may be more relevant to the timing of cardiovascular events.

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0157

CIRCADIAN RHYTHMS IN YOUNG ADULTS FOLLOWING PINEALECTOMY

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Introduction: Melatonin is a neurohormone secreted mainly by the pineal gland, controlled by the suprachiasmatic nucleus which modulates circadian rhythms. We present an prospective study of patients after treatment combining chemotherapy, surgery and radiotherapy of the pineal region for malignant germ cell tumours.

Methods: A consecutive series of patients were recruited from the pediatric oncology department of the Institut Gustave Roussy. All patients underwent baseline clinical evaluation, sleep studies, actimetry, 24 hour 6-sulphatoxy-melatonin excretion, and psychometric testing. Therapy with slow release melatonin (Circadin 2 mg) at 21h00 was commenced followed by repeat clinical evaluation, sleep studies, actimetry, 24 hour 6-sulphatoxy-melatonin excretion, and psychometric testing.

Results: 5 patients were recruited, aged from 17 - 23, 1 - 4 years after tumour resection. All reported daytime fatigue and insomnia. Actimetry confirmed disorganised sleep-wake time over a 24 hour period. Sleep studies showed sleep maintenance insomnia, without excessive daytime sleepiness on MSLT. 6-sulphatoxy-melatonin excretion was dramatically reduced or abolished in all patients. Reduced professional and education performance was found in 4 patients. One patient developed depression with psychosis and severely disturbed sleep wake rhythm 2 years after tumour resection. Following replacement therapy, supraphysiological levels of 6-sulphatoxy-melatonin were observed in all patients, with a nocturnal peak. Initial results in 3 patients showed a subjective improvement in sleep quality and reduction of fatigue, a normalisation of sleep-wake cycles on actimetry. Psychometric testing showed a marked improvement. Educational performance was improved and psychiatric symptoms improved in a patient, allowing withdrawal of hypnotics and neuroleptic treatment.

Conclusion: Pineal gland resection and radiotherapy for pineal tumours greatly reduces or abolishes melatonin secretion, and leads to circadian rhythm disturbance. Treatment by a slow release melatonin leads to an improvement in symptoms.

0158

AN INVESTIGATION OF THE NEURAL PATHWAYS REGULATING METHAMPHETAMINE-ENTRAINABLE CIRCADIAN RHYTHMS

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Introduction: Previous work has demonstrated that the mammalian circadian timing system contains both a light- and food-entrainable os-

cillator, located in the suprachiasmatic (SCN) and dorsomedial (DMH) hypothalamic nucleus, respectively. Additional studies have suggested the presence of a Methamphetamine-Sensitive Circadian Oscillator (MASCO) that is also independent of the SCN but whose neuronal basis remains unresolved.

Methods: In an effort to locate the MASCO we are performing an unbiased profiling of circadian clock gene expression across the neuraxis as well as recording circadian rhythms in mice provided daily methamphetamine (MA) injections (ip, ZT 5) for 10-12 days. All mice were implanted ip with biotelemetry units for the collection of body temperature and locomotor activity. Baseline recordings (2-3 days) began 2 weeks after surgery.

Results: Our results indicate that following MA administration, Per1 expression is induced in several hypothalamic and extra-hypothalamic areas, particularly in the DMH. Concomitant elevations in activity and body temperature were also seen in these mice following MA administration. Importantly, none of these changes are apparent in control animals provided saline injections. We are currently assessing if these MA-dependent responses develop an anticipatory component.

Conclusion: In summary, our data may indicate that the DMH plays an important role in the control of methamphetamine-entrainable circadian rhythms.

0159

CAN MORNING LIGHT STABILIZE CIRCADIAN PHASE IN TEENAGERS AFTER SLEEPING-IN ON WEEKENDS?

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Introduction: Most teenagers keep later and longer sleep (dark) times on weekends compared to school days, which we predict will phase delay the circadian timing system. We examined whether morning light exposure can stabilize rhythms in teenagers following a delayed weekend sleep/wake schedule.

Methods: Eighteen healthy adolescents (15-16 years, 6 males) have kept a fixed sleep/wake schedule (time in bed (TIB)=7.5 hours) 7 nights before and 4 nights after a weekend where sleep is scheduled to start 1.5 hours later and end 3 hours later than fixed sleep/wake (weekend TIB=9.0 hours). Seven participants (2 males) received short wavelength light exposure (454-484nm, GoLite®, Apollo Health, Inc.) for 1 hour upon waking, and eleven participants were not provided lights or light instructions. We measured evening salivary melatonin every 30 minutes for 6 hours before (Friday) and after (Sunday) late weekend sleep and determined dim light melatonin onset (DLMO) phase using a 4pg/mL threshold. We computed a repeated measured ANOVA (between-subject factor: group=LIGHT vs. NO LIGHT; within-subject factor: day=Friday vs. Sunday).

Results: DLMO phase delayed on average 35 minutes with LIGHT (Friday: DLMO mean=21:22, SD=29 minutes; Sunday: DLMO mean=21:57, SD=58 minutes) and 50 minutes with NO LIGHT (Friday: DLMO mean=21:03, SD=65 minutes; Sunday: DLMO mean=21:53, SD=80 minutes). A main effect of day [F(1,16)=27.2, p=.000] emerged; however, the interaction of day and light group did not achieve statistical significance.

Conclusion: It remains unclear whether morning short wavelength light stabilizes circadian phase when teenagers keep late and long weekend sleep schedules. A larger sample may help clarify this empirical question. Future analysis will also examine vigilance, sleepiness, and mood changes in these groups.

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0160

INDIVIDUAL DIFFERENCES IN THE FUNCTIONAL INTEGRATION OF HOMEOSTATIC AND CIRCADIAN FACTORS IN JUDGMENTS OF DAYTIME SLEEPINESS. A STUDY IN SHORT, LONG AND MIDRANGE SLEEPERS

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Introduction: Short and long sleepers have been known to differ in the amount of homeostatic sleep pressure under which they live, but not at the operational level of the sleep homeostat. Recent findings suggest that the circadian pacemaker's program might be at the origin of the variability in habitual sleep time (HST). These differences may also affect the individual's perception on how time of day and prior sleep affect sleepiness levels during the waking period and subsequently result in sleep quality misperception. The main purpose of this study is to determine the effect of individual differences in HST on the functional integration of homeostatic and circadian factors in sleepiness judgments.

Methods: Thirteen self-reported long sleepers (LS), 13 short sleepers (SS) and 16 midrange sleepers (MS) enrolled in a functional integration task. Judgments of hypothetical sleepiness based on verbal information of prior sleep (process S) and time of day (process C) were obtained by means of the Karolinska Sleepiness Scale (KSS) according to a 3×6 factorial design (S= 1000, 1200, 1400, 1600, 1800 and 2000hrs; C= HST, HST/2, no sleep). Sleep quality was assessed by means of the Pittsburgh Sleep Quality Index (PSQI).

Results: Our results support an additive integration of processes S and C in judgments of daytime sleepiness in all three groups as no significant interactions between process S and process C were observed. Estimations of subjective sleepiness for the no-sleep level of S differed significantly between groups and at the 1000hrs level of S. Sleep quality was similar in all three groups.

Conclusion: Consistent with previous findings, our results support the similarity of the regulatory mechanisms of the sleep homeostat in individuals with dissimilar habitual sleep durations and a greater sensitivity to sleep deprivation for LS. This however, has no implications on subjective sleep quality when controlling for HST.

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0161

MORNINGNESS-EVENINGNESS IN UNDERGRADUATES: CONSEQUENCES OVER SLEEP-WAKE PATTERNS

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Introduction: Uniform class schedules are probably not in tune with individual variations of diurnal type. The aim of the present study was to assess diurnal type in undergraduates, and to examine its relationships to schedules, durations, and regularity of sleep, in a university where classes typically start at 9 a.m.

Methods: A sample of 1654 (55% F) Portuguese undergraduates (University of Aveiro), 17-25 yr old, 1st-3rd curricular years, completed a national version of the Composite Morningness Questionnaire (CMQ), plus a sleep self-response questionnaire including questions on sleep durations, bed and rise times. Answers were used to compute week/week-end irregularities of sleep patterns.

Results: CMQ scores ranged from 15 to 52, M = 32.20 (DP = 5.76), and were higher in women (M = 32.93, DP = 5.35) than in men (M = 31.30,

DP = 6.10), $p < .001$. Lower QCM scores (higher eveningness) were significantly ($p < .001$) associated with later bed and rise times, on week and weekends nights, lower sleep duration on school nights, higher sleep duration on weekend nights, higher perceived sleep needs, and higher week-weekend irregularities both in sleep schedules and durations.

Conclusion: In our sample, eveningness is associated, not only with later phases of sleep-wake cycle, but also with sleep irregularities, more pronounced sleep restriction during the week and higher sleep compensation on weekends. Results suggest a conflict among preferred sleep-wake schedules and externally imposed morning classes in evening-oriented students, with consequences over sleep duration and regularity. Evening type students may thus need a sleep education that helps them to adjust to imposed morning schedules, and would probably benefit from later class schedules.

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0162

CIRCADIAN NEUROVASCULAR IMPAIRMENT IN HYPERTENSION AND OSAS

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Introduction: The 24 hour Ambulatory Blood Pressure Monitoring (ABPM) combined with sleep questionnaires and polysomnography may be a useful non invasive tool to study the neurovascular autonomic control in different pathological conditions.

Methods: Blood pressure circadian pattern and heart rate (HR) were recorded by ABPM in two groups of patients (H = Hypertensive, 117 pts, mean age 58±12, BMI 27 ± 4; SD = Sleep Disorders (OSAS), 185 pts, mean age 54 ±11, BMI 29 ± 4). In the SD group 38 pts (20.50%) were also hypertensive, 28 of them treated with politherapy (diuretics, ACE inhibitors Ca antagonists, sartanics), the remaining untreated. In all patients the ABPM data were combined with sleep-wake diary. The diagnosis of OSAS was confirmed by clinical and polysomnographic criteria. The Nocturnal Reduction Rate (NRR, an index expressing the ratio of the mean diurnal and nocturnal BP values) was calculated in the two groups allowing to classify the patients in 4 subcategories: Dippers (D) NRR≥10%, Non-Dippers (ND) NRR <10%, Extreme-Dippers (ED) ≥20%, and Reverse Dippers (RD) NRR<0%.

Results: In the hypertensive group, (systolic BP 135±12, diastolic BP 78±7 mmHg) the mean systolic NRR was 12.56±14% and the distribution of the 4 subcategory was D 36%, ND 32%, ED 21% and RD 11% whereas in the OSAS group (systolic BP 131±13, diastolic BP 78±8 mmHg) the mean systolic NRR was 9.90±8% and the distribution was D 47%, ND 21% with an equal percentage of ED and RD (16%). The results revealed statistical difference among the groups only for the RD subcategories ($p < 0.001$).

Conclusion: Although many confounding factors may contribute to alter the NRR values, the prevalence of the ReverseDipper pattern and the propensity towards low NRR values (NRR 9.90±8) in the OSAS group may suggest in this patients a progressive impairment of the neurovascular control probably caused by the sleep fragmentation and the overactivity of the sympathetic system.

0163

HABITUAL ACTIVITY AND LIGHT EXPOSURE IN SUBJECTS WITH DELAYED SLEEP PHASE SYNDROME

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Introduction: Delayed Sleep Phase Syndrome (DSPS) is a circadian rhythm sleep disorder characterized by difficulty initiating sleep at the

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desired time and sleepiness upon waking. Due to the delayed sleep period, individuals with DSPS may have a reduction in light exposure during the phase advance portion of the light phase response curve and/or increased exposure to bright light during the phase delay portion, which may result in maintaining or further delaying sleep. The aim of this study was to determine the daily habitual light and activity levels of subjects with DSPS.

Methods: 35 DSPS subjects (mean age 34) as determined by International Classification of Sleep Disorders-2 criteria and 20 healthy controls (mean age 34) wore a wrist activity/light monitor (Minimitter AW-L Actiwatch) and maintained a sleep diary for 7 consecutive days. For each subject, light and activity data was binned (30 minutes) relative to their daily sleep and wake times for the 6 hours prior to bedtime and the 6 hours after waking. Data was analyzed using repeated measures ANOVA for time and condition.

Results: DSPS subjects had sleep times approximately two hours later than controls ($p < 0.001$). Activity prior to bedtime was significantly less for DSPS subjects ($p = 0.007$). Mean light levels prior to bedtime were approximately 100 lux for controls and 35 lux for DSPS and after waking, 800 lux for controls and 550 lux for DSPS. There was no significant difference between groups for light prior to bedtime ($p = 0.06$) and for either activity ($p = 0.08$) or light ($p = 0.4$) after waking.

Conclusion: This data suggests that the primary cause of the phase delay in DSPS is not increased light exposure or physical activity prior to bedtime. However, it does raise the question of whether the phase advance response to light is altered in DSPS as both groups have a similar level of light exposure after waking.

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0164

QUANTIFYING PRACTICE EFFECTS WITHIN GROUPS AND INDIVIDUALS: EXAMPLES FROM A MONTH LONG FORCED DESYNCHRONY PROTOCOL

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Introduction: Practice or learning effects can be a confounding factor in evaluating circadian or homeostatic influences on neurobehavioral performance during multi-day studies. We used fixed-effects modeling to quantify the practice effect on a timed calculation test, for group and individual differences, using data from a month-long inpatient protocol. The method improves on current methods (that use averaging) by providing methods for determining parameter statistical significance and confidence intervals.

Methods: Within the mixed-effects model, different functions representing the practice effects were tested: linear, 3 and 4-parameter logistic growth, 3 asymptotic growth functions, and 1- and 2-time-constant exponentials. We computed group (fixed) and individual (random) effects by computing the maximum likelihood of the marginal density function using S-plus version 8 (Insightful Software). The number of calculations attempted in a 4-minute session were used from 16 subjects (8 Placebo, 8 Caffeine) participating in an inpatient 42.85 hour forced-desynchrony protocol [2004 Wyatt et al Sleep].

Results: The mixed-effects model with the 3-parameter logistic growth function was the only form that converged to a solution for both groups (Caffeine: AIC = 7,260.691; Placebo: AIC = 10,639.99; closer to zero is better) and resulted in unbiased residuals. The overall fit of the placebo group demonstrated an initial rapid increase in performance that quickly reached an asymptotic value that was less than the maximum values of the Caffeine group. In contrast, the rate of increase of performance for the Caffeine group was nearly constant throughout the study. The logistic model also fit the data for all individual subjects, except one subject

for whom the trend in performance was flat (slope = 0) and one subject whose trend was not asymptotic, as required with the logistic model.

Conclusion: Non-linear fixed effects modeling can be used to quantify long-term practice effects. The exact model used may differ for other measures (e.g., addition, memory).

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0165

MEASURING CIRCADIAN ADVANTAGE IN MAJOR LEAGUE BASEBALL: A 10-YEAR RETROSPECTIVE STUDY

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Introduction: In 2005, we studied the effect of time zone travel on Major League Baseball (MLB) teams. Through tracking 'circadian time' throughout the 2004 season, we observed trends towards teams at a more favorable circadian time (more acclimated to their current time zone) winning. We also determined that teams performed better traveling east to west rather than west to east. In this study, we examined these trends over the last ten MLB seasons (1997-2006).

Methods: Using the convention that for every time zone crossed, synchronization requires one day, teams were assigned a daily number indicating the number of days away the team was from resynchronization. Positive values indicate eastward travel, negative values westward, and a value of zero indicate synchronization with the current time zone. With these values, all 24133 games of the season could be classified based on home and away circadian values.

Results: 19084 of the 24133 games analyzed (79.1%) were played between teams at equal circadian times. The remaining 5046 games (excluding 3 tie games) featured teams with different circadian times. In these games, the team with the circadian advantage won 2621 games (51.9%). However, 3681 of these 5046 games were also played with a home field advantage. Isolating games in which the away team held the circadian advantage (1365 games), the away team won 619 games (45.3%). Magnitude of circadian advantage influenced success. When teams held a 1-hour circadian advantage, winning percentage was .517 (1904-1782), and winning percentage with a 2-hour advantage was .517 (620-579). When teams held a 3-hour circadian advantage, winning percentage increased to .603 (97-64). Direction of advantage did not seem to consistently influence game outcome as it did in the pilot study.

Conclusion: These results suggest that magnitude of circadian advantage influences outcomes of MLB games in that teams with greater circadian advantage are more likely to win. The trend seen in the 2004 season of teams traveling west having an advantage over eastward traveling teams was not seen over the ten years studied.

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0166

EATING HABITS IN SUBJECTS WITH DELAYED SLEEP PHASE SYNDROME

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Introduction: Delayed Sleep Phase Syndrome (DSPS) is a circadian rhythm sleep disorder characterized by complaints of difficulty initiating sleep at the desired time and sleepiness upon waking which results in impaired daytime function. Disruption of circadian timing has been associated with altered metabolism and feeding in animals. The aim of this study was to examine the timing of meals in individuals with DSPS.

Methods: 18 DSPS subjects (mean age 38 ± 11.5) as determined by International Classification of Sleep Disorders-2 criteria and 10 healthy age-matched controls (mean age 33 ± 12.2) responded to a questionnaire

regarding sleep and food intake including the timing, number and content of meals. Data was analyzed using one tailed t tests.

Results: DSPTS subjects had significantly later sleep-wake times than controls, with no difference in sleep duration. Fifty-five percent of DSPTS subjects ate regular meals and 66% ate breakfast compared to 100% of controls ($p = .006$, $p = .011$ respectively). Eighty percent of DSPTS reported eating 60% or more of their daily calories in the evening compared to 40% of controls ($p = .009$). DSPTS subjects who ate breakfast, lunch or dinner, ate the meals 1-2.5 hours later than controls ($p < 0.01$). There was a longer duration between dinner and bedtime for DSPTS (6.13 hrs) subjects compared to controls (4.31 hrs, $p = .004$). Overall body mass index (BMI) was similar for DSPTS (26.6) and controls (24.2). There was a trend for the BMI to be higher (29) for those DSPTS subjects that did not eat breakfast.

Conclusion: A delay in the timing of meals is consistent with the delay in circadian timing and sleep-wake behavior in DSPTS. While BMI was higher in the DSPTS group, particularly those who do not eat breakfast, there was no significant difference in BMI between the groups.

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0167

DELAYED SLEEP PHASE SYNDROME AND THE MENSTRUAL CYCLE

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Introduction: Delayed Sleep Phase Syndrome (DSPTS) is a circadian rhythm sleep disorder characterized by difficulty initiating sleep at the desired time and sleepiness during the day that are associated with impaired daytime function. Circadian rhythm disruption has been associated with menstrual irregularities, reproductive disturbances, and sleep disturbances in women. The aim of this study was to determine if there is an association between DSPTS and menstrual cycle irregularity.

Methods: Thirteen female DSPTS subjects (mean age: 48 yrs, range: 24-75) as determined by International Classification of Sleep Disorders (ICSD-2) criteria and 13 female controls (mean age: 25 yrs., range: 15-47) responded to a questionnaire regarding their reproductive health, including regularity of their cycle and premenstrual symptoms, either in the past or present. Controls were healthy and neither type on the Horne-Ostberg questionnaire. The groups were compared using one tailed t-tests.

Results: Twice as many DSPTS subjects reported an irregular menstrual cycle compared to controls ($p = 0.003$). For subjects not using birth control (7 DSPTS and 8 Controls), three times as many DSPTS subjects reported irregular menstruation, compared to controls ($p = 0.001$). Sixty-nine percent of DSPTS subjects reported having pre-menstrual problems, such as cramps and mood swings compared to 16.67% of controls ($p = 0.004$).

Conclusion: More women with DSPTS reported irregular menstrual cycles and premenstrual symptoms than controls. While the data is preliminary, these results suggest that women with DSPTS may be at increased risk for menstrual irregularity associated with circadian misalignment. Further investigation with a larger group of subjects using prospective diary data would be useful to further establish the effects of circadian disruption on reproductive cycles in women with DSPTS.

Support (optional): R01 HL069988

0168

ISCHEMIC STROKE CLINICAL FEATURES ACCORDING TO SEASONS IN A SUBTROPICAL CITY

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Introduction: It is not known if there are seasonal stroke clinical features variation in Brazil. Some studies suggest that the most serious cases occur during winter and among older people in some non tropical countries. Objective: To study clinical and populational ischemic stroke features (gender, age, schooling, monthly income, type of neurological deficit) and cerebrovascular disease risk factors according to seasons.

Methods: Data were collected from 598 patients (298 men), aged 26-92 years (62.0 ± 12.3) with acute ischemic stroke who had come from attention to the Emergency room of the Sao Paulo Hospital from november 1998 to June 2006, participants in the trial "transesophagus echocardiogram in strokes and dose of aspirin." We excluded patients with diagnosis ruled out or doubtful for ischemic stroke, with clinical suspicion of cardiac embolism, and those whose hospitalization for acute phase has been more than 14 days.

Results: There was no significant difference in gender ($p = 0.96$), age ($p = 0.10$), schooling ($p = 0.85$), and monthly income per person ($p = 0.12$). Clinical features: right motor deficit ($p = 0.71$), left motor deficit ($p = 0.98$), aphasia ($p = 0.96$), and posterior cranial fossa injury ($p = 0.55$) did not show significant seasonal differences. Sensitive deficit were present more frequently in the winter ($p = 0.02$). Risk Factors were not seasonal associated to the occurrence of stroke: Hypertension ($p = 0.62$), diabetes mellitus ($p = 0.24$); prior cerebrovascular disease ($p = 0.39$), coronary disease ($p = 0.51$), smoking ($p = 0.91$), and alcoholism ($p = 0.92$). Body mass index was not seasonal related too ($p = 0.39$).

Conclusion: The data suggest that populational characteristics and clinical feature of ischemic stroke (with exception of sensitive deficit) and the risk factors do not suffer seasonal influence.

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0169

ADOLESCENTS EXPOSED TO HOME ELECTRIC LIGHTING HAVE DELAYED SLEEP ONSET

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Introduction: Artificial lighting has a significant influence upon human circadian rhythms. The aim of this study was to compare sleep/wake patterns of adolescents with and without electricity at home.

Methods: A group of 37 adolescents living in a rural area of Paraná State - Brazil, participated in the study. These adolescents, 11 had no electric lighting at home, 5 attended morning school classes (G1), and 6 attended evening school classes (G2); and 26 had electricity at home, 15 attended morning school classes (G3), and 11 attended evening school classes (G4). Sleep patterns were measured using actigraph for 5 consecutive days, in parallel with daily logs.

Results: The data were compared by ANOVA and showed significant effect of school schedule on all sleep variables during school days (Sleep Onset: G1=20:38 \pm 0:50, G2= 23:46 \pm 0:26, G3= 21:51 \pm 1:02, G4= 23:53 \pm 0:44, F= 71,24, $p < 0,01$; Sleep Offset: G1= 6:24 \pm 0:46, G2= 7:22 \pm 0:55, G3= 6:36 \pm 0:30, G4=7:58 \pm 1:09, F=14,7, $p < 0,01$; Sleep Duration: G1= 587 \pm 41, G2= 457 \pm 48, G3= 526 \pm 49, G4=488 \pm 48, F= 19,9, $p < 0,01$), i.e., later timing and more sleep for those with late classes. Those adolescents without electricity at home had earlier sleep onset on school days (F= 4,83 $p < 0,05$).

Conclusion: Our data support the idea that technological advances affect human sleep timing and increase adolescent sleep phase delay.

Category D—Circadian Rhythms

Support (optional): CNPq (Brazil) and Sleep Research Society Foundation (USA)

0170

CIRCADIAN FEATURES OF SLEEP AND NEUROBIOLOGICAL REGULATION IN A RAT MODEL OF INSOMNIA

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Introduction: Abnormal circadian regulation has been an emerged as an important issue in chronic insomniacs. Previously, we have reported that a decrease of total wake time, an increase of total sleep time and an increased hypothalamic orexin A were found in a rat model of insomnia induced by neonatal maternal deprivation (Feng et al 2007, Brain Research). In the following experiment, we will reported the features of sleep, activity and circadian regulation in the same rat model of insomnia.

Methods: Twenty five male Sprague Drawly rats were neonatally treated with ten days of either maternal deprivation (MD group, n=13) or a control procedure (MC group, n=12) from postnatal day 4. All rats were implanted with electrodes at three months of age for polysomnographic recording. 48 hours sleep/wake was recorded after ten days of recovery and adaptation. Five days after end of PSG recording, rats were sacrificed at the early light phase (2 hrs after light was turned on) for brain tissue collection. Hypothalamic levels of Clock protein, clock protein RNA and brain levels of melatonin were quantified using western blot, Real time PCR and radioimmunoassay, respectively.

Results: Compared with the MC group, the MD group had (a) significantly less of REM sleep (-15.86%) in overall of 48 hours, (b) 30.31% of less of REM, 8.54% less of total sleep and 18.02% more of total wake in the total light on period. These changes were toward a reverse direction for all sleep/wake states in the dark phase but the differences were not significant. The optical density of Clock protein was obviously lighter in the MD rats compared with that in the MC rats. The Melatonin levels remains under analysis.

Conclusion: The rat model of insomnia, i.e. the MD rats, had alteration of circadian regulation shown as relocated sleep from light phase to dark phase and may have significant alteration of Clock and brain levels of melatonin. This is consistent with findings from human insomnia which has phase of changes of sleep.

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0171

ASSESSMENT OF URINARY 6-SULFATOXYMELATONIN IN OLDER ADULTS UNDER NATURALISTIC "AT HOME" VERSUS CONTROLLED CONDITION

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Introduction: A significant aspect of the aging process is deconsolidation of the circadian system, including possible alteration of melatonin secretion. The controversy among studies investigating age-related melatonin decline raises the question whether endogenous melatonin levels assessed under controlled conditions relate to those assessed under naturalistic conditions within individuals. The purpose of this study was to compare 24h urinary 6-sulfatoxymelatonin (aMT6) levels under controlled (C) vs. naturalistic (N) conditions within older adults.

Methods: Following a one-week assessment of their rest-activity-cycle and ambient light levels (Actiwatch L-Plus®), 24 community-dwelling older adults (16 women; age 71.2±5.5) underwent a 24h urine collection protocol, first at home (N, habitual sleep-wake schedule), then at

the Stanford GCRC (C, dim light <8 lux during wake, <1 lux during sleep, controlled posture, food intake, no exercise). Urine collection was divided in 12h-collection periods, covering night- versus daytime aMT6 secretion, scheduled to the individual sleep-wake cycle. aMT6 was measured using ELISA (ALPCO®).

Results: We observed no significant differences between melatonin levels assessed under N or C, for 24h mean, daytime, nighttime or amplitude melatonin levels (paired t-test). Regression analysis revealed no significant effect of 'physical activity at home', 'caffeine' and 'alcohol' consumption at home or 'medication' on the intra-subject differences in melatonin measures across conditions. Furthermore, melatonin levels assessed under both conditions lead to the same classification into either high or low secretors (upper and lower 30% or 50%).

Conclusion: Our results suggest remarkably stable within-subject aMT6 levels across N/C conditions in our study population of older adults. If confirmed in a larger sample, assessment of melatonin parameters at home may present a valid, more accessible alternative to gold-standard controlled conditions in older adults. As part of a larger project, we are currently relating melatonin levels with sleep parameters and neuropsychological outcomes in this age group.

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0172

EFFECTS OF MORNINGNESS-EVENINGNESS CHRONOTYPE ON SLEEPINESS ACROSS THE DAY

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Introduction: To determine if the levels of sleepiness across the day differs among college students as determined by their chronotype.

Methods: This was a prospective study of 262 college students who completed a survey offered for extra credit, including the Morningness-Eveningness Questionnaire (MEQ), Epworth Sleepiness Scale (ESS), and Time of Day Sleepiness Scale (ToDSS). The ToDSS consists of three scores that rate sleepiness in the morning, afternoon, and evening. There were 196 females and 66 males with an average age of 20.9±3.2. Mean courseload was 14 semester hours.

Results: Definitely/moderately morning types constituted 5.4% of the sample, 37.6% were neither, 51% were moderately evening, and 6.1% were definitely evening types. Sleep schedules differed significantly by type (p<.001); morning types have a 12:45-6:43 a.m. schedule, neither types a 12:03-8:01 a.m. schedule, moderately evening types a 1:06-8:49 a.m. schedule, and definitely evening types a 1:36-9:43 a.m. schedule. However, subjectively reported total sleep times were comparable. Repeated-measures analysis of ToDSS scores for each type were significant (all p<.02), with different patterns of sleepiness across the day. Morning types' scores are 4±4, 7±5, 10±5; neither types' scores are 6±4, 7±4, 9±4; moderately evening types' scores are 8±5, 7±4, 9±4; definitely evening types' scores are 11±4, 8±3, 7±3. Importantly, there was a time x MEQ interaction (p<.001), where definitely/moderately morning types were significantly less sleepy in the morning (4±4) than moderately evening (8±5) and definitely evening (11±4) types. Additionally, neither types (6±4) were significantly less sleepy in the morning than moderately evening and definitely evening types. Moderately and definitely evening types were comparable. There were no differences between types on ESS.

Conclusion: Most college students are evening types on the MEQ, which was corroborated by their reported sleep schedule. The ToDSS enabled differentiation of a differing pattern of sleepiness across the day and specifically found significant differences in the level of sleepiness in morning scores among MEQ types.

0173

INTERACTION OF CIRCADIAN TIMING SYSTEM AND TIME SINCE EATING ON APPETITE IN HUMANS

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Introduction: It has previously been demonstrated that the “satiety hormone” leptin has an endogenous circadian rhythm in humans, with a peak around the habitual wake time. The current study aimed to identify whether or not there exists a significant circadian rhythm in appetite.

Methods: 8 healthy adults (mean age 27 years, range, 19-42 years) underwent a forced desynchrony protocol in dim light for 13 days, wherein the sleep wake and fasting/eating cycles occurred at all phases of the circadian cycle. This was achieved by scheduling twelve recurring 20-h ‘days’. During each waking period, lasting approximately 13.3-hours, isocalorically balanced meals were provided at 1.25 h (breakfast), 6.45 h (lunch), 10.45 h (dinner), and 12.10 h (snack) from time since scheduled wake. The dietary intake was identical each wake-period. A computer-generated visual analogue scale hunger/satiety questionnaire was administered immediately before breakfast and immediately before scheduled bedtime. Body temperature was used to assess circadian phase (the fitted minimum was assigned 0°). Data was binned in 60°-bins and analyzed with Mixed Model ANOVA, with circadian bin and questionnaire result as independent factors.

Results: As expected hunger levels were affected by time since last meal, with highest hunger in the morning after a 9-h overnight fast and lowest at the end of the “feeding day”, following the ‘evening’ snack, with a peak-to-trough difference of 45.6 % (on a 100% scale) ($P < 0.0001$). This effect occurred independent from circadian phase. There was no circadian rhythm in hunger independent of time since last meal. However, there was a significant interaction between circadian phase and time since last meal ($P = 0.004$). Hunger ratings before bedtime expressed a significant circadian rhythm ($P = 0.009$), with a peak at 240 phase, corresponding to 9pm time in this group. In contrast there was no significant circadian rhythm of hunger rating following sleep.

Conclusion: These data demonstrate that the influence of time since last meal has a greater effect on appetite than circadian rhythms alone. However, there is also a significant interaction between time since last meal and circadian phase. Such an interaction may have implications for the obesity of shift work.

0174

UNIVERSITY CREW ROWING SPEED VARIES BY MORNINGNESS-EVENINGNESS

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Introduction: During adolescent and early-adulthood development humans tend toward evening- (E-type), rather than morning- (M-type) or daytime/neither- (N-type) chronotypes. These morningness-eveningness (M-E) tendencies may affect athletic performance and were evaluated in collegiate crew rowers.

Methods: Subjects were eight male (m) and eight female (f) university crew club athletes (mean age=19.6+/-1.5 years), classified from BALM and MEQ M-E scores as eight E-type (3f/5m), four M-type (2f/2m), and four N-type (3f/1m). In a randomized counter-balanced design, each subject's rowing speed was measured for a 2000-m sprint using a rowing ergometer. Morning and evening test sessions occurred at times similar to near-daily early mornings (0500 to 0700 h) and evenings (1630 to 1800 h) practices. Sessions were separated by three days of rest.

Results: Overall, 13 of the 16 crew members rowed on average 2.4 secs (0.52 %) slower in the evening than morning ($F[1,13]=27.43$, $p < .001$).

However, individual AM-PM rowing speed differences were affected by chronotype (Chronotype x Time interaction ($F[2,13] = 13.59$, $p = .001$), and correlated with chronotype score: BALM ($r = .880$, $p < .001$), MEQ ($r = .863$, $p < .001$). M-types slowed in rowing speed from morning to evening by 4.8 secs (1.1%), twice the group average ($F[1,13]=41.60$, $p < .001$) compared with E-types ($p < .001$) and N-types ($p = .014$), who showed no AM-PM changes ($F[1,13]=0.01$, $p = .907$) and ($F[1,13]=3.05$, $p = .104$), respectively), and did not differ from one another ($p = .390$). Notably, three E-types increased rowing speed from morning to evening by an average of 1.9 secs (0.47%).

Conclusion: Performance of young athletes appears influenced by chronotype effects. Yet, these influences seem modified by routine practice at the same time each day, as suggested by absence of typical circadian evening performance superiority. Understanding personal M-E tendencies could allow young athletes to re-arrange daily training schedules to help counteract any circadian time-of-day influences that might work against their competitive performance.

0175

SENSORY FUNCTION IN THE UPPER AIRWAY OF CHILDREN WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Children with the obstructive sleep apnea syndrome (OSAS) have impaired cortical afferent processing of respiratory stimuli. This may be due to an impairment in respiratory sensation. Therefore, we hypothesized that children with OSAS have diminished upper airway sensation compared to normal controls.

Methods: Inspiratory load perception (ILP), two-point discrimination (TPD) and vibratory threshold (VT) were measured in children with OSAS, and age and BMI matched controls during wakefulness. To determine ILP, children were asked to breathe through inspiratory resistors of 0-20 cm H₂O/L/s. Children rated their ease to breathe according to the Wong-Baker scale. TPD was measured in the anterior tongue, right interior cheek and hard palate using calipers. VT was tested in the soft palate using a Vibratron II.

Results: Eleven children with OSAS (mean age [SD] 11 ± 4 years, mean BMI Z score 2.4 ± 0.5, mean AHI 31 ± 52/hr), and nine controls (age 13 ± 2 years, BMI Z score 2.2 ± 0.5, AHI 0.4 ± 0.5/hr) were tested. Children with OSAS had impaired TPD in the anterior tongue (OSAS median [range] = 9 [4-14] mm, Controls = 3 [1-7] mm, p = 0.002) and hard palate (OSAS median [range] = 6 [5-9] mm, Controls = 3 [1-4] mm, p < 0.001). ILP, TPD in the cheek and VT were similar between OSAS and control subjects. However, our sample size was underpowered to detect negative results.

Conclusion: TPD in the anterior tongue and hard palate is impaired in children with OSAS during wakefulness. A bigger sample size is necessary to detect differences in ILP and VT. We speculate that impaired upper airway sensation in childhood OSAS is a cause of upper airway occlusion during sleep. Alternatively, the impaired sensation may be secondary to neural damage from snoring.

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0176

POLYSOMNOGRAPHIC VALUES IN CHILDREN UNDERGOING PUBERTY: PEDIATRIC VERSUS ADULT RESPIRATORY RULES IN ADOLESCENTS

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Introduction: Polysomnographic respiratory events in children should be scored using pediatric respiratory rules. However, due to a lack of data on adolescents, recently revised scoring rules allow children aged 13-18 years to be scored by either adult or pediatric criteria. To further clarify which scoring criteria to use, we describe the evolution of respiratory events with Tanner stage, and compare those events in children aged 13 - 18 years with the new American Academy of Sleep Medicine adult and pediatric respiratory rules.

Methods: Cross-sectional analysis of healthy, asymptomatic, non-obese subjects aged 8 - 18 years recruited for research purposes. Subjects underwent a physical examination to determine Tanner stage, an overnight polysomnogram, and determination of sexual hormones.

Results: 68 subjects with Tanner stages 1-5 were studied, mean age [SD] = 13 ± [3] years, median AHI [range] = 0.1 [0 - 1.2/hour], median per-

centage of total sleep time (TST) with SpO₂ <92% = 0.1 [0 - 4.2%], median percentage of TST with end-tidal CO₂ >50 torr = 0.1 [0 - 88.6%]. No significant differences in AHI, TST with SpO₂ <92%, and with end-tidal CO₂ >50 torr were observed between Tanner stages. 32 subjects were 13 - 18 years old (Tanner 3 - 5), mean age = 16 ± [1] years. The difference between the paired AHI scored by pediatric (median = 0 [0 - 0.9/hour]) and adult (median = 0 [0 - 0.5/hour]) criteria was statistically significant (p=0.04). However, this difference (mean difference=0.048, SD=0.137, 95% CI=-0.001, 0.098) would not be of clinical relevance.

Conclusion: Respiratory events in normal children between 8 and 18 years of age are rare and unrelated to Tanner stage. Adult or pediatric respiratory rules can be used for scoring polysomnograms in asymptomatic research subjects approaching adulthood. However, further studies are needed in symptomatic children within this age group.

Support (optional): NIH ROI HL58585

0177

TREATMENT OF SLEEP DISORDERS IN CHILDHOOD AUTISM WITH MELATONIN OR BEHAVIORAL THERAPY. A RANDOMIZED WAITING-LIST CONTROLLED STUDY

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Introduction: Sleep disturbances appear as a frequent comorbid condition in children with autism (AD). In autism sleep disorders are mostly the product of a faulty internal clock than bad parenting. This study examines the effectiveness of melatonin (MLT) and behavioral therapy (BT) compared with a waiting-list (WL) control group in reducing sleep disorders.

Methods: Sixty-eight medication-free AD children, ages 4 to 7 years, with chronic sleep disorders entered in an 8-week randomized WL-controlled study of BT and MLT (3- 5 mg). Five did not continue into randomization. Sixty-three patients were randomly assigned to one of the three treatment conditions. Sleep was evaluated by 1-week of actigraphic monitoring at baseline and after 8-week MLT or BT treatment period. Primary outcome measures were actigraphy-derived pre- to post-treatment changes in sleep onset latency (SOL), night-to-night variability, sleep efficiency and total sleep duration. Differences in change over time and between the melatonin, BT and WL group were analyzed by rm-ANOVA. Five patient were discontinued which left 58 cases (20 MLT, 20 BT and 18 WL groups) that would be able to be evaluated. All efficacy analyses were performed using to last-observation-carried-forward (LOCF) to replace missing data.

Results: At pretreatment assessment, there were no significant differences between the 3 groups with respect to the outcome measures. For reducing sleep disorders melatonin was superior. Patients in the MLT group showed a significant improvement in sleep patterns than patient in BT and WL groups. For all outcome measures there were significant main effects for group, and post-hoc showed that SOL, night-to-night variability, sleep efficiency and sleep duration gains in the MLT group were significantly larger than those in BT (p<.01) and WL (p<.001) groups.

Conclusion: Melatonin treatment is highly effective for reducing sleep disorders in children with autism. Although the study was short-term, it still provides evidence of effectiveness of melatonin whereas BT is less effective.

0178

DETERMINANTS OF ADENOTONSILLECTOMY OUTCOMES IN TREATMENT OF OBSTRUCTIVE SLEEP APNEA IN CHILDREN: A MULTICENTER RETROSPECTIVE STUDY

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Introduction: The overall efficacy of adenotonsillectomy (T&A) in the treatment of obstructive sleep apnea (OSA) in children is unknown. Although success rates are likely lower than previously estimated, factors that promote the risk for incomplete resolution of OSA after T&A remain undefined.

Methods: A multicenter collaborative retrospective review was performed of all nocturnal PSG performed both pre- and post-operatively on otherwise healthy children undergoing T&A for the diagnosis of OSA at 3 large pediatric sleep centers. Demographic and clinical confounders were extracted from patient charts with intent to determine risk factors associated with failed resolution of OSA after T&A, as indicated by a post-T&A apnea-hypopnea index (AHI) > 5/hrTST.

Results: To date, 319 children (mean age: 7.9±0.3 years) have been identified. T&A resulted in a significant reduction in AHI from 17.2±6.2/hrTST to 4.7±0.4/hrTST post-T&A (p<0.00001). Of the 319 children, 83 (26%) had residual AHI >5/hrTST. Pre-operative AHI was significantly associated with post-operative AHI, such that higher pre-T&A AHI were more likely to result in residual OSA ($\chi^2=8.0$, p<0.02). Of these, 68.5% were obese (BMI Z-score >1.56). Among children with a pre-T&A AHI >10/hrTST, obese children had a significantly higher post-T&A AHI (14.5±1.7/hrTST) compared to non-obese children (9.7±1.4/hrTST; p<0.05), despite similar AHI prior to T&A.

Conclusion: Initial assessments confirmed that both pre-operative AHI and obesity operate as independent risk factors for the occurrence of residual OSA after T&A. Since data collection is ongoing, it is anticipated that the increased sample size will provide enough power to examine the role of other factors such as allergy, asthma, prematurity, and a family history of OSA in the overall polysomnographic outcomes of T&A in children with sleep-disordered-breathing, and thus permit delineation of a validated algorithm for selection of children who would clearly benefit from a post-operative PSG.

Support (optional): The Children's Foundation Endowment for Sleep Research.

0179

PEDIATRIC OBSTRUCTIVE SLEEP APNEA AND INSULIN SENSITIVITY

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Introduction: Obstructive sleep apnea syndrome (OSAS) has been implicated in the pathophysiology of metabolic syndrome, but its contribution to insulin resistance is complicated by its association with obesity and, in children, pubertal insulin resistance. We hypothesized that OSAS worsens insulin resistance independently of both obesity and puberty by lowering the adipose-derived insulin sensitizer, adiponectin.

Methods: Normal controls and children with suspected OSAS were recruited. Subjects were categorized as pubertal or prepubertal based upon a validated self-assessment tool. Overnight polysomnography (PSG)

was performed. Fasting blood glucose (BG), insulin, and adiponectin were obtained. Homeostatic model assessment of insulin resistance (HOMA)=(BG*insulin)/405 was calculated. The independent effects of PSG parameters upon 1) HOMA and 2) adiponectin following adjustment for puberty and body mass index (BMI-Z) were determined using multivariable linear regression.

Results: (Median, range): 88 children (38 female; 36 prepubertal/52 pubertal), age=10.5 years (4-18), were recruited. Subjects were generally overweight (BMI-Z=2.1, -3 to 4.1) and had wide-ranging insulin sensitivities (HOMA=2.7, 0.5-27) and PSG parameters: apnea hypopnea index (AHI)=0.7, 0-125; arousal index=0, 0-110; %time oxygen saturation<90% (%TiSpO2)=0, 0-40; lowest SpO2=91, 44-97; end-tidal CO2 (ETCO2)=51, 40-63. BMI-Z (p<0.001, R2=0.33), puberty (p<0.001, R2=0.25), adiponectin (p<0.001, R2=0.30), and all PSG parameters were independently associated with HOMA. Following adjustment for BMI-Z and puberty, no PSG parameter was associated with HOMA, but AHI (p=0.01, R2=0.34), %TiSpO2 (p=0.01, R2=0.38), and ETCO2 (p=0.005, R2=0.43) remained negatively associated with adiponectin.

Conclusion: As expected in the pediatric population, puberty and obesity were significant determinants of insulin sensitivity. After adjustment for these well-recognized factors, OSAS did not contribute to insulin resistance but was associated with lower adiponectin. Whether OSAS begets lower adiponectin is not known but, if it is causal, the long-term impact of OSAS originating in childhood is potentially significant since hypoadiponectinemia has been implicated in the pathogenesis of insulin resistance, diabetes, and atherogenesis.

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0180

ASSOCIATION OF SLEEP COMPLAINTS WITH SUICIDAL BEHAVIOR AMONG CHILDREN AND ADOLESCENTS WITH DEPRESSIVE EPISODES

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Introduction: Suicide is the third cause of death worldwide among 10 to 20-year-old individuals but no comprehensive study of sleep complaints and suicidal risk exist in young individuals. We determined the association of sleep complaints and suicidal behavior in children and adolescents with Pediatric Bipolar Disorder (PBD) and Pediatric Unipolar Disorder (PUD) during depressive episodes.

Methods: 303 individuals (mean age: 12.8 ± 3.1 years), were assessed for current depressive episode with the Diagnostic Interview for Children and Adolescents (DICA-IV). Demographic and clinical variables were collected at intake with subject and responsible adult. Exclusion criteria: chronic medical illness, psychoactive substance use or dependence; pervasive development disorder; schizophrenia, severe psychotic disorder; institutionalized subjects, homelessness; mental retardation, and substantial learning difficulties. Presence of sleep complaints (initial insomnia, sleep maintenance insomnia, early awakening, and hypersomnia) and suicidal behavior (suicidal ideation, desire to die, suicide plan, and suicide attempt) were detected by face to face interviews during depressive episodes. Data analyses with descriptive statistics and Chi-square tests.

Results: 83.8% of patients with PBD (n= 81) and PUD (n=222) had sleep disturbances. Poor sleep was more frequent among PUD than PBD (92.8% and 58%, p=0.02, respectively). They presented more initial insomnia 63.1% (PUD) vs. 22.2% (PBD), p=0.02; and sleep maintenance insomnia 41.4% vs 22.2%, p<0.05. There was no group difference for early awakening and hypersomnia (p>0.05). The presence of sleep complaints showed a significant association with suicidal behavior (p<0.05). The proportion of subjects who reported suicidal behaviors with sleep complaints was higher among bipolar than unipolar patients, respectively: suicidal ideation: 58% vs. 35.6%, p=0.03; desire to die: 58% vs. 31.5,

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$p < 0.05$; suicide plans: 55.5% vs. 22.3%, $p = 0.003$; and suicide attempt: 40.7% vs. 19.8%, $p = 0.02$.

Conclusion: Sleep complaints during depressive episodes in PBD and PUD must lead to search for suicidal behavior.

0181

TNF- α POLYMORPHISMS AND MORNING PLASMA LEVELS IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: Multiple genetic and environmental factors underlie the development and consequences of OSA. Plasma levels of TNF- α vary among individuals, and correlate with TNF- α gene polymorphisms such as -308G. This specific polymorphism has been implicated in the pathophysiology of OSA in adults. However, the frequency of TNF- α polymorphisms among children with OSA has not yet been explored. Furthermore, the relationship between these polymorphisms and morning plasma levels of TNF- α is unknown. The present study evaluates the relation between four polymorphisms in the TNF- α gene and morning plasma levels of TNF- α in children with OSA.

Methods: Consecutive children (ages 4-10 years) who were polysomnographically diagnosed with OSA (n=154) and age-, gender-, ethnicity-, and BMI-matched control children (n=163) underwent a blood draw the next morning under fasting conditions. Genomic DNA extraction was performed and TNF- α polymorphisms -238, -256, -308, and -948 corresponding to several critical encoding regions of the gene were examined. Genotyping and allelic frequencies were determined using real time PCR TaqMan SNP genotyping assays. Plasma samples were assayed for TNF- α using ELISA.

Results: The frequencies of TNF- α 238 (A/G), 308 (A/G), 256 (G/T), and 948 (A/C) polymorphisms were similar between OSA and control children. Plasma TNF- α levels were significantly increased in children with OSA compared to control groups. No differences in circulating TNF- α levels emerged among 238, 256, and 948 single nucleotide polymorphisms. In contrast, plasma TNF- α levels were markedly higher in children with OSA harboring the -308G polymorphism.

Conclusion: The TNF- α promoter polymorphism (-308G/A) might be associated with inflammatory responses in children with OSA, and thus, this TNF- α polymorphism may operate as a disease-modifying gene in OSA.

Support (optional): NIH grant HL-65270 and the Children's Foundation Endowment for Sleep Research.

0182

NEIGHBORHOOD AIR QUALITY CHARACTERISTICS AND PREVALENCE OF HABITUAL SNORING IN SCHOOL-AGED CHILDREN RESIDING IN TEHRAN, IRAN

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Introduction: Multiple studies have evaluated the frequency of habitual snoring (HS) in pediatric populations. However, while exposure to cigarette smoke (ECS) has been found to increase the risk of HS in a dose-dependent fashion, no studies have examined the potential contribution of air quality to HS in children.

Methods: A sleep questionnaire was distributed during 2007 to 6-12-year-old children attending public schools in 5 distinct neighborhoods (4 schools/area) within the city of Tehran. The regions were selected

based on the officially published air quality measures which include carbon monoxide (CO), particulate matter <10 micron in aerodynamic diameter (PM10), nitrogen dioxide (NO₂), ozone (O₃), and sulphur dioxide (SO₂). 6,000 questionnaires were distributed, and 62.5% were completed by parents. HS was defined as loud snoring ≥ 3 nights/week. Information regarding allergies, asthma, previous adenotonsillectomy (T&A), recurrent ear infections, parental smoking, and ECS was obtained. Descriptive statistics followed by adjusted risk assessments were conducted.

Results: Among the 4,322 completed datasets, the prevalence of HS was similar for boys and girls from age 6-10 years (approximately 3.5%), with significantly higher HS rates in boys at ages 11-12 years ($p < 0.02$). HS was increased if allergic rhinitis, asthma, previous T&A, recurrent ear infections, tympanostomy tubes, and parental smoking were concurrently reported ($p < 0.0001$). Furthermore, partition of HS rates according to air quality neighborhood characteristics revealed significantly higher HS frequencies among children residing in a neighborhood with poorer air quality (6.02% vs. 2.65%), whereby the regional variance in HS was primarily accounted for by SO₂, O₃, and PM10, even after controlling for other risk factors.

Conclusion: In addition to previously identified risk factors, environmental air quality emerges as a significant contributor to the risk for developing HS during childhood, further emphasizing the multiplicity of factors that operate as determinants of upper airway lymphadenoid proliferation.

Support (optional): The Children's Foundation Endowment for Sleep Research.

0183

EFFECTS OF BIRTH WEIGHT ON BAROREFLEX RESPONSES TO HEAD-UP TILTING DURING SLEEP IN PREMATURELY-BORN INFANTS

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Introduction: Previously it has been reported that preterm infants have impaired baroreflex responses at term-equivalent age, however there have been no studies of the maturation of baroreflex control of heart rate (HR) and blood pressure (BP) after term-equivalent age. We aimed to assess the maturation of baroreflex responses to head-up tilting during sleep in prematurely-born infants over the first six months corrected age (CA).

Methods: Twenty-seven preterm infants (28-32 wk GA) were studied using daytime polysomnography at 2-3 wk, 2-3 mo and 5-6 mo CA. BP was measured continuously and non-invasively using a photoplethysmographic cuff (Finometer™) placed around the infant's wrist. Infants were tilted 15° head-up to assess baroreflex responses during quiet and active sleep. Infants were divided into low (LBW; 1500-2500g), very low (VLBW; 1000-1500g) and extremely low (ELBW; <1000g) birth weight groups. The effect of postnatal age on responses to tilting was compared using a two-way ANOVA with Student Newman Keuls post-hoc analysis and data expressed as percentage change from pre-tilt baseline.

Results: There were no significant postnatal changes in HR responses to tilting in any of the groups, nor BP responses in the VLBW and LBW groups. In contrast, there was a significant change in quiet sleep BP responses to tilting with postnatal age in the ELBW group, with the maximum BP response falling with increasing age from 2-3 wk to 5-6 mo CA (9% and 2%, respectively; $p < 0.05$).

Conclusion: The BP response to head-up tilting in ELBW premature infants undergoes significant maturation with increasing postnatal age. Altered BP responses to tilting observed at 2-3 wk and 2-3 mo CA may place ELBW premature infants at a greater risk cardiovascular instability during sleep in this critical developmental period. Further studies are

required to compare both sleep state effects and maturation of responses in prematurely-born infants with healthy, age-matched term infants.

0184

URINARY CATECHOLAMINES IN PEDIATRIC OBSTRUCTIVE SLEEP APNEA: EFFECT OF OBESITY. SNOW A, SERPERO LD, SANS CAPDEVILA O, GOZAL D UNIVERSITY OF LOUISVILLE, LOUISVILLE, USA

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Introduction: Obstructive sleep apnea (OSA) is accompanied by increased sympathetic activity in adults, and is associated with increased urinary catecholamines levels. Moreover, urinary catecholamine excretion is altered in obese patients. Thus, our hypothesis was that morning urine catecholamines levels would be correlated with the severity of obstructive sleep apnea and degree of obesity in children.

Methods: Children referred to the pediatric sleep center for habitual snoring underwent overnight polysomnography, and the first morning voided urine sample was then collected. Urinary concentrations of norepinephrine, epinephrine and dopamine were measured and corrected for urine creatinine levels.

Results: 159 children were recruited and completed the protocol. 2 age-matched groups were identified, namely children having OSA (Average apnea-hypopnea index (AHI) = 8.2 events/hour sleep, n=81) and habitual snorers (AHI <1 event/hour sleep, n=78). Each group was further subdivided into 2 groups based on body mass index Z score criteria for obesity and matched for AHI (BMI Z score = 0.12 ±1.1 (non obese) versus BMI Z score = 2.41 ±0.5 (obese)). Patients with OSA had significantly higher urinary norepinephrine levels in comparison to habitual snorers (40.1±24.7ng/mg creatinine versus 31.6±16.2 ng/mg creatinine, P<0.05). There was a positive correlation between AHI and norepinephrine values. Norepinephrine levels were similar among obese and non obese subjects. Adrenaline and dopamine urinary levels were not statistically different between the 4 sub-groups (p>0.05).

Conclusion: In children with OSA, morning urinary norepinephrine levels are significantly higher than those without OSA, and correlate with the severity of the disease. Urine catecholamine levels do not appear to be influenced by the presence of obesity. Thus, altered sympathetic activity in OSA patients may occur independently of the presence of obesity.

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0185

CULTURALLY-BASED INFANT AND TODDLER SLEEP DIFFERENCES

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Introduction: There are little data available comparing sleep in infants and toddlers cross-culturally. The primary aim of this study was to characterize normal sleep patterns in a large sample of children ages 0 to 36 months in multiple predominantly Asian and predominantly Caucasian countries.

Methods: Parents of 21,273 infants and toddlers (4497 United States; 801 United Kingdom, 1071 Australia, 1077 New Zealand, 502 Canada, 1044 Hong Kong, 1033 Korea, 882 Taiwan, 989 Thailand, 967 Indonesia, 872 Japan, 7505 China) completed an expanded version of the Brief Infant Sleep Questionnaire. All questionnaires were administered online, except face-to-face interviews were conducted in Thailand.

Results: Significant variability in bedtimes were found, ranging from 19:27 (NZ) to 22:17 (HK), p<.001. Variability in total sleep time was also found, ranging from 11.6 (JN) to 13.3 (NZ) hours, p<.001. There were limited differences with no clinical significance in night wakings and naps. Room-sharing ranged from 15.1% in Canada to 94.5% of in Thailand. There was also a wide range in the percentage of parents who perceived that their child had a small or severe sleep problem (11% in Thailand to 76% in China). Overall, children from predominantly Asian countries (HK, KR, TW, TL, IN, JN, CN) had significantly later bedtimes, shorter total sleep times, increased parental perception of sleep problems, and were more likely to room share than children from predominantly Caucasian countries (US, UK, AU, NZ, CA), p<.001.

Conclusion: Overall, young children in predominantly Caucasian countries obtained more overall sleep, had earlier bedtimes, and were less likely to room-share than young children in predominantly Asian countries. No differences were found in night wakings or napping behaviors. These results indicate substantial differences in sleep patterns in young children throughout the world. Further studies to understand the basis for and impact of these interesting differences are needed.

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0186

TNF- α PLASMA LEVELS ARE INCREASED IN EXCESSIVELY SLEEPY SCHOOL-AGED CHILDREN WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Sleep disordered breathing (SDB) in children is associated with severity-dependent increases in excessive daytime sleepiness (EDS) that are only partially explained by the apnea hypopnea index or the severity of desaturation. TNF- α is a cytokine that has been implicated in EDS. We therefore conducted the present study to examine whether TNF- α levels are altered in children with OSA and EDS.

Methods: 16 pre-pubertal children (ages 6-10 years; 50% male; 37.5% AA; 50% obese) who were polysomnographically diagnosed with moderate to severe OSA and were reported by their parents as having EDS (modified Epworth > 11), underwent blood draw the next morning under fasting conditions for TNF- α levels as well as a MSLT, consisting of 5 nap opportunities of 30 min each, every 2 hours. These tests were repeated 6-8 months later, after implementation of effective treatment consisting of adenotonsillectomy and CPAP, the latter if necessary. TNF- α levels were measured using a highly sensitive ELISA.

Results: Mean sleep latency (MSL) was shorter at diagnosis (17.2±2.2 min) compared after treatment (25.6±2.8 min; p<0.001). Similarly, TNF- α levels were higher before treatment (865.7±154.0 pg/ml) compared to after treatment (132.4±45.1 pg/ml; p<0.01). Obese children were more likely to have lower MSL and higher TNF- α levels (p<0.03 vs. non obese). A significant linear correlation emerged between sleep latency and TNF- α levels for the whole cohort.

Conclusion: TNF- α morning plasma concentrations are altered in children with OSA, particularly when EDS is present. Changes in TNF- α levels appear to be proportionate to the severity of daytime sleepiness.

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0187

SLEEP DISORDERED BREATHING OF ANY SEVERITY AFFECTS BLOOD PRESSURE DURING SLEEP IN PRIMARY SCHOOL CHILDREN

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Introduction: Sleep disordered breathing is common in children and ranges in severity from primary snoring (PS) to obstructive sleep apnoea (OSA). OSA has been associated with elevated blood pressure, however the effects of severity of SDB have not been investigated. This study aimed to measure blood pressure non-invasively and continuously during sleep in children with a range of severity of SDB and non-snoring controls.

Methods: 88 children (44M/44F) aged 7-13 y were studied. 68 were referred for assessment of SDB and 20 non-snoring controls were recruited from the community. Routine polysomnography (PSG) was performed and mean arterial pressure (MAP) recorded continuously using a Finometer™ (FMS, BV Arnhem, The Netherlands). None of the children had any significant medical conditions or were on any medication. Children were divided into groups according to obstructive apnoea/hypopnoea index (OAHl). Control children OAHl<0 and no history of snoring (N=20), PS OAHl<1 event/h (N=40), mild OSA OAHl 1-5 events/h (N=14) and moderate/severe OAHl> 5 events/h (N=14). MAP data were grouped into quiet awake (recorded before sleep onset), NREM 1/2, SWS and REM. Data were compared with 2-way ANOVA with Student Newman Kuels post hoc analyses.

Results: There was no difference in BMI, total sleep time, sleep efficiency or sleep latency between groups. Overall MAP was lower in the control group compared with all SDB groups (p<0.001). Awake MAP was lower in the control group (63 ± 3 mmHg) than the PS group (74 ± 2 mmHg, p<0.01) and the moderate/severe group (73 ± 3 mmHg, p<0.05). NREM 1/2 MAP was lower in the control group (61 ± 2 mmHg) than in the PS group (67 ± 2 mmHg, p<0.05), mild OSA group (71 ± 3 mmHg, p<0.05) and moderate/severe group (73 ± 3 mmHg, p<0.1). SWS MAP was also lower in the control group (61 ± 2 mmHg) than the mild OSA group (72 ± 4 mmHg, p<0.05) and moderate/severe group (71 ± 3, p<0.05). REM MAP was lower in the control group (65 ± 2 mmHg) compared to the PS group (73 ± 2 mmHg, p<0.05), the mild OSA group (82 ± 4 mmHg, p<0.01), and the moderate/severe OSA group (80 ± 4 mmHg, p<0.001).

Conclusion: This study recorded MAP continuously overnight and found that SDB was associated with increased MAP during sleep compared to non snoring control children, regardless of the severity of SDB. These findings highlight the importance of considering the long term cardiovascular effects of any severity of SDB in children.

Support (optional): National Health and Medical Research Council of Australia

0188

FEASIBILITY OF PORTABLE MONITORING TO DETECT OBSTRUCTIVE SLEEP APNEA IN-HOME IN ADOLESCENTS: A PILOT STUDY

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Introduction: The increasing prevalence of obstructive sleep apnea (OSA) in adolescents, due in part to the childhood obesity epidemic, will increase demand for diagnostic services. We compared detection of OSA by a portable cardiorespiratory device and concurrent lab-based

polysomnography in teens with suspected OSA, followed by assessment of OSA in the home setting.

Methods: Thirty habitually snoring teens referred for PSG because of suspected OSA [mean age 15 years (range 13-17); males=57%, minority=57%, obese=63%] were enrolled. Patients underwent an in-laboratory PSG concurrent with the ARES™ Unicorder (A-Lab) and wore the Unicorder for 1 or 2-nights in-home (A-Home). PSG-based apnea-hypopneas indices (AHI) were blindly scored using standard pediatric rules with 3% desaturation criteria for hypopnea. The ARES data were auto-scored using a stepped 3% desaturation criteria plus technical review to resolve periods with auto-detected signal quality problems.

Results: Portable monitoring data lost in 2 patients due to early equipment problems. The PSG-total sleep time and A-Lab valid recording time (VRT) were 7.6±1.0 and 7.6±1.4 hours, respectively. In home, 24/28 subjects wore the device in home for two nights [VRT: N1=6.6±2.1, N2=5.9±2.3, overall=11.7±3.9 SD hours]. The relationships between the PSG vs. A-Lab and A-Home showed correlations of 0.94 and 0.73, respectively. Bland-Altman plot mean±SD of 0.9±6.1 for A-Lab and 2.4±11.2 A-Home. Using AHI clinical cut-offs of > 2 and >5, the sensitivity/specificity of the A-Home vs. PSG was 100/44 and 83/82, respectively. PSG and A-Home agreed in 23/28 at AHI threshold ≥2 and in 23/28 at AHI threshold >5.

Conclusion: The device provided comparable results to PSG when worn concurrently. When used in a home setting and compared to PSG, the device appears capable of providing information useful for a clinician to rule-in or out clinically important OSA in 82% of adolescents evaluated and may detect OSA missed by night-to-night variability.

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0189

DOES NECK SIZE PREDICT THE PRESENCE AND SEVERITY OF OSAS IN CHILDREN?

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Introduction: Obstructive sleep-disordered breathing (OSDB) has been shown to have many adverse neurocognitive consequences if left untreated in the child. In the adult population, neck size has been shown to correlate with the presence of OSDB. We hypothesize that neck size is a clinically relevant factor in the pediatric population with OSDB.

Methods: Data were obtained by retrospective chart review and subjected to chi-square and regression analysis. Apnea-hypopnea index (AHI) and mean oxygen saturation values were used as indices of severity of sleep-disordered breathing. Neck size was measured in a sitting and neutral head position. We regressed neck size against age and obtained the percent deviation from predicted neck size (DPN) for each patient.

Results: We looked at 215 children (1½ to 18 years of age) from November 2006 to December 2007 referred to a Pediatric Sleep Center. Obese (BMI>95th%tile for age) patients comprised 37.3% of this population, and had an increased frequency of snoring (chi-square=8.184; p<0.01). DPN correlated with BMI (r=0.680; p<0.01) and weight (r=0.476; p<0.01), and showed no significant correlation with height (r=0.120; p>0.1) or age (r=0.014; p>0.1). DPN showed a higher correlation (r=0.434; p<0.01) with AHI than did BMI (r=0.325), weight (r=0.133) or tonsil size (r=0.158). DPN showed a strong inverse correlation with mean oxygen saturation (r=0.713; p<0.01). DPN was a better predictor of mean oxygen saturation than BMI (r=0.456), weight (r=0.248) or tonsil size (r=0.008).

Conclusion: Kids with bigger age-adjusted neck sizes may be at increased risk for OSDB and increased severity of OSDB. DPN may provide a more anatomically specific risk factor than obesity measures such as BMI. Children with bigger neck sizes for age should be queried about snoring, apnea, hypersomnolence, and hyperactivity. Neck size should be considered in the clinical evaluation of children with a history of snoring and apnea.

Support (optional): University of Virginia Health System Buchanan Grant

0190

COMPARISON OF INFANT AROUSAL RESPONSES BETWEEN DIFFERENT STIMULI

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Introduction: A failed or impaired arousal response from sleep may play an important role in Sudden Infant Death Syndrome. Previous studies have examined infant responses to different respiratory, auditory and tactile arousal stimuli; however with variations in protocols between studies, it is unclear whether these different stimuli are acting via the same neural pathways. The aim of this study was to examine arousal responses to both respiratory and somatosensory stimulation in the same infants throughout the first six months of life.

Methods: 10 healthy term infants were studied longitudinally with daytime polysomnography at 2-4 wk, 2-3 mo and 5-6 mo postnatal age. Infants were challenged with mild hypoxia (15% O₂, balanced N₂) delivered through a silicone nose-mask and air-jet stimulation (a pulsatile jet of air to the nostrils); the starting stimulus was randomized for the first study and alternated for subsequent studies. Arousal responses were scored as sub-cortical activations (SCAs) or full cortical arousals (CAs) using standard infant criteria and were expressed as proportions of total arousal responses. Two way RM ANOVA was employed to assess differences in the proportion of CAs between stimulus types and sleep states, active (AS) and quiet (QS) sleep.

Results: When infants aroused to hypoxia at 2-4 wk, there was a significantly higher proportion of CAs, hence decreased SCAs, observed during AS (75 ± 11%) compared with QS (53 ± 11%, $p < 0.05$). No effects of sleep state were observed at 2-3 or 5-6 mo. In response to air-jet stimulation, AS was associated with increased proportions of CAs at 2-3 mo (75 ± 10%) and 5-6 mo (65 ± 8%) compared with QS (34 ± 7% and 42 ± 8% respectively, $p < 0.05$). When responses were compared between hypoxia and air-jet stimuli, there were no significant differences in the proportions of CAs and SCAs, regardless of sleep state or age studied.

Conclusion: During AS, infants exhibited increased proportions of CAs in response to both hypoxia and air-jet stimulation. This was not unexpected as AS has been well established as a state of increased arousability. Similar trends observed in hypoxia and air-jet induced arousal responses suggest that each involve common neural pathways. Furthermore, this study has provided important information suggesting that data from infant arousal studies using these different stimuli are comparable; and supports nasal air-jet stimulation as an appropriate stimulus for assessing hypoxia-induced arousal in infants.

0191

AUTO-ADJUSTING POSITIVE AIRWAY PRESSURE THERAPY IN SICKLE CELL ANAEMIA CHILDREN: PILOT STUDY

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Introduction: Effects of sleep related breathing disorders (SRBD) on cognitive function may be secondary to intermittent hypoxemia, to sleep fragmentation, or both. It is possible that SRBD influences cognitive performance in sickle cell anaemia (SCA). One of the treatments for SRBD is Positive Airway Pressure (PAP). Although it has proved effective in reducing cognitive morbidity in adults, compliance with PAP is variable. However, no studies have objectively evaluated compliance and the effectiveness of Auto-Adjusting Positive Airway Pressure (APAP) in SCA

children. This abstract reports compliance and its relationship to cognitive outcome from an RCT pilot, to explore feasibility, compliance and safety of six weeks prophylactic, overnight APAP. Clinical, laboratory and neuropsychological measures were obtained at baseline and follow-up, with the aim of obtaining pilot data on endpoints measuring efficacy of this intervention.

Methods: 12 children with SCA were treated with domiciliary APAP for 6 weeks (5/12 male; 11.2+/-3.1 years; Age-standardised BMI -0.3+/-1.1). Effectiveness was evaluated using 7 channel poligraphy. Compliance was measured on a night-by-night basis. Cognitive measures were taken at baseline and post intervention using Wechsler Intelligence Scale for Children (WISC-IV^{UK}). The primary endpoint was Processing Speed Index (PSI), derived from two measures assessing visual attention and working memory skills.

Results: All children completed 6 weeks of treatment. Compliance data showed the mean nightly use was 7.6 +/- 1.3 hours. Total number nights APAP used ≥ 5 hours, median 40, range 35-42. Percentage nights APAP used ≥ 5 hours, median 95%, range 83-100%. APAP was highly effective in this group, with a 10 fold reduction in the apnoea hypopnoea index from 24.1 +/- 10.0 to 2.4 +/- .5 events/hr, $p < .001$. There was a significant relationship between mean hours usage and change in processing speed index, $r(11) = .68$, $p = .022$. Processing speed index improved with treatment, $F(1,9) = 5.8$, $p = .040$, when controlling for hours usage.

Conclusion: APAP appears to be highly efficacious in SCA. There was no bone marrow suppression or rebound pain in any of the participants on treatment and had no adverse effects on general health. APAP improved SRBD symptoms and appears to have a dose dependent impact on cognition. These data suggest APAP is feasible and safe in sickle cell anaemia and justify further investigation to see if APAP reduces the complications of this condition.

0192

SALIVARY DIM LIGHT MELATONIN ONSET (DLMO) AND PHASE ANGLES ARE ASSOCIATED WITH SLEEP INITIATION IN PRESCHOOL CHILDREN

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Introduction: Large scale studies indicate that 11%-54% of preschool children experience reported sleep initiation difficulties (e.g., bedtime resistance, sleep onset delay). Objective data on the role of the circadian system in the development and maintenance of such problems, however, are scarce. In our companion abstract (see Garlo et al.), we report appreciable variability in salivary DLMO (18:13 to 20:31) and relative phase angles in healthy preschoolers. The present analysis examined associations between circadian parameters and sleep initiation as measured by parental report and actigraphy.

Methods: Data were collected on 13 healthy preschoolers (6 males; 11 Caucasians; 30-36 months) with no reported sleep problems. At study start, parents reported on their children's success in going to bed and falling asleep after lights-out with the Children's Sleep-Wake Scale (CSWS; higher scores=better success). Children's sleep during a typical 5-day period was then measured with actigraphy and a daily sleep diary. On day 6, children did not nap and completed a 6hr home-based salivary melatonin assessment under dim light (<4 lux) conditions. Phase angles were computed between DLMO and diary variables (bedtime, midsleep time, rise time) averaged across days 1-5. Sleep onset latency was defined as the difference between reported lights-out on the sleep diary and actigraphically estimated sleep start (3-5 day average).

Results: Children with later salivary DLMOs had (all $p < .05$) longer sleep onset latencies ($r = .45$) and poorer success falling asleep (CSWS; $r = -.48$). Smaller DLMO-bedtime phase angles were associated with poorer success falling asleep (CSWS; $r = .49$, $p < .05$). Smaller DLMO-

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midsleep phase angles were associated (all $ps < .05$) with longer sleep onset latencies ($r = -.57$) and poorer success going to bed and falling asleep (CSWS; $r = .45$ and $r = .53$, respectively). Smaller DLMO-rise time phase angles were more likely in children with shorter sleep onset latencies ($r = -.70$, $p < .01$) and poorer success in falling asleep (CSWS; $r = .50$, $p < .05$). Inspection of scatterplots showed that all associations were linear.

Conclusion: Circadian parameters show moderate-to-strong associations with children's success transitioning from wake to sleep at the beginning of the night. Understanding brain-behavior interactions related to circadian rhythms may inform prevention and treatment of sleep initiation difficulties across early development.

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0193

INSUFFICIENT NIGHTS OF SLEEP AND CHILDHOOD OBESITY IN A NATIONALLY REPRESENTATIVE DATASET

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Introduction: Associations between obesity and insufficient sleep among children have fueled speculation that inadequate hours of sleep could promote obesity. However, few prior studies have considered potential confounders such as sociodemographic factors. Our objective was to determine whether an association exists between obesity and caregiver-reported nights of sufficient sleep, in a nationally representative sample, adjusting for sociodemographic variables.

Methods: The 2003 National Survey of Children's Health (National Center for Health Statistics) used a random digit dialing to contact 76,030 households. Question-items included demographics, height and weight and number of nights of sufficient sleep (0-2, 3-5 or 6-7) obtained in the past week as perceived by a caregiver. Subjects were divided into 2 subgroups by age (6-11 vs. 12-17 years) and also by gender-specific body mass index (BMI, normal weight [5-84 percentile] vs. obese [≥ 95 percentile]).

Results: In 2003, among a population of 34 million US children (weighted), in unadjusted bivariate analysis children aged 6-11 years with 0-2 nights of sufficient sleep had significantly higher odds of being obese in comparison to children with 6-7 nights of sufficient sleep (1.7, 95% CI: 1.2-2.3). Among children aged 12-17 years, the odds of obesity was less among children with 3-5 nights of sufficient sleep in comparison to 6-7 nights (0.8, 95% CI: 0.7-0.9). However, in each age group multivariate logistic regression with adjustment for, race, gender, family income and household education revealed no remaining association between nights of sleep and BMI.

Conclusion: Reported insufficient sleep was associated with obesity mainly among younger children, but adjustment for sociodemographic variables eliminated this association. These findings from a nationally representative sample raise doubts about the role of insufficient sleep in the childhood obesity epidemic.

0194

SLEEP, PSYCHOPATHOLOGY, AND SUICIDAL BEHAVIOR AMONG ADOLESCENTS OF INSOMNIA PARENTS

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Introduction: Sleep disorders have a strong familial aggregation and some degree of genetic transmission. Sleep disorders in parents may not only have negative effects on offspring's sleep but also exert impacts on mental health. However, few studies have explored sleep problems

and psychopathology in offspring of insomnia parents. The current study aimed to examine the extent to which parental insomnia was associated with insomnia and psychopathology among adolescent offspring.

Methods: Participants were adolescents with positive (PH+) or negative (PH-) parental history of chronic insomnia, who had participated in a familial study of sleep and health. Participants consisted of 450 boys and 348 girls, with a mean age of 14.4 years. Adolescents completed a sleep and health questionnaire.

Results: Compared with PH- adolescents, PH+ adolescents were more likely to report insomnia symptoms (OR = 2.8), fatigue (OR = 2.6) and use of hypnotics (OR = 5.6). PH+ adolescents scored significantly higher than PH- on internalizing ($p = .006$) and externalizing problems ($p = .006$). Furthermore, there were significant associations between parental insomnia and suicidal ideation (16.7% vs. 5.3%, $p = .002$), suicide plan (9.5% vs. 1.5%, $p < .001$), and suicide attempt (9.5% vs. 1.7%, $p = .002$) during the past year. After adjustment for age, sex, psychopathology, parental insomnia remained to be significantly associated with suicidal ideation (OR = 3.2) and suicide plan (OR = 7.0) in adolescent offspring.

Conclusion: A history of chronic insomnia in parents is not only associated with elevated risk for insomnia but also with elevated risks for use of hypnotics, psychopathology and suicidal behavior in adolescent offspring. Family sleep interventions may be important to enhance sleep quality and decrease risks for sleep disturbance, psychopathology, and suicidal behavior in adolescents. Further studies are required to examine how and the extent to which genetic and environmental factors interact in determining sleep disturbances and psychopathology among adolescents.

0195

RAPID EYE MOVEMENT SLEEP IS ASSOCIATED WITH OVERWEIGHT IN CHILDREN AND ADOLESCENTS

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Introduction: Recent research indicates that short sleep duration is associated with obesity. However, few studies have examined the relationship between obesity and specific physiologic stages of sleep. This study aimed to examine specific sleep stages, including rapid eye movement (REM) sleep and stages 1-4 of non-rapid-eye-movement (NREM) sleep in relation to overweight in children and adolescents.

Methods: A total of 335 participants (166 children with internalizing disorders, 169 non-psychiatric controls, 66% male, mean age = 10.8 and range = 7-17 years) underwent three consecutive nights of standard polysomnography and weight and height assessment as part of study on the development of childhood internalizing disorders (depression and anxiety). Outcome variables were body mass index (BMI) Z-score and weight status (normal, at-risk, and overweight) according to the CDC BMI percentile for age and sex.

Results: BMI Z-score was significantly and linearly related to total sleep time ($\beta = -.17$, $p = .017$), sleep efficiency ($\beta = -.03$, $p = .010$), and REM density ($\beta = -.26$, $p = .018$). Compared with normal-weight children, overweight children slept about 22 min less, had lower sleep efficiency, shorter REM sleep periods, lower REM activity and density, and longer latency to the first REM period. After adjustment for demographics, pubertal status, ethnicity, and psychiatric diagnosis, one hour less of total sleep increased the odds of overweight by about 2 fold (OR = 1.8), one hour less of REM sleep increased the odds by about 3 fold (OR = 2.9), REM density and activity below the median increased the odds by 2 (OR = 2.18) and 3 (OR = 3.32) fold, respectively.

Conclusion: Our results confirm previous epidemiological observation that short sleep time is associated with overweight in children and adolescents. A core aspect of the association between short sleep duration and overweight may be attributed to reduced REM sleep. Further studies are needed to investigate possible mechanisms underpinning the asso-

ciation between diminished REM sleep and endocrine and metabolic changes that may contribute to obesity.

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0196

SCHOOL-AGED CHILDREN'S REPORT OF SLEEP PATTERNS

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Introduction: Sleep problems are common in school-aged children, but little is known about children's ability to self-report on sleep habits. Parents become less involved with sleep routines for older children, and may not be aware of children's sleep disturbances or daytime sleepiness. This study is the first step in the development of the Children's Report of Sleep Patterns (CRSP), a new self-report measure of children's sleep patterns, sleep hygiene, and sleep disturbances for school-aged children.

Methods: Participants included 120 children (103 primary care and 17 sleep clinic patients; ages 8-12 years) who completed the CRSP, a 67-item measure with nine subscales (bedtime activities, sleep location-bedtime, bedtime worries, sleep disordered breathing, parasomnias, sleep disorders, sleep location-wake time, daytime sleepiness, caffeine use), and the Multidimensional Anxiety Scale for Children-10 item (MASC-10). Parents/caregivers completed the Children's Sleep Habits Questionnaire (CSHQ) and the Children's Sleep Hygiene Scale (CSHS). Fifty-three percent of participants were boys, 66% Caucasian, and 24% African-American.

Results: The CRSP demonstrated adequate internal reliability (total coefficient alpha=.82, subscales alphas=.47-.82). As expected, parent-child agreement (inter-rater reliability) was fair for bedtime (kappa=.35), wake time (kappa=.36), previous night sleep onset latency (kappa=.23), and sleep quality (kappa=.30), all $p < .001$. Twenty-three percent of children reported a night waking the previous night that parents did not report. Concurrent validity was examined, with moderate significant relationships between the CRSP and CSHQ for sleep anxiety, sleep disordered breathing, parasomnias, and sleep disorders/disturbances (r 's=.32-.46, p 's<.001), but not daytime sleepiness (r =.11); between the CRSP and CSHS for caffeine, bedtime routine, sleep onset location, and sleep onset worries (r 's=.26-.37, p 's<.005); and between the CRSP and MASC-10 for bedtime worries (r =.35, p <.001).

Conclusion: This study provides preliminary evidence that the CRSP may be a reliable and valid self-report measure of sleep patterns, sleep hygiene, and sleep disturbances in children ages 8-12 years. Additional data from sleep clinic patients and polysomnography will be used to determine criterion validity. Further validation of the CRSP is warranted, as parental report may be insufficient for determining sleep onset latency, night wakings, and daytime sleepiness in school-aged children.

0197

THE RELATIONSHIP BETWEEN SHORT SLEEP DURATION AND OBESITY IN ADOLESCENTS

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Introduction: Obesity continues to be a major health problem because of increasing prevalence in all age groups and relation to medical comorbidities. In adolescents, there are limited studies on the relationship between obesity and sleep duration, a potentially modifiable risk-factor.

Therefore, the purpose of this study is to determine the association between short sleep duration in adolescents and obesity.

Methods: Data was from the National Longitudinal Study of Adolescent Health (Add Health); a survey of 90,000 youths, ages 12 to 18 years. AddHealth is nationally representative of middle and high school populations, surveyed in three waves. Our study population ($n=13,568$) was from Wave I (1994-1995) and Wave II (1996-1998). Weighted multiple logistic regression was used to identify the relationship between obesity at wave II and sleep duration, having adjusted for skipping breakfast > 2/week; race, gender, parental income, >2 hours TV/day, and obesity at Wave I. Obesity was defined as body mass index (kg/m^2 [BMI]) \geq 95th percentile-for-age and gender.

Results: At Wave I, mean age was 15.96 ± 0.11 yrs, and mean sleep hours were 7.91 ± 0.04 . 10.6% and 11.2% of adolescents were obese at Waves I and II, respectively. Adjusted analyses suggest effect of shortened sleep duration in Wave I does not significantly predict obesity in Wave II ($p < 0.218$). However, parental income ($p = 0.005$), TV viewing > 2hrs/day ($p = 0.008$) and obesity ($p < 0.001$) in Wave I were predictive of obesity in Wave II.

Conclusion: Environmental factors including increased television time and skipping breakfast are significantly associated with weight gain in this large sample of adolescents, while shortened sleep duration is not. Since other recent studies in younger children support shortened sleep duration as independently predictive of obesity, further study is needed to determine whether shortened sleep may have differential effects on body mass index, depending on age.

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0198

MATERNAL DEPRESSION AND SLEEP DEVELOPMENT IN YOUNG CHILDREN: A BIDIRECTIONAL MODEL

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Introduction: Depressive symptomatology in mothers is a consistent correlate of children's sleep problems, but the mechanisms underlying this linkage are unclear. The present study proposes one such mechanism, making use of observations of maternal behavior with their infants at night and mothers' cognitions about their infants sleep behavior.

Methods: Data were collected from 45 families with infants between 1 month and 24 months. Mothers were video recorded interacting with their infants at bedtime and during the night and completed questionnaire items inquiring about how they felt when their infants woke up at night and about mothers' satisfaction with their infants' sleep arrangements and sleep behavior.

Results: Maternal depression correlated with beliefs that "something awful" would happen if mothers did not respond to their infants night waking ($r = .33$, $p = .03$). From video observations, mothers' depression correlated with the percent of time mothers spent with their infants at bedtime ($r = .37$, $p = .02$), and the amount of close contact with their infants at night ($r = .42$, $p = .009$). Importantly, these correlations remained significant even after statistically controlling for infant age and frequency of infant night waking. Finally, depressive symptoms were higher in mothers who were dissatisfied with their infants' sleep location and behavior at bedtime and at night ($r = .48$, $p = .001$).

Conclusion: Depression may predispose mothers to harbor distorted, unrealistic thoughts about their infants' night waking and, in turn, to spend more time at night in close contact with their infants than non-depressed mothers. From previous research, high levels of close mother-infant contact at night lead to increases in infant night waking. In this study, infant sleep difficulties were in turn related to maternal depres-

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sion. Additional evidence in support of this bidirectional model will be presented.

0199

SLEEP COMPLAINTS AFFECTING SCHOOL PERFORMANCE AT DIFFERENT EDUCATIONAL LEVELS

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Introduction: A growing body of work documents an association between disordered sleep and school performance. This study presents data supporting this association in a contiguous community grouping of students extending from Grade 6 through college. It is the authors' contention that the sleep variables affecting school performance in junior high differ from those affecting school performance in high school, and those affecting college students.

Methods: An 18 question frequency scaled (1=never - 5=every night) sleep disturbance questionnaire based on validated and indexed questions was distributed to junior and high school health and science classes, and to college psychology and nursing classes as part of an invited presentation on "Sleep in Young Adults." School performance is based on self reported GPA (Range 2.0-4.0) split at the median for each educational level to form two groups: Low GPA and High GPA. Chi-square analyses were compared using Fisher-exact one-sided tests for each of the sleep variables (grouped according to whether or not the student exhibited the behavior 'at least once a week' or more) with GPA (low and high). This study included 98 junior high students (Grades 6-8), 67 high school students (grades 9-11) and 64 college students; mean age 27.4 (range 17-59).

Results: There were no significant associations between GPA and gender or ethnicity. No sleep variable affected GPA for all groups at a $p < .05$ level of significance. For the junior high students, the complaint of restless/aching legs when falling asleep was significantly more common in the lower GPA grouping ($p = .004$). In high school, lower GPA was significantly associated with falling asleep in class ($p = .010$), difficulty concentrating ($p = .011$), and napping ($p = .009$). In college lower GPA was significantly associated with difficulty falling asleep ($p = .017$), difficulty returning to sleep after waking at night ($p = .028$), and difficulty concentrating during the day ($p = .017$).

Conclusion: This study demonstrates that in students from 6th grade through college disordered sleep has a negative effect on school performance. However, the sleep variables affecting school performance are different for the different educational levels addressed in this study. The complaint of restless legs at sleep onset is associated with poorer performance in junior high students. Daytime sleepiness negatively affects school performance at the high school level, while insomnia has negative effects on the reported GPA for college students.

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0200

POLYSOMNOGRAPHIC FINDINGS IN CHILDREN WITH HEADACHES

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Introduction: Although previous studies have suggested a relationship between headache and sleep disturbances, literature on polysomnographic (PSG) findings in children with headache is sparse. The objective of this study was to describe PSG characteristics and sleep disturbances in children with headaches.

Methods: PSG findings of 90 children referred to our clinic because of headache, who also reported sleep complaints were studied via single-night PSG for presence of primary snoring, sleep disordered breathing (SDB), periodic limb movements of sleep, bruxism, and alterations in sleep architecture. Correlation with frequency of headache, different sub-types of headaches, and impact of medical treatment was analyzed.

Results: Headache types were migraine (60), chronic migraine (11), tension headache (6), and non-specific (13). Migraine headaches were found to be a risk factor for SDB (OR = 2.1; SDB was observed in 56% of the children with migraine versus 30% with non-migraine headache). SDB was also frequent among the non-specific headache patients (54%), in whom children with SDB had higher BMI than those without. Severe migraine was associated with shorter total sleep time (TST), longer sleep latency (SL), shorter REM and slow wave sleep (SWS) percentage. Children with chronic migraine headache had a shorter TST and longer SL, shorter REM sleep, and higher arousal index than children with migraine. Fifty percent of children with tension headache suffered from bruxism versus 2.4% of children with non-tension headache (OR=1.95).

Conclusion: Our results support an association between migraine headache and SDB, and between tension headache and bruxism in children. Additionally, disrupted sleep architecture with reduced REM and SWS in severe and chronic migraine headache may support an intrinsic relationship between sleep and headache disorders.

0201

COEXISTING BEHAVIORAL SLEEP PROBLEMS IN CHILDREN REFERRED FOR EVALUATION OF OBSTRUCTIVE SLEEP APNEA

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Introduction: Although behavioral sleep problems are common in children, they may receive inadequate attention by practitioners when the primary concern is sleep disordered breathing. These coexisting problems may be the consequence of OSA or may be triggered/exacerbated by OSA.

Methods: This was a retrospective chart review. Children 4-12 years of age referred to Cincinnati Children's Hospital for evaluation of obstructive sleep apnea (OSA) from 2005-2006 were included. Assessment included polysomnography (PSG) and the Children's Sleep Habits Questionnaire (CSHQ, Owens et al 2000). The CSHQ assesses sleep habits and behavioral sleep problems (e.g., bedtime resistance). Children with significant neurological disorders, developmental delay or incomplete records were excluded. Published normative data from the CSHQ was used as a reference control.

Results: The sample included 108 OSA patients with an average age of 7.9 ± 2.5 years. No significant differences in age or sex between OSA[s] and control[c] were observed. The average apnea-hypnea index for OSA[s] was 4.5 ± 5.8 years. OSA[s] had higher scores on CSHQ subscales: bedtime resistance (8.89 ± 2.78 [s] vs 7.06 ± 1.89 [c], $P < 0.001$), sleep onset delay (1.78 ± 0.79 [s] vs 1.25 ± 0.53 [c], $P < 0.05$), sleep duration (5.44 ± 1.95 [s] vs 3.41 ± 0.93 [c], $P < 0.001$), sleep anxiety (6.45 ± 2.27 [s] vs 4.89 ± 1.45 [c], $P < 0.001$), night waking (5.06 ± 1.87 [s] vs 3.51 ± 0.89 [c], $P < 0.001$) and parasomnia (11.09 ± 2.37 [s] vs 8.11 ± 1.25 [c], $P < 0.001$). These issues were addressed in 37.4 % (initial) and 29 % (follow up) of clinic visits. Behavioral referral was made in 21.3% (23 of 108) of cases.

Conclusion: Co-existing sleep habits and behavior sleep problem are common in OSA children. These issues may not be adequately addressed in the sleep clinics. It is speculated that the co-existing sleep problems may persist after treatment of OSA and lead to long term consequence independent of OSA.

Support (optional): The research is supported by the Cincinnati Children's Hospital Research Fund.

0202

PROLONGED-RELEASE MELATONIN RESTORE NORMAL SLEEP-WAKE CYCLE IN SMITH-MAGENIS SYNDROME: A CIRCADIAN GENETIC DISORDER

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Introduction: Smith Magenis syndrome (SMS) is a syndrome characterized by mental retardation, dysmorphic features and other congenital anomalies. These are ascribed to an interstitial deletion of chromosome 17p11.2. Another characteristic of SMS is major sleep disturbance and maladaptive daytime behavior, which have been linked to abnormal diurnal rhythm of melatonin. SMS patients display a severe sleep phase advance with sleep attacks, early bedtime, frequent awakenings and early wake-up time. All patients have an extreme phase shift of melatonin secretion. This is the first biological model of sleep disorder in a microdeletion genetic disease, which led us to a novel therapeutic approach including blockade of endogenous melatonin signalling pathways with a beta-blocker combined with the administration of prolonged-release melatonin.

Methods: 34 SMS patients, aged 3 to 23 years, 15 girls and 19 boys, were given a beta-blocker (acebutolol, 10mg/kg/day) in a single morning dose and melatonin (Circadin®, 6mg/day) in a single evening dose over a period of 12 months. Sleep parameters were recorded via diaries and actigraphy recordings.

Results: Following beta-blocker administration, mean melatonin levels decreased at midday. Daytime behaviour improved, naps and sleep attacks disappeared. Adding melatonin in the evening reset the circadian rhythm: exogenous melatonin rose at 10 pm, remained high until 2 am, and decreased until 6 am. Actigraphy recordings were correlated with sleep diaries and showed that mean sleep onset was delayed, patients slept all night and mean sleep duration improved. There was a constant improvement of sleep disorders and no treatment related adverse events.

Conclusion: SMS children have an inversion of the circadian rhythm of melatonin. Treatment with morning beta-adrenergic antagonist and evening melatonin reinstated a normal melatonin circadian rhythm, improved daytime behaviour and restored normal sleep habits, resulting in a greatly improved quality of life for both SMS children and their parents.

0203

PREDICTORS OF SLEEP DURATION IN THE FIRST 6 MONTHS OF LIFE

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Introduction: Insufficient sleep in infants and children is associated with negative effects on cognitive development, mood regulation, and overweight status. Exploring determinants of infant sleep duration may inform interventions to uncouple associations between sleep restriction and health. Few studies have examined a wide range of such factors during infancy. The objective of this study was to examine maternal and infant determinants of sleep duration in the first 6 months of life.

Methods: We studied 1676 mother-infant pairs in Project Viva, a prospective pre-birth cohort study. The primary outcome was mothers' report of their infants' average 24-hour sleep duration at 6 months; we also examined daytime nap and nighttime sleep duration separately. We used

multiple linear regression models to assess the associations between several simultaneous predictors and infant sleep duration.

Results: At 6 months, infants' mean (SD, range) sleep duration was 12.2 h/d (2.0, 5.0 - 19.0), comprising daytime naps (2.9 h/d [1.2, 0 - 11.0]), and nighttime sleep (9.3 h/d [1.8, 1.0 - 14.0]). In multivariable regression models adjusted for maternal age and parity, gender, and overall health, less household income (< \$40k/yr; β -0.57 h/d; 95% CI: -0.97, -0.18) and lower maternal education (< college graduate; β -0.19 h/d; 95% CI: -0.45, 0.08) were associated with shorter infant sleep duration. Compared with white infants, black infants slept 0.94 (95% CI: -1.31, -0.57) fewer total h/d. Also, black, Hispanic, and Asian infants slept more hours during daytime naps (0.52 h/d for blacks, 0.67 for Hispanics, and 0.64 for Asians) but fewer hours at night (-1.46 h/d for blacks, -0.81 for Hispanics, and -1.04 for Asians). Infants whose mothers had a history of depression during pregnancy (β -0.23 h/d; 95% CI: -0.61, 0.14) and those who were being breast fed at 6 months (β -0.15 h/d; 95% CI: -0.37, 0.07) appeared to sleep fewer total h/d. Introduction of solid foods before 4 months of age (β -0.05 h/d; 95% CI: -0.35, 0.24) and attendance of day care outside the home (β -0.04 h/d; 95% CI: -0.25, 0.18) were not associated with infant sleep duration.

Conclusion: Maternal depression during pregnancy, breastfeeding, and lower socioeconomic position were associated with less infant sleep duration at 6 months. However, early introduction of solid foods and day care attendance were not. Our findings of racial/ethnic differences in daytime nap and nighttime sleep duration need further investigation.

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0204

THE IMPACT OF COMORBID ANXIETY ON SLEEP PATTERN IN CHILDHOOD DEPRESSION

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Introduction: Research has shown that up to 90% of depressed adults have sleep complaints. Aim of this study was to assess sleep problems in depressed children in "pure" and comorbid presentation, and to compare results to those of a control group. Since comorbidity with other psychiatric conditions has been reported more frequently than expected, we have tried to gain a deeper comprehension of the impact of comorbid conditions on sleep pattern.

Methods: Participants were 122 children (42 females, 80 males, aged 7-11 years) who met DSM-IV-TR criteria for Major Depressive Disorder. All patients underwent a systematic psychiatric, cognitive and sleep evaluation. All children were medication-free. Depressed children in "pure" presentation and those presenting a comorbid anxious disorder entered the study and were compared with 200 healthy peers.

Results: Clinically, 82% of depressed children reported a problematic sleep compared to 5% of controls ($p < .001$). In depressed group, comorbid children showed a significantly higher frequency of sleep onset insomnia compared to the non-comorbid group (42% vs 29%). They significantly scored higher on Children's Sleep Habits Questionnaire Bedtime Difficulties, Sleep Anxiety and Sleep Duration subdomains than non-comorbid group. ANCOVA results demonstrated that comorbid/non-comorbid depressed children showed a significant tendency to a later bedtime (respectively 50 and 35 min) and a more markedly fragmented sleep than controls. Comorbid depressed children shared more frequently parents' bed than non-comorbid and controls (20% vs 17% vs 5%).

Conclusion: Results demonstrated that depressed children exhibit more disrupted sleep than controls. Among children with depression, comorbid group showed more problematic sleep than non-comorbid group. Thus, certain types of comorbid conditions might be especially disruptive on sleep. Further studies on larger samples with an attention on distinction between types of comorbidity are necessary to better investigate these aspects.

0205

BEHAVIORAL AND COGNITIVE PATTERNS IN CHILDREN WITH OSA AFTER 3 MONTHS OF POSITIVE AIRWAY PRESSURE THERAPY

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Introduction: Patterns of behavioral and cognitive change following automatic positive airway pressure (APAP) therapy in children have not been widely reported. The purpose of this study was to document behavioral and cognitive patterns in children before and after 90 days of remote continuous monitoring (ResTraxx®, ResMed Corp) of APAP treatment.

Methods: Eight children (mean (± s.d)) aged 9.38 (± 1.8) years(2 female), with clinically documented obstructive sleep apnea (OSA) were enrolled prior to APAP titration. Subjects completed several Cambridge Automated Neuropsychological Test and Battery (CANTAB)tests, parents completed the Connors Parental Rating Scale-48 (CPRS-48) to document neurocognitive performance and daytime behavior patterns, respectively. Children underwent overnight titration studies at a University-based research sleep laboratory to determine APAP treatment parameters and were given an APAP system to take home. Daily usage patterns were monitored on-line and entered into a separate spreadsheet for analysis. Descriptive statistics and non-parametric Wilcoxon tests of paired values were used to examine changes in CPRS-48 subscales and CANTAB performance, significance was set at p≤0.05.

Results: Children used APAP an average of 107.6(± 17.7) days between testing periods. APAP was used an average of 6:07 per night, average nightly pressure was 6.1 (±2.0) cm of water and average nightly leak was 0.15 liters (±0.21). CANTAB variables did not change significantly from time 1 to time 2, though several trends toward improvement (p>0.05 to p≤0.10) were evident. Significant decreases in CPRS-48 Anxiety subscale were found from time 1 average t-score=72.0 to t=59.8 at time 2(p=0.03).

Conclusion: Remote continuous monitoring of PAP therapy at home can be used to document objective PAP use patterns in children with OSA. Recruitment for a larger sample size continues, but behavior and cognition may be positively affected by PAP therapy use in children with OSA.

Support (optional): ResMed Foundation Grant(to KHA).

0206

POSITIVE AIRWAY PRESSURE (PAP) ADHERENCE AND THERAPEUTIC PATTERNS IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA: PRELIMINARY RESULTS

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Introduction: Positive airway pressure (PAP) therapy is used to treat obstructive sleep apnea (OSA) in children, but little is known about adherence patterns. The purpose of this preliminary study was to monitor children’s adherence and therapeutic PAP patterns at home with a remote, internet-based monitoring device following initiation of PAP therapy.

Methods: Eight children (mean (±s.d)) aged 9.38 (± 1.8) years (2 female), were enrolled following clinical polysomnography (PSG) which indicated obstructive sleep apnea (OSA). PAP titration studies were performed at a University-based research sleep lab to establish parameters for effective therapy. Children were sent home with an auto-titrating PAP therapy (APAP) system to use for a minimum 90-day period. Attached to each APAP machine was a device to monitor adherence and PAP settings (ResTraxx®, ResMed Corporation). Subject data was reviewed on-line

and entered into a spreadsheet for analysis. We report descriptive statistics of clinical sleep characteristics prior to initiation of APAP therapy, and adherence and therapeutic APAP patterns.

Results: Prior to initiation of PAP therapy, average apnea/hypopnea index (AHI) was 6.3(±2.4), 63% (n=5) were status post adenotonsillectomy, and BMI was 23.9(± 8.8). Children used APAP an average of 107.6 (±17.7) days (range 89-145) for 6:07 per night (range 1:33-9:20). Average nightly pressure was 6.1(±2.0) cm of water (range 3.3-9.8). Maximum average pressure was 9.7(±2.3) (range 5.3-12.5) cm of water. Masks were removed and put back on an average of 0.69(± 0.6) times a night, with a range of 0.19 times to 1.7 times per night.

Conclusion: Children used PAP therapy for over 6 hours per night on average. Patterns of mask removal and replacement during the night were frequent, and parents should be encouraged to check mask placement at least once per night during initial APAP therapy.

Support (optional): ResMed Foundation Grant (to KHA)

0207

LATE STARTING CITY MIDDLE SCHOOLS: ROLE OF FAMILY INCOME AND HEALTH CARE ON 7TH GRADERS’ SLEEP PATTERNS

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Introduction: Later school start times are advantageous for middle/high school students’ sleep needs. Other factors, however, play a significant role. Recent findings demonstrate that income level influences sleep/wake behaviors (e.g., Moore et al., 2002). Current work, however, doesn’t adequately address the impact of income and health care on adolescents’ sleep patterns. Controlling for later school start times, this study examined effects of family income and use of health care on young adolescents’ sleep/wake patterns.

Methods: Seventh graders (N = 96) were recruited for a longitudinal study of sleep and behavior. Parents provided background information (24 family incomes < \$20,000; 11 were > \$80,000). Students completed the School Sleep Habits Questionnaire (school/weekend sleep variables, caffeine use) and assessed sleep for 8 days via diaries and actigraphy (AMI). Using Action-W2 software, sleep period, onset, offset, and mid-sleep times were estimated for school/weekend nights. Effects of sex, family income, and access to health care were analyzed.

Results: Thirty-seven percent of 7th graders were falling asleep after 11 pm with 66% getting less than 9 hours on school nights. Family incomes below \$40,000 were significantly associated with more delayed onset, offset, and mid-sleep times on weekend, but not school-nights (Multivariate F = 6.86, p = .002; Onset: M(low) = 12:22am vs. M(high) = 11:30pm; Offset: M(low) = 9:20am vs. M(high) = 8:43am). Although income was not associated with regular physician use, 7th graders with physicians had healthier school-night sleep patterns than those without health care (Multivariate F = 3.70, p = .03; e.g., 25 min. more sleep, 30 min. earlier onset, less delayed mid-sleep). Self-reported sleep variables showed similar trends and there were no gender differences. Students from lower income families reported more caffeine use (F = 4.54, p = .04).

Conclusion: Findings demonstrate that the trend for delays and reductions of school-night sleep begin early in adolescence, even with delayed school start times. Other demographic factors exacerbate adolescents’ sleep patterns. Middle schoolers from families with either low income or poor access to physicians obtained less sleep, had more delayed schedules, and reported more frequent caffeine use.

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0208

SLEEP AND REST ACTIVITY CYCLES IN INFANTS WITH AND WITHOUT A MATERNAL FAMILY HISTORY OF DEPRESSION

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Introduction: Major depressive disorder (MDD) is associated with sleep disturbances, abnormalities in the timing of REM and NREM sleep and with damped amplitude circadian rhythms. These findings are evident in both children and adults with MDD and in those at high-risk for MDD, based on positive maternal history. Damped amplitude rest activity cycles have also been reported in very young children with MDD. These findings raise the possibility that the entrainment of sleep and circadian rhythms may be impaired in MDD. The purpose of this study was to compare sleep and circadian rest activity cycles in infants born to mothers at high and low risk for MDD.

Methods: Four infants in the study were categorized as low risk, with no maternal history of depression and 11 infants were categorized as high risk, based on past or current maternal MDD (total infant n = 15). Sleep and circadian rest activity cycles were measured from light and motion sensing actigraphs for a minimum of 1 week every month starting at 2 weeks post partum and continuing until 30 weeks post partum. Data were coded by group and total nocturnal sleep time, sleep latency, sleep efficiency, the number of day sleep episodes and their durations, and strength of circadian rest activity cycles were compared at 2 and at 30 weeks, using repeated-measures ANOVA.

Results: The high-risk infants had significantly longer nocturnal sleep latency, lower sleep efficiency, and more daytime sleep than did low-risk infants at 2 and 30 weeks post partum. Circadian rest activity cycles were slower to entrain in the high-risk group and remained significantly lower amplitude than the low risk infants at 30 weeks of age.

Conclusion: These findings suggest that sleep and rest activity cycles are poorly entrained in infants from a maternal family history of depression.

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0209

NON-MEDICAL PSYCHOSTIMULANT USE AND SLEEP AMONG UNDERGRADUATE STUDENTS

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Introduction: Studies of the prevalence of psychostimulant use among undergraduate students have not measured sleep concurrently. Considering the known relations between sleep and other stimulants such as caffeine, the relation between sleep and psychostimulant use may be important. The current study explores the pervasiveness of psychostimulant use, factors surrounding that drug use, and measures of sleep efficiency (SE) and sleep quality (SQ).

Methods: The Pittsburgh Sleep Quality Index (PSQI) and psychostimulant use measures were disseminated to undergraduate students living in residence halls at West Virginia University. Data were analyzed with a 2x2 between-subjects multivariate analysis of variance (MANOVA) using SE and SQ as dependent variables and psychostimulant use and membership in a fraternity or sorority as independent measures.

Results: The prevalence of psychostimulant use for non-medical reasons in this sample of 343 undergraduates, 94% of whom were age 18-20, was 10.1%. Among those with a lifetime history of psychostimulant use, 17.6% used Methylphenidates (Ritalin) and 67.6% used Mixed-Salt Amphetamines (Adderall). Though the majority (82.8%) of users reported administering psychostimulants orally, 17.2% reported nasal administration. SE and SQ subscales of the PSQI were significantly affected by non-medical psychostimulant use, ($p < .05$) but not by membership in

sororities or fraternities ($p > .05$) or by the interaction of psychostimulant use and Greek membership ($p > .05$). To examine the impact of psychostimulant use on SE and SQ separately, univariate ANOVA's showed that non-medical psychostimulant use was significantly related to self-reported SQ ($p < .01$), but not SE ($p = .72$).

Conclusion: Our results reiterate previous findings of an alarming prevalence of non-medical psychostimulant use among university students. This prevalence rate is even more concerning in light of our finding that students reporting use of these drugs also experience poorer sleep quality. The combination of drug use and poor sleep could lead to decrements in health and daily functioning.

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0210

INDIRECT EFFECT OF TOOTH GRINDING ON PRESCHOOL PERFORMANCE

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Introduction: Tooth grinding during sleep is a nonfunctional behavior that may indicate bruxism and is relatively common in children (up to 20% of those <11 years). Bruxism is a condition that is linked to stress, can result in occlusal wear, facial and temporomandibular joint pain, headaches, and arousals from sleep which are associated with elevated behavior and attention problems. The associations between tooth grinding, daytime behavior, and performance have not been previously studied in children and were the focus of the current work.

Methods: As part of a larger study, parents of financially disadvantaged preschool children enrolled in the Early Jump Start program in Louisville, Kentucky completed a questionnaire that included frequency of tooth grinding during sleep, preschool performance items, and items from the Child Behavior Checklist. A structural regression model and the Sobel test for mediation were calculated to assess the effect of tooth grinding on preschool performance.

Results: Participants (N=1,956) were 4.3 (SD±.52) years, 46% female, 45% White, and 39% Black. Overall, 36.8% were reported to grind their teeth ≥ 1 time per week and 6.7% reported this behavior ≥ 4 times per week. Within our model 'tooth grinding' and 'withdrawn behavior' were single item observed variables and 'preschool performance' was a multiple item latent variable. Model fit was $\chi^2=7.77$, $df=7$, CFI=1.00; where 'tooth grinding' was positively associated with 'withdrawn behavior' ($p < .001$) and 'withdrawn behavior' was negatively associated with 'preschool performance' ($p < .001$). 'Withdrawn behavior' was a mediator ($p < .001$) between 'tooth grinding' and 'preschool performance'.

Conclusion: The frequency of tooth grinding in this pediatric sample was higher than expected; this high risk population should be targeted for evaluation of bruxism. Our findings indicate that tooth grinding has a negative effect on preschool performance when withdrawn behavior is present. This dynamic relation between tooth grinding and withdrawn behavior yields a non-obvious influence on preschool performance.

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0211

SLEEP & ACTIVITY DISTURBANCES IN 22Q11 DELETION SYNDROME USING ACTIGRAPHY

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Introduction: 22q11 Deletion Syndrome (22q11DS) is poorly understood although it is the second most common genetic birth defect. It is best known for causing serious cardiac defects, cleft lip/palate, prominent speech/articulation difficulties, learning disabilities, autism spectrum disorder and mental illness in young adulthood. This is the first study to examine sleep and activity in 22q11DS and one of very few studies to examine young adults with this disorder.

Methods: A sample of 20 teens/young adults (50% Male; Asian=1, AA=3; Age: M=21.5, SD=4.7, Range 15-31) with a genetic diagnosis completed 7 days of actigraphy. One additional subject (age 17) was not included in this analysis because he was autistic and his sleep/wake patterns were too erratic to compare. A battery of sleep instruments was administered jointly with parents to validate responses.

Results: A board certified sleep physician independently examined the actograms and recommended follow-up polysomnography for 12 subjects (60%). Reasons for further evaluation included disrupted sleep and/or irregular sleep/wake patterns. When comparing the 12 subjects referred for further evaluation to the 8 subjects with more normal sleep wake patterns there were statistical differences ($p < 0.05$) during sleep intervals for several variables including: Mean Activity Counts/minute; Mean Sleep Efficiency; Mean Wake Time, Mean Percent Wake; and Mean Percent Sleep. Subjects did not report sleep problems when interviewed using the Pittsburgh Sleep Quality Instrument, the Sleep 50 instrument or the Pediatric Sleep Questionnaire. Parents reported bipolar disorder (n=1); mood disorders (n=5), depression (n=5), social immaturity (n=13), obsessive compulsive disorder (n=5), anxiety disorder (n=8) and phobias (3).

Conclusion: These findings suggest that persons with 22q11DS may have disrupted sleep and or irregular sleep/wake patterns that are not identified with standard questionnaires or structured interviews. As poor sleep can exacerbate psychological or behavioral problems we propose that this patient population undergo actigraphy and/or polysomnography to identify latent sleep disruptions that would otherwise not be detected.

Support (optional): Dean's Research Award, University of Alabama School of Nursing (MGU), University of Alabama at Birmingham

0212

USE OF PEDIATRIC SLEEP QUESTIONNAIRE TO PREDICT OSA RELATED OUTCOMES IN ADOLESCENTS WITH SEVERE OBESITY UNDERGOING GASTRIC BYPASS SURGERY

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Introduction: Obstructive sleep apnea (OSA) is highly prevalent in adolescents with severe obesity and surgical weight loss results in reduction of OSA severity. With increasing number of adolescents with severe obesity seeking surgical weight loss treatment, there is a need for clinical tools to assess OSA status after surgery. Our goal is to describe the use of

the pediatric sleep questionnaire (PSQ) to predict OSA related outcomes of gastric bypass surgery in adolescents with severe obesity.

Methods: We reviewed the anthropometric and polysomnography (PSG) data on adolescents with severe obesity who underwent laparoscopic Roux en Y gastric bypass surgery at Cincinnati Children's Hospital Medical Center from July 2005 to July 2006 and whose parents completed the 22-item Sleep-Related Breathing Disorder (SRBD) scale of the PSQ. Comparisons were made between pre- and postoperative SRBD score data. OSA was defined as apnea-hypopnea index ≥ 5 per hour of sleep on the PSG and a PSQ SRBD score of ≥ 0.33 was considered indicative of OSA.

Results: Nine subjects (mean age 16.4yrs \pm 1.1, mean BMI 63.9 kg/m² \pm 10.9, 78% female) had PSQ data before and after surgical weight loss. After significant weight loss (mean BMI change 17.0 kg/m²), PSQ SRBD score significantly decreased in all patients (baseline 0.44 \pm 0.1 vs. 0.17 \pm 0.1 after weight loss, $p < 0.01$). Five of the 9 subjects had PSG data before and after surgical weight loss. All the 4 subjects with PSG resolution of OSA after surgical weight loss had a PSQ SRBD score of < 0.33 .

Conclusion: Our study indicated that the significant weight loss after gastric bypass is associated with a marked reduction in PSQ SRBD score with a score of < 0.33 predicting OSA resolution. This supports the use of PSQ SRBD to predict OSA related outcomes of gastric bypass surgery in adolescents with severe obesity.

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0213

OBESITY INDEPENDENTLY ALTERS ENDOTHELIAL FUNCTION IN CHILDREN

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Introduction: Endothelial dysfunction has been recently identified as a consequence of obstructive sleep apnea (OSA) in non-obese children with adenotonsillar hypertrophy. However, little information is currently available on the impact of obesity on vascular function in children with OSA. We therefore examined endothelial function in obese and non-obese children without OSA.

Methods: All pre-pubertal children participating in research studies at Kosair Children's Hospital Pediatric Sleep Center in Louisville, KY, were approached for recruitment. Endothelial function was assessed using a modified hyperemic test after cuff-induced occlusion of the radial and ulnar arteries. A laser Doppler sensor (Perimed, Periflux 5000, Järfälla, Sweden) was utilized to assess perfusion kinetics which was performed prior to sleep onset, and the test was repeated twice in each child. Anthropometry was assessed in all children using the InBody 320 scale (Biospace) assessing bioelectrical impedance to assess body fat distribution.

Results: 19 children (mean age 7.7 \pm 0.4 years) have been evaluated to date, and 13 of these had BMI-Z scores > 1.56 and were therefore considered as obese. All children underwent an overnight sleep study which revealed completely normal sleep architecture and absence of any cardiorespiratory pattern abnormality. As expected, body fat percentage was significantly elevated in the obese children (39.1 \pm 2.0% vs. 21.0 \pm 2.6% body fat in non-obese; $p < 0.01$), with increased visceral-truncal fat distribution in the obese group as well. During reactive hyperemic tests, there was a significant delay to peak capillary perfusion after release of the occlusion in obese children compared to non-obese children (46.2 \pm 4.7 sec vs. 32.9 \pm 1.6 sec, $p < 0.02$), but no differences in the magnitude of hyperemia.

Conclusion: These preliminary data confirm and extend on previous studies indicating that endothelial dysfunction occurs very early in life secondary to obesity. Exploration of the impact of OSA on endothelial function in obese children is planned and follows the assumption that

OSA and obesity may interact to enhance their individual adverse effects on endothelial integrity.

Support (optional): NIH grant R01HL-65270 (DG), and The Children's Foundation Endowment for Sleep Research

0214

USE OF POLYSOMNOGRAPHY (PSG) IN MANAGEMENT OF NEWBORNS WITH PIERRE ROBIN SEQUENCE (PR) AND OBSTRUCTIVE SLEEP APNEA (OSA) WITH MANDIBULAR DISTRACTION (MD)

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Introduction: Pierre Robin sequence (PR) consists of micrognathia, glossoptosis and high arched or cleft palate. Some infants have severe OSA in prone position causing respiratory distress. Treatments may include tongue lip adhesions or tracheostomy. MD is a newer technique used to improve the upper airway obstruction and avoid tracheostomy. This study explores the relationship between PSG findings, surgical selection and perioperative management of these infants.

Methods: 13 infants with PR were referred during the past 2 yrs with 11 infants undergoing MD. All except 1 intubated infant underwent preoperative PSG. All had postoperative PSGs.

Results: Daytime preoperative PSG showed average sleep time of 276 minutes (range=201-331). Average AHI - 27.3 (range=11-68) vs. 4.5 (range=2-7) for 2 infants referred for MD but managed without surgery. Maximum ETCO₂ averaged 69 torr (range=51-85), lowest oxygen saturation (LOS) averaged 72 torr (range=50-86) with 7 infants requiring supplemental FiO₂. Infants began MD at an average age of 26 days (range=10-49). Postoperative PSG repeated after mean advancement of 11 mm (range=6-17) and 16 days (range 10-25) showed an average AHI-2.2 (range=0.2-6.0). Five infants improved to normal UAO (AHI<2), the other 6 improved to mild UAO (AHI=2-6). None required supplemental oxygen postoperatively. Improvement in AHI, LOS, and maximum ETCO₂ were significant (p=0.001, 0.008, 0.001). Partly based on the postoperative PSG, distraction continued for 6 infants resulting in an average total distraction of 14.4 mm (range=10-20, n=11). PSG performed before cleft palate repair (average age=300 days, range=271-391) showed average AHI - 1.3 (range=0.4-4.0, n=5).

Conclusion: MD dramatically improves UAO in infants with PR. Day-time PSG documents improvement of UAO thereby guiding degree of MD.

0215

CLINICAL CHARACTERISTICS OF 45 CONSECUTIVE REFERRALS TO A NEWLY ESTABLISHED MULTIDISCIPLINARY PEDIATRIC SLEEP CENTER

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Introduction: Cross-sectional studies identify sleep problems in 15% to 35% of children. Despite the explosion of sleep centers across the country, few services target children with their unique etiologies and interventions. The current study represents a retrospective clinical database review, tracking patients attending a newly established pediatric sleep center.

Methods: Patients included 45 consecutive referrals to a pediatric sleep center in a Midwest children's hospital. Patients presenting symptoms of physiological sleep disorders (e.g., apnea, EDS) were evaluated by a board certified pediatric sleep physician; those presenting symptoms of

non-physiological sleep disorders (e.g., behavioral insomnia of childhood) were evaluated by a pediatric psychologist certified in behavioral sleep medicine; some with multiple symptoms were evaluated by both. Data described were obtained from new patient visits only.

Results: Two-thirds of referrals came from primary care physicians (53% pediatricians; 13% family practice). Most patients (81%) lived within 30 miles of clinic; 6% traveled over 100 miles. Patients presented a mix of physiological and behavioral symptoms, with 21 evaluated by the sleep physician, 19 by the behavioral specialist, and 5 by both. Children attending behavioral services tended to be younger and male (mean 6 yrs; 68% male) compared to medical sleep services (mean 12 yrs; 48% male; bmi 28.9). Primary complaints included snoring (38%), undesirable co-sleeping (18%), insomnia/sleep initiation (13%) and parasomnias (11%). Secondary complaints included frequent night-time awakenings (24%) and EDS (13%). Initial diagnosis was dominated by snoring (31%), followed by DSPS (20%), and parasomnias (15%). Secondary diagnosis most commonly included behavioral insomnia of childhood (11%) and anxiety (9%). Consistent with past studies, medical (78%) and psychiatric co-morbidities (27%) were common.

Conclusion: These data support the view that pediatric sleep problems are multi-faceted, tapping the expertise of more than one subspecialty. Future studies are needed to track clinical outcomes and describe the diagnostic results of PSG studies.

0216

ACCEPTABILITY OF EMPIRICALLY-BASED INTERVENTIONS FOR BEDTIME PROBLEMS AND NIGHT WAKINGS: RATINGS BY PARENTS OF CLINICALLY REFERRED YOUTH

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Introduction: An American Academy of Sleep Medicine (AASM) task force recently published a clinical review and practice parameters for the behavioral treatment of bedtime problems and night wakings in young children. The review concluded that behavioral therapies, particularly extinction-based approaches, are highly effective in improving child sleep and enhancing child and family well-being. In clinical practice, however, the effectiveness of a given treatment may be compromised if parents or professionals do not perceive it in a positive manner. The purpose of the current study is to extend our previous work assessing treatment acceptability by pediatricians and parents in the general community. Due to past treatment efforts, parent of children with clinically significant sleep problems may view interventions differently than parents in the general population.

Methods: Participants included 25 parents of children 2-8 years of age, referred to a behavioral sleep medicine clinic. Most patients received diagnoses (ICSD, 1997) of Sleep Onset Association Disorder (47%) and Limit-setting Sleep Disorder (26%). Parents were provided a written vignette describing a 2-year-old child who has "never slept through the night." The child cries when the parents place her/him in bed, then awakens frequently at night and has difficulty settling after each awakening. Eight treatments were selected from a review of the literature. The Treatment Evaluation Inventory-Short Form (TEI-SF) served as the outcome measure.

Results: Treatment acceptability ratings did not differ by patient diagnosis. Graduate Extinction was rated more acceptable than Sedative Medication, Scheduled Awakenings, Quick Check, and Bed-sharing (all p's <.05). There were no differences between Extinction, Quick Check, Scheduled Awakenings, Faded Bedtime, Extinction w/Parental Presence, and Sedative Medication (p's >.05). Bed-Sharing was rated to be the least acceptable option (p's <.05).

Category E—Pediatrics

Conclusion: Consistent with our previous data, these parents rated Graduate Extinction (e.g., the “Ferber” procedure) to be the most acceptable treatment for bedtime problems and night waking. Contrary to our hypothesis, Unmodified Extinction was perceived to be an acceptable option. TEI-SF scores were remarkably similar to those of community-based parents and primary care pediatricians, except that parents of clinically-referred children more readily endorsed Sedative Medication as a viable treatment option.

0217

SLEEP, HUNGER, SATIETY, FOOD CRAVINGS, AND CALORIC INTAKE IN ADOLESCENTS

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Introduction: The prevalence of adolescent obesity has more than tripled in the last two decades. Although diet and exercise patterns are major determinants of weight, recent studies with children and adults have shown that total amount of sleep is inversely associated with body mass index (BMI). The purpose of this study was to examine the association among total sleep time (TST), hunger, satiety, food cravings, and caloric intake in a sample of otherwise healthy adolescents.

Methods: Subjects were recruited from the community and a local high school. Demographic data, sleeping and waking habits, pubertal status, food cravings, caloric intake, physical activity, height and weight were collected between October 2006 and April 2007. Subjects also completed a 7-day sleep/hunger/satiety diary. Descriptive and parametric procedures were used for data analyses ($\alpha = .05$).

Results: The sample included 56% females ($n = 48$), 76% Black ($n = 65$) adolescents. The mean age was 15.6 ± 1.4 years and mean BMI was 24.3 ± 5.4 kg/m². The mean reported cumulative nocturnal sleep was $52.9 (\pm 6.0)$ hours and mean reported cumulative daytime sleep (napping) was $3.7 (\pm 3.4)$ hours. Multiple regression analyses revealed that perceived cravings for high fat foods was greater in Black adolescents and those with increased daytime sleep. Cravings for sweets were greater in female adolescents and cravings for carbohydrates/starches were greater in Black adolescents and those with increased daytime sleep. Cravings for fast foods were greater in Black female adolescents. Total perceived food cravings were greater in younger Black adolescents and were associated with increased daytime sleep. Caloric intake was higher in younger male adolescents and increased daytime sleep.

Conclusion: These findings support an unexpected association between increased daytime sleep and eating behaviors that potentially lead to obesity. Future longitudinal studies using objective measures of sleep, appetite regulation, and caloric intake are needed to better understand how daytime sleep may affect appetite regulation in adolescents from different racial and gender subgroups.

Support (optional): The project described was supported by Grant Number F31NR009897 from the National Institute of Nursing Research.

0218

SLEEP DISORDERS IN CHILDREN WITH EPILEPSY: CLINICAL HISTORY AND POLYSOMNOGRAPHIC COMPARISON WITH NON-EPILEPSY CHILDREN PRESENTING AT A SLEEP DISORDERS CENTER. THE NYU COMPREHENSIVE EPILEPSY CENTER EXPERIENCE. A RETROSPECTIVE STUDY

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Introduction: Sleep disorders in children are common. Several studies have found an increase frequency of sleep problems in children with epilepsy when compared with normal controls. There have been no studies

comparing the prevalence of sleep disorders of children with epilepsy and controls with no epilepsy who present to a Sleep Disorders Center for evaluation.

Methods: We reviewed retrospectively all the children who presented at the New York Sleep Institute from December 2005 to July 2007. We included all the children ages 1 to 20 years-old. We noted the different sleep complaints, Polysomnographic data and final diagnoses and compared children with epilepsy with children referred from the community who did not have epilepsy. We compared the results using chi square and t-student using the JMP program for statistical analysis.

Results: Forty seven children met our inclusion criteria. Twenty two children had epilepsy. The average age was 9.7 years in the epilepsy group and 7.0 years in the non-epilepsy group. The two groups had similar prevalence of symptoms of excessive daytime sleepiness, snoring, difficulties staying asleep, non-restorative sleep, parasomnia and restless sleep. The epilepsy group had more difficulties to fall asleep than the non-epilepsy group ($p = 0.0238$). The Polysomnography results in children with epilepsy showed a sleep efficiency of 88.7% and a sleep latency of 19.0 minutes. Stage 1 sleep represented 2.6 %, stage 2 sleep 37.0%, slow wave sleep 50.2% and REM sleep 10.1%. The percentage of slow wave sleep was significantly higher in the epilepsy group compared with the control group ($p = 0.0135$). There was a trend towards a higher PLMS index in the patients with epilepsy compared to controls. Among children with Epilepsy, there were 8 patients with Obstructive Sleep Apnea (OSA), 10 patients with Restless Legs Syndrome, 5 patients with Parasomnias, 2 patients with Delayed Sleep Phase Syndrome and 6 patients with Excessive daytime sleepiness. There were 13 patients with more than one diagnosis.

Conclusion: Children with epilepsy present with more problems to fall asleep as compared with children from the community referred to a sleep disorders center. There is a trend towards a higher number of PLMS in children with epilepsy and these children also show a higher percentage of slow wave sleep. Ten of 22 children with epilepsy had RLS.

0219

EARLY IDENTIFICATION OF SLEEP APNEA IN INFANTS WITH PRADER WILLI SYNDROME

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Introduction: Children with Prader Willi Syndrome (PWS) develop hyperphagia and subsequently obesity at around age 3 years. Recent studies in prepubertal children with PWS have reported higher prevalence of sleep hypoxemia and apnea. However, there have been no studies to date that describe sleep disordered breathing in infants with PWS, younger than age 3 years, prior to the development of hyperphagia and/or obesity. Concerns about the associated mortality due to apnea in children with PWS while on growth hormone, has prompted our center to screen growth hormone candidates for the possibility of sleep disordered breathing. The purpose of this study is to identify the presence of sleep disordered breathing in infants with PWS, younger than 3 years of age, prior to the initiation of growth hormone treatment.

Methods: Fourteen infants (9 boys, 5 girls) under the age of 3 years (mean age 24.3 ± 12.6 months; Mean BMI 16.8 ± 2.58) were referred to the sleep center for a routine evaluation before starting on growth hormone therapy. The following parameters were analyzed: Respiratory Disturbance Index (RDI); baseline oxygen saturation; lowest saturation level; time spent at oxygen saturation <90% and desaturation index (defined as number of desaturations >3%/hour of sleep).

Results: Seventy (70%) percent of our patients were reported to be snorers. Three of the 14 (21%) had RDI < 1 and were considered free of sleep disordered breathing. The majority of the infants (79%) demonstrated sleep disordered breathing, with RDI ranging from 1.1-6.5 (mean 2.3 ± 1.8). Apnea classification showed 26% central apneas (mean = 4.88 ± 5.7); 15% obstructive apneas (mean = 2.9 ± 3.56); and 58% hypopneas

(mean 11.6 ± 7.38). Mean baseline oxygen desaturation was 97.3 ± 1.1 . Mean lowest saturation was 85.9 ± 4.8 . Mean desaturation index was 6.67 ± 6 .

Conclusion: Infants with PWS younger than 3 years of age, may present with sleep disordered breathing even before obesity develops. The presence of sleep disordered breathing at a very early age in non-obese patients with PWS highlights the need for early screening.

0220

SLEEP COMPLAINTS IN CHILDREN AND ADOLESCENTS WITH UNIPOLAR DEPRESSIVE DISORDER

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Introduction: Common sleep complaints in pediatric depressive disorders (DD) include insomnia, hypersomnia, sleep continuity problems (awakening at night), and sleep wake reversal. Some studies indicated that clinical profiles differ between depressed children without and with sleep disturbance and with more severe depression in the later. We explored sleep complaints and their type in young individuals with Unipolar Depression (UD).

Methods: 222 pediatric cases (6-17 years) with Unipolar Depression (UD) (DSM-IV criteria for Depressive Disorders "Diagnostic Interview for Children and Adolescents" DICA-IV) were investigated for sleep disorders through face to face interviews. Exclusion criteria were: chronic medical illness, mental, physical handicap; history of substance abuse or dependence in the last two weeks; pervasive development disorder; schizophrenia, severe psychotic disorder; institutionalized subjects, homelessness, mental retardation, substantial learning difficulties, inability to complete interview procedures. Subjects were subdivided in three groups based on sleep complaint: presence of initial insomnia; insomnia plus hypersomnia; and only hypersomnia. Analysis was done by descriptive statistics and Chi-square test.

Results: The final sample consisted of 207 subjects: 119 boys (11.8 ± 2.1 years old) and 88 girls (13.4 ± 3 years old). There was no gender difference in report of sleep complaints, but 88% of the sample reported sleep problems during their depressive episodes with initial insomnia as the most common ($p < 0.01$), and this specific complaint was significantly associated with report of school problems ($p < 0.05$). But the investigation of the different types of sleep complaints did not reveal any difference in disease severity based on these criteria as suggested in adults.

Conclusion: Our findings suggest sleep complaints are very common in children and adolescents with Unipolar Depression, and the most common complaint is sleep onset (initial) insomnia. There are many studies of sleep disorders and depression in adults, but less in pediatric cases, despite possible interaction between both types of health problems.

0221

EFFECTS OF PREMATURE MANDIBULAR ADVANCEMENT WITH HERBST APPLIANCE IN SLEEP PATTERN AND UPPER AIRWAY VOLUME IN ADOLESCENTS

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Introduction: This prospective study assessed relevant information from each four variables: sleep pattern, adolescents, mandibular retrognathism, and early orthopedic-functional treatment, as well as shed some light upon their likely interaction.

Methods: Telerradiography and magnetic resonance imaging of the neck were obtained prior to and after treatment (12 months) with Herbst appliance, as were four polysomnographic recordings with pressure nasal cannula. The sample consisted of 16 adolescents with Class II, divi-

sion 1 malocclusion with mandibular retrognathism and at stage 3 or 4 of skeletal maturation.

Results: The length of mandible was increased leading to a more anterior positioning of the chin, the antero-posterior position of maxilla remained stable and its length was increased. The posterior airway space was enhanced, the length of the tongue was preserved and its height increased, the hyoid bone was in a more anterior position. The polysomnographic data revealed that sleep efficiency, REM sleep, sleep latency and REM sleep latency remained stable, a reduction in the percentage of sleep was verified in stages 1 (4.30 ± 1.99 to 2.61 ± 1.83) and 3-4 (25.78 ± 7.00 to 19.17 ± 7.58), an increase in the percentage of stage 2 after treatment (49.03 ± 6.25 to 56.90 ± 6.22). There was a reduction in the number of events of respiratory effort-related arousal (7.06 ± 5.37 to 1.31 ± 1.45) due to an increase in the volume of the airway as a result of redirecting growth of the jaw.

Conclusion: The immediate benefits of this treatment were lead to a less convex profile of the face, improved the relation between maxilla and mandible, the function of the maxillofacial complex was facilitated and the increase in the space within the airway allowed the patients to have easy nocturnal breathing. The long-term benefit was eliminate a predispose factor to OSAS in adults.

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0222

OBJECTIVE AND SUBJECTIVE MEASURES OF SLEEP IN SMITH-LEMLI-OPTIZ SYNDROME (SLOS)

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Introduction: SLOS is an autosomal recessive disorder due to inborn errors of cholesterol metabolism. SLOS has broad spectrum of phenotypic abnormalities including mental retardation, developmental delay, facial anomalies and behavioral abnormalities including sleep disturbances. There are reports of sleep disturbance in as high as 70 % of SLOS patients.

Methods: A convenience sample of a larger study exploring cholesterol synthesis in SLOS was asked to complete the Child Sleep Habits Questionnaire (CSHQ) and wear an actigraph at time of hospital admission. Sleep efficiency (SE) and total sleep time (TST) were estimated by actigraphy. Parental concerns regarding sleep problems were subjectively evaluated by the CSHQ questionnaire.

Results: 5 males and 6 females with SLOS were evaluated, 5 under the age of 2 and 6 over the age of 3. The SE for ages 1 to 2 ranged from 72.4 - 84; mean: 78.3 and standard deviation (SD): 5.6. SE for 3-13-year-olds ranged from 82.2 - 88.81; mean: 86.3; SD: 2.9 when one outlier with SE of 63.35. Mean with the outlier included was 82.5; SD: 9.7. TST for 1-2 year olds ranged from 390.5 - 514.61; mean: 472.0 and SD of 51.9. TST for the 3-13 year old was 414.6 - 565.6; mean: 463.4; SD: 73.5. The outlier for SE mentioned above presented a TST of 359.1, the lowest score for either group. The CSHQ scores ranged from 42 to 60 with one outlier at 86. Means were 48 for both age groups with the outlier removed, though SD was 4.9 for the 1-2 group and 9.1 for the older group.

Conclusion: In a cohort of 11 SLOS patients, we found low TST and SE in the 1-2 year age group. The 3-13 year old presented nearly normal SE and TST except in one patient (outlier) who received a relatively high parasomnia score on that CSHQ subscale. This is a small sample size but objective measures showed a trend in improved TST and SE in the older SLOS child.

0223

SLEEP PROBLEMS AND THEIR RELATION TO COGNITIVE FACTORS, ANXIETY AND DEPRESSIVE SYMPTOMS IN CHILDREN AND ADOLESCENTS

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Introduction: Childhood sleep problems are common in the general population yet few data are available examining unique relationships between sleep, anxiety, cognitive symptoms, and depression in non-clinical samples of youth. In addition, although it has been suggested that sleep disturbance may be more closely associated with anxiety during childhood and with depression during adolescence (Dahl & Carskadon, 1995), available data are somewhat conflicting.

Methods: The current study examined these associations and relationships among a large community sample (N=175) of children and adolescents ages 6-17 (mean=11.4 years, SD=3.4). Participants' socio-demographic backgrounds were characteristic of the urban area from which they were recruited (New Orleans, LA).

Results: Overall significant associations between sleep problems, depression and anxiety were found, though depressive symptoms showed a stronger relationship with sleep problems among adolescents ($r=.58$, $p<.001$) and anxiety symptoms were associated with sleep problems in youth of all ages. Sleep problems were associated with all types of childhood anxiety, but significant correlations with generalized anxiety ($r=.34$, $p<.01$), panic ($r=.27$, $p<.05$) and social anxiety ($r=.49$, $p<.01$) only were found for adolescents. Cognitive factors linked with anxiety and depression also were associated with sleep problems among adolescents ($r=.29$, $p<.01$), though correlations were no longer significant after controlling for internalizing symptoms.

Conclusion: Findings are consistent with the suggestion that childhood sleep disturbance is more closely associated with anxiety, while adolescent sleep problems are linked to depression. Results also suggest links between sleep and anxiety to be non-specific in non-clinical samples of children, though this association may become more explicit by the teenage years.

0224

ERYTHROPOIETIN CONCENTRATIONS IN UMBILICAL CORD BLOOD OF SNORING WOMEN

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Introduction: Physiologic changes that occur during pregnancy, particularly during the third trimester place women at risk for developing SDB. Indeed, habitual snoring is common in pregnancy during the third trimester. Early reports suggest that maternal SDB may represent a risk factor to the fetus. We have recently shown increased umbilical cord levels of nucleated red blood cells (nRBCs) in women who snored during pregnancy indicating some degree of increased fetal erythropoiesis which is most likely mediated by the intermittent hypoxia. In order to further investigate the effect of maternal SDB on fetal erythropoiesis we aimed to measure umbilical cord concentrations of erythropoietin as a marker for tissue hypoxia.

Methods: Parturients with singleton, full-term uncomplicated pregnancy were recruited during labor at the delivery room. All participants together with their sleep partners completed a questionnaire on snoring, sleep pauses and sleepiness (ESS) during the current pregnancy. Cord-blood was obtained immediately following delivery and erythropoietin concentrations were measured using commercially available ELISA kit (R&D systems).

Results: Fifty-nine women participated in the study. The mean age was 29.7±4.5 years (range: 20-41y), the mean BMI was 27.3±3.1 kg/m² (range: 20.7-37.6 kg/m²) and the mean weight gain through pregnancy was 13.8±4.8 kg (range: 3-26 kg). 28/59 (47%) reported on snoring during the current pregnancy. No significant difference was found in umbilical cord erythropoietin concentration between snorers and non snorers (30.5 vs. 25.5 mIU/ml, respectively, $p=NS$). Cord blood erythropoietin concentration weakly correlated with ESS score ($r=0.26$, $p=0.04$). No differences were found in birthweight percentiles of the newborns of snoring mothers compared with non-snoring mothers (60.3±22.7 vs. 54.1±27.0 respectively, $p=NS$).

Conclusion: In contrast to our previous findings on circulating nRBC's, no significant difference was found between cord-blood levels of erythropoietin in snoring women compared with non-snoring women. We speculate that other mechanisms play a role in modulating circulating nRBC's level in the umbilical cord.

0225

RECOVERY FROM 1-WEEK MILD SLEEP RESTRICTION IN 4-8 YEAR-OLD HEALTHY CHILDREN

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Introduction: A profound effect of sleep deprivation and restriction involves neurobehavioral function. However, children frequently face mild sleep restrictions due to delayed bedtimes. We sought to investigate how long it will take children between the ages of 4-8 years to compensate for their loss in sleep if such sleep restrictions (SR) are corrected.

Methods: 163 children (mean = 6.6 ± 1.2 years; 58% female) who were reported to be healthy children and non-snorers participated in the study. Children with normal PSG wore an actigraph on their non-dominant wrist, and maintained a sleep log. 23 children were dropped due to non-compliance. Children continued their normal bedtimes and rise times during week 1 and were randomly assigned to one of 2 groups for week 2, SR (delayed bedtime by 1 hour) and control (CO). Then were requested to go back to their routine sleep habits for a week, and after a month were asked to wear the actigraph for a fourth week.

Results: Total sleep time in CO was 496±34 vs. 499±31 min in SR. SR children slept 43 minutes less in their week 2 (453±33 min) compared to week1 ($p < 0.00001$). During the 3rd week, children returned to pre-SR sleep duration (489±35 min) and similar findings were also documented in the 4th week of recording (494±37 min; $p=NS$), suggesting that after a week of mild SR children return to their pre-restriction sleep routines without rebound sleep. Median sleep efficiency (±80%), sleep onset latency (24±22 min) remained unaltered during SR week and recovery weeks.

Conclusion: One week SR of 45 min/night in otherwise healthy children does not seem to be associated with changes in bedtime or with any actigraphic sleep measures during subsequent recovery. Suggesting that habitual sleep/wake schedules are either sufficient for sleep recovery or that families can't provide additional sleep opportunities.

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0226

SLEEP PATTERNS OF HIGH SCHOOL STUDENTS BEFORE AND AFTER DELAYED SCHOOL START TIME

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Introduction: Adolescents generally do not obtain adequate sleep, adversely affecting daytime function, including mood, alertness and performance. Delaying high school start times affords the opportunity for more sleep. A common concern among parents and educators, however,

is that the extra time would not be used for sleep. The aim of this study was to assess the sleep patterns of high school students before and after a delay in 40 minutes of school start time from 07:35 am to 08:15 am.

Methods: In fall 2001 and spring 2002, 259 students (grades 9 -12) completed the condensed School Sleep Habits Questionnaire. These data were compared to the results of the same questionnaire administered to the entire high school (N= 977) in fall 2004 after the start time was delayed.

Results: Students slept significantly longer on school nights after the delay. Total sleep time on school nights increased 33 minutes, from (mean \pm SD) 422.1 \pm 59.5 to 455.6 \pm 55.2 min ($p < 0.001$). This increased sleep was due mainly to later rise time (6:12 a.m. \pm 24.1 vs. 6:53 a.m. \pm 28.4 min, $p < 0.001$). These changes were consistent across all age groups. Students' bedtime on school nights was marginally later, 10:52 pm \pm 48.5 to 11:00 pm \pm 61.8 ($p = .03$), and weekend night sleep time decreased slightly, from 584.6 \pm 83.8 to 567.7 \pm 84.9 min ($p = 0.004$). More students reported "no problem" with sleepiness after the schedule change (6.6% before vs. 13.8% after delayed start time, $p < 0.001$).

Conclusion: Following a 40 minute delay in start time, high school students utilized 83% of the extra time for sleep. Although students stayed up later and had less weekend sleep, these were not clinically significant changes. Some students reported lower levels of daytime sleepiness after the schedule change.

0227

COMBINED TOPICAL AND SYSTEMIC ANTI-INFLAMMATORY THERAPY IN PEDIATRIC UPPER AIRWAY RESISTANCE SYNDROME (UARS)

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Introduction: About 10-12% of all school-aged children present with habitual snoring during their sleep. While some of these children will suffer from frank obstructive sleep apnea which requires surgical intervention, a substantial proportion will be categorized as having UARS. Currently, there are no clear guidelines for the treatment of children who fall under such category. Although UARS is not a life threatening condition, it may impose a significant adverse impact on child behavior, cognition, and quality of life that warrants the need for non-surgical therapeutic alternatives. Since there is evidence of increased inflammation in the upper airway of children with sleep apnea, we hypothesized that use of anti-inflammatory medication will reduce the severity of UARS.

Methods: A total of 41 children ages 2-14 years (17 Female) fulfilling the criteria for UARS were prospectively recruited for an open trial of 16 weeks duration consisting of a combination of oral montelukast and intranasal corticosteroids. Subjects underwent a second overnight sleep study after completion of the 16-week course.

Results: There was a significant improvement in obstructive AHI 3.6 \pm 0.3/hTST at diagnosis vs. 2.2 \pm 0.1/hTST; P value < 0.0001). The respiratory arousal index, was also markedly improved (from 3.5 \pm 0.2/hTST to 1.3 \pm 0.1/hTST ; P value < 0.0001). There were no changes in lowest SaO₂ over time.

Conclusion: These findings suggest that combined intranasal corticosteroids and oral montelukast therapy once daily for 16 weeks is associated with objective ameliorations in sleep fragmentation and respiratory disturbance in children with UARS whom otherwise would not be candidates for surgical removal of tonsils and adenoids. Anti-inflammatory therapies aiming to improve nasopharyngeal resistance may provide both short and long-term non-surgical options in children with mild sleep-disordered breathing. Thus, further randomized controlled trials aiming to delineate potential additive or synergistic effects of leukotriene modifiers and topical steroids are needed.

Support (optional): Study funded by The Children's Foundation Endowment for Sleep Research.

0228

PEDIATRIC OBSTRUCTIVE SLEEP APNEA (OSA): A POTENTIAL LATE CONSEQUENCE OF RESPIRATORY SYNCYTIAL VIRUS (RSV) BRONCHIOLITIS

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Introduction: Adenotonsillar (AT) hypertrophy is the most common cause of OSA in young children, and has a substantial impact on cognitive development, cardiovascular function, growth, and quality of life. AT tissues harvested from children diagnosed as having OSA exhibit high levels of nerve growth factor (NGF) mRNA, its high-affinity tyrosine kinase receptor (trkA), neurokinin 1 (NK1) receptor, and substance P, and these findings are strikingly similar to the changes observed in the lower airways following RSV infection. Therefore, we hypothesized that children who suffered from severe RSV bronchiolitis during infancy may be at higher risk for OSA later in childhood.

Methods: An initial survey of Kosair Children's Hospital medical records allowed us to identify potential candidates for the study. 17 randomly selected children (mean age \pm SD: 5.0 \pm 1.7 years) with a history of verified RSV-induced bronchiolitis during their first year of life underwent overnight PSG. Children recruited from the general population with no history of RSV bronchiolitis served as a control group. After matching for age, gender and BMI z scores, 69 control subjects (mean age \pm SD: 5.1 \pm 0.7 years) were identified and went through an overnight PSG as well.

Results: Children who had RSV bronchiolitis as infants had significantly higher obstructive AHI compared to controls (2.3 \pm 1.7 vs. 0.6 \pm 0.7 /hrTST; $p < 0.05$). In addition, significantly higher respiratory arousal indices were apparent among children with previous RSV bronchiolitis compared to controls (1.5 \pm 1.0 vs. 0.1 \pm 0.2 /hrTST; $p < 0.05$). There were no significant differences between the groups in the lowest SpO₂ recorded.

Conclusion: Our findings are supportive of the concept that RSV bronchiolitis may contribute to the pathophysiology of OSA in vulnerable children. Future randomized trials aiming at prevention of RSV bronchiolitis during infancy using currently available passive immunization strategies should provide further insights into whether a reduction in OSA indeed occurs.

Support (optional): NIH grant HL 65270 and the Children's Foundation Trust for Sleep and Neurobiology Research.

0229

EFFECT OF ADENOTONSILLECTOMY ON NEUROCOGNITIVE AND PSYCHOSOCIAL FUNCTIONS IN PRESCHOOLERS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Little is known about neurocognitive functions in preschoolers with obstructive sleep apnea syndrome (OSAS), and even less on the effect of adenotonsillectomy (T&A) on neurocognitive and psychosocial functions, at this age.

Methods: The purpose of this study was to evaluate neurocognitive and psychosocial functions and health-related quality of life (HRQL) in children aged 2.5 to 5 years with OSAS (AHI > 1), before and after T&A. Study group included 45 otherwise healthy children with OSAS (mean age 46 \pm 9 months, range: 32-61), and 26 healthy controls (mean age 49 \pm 8, range: 31-61), matched by age and socio-economic status. Comprehensive neurocognitive and psychosocial evaluation was performed before (n=45 OSAS and 26 controls) and one year following T&A (n=23 and 18, respectively). Evaluation included polysomnogra-

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phy (before T&A, OSAS only), sleep questionnaires, behavioral questionnaires (CBCL), intelligence tests (Kaufman ABC), specific tests for executive functions, and tests for cognitive functions such as attention, vocabulary and memory, and HRQL.

Results: Before T&A, preschoolers with OSAS had significant impaired executive functions (verbal and motor fluency, and planning), and in visual attention and vocabulary as compared to normal controls. In addition, preschoolers with OSAS presented significantly more behavioral problems and decreased HRQL. One year after T&A, the 23 children with OSAS significantly improved the visual attention and vocabulary when compared to the 18 controls. Following T&A, there was no significant difference in any of the functions tested between patients and controls.

Conclusion: We conclude that OSAS is associated with impaired attention and vocabulary but not intelligence, and in HRQL, as early as in preschool age. T&A significantly improves neurocognitive and psychosocial functions, to the level of healthy children.

0230

OBESITY, SNORING, AND PHYSICAL ACTIVITY IN SCHOOL-AGED CHILDREN

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Introduction: After sleep deprivation feeling more hungry is commonly reported. In addition, overweight and obesity have been associated with poor or short sleep, and also with reduced physical activity. Sleep disordered breathing disrupts sleep. We hypothesized that obese children with sleep disordered breathing (SDB) may have an increased appetite, may crave particular foods, and may also be less likely to engage in physical activities.

Methods: Participants were recruited from the Louisville public schools. Otherwise, healthy 5- to 9-year-old children ($n=549$, mean age: 6.78 ± 0.60 , 56.28% boys, 64.33% Caucasian, 27.89% African American, 7.78% other ethnicity), with or without SDB (obstructive AHI >2) and/or obesity (BMI z-score >1.56), were selected. The morning after PSG recording, while children underwent a neuropsychological evaluation, parents filled out a food and physical activity questionnaire.

Results: Overall, compared to non-obese children, obese children were more likely to report "good" appetite ($\text{Chi}^2(3) = 12.40$, $p = .0061$). The dietary habits of the obese SDB children showed reduced consumption of fruits and bread compared to control children ($\text{Chi}^2(1) = 4.426$, $p=0.035$ and $\text{Chi}^2(1) = 7.121$, $p=0.008$). Both obesity and SDB decreased the frequency of engaging in physical activities such as walking, running, and bicycling when compared to controls. Indeed, obese-SDB children are physically active fewer days per week (1-2) compared to controls, and the duration of their activity when present is also more likely to be of shorter duration (not more than 15 to 60 minutes per day ($\text{Chi}^2(3) = 8.240$, $p = .041$).

Conclusion: Maintaining a healthy weight has emerged as a critically important approach to reduce the risk of SDB even in children. Our findings suggest that obesity is associated with increased appetite and reduced activity, and that SDB further adversely impacts on dietary preferences, and is particularly detrimental to daily physical activity levels.

Support (optional): NIH HL-65270 and the Children's Foundation for Sleep Research

0231

GHRELIN AND VISFATIN PLASMA LEVELS IN OBESE AND NON-OBESE SCHOOL-AGED CHILDREN WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA

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Introduction: Ghrelin is an endogenous ligand of the growth hormone secretagogue receptor. It is hypothesized to play a key role in energy balance stimulating food intake and body weight. Sleep disruption has been associated with increased obesity rates, and has been associated with increases in ghrelin levels. Obstructive sleep apnea (OSA) in children is associated with varying levels of sleep fragmentation in addition to gas exchange abnormalities. We therefore aimed to examine how obesity and OSA affect morning ghrelin levels in children, as well as those of visfatin, a newly reported fat derived cytokine.

Methods: Consecutive children (ages 4-10 years; $n=189$) who were polysomnographically diagnosed with OSA and age-, gender-, ethnicity-, and BMI-matched control children underwent blood draw the next morning under fasting conditions for ghrelin levels, which were measured using a highly sensitive ELISA. In addition, plasma visfatin levels were also measured.

Results: Compared to non obese controls, plasma ghrelin levels were borderline higher in obese, non snoring children ($p=0.05$). The presence of OSA was associated with increased ghrelin levels, particularly when obesity was also present ($p<0.001$). Linear relationships emerged between ghrelin levels and obstructive AHI, respiratory arousal index, and lowest SpO₂ for the whole cohort. In contrast, plasma visfatin levels were similar, independently from BMI or the presence of OSA (p - not significant; $n=40$).

Conclusion: Ghrelin morning plasma concentrations are altered in children with OSA, particularly when obesity is present, and changes are proportionate to the severity of sleep disturbance. These findings suggest the presence of increased appetite and caloric intake in patients with OSA, which in turn may further promote the severity of obesity and OSA.

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0232

SOMATIC SYMPTOMS IN OBESE CHILDREN WITH SLEEP DISORDERED BREATHING

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Introduction: A risk factor of obesity is sleep disordered breathing (SDB) resulting in fragmented sleep. SDB adversely affects neurobehavioral function and quality of life. However, few studies have explored the effect of fragmented sleep on somatic symptoms in obese children. The purpose of the current study was to explore the role of SDB and obesity in the frequency of somatic complaints.

Methods: As part of an ongoing study, 549 otherwise healthy children (mean = 6.8 ± 0.6 years; 56.3% male; 64.3% Caucasian, 27.9% African American) participated in an overnight PSG followed by neurocognitive testing. During testing, parents completed a set of behavioral measures: Conners' Behavior Rating Long Version (Conners') and Achenbach Child Behavior Checklist (CBCL). Children were categorized into 4 groups based on the overnight PSG obstructive AHI (>2/hrTST) and BMI-z score (>1.56).

Results: A significant overall effect was found ($F(3,163) = 4.25$, $p = 0.006$) indicative for obesity and SDB together increasing the frequency of somatic complaints manifested by the child. More specifically, obese children with SDB exhibited more somatic symptoms on both question-

naires, than control children (Conners': 5.0 ± 4.0 vs. controls = 2.3 ± 3.0 , Bonferroni post hoc $p = 0.007$; CBCL: 4.3 ± 3.0 vs. controls = 1.8 ± 2.3 , Bonferroni post hoc $p = 0.004$). The presence of either obesity or SDB alone failed to significantly increase somatic complaints as reported by the parents. No gender differences were found.

Conclusion: Obese children with SDB clearly express more somatic complaints, and such symptoms are absent when either obesity or SDB occur in isolation. These preliminary findings underline the importance of the interaction between SDB and obesity in amplifying sub-threshold effects. Since being obese contributes to increase the risk of SDB, it will be important to assess the relationships of these somatic complaints on other morbidities and whether they contribute to decrease overall quality of life.

Support (optional): NIH grant R01HL-65270 (DG), and The Children's Foundation Endowment for Sleep Research.

0233

SELF-SELECTED VERSUS STABILIZED SLEEP SCHEDULES: ACTIGRAPHIC SLEEP ESTIMATES IN CHILDREN, ADOLESCENTS, AND YOUNG ADULTS

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Introduction: Developmental changes in sleep occur across childhood and adolescence and into young adulthood. This analysis examined sleep pattern differences for participants sleeping on their own schedules and then on stabilized schedules.

Methods: Two weeks of wrist actigraphy measured sleep patterns of 3 groups: ages: 9-10 years (5 females, 6 males), 15-16 years (8 females, 9 males), 20-23 years (3 females, 8 males). During week 1, participants followed self-selected sleep schedules; during week 2, participants were placed on stabilized sleep schedules designed to provide age-based sufficient sleep quantities, i.e., at least 10 h, 9 h, and 8.5 h for respective age groups. Nine actigraph variables for each week were assessed with MANOVA.

Results: Self-selected schedule: a significant age-group effect was found for sleep period duration ($F(2,36)=5.37$, $p<.01$), with an average of 527 minutes for 9-10, 469 minutes for 15-16, 476 minutes for 20-23 year olds. Stabilized schedules: a significant age-group effect was found for sleep period duration and minutes scored as sleep, confirming the schedule manipulation. Sleep period duration increased by an average of 24 minutes in 9-10 year olds, 31 minutes in 15-16 year olds, and decreased by an average of 46 minutes in 20-23 year olds. Age group differences were found for wake after sleep onset, sleep efficiency, duration of awakenings, and total minutes scored as wake (all $p<.05$).

Conclusion: These actigraphic estimates of sleep indicate that self-selected schedules restrict opportunity for sleep, particularly in mid-adolescents. Restricted sleep schedules in adolescents likely reflect a response to environmental factors (e.g., school start time) and intrinsic sleep regulatory processes. When sleep opportunity is extended via experimental manipulation, children and adolescents slept more according to actigraphy, whereas young adults slept less. Additional factors to be examined include parental alcohol history, mood and circadian phase preference.

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0234

PREDICTORS OF HOW ADOLESCENTS RESPOND TO EXPERIMENTAL SLEEP RESTRICTION

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Introduction: Many adolescents obtain inadequate sleep, which is associated with poor behavioral and academic outcomes that could affect long-term development. Adult research suggests that some individuals are more vulnerable (less resilient) to the adverse effects of sleep restriction than others. To our knowledge, there have been no studies of this phenomenon in adolescents. Here we report on several potential predictors of resilience to sleep restriction in a small sample of adolescents.

Methods: 19 healthy adolescents completed a three-week experimental protocol, including a baseline week followed in counterbalanced order by a sleep-restricted week (SR; Monday-Friday nights limited to 6.5 hours in bed) and an optimized-sleep week (OS; 10 hours in bed Monday-Friday nights). During baseline, subjects were asked to report their habitual sleep duration on school and weekend nights, and to predict how the sleep manipulation would impact their levels of vigor and fatigue. These were then correlated with the actual effect of the sleep manipulation on vigor and fatigue, as reflected in differences across conditions on validated self-report measures.

Results: Participants had markedly less sleep, and reported less vigor and more fatigue, in the SR than the OS condition. Subjects who *predicted* more resilience to sleep restriction habitually slept longer on school nights ($p<.05$) but not on weekend nights ($p>.5$). Conversely, subjects who showed the greatest *actual* effect of our sleep manipulation on fatigue and vigor habitually slept shorter on weekend nights ($p<.05$) but showed no difference on school night sleep duration ($p>.8$). Finally, subjects' predictions of how vigorous they would feel during the experimental weeks were fairly accurate ($p<.01$), but their predictions regarding levels of fatigue were not ($p>.5$).

Conclusion: These pilot data suggest that adolescents' expectations of their resilience to sleep restriction show some relationship to their actual resilience and to their habitual sleep patterns.

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0235

EFFECT OF CHRONIC SLEEP RESTRICTION ON ADOLESCENTS' LEARNING AND BRAIN ACTIVITY IN A SIMULATED CLASSROOM: A PILOT STUDY

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Introduction: Correlational studies have associated sleep restriction during adolescence with academic difficulties, but relevant experimental data have been scant. This pilot study assessed the causal effect of adolescent sleep restriction on learning and brain activity in a simulated classroom setting.

Methods: 16 healthy adolescents aged 13.9-16.9 years completed a three-week experimental protocol that included a baseline week followed in counterbalanced order by a sleep-restricted week (SR; Monday-Friday nights limited to 6.5 hours in bed) and an optimized-sleep week (OS; 10 hours lights-out in bed Monday-Friday nights). Assessments were conducted on the Saturday morning at the end of each week. After the baseline week, subjects completed an IQ screener. After the SR and OS weeks, each subject participated in a simulated classroom comprised of viewing one of two half-hour prerecorded lectures, followed by a relevant quiz. A subgroup of 8 subjects did so while undergoing EEG monitoring and being videotaped. A condition-blind rater coded video-

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tapes for off-task behaviors in 30-second epochs. EEG data from C3/A2 underwent spectral power analysis, focusing on the theta frequency range based upon prior adult sleep deprivation research.

Results: All subjects had markedly less sleep in the SR condition than the OS condition. After covarying for estimated IQ, subjects performed significantly worse on the quizzes after SR than after OS ($p=.05$). In the EEG-monitored subgroup, subjects displayed more off-task behaviors ($p<.05$) and higher theta power ($p=.08$) after SR than after OS. Theta power was associated with inattentive behaviors in the SR condition ($r=.69, p<.05$) but not the OS condition ($r=-.11, ns$).

Conclusion: Chronic sleep restriction during adolescence hampers academic performance and alters brain activity, potentially affecting neurobehavioral development. These pilot findings build upon prior work by using an experimental design with objective measures of learning and brain activity in an ecologically-valid simulated classroom.

Support (optional): Grants #K23 HL075369 and M01 RR 08084 from the National Institutes of Health.

0236

THE EFFECTS OF POSITIVE AIRWAY PRESSURE THERAPY ON COGNITIVE FUNCTION IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA SYNDROME: PRELIMINARY FINDINGS

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Introduction: Children with obstructive sleep apnea syndrome (OSAS) have cognitive impairments. Adult studies indicate CPAP treatment results in improved cognitive function. This study investigates the effects of CPAP/BiPAP therapy on cognitive function in children with OSAS.

Methods: Twenty-two participants (13 boys), 8-16 years of age (mean =12.3) with suspected or documented OSAS were recruited. All subjects or their caregivers filled out the Epworth Sleepiness Scale (ESS) and either the Child Sleep Habit Questionnaire (CSHQ) or the Pittsburgh Sleep Quality Index (PSQI). Participants self-reported daily therapy adherence. Participants performed sections of standardized cognitive tests (WISC-IV, D-KEFS, TEA-Ch, and WRAML-2) to assess their general intelligence, executive function, attention, and memory, respectively. The normative mean for each test is 10. Participants were tested before and 5-6 months after the initiation of PAP therapy. Five participants completed post-therapy testing.

Results: Pre-therapy, mean weight was 95.6±39.8 kg, height was 157.9±13.5 cm, and BMI was 36.8±11.4 (86% overweight). Mean score for ESS was borderline normal (8.9±6.5). CSHQ suggest increased sleep disordered breathing. Participants scored below the normative mean on tests of general intelligence, executive function, sustained attention, and memory. Post-therapy measures indicated an increase in age-corrected standard scores in WISC-IV Block Design (8.0 to 9.6); D-KEFS Letter Sequencing (8.6 to 10.0) and Number-Letter Switching (6.0 to 8.0); TEA-Ch Sky Search (8.8 to 10.4) and Score (7.6 to 9.4); WRAML-2 Design Memory (6.0 to 9.0) and Design Memory Recognition (8.4 to 10.6). The participant least adherent with therapy scored the same or worse on all tests analyzed, with the exception of Design Memory Recognition. The three participants with the greatest adherence demonstrated the most improvement.

Conclusion: Children with OSAS have deficiencies in executive function, memory, learning, and nonverbal intelligence. Post-PAP therapy testing suggests improvement in these deficits. The remaining 11 participants are scheduled for post-therapy assessment.

0237

EFFECTS OF A CONSISTENT BEDTIME ROUTINE ON TODDLER SLEEP

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Introduction: Establishment of a consistent bedtime routine is often recommended to parents of toddlers, especially those with sleep difficulties. However, no studies have investigated the efficacy of such a routine independent of behavioral intervention. Thus, the purpose of this study was to examine the effects of a consistent bedtime routine on toddler sleep.

Methods: 199 mothers (ages 18-49 years) and their toddlers (ages 18-36 months; mean =27.6 months; 48% males) participated in a 3-week study. Families were randomly assigned to either a control or routine group. The first week of the study served as a baseline during which the mothers were instructed to follow their usual bedtime routine. In the second and third weeks, mothers in the routine group were instructed to conduct a specific bedtime routine, including a warm bath, application of lotion, and quiet bedtime activities (e.g., reading), while the control group continued their usual routine. All mothers maintained a daily sleep diary and completed the Brief Infant Sleep Questionnaire (BISQ) on a weekly basis.

Results: The bedtime routine resulted in significant reductions in problematic sleep behaviors according to the BISQ. Significant improvements were seen in latency to sleep onset (20.2 vs. 16.3 minutes; -20%) and number (1.3 vs 0.6 times, -51%) and duration of night wakings (14.8 vs 8.2 minutes; -45%), $p<.001$. Sleep continuity significantly increased by more than 1 hour from 8.1 hours to 9.2 hours, $p<.001$. In addition, three times more mothers of toddlers reported sleep was not a problem, $p<.001$. Control group sleep patterns did not significantly change over the three-week study period, $p>.05$.

Conclusion: These results suggest that a consistent bedtime routine is beneficial in improving multiple aspects of toddler sleep, especially wakefulness after sleep onset and longest continuous sleep period.

Support (optional): This study was supported by JOHNSON & JOHNSON Consumer Companies, Inc.

0238

FIRST NIGHT EFFECT IN CHILDREN WITH ACTIVE AND INACTIVE JUVENILE RHEUMATOID ARTHRITIS (JRA)

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Introduction: Based primarily on parental report, children with Juvenile Rheumatoid Arthritis (JRA) experience sleep disturbances, but few polysomnographic studies have been reported in children with JRA. The purpose of this study was to examine PSG sleep variables between children with active and inactive JRA.

Methods: Seventy children 6-to-11 years of age (mean 8.5 ±1.9 years) with active (n=35) or inactive (n=35) JRA (84% female) participated in the study. Polysomnography (PSG) and self-report measures of sleep were obtained for 2 consecutive nights in a sleep laboratory. Bedtime and rise time was based on the child's usual home schedule, and remained consistent for both study nights. Because sleep efficiency of < 85% is often used as PSG indicator of poor sleep, we grouped the children into those above and below this value for each night. A pediatric rheumatologist rated active disease as inflammation of one or more

joints with swelling, limited range of motion, or tenderness (> 1 on a scale of 0 'no disease' to 10).

Results: During the first night, 40% (n=28) of the children with a sleep efficiency of < 85% had a mean total sleep time of 456 + 44 minutes, a mean sleep latency of 41 + 30 minutes, and a mean sleep efficiency of 77 ± 7.0%. During the second night, 13 % (n=9) of children with a sleep efficiency of < 85% exhibited poor sleep efficiency with mean total sleep time of 500 + 26 minutes, a mean sleep onset latency of 31 + 30 minutes, and a mean sleep efficiency of 82 + 1.9%.

Conclusion: A marked "first-night" effect was found regardless of disease activity. These findings suggest that valid sleep laboratory assessments in children with JRA require an adaptation night.

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0239

IMPACT OF CEREBRAL INJURY ON POSTNATAL SLEEP MATURATION IN A COHORT OF VERY PRETERM NEWBORNS

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Introduction: Very preterm newborns are at high risk of neurological injury. Little is known about the impact of neurological aggression on maturation of sleep architecture in this population.

Methods: The sleep organisation of preterm newborns with normal or poor neurological outcome were compared at term corrected gestational age (GA). The children born less than 28 weeks GA, or less than 1 kg were recruited from 1996 to 2003 at Erasmus Hospital. A neuropsychiatric follow-up of these infants was organised. Two groups were constituted: a first one with children with normal evolution and a second group with children with at least one of these impairments including cerebral palsy, language or mental retardation, visual or hearing disability, behavioural or attention disorder. A MIMIC (Multiple Indicator Multiple Cause) model was used to study the relationship between neurological development status and two sleep latent variables: the "spontaneous arousability" latent variable, described by the number of awakenings or movements/h of quiet sleep (QS) or of active sleep (AS) and the "QS organisation", described by the median duration of QS cycle and the percentage of QS.

Results: 45 neonates were included in the analysis, 19 with a normal neurological outcome, 26 with at least one disability. The preterm infants were born at 27 weeks GA [25-32], weighted 910g [470-1190], were recorded at 38.7 weeks [36.3-44.4] and were followed until 54.5 months (21.3-116.9). Spontaneous arousability was found to be significantly associated with neurological development status, the number of awakenings or movements/h of QS was multiplied by 1.44 [1.00-2.05], and the number of awakenings or movements/h of AS was multiplied by 1.10 [1.00-1.27] for preterm neonates with normal development.

Conclusion: This study suggests that neurological injury could compromise the spontaneous arousability of the very preterm infants. The clinical relevance of this sleep characteristic needs further investigations.

0240

IS THERE AN INTEREST TO PROLONG CARDIORESPIRATORY RECORDINGS IN PRETERM INFANTS BEFORE DISCHARGE?

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Introduction: Cardiorespiratory recordings (CRR) were used to inform the clinician about maturation of the cardiorespiratory function in preterm infants. The duration of these recordings varies widely among institutions. In our hospital, the recordings last 36 hours. Using these recordings, the objective of this study was to evaluate the agreement between two successive nights and between night and day.

Methods: From October 2005 to November 2007, CRR were recorded during successive 36 hours in preterm infants with persistent apnea and bradycardia (PAB) in neonatal unit or in preterm infants after an ALTE at home (one recording per infant). We evaluated the frequency of bradycardia (< 80 bpm for > 5 sec) every 12-hours (night1:8pm-8am, day: 8am-8pm, night2: 8pm-8am). It was hypothesized that a 12-hours recording is altered if it contains ≥ 1 bradycardia.

Results: 54 infants (32 weeks of gestational age at birth (26-36.5)) were included in this study: 25 infants for PAB and 29 infants for ALTE. The postconceptional age was 39.5 weeks (35-46) at the recording. Two groups have similar demographic data. 39 infants exhibited bradycardia (median 3 (0-17)), the PAB group exhibited more bradycardia than the ALTE group (p=.002). 9 infants who did not have bradycardia for the first 12 hours of the study, have at least one bradycardia for the last 24 hours. The agreement value was moderate between two successive nights for the whole population (kappa = 0.55), was good for the ALTE group (kappa =0.64) and mild for the PAB group (kappa=0.29). The concordance between night and day was moderate (night1/day =0.52 and day/night2=0.44).

Conclusion: The agreement of CRR results between two successive nights was moderate. The best duration of these recordings has to be determined as well as the value of these results for the occurrence of ALTE after discharge.

0241

NADPH OXIDASE P22 SUB-UNIT POLYMORPHISMS AND COGNITIVE FUNCTION IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: A major consequence of pediatric OSA involves neurocognitive dysfunction. However, at any given level of AHI, not all children will develop cognitive deficits. Thus, genetic and environmental factors may be involved. Oxidative stress and activation of NADPH oxidase mediate neural cell losses in a murine model of OSA. One of the major regulatory sub-units of NADPH oxidase is p22 (CYBA). One of the single nucleotide polymorphisms thus far identified as associated with reduced function is 640A>G. We evaluated the relation between 2 polymorphisms in the CYBA gene in children with OSA with and without neurocognitive deficits.

Methods: From a set of consecutive children (ages 5.5-8 years; n=378) who were polysomnographically diagnosed with OSA and underwent cognitive function testing with the DAS and NEPSY batteries, we identified 69 with cognitive deficits (i.e., ≥2 abnormal sub-tests). These children were matched against 47 age-, gender-, ethnicity-maternal educa-

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tion-, BMI-, and obstructive AHI-matched children who did not present with any cognitive deficits. All 116 children underwent a blood draw the next morning under fasting conditions. Genomic DNA extraction was performed and CYBA polymorphisms 640A>G and 673A>G which locates to the same exon but is void of any functional effect on NADPH oxidase activity were examined. Genotyping and allelic frequencies were determined using real time PCR TaqMan SNP genotyping assays.

Results: The frequencies of the 673A>G polymorphism were similar between OSA children with and without neurocognitive deficits. However, 640A>G was significantly more frequent among the children without deficits compared to those with deficits ($p < 0.02$).

Conclusion: Polymorphisms within the NADPH oxidase gene or its functional sub-units, such as CYBA 640A>G may account for important components of the variance in cognitive function deficits associated with OSA in children. Therefore, 640A>G and potentially other functionally relevant polymorphisms NADPH oxidase gene may lead to disease-modifying consequences in pediatric OSA.

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0242

SLEEP ARCHITECTURE IN CHILDREN WITH DOWN SYNDROME

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Introduction: Children with Down Syndrome (DS) are reported to sleep poorly. It has been suggested that up to 60% of children with DS may have sleep-disordered breathing (SDB). However, children with DS may have altered sleep architecture and sleep fragmentation, only partly related to SDB. We sought to identify sleep architecture characteristics of children with DS in comparison to those of typically developing (TD) children from a general sleep clinic population.

Methods: We performed a retrospective case-control study, comparing sleep architectures and other variables on diagnostic polysomnography (PSG) between DS children and age-, gender-, and SDB-severity matched TD children. Data was reviewed and compared using paired t-tests.

Results: A total of 38 PSGs of DS children were identified and matched to those of 38 TD children. Mean ages of DS vs. TD children were 7.3±4.3 years vs. 7.4±4.3 years and mean apnea/hypopnea index was 11.3±11.9 vs. 9.0±9.4. Seventy five percent of subjects were male. As a group, DS children exhibited significantly increased wake after sleep onset (WASO; 61.4±51.0 vs. 49.2±48.0 minutes; $p = 0.013$), despite matching for SDB severity. When subjects were further divided based on age (1-4, 5-9, and 10-16 years), differences in sleep architecture were prominent. Specifically, DS children in the 5-9 year group ($n = 17$) exhibited lower sleep efficiency (SE; 82.1±11.7% vs. 87.1±10.9%; $p = 0.03$), less total sleep time (TST; 380.6±71.1 vs. 425.2±50.7 minutes; $p = 0.007$), increased WASO (65.7±63.7% vs. 36.5±45.3%; $p = 0.002$), more stage 1 (14.5±7.3% vs. 7.9±4.8%; $p = 0.001$), and less REM sleep (11.0±7.0% vs. 16.2±6.2%; $p = 0.012$) compared to TD children. Slow wave sleep (SWS) showed an increasing trend across the DS age groups, and those in the 10-16 year group ($n = 11$) exhibited significantly more SWS than matched TD children (31.5±12.3% vs. 22.9±6.3%; $p = 0.019$). Also, REM sleep was reduced in DS children with increasing age, although this only reached significance in the 5-9 year age group.

Conclusion: Children with DS exhibit more sleep fragmentation and altered sleep architecture compared to TD children, independently of SDB severity. Of interest, decreased REM sleep and increased SWS has been previously reported in DS adults. Our findings suggest that this sleep architecture pattern may emerge during childhood and may reflect a developmental phenotype in this population.

0243

TIMING OF THE NOCTURNAL SLEEP PERIOD DURING EARLY CHILDHOOD

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Introduction: The way children distribute their sleep is influenced by a number of factors (e.g., biological, environmental). In adolescents and adults, a "mismatch" between biological timing and social demands commonly results in sleep deficits and compromised waking function. The significance of such interactions in children is relatively unexplored. The present study examines changes in the timing of the nocturnal weekday sleep period and factors associated with these changes in preschool children.

Methods: Data were collected from a representative community sample of 648 children (70% White non-Hispanic; 51% male) aged 2-5 years from southern Mississippi. Caretakers reported their child's typical weekday and weekend bedtime/rise time, napping patterns, family demographics, and completed the Children's Sleep Wake Scale (sleep quality).

Results: An age-related advance in the timing of the weekday sleep period was evident for 2-5 year olds. The advance was not seen for the weekend sleep period. We attribute this change to family/community pressure for increasingly early weekday wake times (WDWT). From age 2 to age 5, the linear advance in WDWT (47 minutes; $p < .001$; partial $\eta^2 = .07$) was larger than the linear advance in weekday bedtimes (WDBT; 30 minutes; $p < .001$; partial $\eta^2 = .05$), resulting in a cumulative across-the-week deficit in time in bed on weekdays of ~1.5 hours. Earlier WDWTs were associated with more napping ($p = .014$; partial $\eta^2 = .07$), but despite more diurnal sleep, children with earlier WDWTs had less overall time in bed across the week ($p < .001$ partial $\eta^2 = .22$). Associated with less weekday time in bed were indications of sleepiness, including less difficulty going to bed and falling asleep, fewer nighttime awakenings, and increased difficulty waking in the morning. Additionally, earlier WDWTs were associated with sleep extension on weekends ($p < .001$; partial $\eta^2 = .08$).

Conclusion: These findings suggest that contextual variables, presumably related to early WDWTs, make it increasingly difficult for preschool children to spend an adequate amount of time in bed during the week. These variables likely include preschool/daycare attendance (see accompanying abstract by Han et al.). Despite efforts to compensate for lost sleep (e.g., napping, weekend sleep extension), children with earlier WDWTs spend less time in bed during the week. The impact of the advance of the weekday sleep period on neurocognitive and emotional functioning is an area for further exploration.

0244

A PEDIATRIC OBSTRUCTIVE SLEEP APNEA GENETIC REPOSITORY: DESIGN AND METHODS

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Introduction: Although several studies support a genetic basis for obstructive sleep apnea (OSA), the exact genetic underpinnings of this disorder are not yet identified. A pediatric OSA genetic repository was established to study the genetic factors that mediate susceptibility to OSA in children. Our objective is to describe the study methods and the clinical characteristics of participants.

Methods: All children seeking treatment for sleep disordered breathing at Cincinnati Children's Sleep Center were approached for buccal genetic material samples. Children with craniofacial abnormalities, genetic syndromes, neuromuscular disorders, and history of tracheostomy were

excluded. Data on demographic, anthropometric, and polysomnographic variables were entered into an access database. Buccal DNA was obtained by brush sampling and 4 brushes were collected per patient. DNA was extracted using Puregene buccal protocol and stored at -80 degree celsius for future studies.

Results: Of the 830 children eligible, 711 were approached for sample collection and 701 consented. There was no ethnic predisposition to decline buccal genetic sampling (5 vs. 5). The mean age of subjects was 11.26 years \pm 4.6, mean BMI 33.5 kg/m² \pm 13.5, and 45.6 % were male. Caucasian ethnicity was reported in 66%, African American in 33 % and Hispanic in 1%. A high prevalence of overweight (63.3 %) and obesity (51.6 %) was noted. Positive family history of habitual snoring was obtained in 61.7%. Polysomnography revealed AHI \geq 1 in 62% and AHI \geq 5 in 30%. Average DNA yield per brush was 345 ng. Two candidate gene studies using a multiplex genotyping platform have been completed.

Conclusion: Our results demonstrate that use of buccal sampling in pediatric genetic studies results in very high subject recruitment and yields adequate quantity of DNA for genotyping on multiplex platforms. The high prevalence of positive family history of OSA symptoms in children seeking treatment for OSA supports the need for future genetic investigations targeting factors that mediate this susceptibility.

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0245

PERFORMANCE ON ATTENTION TESTS IS ASSOCIATED WITH SLEEP EFFICIENCY IN CHILDREN WITH ADHD BUT NOT IN CONTROLS

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Introduction: Attention-Deficit/Hyperactivity Disorder (ADHD) is characterized by inattention, impulsivity and hyperactivity. It has been suggested that disrupted sleep may underlie the inattention and hyperactivity in children with ADHD symptoms. In the present study, we sought to examine whether the sleep efficiency of children diagnosed with ADHD and Controls moderates their performance on measures of attention.

Methods: Nightly sleep recordings were conducted in 18 children diagnosed with ADHD (DSM-IV) but without comorbid psychiatric problems and in 24 healthy controls aged 7 to 11 years. Children were off-medication and did not consume products containing caffeine for at least 7 days prior to the polysomnography (PSG) study. Standard overnight multichannel PSG evaluation was performed at each child's home by an experienced sleep technician using a portable PSG device. On the seventh day, neurobehavioral functioning was assessed using subsets from The Test of Everyday Attention for Children (TEA-CH) pertaining to sustained attention and attention control.

Results: Subjects were divided into two groups based on the mean sleep efficiency score, with subjects below and above the Median placed in the Poor-Sleep Group (PS) and Good-Sleep Group (GS), respectively. Group differences were found on measures of attention controls with children in the ADHD performing worse than controls F(2,27)=5.29, p<.05. A Sleep Efficiency by diagnostic group interaction was found for the TEA-CH's sustained attention sub-component F(3,26)=4.78 p<.05. Univariate analysis indicated that poor sleepers performed worse on measures associated with sustained attention in the ADHD group, while no differences were found between poor and normal sleepers in the control group.

Conclusion: Good sleepers perform better than poor sleepers on measures of sustained attention in the ADHD group but not in the control group. These results may suggest that sleep intervention could improve

functioning in non-medicated children with ADHD and poor sleep patterns.

Support (optional): This study was supported by Canadian Institute of Health Research (CIHR) and FRSQ

0246

SLEEP DISTURBANCES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A HOME POLYSOMNOGRAPHY STUDY

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Introduction: ADHD, one of the most prevalent conditions in child psychiatry, manifests as an unusually high and chronic level of inattention/impulsivity/hyperactivity. ADHD is estimated to occur in 3% to 7.5% of school age children, and routinely continues into adolescence and adulthood. If left untreated, individuals with ADHD struggle with impairments in crucial areas of life. Sleep problems are clinically reported in an estimated 25-50% of children and adolescents with ADHD. However, objective studies have failed to find consistent differences between children with ADHD and controls. In the present study, we examined measures of sleep architecture measured in the child's home environment as well as reported sleep problems in children with ADHD and normal controls. In our analysis, we considered the roles of several pertinent moderating factors, including adjustment night, comorbid psychiatric problems, and family factors.

Methods: Nightly sleep recordings were conducted in 18 children diagnosed with ADHD (DSM-IV) but without comorbid psychiatric problems and in 24 healthy controls aged 7 to 11 years. Children were off-medication, in good health and did not consume products containing caffeine for at least 7 days prior to the polysomnography (PSG) study. Standard overnight multichannel PSG evaluation was performed at each child's home by an experienced sleep technician using a portable PSG device. The children slept in their regular beds and went to bed at their habitual bedtimes.

Results: Compared to controls, children in the ADHD group had significantly shorter durations of REM sleep (F(1,29)=6.14 p<.05) and total sleep [(F(1,29)=4.29 p<.05)]. The percentage of total sleep time spent in REM sleep was marginally smaller in ADHD children compared to controls (F(1,29)=4.29 p<.06. Latency of stage 3 was shorter in the ADHD group than in the control group (F(1,29)=6.2 p<.05). In addition, the ADHD group had a higher score on the Circadian Sleep Factor compared to children in the control group (F(3,28)=7.28 p<.001).

Conclusion: The present findings support the hypothesis that children with ADHD present with sleep disturbances.

Support (optional): This study was supported by Canadian Institute of Health Research (CIHR) and FRSQ

0247

OBSTRUCTIVE SLEEP APNEA IN CHILDREN: RELATIVE CONTRIBUTIONS OF BODY-MASS INDEX AND ADENOTONSILLAR HYPERTROPHY

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Introduction: The epidemic of childhood obesity has prompted remarkable changes in the relative proportion of overweight or obese children being referred for evaluation of habitual snoring and suspected OSA. However, adenotonsillar hypertrophy is by far the most important de-

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terminant of OSA in children and the contribution of obesity remains undefined.

Methods: The epidemic of childhood obesity has prompted remarkable changes in the relative proportion of overweight or obese children being referred for evaluation of habitual snoring and suspected OSA. However, adenotonsillar hypertrophy is by far the most important determinant of OSA in children and the contribution of obesity remains undefined.

Results: The mean obstructive AHI for the 2 groups was approximately 10/hrTST. For the whole cohort, there was only a small albeit significant association between BMI and AHI in the non-obese cohort but not in obese children ($r:0.2$; $p<0.01$). Adenotonsillar size scores were markedly higher in non-obese children ($p<0.0001$), while Mallampati class scores were significantly higher in obese children ($p<0.0001$).

Conclusion: The magnitude of adenotonsillar hypertrophy required for any given level of OSA severity is more likely to be smaller in obese children compared to non-obese children. Increased Mallampati scores suggest that soft tissue changes and potentially fat deposition in the upper airway may play a significant role in the global differences in tonsillar and adenoidal size in obese and non-obese children with OSA.

Support (optional): NIH grant HL-65270 and the Children's Foundation Endowment for Sleep Research.

0248

SLEEP IN PEDIATRIC SICKLE CELL DISEASE

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Introduction: Research to date has focused on the increased occurrence of specific sleep disorders (sleep-disordered breathing, hypoxemia, nocturnal enuresis) in children with Sickle Cell Disease (SCD), without describing general sleep problems in relation to disease severity. The purpose of the current study is to describe the sleep habits of children with SCD and the relationship to hemoglobin level and SCD genotype.

Methods: Parents of 94 children ages 3-18 (mean = 8.71, SD = 3.80) completed the Children's Sleep Habits Questionnaire (CSHQ) as part of routine clinical care. Blood samples were also taken to determine hemoglobin levels. The hemoglobinopathies represented are HBSS (n = 56), HBSC (n = 28), HBSβ+ Thalassemia (n = 4), HBSβo (n = 3), and S other (n = 3). No children had neurological complications, but 11 children were receiving chronic transfusions.

Results: The average hemoglobin was 9.69 g/dL (SD = 1.90). There was a significant inverse relationship between hemoglobin and reports of daytime sleepiness, $r = -.23$, $p = .034$. Consistent with previous research, patients with HBSS were significantly more likely to wet the bed (F (1, 92) = 6.16, $p = .015$). Additionally, they also had significantly higher scores on the CHSQ subscale related to parasomnias (F (1, 92) = 6.08, $p = .016$) and daytime sleepiness subscale (F (1, 94) = 4.22, $p = .043$). There were no significant differences within the HBSS group between transfused and non-transfused patients.

Conclusion: Daytime tiredness in SCD may be associated with lower hemoglobin levels and more prevalent in HBSS subtype as compared to other genotypes of SCD. Additionally, parasomnias, including enuresis, occur more frequently in children with HBSS. Children on chronic transfusion did not differ in reports of daytime tiredness or total sleep time. It is important for health care professionals to consider genotype when assessing SCD patient's sleep habits.

Support (optional): Department of Health, Human Impact Grant

0249

DOES EXCESSIVE MOBILE PHONE USE AFFECT SLEEP IN TEENAGERS?

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Introduction: Teenagers communicate frequently via cell phone. Can that yield to restlessness and sleep problems?

Methods: We studied 21 healthy subjects with regular working/studying hours and without sleeping problems (age 14-20). Control group (CS, 3 men, 7 women) made less than 5 calls and/or sent 5 text messages a day. Experimental group (ES, 3 men, 8 women) had more than 15 calls and/or 15 text messages a day. Subjects filled a 47-item questionnaire (lifestyle, sleep habits), Epworth Sleepiness Scale and Beck Youth Scale. Sleep-wake profiles were assessed through a one-week actigraphy and sleep diary and one night sleep study at home using the sensor pad technique and pulse oxymetry. Cardiac activity was recorded 2 days continuously with a wireless thoracic belt sensor.

Results: One ES had more than 200 text messages/day. None but one (CS) subjects turned-off cell phone at night. Average Epworth score was 9 (4 ES > 11). No differences in Beck Scale. All CS had breakfast 33 % ES did not have it. ES spent more time on computers, drank more often coke and alcohol than CS. ES had more irregular sleeping hours. Perception of sleep latency was longer in CS but recordings showed longer sleep latency for ES. During the 1st recording sleep hour ES were more agitated with more stage shifts. Sleep efficiency was lower in ES having more arousals, major positions changes and turns. It took longer time for ES to reach "quiet" (SWS) sleep. The light/dark ratio of motor activity was higher in CS, less active at night. ES had more difficulty in waking up in the morning and were more tired before midday. During the week-ends 7 ES woke up after 12 pm (only 2 CS).

Conclusion: Teenagers using excessively their cell phone seem to be more prone to disrupted sleep, restlessness, stress and fatigue.

0250

USE OF EEG SPECTRAL ANALYSIS FOR DETERMINING SLEEP QUALITY IN CHILDREN WITH SLEEP DISORDERED BREATHING

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Introduction: Sleep disordered breathing (SDB) occurs in up to 34% of children ranging in severity from primary snoring (PS) to obstructive sleep apnoea (OSA). SDB is known to disrupt sleep quality in adults due to frequent arousals. In children, conventional methods suggest sleep may be less disturbed, as only ~50% of apnoeic events terminate with an EEG arousal. The present study tested the hypothesis that spectral EEG analysis would provide a more sensitive marker of sleep disturbance in children with SDB than standard visually scored assessment of sleep quality.

Methods: 105 healthy children aged 7-12 y were recruited. 84 were referred for clinical assessment of SDB and 21 were non-snoring controls recruited from the public. Standard polysomnography was performed with EEG bandpass filtered from 0.3Hz to 100Hz and sampled at 500Hz. Recordings were manually sleep-staged in 30s epochs using standard paediatric criteria. Spectral analysis using Fast Fourier Transform was run on consecutive 5s epochs over the entire night, for each hour for the first 6 hours after sleep onset, and in each sleep stage. 5 frequency bands were derived: Delta (0-4Hz), Theta (4-8Hz), Alpha (8-12Hz), Sigma

(12-14Hz), and Beta (14-30Hz). Statistical analysis was performed using 1-way ANOVA with Student Newman Keuls post hoc tests ($p < 0.05$ being considered significant).

Results: Conventional scoring showed the Moderate/Severe OSA subjects slept significantly less than the controls and also had longer sleep and REM latency. The Mild and Moderate/Severe OSA subjects spent increased time in NREM 1 and decreased time in NREM 2 compared to the PS and Control subjects. No other differences were seen. No significant differences were observed between SDB severity groups in the average spectral distribution across the night. Averaged spectral power of the first 6 hours of sleep also showed no significant alterations between groups in the distribution of power as the night progressed. No significant difference was observed in Delta power in any sleep stage.

Conclusion: Both conventional scoring and EEG spectral analysis indicated that sleep quality was not significantly altered by SDB, either across the night, in any specific hour of the night, or in specific sleep stages. The results suggest that reduced daytime functioning previously reported in SDB children is not due to sleep disruption. We speculate that in children, a stronger sleep-drive preserves sleep quality even in severe OSA.

0251

LONGITUDINAL STUDY OF SLEEP PROBLEMS IN CHILDREN WITH PRENATAL EXPOSURE TO COCAINE AND OTHER DRUGS

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Introduction: The purpose of this study was to determine if childhood sleep problems are related to prenatal exposure to cocaine and/or other drugs.

Methods: Sleep data was collected by maternal report in a prospective longitudinal follow-up of cocaine exposed and unexposed children participating in the Providence, RI cohort of the Maternal Lifestyle multi-site study. There were 139 subjects: 23 with no prenatal drug exposure, 55 exposed to cocaine alone or in combination with other drugs, and 61 exposed to drugs other than cocaine. Characteristics differed between exposure groups, including birth weight and head circumference, prenatal care, number of caretaker changes, and maternal poverty, SES, education, marital status, and postnatal drug use. Outcome measures included sleep problems as toddlers, preschoolers, and early school-age, assessed as composites of maternal report items.

Results: Compared to those with no drug exposure, children with prenatal drug exposure other than cocaine experienced greater sleep problems (mean [SD], 5 [4.93] vs 7.7 [4.85], $p = .026$). Prenatal nicotine exposure was a unique predictor of sleep problems ($R^2 = .028$, $p = .048$). Early sleep problems predicted later sleep problems (all p 's $< .01$).

Conclusion: Prenatal drug exposure is related to sleep problems from 18 months to 9 years of age, nicotine has a unique effect, and early sleep problems predict later sleep problems.

Support (optional): This study was funded by National Institute on Drug Abuse (NIDA) and the National Institute of Child Health and Human Development (NICHD) grants N01-HD-2-3159 and U10 HD 27904, respectively.

0252

SLEEP DISRUPTION IN PARENTS OF YOUNG CHILDREN WITH TYPE 1 DIABETES

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Introduction: Parents of children with chronic illnesses experience significant sleep disruption; however, few studies have examined sleep in relation to type 1 diabetes management. This study investigates sleep disruption related to diabetes care in young children.

Methods: Twenty-four parents (88% female) completed parent-report measures about diabetes regimen, and child and parent sleep quality. Children ($N=24$; M age= 4.1 years; 50% female; 75% Caucasian) were in adequate metabolic control (M HbA1c=7.87%). The sample was split between children on conventional insulin regimens (2-3 injections/day; $n=11$) and more intensive insulin regimens (multiple daily injections (MDI); $n=13$). Child age and HbA1c did not significantly differ by regimen.

Results: Parents reported an average of 6.3 blood glucose (BG) checks/day. Children on MDI received significantly more BG checks/day (conventional $M=5.27$; MDI $M=7.15$; $p=.05$). In the MDI group, 85% reported checking their child's BG level after their child went to sleep ≥ 3 nights per week, compared to 27% of the conventional regimen group ($p=.05$). Having a child on MDI was associated with increased parent-reported difficulty sleeping ($p<.01$). 100% of parents of children on MDI reported diabetes disrupted their sleep sometimes (54%) or often (46%), as compared to 36% (sometimes) and 14% (often) of parents of children on conventional regimens ($p=.01$). 54% of children on MDI experienced at least one nighttime awakening lasting ≥ 10 minutes during the past three weeks, as compared to 0% of children on conventional regimens ($p<.01$). 54% of MDI parents report bedtime is stressful ≥ 3 nights per week, as compared to 18% of parents in the conventional regimen group ($p=.05$). Parents slept for an average of 6.57 hours/night.

Conclusion: Results suggest a significant number of parents of young children with type 1 diabetes experience sleep disruption and, further, having a child on a MDI regimen appears to cause increased sleep disruption.

0253

PRIMARY SNORING IN CHILDREN IMPACTS CARDIOVASCULAR FUNCTIONING

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Introduction: Primary snoring (PS) affects up to 30% of children. PS is the mildest form of sleep-disordered breathing (SDB), with OSA representing more severe SDB. OSA is known to negatively affect children's cardiovascular health. PS, however, has traditionally been considered benign, and its impact on cardiovascular functioning has not been reported.

Methods: Participants were 40 children (22F/18M; mean age 8.3 ± 2.2 y) referred for clinical assessment of SDB and matched controls. Overnight polysomnography and wrist actigraphy data were collected. Heart rate (HR) and HR variability (HRV) data from the total sleep period and from periods of uninterrupted sleep were analysed using both time and frequency domain methods. Participants were grouped by clinical diagnosis: PS (OAH1<1; $n=11$), mild OSA (OAH1 1-5; $n=7$), moderate OSA (OAH1 5-10; $n=7$), severe OSA (OAH1>10; $n=8$), and controls ($n=7$).

Results: Significant overall differences were found in HR ($p<0.05$) over the total sleep period and during stable sleep, whereby HR was highest in severe OSA (92 ± 13 bpm), followed by PS (82 ± 15 bpm), moderate

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OSA (76 ± 5 bpm), mild OSA (74 ± 8 bpm), and controls (71 ± 8 bpm). Significant overall differences were also found in all measures of HRV ($p < 0.05$) in both spectral and time domain analyses, whereby the standard deviation of R-R intervals in the time domain was lowest in severe OSA (53 ± 23 ms), followed by PS (59 ± 28 ms), moderate OSA (94 ± 37 ms), mild OSA (107 ± 45 ms), and controls (115 ± 46 ms). In time domain analyses, HRV was significantly lower in PS than in controls ($p < 0.05$). With values corrected for total HRV, there were no significant overall differences reflective of differences in autonomic balance.

Conclusion: PS was shown to have an impact on cardiovascular functioning equivalent to that of moderate OSA, challenging the notion that it is a benign condition. These data have implications regarding the management of PS, particularly when considered together with mounting evidence of neurocognitive, behavioural, and academic dysfunction.

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0254

SLEEPING LIKE A BABY: DOES SWADDLING PROMOTE SLEEP IN INFANTS BY INHIBITING AROUSAL PATHWAYS?

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Introduction: It has been proposed that an impaired ability to arouse from sleep may be involved in the pathophysiology of Sudden Infant Death Syndrome (SIDS). Swaddling is currently being promoted by some Australian SIDS organisations as a method for settling infants in the supine position, with the aim of reducing the incidence of infants being placed prone to improve sleep. Previous studies have shown that swaddling infants reduces spontaneous arousal and increases auditory arousal thresholds during active sleep (AS); however the underlying physiological mechanisms involved are uncertain. The aim of this study was to evaluate the effects of swaddling on infant arousal pathways, particularly the progression of sub-cortical activation (SCA) to full cortical arousal (CA).

Methods: 10 healthy term infants were studied with daytime polysomnography at 3–4 wk and 3 mo after birth; in both swaddled (sw) and non-swaddled (nsw) conditions. During both AS and quiet sleep (QS), arousal was induced with a pulsatile jet of air to the nostrils at increasing pressures. Arousal responses were scored as SCAs or CAs following standard infant criteria, and expressed as proportions of total arousal responses. Arousals observed during uninterrupted sleep between tests were classified as spontaneous and were also examined. Two-way RM ANOVA with post hoc Student-Newman-Keuls test was used to assess the effects of sleep state and swaddling on the proportion of CAs.

Results: No sleep state differences were observed in either induced or spontaneous arousal responses, therefore data were combined. Proportions of induced CAs were similar ($p > 0.05$) between sw and nsw conditions at 3–4 wk (sw $25 \pm 4\%$; nsw $35 \pm 6\%$) and 3 mo (sw $16 \pm 5\%$; nsw $25 \pm 6\%$). Swaddling also had no significant effects on the proportions of spontaneous CAs observed at 3–4 wk (sw $39 \pm 10\%$; nsw $56 \pm 8\%$) and 3 mo (sw $41 \pm 9\%$; nsw $47 \pm 10\%$). Regardless of sleep state and age, swaddling had no significant effect on baseline physiological variables (heart rate, oxygen saturation and abdominal skin temperature) or total sleep time.

Conclusion: We demonstrate for the first time that the arousal pathways to full cortical arousal are not altered by infant swaddling. Furthermore, swaddling does not affect physiological variables during sleep. These data provide important new evidence to support the promotion of infant swaddling as a safe means to settle infants and improve sleep in the supine position.

0255

SLEEP IN CHILDREN DURING EARLY DEVELOPMENT: DATA FROM THE SOUTH AUSTRALIAN PAEDIATRIC SLEEP STUDY (SAPSS)

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Introduction: It is reported that children are sleeping less than ever before, affecting health and daytime functioning. The aims of this study were to examine sleep characteristics by gender and age in a large cohort of children aged 5–10 years, and identify groups at risk through determination of demographic predictors of short sleep.

Methods: A parent-reported questionnaire, combining previously validated tools, was used to gather information on sleep and daytime functioning in children aged 5–10 yrs ($N=1845$) from 32 Adelaide metropolitan schools. A MANOVA was used to determine differences in sleep characteristics by age and gender. Short (<9 h/night), optimal (9–12h/night) and long sleepers (>12 h/night) were identified using NSF guidelines. Sleep time was calculated from reported sleep onset to reported wake time. Analyses of demographic influences are underway.

Results: Overall, results show sleep time on weekends was significantly shorter than on schooldays ($p < .0001$). Girls slept significantly longer than boys across schooldays ($p < .05$) and weekends ($p < .0001$). At the extremes, 10-year-olds slept less than 5-year-olds ($p < .0001$) on schooldays (42.6mins) and weekends (37.2mins). On schooldays, 21% of children were identified as short sleepers. This increased to 34% on weekends, with 14% getting less sleep than recommended every night of the week. Interestingly, there was no difference in sleep time of short sleepers across the age groups.

Conclusion: The group trends found in this study, the first in Australia to collect detailed sleep characteristics of a large paediatric community cohort, are consistent with similar epidemiological studies overseas. However, the high proportion of short sleepers and similar sleep times between short sleepers from 5 to 10 years are concerning as this suggests the greatest sleep deficits are in the younger group. As this is a critical phase of development, reduced sleep quantity may have a serious impact on health and daytime functioning in these children.

0256

HOME NOCTURNAL CARDIORESPIRATORY RECORDING IN CHILDREN

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Introduction: Obstructive sleep apnea syndrome (OSAS) in children is a common pediatric problem with serious complications. The gold standard for diagnosing OSAS is full polysomnography in a sleep laboratory. Unattended home sleep studies using abbreviated portable systems, however, are increasingly recognized as an alternative. Advantages include convenience, improved sleep quality, and cost-effectiveness. The aim of this study is to explore the utility of abbreviated home polygraphy for diagnosis of OSAS in children.

Methods: Prospective study of 100 children, aged 3 to 14 years, referred for suspected OSAS to our Sleep Service between November 2005 and July 2007. Recordings were performed overnight in the childrens homes using an ambulatory cardiopulmonary device. Parameters registered: chest and abdominal wall movements, nasal airflow, snoring, arterial oxygen saturation, pulse rate and body position. We considered mild OSAS when apnea index (AI) >1 or apnea-hypopnea index (AHI) 3–5.9, moderate OSAS when AHI 6–9.9 and severe OSAS when AHI >10 .

Results: We recorded 100 children: A. Results from 14 children (14%) were excluded due to technical deficiencies in the recordings. B. In 86

children (86 %) the study was successful and led to a diagnosis. Mean data overall group: AIH: 15.04+ 0.7, basal oxygen saturation: 98.5+ 0.7, minimum oxygen saturation: 85.7 + 5.0. 1. A 85.7 % (74 children) was OSAS. 2. A 7.8 % (7 children) had bradi-tachycardia without other disorder in studied parameters. In these cases we did a full polysomnography. 3. A 6.5% (5 children) had normal cardio-respiratory parameters. A subgroup of 10 of these children were evaluated twice, using polysomnography in the hospital and home recording and there was concordance in the diagnosis.

Conclusion: Abbreviated home cardiopulmonary sleep studies may be successfully performed at home to evaluate OSAS in children. In our experience we had a good diagnosis in 85.7% of children.

0257

RELATIONSHIP AMONG OBESITY, SLEEP PROBLEMS, AND QUALITY OF LIFE IN SCHOOL-AGED CHILDREN

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Introduction: While sleep problems have been documented in overweight adults, few studies have focused on children's weight and sleep patterns. Furthermore, studies have shown poorer quality of life in children who are overweight or in children who experience sleep problems. Yet, the independent and joint contribution of weight and sleep problems on quality of life has yet to be investigated.

Methods: One hundred children (ages 8-12 years; 60% boys; 58% African-American, 32% Caucasian) and their caregivers completed questionnaires at the child's well-visit. Parents completed a demographic survey, the Children's Sleep Habits Questionnaire (CSHQ), the Pediatric Sleep Questionnaire (PSQ), and the Pediatric Quality of Life 4.0 (PedsQL 4.0). Children completed the PedsQL 4.0. Healthcare practitioners provided children's height and weight, which was used to compute BMI for age-and-sex.

Results: Children who were obese had poorer scores for sleep onset delay, $F(2, 99)=8.71, p<.01$, sleep-disordered breathing, $F(2, 99)=11.95, p<.01$, sleep duration, $F(2, 99)=4.23, p=0.02$, and daytime sleepiness, $F(2,99)=14.26, p<.01$, compared to children who were overweight or healthy weight. Hierarchical regression analyses found weight category was a significant predictor of parent-reported physical, $F(1,99)=11.78, p=.001$, psychosocial, $F(1,99)=13.03, p=.001$, and total quality of life scores, $F(1,99)=13.08, p=.001$, as well as child-reported physical functioning scores, $F(1,99)=28.71, p<.01$ (accounting for 11-23% of the variance). Weight category and sleep problem category were significant predictors of child-reported psychosocial, $F(1,99)=26.86, p<.01$, and total quality of life scores, $F(1,99)=31.97, p<.01$ (accounting for 8-25% of the variance).

Conclusion: These results support previous studies showing an increased prevalence of sleep problems among children who are obese and an association between increased weight and lower quality of life. In this study, sleep and weight each contributed unique variance for quality of life scores, thus indicating the need to evaluate daytime functioning in children with both obesity and sleep problems.

0258

CEPHALOMETRIC MEASURES CAN PREDICT SNORING AND APNEA EVENTS IN MOUTH BREATHING CHILDREN

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Introduction: Children with adenotonsillar hypertrophy are predisposed to sleep-disordered breathing and many of them are mouth breathers. A modified craniofacial morphology can be a predisponent factor for sleep

disordered breathing, and lateral radiography is a common approach to recognize this feature. Our hypothesis is that angular and linear measurements might be predictive of polysomnographic changes in sleep-disordered breathing in children. The aim of this study is to investigate possible associations among polysomnographic and cephalometric data of nasal and mouth breathing children.

Methods: Twenty-seven mouth and nasal breathing children aged 7 to 14 years (15 mouth breathing children - MB; 12 nasal breathing children - NB) were subjected to polysomnographic and lateral radiography. The polysomnographic variables were: sleep efficiency, sleep latency, AHI (apnea-hypopnea index), SaO₂, arousal index and snoring. The evaluated cephalometric measures were: SNA, SNB, ANB, NS.PIO, NS.GoGn, 1.NA, 1.NB, SPAS, PAS, MPH and C3H. Statistical analysis was based on Logistic Regression and Multiple Linear Regression.

Results: Snoring MB children had smaller SPAS ($p=0.005$) than NB children. MB children with oxygen desaturation had a trend to have smaller SNA measurements ($p=0.09$) and those with AHI greater than 1 event per hour had smaller PAS measurements ($p=0.05$) when compared to the NB children. The multiple linear regression models showed that SPAS measurement and snoring are associated ($p=0.0053$).

Conclusion: Our study showed association among polysomnographic data and cephalometric measures of mouth breathing children. Snoring was the most important variable associated with altered craniofacial morphology. Cephalometric measurements are important to be evaluated in order to predict the presence of sleep-disordered breathing in mouth breathing children.

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0259

A SUB-TYPE OF NOCTURNAL FRONTAL LOBE EPILEPSY OR A NEW EPILEPTIC SYNDROME?

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Introduction: Frontal lobe epilepsy is the most frequent nocturnal epilepsy seen during sleep in adults and children. We want to describe the PSG findings in 30 patients, referred to our epilepsy unit, diagnosed with refractory epilepsy and with neurocognitive and behaviour deterioration that do not fit the classical presentation of the frontal lobe epilepsy.

Methods: 30 patients were studied from January 1990 to January 2005. Age range: 5,5 to 19 years (mean 12,5 years). 11 boys, 19 girls. First seizure appeared at the mean age of 2.9 years. All patients underwent several nocturnal PSG. 29 suffered from frontal epilepsy and only one had occipital epilepsy.

Results: During slow wave sleep the video-EEG showed generalized paroxysmal discharges, focal (frontal or occipital) or unilateral. These paroxysms coincided in all patients with arousal and irregular breathing that occurred several times during NREM sleep (stages 1 and 2) hindering progression to slow wave sleep and altering the structure and organization of sleep cycles. The persistence in time of this phenomenon worsened the cognitive deficit as well as the behaviour of these patients. The MRI showed abnormalities in 50% of the patients. The follow up of the patients ranged from 2 to 15 years. All the patients were on AED (polytherapy). Except for two patients, all the other subjects had a poor outcome with persistent seizures as well as worsening of cognition.

Conclusion: We consider that the particular findings of this group of patients: the electro-clinical findings, cognitive deterioration, bad response to antiepileptic drugs and a poor cognitive outcome, might correspond, clinically and from the EEG findings, to a different group of those with nocturnal frontal lobe epilepsy (NFLE), maybe a sub-type of NFLE, or a new epileptic syndrome.

0260

PARENTAL SMOKING AND SLEEP DISORDERED BREATHING IN CHILDREN; A ROLE FOR URINARY COTININE?

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Introduction: Environmental tobacco smoke exposure (ETS) is a major health hazard and is a key contributor to respiratory disorders in children. Nicotine is a key constituent of tobacco smoke and measurement of the stable metabolite cotinine can be used as a surrogate to ETS exposure. The association between ETS and Sleep Disordered Breathing (SDB) has not been studied in children although an association between ETS and sleep fragmentation in infants has been shown. We conducted a cross-sectional study, with prospective data collection assessing SDB among children differentially exposed to ETS.

Methods: Children undergoing overnight polysomnography (PSG) to rule out Obstructive Sleep Apnea were consecutively enrolled. Both parents filled ETS validated questionnaire and children's urinary samples taken after PSG were assessed for cotinine by a direct ELISA kit.

Results: 40 children (age 5.8±2.4y, 72% boys, BMI 16.3±2.1, AHI 5.0±3.2) were consecutively enrolled. 18 (45%) children had parent/s that reported on current smoking. Children's urinary cotinine concentration correlated with parental reported intensity of ETS (spearman p=0.03, r=0.55, mean cotinine concentration 5.9±5.6 ng/ml). Cotinine concentration did not correlate with Apnea Hypopnea Index (p=0.8). ETS was associated with lower mean nocturnal oxygen saturation (r=0.4, p<0.02). Elevated urinary cotinine level correlated with decreased sleep efficiency (r=0.4, p=0.02) and decreased total sleep time (r=0.36, p<0.05). Arousal index was almost two folds higher in children of parents that reported smoking vs. not smoking (14.4±6.7 vs. 8.6±4.3 events/hr, p<0.05) with no significant effect on sleep architecture (percentage of sleep stages) between the two groups.

Conclusion: The severity of SDB cannot be explained by objective and subjective correlates of exposure to tobacco smoke. Children exposed to ETS suffer from poorer quality of sleep that is correlated to objective urinary cotinine concentration.

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0261

SLEEP DEPRIVATION AMONG ADOLESCENTS IN SINGAPORE

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Introduction: Sleep deprivation in teenagers is associated with emotional and behavioural problems, accidents and poorer academic performance. Relatively little data exists on the scope of this problem in Asian populations. Our objective was to determine the extent of sleep deprivation among school-going adolescents in Singapore.

Methods: A cross-sectional survey of secondary school students from 26 randomly selected schools in Singapore was carried out using detailed self-administered questionnaires on Sleep patterns and related behaviours.

Results: 7 school principals consented to participate in the survey, for a total of 1376 students from secondary school levels 1 through 5, representing different types of schools (autonomous, government, independent, international) and academic streams (Special, Express, Normal Academic, Normal Technical) in Singapore. Ages ranged from 13 to 18 years, with 323 boys (24%) and 1024 girls (76%), of mixed racial composition (81.0% Chinese, 10.9% Malay, 4.7% Indian, 3.4% others). Reported amount of sleep on school nights was categorized as insuff-

icient (<8 hours), borderline (8 to < 9 hours) or optimal (>= 9 hours). Only 3.1% of teenagers reported optimal amounts of sleep, with 80.3% not getting sufficient sleep. Teenagers reported an average of only 6.72 hours sleep on school nights. On non-school nights, more students (66.3%) reported optimal sleep: An average of 9.2 hours, or 2.49 hours more than on school nights. 14.8% of teenagers felt they had sleeping problems, but with only 0.5% reporting these to a doctor. 14.5% reported snoring at least a few nights a month. Those reporting snoring at least a few nights a week had significantly (P<0.05) more problems with falling or staying asleep, concentrating at school, getting along with others, use of caffeinated beverages and higher Depressive Mood Scores than those who rarely or never snore. Symptoms of Restless Legs Syndrome (RLS) were reported in 5.7% of teenagers.

Conclusion: The vast majority of teenagers in the Singapore schools surveyed are not getting enough sleep on school nights, but appear to partially catch up on their sleep debt on non-school nights. Sleep disturbances are generally under-reported to healthcare professionals. Treatable sleep disorders such as sleep disordered breathing and RLS are probably under-diagnosed. Greater awareness of sleep health is needed among adolescents in Singapore in order to improve their wellbeing and school performance.

0262

CARDIAC RESPONSE TO OBSTRUCTIVE EVENTS IN CHILDREN WITH OSAS

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Introduction: Children with obstructive sleep apnea syndrome (OSAS) display significant changes in heart rate and heart rate variability during obstructive episodes. However, the magnitude of the cardiac response is not well documented. We hypothesized that the cardiac response to an obstructive event changes during development.

Methods: We compared the change in heart rate during obstructive events in REM sleep in two groups of children with OSAS; those younger than 11 years of age and those older than 11 years of age. For each subject, we identified all REM epochs containing obstructive events of at least 10 seconds duration, preceded by 10 seconds or more of normal respiration. For each event, the RR interval of the last 10 seconds before the event (Baseline) and the first 10 seconds of the event (OSA) were calculated and the % change between baseline and OSA was determined. Similarly, mean % change between baseline and OSA for all events in each subject and for both groups were determined.

Results: Cardiac response during REM was studied in 11 children younger than 11 years; mean age 5.6±2.5 years (BMI Z-score: 2.0±1.5), and 6 children older than 11 years; mean age 13.3±1.3 years (BMI Z-score: 2.6±0.5, p=NS). We noted significant changes in the magnitude of the cardiac response between the groups. Younger children had a smaller changes in RR interval (8.1±6.9%) compared to older children 17.0±9.2%, p<0.05). In addition, for all children, the % change in RR interval between baseline and OSA increased linearly with age (R=0.55).

Conclusion: These results suggest that older children with OSAS are more prone to develop significant heart rate decelerations during obstructive episodes in REM sleep compared to younger children. Maturation changes in the autonomic nervous system may be responsible for these differences.

0263

QUESTIONNAIRE, CARDIOPULMONARY COUPLING, AND ATTENDED CARDIORESPIRATORY SLEEP STUDIES IN 200 PEDIATRIC SLEEP APNEA PATIENTSGuo D¹, Peng C², Wu H¹, Sun R¹, Chen G¹, Thomas R³

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Introduction: Sleep-disordered breathing (SDB) impairs body growth, intelligent and mental development of children. The optimal method of screening for pediatric SDB remains to be established. An ECG-based cardiopulmonary coupling (CPC) analysis has been applied to the assessment of sleep apnea and sleep stability in adults (Sleep 2005; 8(9):1151-1161). We propose that CPC can also be reliably used in pediatric patients, especially since respiratory sinus arrhythmia, a critical signal used in this analysis, is strong in children.

Methods: Data from 200 pediatric SDB patients (130 male and 70 female, average age 5.7 years), acquired by the Sleep Center of China Beijing Meitan General Hospital, during the period of March to August, 2007, are retrospectively analyzed. Life Quality Questionnaire OSA-18 was completed by each child's parents before sleep study. The questionnaire includes 18 items grouped in 5 domains: sleep disturbances, physical suffering, emotional distress, daytime problems, and parent or caretaker concern. For the CPC analysis, RR and ECG-derived respiration time series were analyzed to calculate the product of the power and coherence of these two signals at a given frequency. A predominance of power and coherence in the low-frequency band (0.01~0.1Hz) is associated with disordered breathing. Attended sleep studies, included nasal pressure (the primary scoring channel), oronasal thermistor, pulse oximetry, pulse transit time, and body position, without EEG recording. Respiratory events are scored both with and without 4% oxygen desaturation.

Results: Preliminary analysis indicates that CPC and respiratory flow analysis correlate with each other, and both correlate with the questionnaire evaluation. The CPC detection of SDB has adequate sensitivity and specificity compared with the respiratory flow scoring. The analysis of all 200 subjects is ongoing.

Conclusion: Compared with questionnaire and the usual scoring of sleep respiration, CPC analysis seems a valuable screening method for pediatric SDB.

0264

EFFECTS OF A NK 1 RECEPTOR ANTAGONIST ON CELLULAR PROLIFERATION OF TONSIL TISSUES DERIVED FROM CHILDREN WITH OSA AND RECURRENT TONSILLITIS

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Introduction: Obstructive sleep apnea (OSA) affects 2-3% of all children. Adenotonsillar tissue hypertrophy (AT) is by far the major pathophysiological contributor to OSA in children. However, the mechanisms of adenotonsillar proliferation are poorly understood. Substance P levels (NK agonist) and expression of NK-1 receptor are significantly higher in patients with OSA compared to recurrent infection (RI). Therefore, we hypothesized that a NK-1 receptor antagonist would reduce proliferative rates of tonsillar tissue in children with OSA in a mixed cell tissue culture model.

Methods: Cell cultures from tonsil samples removed from pediatric patients with OSA (n=15) and RI (n=15) were established in standard medium, transferred into 96-round bottom well plates, and placed in a 5 % CO₂ incubator at 37° for 48 hours. Cells were incubated to evaluate

basal proliferation or stimulated with substance P and NK 1 antagonist (GR-82334). Cells were pulsed for the final 18-20 hours with 0.0185 MBq (0.5 microCi) 3H-Thymidine to determine the cell proliferation. Moreover, cells were also cultured in similar conditions using 24-well plates to determine the specific protein levels and mRNA expression. Each of specific mRNA and protein expression were assessed by real-time RT-PCR and commercial ELISA kits, respectively.

Results: Treatment with a NK-1 receptor antagonist induced significant dose-dependent reductions in the proliferative rates of tonsillar tissues from children with OSA. In basal conditions, TNF-alpha, IL-6, and IL-1 levels were significantly higher in OSA than in RI, and treatment with NK 1 receptor antagonist reduced these cytokines. In addition, thioredoxin mRNA levels, a known anti-oxidant protein, were significantly higher after treatment with NK 1 receptor antagonist.

Conclusion: In a tonsillar mixed cell culture from children with OSA and RI, treatment with a NK 1 receptor antagonist suppresses proliferative responses in a dose-dependent fashion, and significantly reduces IL-6, TNF- α , and IL-1 α release. These findings suggest a potential role for modulators of NK 1 receptor in the treatment of AT associated with OSA in children.

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0265

COMPLIANCE WITH POSITIVE AIRWAY PRESSURE IN A PEDIATRIC POPULATION

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Introduction: Compliance with positive airway pressure (PAP) therapy for treatment of sleep apnea has been well studied in the adult population. Compliance, as defined by greater than 4 hours per night, is reported at 40-60 percent. Many factors related to compliance have been studied (i.e., machine type, interface type, cognitive constructs, disease severity). However, there is a paucity of information regarding PAP compliance in the pediatric population, with the prominent factors studied being machine type or subjective parent report only. The clinic described and studied is dedicated to over 200 pediatric patients on CPAP or BIPAP therapy with the standard of minimal compliance at 50%. As part of a clinic initiative to report overall compliance rates and to identify variables associated with compliance or increased need for intervention, data regarding demographics, weight status, objective rates of compliance by smartcard technology, disease state, and others were gathered and analyzed.

Methods: In an effort to better understand the trends present in the PAP clinic data, several exploratory analyses were performed on variables such as age, weight status, disease state, and compliance across visits over time.

Results: In our pediatric population, overall compliance rate is 52.3%, similar to that found in adults. Adolescents were consistently below 50% compliance. In addition, children at or above the 90th percentile for BMI tend to have a compliance rate lower than 50% (42%), and weight status remains consistent over time. Finally, results indicate that children who are seen frequently in the first few weeks of CPAP/BIPAP initiation have a compliance rate that remains above 50% over time.

Conclusion: In a pediatric CPAP/BIPAP population, results suggest compliance rates are similar to that in adults. Specific subpopulations may need further support to maintain treatment compliance. Planned future studies aim to specify treatment barriers and areas to target for intervention.

0266

PARENTAL ADAPTATION AND SLEEP ARRANGEMENTS IN INFANCY

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Introduction: Decisions about where infants sleep have important ramifications for many aspects of family life and are complexly determined (Germino et al, 2007, Goldberg & Keller, 2007). Parental adaptation to sleep arrangements, however, has received very little attention. The present study examines mothers' and fathers' adaptation to infant sleep arrangements and parents' attitudes about bedsharing.

Methods: Data on 45 families with infants between 1 and 24 months have been collected. Parents completed measures of parental cognitions about infant sleep and attitudes and practices regarding sleep arrangements. A measure of adaptation to infant sleep was derived from five items that inquired about parents' satisfaction with infants' sleep location, and bedtime and nighttime behavior.

Results: Fathers' and mothers' adaptation scores were highly correlated ($r=.58, p<.01$). Parents whose infants spent any time with them at night had poorer adaptation scores than did parents who slept separately from their infants ($t=-3.7, p<.001$ for mothers, $t=-4.3, p<.001$ for fathers). Parents with more lenient attitudes toward bedsharing spent more time with their infants at night than did parents with less lenient attitudes. Interestingly, however, more lenient attitudes toward bedsharing were associated with poorer adaptation in both mothers ($r=.42, p<.01$) and fathers ($r=.35, p<.01$), even after infant age was statistically controlled.

Conclusion: Parental adaptation to infant sleep was poorer when infants spent any part of the night with their parents, even when parents endorsed bedsharing. In a culture that is typically not accustomed to co-sleeping, parents who choose to co-sleep for their child's well-being may be doing so at their own expense. Additional analyses will examine parental adaptation in relation to video recordings of infant-parent interactions at bedtime and nighttime, and actigraph assessment of maternal sleep quality.

0267

BIOLOGICAL AND BEHAVIORAL CORRELATES OF DAYTIME SLEEP/WAKE STATES IN NEONATAL RHESUS MACAQUES

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Introduction: Infant sleep is an important developmental behavior influenced by a complex interplay between endogenous and environmental factors. Non-human primates offer an ideal developmental research model of human sleep, providing greater control over factors, while maintaining high generalizability to humans. This is a preliminary study investigating the relationship between heredity, birth weight, temperament and neonatal daytime sleep patterns.

Methods: The sample composed nursery reared neonatal rhesus macaques ($n = 144$). Infants were kept under experimental control for 30 days post-birth. Sleep/wake states (1=sleep, 2=transition, and 3=wake) were recorded at two hour intervals daily (8am-8pm) and averaged over 30 days. A one-way ANOVA was used to compare the relationship of paternity, co-varied with birth weight, to daytime sleep. An additional one-way MANOVA was used to investigate the relationship between paternity, co-varied with sleep, and the four major factors of the Brazelton temperament test for monkeys: orientation, state control, motor maturity and activity.

Results: There was a significant effect for the ANOVA for both paternity and birth weight to neonatal daytime sleep ($F_{17,123}=2.27, p<0.005$;

$F_{1,12513.03}, p<0.001$, respectively). Follow-up analysis showed that birth weight was negatively correlated with daytime sleep ($r=0.24, df=142, p<0.005$). The MANOVA revealed a significant effect for paternity and sleep to Brazelton factors ($\lambda (17,123)=2.401, p<0.005; \lambda (4,120), p<0.05$). Follow-up ANOVAs showed significant relationships linking paternity to activity ($F_{17,123}=1.98, p<0.05$) and sleep to state control ($F_{1,123}=8.90, p<0.005$). Correlation analysis showed a positive relationship between state control and daytime sleep ($r=0.27, df=142, p<0.005$).

Conclusion: Rhesus monkeys provide an ideal model for developmental sleep research. The results of this analysis highlight the potential in this area. Some of these findings have been observed in human studies; however, additional studies are warranted with greater monitoring of sleep over the lifespan and experimental manipulations which will parse out the complex relationship between genetics, environment, sleep and behavior.

0268

SLEEP-DISORDERED BREATHING AND BEHAVIOR IN CHILDREN WITH A CLEFT PALATE REPAIR

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Introduction: Children with a previous repair of a cleft palate may be at an increased risk of sleep-disordered breathing (SDB). Anecdotal reports suggest that children with cleft palate repair commonly develop neurobehavioral problems, such as hyperactivity, that resemble those seen in association with SDB. The possibility that SDB may contribute to such problems has never been studied.

Methods: Children attending the Craniofacial Anomalies Program for long-term follow-up of a previous cleft repair were recruited. Parents were asked to complete two well-validated instruments: the sleep-related breathing disorder (SRBD) subscale of the Pediatric Sleep Questionnaire, minus the 6 items relating to behavior, and the Conners' Parent Rating Scale-Revised. An SRBD score of ≥ 0.33 identifies risk for SDB. The Conners' Parent Rating Scale has a mean T-score of 50 with a standard deviation (SD) of 10.

Results: Thus far, 35 children have participated. The mean age was 10.2 ± 3 years, mean body mass index (BMI) was 17.6 ± 4.6 , and 57% were male. Twenty-six percent of the subjects had a SRBD score ≥ 0.33 . SRBD scores correlated with age and BMI. After adjusting for both age and BMI, the SRBD score correlated with the Cognitive Problem domain and the DSM-IV domain for Inattention ($r=0.34$ and $r=0.35; p \leq 0.05$ for each). Twenty-three percent of children scored $\geq 2SD$ above the mean on the Cognitive Problem domain while 17% scored $\geq 2SD$ on the DSM-IV Inattention domain.

Conclusion: The proportion of children with repaired cleft palates who are at high risk for SDB is substantially larger than would be expected in a general clinical sample of well children. We have previously shown that only 5% of children attending well clinic visits score above the 0.33 threshold (Archbold et al 2002). Furthermore, SDB may play a role in the some of the behavioral problems clinically observed in these children.

0269

SLEEP-DISORDERED BREATHING: DOES IT PLAY A ROLE IN ANXIETY?Paruthi S¹, Felt BT², Hoban TF^{1,2}, Chervin RD¹, Ruzicka DL¹, O'Brien LM^{1,3}¹Neurology, University of Michigan, Ann Arbor, MI, USA, ²Pediatrics and Communicable Diseases, University of Michigan, Ann Arbor, MI, USA, ³Oral and Maxillofacial Surgery, University of Michigan, Ann Arbor, MI, USA

Introduction: Sleep-disordered breathing (SDB) is a common condition in children and is frequently associated with cognitive and behavioral morbidities, such as hyperactivity. Anxiety in children is often multifactorial and can be associated with other disorders including attention deficit hyperactivity disorder. However, no data exists on anxiety and its association with SDB. We investigated whether anxiety may be associated with SDB.

Methods: Children in grades 2–5 of an urban public school system were surveyed about SDB symptoms as well as behavior. SDB symptoms were assessed using a validated instrument; the sleep-related breathing disorders (SRBD) subscale of the Pediatric Sleep Questionnaire, minus 6 of the 22 items that directly ask about behavior. Anxiety was assessed using the Conners' Parent Rating Scale (CPRS). A score of at least 0.33 on the SRBD subscale indicates risk for SDB and anxiety was identified by a score of at least 2SD above the mean on the domain T-score.

Results: A total of 341 families completed the questionnaires. Thirty three children (9.7%) were identified with anxiety and 66 children (19.4%) had risk for SDB. Children at risk for SDB, compared to those without, were more likely to have anxiety (19.7% vs. 7.3%; $p=0.005$). The SDB score correlated with both the anxiety score ($r=0.33$, $p\leq 0.001$) and hyperactivity score ($r=0.41$, $p\leq 0.001$). After controlling for hyperactivity score there remained a correlation between SDB score and anxiety score ($r=0.2$, $p\leq 0.001$). In a linear regression, hyperactivity and SDB score were both independently associated with anxiety ($p\leq 0.001$). Hyperactivity and SDB score together accounted for 19% of the variance in anxiety score.

Conclusion: Children with high risk for SDB are more likely to have anxiety. This relationship is independent of hyperactivity, which is known to be associated with both SDB and anxiety.

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0270

SLEEP IN HOSPITALIZED PEDIATRIC PATIENTS AND THEIR PARENTSMeltzer LJ^{1,2}, Davis KF¹, Mindell JA^{1,3}¹Children's Hospital of Philadelphia, Philadelphia, PA, USA, ²Pediatrics, University of Pennsylvania School of Medicine, Philadelphia, PA, USA, ³Psychology, Saint Joseph's University, Philadelphia, PA, USA

Introduction: While sleep quantity and quality during hospitalization have been shown to be significantly worse for adults, little is known about the sleep of hospitalized pediatric patients and their parents. The objectives of this study were to determine whether sleep during hospitalization differs from sleep at home and examine potential sleep disruptors.

Methods: 81 children (48% female, 6-21 years) and 82 parents (90% female) completed the Sleep in a Children's Hospital (SinCH) questionnaire, providing information about sleep patterns at home, the previous night's sleep while hospitalized, and sleep disruptors (e.g., pain, noise, procedures).

Results: Sleep patterns significantly differed during hospitalization, with younger children reporting a later bedtime (BT), later wake time (WT), more night wakings (NW), and shorter total sleep time (TST), all $p<0.005$, and older children reporting a significantly later WT, more

NW, and longer TST, $p<0.01$. There was a first night effect for hospitalization of significantly earlier WT and shorter TST, $p<0.02$. Fourteen percent of children took medication for sleep while hospitalized (vs. 2% at home). Parents reported significantly more NW, $p<0.001$. While parent and child sleep variables at home were not correlated, bedtime, SOL, WT, and TST during hospitalization were significantly related (all $p<0.01$). Alarms on medical equipment and people talking in the hallway were the most bothersome noises for both children and parents, while nurses taking vital signs, the child's pain, and noise in the room were the most frequent sleep disruptors.

Conclusion: This study is the first to demonstrate the negative impact of hospitalization on sleep quantity and quality in children and their parents, in particular for younger patients and on the first night of hospitalization. Interventions to dampen noise, manage pain, and decrease the taking of vital signs throughout the night would lead to beneficial effects on sleep for both pediatric patients and their parents.

0271

PRESCHOOL/DAY CARE ATTENDANCE AND SLEEP PATTERNS OF 2- TO 5-YEARS-OLD CHILDRENHan G¹, Cairns AA¹, LeBourgeois MK², Harsh JR¹¹Psychology, The University of Southern Mississippi, Hattiesburg, MS, USA, ²Center for the Study of Human Development, Brown University, Providence, RI, USA

Introduction: Parents send their children to preschool and day care in order to be free to work and/or for educational gains. Preschool/day care attendance requires that at least some children wake earlier in the morning. An earlier awakening requires other changes to the sleep pattern to ensure adequate time in bed. In this study, we examined the association between preschool and/or day care attendance and the sleep patterns of 2- to 5-year-old children.

Methods: Data were collected from a representative community sample of 489 children (50.3% male; 72% White non-Hispanic) aged 2 to 5 years from southern Mississippi. Caretakers reported their child's typical weekday and weekend bedtime/rise time, napping patterns, and family demographics, including preschool/daycare attendance. They also completed the Children's Sleep Wake Scale, a measure of behavioral sleep quality.

Results: The mean start time for preschool/day care was 8:02 (SD = 43 min). In analyses controlling for race, month of data collection, and age, different sleep period distribution patterns were found for children attending vs. not attending preschool/day care. Attending children were out of bed > 50 min earlier on weekday mornings (6:54 vs. 7:45; $p<0.01$) but went to bed only 23 min earlier (20:47 vs. 21:10; $p<0.01$) and thus had 28 min less time in bed on week nights (607 vs. 635 minutes; $p<0.01$). Children attending preschool/day care were reported to have more difficulty waking in the morning ($p<0.01$; effect size = 0.63 SD) and obtained more diurnal sleep during the week (360 vs. 257 minutes; $p<0.01$).

Conclusion: Preschool/day care attendance is associated with differences in how preschool children distribute their sleep. On average, children attending preschool/day care appear less able to obtain adequate weekday nocturnal sleep as evidenced by greater difficulty getting out of bed in the morning and more diurnal sleep. Further study is needed to determine whether these differences have any consequences for neurobehavioral and/or emotional functioning.

0272

FACTORS AFFECTING POSITIVE AIRWAY PRESSURE (PAP) ADHERENCE IN CHILDREN

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Introduction: Positive airway pressure (PAP) is an effective treatment for obstructive sleep apnea in children, but remains a challenge due to poor adherence. The purpose of this study was to identify psychosocial and demographic factors related to PAP adherence in children. We hypothesized that child reported quality of life, daytime sleepiness, age, BMI, maternal education, PAP pressure and polysomnographic (PSG) parameters would affect PAP adherence.

Methods: Nine children (6-16 years of age) and their parents completed a series of psychosocial questionnaires prior to PAP initiation. Objective adherence data was obtained after one month. Children were 78% African American, 67% obese, and 22% developmentally delayed.

Results: One-third of the participants used PAP >4 hours/night. Average minutes of PAP usage over one month was related to child reported quality of life ($r=0.83$, $p=0.01$) and maternal education ($r=0.75$, $p=0.02$), and was inversely related to age ($r=-0.66$, $p=0.05$), and BMI z-score ($r=-0.72$, $p=0.03$). PSG parameters, PAP pressure setting, and daytime sleepiness did not correlate with average minutes of PAP usage over one month.

Conclusion: These results indicate that children who report better quality of life used their PAP more. In addition, PAP usage was higher for younger children, as well as if mothers had more education. Finally, higher BMI z-scores were associated with lower PAP usage. As no PSG variables were related to PAP usage, these results suggest that PAP adherence is related to psychosocial factors rather than severity of sleep apnea. However, these results were limited by small sample size; data collection is ongoing.

Support (optional): Respironics Inc., NHLBI 58585

0273

SLEEP STAGE DYNAMICS DIFFER BETWEEN CHILDREN WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA

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Introduction: Previous studies have shown that sleep stage dynamics, reflected by contiguous sleep and sleep stage durations, follow characteristic statistical distributions (Lo C et al., *Europhys. Lett.*; 57 (5) :625-631, Penzel T et al., *Neuropsychopharmacology*; 28: S48-S53). Whether such distributions or component durations may have diagnostic value has received little study. We examined for the first time these polysomnographic variables in children with and without obstructive sleep apnea (OSA).

Methods: Retrospective analysis of polysomnographic data from the Washtenaw County Adenotonsillectomy Cohort. Selected subjects were 48 children aged 5-12 years with OSA (pediatric apnea/hypopnea index ≥ 1.5) and scheduled for adenotonsillectomy, and 20 control subjects of similar ages without OSA and not scheduled for adenotonsillectomy. Subjects were studied at enrollment, and again one year later in almost all cases.

Results: For most of the subjects, from either group, the distribution of sleep and sleep stage durations could be modeled by an exponential distribution. At baseline, the number of sleep stage changes, proportion of total sleep time occupied by stage 1 sleep, proportion stage 2 sleep, mean stage 2 duration, and mean stage REM duration each distinguished subjects with and without OSA (Wilcoxon rank sum test, $p<.05$), but

only mean stage 2 duration did so independently, after accounting for the remaining variables ($p=.03$). At one-year follow-up, changes in total sleep time, mean stage 2 duration, and mean stage REM duration distinguished OSA from control subjects, but again only changes in mean stage 2 duration did so independently ($p=.01$).

Conclusion: Durations of contiguous sleep and specific sleep stages generally follow exponential distributions in children with or without OSA. The parameters of these distributions - particularly the mean duration of stage 2 sleep periods - may provide a useful addition to standard sleep stage analyses.

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0274

POLYSOMNOGRAPHIC FINDINGS OF SYMPTOMATIC PATIENTS WITH POSSIBLE MITOCHONDRIAL DISORDER

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Introduction: Fatigue is a common complaint in patients with mitochondrial disorders (MD) and sleep-disordered breathing (SDB). Patients with MD are more prone to SDB. We assessed SDB in patients with suspected MD presented with fatigue and symptoms of sleep disruption, who were referred for polysomnography (PSG).

Methods: A retrospective chart review was performed to evaluate the frequency of symptoms and PSG findings in patients with possible MD referred from metabolism clinic for PSG.

Results: Seventy-three patients with a median age of 9 years (range=1-39 years) were identified with fatigue (82%), autonomic dysregulation (53%) and developmental delays (38.4%). According to enzyme and DNA studies 22 patients (30.2%) were diagnosed with MD, 6 patients (8.2%) with other disorders; while 61.6% of patients have no diagnosis (negative for MD or still on going). Restless sleep (71%), excessive daytime sleepiness (69%) and snoring (62%) were the common symptoms. The median sleep time was 6.9 hours (range=1.9-8.7 h) with a median sleep efficiency of 87% (range= 32-97.6%). While the median latency to first epoch of sleep was within normal limits (21.3 min), the median REM latency was lengthened (189 min). Median total arousal number was high (108.5 events) with a median index of 17 (range=0-62). Ninety-five percent of the children (61/64 pts) were diagnosed as obstructive sleep apnea (OSA) with a median respiratory disturbance index of 7.4 (range=2-62), while 2 children got insufficient data and SDB was ruled out in 1 child. Forty of these pediatric patients had median awake and peak end-tidal carbon dioxide 41 and 50 torr, respectively. Seven of nine adult patients (77.8%) were also diagnosed as OSA with a median respiratory disturbance index of 14 (range=5.5-29).

Conclusion: We describe a high prevalence of SDB, particularly OSA, in symptomatic patients with suspected MD, especially children.

0275

PARENT REPORTED SLEEP COMPLAINTS IN YOUTH DIAGNOSED WITH AUTISM SPECTRUM DISORDERS

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Introduction: Children with Autism Spectrum disorders (ASD) have myriad sleep problems that place a significant burden on families. This study describes: a) specific sleep complaints reported by caregivers of children diagnosed with ASD and; b) the relationship between sleep complaints and psychiatric symptoms.

Methods: Intake data from 13 children with ASD presenting to a pediatric behavioral sleep medicine clinic were examined. Fifty three percent

had language and motor delay, 30% were nonverbal, and 69% received special academic services. Data were collected via preliminary phone interview, 1-2 hour in-person interview and observation of the caregiver and child, behavioral rating scales including a child sleep questionnaire (CSQ) and the Child Behavior Checklist (CBCL). Associations between the CSQ and CBCL were explored.

Results: Eighty five percent of subjects presented with difficulty initiating or maintaining sleep and 15% had irregular sleep-wake cycles. Following consultation, 77% met diagnostic criteria for Dyssomnias, 15% for sleep problems related to a medical condition and 8% for sleep-wake transition disorder. Of the 77% with dyssomnias, 70% had psychophysiological insomnia, 20% limit setting and, 10% sleep onset association disorder. On average caregivers reported bedtime resistance on 3 or more nights per week with an average sleep onset latency of 129 (+/-122) minutes and average wake time after sleep onset of 113 (+/-143) minutes. Examination of CBCL subscales revealed clinically significant values for thought problems, mean t score = 76 (+/- 6) and attention problems, mean t score = 69 (+/-8). Correlations among the CSQ items and CBCL subscales indicated bedtime resistance to be significantly associated with increased externalizing problems ($r=0.57$, $p<0.05$).

Conclusion: Sleep complaints, especially problems initiating and maintaining sleep, are highly prevalent among youth diagnosed with ASD. Overall, findings suggest that self-regulatory skills necessary for sleep onset and maintenance present a significant challenge for ASD youth and should be a priority of treatment.

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0276

OCCASIONAL SNORING DURING SLEEP IN CHILDREN AND IMPAIRMENTS ON A SPEECH DISCRIMINATION TASK

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Introduction: Neurocognitive morbidity has been frequently reported in children with sleep-disordered breathing (SDB), with associations being found between neurobehavioral impairment and polysomnographic (PSG) measures. Even habitually snoring children are at higher risk for neurobehavioral and cognitive deficits. To examine whether even occasional snoring is associated with altered brain functions, this study investigated brain activation and speech sound processing in children reporting snoring as “rarely” or “occasionally.”

Methods: Differences in auditory event-related potentials (ERPs) were investigated in 26 children (mean age 6.0 yrs, 16 females, 13 controls) using a 128-electrode net during a speech discrimination task. ERP data was analyzed using temporal principal components analysis (PCA) with subsequent factor loading scores serving as the dependent variable in the analysis of variance. Snoring frequency was documented using parental reports and overnight PSG was performed.

Results: Independent t-tests showed no significant differences in PSG variables between snorers and controls. PCA identified 4 regions accounting for 83.9% of total variance. One factor (peak at 308ms) accounted for 23.994% of the total variance. Significant Group*Electrode*Hemisphere ($F=1.084$, $p=0.047$) and Group*Electrode*Stimulus effects ($F=6.073$, $p=0.048$) characterized this factor. Post-hoc corrected t-tests indicated larger ERP amplitude in snoring children versus controls, possibly reflecting more effortful processing and increased resources needed for speech perception. Snoring children exhibited more positive ERP amplitudes across central electrode sites and larger negative peaks over occipital sites. This suggests that, although occasional snorers did not meet criteria for SDB, alterations in neural processing in these children emerged. This was especially pronounced in response to the “da” stimulus.

Conclusion: Neural processing appears to change in children who snore as little as once a week. This could reflect more effortful evaluation of speech stimuli or a decrease in cognitive resources available for the task. This raises the possibility that snoring—even if only occasional—is not benign.

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0277

DEVELOPMENT DIFFERENCES IN PARENTAL STRESS AND CHILD SLEEP DISTURBANCES IN AN AFRICAN-AMERICAN SAMPLE

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Introduction: Bedtime can be a stressful period for children, adolescents and their families. There is abundant anecdotal evidence that parents are stressed by their children’s sleep problems and can develop negative feelings about their children when the problems are chronic. This may ultimately make it difficult for parents to implement strategies to address their child’s sleep disturbances. This study examines the associations between parent’s perceptions stress, behavior, and sleep problems in their children.

Methods: Sleep, behavior, and parenting stress were evaluated in 73 African-American children (ages 6-18; mean age = 11(3.3) years); and 57% female. Measures consisted of a child sleep questionnaire (CSQ), the Child Behavior Checklist (CBCL), and the Parenting Stress Index/Short Form (PSI). Regression analyses were used to evaluate the association between parent stress, and their children’s bedtime and other behavior problems.

Results: Fourteen subjects (19%) met our criteria for having sleep onset problems (i.e., bedtime resistance and/or >2 call outs to caregiver on more than 3 nights a week) and 10 subjects (13%) were in the borderline or clinical range on the CBCL. Overall parental ratings of stress were significantly higher among youth with sleep problems ($p < .02$) as were ratings on CBCL Total, Anxious/Depressed and Externalizing scales ($p < .01$). When divided into child (6-11) and adolescent (12-18) groups, parental ratings of their own stress accounted for more of the variance in child sleep problems ($R^2=0.12$ $p < .05$) and parent ratings of adolescent behavior problems (PSI and CBCL) accounted for more of the variance in adolescent sleep problems ($R^2=0.20$ $p < .01$).

Conclusion: Increased parental stress and child behavior problems are associated with sleep problems in children. The associations or parental attributions appear to differ across development. Evaluating parent stress and perceptions of their children may inform treatment approaches and improve parent and child adherence to recommendations.

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0278

PREVALENCE OF PEDIATRIC SLEEPINESS

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Introduction: Prevalence estimates for sleepiness are appreciable in adolescents (15%-50%) and adults (9%-25%). Sleepiness in these populations is associated with compromised cognitive, behavioral, and emotional functioning. Although sleepiness may be equally significant in childhood, studies on its prevalence are relatively sparse. This report provides results of a review of epidemiology studies investigating pediatric sleepiness in the general population (GP) and in various clinical populations (CP).

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Methods: Searches of *Pub Med* and *Psych Info* identified reports of sleepiness in children aged 2-12 years. Keywords used were related to sleepiness, pediatrics, and epidemiology. For each article, we recorded geographical region, age, sampling method, definition of sleepiness, prevalence data, and risk factors. Articles were excluded if “sleepiness” was not clearly defined.

Results: Out of a total of 19 GP studies and 21 CP studies, 6 were excluded (retention 85%). Prevalence of sleepiness in GP studies ranged from 1.5% to 73.0% with a median of 12.0%. The variance in prevalence was related to how sleepiness was defined. For studies assessing Perception of Sleepiness by caretakers, the median prevalence was 19.5%, (range 4.0%-73.0%). Surveys assessing Inadvertent Sleep/Problematic Sleepiness yielded a median of 5.5% (range 1.5%- 34.0%). The greatest risk for sleepiness was associated with evening chronotype, rhinitis, and cough. Among CP studies, sleepiness was most prevalent for Asperger’s Syndrome (75.0%), Epilepsy (61.0%), and Dialysis (60.0%). Pronounced differences were found across geographic regions, but these differences may in large part be due to how sleepiness was defined.

Conclusion: The prevalence of pediatric sleepiness appears to be high and an important social concern given the short and long-term consequences known to be associated with sleepiness in this population. Parents, educators, and other caretakers should be aware of the common risk factors, especially when sleepiness may be excessive and unnecessary. The high rate of sleepiness in some clinical populations suggests considering sleepiness as a therapeutically-important symptom/feature.

0279

SLEEP PATTERNS IN HOSPITALIZED CHILDREN

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Introduction: Sleep is a complex function where all physiological processes change and it may be considered a protecting activity essential to survival. Hospitalization may affect a child’s quality of life, since it is a sudden interruption in his/her daily activities. It may represent a stressful experience involving a number of adaptations to deal with new routines. This study verified sleep patterns in hospitalized children (HC) concerning gender and age.

Methods: We studied 128 children hospitalized for respiratory diseases, from 4 to 14.91 years, about sleep patterns: total sleep time (TST), sleep latency (SL), sleep efficiency (SE), amount of naps (AN), duration of nap (DN), awakening after sleep onset (WASO), and duration of awakenings (DA). Sleep logs filled every morning by trained researches where used to assess sleep parameters.

Results: Considering the role sample, the TST was 590.3±560.5min, SL was 17.71±8.8 min, SE was 94.27±4.71%, AN was 0.52±0.38, DN was 55.92±40.11min, WASO was 0.27±0.43, and DA was 14.14±22.45min. TST was longer for boys (647.8±774.6min) than for girls (529±85.50min; p=0.03). Regarding age, we observed that 4-7 years old children presented TST 643.6±747.7min, 7.01-11 years old children presented TST 530.4±75.45 min, and 11.01-14 years old children presented TST 501.4±68.07 (p=0.0087). Young children (4-7 years old) showed SE higher than 7.01-11 and 11.01-14 years old children (94.99±4.2%; 93.96±4.8%; 92±6.2 %; p= 0.05). Other parameters were not significantly different considering gender and age.

Conclusion: TST declines with age in HC as well as in not HC. HC tend to sleep more than not HC according to literature data for Brazilian children. There are no information showing differences in TST regarding gender, but it could be hypothesized that boys react to the stress of hospitalization by increasing TST.

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0280

MIGRAINE AND SLEEP DISORDERS IN CHILDREN

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Introduction: Primary headache and sleep disorders are very common in children. According to several reports, about 10% of children fill the International Headache Society criteria for migraine headache. Children with migraine have a higher prevalence of various sleep problems as snoring, bruxism, and parasomnias compared to children without headache. Both migraine and sleep disturbances have serious consequences in child’s quality of life. Objective: The aim of this study is to verify the association between migraine and sleep disorders.

Methods: We study 46 outpatients of pediatric neurologic clinic with migraine (24 male) and 46 outpatients without headache (28 male), aged 7 to 14 years, from January to November, 2007. A complete clinical neurological assessment evaluating pain features were done by a trained neurologist to identify those with migraine.

Results: Sleep disorders were presented in 28 children with migraine and in 7 no headache children (p=0.00002). The sleep disorders found in children with migraine were parasomnias (14), snoring (11), bruxism (8), excessive sleepiness (3), and enuresis (2).

Conclusion: Children with migraine have more frequent sleep problems than those without headache. This association is yet unknown, but the intervention in sleep habits is reported to improve headache symptoms and an adequate treatment of migraine improves sleep. It is important a controlled research taking in account headache frequency, intensity, and duration, to verify the association among sleep disorders, headache, and the impact in the quality of life of the children.

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0281

RESTLESS LEGS SYNDROME AND COGNITION IN CHILDREN

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Introduction: The complaints on disorders of learning are the main reasons for children psychotherapy, becoming a challenge for the involved professionals in education and learning. The sleep disorders children present disorders of learning, memory, attention, and concentration. It is important to find easy tools to evaluate cognition in children to be applied in an outpatient clinic set and the Bender Gestalt screening (BG) could be one of these tools. OBJECTIVE: The present study aim to verify if BG can help on diagnosis of cognitive dysfunction in Restless Legs Syndrome (RLS) children.

Methods: 11 children (6 girls) aged 4 to 13 years, from elementary school, with sleep disorders complaints, referred to Neuro-Sono outpatients clinic of UNIFESP, Sao Paulo, Brazil, from February to December, 2007, were evaluated throughout BG. A trained psychologist and sleep specialist evaluated the children in the first clinical visit.

Results: All children had RLS diagnosed according to specific criteria of the International RLS Study Group. Three of them had isolated RLS and the remaining 8 children had comorbidities like learning complaints, attention deficits, hyperactivity, and delay in cognitive acquisition. BG disclosed cognitive dysfunction in all 8 children with RLS associated to comorbidities and was normal in those 3 children with pure RLS complaints.

Conclusion: BG was a tool that can easily check cognitive dysfunction in RLS children, allowing the health care team to treat these children not only in their RLS complaints but also their cognitive deficit, providing orientation to their families, teachers, and educators.

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0282

PREVALENCE OF NASAL CONGESTION IN CHILDREN PRESENTING TO THE SLEEP DISORDERS CLINIC

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Introduction: It has been shown that chronic nasal congestion may compound obstructive sleep apnea (OSA) and as such, is a modifiable risk factor for OSA. Recent literature has discussed that treatment of nasal congestion may improve symptoms of mild to moderate OSA [1]. However, despite this, nasal congestion is often under recognized as a confounder for sleep disruption and is often left untreated in the pediatric population. Objectives: To evaluate the prevalence of reported nasal congestion in children undergoing polysomnography (PSG) for suspected OSA.

Methods: At the Hospital for Sick Children, Toronto, we reviewed 200 parent questionnaires of patients who underwent formal PSG in 2007.

Results: Of the 200 questionnaires reviewed, 89 (45%) reported current symptoms of nasal congestion. Of those 89 patients, 5 patients (6%) were currently receiving treatment with nasal corticosteroids, 1 patient (1%) was currently treated with oral decongestant and 83 patients (93%) were not reported to be receiving any treatment for nasal congestion.

Conclusion: These findings would suggest that nasal congestion is commonly identified in children requiring assessment for sleep disordered breathing. Future recommendations may include screening and treatment of nasal congestion prior to formal PSG.

Support (optional): [1] Alexopoulos, E.I, et al. *Pediatric Pulmonology* 38: 161-167 (2004)

0283

NAP DEPRIVATION EFFECTS ON EMOTION REGULATION STRATEGIES IN PRESCHOOL CHILDREN

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Introduction: A vast literature in adolescents and adults shows that insufficient sleep leads to decrements in mood, behavior, and performance. In preschool children, little-to-no well controlled data on such relationships exist. Considering that 7%-24% of preschoolers have reported behavioral/emotional problems, identifying early risk factors, such as sleep regulation, is crucial. This study examined the effects of nap deprivation on emotion regulatory strategies employed during a solvable and unsolvable puzzle task assessment.

Methods: Data were collected on 8 healthy preschoolers (2 males; 6 Caucasians; 30-36 months) with no sleep/emotion/behavior problems. Children followed a strict sleep schedule for 5 days before emotion assessments that optimized sleep (12.5+ hrs TIB/24hrs). Emotion assessments occurred on two afternoons in the children's home: one after an afternoon nap of at least 60min (verified with actigraphy), the under a no-nap condition. Children were instructed to solve two puzzles. The unsolvable puzzle included an incorrect piece, and at a frustration point children were told to, "Solve the puzzle" for 1min and then asked, "What can you do to solve the puzzle?" Behavioral responses were videotaped and coded as the following emotion regulation strategies: soliciting help, healthy skepticism, self-talk, physical self-soothing, disruptive behaviors, alternate strategies, and negative self-appraisals.

Results: On the unsolvable puzzle task, a Wilcoxon matched-pairs signed-ranks test revealed a significant difference in measures of healthy skepticism, alternate strategies, and negative self-appraisal ($N_s=16$,

$p_s<.05$). Children in the no-nap condition spent significantly less time using healthy skepticism behaviors ($Z= -2.5$; Nap: $M=14.1$, $SD=10.7$; No nap: $M=4.1$, $SD=4.8$), more time using alternate strategies ($Z=-2.0$; Nap: $M=4.1$, $SD=4.5$; No nap: $M=13.5$, $SD=11.9$) and less time verbalizing negative self appraisals ($Z= -2.2$; Nap: $M=5.6$, $SD=6.4$; No nap: $M=2.5$, $SD=4.7$). No significant differences in emotion regulation across conditions (nap versus no-nap) were found during the solvable puzzle task.

Conclusion: Results suggest that nap deprivation affects children's use of behaviors related to regulation of frustration. Decreased use of healthy skepticism and negative self-appraisal in the nap-deprivation condition demonstrates impaired verbal regulation strategies of a more cognitive nature, while increased use of alternate strategies indicates more physically-bound approaches to frustration.

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0284

SLEEP DISORDERED BREATHING AND SLEEP HYPERHYDROSIS: LINKED REACTIONS TO STRESS AND COPING STRATEGIES

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Introduction: Sleep disorders can lead to chronic stress, with prolonged physiological responses that may damage the body worsening diseases processes. Night sweating is a common symptom of obstructive sleep apnea syndrome although the pathogenic mechanism is still unclear. The aim of this study is verify if play reduces stress in children with sleep breathing disorders and sleep hyperhydrosis.

Methods: We studied 329 children that came to the laboratory for blood tests, ages from 4-14.91 years, for mean levels of seric cortisol (cortisol) from March to December, 2005. The children were separated in groups that played (PG), refused to play (RPG), and did not play (NPG) in consecutively alternating weeks. Caretakers answered a sleep questionnaire to establish which children presented sleep disordered breathing associated to sleep hyperhydrosis (SDB-SHY), other sleep disorders (SD), and normal sleeping (NS), following Bruni's criteria. All blood samples were collected at 8:00 AM.

Results: We observed that 29 (8.78%) children with SDB-SHY showed lower cortisol than the 165 (50.15%) NS children ($10.44\pm 4.88\mu\text{g}/\text{dl}$; $12.21\pm 4.61\mu\text{g}/\text{dl}$; $p= 0.06$). There was no cortisol difference for SDB-SHY and NS children compared to the 42 (12.7%) SD children ($11.93\pm 4.46\mu\text{g}/\text{dl}$; $p=0.8$). Considering playing activities, SD children did not show differences in cortisol compared to the other groups ($p= 0.98$). Among the 29 SDB-SHY children, the 7 (1.82%) NPG showed higher cortisol than the 15 (4.5%) PG ($15.68\pm 5.56\mu\text{g}/\text{dl}$; $9.98\pm 3.36\mu\text{g}/\text{dl}$; $p= 0.001$) and than the 7 (2.12%) RPG ($9.48\pm 4.87\mu\text{g}/\text{dl}$; $p=0.04$).

Conclusion: Our data show that SDB-SHY are associated to cortisol level in children and play seems to have a positive impact on this group.

Support (optional): FAPESP AND UNITER-SONO

0285

THE MODERATING IMPACT OF PARENTING ON LINKAGES BETWEEN TEMPERAMENT AND THE DEVELOPMENT OF INFANT SLEEP

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Introduction: Temperament is frequently cited as a contributor to infant sleep quality, but findings are inconsistent. A largely unexplored role of temperament may be the manner in which it moderates the impact of parenting on infant sleep behavior. Such an approach is consistent with

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transactional perspectives on child development, which consider both parent and child influences. The present study examines this question.

Methods: Data were collected from 45 families with infants between 1 month and 24 months of age. Mothers and fathers completed measures of infant temperament, reports of their parenting behaviors regarding their infant's sleep, and daily infant sleep diaries. Infants were videotaped sleeping for one night to assess infant sleep and parenting behaviors.

Results: A number of direct, significant correlations emerged between temperament and infant waking frequency at night. However, after infant age was statistically controlled, the number of these associations was greatly reduced. Importantly, regression analyses controlling for infant age revealed a number of significant temperament X parenting interactions in predicting infant waking frequency. For example, putting infants down to sleep while still awake interacted with perceptual sensitivity in predicting waking frequency such that more perceptually sensitive infants had fewer night wakings if they were put down awake. For infants low in perceptual sensitivity, putting down awake was not associated with waking frequency. Other interactions, too numerous to report here, support the premise that the impact of specific parent behaviors on infant sleep quality depends on infant temperamental difficulty. These interactions will be presented in the final poster.

Conclusion: As these data suggest, the role of infant temperament in infant sleep development may best be understood in the context of specific parenting practices used to put infants to sleep. Direct and indirect contributions of infant temperament to infant sleep will be discussed.

0286

SLEEP DISORDERED BREATHING, OVERWEIGHT AND DAYTIME SOMNOLENCE IN A SAMPLE OF AFRICAN AMERICAN CHILDREN

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Introduction: Prevalence rates of overweight in children have increased dramatically over the last decade. While the association between obesity and obstructive sleep apnea (OSA) is well established in adults the association between overweight status and sleep in children is only recently being addressed. This study investigated the hypothesized associations between overweight status, sleep problems and daytime sleepiness in sample of urban African American youth.

Methods: The study sample consisted of 130 African American children (ages 6-18, mean age of 9.5(2.8) years and 50% female who were recruited from the community or referred for a polysomnography (PSG) to rule out OSA. Parents and children completed measures assessing sleep habits, behavior and psychiatric symptoms. Sleep parameters were derived from standard PSG and criteria for OSA severity were respiratory disturbance index (RDI): no Dx<1; mild 1-4; moderate 5-9 and severe >10. Overweight was classified as Body Mass Index (BMI) percentile corrected by age >85% (BMI%). Daytime sleepiness was estimated from a non-standardized modified Epworth Sleepiness Scale for children.

Results: OSA diagnoses for the normal weight/overweight groups were: no Dx=47%/36%, mild=38%/28%, moderate=8%/22% and severe 8%/14% ($p < .05$). The RDI did not differ between the normal (3.6+/-7.7) and overweight (5.9+/-11.5) groups ($p = .18$) and was not correlated with BMI% ($r = .08$, ns), although a rank order correlation was significant ($\rho = .18$, $p < .05$). The Epworth did not differ among the OSA severity groupings or among the BMI groups, however there was an association between the Epworth and RDI ($r = .26$, $p < .005$) but not between the Epworth and BMI% ($r = -.11$, ns).

Conclusion: Given the significant increased rates of overweight children and adolescents, understanding the interaction between inadequate sleep, overweight and sleep disordered breathing is of particular importance. These preliminary results suggests that degree of overweight is

not associated with OSA severity, but both overweight and OSA severity may contribute to daytime somnolence.

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0287

RELATIONSHIP BETWEEN SLEEP PROBLEMS AND BEHAVIOR PROBLEMS AMONG PRIMARY SCHOOL CHILDREN IN JAPAN

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Introduction: Sleep problems are common in children, and they are known to affect emotional, cognitive and social development of children. Pediatric sleep problems are mostly treatable, therefore, early recognition and treatment of sleep problems are important. The aim of the study was to identify the relationship between sleep problems and behavior problems among Japanese school children.

Methods: The study was conducted at a primary school located in the suburbs of the second largest city of Japan. Children's Sleep Habits Questionnaire (CSHQ) and Strengths and Difficulties Questionnaires (SDQ) was given to all students of the school and was filled out by the parents or caregivers. 509 subjects (252 males, 257 females, mean age : 9.0 SD 1.8) who responded to the questionnaire properly (response rate : 86.9%) were included in the analysis. Multivariate logistic regression analyses were performed to examine the sleep problems associated with behavior problems. Six logistic models that use SDQ total and subscale scores as response variables were created. As covariates, CSHQ total and subscale scores were used in common.

Results: Sleep onset delay and daytime sleepiness were shown to be independently associated with conduct problems and elevated total SDQ score. Daytime sleepiness was also associated with hyperactivity / inattention. Sleep anxiety was associated with peer relationship problems. Shortened sleep duration and parasomnias were associated with prosocial behavior. Elevated total CSHQ score was associated with emotional symptoms and elevated total SDQ score.

Conclusion: Sleep problems identified by the CSHQ were related to behavior problems. Early recognition and treatment of sleep problems in children may be important in improving or preventing behavior problems.

0288

AIRWAY FINDINGS IN DOWN SYNDROME CHILDREN WITH SLEEP DISORDERED BREATHING: A CASE CONTROL STUDY

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Introduction: Down syndrome (DS) children have a high prevalence of sleep disordered breathing (SDB) and are at high risk of post-surgical complications. Although adenotonsillectomy is considered the first line of treatment for pediatric SDB, there is emerging evidence that this surgical procedure may not be curative for all children with SDB. Objective: Identify the pattern of airway obstruction in DS children with SDB compared to healthy children referred for SDB.

Methods: DS children presenting with SDB were identified from a prospectively kept surgical database. Only those who had undergone sleep nasopharyngoscopy (NP) were included. All NP are performed under spontaneous respiration using a uniform anaesthetic technique. Age, and gender pair-matched controls were identified. The videos for these patients were reviewed. A count for obstructive and collapse findings

was performed for the study and control groups. Only DS and healthy controls with SDB were included.

Results: 11 consecutive DS children were identified (4 girls; 7 boys; age 7.25 years). They were matched with 11 controls with SDB (mean age 6.9 years). The average BMI of DS children versus controls was: 18.7 kg/m² versus 16.9 kg/m². The DS children compared to controls had comparable adenotonsillar obstruction (n.s). However, the DS children versus controls exhibited more circumferential (4 vs. 0) and lingual collapse (7 vs 2). The proportion of DS exhibiting dynamic collapse (17 vs. 5) was statistically significant compared to static collapse (22 vs. 24) ($P < 0.05$).

Conclusion: The results support the role of nasoendoscopy to direct the surgical treatment, and may explain failures of indiscriminate application of adenotonsillectomy to children with DS. Children with dynamic collapse are more likely to need positive airway pressure therapy as a treatment option rather than surgery with potential complications.

Support (optional): None

0289

BARRIERS TO ADHERENCE IN CHILDREN USING POSITIVE AIRWAY PRESURE TO TREAT OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive Sleep Apnea (OSA) is associated with significant morbidity in children. Positive airway pressure (PAP) is an effective alternative to surgery for pediatric OSA. However, nonadherence to PAP is common. Although nonadherence to PAP in adults has received much attention in the literature, little has been published regarding factors associated with PAP nonadherence in children. This preliminary investigation examined PAP adherence and treatment barriers in pediatric OSA.

Methods: Retrospective chart review. Subjects underwent PAP titration polysomnography (PSG) during January - December 2005. All outpatient clinic notes for each patient were reviewed up through 2007. Variables collected included: demographics, PSG data, level of adherence documented by sleep clinician, and barriers to PAP adherence.

Results: Subjects included sixty patients who were predominantly male (73.3%) and Caucasian (65.0%). The mean age at time of initial diagnostic PSG was 10.84±5.38 years. Severity of OSA varied (mean respiratory disturbance index was 22.26, range = 2.70-166.2). Most children (88.3%) returned for follow up management and were seen for a mean of 2.23±1.85 clinic visits after their initial referral to the sleep center. Clinician comments regarding adherence were documented for the majority (93.87%) of clinic visits. Less than 20% of the sample was rated as using PAP as prescribed. Barriers to adherence were varied (e.g., lack of insurance coverage; poor mask fit; blower/mask malfunction; skin irritation; nasal congestion; anxiety/clostraphobia; noncompliance; limited parent supervision).

Conclusion: Adherence to PAP was suboptimal in most cases. Factors affecting PAP nonadherence varied across subjects. These preliminary data reveal systemic, technical and patient/family-specific barriers to adherence that have implications for future research targeting improved PAP adherence in children.

0290

SLEEP BEHAVIORS AND SLEEP QUALITY IN CHILDREN WITH AUTISTIC SPECTRUM DISORDERS

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Introduction: Children with Autistic Spectrum Disorders (ASD) are at increased risk for sleep disturbances. Core deficits of ASD and their underlying neurophysiology may predispose children to intrinsic and extrinsic stressors that threaten sleep. Poor sleep in children can alter learning, attention and performance. Approximately two-thirds of parents report a sleep disturbance with their ASD child. Few rigorous epidemiological studies have been conducted in this population. Characterization of sleep in a well described ASD group utilizing subjective and objective standardized measures contributes solid descriptive baseline data and provides an important first step in building a foundation for future studies of etiology and intervention. The aims of this descriptive epidemiological study were to estimate the prevalence of sleep disturbances in children with ASD as compared to controls and to describe their sleep behaviors and sleep quality.

Methods: Participants were randomly selected from the Regional Autism Center Registry at the Children's Hospital of Philadelphia. The ASD cohort of 59 children, ages 4-10, 26 autism, 21 PDD-NOS, and 12 Asperger Disorder were compared to 40 typically developing (TD) controls. Diagnosis was confirmed with the Autism Diagnostic Observation Schedule or Asperger Syndrome Diagnostic Scale. Controls were screened using the Social Communication Questionnaire. Data was obtained with the Children's Sleep Habits Questionnaire (CSHQ), sleep diaries and ten nights of actigraphy. Actigraphic data was analyzed with the Sadeh algorithm and Scoring Analysis program.

Results: 66.1 % of parents of children with ASD (62.5% autism, 76.2% PDD-NOS, 58.3% Asperger) and 45% of parents of the TD controls report sleep problems on the CSHQ. 66.7% of actigraphic data of children with ASD (75% autism, 52.4% PDD-NOS, 75% Asperger) and 45.9 % of TD controls shows disturbed sleep.

Conclusion: Insomnia in the ASD population was endemic and 45% of TD controls from the Philadelphia Area were sleepy.

0291

INCREASE IN TOTAL SLEEP TIME IS ASSOCIATED WITH IMPROVEMENTS IN COGNITION IN ALZHEIMER'S DISEASE PATIENTS TREATED FOR OSA

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Introduction: Cognitive dysfunction related to obstructive sleep apnea (OSA) is attributed to hypoxemia. We previously showed that continuous positive airway pressure (CPAP) treatment of OSA in Alzheimer's disease (AD) patients results in cognitive improvements. This study evaluated variables associated with cognitive change.

Methods: 52 subjects (mean age=77.8 years, SD=7.3) with AD and OSA (mean AHI=28.5, SD=16.2) were randomized to 6 weeks of therapeutic CPAP or 3 weeks placebo CPAP followed by 3 weeks therapeutic CPAP. Subjects underwent neurocognitive testing at baseline, 3 weeks and 6 weeks. Sleep (Embla) was analyzed and scored for %-sleep stage, TST, WASO, and oximetry. Multiple regression analyses were performed using change in the composite neurocognitive score (after 3 weeks of real CPAP for both groups) as the primary outcome variable, adjusting for baseline cognition, with changes in oxygenation and sleep entered separately and jointly.

Results: When sleep and oxygenation variables were entered in the model jointly, increase in TST was the only variable that was significantly associated with improvement in the composite neurocognitive score. With TST and % time SpO₂<90% added to the baseline cognition model, TST had a significant association while SpO₂ did not (TST beta-coefficient=0.007, p=0.02; SpO₂ beta-coefficient=0.005, p=0.15). The explained variation for the models was: basic model R²=0.01; basic + TST R²=0.10; basic + % time SpO₂<90% R²=0.03; basic + TST + SpO₂ R²=0.20. None of the other saturation or sleep variables were significant when entered in the models.

Conclusion: Increases in TST, but not improvements in oxygenation, related to treatment of OSA with CPAP are associated with improvements in cognition in AD patients. This finding implies that the cognitive impairment associated with OSA in AD patients may not be a function of oxygenation but rather the effects of short sleep time and warrants further investigation.

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0292

SELF-REPORTED SLEEP QUALITY PREDICTS MORTALITY WITHIN ONE YEAR OF POST-ACUTE REHABILITATION AMONG OLDER PEOPLE

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Introduction: Our prior work has demonstrated that more daytime sleeping during an inpatient post-acute rehabilitation stay predicts less functional improvement among older people recovering from an acute health event, and this relationship persists for up to 6 months after enrollment. The present analyses extend our prior work, exploring whether self-reported sleep disturbance during rehabilitation predicts mortality within 1 year of admission to a post-acute rehabilitation facility.

Methods: This prospective, descriptive study enrolled 245 older adults on admission to two post-acute rehabilitation sites (one VA, one commu-

nity). Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI) performed once on admission (inquiring about sleep prior to the health event that precipitated hospitalization; i.e., pre-morbid PSQI) and again 7 days later (inquiring about sleep during the inpatient rehabilitation stay; i.e., inpatient PSQI). Participants were contacted for 3, 6, 9 and 12 month follow-ups, and for those who died, date of death was recorded. Inpatient (7-day) PSQI score was examined as a predictor of time to death in a multi-variable Cox survival model, controlling for pre-morbid PSQI, medical comorbidities (Cumulative Illness Rating Scale-Geriatrics; CIRSG), cognitive functioning (Mini-Mental State Examination; MMSE), depression (Geriatric Depression Scale-15; GDS-15), age and gender.

Results: For the entire sample, mean (SD) age was 81 (7) years, 38% were female, 80% were non-Hispanic white, and the mean length of rehabilitation stay was 21 (12) days. The mean pre-morbid PSQI was 5.2 (3.8) and the mean inpatient (7-day) PSQI was 8.3 (4.4). Mean CIRSG was 22.6 (5.8), mean MMSE was 24.1 (6.2), and mean GDS-15 was 4.1 (3.3). At 1 year, 57 participants (23%) were deceased. In the multi-variable model (X²=41.1, df=7, p<.001), inpatient PSQI (p=.008), CIRSG (p=.002), and MMSE (p=.002) remained significant independent predictors of time to death while pre-morbid PSQI (p=.99), gender (p=.08), age (p=.21) and GDS (p=.05) did not.

Conclusion: 1-year mortality rates are high and reported sleep disturbance during the rehabilitation stay is a significant predictor of mortality among older people admitted to inpatient post-acute rehabilitation. Interventions targeting sleep in the inpatient rehabilitation setting may reduce mortality risk among these vulnerable older people.

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0293

EFFECT OF EXOGENOUS MELATONIN ON EEG SPECTRAL ACTIVITY IN HEALTHY OLDER SUBJECTS

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Introduction: Exogenous melatonin given prior to sleep scheduled during the biological day decreases sleep latency and increases sleep efficiency. In young subjects, exogenous melatonin has also been shown to reduce EEG slow-wave activity and enhance EEG spindle frequency activity during daytime sleep. In the present study we examined the effects of exogenous melatonin on the EEG sleep spectra in older subjects.

Methods: 24 healthy subjects (13f, 11m; mean age 64.2; SD ± 6.3yrs) participated in a 32-day forced desynchrony study during which they were scheduled to a 20h sleep-wake cycle (13.3h wake, 6.7h sleep) for 30 cycles. Following 3 8-h baseline nights, each subject participated in both placebo and melatonin conditions, and was randomly assigned to receive melatonin for the first 12 cycles or the final 12 cycles. Half the subjects received 0.3 mg melatonin while the other half received 5.0 mg, and placebo/melatonin was given 30 min before lights out. Polysomnographic recordings were collected for each sleep episode, visually scored according to standard criteria, and subjected to spectral analysis.

Results: A total of 790 sleep episodes were analyzed and collapsed into 0.25 Hz bins. Compared to baseline nights, the placebo condition showed a significant increase (p<0.05) in the frequency range from 1-8, 10.5-11.25 and 15-16 Hz during NREM sleep. Melatonin showed a significant increase in the frequency range between 1.5-1.75, 2-2.25, 7.75-8, 11-11.25, 11.5-11.75, and 14.75-17 Hz compared to baseline nights, with no significant differences between the two melatonin doses (p>0.1). During the forced desynchrony, melatonin produced a significant decrease in spectral activity in the EEG frequency range between 0.75 and 7 Hz when compared with placebo (2-way tANOVA; p<0.05).

Conclusion: Exogenous melatonin of both doses exerted a similar reduction of EEG spectral activity in the lower frequency range during

NREM sleep in these older subjects, similar to what has been reported previously in young adults.

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0294

EXPERIMENTAL SUPPRESSION OF SLOW WAVE SLEEP IN HEALTHY YOUNG MEN IS ASSOCIATED WITH DECREASED GROWTH HORMONE SECRETION

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Introduction: In the course of normal aging, a marked reduction in slow wave sleep (SWS) and a decrease in growth hormone (GH) secretion occur with similar chronologies. However, it is not known whether the decrements in SWS contribute to the well-known decrease in GH secretion in late life. GH secretion is stimulated during sleep and, in men the majority of daily GH secretion occurs during early sleep in association with SWS. In the present study, we selectively suppressed SWS in healthy young men to the levels that occur in late life, and assessed the amounts of GH secretion.

Methods: Nine healthy lean men (mean age: 23±1 yrs) were studied under two conditions (baseline, SWS suppression) with controlled caloric intake and activity in a randomized crossover design. All subjects were normal sleepers and sleep disorders were ruled out by polysomnography. The baseline condition involved recording undisturbed sleep for two consecutive nights (B1, B2). In the SWS suppression condition, sleep was continuously monitored and acoustic stimuli (1000-2000Hz, 40-110dB) were administered during NREM sleep to suppress SWS for three consecutive nights (S1, S2, S3). Blood samples were collected at 15-30min intervals for 24-hr after the nights B2 and S2 for measurement of plasma GH levels. GH secretory rates were estimated from plasma levels using a deconvolution method. Significant pulses of GH secretion were identified using a computerized algorithm (Chronobiological Series Analyzer, Chicago, USA). The amount of GH secretion over 24-hr, nighttime and daytime was determined by summing the amounts secreted in each of the pulses during that time interval.

Results: The amount of SWS was markedly decreased (min; 90±14 on baseline vs 4±1 on S1, 8±2 on S2, 13±4 on S3; p<0.0001) despite no differences in total sleep time (min; 481±5 on baseline vs 465±6 on S1, 476±5 on S2, 467±6 on S3; p=0.14). SWS suppression as compared to baseline was associated with decreases in 24-hr (ng; 863±105 vs 668±95, p=0.05), nighttime (652±98 vs 424±106, p=0.04), and sleep onset (ng; 606±103 vs 363±108, p=0.04) GH secretion. There was no difference in daytime GH secretion (ng; 211±34 vs 244±58, p=0.48).

Conclusion: These findings provide the first evidence that selective suppression of SWS results in decreased GH secretion in healthy young men. Our data suggest that decrements in SWS that are typical of normal aging could play a role in the decline in GH secretion leading to decreased lean body mass and increased fat mass in later life.

0295

IMPACT OF SLEEP DEPRIVATION ON POSTURAL CONTROL IN YOUNG AND OLDER SUBJECTS

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Introduction: Falls increase with age and cause significant injuries in the older population. While a few studies suggest that sleep influences postural control, the impact of age-related changes in sleep mechanisms on postural control is still unknown. This study aimed to determine

whether age modulates the interactions between sleep deprivation (SD), attention, and postural control.

Methods: Eight young (24,8±1.9 y.) and nine older adults (64,4±4.0 y.) stood still on a force plate in two counterbalanced sleep conditions: after a night of sleep and after a night of total SD (25h of wakefulness). Two hours after wake time, center of pressure (CoP) displacements were measured in six postural conditions: eyes open (EO) and eyes closed (EC), while doing an interference task, a control task, or no task. Three-way ANOVAs (2 age groups * 2 sleep conditions * 6 postural conditions) were executed on anteroposterior CoP range and speed parameters.

Results: Only older subjects presented an increased CoP range after SD in the "EO - control task" condition and in all EC conditions (age*sleeppostural conditions*postural conditions interaction p<0.002; all contrasts p<0.05). SD increased CoP speed in the "EO - no task" condition and in all EC conditions for all subjects (sleeppostural condition interaction p<0.007; all contrast p<0.005).

Conclusion: SD increased CoP speed in both age groups. However, in older subjects, the CoP did not only move faster, but also shifted further away, suggesting an even higher risk of crossing postural stability boundaries. Importantly, while the effects of SD on CoP range seemed to depend on tasks and visual input, CoP speed reacted to SD even when visual information was available and no cognitive task was performed, revealing a direct impact of SD. These results suggest that SD may be a significant factor putting older people at higher risk of falling.

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0296

VARIABILITY IN CORTISOL AMONG THE AGING: RELATIONSHIP TO GOOD SLEEP AND CHRONIC STRESS

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Introduction: Variability in cortisol concentrations has been observed among the aging, including hypocortisolism and blunted diurnal variation (O'Hara, 2006). Contradictory findings are due to great inter-individual variability in cortisol production, as well as age-related cortisol changes that are often difficult to distinguish from changes linked to disturbed sleep or stressful conditions (Ferrari et al., 2007).

Methods: We provide initial descriptive data on the relationship among subjective sleep, indices of stress, and salivary cortisol concentrations in a 24-hour period (AUC) in two groups of "stressed" individuals: bereaved (BR) (N = 27, 71.6 ± 6.4 yrs, 76% female) and spousal caregivers (CG) of patients with dementia (N = 42, 73.5 ± 7.1 yrs; 74% female), and in a group of elders (HC) without significant sleep complaints or medical comorbidity (N = 49, 79.4 ± 3.2 yrs; 47% female). Data are from the baseline assessment during which participants completed sleep diaries, questionnaires (the Pittsburgh Sleep Quality Index, Hamilton Depression Scale, and Perceived Stress Scale), and provided five saliva samples (wake-up, wake-up + 30 minutes, 3pm, 8pm, and bedtime) using Salivettes.

Results: HC (M = 11278.9 ± 4117 µg/dl) had higher cortisol levels than either the BR (7794.6 ± 2804 µg/dl) or the CG (9513.5 ± 3365 µg/dl (F (3,117) = 9.0, p < .001). No association between depressive symptomatology or perceived stress and cortisol was observed (all groups p's > .05). Higher 24-hr cortisol values, only among the HC, were associated with shorter sleep latency (r = -.34, p < .05) and greater sleep efficiency (r = .39, p < .05), as well as fewer sleep complaints as assessed by the PSQI (r = -.42, p < .01).

Conclusion: These data suggest that older adults enduring a chronic stressor have blunted 24-hr levels of cortisol. Hypocortisolism may be causally related to disinhibition of inflammatory processes thereby increasing stress-related pathology. These data also suggest that "appropriate" cortisol secretion across a 24-hr period, and subsequent reduced

Category F—Aging

medical morbidity, may be facilitated by good sleep. A better understanding of these complex interactions is needed to identify sub-populations at risk of medical morbidity.

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0297

CARDIAC AUTONOMIC FUNCTION DURING DIFFERENT SLEEP STAGES IN THE ELDERLY: RESULTS FROM THE SLEEP HEART HEALTH STUDY

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Introduction: Different sleep stages are associated with different degrees of sympathetic and parasympathetic activity. Autonomic activity can be measured using heart rate variability (HRV). The relationship of HR (heart rate) and HRV to sleep stage in the elderly is unknown.

Methods: PSG (polysomnogram) ECGs were analyzed on a MARS 8000 Holter scanner (GE Medical Systems, Milwaukee, WI) using standard research Holter techniques in 116 participants from the Sleep Heart Health Study (SHHS) age 77 ± 4 yrs, with usable HRV data in every sleep stage. HR/HRV was calculated for every 2 min scored in the same stage and averaged by stage. S4 sleep was omitted because only 11 subjects had stage 4 data. A repeated-measures ANOVA compared HR/HRV by sleep stage. We also compared HRV by sleep stage between participants with and without severe sleep apnea (categorized as OAH cut at 20) using t-tests. SPSS 14 (SPSS, Chicago, IL) was used for statistical analyses. Results are shown as mean \pm SEM.

Results: Significant changes in at least some HR/HRV measures were seen for every sleep stage relative to the others. Unlike prior reports, HRs during REM (65 ± 1 bpm) were lower than during wake (69 ± 1 bpm), but HRV was not different. HRs were lowest in stage 2 (64 ± 1 bpm). Vagally-modulated HRV (rMSSD, the root mean square of successive differences in normal-to-normal interbeat intervals) was highest in stages 1, 2 and 3 (26 ± 2 - 27 ± 1) ms and not different between wake and REM (23 ± 1 ms for each). HRV was generally lowest in stage 3. For example, SDNN (the standard deviation of normal-to-normal interbeat intervals) was 30 ± 2 ms in stage 3, 37 ± 1 ms in wake, 35 ± 2 ms in stage 1, 37 ± 2 ms in stage 2 and 39 ± 2 ms in REM sleep. Only very low frequency power (VLF), which captures variations in heart rate at the same underlying frequency as apneas, was significantly higher with severe sleep apnea [stage 1 ($p=0.023$), stage 2 ($p<0.001$), and stage 3 ($p=0.02$)]. VLF differences were borderline for REM ($p=0.06$) and not significant during wake.

Conclusion: HR and HRV reflecting autonomic changes during different sleep stages persist in the elderly but may not follow previously-reported patterns in younger people. Except for VLF power, the presence of severe sleep apnea does not greatly affect the relationship or HRV and sleep stage in the elderly.

Support (optional): U01HL63463 and R0-1 HL62181 from the National Heart, Lung, and Blood Institute.

0298

HOW VARIABLE IS NAPPING BEHAVIOR IN OLDER ADULTS? WITHIN-PERSON VARIABILITY IN NAPPING IN OLDER ADULTS IN RELATION TO SLEEP

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Introduction: Individuals with insomnia have highly variable sleep patterns. Napping, a behavior associated with sleep in older adults, is highly variable in terms of nap duration. Compared to traditional between-person research, within-person variability refers to behavior changes within the individual. The examination of within-person variability has been described as “absolutely essential” for accurately capturing behaviors

within the individual (Nesselrode, 2002). Within-person variability has been studied across a variety of domains but has yet to be examined in sleep and napping. The present study examines between and within-persons variability in napping/sleep and the association between variability in napping and overall sleep.

Methods: 103 community-dwelling older adults ($M_{age}=72.81$, $SD=7.12$) wore an Actiwatch-L® (24hs/day) for 14 days and concurrently completed daily sleep diaries.

Results: Indices of between-person variability (Sample Standard Deviation-SD) and within-person variability (Individual Standard Deviation-ISD) were computed after de-trending the variables to control for systematic growth in the data. Individuals were found to vary at least 80% as much within-persons as they did between-persons in terms of objective WASO, TST, and subjective nap duration. For actigraphically-measured napping, individuals varied almost twice as much within-persons as they varied between-persons. Bivariate correlations indicated that longer actigraphically-measured nap duration was associated with less variable objective WASO ($r=.26$, $p<.05$). More consistent WASO was associated with decreased WASO on average ($r=.72$, $p<.01$).

Conclusion: Previously, within-person variability has been described as ‘noise’ or ‘error’. The current study shows that nap duration is so variable within-persons that, overall, an individual’s daily nap duration varies more day-to-day than it varies between-persons. While variability in napping does not appear to be associated with impaired sleep, longer naps are associated with decreased variability in night-to-night WASO. Decreased variability in WASO is associated with overall less WASO and consequently better sleep. Results have implications for traditional CBTi treatment recommendations regarding napping.

0299

THE RELATIONSHIP BETWEEN SENILE CATARACT AS DETERMINED BY THE LOCS (LENS OPACITIES CLASSIFICATION SYSTEM) III AND DURATION OF SLEEP, WAKE-UP TIME AND SLEEPING TIME

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Introduction: This study was undertaken to evaluate the relationship between cataract and the general aspects of sleep.

Methods: Clinical interview and ophthalmological examination was done on 96 patients. Severities of cataract in total (lenticular opacity) and nucleosclerosis (lenticular nucleosclerosis) were determined by the LOCS (Lens Opacities Classification System) III. Duration of sleep, wake-up time and sleeping time were evaluated by questionnaire. Epworth Sleepiness Scale and Hospital Anxiety-Depression Scale were performed. The relationship between duration of sleep, wake-up time and sleeping time were evaluated with the severity of total cataract and nucleosclerosis.

Results: Earlier sleeping and wake-up time was related to more severe cataract and nucleosclerosis, but only the relationship between sleeping time and nucleosclerosis was significant ($p=0.015$). Duration of sleep showed negative correlations with the severity of both cataract and nucleosclerosis but were not significant.

Conclusion: Earlier sleeping and wake-up time occurs with advancing nucleosclerosis. Stimulus by light of appropriate wavelength to the eye is necessary for the physiologic regulation of sleep.

0300

SLEEP AND CIRCADIAN RHYTHMS IN SPOUSALLY BEREAVED SENIORS

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Introduction: For most people, spousal bereavement is the most devastating life event that they will ever experience. It happens in the lives of more than 800,000 older Americans every year. Both laboratory and epidemiological studies have confirmed that sleep disruption is a major consequence of bereavement, with the latter showing bereavement to increase the risk of sleep disorders by 67-90%. One possible pathway to sleep disruption might be through circadian dysfunction in the bereaved, whose lives are often radically restructured by the loss of their spouse, and who are often depressed. There appear to be no studies simultaneously measuring both sleep and circadian rhythms in bereaved seniors.

Methods: A laboratory study of sleep and circadian rhythms was undertaken in 28 spousally bereaved seniors (24F, 4M, 60y+) at least 4mos. after the loss event. Measures taken included 2 nights of polysomnography, ~36h of continuous core body temperature monitoring, and 4 assessments of mood and alertness throughout a day. Preceding the laboratory study, 2-week diaries were completed, allowing the assessment of lifestyle regularity (SRM), and the timing of sleep. Also assessed was grief (TRIG), depression (HRSD), and sleep quality (PSQI).

Results: Grief was still present (TRIG≈60, HRSD≈9). Sleep was subjectively poor (PSQI=6.4), short (TST≈6h) and fairly inefficient (SE≈80%). There was a slight trend for higher grief to be associated with less time spent asleep ($\rho=-0.35$, $p=0.07$), and with reduced alertness at 20:00 ($\rho=-0.37$, $p=0.05$). However, the circadian temperature rhythm (Tmin=02:57, Trange=0.8°C) and timing of sleep (23:01-06:39) seemed very normal for this age group, although SRM was slightly reduced (SRM=3.7).

Conclusion: When studied at least 4mos. after the loss event, there appears to be some sleep disruption in widow(er)s. However, this disruption does not appear to be due to bereavement-related disruptions in the circadian system.

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0301

CHANGES IN SLEEP QUALITY OF COMMUNITY-DWELLING OLDER WOMEN OVER 10 YEARS

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Introduction: Sleep disruption is a significant problem affecting one in three older adults. Disrupted sleep is associated with anxiety, functional decline, poor self-rated health, and interference with normal daytime functioning. Over time sleep disruption has been associated with depression, injury, and premature death. The purpose of this study was to describe changes in sleep quality of older women over time and to determine whether health and well-being factors predict changes in sleep quality.

Methods: Participants were 115 community-dwelling elderly women (baseline mean age = 66.9, SD = 7.18) from the Later Life Resiliency Study (Kwan, Love, Ryff, & Essex, 2003). Measures of sleep quality (Pittsburgh Sleep Quality Index), health, and well-being were examined at baseline, 8, and 10 years. Growth mixture modeling was used to examine whether there were different sleep classes (trajectories) over time and whether health (subjective health, number of illnesses) and well-being (depression, anxiety, psychological well-being) factors predict class membership. Latent growth modeling was used to determine whether

changes in physical health or psychological health predict changes in sleep quality over time.

Results: Overall, older women experienced a reduction in sleep quality with age ($\beta=0.14$; SE=0.05; $p<.05$). Three classes of sleep quality were found (significant decrease in good sleep quality over time [$\beta=0.09$; SE=4.06; $p<.05$; $n=88$]; no change in sleep quality [$\beta=0.23$; SE=7.34; $p>.05$; $n=24$]; a significant reduction in already poor sleep quality [$\beta=0.61$; SE=10.61; $p<.05$; $n=4$]). Baseline depression, pain interference, number of illnesses, and several dimensions of psychological well-being predicted sleep class membership.

Conclusion: Community-dwelling older women experience differing trajectories of sleep quality with aging. Higher baseline depression, pain, and illness and lower baseline psychological well-being predicted reduced sleep quality with age. However, changes in health and well-being over time did not predict class membership.

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0302

AGE, GENDER AND TOPOGRAPHICAL DIFFERENCES IN SLEEP SPINDLES: RESULTS FROM AUTOMATIC DETECTION

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Introduction: Sleep spindles are waxing-and-waning 12-14 Hz rhythmic waves during NREM sleep. Their functional significance is debatable but they are associated with brain plasticity and sleep protection mechanisms. Older participants show lower number and duration of spindles. Surprisingly, little is known about interaction between age, gender and topography of spindles. We used an automatic algorithm to assess these relationships.

Methods: Eighty-seven healthy volunteers with no sleep disorders were separated in two groups: Young (22W, 26M; 23.3y ±2.4), and Middle-aged (21W, 18M; 51.9y ±4.6). Spindle detection was performed on artefact free sections of NREM sleep for Fp1, F3, C3, P3, and O1 (linked-ears), using a bandpass filter (-3 dB at 11.1 and 14.9 Hz), then thresholding the RMS values of the filtered signal at the 95th percentile. Three-way ANOVAs (Factors: Age groups, Gender, Derivations) were performed on spindle density (nb/min), duration and periodicity (number of seconds between two spindles within a spindle burst).

Results: Spindle density was lower in older compared to young participants and this effect was stronger in Fp1, F3, C3, and O1 than in P3 (age*derivation interaction, $p=.01$). Spindle duration was shorter in older compared to young participants in C3, P3 and O1 (age*derivation interaction, $p<.001$). Older participants showed shorter periodicity (6.9 vs. 7.4; age effect, $p=.01$). Women showed higher spindle density than men, but only in the frontal derivations (Fp1, F3; gender*derivation interaction, $p=.01$). No age*gender interactions were found.

Conclusion: These results suggest that the effects of aging and gender on sleep spindles vary over scalp topography. While age-related reduction in spindle density is more prominent in fronto-centro-parieto derivations, the decline in spindle duration is observed only at central and posterior derivations. Importantly, effects of aging on spindle characteristics did not differ between men and women, but women showed higher spindle density in frontal derivations. These results may help understanding brain mechanisms underlying age and gender effects on sleep.

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0303

EARLIER AND LATE COMPONENTS OF THE EVENT-RELATED POTENTIALS IN AGED PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: The earlier event-related (ERP) components (N1 and P2) are known to vary with initial orienting while the late components (N2 and P3) are associated with cognitive variables such as attention, decision making, expectancy and memory. Our aim was to characterise the cognitive impairment in aged patients with obstructive sleep apnea syndrome (OSAS) and to assess whether there was a correlation among ERP findings and polysomnographic (PSG) parameters.

Methods: 19 male patients aged 63-75 (68.2 ± 2.9 y) were evaluated and compared to 12 healthy male controls, matched by age and IMC. All of them were submitted to full night PSG studies. The ERP was performed around 9 AM, with the oddball paradigm. N1 and P2 latencies were measured after both standard and target tones (50-150ms and 125-230 post-stimulus respectively), while N2 and P3 latencies were measured after target tones only (175-400 and 250-500ms post-stimulus respectively).

Results: The PSG data of controls and OSAS patients were (mean \pm sd): apnea/hypopnea index (AHI): 4.82 ± 2.68 and 39.54 ± 4.13 ; number of arousals/hour: 13.3 ± 6.7 and 29.7 ± 14.8 . The ERPs of OSAS patients showed increased N2 and P3 latency values in relation to controls ($p < 0.01$ and $p < 0.001$, respectively). There was no significant difference in relation to earlier N1 and P2 components. There was a moderate correlation between the P3 latency and the number of arousals/hour ($r = 0.53$).

Conclusion: There were different effects in relation to earlier and late ERP components performed by OSAS patients. These results suggest that there was a preservation of initial orienting (no change in N1 and P2) and then an important reduction in resource allocation (affecting N2 and P3 latencies). The moderate correlation between the number of arousals/hour and the P3 latency may suggest that the sleep fragmentation and consequent sleepiness were linked to the cognitive deficits found here.

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0304

STRESS, DEPRESSION, ANXIETY AND WORRY IN MID-LIFE WOMEN: WHAT'S SLEEP GOT TO DO WITH IT?

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Introduction: Complaints of poor and non-restorative sleep increase during the menopausal transition yet little is known about their consequences. The present study evaluated the impact of sleep, including its day-to-day variability, on subsequent indices of stress, worry, anxiety and depression in a multi-ethnic sample of mid-life women. We hypothesized that poor and more variable sleep would be associated with elevated levels of subsequently measured stress, worry, anxiety and depression.

Methods: SWAN Sleep Study participants with at least 28 days of sleep diary and actigraphy data were included in these analyses ($n = 233$). Sleep quality and duration were measured by diary and sleep efficiency was assessed by actigraphy; means and standard deviations were calculated for each over the first 3/4 of the protocol. Stress, worry, anxiety and depression were assessed at the beginning and end of the protocol. Re-

gressions adjusted for each measure at baseline and age, race, study site and menopausal status.

Results: Higher mean sleep duration was associated with higher levels of anxiety ($p < .05$). Greater variability in sleep efficiency was associated with more severe nighttime worry ($p < .05$). Sleep was unrelated to stress and depression. Results apply to all three races.

Conclusion: In a multi-ethnic sample of mid-life women, daily measures of sleep duration and continuity correlated significantly with anxiety and nighttime worries measured one to two weeks later. The relationship between sleep duration and anxiety may bear on observed relationships among long sleep duration and adverse health outcomes including increased body mass and diabetes risk in mid-life women. Results linking variability in sleep efficiency to nighttime worry severity are consistent with the hypothesized role of worry in the maintenance of insomnia which is prevalent in mid-life women. Measures of variability may reveal important characteristics and potential consequences of sleep in mid-life women beyond those shown by mean values.

0305

SLEEP AND SUCCESSFUL AGING IN WOMEN OVER AGE 60

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Introduction: As sleep is often considered a "vital sign", we investigated the relationship between successful aging and various sleep variables. The definition used for successful aging was correlates of self-rated successful aging: independent living, positive adaptation, active engagement with life, mastery/growth, life satisfaction/well-being, freedom from disability, and absence of physical disease.

Methods: As part of a larger cross-sectional study of successful aging affiliated with the Women's Health Initiative (WHI), data from 2226 women age 60 or older were examined. The WHI Insomnia Rating Scale (WHI-IRS), a 10-item scale that assesses use of sleeping aids, daytime somnolence, napping, sleep latency, sleep maintenance insomnia, early morning awakening, snoring, overall perceived sleep quality, and sleep duration was assessed.

Results: 20.8% of the women were categorized as "successful agers." In logistic regression, lower scores on the WHI-IRS (i.e. less sleep disturbance) were predictive of being categorized as a successful ager ($p < 0.001$), and this relationship persisted even after controlling for depression scores on the Center for Epidemiologic Studies Depression Scale ($p = 0.02$). Items related to less daytime napping and fewer complaints of sleep maintenance insomnia best predicted successful aging. There was no direct relationship between use of sedative-hypnotics and successful aging. Specific individual criteria for successful aging that were most strongly predicted by sleep disturbance scores included: freedom from disability, life satisfaction, sense of mastery, and positive psychological adaptation. Increased severity of sleep disturbance also predicted lower self-rated "successful aging" and a greater difference between perceived and actual age, and this result again remained significant after controlling for depressive symptom severity.

Conclusion: The importance of normal sleep for healthy aging was reinforced by these findings, and the relationship between sleep and successful aging should be further investigated in future longitudinal studies.

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0306

UNDERSTANDING SUBJECTIVE DAYTIME FUNCTIONING ESTIMATES IN OLDER ADULTS ACCORDING TO SLEEP DURATION AND QUALITY

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Introduction: The use of subjective daytime functioning measures can aid in the understanding of sleep disorders, although the relationship with objective polysomnography (PSG) variables is not well defined. Interestingly, older adults often report lower scores on daytime functioning estimates, further complicating the interpretation with other sleep measures. This study attempts to look at the relationship between various subjective sleep estimates and PSG variables to better understand the relationship between older adults and daytime functioning estimates.

Methods: A total of 238 patients, ages 55-80 years old who presented to a Midwestern metropolitan sleep center for diagnostic PSG from November 2006-June 2007 participated in this study. Participants completed subjective sleep measures including the Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS), Clayton Daytime Functioning Scale (CDFS), and the Pittsburgh Sleep Quality Index (PSQI). Study criteria include no shift work, no prior sleep disorder diagnosis, and no split-night studies.

Results: A one-way ANOVA using a split median of habitual sleep duration revealed significant correlations ($p < .05$) with all subjective measures, but higher scores were observed on all measures in the group with less sleep duration. Comparing groups using a one-way ANOVA according to severity of arousal index (mild $< 15/hr$, moderate $15-30/hr$, severe $> 30/hr$) demonstrated a negative trend in subjective measures. However, the mild arousal index group had significantly lower sleep duration. Path analysis regression revealed that sleep duration fully mediates the significant predictive relationship between the CDFS and PSQI ($p < .001$), accounting for 55% of the variance.

Conclusion: Interpretation of the results could suggest that daytime functioning estimates are more sensitive to sleep duration rather than sleep quality, especially when compared with objective sleep measures. Underestimation due to habituation of symptoms must also be considered. Further work in understanding these relationships is needed as well as consideration of subjective sleep duration with daytime functioning scales when interpreting level of impairment.

0307

THE RELATIONSHIPS AMONG COGNITION, FUNCTIONAL PERFORMANCE, AND NIGHTTIME SLEEP IN NURSING HOME RESIDENTS WITH DEMENTIA

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Introduction: Symptoms of dementia are grouped into four areas: cognition, behavior, function, and affect. One behavioral symptom that may have additive adverse effects on cognition and function is sleep distur-

bance. The primary objective of this study was to examine the relationships among cognition, functional performance, and nighttime sleep in nursing home residents with dementia.

Methods: This descriptive correlational study ($n = 90$) measured cognition with the Mini Mental State Examination, functional performance with the Nursing Home Physical Performance Test and nighttime sleep with 2 nights of attended polysomnography.

Results: Improved cognition was associated with decreased total sleep time (TST) ($r = -0.21$, $p < 0.04$) and fewer awakenings ($r = -0.25$, $p < 0.02$). Improved functional performance was associated with improved cognition ($r = 0.68$, $p < 0.00$) and decreased TST ($r = -0.30$, $p < 0.00$). Awakenings were categorized by type (respiratory [55%], spontaneous [39%], bathroom [5%], and periodic limb movements [1%]). Further analysis determined that fewer respiratory awakenings and a higher SaO₂ nadir were associated with improved cognition ($r = -0.24$, $p < 0.03$; $r = 0.23$, $p < 0.04$). In this sample of persons with dementia 60.8% had an AHI > 5 , indicating a diagnosis of obstructive sleep apnea.

Conclusion: Cognition explained a significant amount of variation in functional performance in this sample and improved cognition was associated with fewer respiratory awakenings and higher SaO₂ nadir. In this sample, improved cognition and functional performance were associated with decreased TST. Although correlation does not establish causation, these results suggest the possibility that interventions to decrease respiratory awakenings and maintain SaO₂ have the potential to support cognition and functional performance.

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0308

FEASIBILITY STUDY: HOME REACTION TIMES IN PERSONS WITH ALZHEIMER'S DISEASE (PWAD)

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Introduction: Sleep contributes to optimal cognitive performance and in healthy people, we know that changes in cognitive performance reflect both circadian rhythm and sleep homeostasis. These patterns have been studied in the laboratory with healthy adults using repeated Psychomotor Vigilance Task (PVT) trials. Unfortunately, in PWAD, the unfamiliar laboratory may preclude optimal performance and produce erroneous results. Therefore, the purpose of this study was to explore the feasibility of obtaining repeated PVT trials in the home for PWAD. The research questions were: 1) Can laboratory controls (temperature, sound, light) be replicated in the home? 2) Where do PWAD perform PVT trials optimally?

Methods: This study involved two steps: 1) PWAD completed 12 PVT trials every two hours for two days in alternating sequence, one day in the laboratory and one in the home, 2) participants were surveyed to determine preferences.

Results: The sample consisted of five men and six women, average age 78.3. The average Mini Mental State Exam score was 18.2. There were no significant differences in temperature ($t = -0.11$, $p = -0.92$) or sound ($t = -0.12$, $p = 0.91$). There were significant differences in light ($t = -14.75$, $p < 0.01$). All participants were able to complete all trials. There were no significant differences in performance between the home and the laboratory (good reaction times [$t = -0.04$, $p = 0.73$], mean reaction time [$t = .017$, $p = .99$], total errors [$t = 0.45$, $p = 0.65$]). Further, 100% of participants voiced a preference for home testing.

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Conclusion: Home reaction time testing is feasible and laboratory controls can be maintained. There were significant differences between lighting in the two settings; this difference can be remedied with appropriate task lighting. Performance did not vary between settings and respecting participant preferences could positively influence participant recruitment.

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0309

SLEEP ARCHITECTURE IN PERIMENOPAUSAL AND POSTMENOPAUSAL WOMEN

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Introduction: Women often complain of disturbed sleep during the menopausal transition. However, using objective measures of sleep quality, most studies have found either no differences in sleep between peri- and postmenopausal women, or better sleep among postmenopausal compared to perimenopausal women.

Methods: As part of a longitudinal cohort study of sleep-disordered breathing in mid-life women, we performed full overnight home polysomnography on 60 peri- and postmenopausal women who were current or former residents of Philadelphia County. If subjects reported a menstrual period in the past 60 days, the sleep study was performed within 6 days of next onset of bleeding (i.e. early follicular phase). Subjects were classified as perimenopausal if they had ≥ 2 cycles with changes of ≥ 7 days in cycle length compared to the subject's baseline, and postmenopausal if they had greater than or equal to 12 months of amenorrhea. Sleep study data was manually scored by trained PSG technologists according to standards established by the American Academy of Sleep Medicine. The Wilcoxon rank sum test for unpaired nonparametric data was used to compare measurements of sleep architecture.

Results: We studied 38 peri- and 22 postmenopausal women. Although total sleep time (SD) [333(116) min v 383 (41.4), $p=0.20$] and sleep efficiency [80.6(18.3)% v 86.8 (7.8), $p=0.62$] were higher among postmenopausal than perimenopausal women, differences were not statistically significant. Differences in the latency to sleep onset [17.6 (40.5) min v 11.0(16.9), $p=0.70$], amount of delta [8.8(11.3) min v 14.0 (16.4), $p=0.40$] and REM sleep [60.4(32.1) min v 76.3 (23.9), $p=0.23$] between peri- and postmenopausal women were also not significant.

Conclusion: Peri- and postmenopausal women had similar sleep architecture measured by home overnight polysomnography. Our results concur with other studies of objective sleep quality in mid-life women. However, objective sleep measurements may not fully capture the subjective experience of good or poor sleep, which may be affected by menopausal symptoms such as hot flashes or depressive symptoms.

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0310

AGE DIFFERENCES IN STAGE 2 SPINDLE DENSITY, BUT NOT REM DENSITY

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Introduction: Previous studies have examined age differences in spindle density and REM density. It is difficult, however, to compare the magnitude of age differences for these two phasic events as few studies have examined them in the same participants. The purpose of this study was to examine age differences in spindle density and REM density in the same participants.

Methods: Participants included 22 young adults (17-25 yrs; 10 female) and 22 elderly adults (62-79 yrs; 12 female). In-home polysomnographic sleep recordings were performed on two consecutive nights; the data reported here are from the second night. Stage 2 spindles and REMs during REM sleep were counted visually. Independent t-tests were used to compare the two age groups on whole night spindle and REM density measures. Separate 2(Age: Young, Elderly) by 3(Thirds: First, Second, Last) mixed ANOVAs were used to determine whether there were age differences in the density of spindles and REMs across each third of the night.

Results: The density of Stage 2 sleep spindles was significantly lower in elderly participants ($M=1.96$; $SD=1.56$) than in young participants ($M=4.94$; $SD=2.06$), $t(42)=5.40$, $p<.001$. The difference in REM density between elderly ($M=13.22$; $SD=7.14$) and young participants ($M=13.12$; $SD=5.10$) was not significant, $t(42)=.05$, $p=.958$. There was a significant Age by Thirds interaction for spindle density, $F(2,84)=8.47$, $p=.002$. Although spindle density increased significantly across the night in young participants, $F(2,42)=4.68$, $p=.032$ it dropped significantly across the night in elderly participants, $F(2,42)=5.51$, $p=.009$. For REM density, only the main effect of Thirds approached significance, $F(2,84)=3.03$, $p=.062$, suggesting a slight increase across the night in both age groups.

Conclusion: Age differences in this study were much more pronounced for spindle density than for REM density. These results suggest that age differentially affects the brain areas involved in generating these two types of phasic events.

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0311

HEART RATE VARIABILITY DURING SLEEP: THE SLEEPScore STUDY

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Introduction: Disturbed sleep is a risk factor for cardiovascular disease (CVD) morbidity and mortality, yet little is known about the pathways that link sleep to CVD. We evaluated heart rate variability (HRV) during sleep and its association with psychological and physiological risk factors for CVD in mid-life men and women.

Methods: Participants for the SleepScore study were recruited from a larger community-based cohort study, HeartScore, which focuses on nontraditional risk factors for cardiovascular disease including brachial artery diameter (BAD), peripheral arterial tonometry (PAT), and nocturnal blood pressure (BP) dipping. Stress, depression and anxiety were evaluated in conjunction with in-home PSG. Quantitative HRV was computed from the Night 2 EKG records of 96 SleepScore participants (mean age 58 years, 51% female, 49% African-American). HRV and visually-scored sleep were linked in 2-minute epochs to generate measures of vagal (HF band) and sympathovagal (LF:HF ratio) tone during NREM sleep. Analyses adjusted for medications that affected HRV.

Results: Repeated measures ANCOVA revealed that vagal tone increased across the night during NREM sleep ($p < .001$). The opposite pattern was seen for sympathovagal tone. Higher perceived stress ratings were associated with decreased vagal tone during the first two sleep cycles ($r = -0.34$, $p < .001$) but were unrelated to vagal tone during the last two sleep cycles. More modest associations were observed for depression ($p's < .05$). Higher sympathovagal tone during NREM sleep was associated with greater BAD ($r = 0.33$, $p < .01$). HRV during NREM sleep was unrelated to hostility, PAT and BP dipping.

Conclusion: Vagal and sympathovagal tone change across successive NREM sleep cycles. Quantitative HRV profiles during sleep are linked to several key CVD risk factors including stress, depression and brachial artery diameter. More work is needed to evaluate the extent to which these relationships affect disease endpoints such as hypertension or myocardial infarction.

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0312

LATENCY TO STAGE 2 SLEEP INCREASES WITH BOTH PLMS FREQUENCY AND AGING IN A SLEEP DISORDERS CENTER PATIENT POPULATION

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Introduction: Sleep latency, Periodic Limb Movements in Sleep (PLMS), and arousals increase with age while deep sleep declines. The goals of this study were to determine 1) if similar changes occur in clinical populations and 2) if increased PLMS are associated with longer latency for stage 2 sleep (SL2).

Methods: Following IRB approval, this study examined 100 charts in each of four patient age groups: young (18-34 years), middle-age (35-54 years), old (55-74 years) and old-old (>75 years) that received polysomnograms from 2004-2007. Primary variables were stage 2 sleep latency (SL2), sleep efficiency, arousal index, deep sleep percent, PLMS index, and sleep apnea index.

Results: Age affected all variables. Means \pm S.D. from youngest to oldest groups while controlling for BMI and number of medications were: Stage 2 latency increased, 19 ± 18 minutes to 39 ± 40 minutes, $p < 0.001$; Sleep efficiency declined, $86\% \pm 10$ to $66\% \pm 17$, $p < 0.001$; Arousal Index increased, 31 ± 22 to 38 ± 22 , $p < 0.003$; Deep sleep% declined, 7.6 ± 7.7 to 1.1 ± 3.5 , $p < 0.001$; PLMS index increased, 10 ± 13 to 28 ± 41 , $p < 0.001$; Sleep apnea index increased, 18 ± 31 to 26 ± 26 , $p < 0.02$. For polysomnographic variables, SL2 more closely correlated with the PLMS index ($r = 0.29$, $p < 0.001$) than with other measures that might be expected to delay reaching stage 2 sleep, such as AHI ($r = -0.06$, ns) and arousal index ($r = 0.09$, ns). There was no significant correlation with SL2 for sex, pre-sleep pain score, BMI, time supine, and low oxygen saturation although the number of medications did correlate with SL2 ($r = 0.31$, $p = 0.01$).

Conclusion: Even in a sleep disturbed population, aging is associated with further deterioration of sleep. Additionally, patients with PLMS have longer latencies to stage 2 sleep.

Support (optional): Internal

0313

SLEEP AND HEALTH BEHAVIORS IN A MULTI-ETHNIC SAMPLE OF MIDLIFE WOMEN

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Introduction: Complaints of poor and non-restorative sleep increase during the menopausal transition. Little is known about the extent to which health behaviors impact sleep disturbances in mid-life women or the extent to which these differ in women from different racial groups. In the present study, we evaluated relationships among health behaviors and sleep in a multi-ethnic sample of mid-life women.

Methods: Participants were 358 midlife women (167 Caucasians, 133 African Americans, and 58 Chinese) enrolled in the Study of Women Across the Nation (SWAN) Sleep Study who had complete health behaviors and sleep data. Sleep was measured by in-home polysomnography (PSG) and self-report sleep quality (PSQI). Alcohol and caffeine use, smoking and exercise were measured with daily diaries. Smoking was not evaluated given its low prevalence in this sample. Linear regression adjusted for age, menopausal status, race and study site.

Results: Women who consumed moderate amounts of alcohol spent more time asleep (PSG) compared to women who did not consume alcohol. Similar to other studies, women who exercised reported better sleep quality (PSQI) compared to women who did not exercise. Additionally, results showed an association between race and alcohol consumption and race and exercise. Caucasians were more likely to consume alcohol and engage in exercise compared to African Americans and Chinese. However, racial/ethnic differences in alcohol consumption were not associated with racial/ethnic differences in time spent asleep. The low prevalence of alcohol consumption among African American and Chinese women in this sample may explain this finding. Conversely, racial/ethnic differences in exercise were associated with racial/ethnic differences in sleep quality.

Conclusion: Caucasian women engaged in health behaviors associated with more time spent asleep and better sleep quality. Factors contributing to racial/ethnic differences in these health behaviors are unknown. It is important to understand these differences in health behaviors in order to suggest lifestyle modifications that can promote better sleep in non-Caucasian groups.

0314

WITHIN-PERSON VARIATION IN SLEEP AND AFFECT IN SPOUSAL CAREGIVERS OF INDIVIDUALS WITH ALZHEIMER'S DISEASE

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Introduction: Sleep and affect are typically measured on a daily basis, but the data are frequently 'averaged' to reduce 'error.' However, studies now show that daily fluctuations in an individual's responses (within-person variation) provide unique, meaningful information that can be reliably distinguished from error (Hultsch et al. 2000). The present study examines within- and between-person variability in sleep and affect in older caregivers.

Methods: 30 participants (M=61.55years, SD=11.20) wore an Actiwatch-L® (24hs/day) for 7 days and concurrently completed sleep diaries and the PANAS-short. Sleep variables analyzed included: subjective total wake time(TWTS), objective total wake time(TWTO), and sleep misperception[(TWTS-TWTO)/TWTO*100].

Results: Variables were de-trended to control for systematic growth and then indices of between-person variability and within-person variability were calculated. Results revealed that within-person variability is a significant portion of the total variance measured. Specifically, caregivers varied at least 60% as much within-person as they did between-person in terms of affect, TWTs, TWTo, and sleep misperception. Bivariate correlations indicated that variability in sleep misperception was significantly associated with greater overall negative affect ($r = .50$, $p < .01$); otherwise, sleep was not related to affect. Not surprisingly, several sleep variables exhibited significant within- and between-person associations with each other [(TWTs/TWTo: within- $r = .63$, $p < .01$; between- $r = .60$, $p < .01$), (TWTs/sleep misperception: within- $r = .50$, $p < .01$; between- $r = .84$, $p < .01$)]. Positive and negative affect were significantly associated at the within-person level only ($r = .51$, $p < .01$).

Conclusion: This study indicates caregivers' sleep and affect vary more day-to-day within an individual than they do between-persons. Surprisingly, neither objective nor subjective nightly wake time was strongly

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related to affect either within- or between-persons. Interestingly, greater variability in the mismatch between subjective estimates of nightly wake time and actigraphic estimates was associated with increased negative affect. Results suggest interventions that decrease daily fluctuations in sleep perceptions may also reduce negative affect in caregivers, and vice versa. Future research examining the day-to-day sleep/affect relationship in caregivers is warranted.

0315

NIGHTLY SLEEP PATTERNS IN OLDER ADULTS: NIGHT-TO-NIGHT FLUCTUATIONS IN THE SLEEP OF OLDER GOOD-NONCOMPLAINING, GOOD-COMPLAINING, POOR-NONCOMPLAINING, POOR-COMPLAINING/INSOMNIA, AND CAREGIVERS

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Introduction: Experts have commented on the relevance of individual variability in sleep patterns for broadening our understanding of sleep (Espie, 1991). While night-to-night fluctuations in sleep have received some attention in the literature, the majority of research has focused on other aspects of sleep and then commented on the considerable intraindividual variability observed in the data. The present study quantified the amount of nightly inconsistency in the sleep of five distinct groups of older adults and examined the relationship between inconsistency in sleep and overall amount of sleep.

Methods: 151 community-dwelling older adults, categorized as good-noncomplaining, good-complaining, poor-noncomplaining, or poor-complaining/insomnia (McCrae et al., 2003) ($M=71.36$, $SD=7.18$) and 42 community-dwelling older adult caregivers ($M=65.71$, $SD=9.62$) wore an Actiwatch for 7 days and concurrently completed daily sleep diaries.

Results: Indices of between-person variability (Sample Standard Deviation) and within-person variability (Individual Standard Deviation) were computed (controlling for systematic growth). All individuals were found to be highly inconsistent sleepers, objectively and subjectively. Across the parameters of SOL, WASO, and TST good-noncomplaining displayed 28% - 179%, good-complaining displayed 39% - 154%, poor-noncomplaining displayed 77% - 130%, poor-complaining/insomnia displayed 71% - 108%, and caregivers displayed 73% - 113% of the amount of between-person variability within-persons. In all groups increased inconsistency in sleep was associated with poorer overall sleep.

Conclusion: The results suggest that characterizing individuals by their mean sleep may not provide the most accurate estimates of their behavior. Results suggest the need to systematically study how individuals' sleep varies from night-to-night. Averaging multiple nights of sleep to produce single indices of sleep parameters overlooks nightly variations and may result in erroneous findings. Results imply increasing consistency in sleep as a possible treatment avenue.

Support (optional): Research supported by NIH/NIA AG024459-01- (McCrae, PI).

0316

SLEEP DISTURBANCES, MOOD AND NOCTURIA IN COMMUNITY DWELLING ELDERERS IN THE US AND GERMANY

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Introduction: Sleep disordered breathing (SDB) is commonly associated with nocturia and declines in daytime functioning and affect. This study examined the association of SDB, nocturia, and mood in community-dwelling elders residing in Germany and the United States.

Methods: A sample of persons age ≥ 60 years ($N=1290$, male= 39%, 70.75 ± 10.47 years, age range 60-101) was recruited using random digit dialing phone calls to households in the US ($n=608$, male=35%) and Germany ($n=682$, male=42%). German and US sub-samples were matched by age. Subjects responded to a telephone survey that included sleep disturbance items (sleep duration, trouble falling asleep, trouble maintaining sleep), SDB symptoms (loud snoring, snorting/gasping, breathing stops), nocturia (frequency) and bladder function items (bladder emptying, frequency, delaying urination, weak stream, problem starting urination) and questions related to mood (bothered, poor concentration, depression, exertion, fearful, lonely, sad, inert, feeling disliked). Indexes were independently calculated for SDB symptoms, bladder symptoms, and mood disorder symptoms.

Results: Most elders (85.8%) had acceptable sleep durations (5-8 hours) and some degree of nocturia (0=22%, 1=22%, $\geq 2=56%$; mean=2.78 + 2.8). Over 20% reported an inability to return to sleep ($>$ once a week) after nocturnal voiding. While controlling for age, gender and financial situation, SDB symptoms had a significant impact on daytime mood ($F[15, 1047]=6.99$, $p<.0001$). Using a composite index of bladder symptoms, elders with more symptoms of SDB had more bladder symptoms ($F[15, 974]=4.13$, $p<.0001$) even when controlling for age and gender. In a similar analysis, SDB symptoms also predicted greater frequency of nocturia ($F[15, 1041]=2.03$, $p<.001$).

Conclusion: Even though age, gender and financial situation have an effect on mood, these data show that SDB plays an important role on symptoms of impaired mood. Likewise, SDB may also have an impact on the report of bladder symptoms and nocturia among elderly men and women.

0317

SLEEP QUALITY AND DEPRESSIVE SYMPTOMS IN DIVERSE MIDLIFE WOMEN: A LONGITUDINAL STUDY

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Introduction: The purpose is to describe changes in subjective sleep quality in relation to depressive symptoms and patterns over time in midlife women. Few studies have examined diverse women in the decade prior to menopause.

Methods: This secondary analysis of a longitudinal study (5 years) included 347 community-based regularly menstruating women between 40-50 years of age. Women were originally excluded if they were on hormones, antidepressants or had a hysterectomy. At 6 month intervals, Pittsburgh Sleep Quality Index (PSQI) assessed sleep quality and Center for Epidemiological Studies-Depression (CESD) scale was used to indicate frequency of depressive symptoms. Because of non-normal distributions, negative binomial regression models were used to predict PSQI scores over time.

Results: At baseline, the mean age was 43.5 ± 2.4 years. The 88 African Americans had higher PSQI scores (6.03 ± 3.43 , 48% scored greater than 5) compared to 160 European Americans (4.98 ± 2.67 , 32.5% scored greater than 5) and 95 Latina (5.68 ± 3.30 , 39% scored greater

than 5) ($F_{2,340} = 3.76, p = .024$). At baseline, body mass index (BMI) correlated with PSQI ($r = .228, p < .001$) and CESD ($r = .180, p = .001$). In the first negative binomial regression model, the significant predictors were income ($p = .003$) and ethnicity (African American vs. European American, $p = .026$). When CESD was added to the regression model, significant predictors of PSQI were ethnicity (African American vs. European American) [Incidence Rate Ratio (IRR) = 1.129, $p < .05$] and CESD [IRR = 1.020, $p < .001$]. Income was no longer significant. Additional covariates will be tested in a larger model over time.

Conclusion: When clinicians are assessing and treating women's sleep complaints, they should also assess for depressive symptoms. More research is needed about the temporal relationship between sleep quality and depressive symptoms in midlife women and the interactions of ethnicity and socioeconomic status as well as BMI and other health variables.

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0318

THE RELATIONSHIP OF SLEEP STAGES TO COGNITIVE PROCESSING IN OLDER ADULTS

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Introduction: There is a significant literature implicating sleep disturbance in cognitive functioning (Banks S. et al, 2007). Many studies find sleep deprivation causes impaired cognition and decreased attention in children and adults. Sleep in elderly adults is characterized by an increase in the number of sleep stage shifts, increase in the number of awakenings and a shift towards the sleep stages 1 and 2. (Normal Sleep, 2007) To date, few studies have examined the relationship of the different stages of sleep to cognitive function in later life. In the current study we aimed to examine this issue.

Methods: 110 community-dwelling older adults participated, aged 55 to 90 years, mean age 70.90 years, 64 females and 46 males participating. All participants were assessed with in-home full ambulatory polysomnography (PSG). Which measured the different stages of sleep; namely REM, Stage1, Stage2, Stage3 and Stage4. Participants were also administered a full neuropsychological test battery that tested four main cognitive domains: Memory with the Rey Auditory Verbal Learning Test immediate and delayed; Attention with The Symbol Digits Modality Test and The Stroop Color-Words Test; Visuo-spatial ability by The Judgment of Line Orientation Test; and Verbal Ability using the Boston Naming Test.

Results: A Multivariate analysis found a significant association between the percentage of time spent in Stage 3 and 4 sleep and performance on the measure of memory ($P < .02$) and attention ($P < .009$), after controlling for age. Older individuals who had a greater percent of Stage 3 sleep had significantly higher performance on the measure of attention. Although very few participants had Stage 4 sleep, those that did had significantly better performance on the measure of delayed recall, independent of age.

Conclusion: Independent of age, different stages of sleep appear to differentially impact cognitive function in older adults. Implications of these findings for the literature will be discussed.

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0319

RELIABILITY OF POLYSOMNOGRAPHY DATA IN ELDERLY WITH DEMENTIA

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Introduction: Randomized controlled trials of pharmacological and behavioral interventions to improve sleep in elders with dementia have often failed to show statistically and clinically significant improvements. High night-to-night variability in sleep, limb movements, and breathing of elders with dementia may partially account for these non-significant findings. The purpose of this study was to determine the estimated reliability of polysomnography (PSG)-derived sleep quality measures, the periodic limb movement index (PLMI), and the apnea-hypopnea index (AHI) across two nights.

Methods: Attended PSG, using standard methods, was carried out in the homes of persons with dementia for two consecutive nights. All non-rapid eye movement sleep (NREM) stages were collapsed into NREM. The measures on the two nights of data were examined by a random effects model (Stata: xtreg, maximum likelihood) program. The analyses allowed us to estimate the reliability of the PSG measurements using the Spearman-Brown estimations.

Results: There were 19 females and 41 males and their mean Mini-Mental State Examination Score was 20.02. Using a .70 cut-point for reliability, AHI, PLMI, and wake after sleep onset were reliable based on two nights. The Spearman-Brown indicated that 3 nights of PSG would be needed for total sleep time. Four nights of PSG would be needed for minutes NREM and REM. The variable sleep efficiency would need from 5 - 6 nights of PSG to reach the .70 cut-point for reliability. Sleep onset latency was totally unreliable.

Conclusion: Multiple nights of PSG are needed for reliable sleep quality data in persons with dementia. Wake after sleep onset, AHI, and PLMI are the most reliable variables.

Support (optional): Sources of support for this study included the Veterans Administration (VA NRI 01-077-1) and the John A. Hartford Foundation.

0320

POSSIBLE RESTLESS LEGS SYNDROME PREDICTS NIGHTTIME BEHAVIORAL DISTURBANCES IN ELDERLY WITH DEMENTIA

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Introduction: Nocturnal behavioral disturbances are prevalent among elders with dementia. We hypothesized that nighttime behavioral disturbances may be associated with obstructive sleep apnea syndrome, periodic limb movement disorder, and restless legs syndrome (RLS).

Methods: A sleep technician conducted two overnight attended polysomnography (PSG) studies in the homes of the 60 participants (41 males). Within one week, a trained research assistant (RA) observed participants continuously in their homes for 3 nights (19 hours) for nighttime behavioral disturbances using the Cohen-Mansfield Agitation Inventory. We used these observations to calculate behavioral disturbances per hour [Behavioral Disturbance Index (BDI)]. The RA also observed for specific RLS behaviors, such as rubbing the legs every 5 minutes. RA interrater reliability ranged from .90 - .95. One registered polysomnographic technologist, blinded to BDI, scored the overnight PSG studies. Since older adults with dementia often do not have the cognitive skills to answer the RLS diagnostic interview questions, 2 RLS experts independently rated each participant as possible RLS or no RLS based

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on the following data: 1) diagnoses and medications, 2) caffeine and alcohol intake, 3) chief sleep complaint (from caregiver and/or elder), 4) RLS diagnostic interview per caregiver, 5) polysomnography data including apnea-hypopnea index (AHI) and periodic limb movement index (PLMI), and 6) RA observations of RLS signs. The experts were blinded to the BDIs. The BDI was the dependent variable in zero-order and multiple regressions. Only significant zero-order r 's with the BDI criteria were used in the multiple regressions. Square-root adjustments substantially improved BDI normality; the AHI predictor required a log transformation.

Results: Mean age was 79.05 years (s.d. = 6.03) and mean Mini-Mental State Examination (MMSE) score was 20.02 (s.d. = 7.33). The most common behavioral disturbance was general restlessness. RLS, MMSE, and log AHI significantly predicted BDI ($R^2 = .31$, $N = 57$, $F(3,53) = 9.40$, $p = .000$). All three predictors were uniquely significant.

Conclusion: Possible RLS, a lower MMSE and a lower AHI were associated with objectively measured nighttime behavioral disturbances, such general restlessness and wandering, in elders with dementia. Valid objective diagnostic measures for RLS and effective treatment may reduce nighttime behavioral disturbances and improve quality of life of elders with dementia.

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0321

SLEEP HABITS, EMOTIONAL DISTURBANCE, AND ADHD IN HIGH SCHOOL FRESHMAN

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Introduction: The trend toward fewer hours of sleep among adolescents is accelerating and there is growing concern about the rise of academic, psychological, and behavioral problems during the high school transition. This study focuses on the relations between hours of sleep and academic performance, motivational states, emotional problems, and ADHD symptoms among high school freshman.

Methods: A total of 882 grade nine students provided information about their sleep habits and school grades and completed psychological and behavioral assessments from the Behavior Assessment System for Children, Second Edition (BASC-2) and the Children's Academic Intrinsic Motivation Inventory. A global indicator of emotional disturbance was computed from the BASC-2 subscales social stress, anxiety, depression, and sense of inadequacy. Elevated scores on this index (70 or above) "almost always signal the presence of serious emotional disturbance" (Reynolds and Kamphaus, 2004). An ADHD composite index was computed by combining the inattention and hyperactivity subscales. Scores exceeding 70 on this index indicate that the student is at risk for a diagnosis of ADHD. Linear and logistic regression analyses were used to test the degree of association between sleep hours and gpa, intrinsic motivation, emotional disturbance, and ADHD.

Results: Students reported sleeping, on average, 7.6 hours per school night with 48% reporting less than 8 hours. After controlling for gender and race/ethnicity, hours of sleep per school night were significantly positively associated with gpa and intrinsic motivation, and significantly negatively associated with clinically significant levels of emotional disturbance and ADHD. Each additional hour of sleep on school nights lowered the odds of scoring in the clinically significant range of emotional disturbance and ADHD by 25% and 34%, respectively.

Conclusion: Insufficient sleep among adolescents may not only contribute to lower grades and intrinsic motivation but may also increase the odds of serious levels of emotional and behavioral disturbance.

0322

SLEEP RESTRICTION FOR ONE WEEK REDUCES INSULIN SENSITIVITY MEASURED USING THE EUGLYCEMIC HYPERINSULINEMIC CLAMP TECHNIQUE

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Introduction: Sleep restriction appears to have adverse effects on glucose metabolism. The purpose of this study was to determine the effects of sleep restriction, with and without modafinil treatment, on insulin sensitivity.

Methods: Healthy, non-obese adult men 20-35 years of age (n=20, BMI 21-30 kg/m², fasting plasma glucose levels of 90±1 mg/dL) were studied in a randomized, double-blind, placebo-controlled clinical trial including an 12-day inpatient admission to a General Clinical Research Center. Subjects were scheduled to 10 hours/night of time in bed for one week while at home (pre-study) and for the first 3 inpatient nights ('sleep replete' baseline). Subjects were then limited to 5 hours/night of time in bed for 7 days ('sleep restriction'). Subjects were randomized to receive modafinil (300 mg/day; 200 mg at 0600, 100 mg at 1300 hrs) or placebo during the week of sleep restriction. Diet was controlled for micro- and macro-nutrient content and calories. Each subject underwent two euglycemic hyperinsulinemic clamps performed at the end of the sleep replete baseline, and after 7 days of sleep restriction. Regular human insulin was infused at 40 mU per meter² of body surface area per min for 3 hrs

with variable infusion of 20% dextrose to maintain blood glucose at 5.0 mmol/l. Insulin sensitivity (mg glucose/kg/minute) was calculated from the last hour of the procedure in (mg glucose)/(kg body weight)/(minute). Data was analyzed by non-parametric statistical tests and results reported as mean±SEM.

Results: Sleep restriction reduced insulin sensitivity from a baseline 7.4±0.8 mg/kg/min to 6.7±0.8 mg/kg/min with placebo (Wilcoxon P<0.05) and from 7.1±0.9 mg/kg/min to 6.1±0.7 mg/kg/min with modafinil. There was no difference in the change in insulin sensitivity with sleep restriction between placebo (-10±4%) and modafinil (-12±7%) treatments. The mean change in insulin sensitivity due to sleep restriction, compared to the sleep replete baseline, was -11±4% (P=0.002), across all subjects. Changes in insulin sensitivity could not be explained by changes in 24-hr urinary epinephrine or afternoon/evening salivary free cortisol levels.

Conclusion: Sleep restriction (5 hrs/night) for one week significantly reduces insulin sensitivity in non-obese, healthy men whereas treatment with modafinil during sleep restriction had no effect on insulin resistance. These data support the hypothesis that reduced sleep duration increases risk for obesity and diabetes by increasing insulin resistance.

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0323

TOPOGRAPHY OF THE EFFECTS OF A PER3 POLYMORPHISM ON ALPHA ACTIVITY IN REM SLEEP UNDER BASELINE AND RECOVERY CONDITIONS

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Introduction: EEG characteristics are among the most heritable traits in humans. We previously reported that individuals homozygous for the longer allele of a variable number tandem repeat (VNTR) polymorphism in PER3 have increased alpha activity during REM sleep under both baseline conditions and during recovery from acute sleep deprivation. Alpha activity during REM sleep is known to vary across EEG derivations and to be most pronounced in occipital derivations. We investigated whether this polymorphism affects the topographical distribution of alpha activity in REM sleep and compared its effects to those of sleep deprivation.

Methods: The dynamics of alpha activity in REM sleep were assessed in 24 healthy volunteers who were homozygous for either the long (PER35/5) or short allele (PER34/4) of a PER3 VNTR. Sleep EEG in frontal, central, parietal and occipital brain regions was recorded during baseline sleep and recovery sleep, after a 40h constant routine.

Results: During baseline sleep, PER35/5 participants displayed greater theta- alpha activity in all derivations. Thus EEG power density differed significantly between the two genotypes in frontal (7-12Hz, P<0.05), central (8-11Hz, P<0.05) parietal (8-10Hz, P<0.05) and occipital (9-10Hz, P<0.05) derivations. Repeated measures ANOVA revealed a significant interaction between genotype, derivation and frequency (P=0.02). A very similar pattern was seen during recovery sleep, although smaller differences were also present in slow wave and beta ranges. In contrast, sleep deprivation led to an increase in EEG activity in REM sleep over slow wave and theta activity ranges (Frontal: 2-4Hz; Central 2-5Hz; Parietal 2-7Hz and occipital 3-5Hz, P<0.05).

Conclusion: The polymorphism has a robust effect on EEG activity in REM sleep, which is most pronounced in alpha activity in occipital and parietal derivations which contrasts the effects of sleep deprivation and implies that the polymorphism affects aspects of the EEG that are separate from the effects of sleep homeostasis.

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0324

CUMULATIVE EFFECTS OF REPEATED SLEEP RESTRICTION ON THE METABOLIC PHENOTYPE OF RATS

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Introduction: A single episode of sleep restriction lasting 10 days has previously been shown to result in a negative energy balance in rats. The purpose of the present study was to investigate physiological adaptations in response to repeated sleep restriction over time. Changes in food intake and body weight were determined during six consecutive cycles of 10 days of sleep restriction followed by 2 days of sleep recovery over a 10-week period, as a first step in studying effects of sleep restriction on the metabolic phenotype.

Methods: Rats with electrodes for sleep recordings were housed in Bergmann-Rechtschaffen disk apparatuses. Sleep restriction (SR, N=10) for each of the six 10-day cycles was produced by applying a 6-sec ambulatory requirement according to a schedule previously shown to heavily fragment and reduce sleep by nearly 40%. Locomotor control (LC) rats (N=10) received the same ambulatory requirement of 26% of time, only scheduled in consolidated periods to permit uninterrupted sleep. Sleep recovery was allowed for 2 days after each of the six 10-day SR or LC periods. Weight and food intake were measured daily.

Results: Each SR cycle resulted in greater food intake and lower weight. During Cycle 6, the change from baseline peak 48-hr food intake was +311 (73.2 SD)% and the change in weight was -15 (6.3 SD)% in SR rats, compared with +160 (26 SD)% and +8.4 (5.8 SD)% for LC rats [t16=8.2 and t18=6.1, P<0.001]. The trajectories of food intake increases and weight losses in SR rats were arrested during recovery sleep periods. Two SR rats died during the 6th cycle, despite both having obtained partial sleep throughout and having consumed 50 to 235% of baseline food intake just 24 hr beforehand. All SR rats developed abnormalities of the skin and fur, and loss of fattiness in depots and connective tissue. LC rats remained healthy.

Conclusion: Short-term sleep restriction in humans and rats previously has been shown to result in, among other signs, decreased circulating leptin, a reliable marker of a negative energy balance. The present results show that the effects of repeated sleep restriction are cumulative and that severe consequences ensue if recovery sleep is insufficient. Consistent with restrictions of nutrition or hydration, chronic sleep restriction results in metabolic dysfunction and severe pathology. The progressiveness of the changes suggest that less persistent sleep restriction also undermines health and promotes disease.

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0325

SLEEP EXTENSION IMPROVES ALERTNESS AND PERFORMANCE DURING AND FOLLOWING 7 NIGHTS OF SUBSEQUENT SLEEP RESTRICTION

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Introduction: The effects of one week of sleep extension on performance and alertness during a subsequent week of sleep restriction, and during a 5-day post-restriction recovery period, were determined.

Methods: Eleven males and 13 females [mean (SD) age = 25 (6.5) years] were randomly assigned to either an Extended [10 hours time in bed (TIB)] (n = 12) or Habitual [mean (SD) = 7.09 (0.7)] (n = 12) sleep group for one week followed by one baseline, seven sleep restriction (3 hours TIB), and five recovery nights (8 hours TIB). Throughout baseline, restriction, and recovery, volunteers were administered the Psychomotor Vigilance Task (PVT), Maintenance of Wakefulness Test (MWT), and Stanford Sleepiness Scale (SSS) between 0800 and 1800. PVT speed (1/RT) and lapses (RTs > 500 ms), MWT latency (minutes

to 3 epochs stage 1), and SSS ratings were analyzed using mixed-model ANOVA and post-hoc t-tests (Bonferroni correction).

Results: Sleep latency was longer for Extended v. Habitual sleep groups (p < 0.05) on Day 1. During restriction, PVT performance and alertness declined in both groups, but declines were faster for the Habitual group (p < 0.05). During recovery, Extended group PVT performance was restored to baseline after the first recovery night, although alertness scores remained low. For the Habitual group, PVT performance failed to recover, although SSS and MWT scores were restored to baseline after 1-2 nights of recovery sleep.

Conclusion: One week of sleep extension improved resilience during subsequent sleep restriction, and facilitated recovery thereafter - showing that nightly sleep duration exerts long-term (days, weeks) effects. Neurobiological changes underlying these effects may relate to changes in adenosine receptor density as a function of nightly sleep duration.

0326

ACUTE SLEEP DEPRIVATION AUGMENTS COCAINE SEEKING AND TAKING IN RATS

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Introduction: Substance abuse is a major concern within the United States, compounded by the propensity of many addicted individuals to relapse. The clinical literature suggests sleep deprivation is a factor that can induce relapse in humans. Despite the prevalence of sleep deprivation in our society, the effect of this factor on relapse has received relatively little attention in the laboratory, and currently no animal model exists. The present study developed the first rodent model to begin to address this question.

Methods: Forty-two naïve male Sprague-Dawley rats were trained to self-administer cocaine and then were divided into two sub-populations: low drug-takers (n=20) and high drug-takers (n=22). Extinction training followed, and then the effects of sleep deprivation (0, 4, or 8 h) on drug-induced reinstatement and on the motivation to work for drug were tested.

Results: Interestingly, while acute sleep deprivation did relatively little to augment behavior in the highly motivated high drug-taking rats, it reliably elicited drug-seeking and drug-taking behaviors in the previously unresponsive low drug-taking group. Thus, acute sleep deprivation caused a decrease in inter-infusion interval (i.e., the amount of time between infusions became shorter), a decrease in load-up latency (i.e., the amount of time to self-administer the first five infusions became shorter), and an increase in goal-directed behavior (i.e., efforts were focused more exclusively upon the active than the inactive spout).

Conclusion: These data are the first to demonstrate a direct link between sleep deprivation and drug relapse and, in so doing, provide a new model to study the neural mechanisms by which sleep deprivation may facilitate the acquisition and reinstatement of drug-seeking behavior. In addition, these findings also have profound clinical implications, and may shed light on a heretofore unrecognized factor in the early transition from substance use to substance abuse.

0327

ROLE OF ALPHA-1-ADRENORECEPTORS IN REM SLEEP MODULATION DURING RECOVERY FROM TOTAL SLEEP DEPRIVATION AND ITS POSSIBLE THERAPEUTIC APPLICATION IN DEPRESSIVE ILLNESS

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Introduction: Sleep deprivation (SD) increases the expression of several types of genes in the brain, including those of neurotransmitter recep-

tors. But the physiological implication of synaptic receptor up-scaling after SD is not understood. Additionally, the central monoamine enhancing drugs and SD are currently used to cure depressive illness; but an increased rapid eye movement sleep (REMS) density during recovery after SD reflects a poor response to sleep-restriction mediated psychotherapy for depression. Here, we report that REMS is inhibited by inactivating alpha-1-adrenoreceptors during recovery sleep after 6 hour-SD; which could have possible therapeutic application in depressive illness.

Methods: Male Sprague-Dawley rats (n=5) were prepared for polysomnographic recordings. After recovery, the same animal was studied under seven groups (experiments adequately spaced-out): baseline, non-SD+vehicle, SD, non-SD+prazosin (lower/higher dosage) and SD+prazosin (lower/higher dosage). Sleep was recorded from 1PM - 7PM in baseline and non-SD groups. In SD groups, rats were sleep deprived from 7AM - 1PM and allowed to recover from 1PM - 7PM. Sleep was recorded continuously during these periods. Two different dosages of prazosin (2 mg/kg and 4 mg/kg) and vehicle were injected (i.p.) at the end of SD. Changes in sleep measures were compared statistically (one-way ANOVA, tukey posthoc test).

Results: Prazosin, an alpha-1-adrenoreceptor blocker, inhibited REMS dose dependently only during recovery after SD. The mean±S.E.M. of sleep measures in different groups were; baseline—NREMS: 46.70±3.93, REMS: 8.93±0.72, Wake: 44.36±4.40; non-SD+vehicle—NREMS: 47.04±1.98, REMS: 7.93±1.10, Wake: 45.01±2.00; SD—NREMS: 61.58±2.89**, REMS: 13.63±1.47*, Wake: 24.77±3.90**; non-SD+prazosin(2mg/kg)—NREMS: 53.82±6.54, REMS: 7.58±1.28, Wake: 38.60±6.25; SD+prazosin(2mg/kg)—NREMS: 63.63±6.60*, REMS: 4.15±1.27, Wake: 32.21±6.80; non-SD+prazosin(4mg/kg)—NREMS: 61.72±4.13*, REMS: 5.73±2.01, Wake: 32.55±5.31; SD+prazosin(4mg/kg)—NREMS: 70.37±4.53**, REMS: 2.23±1.22**, Wake: 28.13±4.46** (*= $p<0.05$; **= $p<0.01$).

Conclusion: Our results suggest the significance of alpha-1-adrenoreceptor modulation after SD, resulting in restricted appearance of REMS during recovery and its possible therapeutic use for depressive illness.

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0328

METYPAPONE AND CORTICOSTERONE DECREASE SLOW WAVE SLEEP IN PARADOXICAL SLEEP-DEPRIVED RATS

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Introduction: In order to evaluate the role of corticosterone on the sleep rebound induced by paradoxical sleep deprivation (PSD), rats were treated with corticosterone or with the corticosterone synthesis inhibitor, metypapone, throughout the 96h period of PSD.

Methods: Male Wistar rats were implanted with electrodes for recording of sleep-wake cycle during a baseline condition and 72h recovery period following a 96h of PSD. Corticosterone (5mg/kg; s.c.) or metypapone (100mg/kg; i.p.) were administered twice/day (at 7:00h and 19:00h + 1 injection at the end of PSD). Plasma concentrations of ACTH and corticosterone were assessed, together with sleep parameters and compared to appropriate control groups. Statistical analysis was performed by ANOVAs followed by Newman-Keuls tests.

Results: PSD+metypapone-treated animals did not present the corticosterone rise induced by PSD and their levels were very similar to control (CTL) animals, whereas ACTH levels were 9 fold higher than CTL ($p<0.0001$) and 4 fold higher than PSD+vehicle-treated rats ($p<0.0001$). On the contrary, PSD+corticosterone-treated rats exhibited plasma levels that were 82% higher than PSD+vehicle ($p<0.03$) and 304.39% higher than CTL group ($p<0.0001$). ACTH levels were 3.5 fold lower than CTL ($p<0.04$) and 8.7 lower than PSD-vehicle ($p<0.0001$) groups. Despite no alterations on paradoxical sleep, both treatments decreased slow wave sleep (low amplitude: PSD+metypapone: -22.81%; $p<0.01$; PSD+corticosterone: -40.34%; $p<0.0004$; and high amplitude:

PSD+metypapone: -37.43% ($p<0.0002$); PSD+corticosterone: -17.28%; ($p<0.02$), however the slow wave activity (1-4Hz) was increased in PSD+corticosterone (+72.46%; $p<0.01$), during the first 12h (lights on) of sleep recovery when compared to PSD+vehicle group.

Conclusion: These results indicate that the increase in the activity of the HPA axis impairs SWS homeostasis. By inhibiting corticosterone synthesis and, consequently, freeing the system from negative feedback, metypapone induced increased CRH release (reflected by elevated by ACTH levels), which impairs SWS. The treatment with high dose of corticosterone also modulates SWS recovery, probably via activation of GR subtype receptors.

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0329

INFLUENCE OF SLEEP DEPRIVATION AND RECOVERY SLEEP ON 24 HOUR ENERGY EXPENDITURE

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Introduction: A proposed function of sleep is that it contributes to energy homeostasis (e.g., by conserving energy), but little research has been done to study this proposed function of sleep in humans. The aim of this study was to determine the metabolic costs of missing one night of sleep and of recovery sleep on 24h energy expenditure.

Methods: Seven healthy participants (5 men, 2 women), aged 22.43±4.76 (Mean±SD), maintained an ~8h per night sleep schedule for one week at home and consumed an outpatient isocaloric diet for three days prior to an ~90h GCRC protocol. Following an 8h sleep disorders screening night, subjects lived in a whole room indirect calorimeter and were scheduled to a 16 h wakefulness:8 h sleep baseline, followed by 40h of total sleep deprivation and 8h recovery sleep. Subjects were studied under modified constant routine conditions of dim light (< 8lux) during scheduled wakefulness, constant ambient temperature, bedrest and polysomnographic recordings. Breakfast, lunch, dinner, snack, sleep and wake times were scheduled relative to habitual waketime as determined by at home actigraphy recordings.

Results: Twenty-four hour energy expenditure was significantly greater during the first 24h of sleep deprivation compared to the 16h wakefulness:8h sleep baseline ($p<0.05$); whereas, 24h energy expenditure was significantly lower during sleep deprivation hours awake 25-40 and 8h recovery sleep compared to baseline ($p<0.05$). The largest differences in energy expenditure between 24h days occurred at night.

Conclusion: Missing one night of sleep increases 24h energy expenditure, whereas recovery sleep decreases 24h energy expenditure indicating that alteration of sleep homeostasis influences energy use. Although energy expenditure during sleep has been reported to be lower compared to pre-sleep wakefulness, this is the first study to quantify the metabolic costs of staying awake all night and of recovery sleep following total sleep deprivation.

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0330

THE SLEEP-DEPRIVED BRAIN AT REST: A DOUBLE-DISSOCIATION IN ABNORMAL “DEFAULT-MODE” ACTIVITY

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Introduction: To date, the sleep-deprived brain has principally been characterized by examining dysfunction during cognitive-task performance. Far less attention has been afforded to the possibility that sleep deprivation may be as, if not more, accurately characterized on the basis of abnormal resting-state or “default-mode” brain activity. Here we examine whether one night of sleep deprivation disrupts the canonical signature of resting-state brain activity and connectivity.

Methods: Twenty-eight health young subjects were randomly assigned to either a sleep-control group or sleep-deprivation group (who remained awake for 35hr prior to scanning). The event-related fMRI session involved a picture-slide learning task, interspersed by fixation trials. Analysis focused on these baseline fixation periods, thereby mapping the resting-state of brain activation.

Results: With both groups combined, there was archetypal resting-state activity in the anterior cingulate (ACC), posterior cingulate (PCC), medial temporal and superior parietal cortex. However, when compared between groups, a remarkable double-dissociation emerged, with significantly stronger resting-state activation in the ACC in the sleep-control group, yet greater PCC activity in the deprived group; patterns that were predictive of subsequent memory performance. Indeed, activity in these regions alone discriminated sleep-deprived from sleep-control subjects with a 93% sensitivity and 92% specificity. Finally, connectivity analysis revealed that these ACC-PCC differences significantly altered resting-state connectivity networks between the two groups, most evident in sensory thalamic regions.

Conclusion: The state of sleep deprivation appears to be associated with dysfunctional alterations in the resting-state of brain activation, with doubly-dissociable changes in anterior versus posterior cingulate activity. Moreover, these different resting-state patterns were not only associated with subsequent behavioral performance, but also with marked alterations in ensuing neural connectivity, suggesting that such changes are functional, not epiphenomenal. Thus, the brain-state of sleep deprivation maybe as accurately characterized by impaired regulation of/disengagement from resting-state activity, as it is impaired on-task activity.

0331

EXPERIMENTAL SUPPRESSION OF SLOW WAVE SLEEP IS ASSOCIATED WITH INCREASED HUNGER AND DECREASED VIGOR AND MOOD

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Introduction: In the course of normal aging, a marked reduction in slow wave sleep (SWS) and an increased risk of weight gain occur during the transition from young adulthood to midlife. While there is epidemiologic and laboratory evidence to indicate that reduced sleep *duration* may increase the risk of obesity, it is not known whether reduced sleep *quality* could also have deleterious effects on appetite regulation. The present study examines the impact of 2 nights of SWS suppression without change in sleep duration on hunger, vigor and mood in young adults.

Methods: Thirteen healthy lean normal sleepers (mean age: 24+/-1 years; 4 women) were studied under two conditions (baseline, SWS suppression) with controlled caloric intake and activity in a randomized crossover design. The baseline condition involved recording undisturbed sleep for two consecutive nights (B1,B2). In the SWS suppression condition, sleep was continuously monitored and acoustic stimuli (1000-

2000Hz, 40-110dB) were administered during NREM sleep to suppress SWS for two consecutive nights (S1,S2). At the end of each condition, subjects completed 10-cm visual analog scales for hunger and vigor, and the Positive and Negative Affect Schedule (PANAS) for mood every 2 hours from 16:00 to 22:00.

Results: The amount of SWS was markedly decreased (min; 87+/-10 on baseline vs 6+/-1 on S1, 10+/-2 on S2, p<0.0001) despite no differences in total sleep time (min; 473+/-6 on baseline vs 465+/-4 on S1, 473+/-4 on S2; p=0.36). Two nights of SWS suppression, as compared to baseline, was associated with a 19% increase in hunger ratings (mean ± SEM, 5.1+/-0.5 vs 4.3+/-0.4; p=0.03), 22% decrease in vigor ratings (5.6+/-0.5 vs 7.2+/-0.3; p<0.0001), and 11% decrease in positive affect (2.3+/-0.2 vs 2.5+/-0.2; p=0.02). There was no change in negative affect (1.1+/-0.1 at baseline vs 1.1+/-0.1 after SWS suppression; p=0.90).

Conclusion: These findings provide the first evidence that suppression of SWS without a decrease in total sleep time is associated with increased hunger and, similar to sleep restriction, suggest that disruptions in sleep quality may also be involved in excessive food intake and weight gain. Our data also suggest that a reduction in SWS due to a disorder such as sleep-disordered breathing may result in increased daytime sleepiness and lower mood.

0332

EVALUATING WORKING MEMORY TASKS UNDER SLEEP DEPRIVATION CONDITIONS

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Introduction: Working memory is generally considered to be a basic underlying cognitive mechanism that permits higher order cognitive processing. The purpose of the current study was to determine whether short-term sleep deprivation had a differential effect on visual versus verbal working memory.

Methods: Twenty-five participants (age: 21.1 ± 2.6) completed a number of tasks under sleep deprivation conditions. Code Substitution was a visual working memory task requiring participants to match symbols with numbers. Participants first completed a practice session of the task and then completed 2 memory conditions: an immediate recall session and a delay recall session 8 minutes later. The Clemson Verbal Substitution Task was a verbal working memory task requiring participants to match 2 words. The Verbal Substitution task also consisted of a practice session, an immediate recall and a delay recall condition. Different versions of each task were administered four times during 30 hours of acute sleep deprivation.

Results: A 2x4 ANOVA was completed on percent accuracy on the two tasks across the four administrations (time). Percent accuracy on both tasks decreased significantly (p=.001) across time during the practice condition. Percent accuracy was significantly greater on Code Substitution than Verbal Substitution (p=.001) and decreased significantly on both tasks (p=.001) across time during the immediate recall condition. Percent accuracy was also significantly greater on Code Substitution than Verbal Substitution (p<.001) and decreased significantly on both tasks (p<.001) across time during the delay recall condition. The interaction (task*time) was not significant under any of the 3 testing conditions.

Conclusion: The current results suggest that sleep deprivation negatively affected verbal working memory more than visual working memory. These results suggest that acute sleep deprivation could have previously unrecognized effects in many of our current work environments where employees are frequently “knowledge workers” and are required to work with language on many levels to successfully complete their assigned tasks.

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0333

REGIONAL SLOW-WAVE SLEEP HOMEOSTASIS IN THE PIGEON (*COLUMBA LIVIA*)Lesku JA¹, Martinez-Gonzalez D¹, Wilzeck C², Rattenborg NC¹¹Sleep and Flight Group, Max Planck Institute for Ornithology, Seewiesen, Starnberg, Germany, ²Johann Wolfgang Goethe-Universität, Frankfurt, Germany

Introduction: The hallmark of mammalian slow-wave sleep (SWS) homeostasis is an increase in low-frequency EEG power density during SWS following extended periods of wakefulness. We recently demonstrated that birds also show a compensatory increase in SWS-related low-frequency power in response to sleep deprivation (Martinez-Gonzalez et al. JSR. In press). However, it is unclear if this increase can occur regionally in the avian brain as a function of prior use during wakefulness.

Methods: Seven adult homing pigeons (*Columba livia*) were housed individually on a 12L:12D photoperiod. Electrodes were implanted over the hyperpallium (i.e., visual Wulst) of each hemisphere. EEG and video were recorded for 48 hrs. The first 24 hrs served as a baseline; 4 hrs after lights-on on the second day, the birds were kept awake for 8 hrs. During sleep deprivation, the right eye was oriented towards a monitor showing video of wild birds and the left eye was occluded. Because each hyperpallium receives projections primarily from the contralateral eye, we predicted that the left hyperpallium would show a greater increase of SWS-related low-frequency power density relative to the right hyperpallium.

Results: As predicted, during the first 3 hrs of recovery, the increase in low-frequency (1.56 - 4.30 Hz) power density during SWS was significantly greater in the left hyperpallium when compared to the right hyperpallium (paired t-tests: $P < 0.05$). The time spent in SWS during this 3 hr period was not significantly different from baseline ($P > 0.40$).

Conclusion: We demonstrated previously that birds show a mammalian-like increase in SWS-related low-frequency power density following sleep deprivation. Here, we show that unilateral visual stimulation in birds sleep-deprived for 8 hrs results in an asymmetrical rebound in low-frequencies during SWS, with the increase being greatest in the visually stimulated hemisphere. These results indicate that, as in mammals, low-frequency power density during SWS is a function of regional brain use during prior wakefulness.

Support (optional): This study was supported by the Max Planck Society.

0334

PHENOTYPIC NEUROBEHAVIORAL RESPONSES TO SLEEP RESTRICTION: RELATIONSHIP TO COGNITIVE AND SUBJECTIVE MEASURES

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Introduction: Differential vulnerability to sleep loss assayed by neurobehavioral responses has recently been demonstrated in subjects undergoing sleep restriction. This study investigated the various relationships between our neurobehavioral PVT phenotype variable and standard cognitive and subjective measures in response to sleep restriction.

Methods: $N = 155$ healthy adults ($M = 29.9y \pm 7.0y$; 80 women) completed 2 baseline sleep nights (TIB=10h) followed by 5 sleep restriction nights (TIB=4h) in a laboratory under carefully controlled conditions. The 10-min Psychomotor Vigilance Test (PVT), Digit Symbol Substitution Task (DSST), Digit Span working memory capacity test (DS), Karolinska Sleepiness Scale (KSS), and “Fresh-Tired” visual analog scale (VAS) were administered every 2h during wakefulness on all days. Neurobehavioral phenotypic responses to sleep restriction were characterized using a mean difference PVT lapses/trial metric. This continuous metric is calculated as the mean deprivation lapses/trial (using

all deprivation bouts) – mean baseline lapses/trial (using all baseline bouts), whereby lapses were defined as > 500 ms response time. Difference scores were similarly calculated for DSST (total number correct), DS (forward and total number correct), KSS, and VAS. Spearman’s rho correlation coefficient analyses quantified the various relationships between measures.

Results: The DSST ($\rho = -0.51$, $p < 0.001$), and forward ($\rho = -0.26$, $p < 0.001$) and total correct ($\rho = -0.22$, $p = 0.006$) DS scores showed significant negative relationships to the difference lapses/trial phenotype. By contrast, KSS scores showed a significant positive relationship to the PVT phenotype ($\rho = 0.20$, $p = 0.01$); VAS fatigue scores were also positively correlated but did not reach significance ($\rho = 0.14$, $p = 0.08$).

Conclusion: Subjects most severely affected by sleep restriction as manifested in greater increases in lapses during PVT performance also had the greatest cognitive throughput (DSST) and memory capacity (DS) deficits in response to sleep restriction, and the greatest increases in sleepiness and fatigue self-rated scores. Psychometric properties, learning components and shared biology may all contribute to the observed relationships.

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0335

A PERIOD 3 POLYMORPHISM PREDICTS FMRI ASSESSED BRAIN RESPONSES FOLLOWING SLEEP LOSS

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Introduction: A variable number tandem repeat polymorphism in the clock gene PERIOD3 (PER3) is a genetic marker for inter-individual differences in effects of sleep loss. Individuals homozygous for the longer repeat (PER35/5), previously associated with morningness, are more susceptible than individuals homozygous for the shorter allele (PER34/4). It was hypothesized that the effects on cognitive decline during sleep loss are mediated through the polymorphism’s effects on sleep homeostasis, rather than on circadian phase. However, the brain bases of the effects of this polymorphism on cognitive performance are unknown.

Methods: Fifteen PER344 and 13 PER355 healthy individuals were recruited solely on the basis of their PER3 genotype. Brain responses to an auditory 3-back working memory task were recorded in 4 fMRI sessions during 2 separate visits. In each visit, they were recorded in the evening and the following morning. In one visit they slept in the laboratory between both sessions, while in the other, they remained awake (24h sleep deprivation). Sleep deprivation and sleep visits were counterbalanced within and between genotypes.

Results: Performance and fMRI results showed that subjects could perform the task in all 4 sessions and were affected by sleep deprivation. fMRI data revealed striking differences between PER34/4 and PER35/5 in the changes in brain responses observed after 24h of sleep deprivation, even though performance did not yet differ significantly between the genotypes. In PER34/4 activity increased in frontal and temporal cortices and in the thalamus, cerebellum, and parahippocampus. In contrast, PER35/5 exhibited marked deactivations in frontal, temporal, parietal and occipital cortices and no activations.

Conclusion: The ability to recruit higher cognitive prefrontal areas after extended wakefulness is maintained in PER34/4 but not in PER35/5 individuals. These data provide a brain basis for genetically determined inter-individual differences in susceptibility to sleep loss.

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0336

CHANGE IN NEURAL NETWORKS FOLLOWING TOTAL SLEEP DEPRIVATION AND RECOVERY SLEEP

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Introduction: We previously reported specific neural networks involved in verbal learning (including bilateral inferior frontal gyri and left superior and inferior parietal lobes) and showed that one night total sleep deprivation (TSD) alters the connections among regions within these networks. Here, we extend these a priori models across a second night of TSD and two recovery nights.

Methods: Thirty-three subjects (age=23.9±5.1yrs; 14F) performed both Easy and Hard versions of the verbal learning task during fMRI while well-rested (WR), after 36 and 62hrs TSD, and after each of 2 recovery nights (REC1, REC2). SEM using a χ^2 test and RMSEA was used to test the models. Δ RMSEA was used to examine the relative strength of each path within the models.

Results: For Easy words, the model significantly fit the data for each condition. The model fit the WR data the best, with decreased model fit for all TSD and REC conditions. For Hard words, the model significantly fit the data only during WR and 36hrs TSD, with WR model fitting better. The model did not fit after 62hrs TSD or either REC. Overall, compared to the WR condition, the relative strengths of various connections within the models changed and varied depending on the length of TSD and REC sleep.

Conclusion: Results confirm the influence of task difficulty on neural networks and show difficulty interacts with length of TSD and REC. For Easy words, we observed weakening of several connections but strengthening of (compensation in) intra-parietal connections after 36hrs TSD, weakening of the entire network after 62hrs TSD, partial return of connection strength after REC1, and return only to the 36hrs TSD pattern after REC2. For Hard words, we saw compensation in frontal-parietal connections after 36hrs TSD, but weakening in the network in all other conditions, suggesting the brain may use alternative networks when heavily taxed.

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0337

PROSTAGLANDIN E2 INCREASES DURING PROLONGED TOTAL SLEEP DEPRIVATION (TSD) AND IS ASSOCIATED WITH INCREASED SPONTANEOUS PAIN IN HEALTHY VOLUNTEERS

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Introduction: The development and augmentation of pain under conditions of insufficient sleep duration and quality is increasingly recognized, but it is still an open question which mechanisms are responsible for the pain-enhancing effect of sleep loss. Prostaglandins are critical mediators in sensitizing the pain system and are involved in the regulation of sleep-wake behavior. Thus, they may be excellent candidates in mediating sleep loss-induced pain. Here, we investigated whether pain developing throughout sleep deprivation is related to changes in prostaglandin E2 production.

Methods: Following two 8h-baseline nights of sleep, 31 healthy participants were randomly assigned to either 88 hours of TSD (N=20) or three nights of 8h-control sleep (23-07h; N=11). Starting on the 2nd baseline day, participants were equipped with intensive recording devices

to monitor blood pressure, temperature, EEG, and blood and urine were also collected. Computerized visual analog scales (VAS) were presented every 2 hours to assess emotional well-being and regional (e.g. headache, backpain) and generalized physical symptoms (e.g. body pain, physical discomfort). Single self-rated pain items were compiled to a global pain variable. Prostaglandin E2 (PGE2) was measured in 24h-urine samples at baseline and again for a 24h-period following 48 hours of sleep deprivation. Values were calculated as amount per 24h-urine output.

Results: Spontaneous pain increased throughout three days of TSD by 9%, compared to an increase of 2% in the 8h-sleep condition ($p<0.01$ for interaction effect), reaching significance after the first night of TSD ($p<0.01$), and dropping back to baseline values after recovery sleep of 12 hrs. The amount of subjective stress (N=13) increased by 14% in the TSD condition, compared to an increase of 8% in the sleep condition. After controlling for stress ratings, the pain response to TSD remains significant ($p<0.01$). Urinary PGE2 levels (N=11) increased from baseline to the third night of TSD from 1593±404 ng/day to 2528±571 ng/day (mean ±SEM) in 10 out of 11 participants ($p<0.005$). Sleep loss-induced increases in spontaneous pain were positively correlated with change in PGE2 levels ($R=0.63$, $p<0.03$).

Conclusion: The current preliminary findings support the hypothesis that the development of spontaneous pain in response to TSD is of inflammatory origin, involving a prostaglandin-mediated pathway. Analyses are underway to determine PGE2 levels in the remaining sleep-deprived and control participants.

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0338

DISTURBED SLEEP, PSYCHOLOGICAL DISTRESS, AND LIFE SATISFACTION IN A COLLEGE SAMPLE

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Introduction: Sleep disruption has been associated with a number of health and daytime functioning problems, especially among adolescents and young adults. College students, in particular, are notorious for poor sleep and there is growing concern that this may significantly impact the quality of their university experience and their overall life satisfaction. This study uses structural equation modeling (SEM) to test the hypothesis that sleep disruption increases psychological distress which, in turn, lowers life satisfaction.

Methods: A comprehensive health and psychological functioning questionnaire was administered to 240 undergraduates. Measures included questions concerning sleep disruption, 21 items from the Depression Anxiety Stress Scale (DASS-21), 7 items from the Rosenberg Self-Esteem scale, and 4 items from the Brief Multidimensional Students' Life Satisfaction Scale. First- and second-order confirmatory factor analyses were conducted to establish that the factor structures of the three DASS scales and the Self-Esteem scale were such that these scales both reflected separate facets of psychological distress and contributed to a higher-order distress factor in this group of college students. SEM procedures were used to test the proposed causal model.

Results: Three sleep discontinuity questions comprised a latent variable "Disturbed Sleep"; seven items each for depression, anxiety, stress, and low self-esteem comprised a latent variable "Psychological Distress"; four items reflecting satisfaction with social, academic, extracurricular, and overall university experiences comprised a latent variable "Life Satisfaction". Disturbed sleep was significantly related to increased psychological distress which, in turn, was significantly related to lower life satisfaction. The direct effect of disturbed sleep on life satisfaction was not significant, but the indirect effect of disturbed sleep (due to its effects on psychological distress) accounted for 45% of the variance in life satisfaction.

Conclusion: Sleep disruption is strongly related to life satisfaction among college students and this relation is mediated through sleep disruption's effect on psychological distress.

0339

EFFECTS OF SLEEP DEPRIVATION, SLEEP SATIATION, AND AD-LIBITUM SLEEP CONDITIONS ON DAYTIME SLEEP LATENCIES, DROWSINESS, AND VIGILANCE TASKS IN COLLEGE STUDENTS

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Introduction: Since individuals have varying total sleep time (TST), people with reduced TSTs are expected to have short daytime sleep latencies; conversely, individuals with increased TSTs are expected to have long daytime sleep latencies. Young adult subjects' objective and subjective TSTs, during ad-lib sleep (AL), partial sleep deprivation (SD), and sleep satiation (SS), were compared to their MSLT results. Further comparisons included subjects' TSTs to results of their sleepiness scales, daily sleep logs, peak drowsiness assessments, and vigilance tasks, plus subjects' sleepiness rated by observers.

Methods: 12 college students (7F,5M) were divided into 3 groups: AL, usual sleep-wake pattern; SD, a 2-h delayed bedtime, with usual morning time awakening (MTA); and SS, a 2-h advanced bedtime, with usual MTA. Subjects were separated into 3 teams, each consisting of 2 subject-blinded observer pairs. Stanford sleepiness scale (SSS) scores and activities were noted at 1/2-h intervals. Daily sleep amounts by sleep logs and actigraphy, sleep quality, alertness levels, and peak drowsiness times were recorded. Observers rated subjects using the SSS at 1/2-h intervals and recorded peak drowsiness times. After 3 nights in each condition, MSLT and vigilance tasks (4-Choice, SteerClear) were conducted.

Results: The MSLT latencies for subjects with shorter TSTs were longer than those for subjects with higher TSTs ($r = -0.85$). In general, subjects with the shortest TST had higher SSS scores in the SD condition vs. AL and SS, and these subjects reported peak drowsiness more frequently during SD. SSS scores by observers confirmed that the low AL TST subjects were most affected (i.e., highest SSS scores) during SD. SSS and MSLT results showed no time-of-day effects. No consistent patterns were detected in comparing the TST with SteerClear and 4-Choice results.

Conclusion: Subjects with less sleep had long MSLT sleep latencies. Further, subjects with the shortest TSTs for the AL condition had the shortest TSTs for the SD and SS conditions. Subjects with short AL TSTs were more sensitive (i.e., higher SSS scores) to less sleep and were drowsier throughout the day compared to other subjects with higher AL TSTs, perhaps indicating that these subjects with short TSTs had efficient sleep and less inherent reserve to compensate for added sleep loss. There were no meaningful relationships between time of day and drowsiness, and sleep amounts had no significant effect on vigilance as measured by the performance tasks.

0340

SLEEP ADEQUACY ASSOCIATED WITH MORE HEALTHFUL FOOD CHOICES AND POSITIVE WORKPLACE EXPERIENCE IN MOTOR FREIGHT WORKERS

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Introduction: Insufficient sleep in a laboratory setting has been associated with increased appetite, and in a population study, higher Body Mass Index (BMI). Other studies have linked sleep difficulties with job strain and negative workplace experiences. In this study, we test the hypothesis that adequate sleep in motor freight workers is linked to more healthful eating behaviors and mediates the effects of workplace experience.

Methods: The Gear Up for Health Study was designed to test a workplace intervention to promote tobacco use cessation and weight management using a social-contextual model to describe the roles that work experiences and job conditions play in shaping worker health behaviors. Data are from a baseline survey of International Brotherhood of Teamsters members employed at 8 trucking terminals affiliated with the Motor Freight Carriers Association. Eligible permanent employees worked ≥ 15 hrs/week as over-the-road truck drivers, pick-up and delivery truck drivers, dockworkers or a combination of these. Bi-variate and multi-variate regression models examine relationships between sociodemographic and social context characteristics and health, specifically, the relationships between work environment, sleep adequacy, and dietary choices.

Results: The sample ($n=542$; response rate of 78%) was 83% white, 49 ± 8 years, with BMI of 30 ± 5 kg/m². Job satisfaction was 87.5%, but 30% reported job strain (high demand, low control). 51% reported adequate sleep (often or very often get enough sleep to feel rested). In a first logistic regression model, no job strain (OR=0.57; 0.38,0.85; $p < 0.006$), and supervisor support (OR=0.91; 0.86,0.97; $p < 0.003$) were associated with higher odds of adequate sleep. In a second set of linear regression models for each of 3 healthful diet choices (Fruits and Vegetables servings/day, not french fries; Drinks With Added Sugar servings/day; Sugary Snacks servings/day), at least two of these more healthful eating choices were significantly associated with education (some college or more), age, and adequate sleep (all $p < 0.05$). Job strain, hours worked, supervisor support and job satisfaction were not significant predictors of food choices when adequate sleep was included in the model.

Conclusion: Adequate sleep is associated with more healthful food choices in this sample of motor-freight workers, and may mediate in part the effects of positive workplace experiences.

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0341

AUTOMATIC DETECTION OF CHANGES IN SPEECH CLARITY DURING SLEEP DEPRIVATION

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Introduction: There is a common perception that speech articulation becomes more "sloppy" under sleep deprivation conditions. To date, these impressions have been difficult to quantify in a time-efficient manner. We present an automated method for detecting abrupt changes in the speech spectrum that reflect important articulatory events, and thus

Category G—Sleep Deprivation

the degree to which speech is spoken clearly. We applied this method to speech recorded in a sleep deprivation protocol.

Methods: Participants were recorded reading aloud a standard 3-paragraph passage at intervals over a 28-hour period of sleep deprivation. The continuous acoustic signals (about 1.5 minutes of speech) from the first (FIRST) and last (LAST) sessions were submitted to our automated analysis method for detecting abrupt acoustic events, or landmarks (Stevens, 1991). A parallel analysis was performed on speech recorded by subjects using maximally intelligible (CLEAR) and typical (CONVERSATIONAL) speaking styles. While both CLEAR and CONVERSATIONAL styles of speech are intelligible under ordinary speaking conditions, CLEAR speech is more carefully articulated, and more intelligible, under challenging listening conditions.

Results: There was a strong and statistically significant difference between speech recorded by subjects in the FIRST and LAST conditions. These results resembled in kind differences found between CLEAR and CONVERSATIONAL speaking styles.

Conclusion: Subtle changes in speech production occur during sleep deprivation, and these changes follow well-established patterns of change in articulatory clarity and intelligibility. Detection of these changes via automatic procedure has the potential to improve monitoring of sleep-related changes in performance.

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0342

EFFECT OF SLEEP DEPRIVATION ON NEURAL ACTIVATION DURING LANGUAGE COMPREHENSION AND PRODUCTION

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Introduction: Sleep deprivation impairs a range of cognitive abilities but its effect on language ability is not commonly studied. Impairment on a Word Fluency task (word production, phonological similarity) following sleep deprivation has been reported (Harrison & Horne, 1997), but sentence-level language production and language comprehension following sleep deprivation have not been comparatively studied. We report results from a functional magnetic resonance imaging (fMRI) study of neural activation during word- and sentence-level, comprehension and production language tasks following sleep deprivation.

Methods: Eighteen healthy, right-handed, native North American English-speaking participants (8 male, 10 female, average age 25 years) completed a series of language tasks during fMRI in 2 conditions: 15 hours after sleep (NORMAL) and 39 hours after sleep (SLEEP DEPRIVED). fMRI scans were conducted between 9 p.m. and 10 p.m. The 16-minute series of language tasks was comprised of 4 serial 4-minute tasks: 1) word comprehension (word v. non-word discrimination; button press response), 2) sentence comprehension (grammatically correct v. incorrect sentence discrimination; button press response), 3) word production (generate words that begin with a seed letter; overt speech response), and 4) sentence production (generate sentences that include with a seed verb; overt speech response). All stimuli for language tasks were auditory.

Results: Button press responses during language comprehension were scored for accuracy, and overt speech responses during production were scored by count of generated items. Behavioral performance on the 4 language tasks was maintained between NORMAL and SLEEP DEPRIVED conditions. Neural activation showed expected decrease with

sleep deprivation during language comprehension and unexpected increase during language production.

Conclusion: These results are novel in the study of sleep deprivation effects on language and are further support for task specificity of changes in neural activation following sleep deprivation (e.g., Drummond et al., 2005).

0343

THE RELATIONSHIP BETWEEN BODY WEIGHT AND SLEEP DURATION AND QUALITY

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Introduction: The link between the rise of obesity and the decline of sleeping hours in modern societies suggests a potential role for sleep in weight regulation. Most epidemiological studies examining this question have focused on sleep duration without considering the potential role of sleep quality. The present study seeks to examine the relationship between weight and both sleep duration and quality.

Methods: Data were derived from a larger study examining the natural history of insomnia in a population-based sample of French-speaking residents of the province of Quebec. Participants were individuals with and without insomnia (870 adults, mean age = 43.7 years, 60% women) who completed questionnaires assessing sleep, physical and mental health, lifestyles habits, and demographics. Sleep duration was self-reported from a single item. Measures of insomnia and sleep quality were derived from the Insomnia Severity Index (ISI) and Pittsburgh Sleep Quality Index (PSQI). Body mass index (BMI) was calculated from self-reported height and weight. Participants were categorized into normal weight (BMI < 25; 53.9%), overweight (BMI ≥ 25 and < 30; 30.2%), and obese (BMI ≥ 30; 15.9%). These groups were then compared on sleep quality and duration variables.

Results: Mean self-reported sleep durations for normal weight, overweight, and obese individuals were 7.27 (SD = 1.24), 7.25 (SD = 1.16), and 7.14 (SD = 1.27) respectively. Mean ISI scores were 7.25 (SD = 5.6), 6.55 (SD = 5.37), and 7.47 (SD = 5.91) for the same three groups, respectively. Mean PSQI scores were 5.54 (SD = 3.33), 5.08 (SD = 3.2), and 5.67 (SD = 3.52) for the same three groups, respectively. There were no group differences on measures of sleep duration, sleep quality, or insomnia severity; however, when the analyses were conducted separately by age and gender groups, it was found that obese women, aged 35-50 years, slept significantly less than normal weight and overweight women of the same age.

Conclusion: These results, which are not entirely consistent with previous studies, suggest that the sleep and obesity relationship may be specific to certain age and gender subgroups.

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0344

RECOVERY SLEEP AFTER PARTIAL SLEEP DEPRIVATION: BENEFICIAL EFFECTS ON DAYTIME SLEEPINESS, PERFORMANCE AND IL-6 LEVELS

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Introduction: One week of modest sleep restriction (from 8h to 6h of sleep/night for 1 wk) impacts adversely sleepiness, performance and inflammatory cytokines. Many individuals in modern societies try to overcome these adverse effects by extending their sleep during non-work days, usually on weekends. The aim of this study was to assess objectively this common practice, i.e. two days of extended ("recovery") sleep following one week of sleep curtailment.

Methods: Ten young, healthy, normal sleepers, mean age \pm SE 24.9 \pm 1.3 years, were studied for 13 consecutive nights in the sleep laboratory. The first 4 nights served as baseline nights (8 h/night), followed by 6 nights of partial sleep restriction (6h/night), followed by 3 recovery nights (10h/night). Daytime sleepiness [Multiple Sleep Latency Test (MSLT)] and serial plasma cytokines' levels were measured on days 4 (baseline), 10 (after one week of sleep restriction) and 13 (after 2 nights of recovery sleep).

Results: Preliminary analysis showed that sleep latency in MSLT was significantly decreased after restriction, compared to baseline overall ($p=0.001$). Sleep latency improved significantly after recovery sleep, compared to restriction overall ($p<0.0001$). Also 24-hour plasma levels of IL-6 increased significantly during the sleep restriction period whereas they dropped to baseline after two nights of extended recovery sleep. (2.6pg/ml vs 3.2pg/ml vs 2.4pg/ml $p<0.05$).

Conclusion: Extended recovery sleep of two days reverses the impact of one work-week of mild sleep restriction on daytime sleepiness and fatigue and IL-6 secretion. These data suggest that IL-6 levels correspond to sleepiness/alertness in humans, following sleep restriction and recovery respectively. The common sleep pattern alternating weekday restriction/weekend recovery sleep may lead to intermittent low grade inflammation of which long-term sequelae are unknown.

0345

SLEEP, SLEEPINESS AND NEUROCOGNITION IN 12-HOUR NURSES: PRELIMINARY RESULTS

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Introduction: Shifts of 12 hours or more are common among ICU nurses, combined with a compressed workweek to maximize time off. Such schedules may cause fatigue-related decrements in nurses' attention, vigilance and executive functioning. Partial sleep deprivation and associated neurocognitive decline over successive workdays has been studied under laboratory conditions, but real-world studies of nurses performance are lacking. This paper presents early findings of a study examining achieved sleep, sleepiness, and neurocognitive performance in nurses over 3 successive 12-hour workdays.

Methods: We recruited a convenience sample of female RNs working 3 consecutive 12-hour shifts preceded by 2 days off. Sleep was measured by actigraphy, with alarms cueing input of the Karolinska Sleepiness Score every two hours during their work shift. Neurocognitive tests (Walter Reed PVT, ARES battery) were delivered post shift using a personal digital assistant. Nurses with a high prior probability of sleep apnea were excluded (Berlin Scale).

Results: 46 nurses were screened and 26 qualified for the study, with 65% of disqualifiers for elevated Berlin score. Twenty nurses completed the protocol. Mean age of those enrolled was 40.1 (24-57) years. Total sleep times (TST) were short, with 39% below 6 hours between shifts, and the shortest sleepers having sleep broken into segments. TST did not influence cognitive throughput during the first two shifts, but had a significant influence on the third consecutive 12-hour shift. Overall, sleepiness scores were low, showed circadian variation, and did not correlate with TST. Yet catch-up sleep was seen at the end of the work cycle. Data collection is ongoing and data will be provided incorporating additional results.

Conclusion: Sustained shifts with compressed schedules resulted in partial sleep deprivation over work days, with some decrements in neurocognition observed.

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IMPAIRED SLEEP, WORK SCHEDULE AND HOME DEMANDS IN NURSES

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Introduction: Work schedules that contain long shifts, mandatory overtime, and quick returns (work with <10 hours between shifts) can influence the quality and amount of sleep amount obtained. Excessive work demands also can produce slow unwinding, interfering with sleep quality. In addition, home demands can also interfere with obtaining needed rest. This study describes the association between work schedules and home demands on restless or insufficient sleep in a large population-based sample of registered nurses (RNs).

Methods: Data were analyzed from Wave 1 of a longitudinal survey of RNs (N= 2273). Work schedule variables included hours per day and per week, days per week, weekends/month, shift typically worked, quick returns, mandatory overtime, on-call, and circadian mismatch. Sleep was measured by two items: "My sleep was restless" and "I got less sleep than I thought I should" with responses dichotomized to 3 or more nights per week as the indicator. Respondents were also asked about home demands including time spent on childcare, dependent elderly care, and domestic chores. Bivariate odds were estimated for each work schedule item in relation to sleep.

Results: Restless sleep was predicted by workdays > 12 hours long (OR 1.56, 95% CI 1.11-2.19), quick returns (1.66, 1.03-2.69), and mandatory overtime at least weekly (1.63- 1.17-2.26). Insufficient sleep was predicted by nightshift (1.63, 1.17-2.27), weekend work (OR 1.33-1.46 by frequency) quick returns (OR 1.61 to 2.04 by frequency), mandatory overtime (1.49, 1.09-2.05), and circadian mismatch (OR 1.51, 1.22-1.87). Child and eldercare and household chores also interfered with sleep.

Conclusion: Sleep quality and amount were negatively influenced by adverse work schedules and additional home demands. These results have implications for both worker and patient safety, as sleep adequacy affects job performance.

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0347

DIFFERENTIAL EXPRESSION OF CLOCK-RELATED GENES IN THE CEREBRAL CORTEX OF INBRED MOUSE STRAINS IN RESPONSE TO SLEEP DEPRIVATION

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Introduction: Sleep deprivation (SD) results in increased electroencephalographic delta power during subsequent sleep and is associated with changes in the expression of circadian clock-related genes in the cerebral cortex (Cx). The rate of increase of non-rapid eye movement sleep delta power as a function of prior wake duration varies among inbred strains of mice. We sought to determine whether SD-dependent changes in clock gene expression parallel strain differences previously described at the EEG level.

Methods: Three different strains of mice that differ in the magnitude of the increase in delta power after SD (AKR, C57BL/6 and DBA/2; n=8/group) were subjected to enforced wakefulness of incremental durations (2, 4 or 6 h). At the end of SD (ZT6), animals were euthanized and the brain was dissected. Real-time RT-PCR was used to assess the expression of circadian clock genes (bmal1, clock, cry1, cry2, csnk1e, npas2, per1 and per2) in the Cx.

Category G—Sleep Deprivation

Results: Changes in expression of the transcripts encoding *bmal1*, *clock*, *cry1*, *cry2*, *csnk1ε* and *npas2* occurred in response to SD in a strain-specific manner. The expression of these genes subsequent to SD was proportional to the increase in delta power that occurs in inbred strains: the strain that exhibited the most robust electroencephalographic response to SD (AKR) exhibited the most dramatic increase in expression of *bmal1*, *clock*, *cry1*, *cry2*, *csnk1ε* and *npas2*, while the strain with the least robust electroencephalographic response to SD (DBA/2) exhibited either no change or a decrease in the expression of these genes. Expression of the *per1* and *per2* was rapidly elevated in all strains after 2 h of SD.

Conclusion: These data demonstrate a molecular concomitant to previously-described strain differences in the EEG effect of SD, and raise the possibility that genetic differences underlying clock gene expression may mediate electroencephalographic differences among these strains.

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0348

EXTENDED DRIVING IMPAIRS NOCTURNAL DRIVING PERFORMANCES

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Introduction: Though fatigue and sleepiness at the wheel are well-known risk factors for traffic accidents, many drivers combine extended driving and sleep deprivation. Fatigue-related accidents occur mainly at night but there is no experimental data available on the relationship between duration of driving and nocturnal accidental risk. We studied whether 2, 4 and 8 hours of nocturnal driving affect differently driving performance.

Methods: A cross-over study using a balanced repeated design was planned. Participants drove in 3 nocturnal driving sessions (3-5am, 1-5am and 9pm-5am) on an open highway. Fourteen young healthy men (mean age [± SD]=23.4 [±1.7] years) were recruited. Inappropriate line crossings (ILC) in the last hour of driving of each session (3-5am, 1-5am and 9pm-5am), sleep variables, self-perceived fatigue and sleepiness were analyzed.

Results: Compared to the 3-5am driving session, the incidence rate ratio of inappropriate line crossings increased by 2.6 (95% CI, 1.1 to 6.0; $P<.05$) in 1-5am driving session and by 4.0 (CI, 1.7 to 9.4; $P<.001$) in 9pm-5am driving session. Compared to the reference session (9-10pm), the incidence rate ratio of inappropriate line crossings were 6.0 (95% CI, 2.3 to 15.5; $P<.001$) in the 3-5am driving session, 15.4 (CI, 4.6 to 51.5; $P<.001$) in the 1-5am driving session and 24.3 (CI, 7.4 to 79.5; $P<.001$) in the 9pm-5am driving session. Self-rated fatigue and sleepiness scores were both correlated to driving impairment in the 1-5am and 9pm-5am driving sessions and increased significantly during the nocturnal driving sessions compared to the reference session.

Conclusion: At night, extended driving impacts on driving performances and therefore should be limited. Revision of driving regulations should take into account these new findings to reconsider the maximal nocturnal non stop driving duration.

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0349

RELATIONSHIP BETWEEN NEUROBEHAVIORAL ASSESSMENTS OF COGNITIVE PERFORMANCE AND SLEEPINESS AFTER SLEEP RESTRICTION

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Introduction: While it has been widely established that chronic sleep restriction adversely affects neurobehavioral performance and tests for sleepiness, the relationship among these measures has not been examined closely. Five tests that measure different cognitive and performance domains (vigilant attention, cognitive throughput, ability to resist sleep, and subjective sleepiness and fatigue) were examined in a sleep restriction protocol.

Methods: N=79 healthy subjects (30±6.6yrs; 47 males) participated in a laboratory-controlled sleep restriction protocol. Subjects underwent 2 nights of baseline sleep (10h TIB/night) followed by 5 nights of sleep restriction (4h TIB/night). Subjects completed the Psychomotor Vigilance Task (PVT; vigilant attention), the Digit Symbol Substitution Task (DSST; cognitive throughput), Profile of Mood States fatigue subscale (POMSf; subjective fatigue) and the Karolinska Sleepiness Scale (KSS; subjective sleepiness) every 2h during wakefulness, and a modified Maintenance of Wakefulness Test (MWT; ability to resist sleep) on the second baseline day (B2) and after the fifth night of sleep restriction (SR5). Change scores (SR5-B2) were calculated for each test and then Spearman correlations were calculated.

Results: MWT correlated weakly with KSS ($\rho=-0.19$, $p=0.03$), while PVT lapses correlated with DSST ($\rho=-0.32$, $p=0.001$), KSS ($\rho=0.39$, $p<0.001$), and POMSf ($\rho=0.29$, $p=0.002$). KSS and POMSf were highly correlated ($\rho=0.61$, $p<0.001$). All other relationships were not significant ($p>0.05$).

Conclusion: Subjective sleepiness (KSS) and fatigue (POMSf) and Cognitive Throughput (DSST) all co-varied with PVT lapses, while MWT (ability to resist sleep) only co-varied with subjective sleepiness (KSS). Some neurobehavioral assessments appear to measure distinctly separate domains (i.e. DSST vs. MWT). Therefore in order to accurately assess impairment due to sleep restriction it is important to use a wide range of assessments that cover several cognitive and performance domains.

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0350

'SLEEPINESS' AND 'FATIGUE': SEPARATED AT BIRTH?

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Introduction: High levels of sleepiness and fatigue are well-documented among postpartum mothers. However, the two constructs are often described interchangeably. The purpose of this study was to explore whether standard instruments used to measure 'Sleepiness' and 'Fatigue' identify these two constructs among sleep disturbed postpartum mothers.

Methods: As part of a larger study, mothers (N=24; 28.7 SD±4.7 years, 88% White, with 16.6 SD±2.5 years of education) completed objective and subjective outcome measures during postpartum weeks 8 through 16. The Psychomotor Vigilance Test (PVT) was completed once daily. The Epworth Sleepiness Scale (ESS), Stanford Sleepiness Scale (SSS), and 100-point Visual Analogue of Fatigue (VAF) scale were completed several times daily. Each measure was averaged across postpartum weeks 10 and 16 to correspond with administration of the Beck Depression Inventory-II (BDI-II), from which two items were used relating to loss-of-energy and tiredness-or-fatigue. Exploratory Factor Analysis with Principle Components Analysis for eigenvalues ≥ 1 was calculated.

Results: Postpartum mothers' average PVT reaction time was 422.7 msec (SE±20.6), they had 16.8% (SE±2.9) lapses and 20.9% (SE±4.2)

fast responses. SSS scores were 3.0 (SE±.18), total ESS scores were 8.7 (SE±.70), and VAF ratings were 53.1 (SE±2.5). BDI-II loss-of-energy score was .69 (SE±.12) and tiredness-or-fatigue score was .64 (SE±.11). Four components accounted for 75.8% of the total variance in the model. Component 1 (44.5%) ‘Sleep Propensity’ included the SSS, VAF, and four ESS items. Component 2 (14.5%) ‘Psychomotor Performance’ included PVT measurements. Component 3 (9.6%) ‘Dozing when Idle’ included the other four ESS items. Component 4 ‘BDI-II Items’ included the two BDI-II items.

Conclusion: Postpartum mothers had high PVT measures, mean ESS and SSS scores in the clinical range, and high variance on all measures. Among postpartum mothers, standard instruments used to measure the constructs of ‘Sleepiness’ and ‘Fatigue’ reveal four distinct components that account for a large proportion of variance.

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0351

ROBUSTNESS OF PARAMETERS IN A CIRCADIAN AND NEUROBEHAVIORAL PERFORMANCE AND ALERTNESS MODEL SUGGEST TRAIT-LIKE CHARACTERISTICS OF THE HOMEOSTATIC PROCESS

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Introduction: A wide range of inter-individual variability in measures of performance and alertness has been observed under conditions of sleep deprivation and sleep restriction. These inter-individual differences may involve both state characteristics that change in an individual depending on conditions and trait-like characteristics that are consistent across studies [Van Dongen et al., 2004]. Using the Circadian Neurobehavioral Performance and Alertness (CNPA) model [Jewett and Kronauer, 1999], we investigated inter-individual differences in parameter values of best-fit models for state- and trait-like characteristics.

Methods: The CNPA model includes both circadian and sleep homeostasis influences to predict neurobehavioral performance on a 0.0 to 1.0 scale relative to data from all subjects. The published model parameters are from grouped (all subjects) data. We used serial addition task data from 66 subjects [Jewett Ph.D. Thesis, Harvard 1997] scheduled to two constant routines (CRs), one occurring before an experimental ocular bright light exposure (CR1) and one after that exposure (CR2); these were a subset of the 147 subjects included in the group parameter calculations. The length of the CRs varied from 26 - 50 h. The relative circadian phase was expected to be different during CR2 than CR1 because of the experimental light exposure. We used a non-linear optimization procedure (MatLab 7.1) to fit parameters to each individual’s data. Five parameters of the model were fit: uC (upper asymptote of circadian amplitude), A (circadian scaling), Hac (circadian-homeostatic interaction), rHw (rate of homeostatic decline during wake) and uH (upper asymptote of homeostatic recovery). Paired t-tests were used to compare the model parameters estimated from CR1 and CR2.

Results: Results of paired t-tests revealed no significant differences between CR1 and CR2 in the parameter values of rHw ($p=0.07$) and uH ($p = 0.32$). Significant differences were found for uC, Hac, and A ($p < 0.001$ for all three parameters).

Conclusion: This analysis suggests that the parameters associated with the sleep homeostat in an individual may be stable across CRs and robust to changes associated with an experimental light intervention, and thus may represent trait-like characteristics. The circadian parameters differed significantly in CR1 and CR2, as would be expected in response to a light intervention, and therefore may represent state characteristics. Replication of these results with other data sets is in progress.

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0352

RELATIONSHIP BETWEEN SLEEP DURATION AND CARDIOVASCULAR DISEASE IN THE HUNGARIAN POPULATION

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Introduction: Sleep disorders are very prevalent in the general population and recent research has demonstrated that both short and long sleep are associated with increased risk of morbidity and mortality. We investigated the association between sleep duration and the prevalence of cardiovascular diseases.

Methods: Data were collected within a framework of a large-scale, cross-sectional survey of health behavior of the Hungarian population. (“Hungarostudy 2002”). The Hungarian National Population Register was used as the sampling frame and a clustered, stratified sampling procedure was employed. The study population represented 0.16% of the population over the age of 18 years according to age, sex and 150 sub-regions of the country. Interviews were carried out in the homes of 12,643 persons.

Results: Forty-five percent of the total study population were males. The average sleep time was 7.5±1.52 hours. Hypertension, myocardial infarction and stroke were reported by 25% [95% confidence interval: 24-25.5], 3% [CI:2.8-3.4] and 4% [CI:3.7-4.4] of the respondents, respectively. We categorized sleep duration into five categories: <5, 5-6, 6-7, 7-8 and >8 hours. The prevalence of hypertension and myocardial infarction was the lowest in people who slept 7 to 8 hours per day (23.6% [CI:21.9-25.4], 2.3% [CI:1.8-3.0], respectively) and the prevalence of stroke was the lowest in individuals who slept 6-8 hours per day: 2.9% [CI:2.3-3.7]. The prevalence of hypertension, myocardial infarction and stroke was the highest in short sleepers (less than 5 hours per day). In multivariate model after controlling for traditional risk factors hypertension, myocardial infarction and stroke was associated with sleep duration. Compared to individuals sleeping 7 to 8 hours per day short sleepers were at higher risk of having hypertension, myocardial infarction and stroke (odds ratio: 1.3 [CI:1.1-1.5], OR:2.1 [CI:1.5-2.9], OR:1.4 [CI:1.0-2.0] respectively).

Conclusion: The present study indicated that sleep loss is associated with an increased risk of cardiovascular disease and suggests that more than 8 hour of sleep increases the risk of myocardial infarction and stroke in the Hungarian population.

Support (optional): The authors would like to thank the other members of the “Hungarostudy 2002” team (Csilla Csoboth, György Gyukits, Katalin Hajdú, János Loke, Andrea Odor, János Réthelyi, Sándor Rózsa, Árpád Skrabski, Adrienne Stauder, András Székely, László Szucs) for their work and to the network of community nurses for the home interviews, and for the National Population Register for the sample selection. Funding: This study was supported by the NKFP 1/002/2001 project, by the United Nation Development Program (UNDP), project No HUN/00/002/A/01/99, and the National Research Fund (OTKA) projects No: T-32974 (2000), TS- 040889, T038409 (MN, IM) and TeT Foundation (2005/06, MN).

0353

RELATIONSHIP BETWEEN SLEEP DURATION AND DIABETES MELLITUS IN THE HUNGARIAN POPULATION

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Introduction: The prevalence of diabetes mellitus has increased dramatically over the past few decades. Both laboratory and epidemiological studies have shown that sleep deprivation is associated with impairments in glucose metabolism and increases the risk of developing diabetes mellitus. We assessed the association between sleep duration and the prevalence of diabetes mellitus in the Hungarian population.

Methods: Data were collected within a framework of a large-scale, cross-sectional survey of health behavior of the Hungarian population. (“Hungarostudy 2002”). We used the Hungarian National Population Register as the sampling frame and implemented a clustered, stratified sampling procedure. The study population represented 0.16% of the population over the age of 18 years according to age, sex and 150 sub-regions of the country. Interviews were carried out in the homes of 12,643 persons.

Results: Forty-five percent of the total study population were males. The average sleep time was 7.5+1.52 hours. Diabetes mellitus was reported by 6.2% [95% confidence interval: 5.8-6.6] of the respondents. We categorized sleep duration into five categories: <5, 5-6, 6-7, 7-8 and >8 hours. The prevalence of diabetes mellitus was lower in people who slept 6 to 7 hours per day in contrast to short (<5h) and long sleepers (>8h): 4.4% [CI:3.6-5.3] vs. 11.8% [CI:9.8-14.1] and 7% [CI:6.1-8.0] respectively. In multivariate model after controlling for age, gender, body mass index, level of education, self-assessed financial status and physical activity, we found that compared to individuals who slept 6 to 7 hours, short and long sleepers have a higher risk for the presence of diabetes mellitus (odds ratio:1.8 [CI:1.4-2.5], OR:1.6[CI:1.3-2.1] respectively).

Conclusion: The present study suggests that both sleep loss and too much sleep are associated with increased risk of diabetes mellitus in the Hungarian population.

Support (optional): The authors would like to thank the other members of the “Hungarostudy 2002” team (Csilla Csoboth, György Gyukits, Katalin Hajdú, János Loke, Andrea Odor, János Réthelyi, Sándor Rózsa, Árpád Skrabski, Adrienne Stauder, András Székely, László Szucs) for their work and to the network of community nurses for the home interviews, and for the National Population Register for the sample selection. Funding: This study was supported by the NKFP 1/002/2001 project, by the United Nation Development Program (UNDP), project No HUN/00/002/A/01/99, and the National Research Fund (OTKA) projects No: T-32974 (2000), TS- 040889, T038409 (MN, IM) and TeT Foundation (2005/06, MN).

0354

THE TEST-RETEST RELIABILITY OF AN OCULAR MEASURE OF DROWSINESS

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Introduction: A new method has been proposed for measuring drowsiness by infrared reflectance oculography (Optalert™, Sleep Diagnostics Pty Ltd, Melbourne, Australia) using a new scale, the Johns Drowsiness Scale (JDS). JDS scores (0-10) are based on a weighted combination of variables relating to eye and eyelid movements measured every minute.

The aim of this investigation was to measure the test-retest reliability of mean JDS scores at different levels of drowsiness.

Methods: 14 healthy volunteers (M/F=10/4, ages 21-32 yr) performed 15-min psychomotor vigilance tests (the Johns Test of Vigilance, JTV) twice within about 2 hr under three different conditions -a “not sleep-deprived” condition on one day, with tests at 1200 and 1400 hr after a normal night’s sleep, and two “sleep-deprived” conditions on another day after missing the previous night’s sleep, with tests at 0945 and 1130 hr, and again at 1440 and 1545 hr, ie after being awake for 27-33 hr. The order of days was randomized. The mean JDS score per JTV test was taken as the measure of drowsiness at the time. Between each pair of JTVs, subjects were mostly sitting and taking part in the same activities.

Results: Repeated measures ANOVA for mean JDS scores showed a significant effect of Condition (sleep deprivation) (F (2,39)=5.049, p=0.01), but not of Session (test-retest) (F(1,39)=0.980, p=0.33), or Condition-Session interaction (F(2,39)=0.863, p=0.43). A paired t-test between test and retest mean JDS scores, combining all 3 conditions, showed no significant difference (mean diff = 0.19 +/- 0.19 standard error, n = 42, p>0.3), and there was a high intraclass correlation (r = 0.80, n = 42, p<0.001).

Conclusion: The mean JDS score per 15-min JTV test increased after sleep deprivation and those scores were very reliable, at least in the short-term.

Support (optional): Research supported by Sleep Diagnostics Pty Ltd

0355

SLEEP RESTRICTION RESULTS IN INCREASED CONSUMPTION OF ENERGY FROM SNACKS

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Introduction: Short sleep is associated with obesity and may alter the regulation of hunger and appetite. Our goal was to determine if experimental bedtime curtailment will be accompanied by increased intake of energy from meals and snacks.

Methods: Eleven healthy volunteers (5/6 F/M; mean [SD] age 39 [5] y; BMI 26.5 [1.5] kg/m²) each completed two 14-day studies in random order at least 3 months apart. Studies were carried out in the laboratory with 5.5-h (restricted, R) or 8.5-h (control, C) bedtimes and ad lib food intake. We monitored caloric intake from meals and snacks (daily counts), total energy expenditure (doubly labeled water; n=10), body weight (scale), body composition (DXA), and sleep (polysomnography). Serum leptin and total ghrelin levels (Linco) were sampled every 30 min for 24 hours before and after each study.

Results: Total sleep times were 311 [7] and 433 [26] min with 5.5 and 8.5-h bedtimes (P<0.01) Meal intakes remained similar (R: 2611 [873] vs. C: 2536 [943] kcal/day, NS), but subjects consumed more energy from snacks during the 5.5-h bedtime period (1087 [541] vs. 866 [365] kcal/day; P=0.02). The carbohydrate content of ingested snacks also increased during the period of bedtime restriction (65[7] vs. 61[6]%; P=0.04). Total energy expenditure was comparable between the two sleep conditions (R: 2556 [556] vs. C: 2421 [375] kcal/day; NS). Both interventions were accompanied by a positive energy balance and comparable gains in body weight (R: 1.9 [1.6] vs. C: 2.1 [2.1] kg; NS) and adiposity (R: 1.7 [0.8] vs. C: 1.5 [1.0] kg; NS). Mean 24-h leptin levels increased (change after R: 2.6 [3.7] vs. C: 3.1 [4.5] ng/ml; NS) and reflected the final degree of adiposity of the subjects equally well (R: 0.57 [0.40] vs. C: 0.58 [0.51] ng/ml/kg body fat; NS) irrespective of the presence or absence of sleep loss. There were no detectable changes in ghrelin levels (n=9) during either of the two sleep conditions.

Conclusion: Bedtime restriction in an environment that promotes overeating and inactivity is accompanied by increased intake of calories from snacks. This behavior may contribute to the increased risk of

weight gain and obesity associated with short sleep hours. Since energy expenditure, leptin, and ghrelin levels were similar during both sleep conditions, alternative factors, such as longer exposure to an environment with unlimited access to food and changes in reward seeking and motivation, may underlie the increased consumption of snacks associated with recurrent bedtime curtailment.

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0356

AN OCULAR MEASURE OF DROWSINESS AND THE EEG: CHANGES WITH SLEEP DEPRIVATION

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Introduction: We have developed a new scale for measuring drowsiness, the Johns Drowsiness Scale (JDS), based on multiple characteristics of blinks as measured by infrared reflectance oculography (Optalert™, Sleep Diagnostics Pty Ltd, Melbourne, Australia). We aimed to investigate the relationship between JDS scores and EEG power, as they changed with sleep deprivation.

Methods: 19 volunteers had their drowsiness measured every minute while performing a 15 minute visual reaction-time test (JTV) in 3 conditions - first when alert after a normal night's sleep, second after 25 hrs of sleep deprivation, and third, after 29 hrs of sleep deprivation. EEG was recorded from several scalp sites but the results are presented for 02-A1. Following eye movement artifact rejection, power spectra were calculated by FFT for the remaining periods of 5117.5 msec (2048 samples) before each visual stimulus, presented at intervals of 5 to 15 seconds. Mean power density was calculated for alpha (8 - 12 Hz) and theta (4 - 7 Hz) frequency bins. Changes in EEG power were standardized as a percentage of each subject's power when alert. The mean JDS score during each JTV was used as the measure of drowsiness at the time.

Results: Standardized theta power was significantly correlated with the mean JDS score recorded during each test ($r = 0.40$, $n = 55$, $p < 0.01$). Standardized alpha power was not significantly related to JDS scores ($p > 0.1$). Nor was the absolute alpha or theta power correlated with JDS scores ($p > 0.1$).

Conclusion: As drowsiness and mean JDS scores increased so did EEG theta power, but only when differences in the EEG between subjects were removed. A relationship between theta power and drowsiness has been reported by others using different methods. Alpha power is not a reliable measure of drowsiness perhaps because it is heavily influenced by the eyes being open or closed at the time.

0357

COLLEGE STUDENTS' USE OF "ALL-NIGHTERS": GPA GROUP AND INDIVIDUAL DIFFERENCES ON MEASURES OF COGNITIVE PERFORMANCE

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Introduction: Previous research demonstrated that students who use single nights of total sleep deprivation (SN-TSD), or all-nighters, for studying have lower group grade point averages (GPA) than those who deny ever engaging in SN-TSD. However, some students who report frequent use of SN-TSD maintain high GPAs. This study was designed to examine if students differ in their ability to maintain performance after a SN-TSD by GPA group status.

Methods: Paid participants ($N = 12$) were recruited for using 3+SN-TSD per semester and high ($\geq 3.4/4.0$) or low ($\leq 2.8/4.0$) GPA. Participants

completed three iterations (afternoon baseline, 06:00 after SN-TSD, and recovery 3.5d later) of a cognitive battery tasking primarily memory, working memory, and response speed. Exclusion criteria included history of bipolar disorder; current treatment of depression or use of psychiatric medication; and history of head injury. Participants wore actigraphs for 10 days minimum, kept sleep diaries, and completed measures of morningness/eveningness (MEQ), mood (BDI-II), substance use, SN-TSD history, and sleep quality (PSQI).

Results: Groups did not differ in age ($20.3 \pm 1.0y$), gender (50%F), class year, MEQ (43.6 ± 7.8), BDI-II (11.0 ± 7.4), substance use (all used caffeine, mean #substances reported beyond caffeine = 3.4), average #SN-TSD/semester (8.6 ± 10.9), PSQI (8.1 ± 3.4), and self-reported total sleep time (TST, $5.8h \pm 1.4$). Self reported GPA was low: 2.6 ± 0.3 , high: 3.7 ± 0.2 ($F[1,10] = 44.2$, $p < 0.0001$). Repeated measures ANOVA indicated no significant cognitive battery performance differences between GPA groups, except during the second iteration of a digit symbol substitution task where the high GPA group performed better ($F[1,10] = 7.57$, $p < 0.03$). Pearson's r correlations revealed that more frequent use of SN-TSD was correlated with decreased sleep quality ($r = 0.76$, $p < 0.01$), shorter TST ($r = -0.60$, $p < 0.04$), and more substances used ($r = 0.76$, $p < 0.01$).

Conclusion: Due to individual variability in performance, almost no significant differences by GPA group were observed. Individuals displayed a maintained or improved level of performance on some tasks, while demonstrating decrements in performance on others. Trait variability or individual differences thought to underlie tolerance of sleep deprivation could explain why some Participants who use SN-TSD maintain excellent GPAs.

0358

PRIOR SLEEP EXTENSION FACILITATES LEARNING OF A MATHEMATICAL PROCESSING TASK DURING SLEEP RESTRICTION AND RECOVERY

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Introduction: Prior sleep history and chronic sleep restriction impairs performance on simple tasks (see Rupp et al., this volume). However, it is unclear how learning per se is affected. We used a mathematical processing task that shows practice effects to assess the effects of prior sleep history on task acquisition during sleep restriction and subsequent recovery.

Methods: Eleven males and 13 females [mean (SD) age = 25 (6.5) years] were assigned to either an Extended [10 hours time in bed (TIB)] ($n = 12$) or Habitual [Mean (SD) = 7.09 (0.7)] ($n = 12$) sleep group for one week followed by one baseline night, seven sleep restriction nights (3 hours TIB), and five recovery nights (8 hours TIB). Throughout baseline, restriction, and recovery, volunteers were administered a computerized mathematical processing task hourly each day (0800-1800). Throughput (speed * accuracy product) was analyzed (a) using a mixed model ANOVA with fixed effects for sleep group, day, and time of day followed by post-hoc t-tests (Bonferroni correction); and (b) by fitting slopes to performance data separately for each Sleep Group and for restriction versus recovery nights.

Results: During restriction, throughput improved for both groups (particularly across the first several days) but more so for the Extended group versus the Habitual group ($p < 0.05$). This pattern persisted into recovery, with the Extended group continuing to accrue larger gains in performance compared to the Habitual group.

Conclusion: Extending sleep amounts for one week prior to a sleep restriction challenge facilitated task acquisition during subsequent sleep restriction and recovery. Thus, prior sleep history impacts task acquisition. These effects persist into - and intensify during - subsequent recovery.

0359

BASELINE SLEEP PROPENSITY PREDICTS INDIVIDUAL DIFFERENCES IN PERFORMANCE DURING SUBSEQUENT SLEEP DEPRIVATION

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Introduction: There are substantial individual differences in sensitivity/resiliency to the effects of sleep deprivation. Likewise, mean sleep latency on the Multiple Sleep Latency Test (MSLT) can vary greatly, even among normal controls who have undergone two weeks of sleep extension. For the present study, it was hypothesized that normal controls with shorter baseline sleep latencies would exhibit poorer performance during subsequent total sleep deprivation.

Methods: For seven days before reporting to the laboratory, 15 participants (age range: 21-32 years old) obtained an amount of sleep that approximately met their reported daily need (verified by actigraphy). A nocturnal polysomnogram (eight hours time in bed) was followed by an MSLT and 36 hours of total sleep deprivation with a battery of performance tests administered every two hours. MSLT mean sleep latency (range: 0.50-16.7 minutes) was correlated with mean performance for each test across all administrations.

Results: There was a significant correlation with mean Psychomotor Vigilance Test 0.5-second lapses ($r(13) = -0.51, p < 0.05$). There was a marginally significant correlation with risk-taking behavior as measured by pumps on the Balloon Analog Risk Task ($r(13) = 0.43, p < 0.10$) and with short-term memory errors as measured by repeated moves (i.e., moves without a match) on the Memory Cards Test ($r(13) = -0.37, p < 0.10$).

Conclusion: The hypothesis of this study was supported: shorter sleep latencies were associated with poorer performance. Baseline MSLT mean sleep latency could prove useful as a screening tool for occupations involving sleep deprivation (given this variable shows high test-retest reliability across several months), and contribute to the development of an index that could be used to individualize sleep/performance prediction model parameters.

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0360

ALTERED EXPRESSION OF CERULOPLASMIN IN CAVERNOSAL TISSUE FROM PARADOXICALLY SLEEP DEPRIVED RATS

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Introduction: Paradoxical sleep deprivation (PSD) markedly promotes an increase of penile erection and influences sexual motivation in rats. Nitric oxide (NO) appears to play a role in the vasodilatation and relaxation of corpus cavernosum, which will ultimately lead to erection. It has been shown that Ceruloplasmin (Cp), a multi-copper oxidase, affects the NO homeostasis and nitrite synthesis, as well as vascular response. This study was designed to evaluate the mRNA expression of two Cp splice variants (CpGPI; membrane anchored and Cp serum) in cavernosal tissue from animals exposed to selective PSD.

Methods: Adult male Wistar rats were assigned into three groups (6-7/group): home-cage (control), PSD (96h) or rebound (24h). After the experimental period, the rats were killed for blood and tissue collection. Real time RT-PCR was performed on an ABI PRISM 7500 using the SYBR® Green I chemistry. The comparative CT method was used for

the relative quantification of expression with beta-actin as the house-keeping gene.

Results: The analyses demonstrated a similar increase in the expression of both Cp serum (1.7 fold) and Cp-GPI isoforms (1.8 fold) in sleep deprived rats for 96 hours. Moreover, the elevated mRNA expression returned toward control levels during the sleep recovery period in the rebound group.

Conclusion: The results suggest that the expression of Ceruloplasmin gene in cavernosum corpus of rats is influenced by sleep deprivation. Given the well-established association between PSD and increase penile erection, we speculate that Cp might influence normal erectile function through the modulation of bioavailability of NO.

Support (optional): AFIP, FAPESP (CEPID #98/14303-3 to ST and 06/58274-5 to T.A.F.A.).

0361

EFFECTS OF ACUTE AND CHRONIC SLEEP LOSS ON IMMUNE MODULATION OF RATS

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Introduction: Although sleep is now viewed by a significant body of researchers as being essential for the proper working of a host of defense systems, the consequences of lack of sleep on immune function remains to be fully comprehended. **OBJECTIVES:** To investigate how paradoxical sleep deprivation (PSD) for 24 and 96 hours and sleep restriction (SR) for 21 days by the multiple platform method, and their respective 24h recovery periods, affect immune activation in rats.

Methods: Adult male Wistar-Hannover were distributed into seven groups (N=10/group): a) Control, b) PSD 24 hours, c) PSD 24 hours with 24 hours of recovery, d) PSD 96 hours, e) PSD 96 hours with 24 hours of recovery, f) SR 21 days (18 hours of PSD followed by 6 hours of sleep per day), g) SR 21 days (18 hours of PSD followed by 6 hours of sleep per day) with 24 hours of recovery. After the sleep deprivation procedure, we assessed circulating white blood cell counts, lymphocyte count within immune organs as well as immunoglobulin (Ig) and complement production.

Results: PSD for 96h increased complement C3 and corticosterone concentration in relation to the control group. In contrast, the spleen weight, total leukocytes, and lymphocytes decreased during SR for 21 days when compared with the control group, although production of a certain class of immunoglobulin, the IgM, did increase. After recovery sleep, lymphocyte count in axillary lymph nodes grew when rats had rebound sleep after PSD for 24h, neutrophils increased after PSD96h and lymphocytes numbers were higher after SR21d.

Conclusion: Such alterations during sleep deprivation suggest only minor alterations of nonspecific immune parameters during acute PSD, and a significant impairment in cellular response during chronic SR.

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0362

SLEEP DEPRIVATION REDUCES LYMPHOCYTES IN NON-OBESE DIABETIC (NOD) MOUSE MODEL OF TYPE 1 DIABETES MELLITUS

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Introduction: Viewing sleep deprivation (SD) as a stressor this study aimed to assess whether loss of sleep would promote alterations in the number of lymphocytes in a Type 1 diabetes model (NOD) and to verify whether SD would exert distinct influence on female and male subjects of that strain in relation to Swiss strain.

Methods: Adult male and female Swiss and NOD mice were distributed in control (CTRL) and SD groups, according to gender and strain. The

groups were subjected to SD for 24 and 96h using the multiple platform method (placing five mice inside cages containing 14 circular platforms with water up to 1 cm of their upper surface) or maintained in their home-cages (control groups).

Results: SD for 96h significantly reduced lymphocytes in male Swiss in relation to control (4.1 ± 0.7 vs. 8.6 ± 2.1 , $p < 0.02$). In NOD, 24h and 96h SD caused a significant decrease of 65% (1.6 ± 0.5 vs. 4.4 ± 0.3 , $p < 0.001$) and 79.5% (0.9 ± 0.1 vs. 4.4 ± 0.3 , $p < 0.00001$) of lymphocytes respectively compared to control. Lymphopenia was also observed in the male NOD strain in relation to Swiss at the same time-points of both SD groups (PS24h: 1.6 ± 0.5 vs. 7.1 ± 1.0 , $p < 0.001$; PS96h: 0.9 ± 0.1 vs. 4.1 ± 0.7 , $p < 0.001$). In female Swiss, SD24h (4.5 ± 0.5 vs. 7.5 ± 0.5 , $p < 0.001$) and 96h (4.4 ± 0.6 vs. 7.5 ± 0.5 , $p < 0.001$) and in NOD, SD24h (1.8 ± 0.2 vs. 4.0 ± 0.6 , $p < 0.01$) and 96h (1.2 ± 0.4 vs. 4.0 ± 0.6 , $p < 0.01$), both, induced a significant reduction in the number of lymphocytes in relation to respective controls.

Conclusion: Since lymphopenia may facilitate the destructive process that characterizes autoimmunity and that the NOD strain proved to be more susceptible to SD than Swiss strain, our results suggest that SD should be considered a risk factor in the onset of autoimmune disorders.

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0363

THE EFFECTS OF COCAINE, METHAMPHETAMINE AND MODAFINIL CHALLENGE ON SLEEP REBOUND AFTER PARADOXICAL SLEEP DEPRIVATION IN RATS

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Introduction: The problems most frequently reported by psychostimulant users are sleep disturbances. Since substances that increase the release of dopamine are commonly used as psychostimulants and paradoxical sleep deprivation (PSD) plays a crucial role in the dopaminergic system. Compare the sleep patterns in rats challenged with cocaine, methamphetamine or modafinil subsequent to a 96h of PSD.

Methods: To record cortical electrocorticogram in adult Wistar rats two pair of screw electrodes were placed through the skull. Subsequent to the recovery period of the surgery, the animals were distributed into home-cage or 96h PSD group. The PSD method consists of placing animals inside a tiled tank filled with water to within 1 cm of the upper surface of the platform. Subsequent to this period, the rats were challenged with: saline, cocaine (7mg/kg, i.p.), methamphetamine (7mg/kg, i.p.) or modafinil (100mg/kg, i.p.). Electrophysiological signals were recorded during 48 hours.

Results: Home-cage rats injected with modafinil and methamphetamine showed a reduction in slow wave sleep (SWS) compared with the saline group. Cocaine was the psychostimulant that led to the lesser alterations in the sleep pattern in relation to those observed in the saline group. Methamphetamine reduced paradoxical sleep (PS), SWS and sleep efficiency after PSD when compared with their respective saline groups. PSD rats injected with psychostimulants presented lower percentages of PS when compared to those injected with saline. As for SWS, rats injected psychostimulants after PSD presented a rebound on the second night after the injection when compared to PSD rats injected with saline.

Conclusion: The association of these psychostimulants with a PSD paradigm aggravates their impact on sleep and different pharmacological profiles of psychostimulants lead to sleep rebound after PSD. Our data suggest that its function is to enhance sleep recovery by restoring the physiological and functional concentrations of catecholaminergic neurons.

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0364

RATS EXPERIENCE SLEEPINESS DURING CHRONIC SLEEP RESTRICTION

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Introduction: Under chronic sleep restriction (CSR), human subjects experience only a mild increase in subjective sleepiness, but significant impairment in objective measures of sleepiness and vigilance performance. Rats exposed to CSR fail to express homeostatic sleep drive, as indicated by an absence of compensatory increases in sleep time and sleep intensity (measured by EEG NREM delta power). Thus, the sleep responses to CSR in mammals are fundamentally different from the responses seen after short-term total sleep deprivation. Herein the objective sleepiness of rats was assessed in a CSR paradigm.

Methods: Sleep deprivation (SD) wheels were used to produce 18h of SD followed by 6h of sleep opportunity (SO) for 5 consecutive days. The SO was given during the first 6h of the light period. Sleep onset latencies were measured at 1h after the end of SD, and 1h before the start of SD.

Results: The 18h SD procedure produced 95.8% wakefulness. During the 6h SO periods of days 2 to 5, sleep time and NREM delta power were not elevated compared to baseline. Sleep latencies at 1h after the end of SD were significantly reduced, (e.g., 1.8 min on SR day 1, and 2.1 min on SR day 4) compared to baseline (9.4 min). After 5h free SO, sleep latencies resembled baseline (especially on CSR days 1 to 3, but still showing reduced latency on SR days 4 and 5). Sleep latencies were not decreased during 3 days of free recovery sleep following the 5 days of CSR.

Conclusion: Although sleep time and sleep intensity were not elevated during SO on CSR days 2 to 5, the decrease in sleep latencies indicated that the rats experienced sleepiness throughout the 5 days of CSR. These results suggest that there are at least 2 different sleep regulatory systems: one mediating sleep time/intensity, and the other mediating sleepiness.

Support (optional): Department of Veterans Affairs

0365

THE EFFECTS OF SLEEP DEPRIVATION INTO MICE SPLENIC LYMPHOCYTES CALCIUM SIGNALING

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Introduction: Calcium is an important second messenger in eukaryotic cells and responsible for regulation of many cellular events like protein expression and cellular metabolism. Physiological changes induced by sleep deprivation (SD) are described by many authors. In the present study we are verifying the possible changes in spleen lymphocytes calcium signaling after SD.

Methods: Male Swiss mice were sleep deprived for 24, 48 and 72h before isolation of spleen lymphocytes for loading with cytosolic calcium dye Fluo-3 AM (40min at 37°C). We performed calcium fluorescent measurements using confocal microscopy and fluorimetry. Cytosolic calcium mobilization was induced by addition of endoplasmic reticulum Ca²⁺-ATPase inhibitor thapsigargin (10µM), ionophore K⁺/H⁺ nigericin (10µM) and TNF-α (50ng/mL).

Results: SD (48 and 72h) produced significant reduction on calcium mobilization from endoplasmic reticulum stores using thapsigargin 47% ($p < 0.05$) and 60% ($p < 0.001$), respectively. A subsequent addition of nigericin ionophore promoted a calcium flow from acidic compartment (lysosomes), and we verify reductions of 70% (48h) and 80% (72h) on calcium cytosolic concentrations. These reductions could lead to a deficiency of intracellular signaling from stimulus like agonist TNF-α. Our data reveal a reduction of 45% of calcium cytosolic fluorescence increase with TNF-α (50ng/mL) after 72h of SD compare to control cells.

Category G—Sleep Deprivation

Conclusion: These results provided novel information about physiological changes induced by SD. Immune cells from spleen show a reduction of calcium maintenance and consequent lower calcium signaling after cellular stimulus. We hypothesize that these changes could lead to reduction of immune system efficiency during pathogenic infection events.

Support (optional): AFIP and FAPESP (CEPID 98/14303-3).

0366

MORNING WAKING EEG AND PROCEDURAL LEARNING AFTER ONE NIGHT OF SLEEP DEPRIVATION IN YOUNG ADULTS

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Introduction: Sigma EEG activity during wake correlates negatively with spatial orientation in a human-size maze, which involves sensorimotor integration (Chouinard and al., *Brain & Cognition*, 2003). We investigated this issue further by searching for a correlation between wake Sigma EEG activity and performance on a sensorimotor implicit memory task, after a night of sleep deprivation in young healthy adults.

Methods: Twenty-eight healthy young adults were recorded for two consecutive nights. On the second night, 14 were allowed to sleep while the 14 others were totally sleep deprived (TSD). On the following morning, waking EEG was recorded for 5 minutes, with eyes closed. Spectral analysis was performed on 12 to 15 four-second artifact-free epochs and five frequency bands were generated: Delta (0.75-3.75Hz), Theta (4.0-7.75Hz), Alpha (8.0-12.75Hz), Sigma (11.75-14.75Hz), Beta (13.00-30Hz). The same morning, all participants were tested on the rotary pursuit task. Comparisons between groups on Sigma EEG spectral power and performance on the pursuit rotor task were achieved with T-tests; the correlation between Sigma EEG activity and performance was estimated with Spearman's rho coefficient.

Results: Compared to controls, TSD participants showed more Sigma EEG power than controls over frontal and temporal regions. The performance of TSD participants on the rotary pursuit was impaired and deficits were positively correlated with Sigma power.

Conclusion: These results show that waking fronto-temporal EEG Sigma activity reflects a thalamo-cortical EEG generating system that is associated with the quality of sensorimotor procedural memory. The fact that sleep spindle activity has been reported to correlate in the opposite direction with sensorimotor procedural memory suggests that these two EEG markers represent different dimensions of procedural memory substrates.

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0367

VOLUNTARY SLEEP RESTRICTION IN RATS IS ASSOCIATED WITH SLEEP REBOUND

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Introduction: Animal models involving sleep deprivation or sleep restriction rely upon experimenter-imposed adverse stimulation to keep the animal awake. Such deprivation-associated techniques are likely stressful due in part to the animals' inability to control what is happening to them. Rats will self-stimulate for prolonged periods if electrodes are in the lateral hypothalamus. In contrast, in human studies sleep loss

is voluntary, understandable, and often self-imposed due to socio-economic reasons. The effects of self-stimulation on rat sleep are reported herein.

Methods: Male Sprague-Dawley rats received EEG and EMG electrodes and a bipolar stimulating electrode implanted into the medial forebrain bundle at the level of the lateral hypothalamus. After recovery, a 24h baseline recording was obtained then rats were allowed to self-stimulate in the last 6h of the light period. EEG and EMG recordings continued during the stimulation and for an additional recovery day.

Results: Self-stimulation induced a 2-fold increase in the amount of non-rapid-eye movement sleep (NREMS) and a dramatic increase in EEG slow wave activity (SWA) during NREMS during the 12h following stimulation. In the subsequent light period, NREMS and EEG SWA returned to baseline. Changes in REMS were biphasic. During the first 12h after stimulation (dark period) REMS increased almost 3 fold, then it decreased below baseline for the next 12h.

Conclusion: Voluntary sleep deprivation by intracranial self-stimulation induced substantial changes in the sleep-wake activity of rats. These changes were significant and qualitatively similar to those observed after imposed sleep deprivation. The extent of similarities between the homeostatic sleep response after voluntary vs imposed sleep loss has not yet been determined. Since the sleep restriction used in this study was also associated with increased food intake, this model may serve as an animal model for the sleep restriction-metabolic syndrome link.

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0368

HAZARD PERCEPTION WHEN SLEEPY IN EXPERIENCED AND INEXPERIENCED DRIVERS

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Introduction: Young drivers are disproportionately involved in all serious vehicle crashes, and this is particularly true of sleepiness-related crashes. Specific difficulties in perceiving road hazards, and further impairment of this skill when sleepy, may contribute to this problem in young and inexperienced drivers. Perception, and response, to potential driving hazards is typically better in experienced drivers than in inexperienced drivers. However, the relationship between driver experience and sleepiness is not known.

Methods: 18 experienced and 24 inexperienced drivers completed a 20-minute hazard perception task (real video driving simulation - the Queensland Spatial Hazard Perception Test) at 10am and at 3am in a counterbalanced repeated measures design. Past driving experience, habitual sleepiness and habitual sleep quality were also assessed.

Results: Experienced drivers had shorter hazard perception response latencies than inexperienced drivers overall ($p=.007$). A significant interaction was found between group (inexperienced versus experienced) and time of day (10am and 3am), $p=.039$. Simple effects analysis found worse hazard perception at night for the inexperienced group ($p=.018$), but not for the experienced group ($p=.562$).

Conclusion: The inexperienced drivers were disproportionately slower at detecting driving hazards when they were sleepy, when compared to the more experienced drivers. The results may help to explain the increased risk of driving while sleepy for young adult drivers. Sleepiness impairs elements of driving performance that are critical to safe driving, including hazard perception.

Support (optional): Australian Transport Safety Bureau Road Safety Research grant to Dr Smith and Dr Horswill

0369

SLEEP INERTIA: THE EFFECTS OF TYPE OF TASK AND SLEEP EPOCH PRIOR TO AWAKENINGGrossman ES¹, Babkoff H^{2,3}¹The Interdisciplinary Department of Social sciences, Bar Ilan University, Ramat Gan, Israel, ²Psychology, Bar Ilan University, Ramat Gan, Israel, ³Psychology, Ashkelon Academic College, Ashkelon, Israel

Introduction: The intensity of sleep inertia (SI) is dependent on whether the sleep epoch prior to awakening was normal or recovery sleep following sleep deprivation. SI may not impact all cognitive functions in a similar manner. This study addresses the question as to whether SI after normal and recovery sleep differ in their impact on different cognitive functions. In addition, both types of SI are compared to the impact of sleep deprivation on performance.

Methods: Twenty-two healthy adults (11 men, 11 women), aged 20-27, participated in the study. Subjects slept five and one-half hours on average during the normal- and recovery- sleep nights. Performance on choice RT; verbal working memory; spatial discrimination; psychomotor tracing and subjective arousal were measured during each of eight- 13 minute sessions extending over two hours after awakening (0600-0800) and on the morning following a night of sleep deprivation.

Results: Recovery sleep was characterized by more SWS than normal sleep (89.50(29.87)min., (71.81(22.64)min. respectively) (F1,17=5.33; p<.05) and shorter SWS latency (12.97(9.74)min., 31.25(27.51)min.) (F1,17=7.13; p<.05). Task performance and subjective arousal during sleep deprivation were worse than during SI. Performance speed showed the classical effects of SI. Performance speed during the first session was significantly slower than baseline level (average of last two sessions) (all p's < .01) and improved significantly, by the end of the first hour. Intensity of SI after recovery sleep differed significantly from that after normal sleep only for working memory (F1,21) = 5.66, p<.05) but not for any other cognitive or psychomotor task.

Conclusion: The finding that working memory is more sensitive to SI following recovery sleep than other cognitive and psychomotor tasks is of theoretical interest. Does this reflect the influence of increased SWS during recovery sleep on prefrontal cortical regions or does it reflect the continued effect of prior sleep deprivation?

0370

MODULATION OF SLEEP HOMEOSTASIS BY THE CRH SYSTEM IN PARADOXICAL SLEEP-DEPRIVED RATS

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Introduction: Activation of the CRH system is a common feature of the stress response and is also implicated with its effects on sleep. In order to examine the relationship of the CRH system with sleep homeostasis and the stress, corticotrophin releasing hormone or its antagonist α -helical-CRH(9-41), were administered intracerebroventricularly to rats throughout the 96h period of paradoxical sleep deprivation - PSD.

Methods: Male Wistar rats were implanted with a cannula on the lateral ventricle and with electrodes for recording of the sleep-wake cycle during a baseline condition and 72h recovery period following a 96h of PSD. CRH (3 μ g/animal) or α -helical-CRH(9-41)(20 μ g/animal) was administered twice/day (at 7:00h and 19:00h + 1 infusion at the end of PSD). Plasma ACTH and corticosterone levels were assessed, together with various sleep parameters and compared to appropriate control groups. Statistical analysis was preformed by ANOVAs followed by Newman-Keuls tests.

Results: Repeated CRH treatment of PSD animals led to increase of ACTH (+42.8%; p<.05) and corticosterone (+213.62%; p<.0002) levels when compared to PSD+veh (artificial cerebrospinal fluid)-treated animals. Chronic treatment of PSD rats with α hCRH also resulted in elevated corticosterone (+293.48%; p<.0002) when compared to PSD+veh group, whereas ACTH levels did not differ between the groups (p=.73).

During the first 3h of sleep recovery, PSD+CRH rats displayed less total sleep (-64.37%; p<.05) and paradoxical sleep (-59.87%; p<.05), greater number of awakening episodes (+44.83%; p<.040) and of longer latency to paradoxical sleep (4.2 times; p<.004) when compared than PSD+veh group. Persistent effects of these peptides were observed in the number of awakenings episodes (PSD+CRH: +48.8%, p<.05) and in the length of paradoxical sleep episodes (PSD+CRH: -45.96%; PSD+ α hCRH: -40.0%; p<.05) during the first 12h (lights on) of the recovery period.

Conclusion: Although administered chronically during the entire 96h of the PSD period, CRH showed only transient deleterious effects on sleep homeostasis. Treatment with α -helical-CRH(9-41) did not prevent the ACTH and corticosterone rise induced by PSD and had little effect on sleep homeostasis.

Support (optional): AFIP, FAPESP/CEPID# 98/14303-3, FAPESP# 04/02213-2, CNPq.

0371

REPEATED FOOTSHOCK STRESS INCREASES PARADOXICAL SLEEP REBOUND IN SLEEP DEPRIVED RATS: ASSOCIATION WITH PROLACTIN LEVELS AND HYPOTHALAMIC SEROTONIN CONTENT

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Introduction: We have previously demonstrated that chronic footshock (FS) stress associated with paradoxical sleep deprivation (PSD) increases the paradoxical sleep rebound dramatically (Machado et al., Sleep, 29:A354, 2006). Since plasma levels of stress hormones and catecholamines did not explain this phenomenon, we investigated the role of central monoamines and plasma prolactin levels.

Methods: Male Wistar rats were implanted with electrodes for recording of sleep-wake cycle and heart rate during the entire experimental period (96h of PSD followed by 72h of recovery). Control non-PSD (CTL) and PSD groups were distributed in 1)Non-Footshock (NFS); 2) Single FS stress (SFS - 40 min; 2mA; 0.1s; 5-7 shocks/min at the end of PSD); 3) Multiple FS stress (MFS - same characteristics, applied twice/day, at 7:00h and 19:00h + 1 session at the end of PSD). Plasma prolactin was evaluated by immunoenzymatic assay and brain monoamines, by HPLC. Statistical analysis was carried out by a two-way ANOVA and Pearson's correlation tests.

Results: PSD+MFS rats showed the highest PS rebound and the highest levels of prolactin (Pearson's correlation test, r = 0.53, N=19; p < 0.02 for percentage of PS; r=0.71; p < 0.001 for length of paradoxical sleep episodes). PS deprivation increased serotonin content and/or serotonin turnover in the pons, medulla, hypothalamus, but reduced serotonin content in the hippocampus and frontal cortex. In addition, augmented dopaminergic turnover in the medulla may be responsible for the augmented heart rate in PSD rats.

Conclusion: Increased prolactin secretion was associated with over-expression of PS during the sleep recovery period and serotonin content in the hypothalamus seemed to regulate this phenomenon. Persistent increase in heart rate in PSD rats may be the consequence of diminished vagal tone and increased dopaminergic turnover in the medulla.

Support (optional): AFIP, FAPESP/CEPID# 98/14303-3, FAPESP# 04/02213-2 and CNPq.

0372

NAPPING DURING NIGHT SHIFT: EXPERIENCES OF CRITICAL CARE NURSESMcMillan DE¹, Fallis WM¹, Edwards MP¹¹Faculty of Nursing, University of Manitoba, Winnipeg, MB, Canada,²Victoria General Hospital, Winnipeg, MB, Canada

Introduction: The critical care environment demands specialized nursing care, rapid decision-making, as well as enhanced organizational, assessment, and motor performance skills on a round-the-clock basis.

Category G—Sleep Deprivation

These patient care demands place critical care nurses at risk for sleep deprivation, which in turn leads to threats to patient safety and the health and safety of nurses. Napping has been suggested as a strategy to improve performance, reduce fatigue, and increase vigilance in other shift work environments. This study aims to explore nurses' perceptions, experiences, and barriers related to napping/not napping during night shift, with the goal to develop an effective napping intervention for the critical care environment.

Methods: This qualitative descriptive study used a convenience sample of critical care nurses working night shift at an acute care hospital in mid-western Canada. Participants met individually with one of the researchers and completed a tape-recorded semi-structured interview exploring demographics, work schedule and environment, and napping/nonnapping experiences, perceptions, barriers, and preferences. Analysis of the data involved constant comparison of transcripts and identification of categories and themes. Sampling continued until saturation was achieved. Attention was paid to ensuring data integrity and trustworthiness.

Results: Thirteen critical care nurses participated. The majority were female (82%), married (82%), 31-50 years of age, had dependents (55%), worked full-time (55%) in a night-day or night-evening rotation, with an average of 16 years experience. Ten nurses were regular nappers. Emergent themes speak to the complexity, dynamic nature, and unpredictability of the critical care environment. Participants identified the need for and benefits of napping during night shift break. The ability to achieve a restorative nap was impacted by complex factors including the demands of patient care and safety, staffing needs, shiftwork rotation, and organizational and environmental factors.

Conclusion: Nurses identified a number of personal health, safety, and patient care issues that support the need for a restorative nap during night shift. Currently, barriers exist both within the organization and work environment for achieving naps. A strategy to assist nurses to promote sleep health within the complex context of their own sleep needs, organizational demands, and domestic responsibilities is greatly needed for both critical care nurses and the patients in their care.

Support (optional): Manitoba Nursing Research Institute, Outcomes Research Grant, Faculty of Nursing, University of Manitoba; Dr. John Wade Research Award, Manitoba Institute for Patient Safety.

0373

ACUTE SLEEP FRAGMENTATION OR DEPRIVATION REDUCES BODY TEMPERATURE AND GROSS MOTOR ACTIVITY IN SOCIALLY ISOLATED MICE

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Introduction: Sleep deprivation (SD) and sleep fragmentation (SF) are potential methodological strategies to evaluate sleep homeostasis. Prolonged wakefulness increases the propensity to sleep and enhances delta power during slow wave sleep (SWS). However, studies involving interrelationship between core body temperature (Tb) and gross motor activity (Ag) during SD and SF in a social contextual setting have not been explored.

Methods: C57/BLJ male mice were chronically implanted with a telemetric transponder to measure EEG, EMG, Tb and Ag. They were exposed to SD and SF using a custom designed instrument that elicits minimal stress and is not associated with forced locomotion. Telemetric polygraphic recordings including Tb and Ag were carried out before, during and following the interventions, which consisted of 6h of either SD or SF starting 7AM followed by 18h of recovery. Recordings were carried out under social conditions (mice were paired: PAIR) or under socially-isolated condition (single-no pairing for 5 weeks: ISO).

Results: There was an overall increase in Tb during SD in both PAIR and ISO groups. SF showed an initial increase in Tb but the latter returned to baseline after a couple of hours. During the dark period (7.00 pm to 1.00

am), there were significant decreases in Tb ($F(4,35) = 4.359$ $p < 0.001$) and Ag ($F(4,35) = 5.316$ $p < 0.001$) in ISO group when compared to the PAIR group. Although both SD and SF group in ISO showed a significant decrease in Tb, the effect was more prominent in the SD mice.

Conclusion: We present evidence supporting the use of a novel approach to induce either SD or SF in a murine model that is void of elevated stress responses or forced locomotion. Furthermore, we show that social interactions in the context of SF or SD play an important role in modulating Tb and Ag, thereby emphasizing the need to incorporate the contextual social setting in future experiments aiming to determine the regulation of sleep homeostatic responses.

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0374

SLEEP, FATIGUE, AND DEPRESSION IN MOTHERS OF TWINS

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Introduction: Parenting newly born twins poses high childrearing demands, placing parents at risk for sleep restriction. Furthermore, over half of twins are delivered preterm. Preterm infants are more fragile, require more vigilant care, and show preference for nighttime wakefulness. Fatigue and sleep restriction are associated with the development of depression in postpartum women. This study examined relationships between sleep patterns, fatigue, sleep quality, and depression in mothers of twins.

Methods: A descriptive longitudinal repeated measures design was used. Data were collected over 3-day periods at 40 weeks post-menstrual age of the twins, and 8 and 12 weeks post-hospital discharge. Measures included actigraphy, sleep diaries, and standardized instruments for fatigue, sleep quality, and depression. Data for 14 mothers of twins at two data points were examined.

Results: Mothers delivered at a mean of 36.6 weeks gestation. Mean 24-hour sleep time was 321.2 minutes (SD = 55.1) at Time 1 and 335.3 minutes (SD = 48.4) at Time 2. Over 70% of women had < 6 hours sleep, although fewer (21.4%) had < 5 hours sleep by Time 2. Mean number of sleep episodes at Time 1 was 15.1 (SD = 5.4) averaging 22.4 minutes in length (SD = 8.1); mean number at Time 2 was 12.8 episodes (SD = 5.7) averaging 31.8 minutes (SD = 21.3). Based on the CES-D and Postpartum Depression Screening Scale, 42.9-50% of women at Time 1 and 14.3-21.4% of women at Time 2 reported mild to severe depressive symptoms. Fatigue levels decreased while subjective sleep quality increased over time.

Conclusion: Preliminary results document significant sleep restriction in postpartum mothers of twins. Although total sleep time remained consistent, sleep was less fragmented over time, corresponding with improved subjective sleep quality. Compared to previous research in mothers of singleton infants, more mothers of twins had significant depressive symptoms. Further study is needed to clarify factors associated with sleep restriction.

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0375

SLEEP DEPRIVATION INDUCED EMOTIONAL VISUAL AGNOSIA

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Introduction: While the effects of sleep-deprivation on cognitive function have received considerable research interest, the impact of sleep loss on emotional processing remains surprisingly understudied. Here we demonstrate that a single night of sleep-deprivation induces a selective impairment in the ability to recognize human emotions; an effect that was reversed following recovery sleep.

Methods: The task involved evaluating three different affective face categories: Sad, Happy and Angry. For each emotion, ten picture-slides, ranging in a gradient from neutral to increasingly emotional, were presented in a random order, with subjects required to make an emotional-strength rating for each face-slide. Prior to performing the task, subjects either slept normally, or were sleep deprived. Following a recovery night of sleep, both groups repeated the task.

Results: Under conditions of sleep-deprivation, there was a significant impairment (blunting) in the recognition of happy and particularly angry facial expressions ($p=0.01$ and $p=0.004$, respectively), yet a preservation in the recognition of sad expressions. Moreover, these effects were far greater in females than males. This selective “emotional visual agnosia” was, however, ameliorated following a night of recovery sleep, with performance returning to similar profiles observed in the control group.

Conclusion: Together, these data demonstrate that sleep-deprivation significantly and selectively disrupts affective processing, impairing the ability to recognize human emotions in others. Such specificity suggests that sleep-deprivation impacts discrete neural systems, rather than imposing a global brain deficit, and may offer clinically relevant insights into the co-occurrence of sleep abnormalities in psychiatric mood disorders, including major depression and post-traumatic stress disorder.

0376

USING BRIGHT LIGHT THERAPY TO PROMOTE SLEEP IN MOTHERS WITH A LOW BIRTH WEIGHT INFANT: A PRELIMINARY REPORT

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Introduction: Having a low birth weight (LBW) infant in the intensive care unit (ICU) can intensify sleep disturbances because of extended periods of exposure to the artificial dim light in the ICU and stress related to the infant’s medical condition. Impaired sleep may have a negative impact on mother’s well-being. The purpose of this pilot study is to examine whether a bright light therapy will lead to clinically significant improvements in sleep, fatigue, depression, and physical health of mothers of LBW infants.

Methods: Sixteen first-time mothers with a LBW infant hospitalized in the ICU were randomly assigned to two groups: the treatment group mothers received a 10,000 lux blue-green bright light therapy (BL; $n=9$) for 4 weeks and the control group mothers received a placebo dim red light therapy (RL; $n=7$). Data collected at baseline and after the 4 week intervention period included: 1) Perceived Stress Scale (PSS), Impact of Events Scale (IES), General Sleep Disturbance Scale (GSDD), Numerical Rating Scale for Fatigue, Edinburgh Postnatal Depression Scale (EPDS), and Medical Outcomes Short Form-36version 2 (SF36v2). Total sleep time (TST) during the day and night was measured by obtaining averaging the data obtained from two consecutive days of wrist actigraphy monitoring.

Results: Post treatment, the average nocturnal TST increased from 383 minutes ($SE= 34$) at the baseline to 424 minutes ($SE= 13$) for the BL group. However, the TST in the RL group mothers worsened from 413 minutes ($SE= 38$) to 373 minutes ($SE=20$). After the 4-week intervention, the BL group mothers’ daytime TST decreased from 114 to 39

minutes; the means scores of GSDD, EPDS, and IES had significant decreases over time ($p<.05$), while the SF36v2 aggregated physical health component had a significant increase over time ($p=.025$).

Conclusion: Results indicate that bright light therapy may improve a mother’s nocturnal sleep, decrease daytime sleepiness, and be beneficial to her well-being. The positive findings of this pilot study suggest a larger scale randomized clinical trial testing the effects of bright light therapy in this population is warranted.

Support (optional): This study was supported by Georgia State University and the Association of Women’s Health, Obstetric and Neonatal Nurses (AWHONN).

0377

IMPAIRED SLEEP AND HEALTH-RELATED QUALITY OF LIFE AMONG MOTHERS WITH A LOW BIRTH WEIGHT INFANT IN THE ICU

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Introduction: Mothers with low birth weight (LBW) infants hospitalized in the intensive care unit (ICU) are at a higher risk for impaired sleep and related adverse health outcomes such as fatigue, depression, and poorer health-related quality of life. The aim of this study was to describe mothers’ sleep, fatigue, and quality of life while their LBW infants were hospitalized in the ICU.

Methods: Eighteen first-time mothers who had a LBW infant hospitalized in the ICU were enrolled during their 7-10 day postpartum period. Total sleep time (TST) and wake after sleep onset (WASO) were measured by averaging data from two nights of wrist actigraphy monitoring. Self-report data were collected with the Perceived Stress Scale (PSS), Impact of Events Scale (IES), General Sleep Disturbance Scale (GSDD), Numerical Rating Scale for Fatigue, Edinburgh Postnatal Depression Scale (EPDS), and the Medical Outcomes Short Form-36version 2 (SF36v2).

Results: The average nocturnal TST was 400 minutes ($SE= 22.3$) and the average WASO was 18.4% ($SE= 2.3$). The GSDD mean score was 2.8 ($SD=0.8$), indicating those mothers were poor sleepers. The fatigue mean scores were 3.9 and 5.3 for morning and evening respectively, indicating a moderate fatigue severity for mothers. The EPDS mean score was 14.6 ($SD=5.9$), indicating that the mothers experienced a moderate amount of depressive symptoms. The mean scores for the IES and PSS were 35.8 ($SD= 12.9$) and 21.1 ($SD= 5.9$) respectively, indicating the mothers perceived moderate stress levels from their infant’s hospitalization, and their stress level was higher than the norm for female adults. The mother’s physical and mental health scores (SF36v2) were about 1 SD below the normative scores for age-matched females in the U.S. general population.

Conclusion: Mothers of LBW infants demonstrated sleep disturbances, decreased psychological health, and health-related quality of life below that of women of similar age in the general population. Further research is needed to develop and test interventions to promote sleep and well-being in mothers of LBW infants and to determine if interventions are effective in supporting mothers as they transition from the hospital to becoming the infant’s primary caregiver in the home.

Support (optional): This study was supported by Georgia State University, and Association of Women’s Health, Obstetric and Neonatal Nurses (AWHONN).

0378

SLEEP DURATION AND FUNCTIONAL CAPACITY IN THE US: RESULTS OF THE NATIONAL HEALTH INTERVIEW SURVEY

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Introduction: Evidence suggests that individuals reporting extreme sleep scores are often obese and are at risk for hypertension, diabetes, and cardiovascular disease. Evidence also suggests that individuals with cardiovascular disease have reduced functional capacity. Using data from the National Health Interview Survey (NHIS), we assessed whether sleep duration and functional capacity are independently associated.

Methods: Data were obtained from 29,818 Americans (age range: 18-85yrs) who participated in the 2005 NHIS; 85% of the sample was white, and 56% was women. The NHIS is a cross-sectional household interview survey, which uses a multistage area probability design. Probability samples of the civilian population of all 50 states and DC were obtained. During face-to-face interviews by trained interviewers from the U.S. Census Bureau, respondents provided socio-demographic data and information about physician-diagnosed chronic conditions. They estimated habitual sleep duration and indicated their functional capacity, anchored by ability to walk one-quarter mile without assistance.

Results: Of the sample, 28.3% reported hypertension; 8.3%, heart disease; 7.9%, cancer; 8.4%, diabetes; 23.4%, arthritis; 10.2%, vision problem; and 61.5% were overweight/obese. Altogether, 17.2% reported extreme sleep scores, defined as sleep duration \leq 5hrs or \geq 9hrs. Based on logistic regression analysis, sleep duration was associated with functional capacity [odds ratio=2.84, 95% CI: 2.65—3.05, $p < 0.0001$]. After adjusting for heart disease, odds ratio diminished slightly: 2.76 [95% CI: 2.57—2.96, $p < 0.0001$]. With further adjustment for demographic, medical, and risk factors, the odds ratio was: 2.20 [95% CI: 2.02—2.40, $p < 0.0001$].

Conclusion: Even after adjusting for effects of covariates, the odds of reporting reduced functional capacity for individuals characterized by extreme sleep scores were twice as great as that of individuals sleeping within the healthy range. While it can't be said that increased sleep duration would enhance functional capacity, individuals reporting extreme sleep scores should be the focus of interventions aimed at achieving optimal sleep.

Support (optional): This research was supported by funds from NIH(1R24MD001090 and HL085042).

0379

SLEEPINESS AND IMPAIRMENT OF SUSTAINED ATTENTION PRODUCED BY SLEEP DEPRIVATION

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Introduction: Sleepiness, defined as the propensity to fall asleep, has been indicated in basic research with electrographic analysis. Our laboratory has recently developed methods to objectively measure sleepiness by means of behavioral evaluation. Rats were exposed to 24 hours of sleep deprivation (SD), and sleepiness was evaluated following treatment. Electrographic indicators of sleepiness were measured during the first 3 hours of recovery following SD. Sleepiness was objectively measured by means of a rat multiple sleep latencies test (rMSLT) and the rat

psychomotor vigilance task (rPVT), both animal analogues of clinical measures.

Methods: SD was produced by slow rotation of an activity wheel, producing approximately 94% wakefulness. In one group of rats, recovery after SD was left undisturbed, in order to document changes in NREM sleep episode duration, delta activity, and total amounts. In another group, the rMSLT was performed, with 6 latency trials conducted in the 3 hours of recovery. In a third group, the rPVT was performed in recovery, and measures such as response latencies and performance lapses were evaluated.

Results: Measures of NREM sleep episode durations (1 min, 51 s baseline vs. 4 min, 23 s post-SD), NREM delta power (171% increase post-SD compared to baseline values), and total NREM amounts (39.5% of total time in NREM baseline vs. 55.56% post-SD) were increased during uninterrupted recovery. Sleep latencies in recovery were significantly decreased compared to time-of-day matched baseline (8 min, 46s baseline vs. 3 min, 15 s post-SD). Performance lapses increased significantly during rPVT sessions immediately following SD (9.2 lapses baseline vs. 18.33 lapses post-SD).

Conclusion: The propensity to fall asleep following SD was evident with conventional electrographic measures (post-SD EEG/EMG analysis). SD produced behavioral impairment in novel tests of sleepiness (rMSLT) and sustained attention (rPVT) analogous to that shown by sleep disrupted human subjects.

Support (optional): Dept. of Vet. Aff., NIH HL060292, MH039683, and MH070156.

0380

ERRORS IN GRAMMAR AND SYNTAX FROM WRITTEN LANGUAGE SAMPLES INCREASE DURING A NIGHT OF TOTAL SLEEP DEPRIVATION

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Introduction: Writing is a complex task involving attention and planning, both frontal lobe functions. Frontal lobe function is thought to be impaired during sleep deprivation. We examined samples of participants' writing obtained at two-hour intervals during a night of total sleep deprivation (SD). We compared those writing samples to those collected two weeks later from the same participants, after participants had had two weeks of ad lib sleep. Samples were compared with respect to errors of grammar, spelling, syntax, and other categories of written language production.

Methods: Fourteen participants wrote about their cognitive, physical, and affective state during a night of total sleep deprivation. Two weeks later they again wrote descriptions of how they remembered feeling during that night. Two raters, blinded to condition, examined the passages and identified errors in the writing samples including misspellings, grammatical and syntactical errors, contradictions, and perseverative phrases. A within-subjects ANOVA was calculated to compare SD to retrospective ratio of total errors to total number of words used.

Results: Participants' error rates for SD writing samples were 18 per thousand words, significantly worse than that obtained from the same participants two weeks later, calculated to be eight per thousand words ($F[1,26]=6.48, p < .02$). Most frequent error during the night was a syntactical or grammatical error; misspellings were least common. No single error was more common during the day-time samples of writing.

Conclusion: Errors in written language may be more common during SD. Errors in syntax and grammar may represent an overall difficulty with written language that may reflect poorer frontal lobe function during the night, during sleep deprivation, or may represent more focal problems in areas of the brain which are involved in production of written language.

0381

SLEEP AND ACADEMIC PERFORMANCE IN A COMMUNITY COLLEGE

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Introduction: Sleep is important for learning but is often compromised in college students. We sought to describe sleep habits in a community college and to correlate these habits with academic performance.

Methods: An anonymous 30-question survey was administered randomly to query students on bedtimes, waketimes, naps, jobs, and grade point average.

Results: Of 157 surveys (81 men), median age was 20y (range 17-69y), 66 white, 28 hispanic, 23 black, 21 asian, 20 other. Mean bedtime on nights before class was 12:16 AM (range 9 PM-4 AM), waketime 7:37 AM (range 3:30 AM-12:30 PM), with nightly sleep time of 7h23m. Mean total sleep time (including naps) was 7h32m. On nights with no class, bedtime was an hour later (1:12 AM) and wake time 2.5 hours later (9:58 AM) with nightly sleep time 8h43m. Students in the lowest quintile for grades (GPA<2.7) slept more (but not significantly, $p=0.87$) than students in the highest quintile for grades (GPA>3.5). Students with low grades had nightly sleep time before class days of 7h35m while students with high grades slept 7h29m before class days. Similarly sleep time before days off was 8h49m vs 8h39m. Students with lowest grades reported mean study time of 2h23m per day. Students with highest grades reported mean study time 2h47m (mean increase of 24m between low and high performers, $p=0.4$). Mean GPA for women (3.3+0.5) and men (3.2+0.5) was not different ($p=0.3$). 42 students did not work and reported GPA=3.0 and total sleep time 7h45m. 47 students worked 20h/week or less, and reported GPA=3.3 and total sleep time 7h18m. 22 students worked more than 20h/week and reported GPA=3.16 and total sleep time 7h13m.

Conclusion: In a community college setting with balanced gender and mixed races, average sleep time was less than current guidelines recommend. There was substantial variability in bedtime and waketime between nights before class and before days off. Substantial variability of sleep times was also observed between individuals, manifesting in a wide range of bedtimes and waketimes. Sleep time for students with high grades did not differ statistically from those with low grades. Gender and homework time did not predict scholastic performance. Employed students slept less but maintained higher grades than students without jobs. Students who worked more than half-time (>20h/week) slept the least and reported grades in-between part-time workers and unemployed students.

0382

IMPACT OF NIGHT VS. DAY SHIFT WORK IN RESIDENTS ON SLEEP, PERCEPTIONS OF SLEEP AND MOOD

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Introduction: In response to the belief that resident fatigue resulting from long work hours leads to medical errors, ACGME instituted work regulations. Thus, most training programs have implemented shift systems such as a night float admitting team, to achieve compliance. The impact of night float systems on residents' sleep, perceptions of sleep and mood is unknown. We postulated night float residents would have reduced hours of sleep, increased subjective sleepiness and decreased mood compared to day shift.

Methods: Residents on general medicine ward rotations were asked to participate in a three-week study. Twenty-nine subjects wore wrist actigraphs and kept sleep logbooks which included daily assessments of sleepiness using a Likert scale. Sleep time (ST), nap time (NT), total sleep time (TST=ST+NT), and number of naps were measured with actigraphy. Sleepiness was assessed with Epworth Sleepiness Scale (ESS) and Stanford Sleepiness Scale (SSS) at baseline and weekly. Mood was assessed by the Center for Epidemiologic Studies Depression scale (CESD). Dependent t-tests and Wilcoxon tests determined differences between nights and days.

Results: All measures indicated sleepiness was significantly higher in residents on nights versus days (all $p<0.001$). At the end of night float week, 75-92% of residents rated themselves as excessively sleepy by ESS and 60-67% by SSS. Over two-thirds of residents had ESS ≥ 16 , placing them in an impaired range comparable to those with narcolepsy and moderate to severe OSA. ST was lower ($p=0.028$), while number of naps ($p<0.001$) and depression ($p=0.030$) were higher on nights compared to days; however amount of NT and TST did not differ. Most correlations between subjective and actigraphy measures were low.

Conclusion: During night float, residents reported excessive sleepiness, less sleep, more naps, and higher depressive symptoms. Low correlation with actigraphy suggests that the change in day-night cycle rather than actual time asleep influences subjective symptoms.

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0383

PREDICTING BLOOD PRESSURE RESPONSE UNDER SLEEP DEPRIVATION CONDITIONS

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Introduction: Biopsychological models of disease suggest that persons with exaggerated physiological responses to acute stressful states are at a greater risk of developing cardiovascular disorders. Although several studies have attempted to relate measures of mood and cardiovascular output under emotional stressful conditions, few studies have examined the effects of sleep deprivation. The purpose of the current study was to examine how well a variety of subjective mood indicators predict blood pressure under sleep deprivation and sustained operations conditions.

Methods: Sixty-three participants (age: 23 ± 2.5) took part in a 30 hour acute sleep deprivation study. The participants completed a wide range of tasks during an 18-hour sustained work period from 6:00 PM on day 1 to noon on day 2. Prior to the work period, the participants completed several subjective surveys on mood and anxiety. Resting blood pressure (BP) was assessed using the GE Dinamap Pro 100 at the beginning of the work period when the participants were well rested (between 6:30 and 10:30 PM) and at the nadir of the circadian cycle (between 3:30 and 7:30 AM).

Results: A series of backwards regression models were completed to determine the best predictive model of systolic and diastolic BP when the participants were well-rested (time 1) and at the nadir of the circadian cycle (time 2). Of the subjective variables assessed, the POMS mood measure, PANAS affect measure, a measure of neuroticism (NEO) and a measure of state anxiety (STAI) resulted in the best over-all predictive model of systolic and diastolic BP. When predicting systolic BP, the mood and anxiety scales resulted in an r-square of .260 ($p=.028$) at time 1 and an r-square of .206 ($p=.05$) at time 2. At time 1, PANAS positive and negative affect were the best predictors of systolic BP. At time 2, PANAS negative affect and the NEO were the best predictors of systolic BP. The measures of mood and anxiety used in the current regression models did not significantly predict diastolic BP at either time 1 or 2.

Conclusion: The current results indicate that subjective measures of mood and anxiety can predict systolic but not diastolic BP under well-rested and sleep deprivation conditions. These results agree with previous studies concluding that ambulatory systolic BP but not diastolic BP

Category G—Sleep Deprivation

could be predicted by subjective measures of mood and further indicate that this relationship may be independent of any effects due to endogenous circadian rhythms.

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0384

EXTENDED SLEEP AND THE EFFECTS ON MOOD AND ATHLETIC PERFORMANCE IN COLLEGIATE SWIMMERS

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Introduction: Relatively few studies have clearly elucidated the immediate and long term effects of extended sleep. In particular, little research has thoroughly investigated the impact of multiple nights of extra sleep over a prolonged period of time and specifically, how extended sleep affects athletic performance.

Methods: In this ongoing study, five healthy students (age 18 - 22) on the Stanford men's and women's swimming teams established a two week baseline in which they maintained their usual sleep/wake patterns. Athletes then extended their sleep to 10 hours per day for 6-7 weeks. Following each regularly scheduled swim practice, swimmers were assessed for athletic performance including 15m sprint, reaction time off the block, and turn time. To monitor daily sleep/wake activity, actigraphy and self-reported sleep logs were recorded throughout the study. The Epworth Sleepiness Scale assessed daytime sleepiness and the Profile of Mood States (POMS) monitored weekly changes in mood.

Results: Indicators of athletic performance significantly improved following the extended sleep period. Improvements included faster 15m sprint (6.98 ± 0.99 seconds at baseline, 6.47 ± 0.64 seconds at end sleep extension, $p < 0.05$), faster reaction time (0.88 ± 0.20 at baseline, 0.73 ± 0.13 at end sleep extension, $p < 0.05$), improved turn time (1.10 ± 0.20 at baseline, 1.00 ± 0.22 at end sleep extension, $p < 0.05$), and increased kick strokes (26.2 ± 1.53 at baseline, 31.2 ± 1.84 at end sleep extension, $p < 0.05$). Swimmers also demonstrated mood improvements including POMS vigor ratings (42.9 ± 3.80 at baseline, 65.3 ± 5.08 at end sleep extension, $p < 0.05$) and decreased POMS fatigue scores (57.9 ± 4.86 at baseline, 34.1 ± 0.22 at end sleep extension, $p < 0.05$). Epworth scores decreased from 11.0 ± 3.32 at baseline to 2.40 ± 2.07 , $p < 0.05$ at end sleep extension.

Conclusion: Significant improvements in measures of athletic performance and mood were observed in collegiate swimmers after extended sleep.

0385

RELATIONSHIP BETWEEN SLEEP PHYSIOLOGY AND EXECUTIVE FUNCTION DURING CHRONIC PARTIAL SLEEP RESTRICTION

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Introduction: Research suggests total sleep loss affects the prefrontal cortex, which is important for executive function (EF). However, little data exist on the relationship between sleep physiology during chronic partial sleep restriction and EF. This study was designed to assess this issue.

Methods: N=120 participants (22-45y, 68m, 52f.) completed one of two identical sleep restriction protocols of 4h time in bed (TIB) for sleep on 5 consecutive nights after 2 baseline nights of 10h TIB. On the day after the 5th sleep restriction night, the Hayling Sentence Completion Test and

Brixton Spatial Anticipation Test were administered and scored according to standard criteria. The Hayling test measured response inhibition (total errors), response initiation (response latency), and divergent thinking (type B errors). The Brixton test measured cognitive flexibility (total errors). A measure of overall EF was also derived (Hayling + Brixton scaled scores). PSG was recorded using a standard montage (EEG-C3/A1, EOG, EMG), and scored to derive slow wave sleep (SWS), REM sleep, and stage 2 sleep times (minutes). A stepwise linear regression was conducted to identify which sleep parameters best related to EF measures.

Results: SWS on the final night of sleep restriction was the best PSG predictor of each EF measure, but SWS explained $\leq 8\%$ of the variance in EF dependent measures. Significant negative associations were demonstrated between SWS and response inhibition ($\beta = -0.21$, $p = 0.02$); response initiation ($\beta = -0.26$, $p < 0.01$); divergent thinking ($\beta = -0.20$, $p = 0.03$); and cognitive flexibility ($\beta = -0.23$, $p = 0.01$). SWS was positively associated with overall EF ($\beta = 0.29$, $p < 0.01$).

Conclusion: Having more SWS during sleep restriction predicted fewer errors, shorter response latencies, and better overall performance on tests of EF. It remains to be determined whether these associations reflect physiological causality

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0386

FIVE NIGHTS OF PARTIAL SLEEP RESTRICTION INCREASED PLASMA LEPTIN LEVELS IN HEALTHY ADULTS

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Introduction: Sleep deprivation has previously been shown to affect a number of inflammatory and neuroendocrine markers related to health. Leptin, a pro-inflammatory hormone produced by adipocyte tissues in humans, plays an important role in obesity and metabolic function. Limited previous research has observed that leptin levels decrease in response to total and partial sleep deprivation; however, sample sizes have been small and generally included only male participants.

Methods: N=112 healthy adults (mean age 30.2 ± 7.1 years, 46% men, 44% Caucasian) underwent an 11-day inpatient sleep protocol. Following 2 nights of full (10h) baseline sleep, 106 participants received 4h time in bed (TIB) for the next five nights. N=8 participants served as controls and received 10h TIB each night. 10mL samples of venous blood were collected between 0900-1100 following the second night of baseline sleep (B2) and the fifth night of partial sleep restriction (P5).

Results: While there were no significant differences between groups at either the B2 or P5 time points, sleep restriction resulted in a significant (within-group) increase in leptin levels from B2 to P5 ($Z = -7.55$, $p < .001$); the control group showed no significant changes. Significant gender and ethnicity differences were also observed at both B2 and P5 within the deprivation group: women and African-Americans had higher leptin levels than men and Caucasians, respectively (all p 's $< .02$). Within the deprivation group, women demonstrated a significantly greater increase in leptin levels compared to men ($Z = -4.44$, $p < .001$). There was no significant difference in response to sleep deprivation between ethnic groups.

Conclusion: In a large sample, plasma leptin levels increased significantly, particularly in women, in response to five nights of partial (4h TIB) sleep restriction. These results have implications with respect to the role of sleep duration and obesity and other metabolic disorders.

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0387

CLINICAL STUDY OF VSF-173 IN A MODEL OF EXCESSIVE SLEEPINESS

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Introduction: VSF-173 is an investigational compound of unknown mechanism of action that has previously demonstrated wake-promoting properties in a rat model measuring sleep. We studied the effects of this novel compound on wakefulness in humans under the condition of a single night of sleep deprivation when the subjects would normally have been asleep in this proof-of-concept study.

Methods: A randomized, double-blind, placebo-controlled, single-center study of 55 healthy adults was conducted. Sleepiness was measured under the condition of keeping subjects awake past their habitual bedtime and through the next day. Subjects received a total nighttime dose of 50mg, 100mg, 200mg VSF-173 or placebo. Wakefulness was assessed every two hours starting one hour after habitual bedtime using the maintenance-of-wakefulness test (MWT). After the sleep deprivation assessments, the subjects had a recovery sleep which was measured by polysomnography (PSG).

Results: Averaging the first 4 MWTs, MWT sleep onset for 50 mg, 100 mg and 200 mg, and placebo groups were 10.3, 12.9, 10.6 and 9.2 minutes (n.s.s.). However, in a subset of 37 subjects with no observed impairment in pre-dose daytime wakefulness (daytime MWT), the mean MWT scores for the 50 mg, 100 mg and 200 mg groups showed improvements of 2.1, 3.4 and 2.1 minutes, respectively, compared to placebo ($p < 0.05$ for 100mg). PK/PD modeling revealed a greater-than 5 minute wakefulness effect ($p < 0.05$) for those who reached a threshold of exposure to VSF-173 early in the night. In addition, wakefulness as measured by WASO in the first 3 hours of the sleep period showed a statistically significant dose and exposure-response profile.

Conclusion: The results in this proof-of-concept trial suggest exposure-dependent wake-promoting properties for VSF-173. Further information gained from PK/PD Modeling will help to guide timing of administration and dosage in future studies. In this trial, VSF-173 was safe and well tolerated.

Support (optional): Vanda Pharmaceuticals sponsored this study.

0388

TIME AWAKE AND NOCTURNAL DRIVING PERFORMANCES

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Introduction: Epidemiological studies have shown that driving at night is a major cause of sleep-related accidents, especially between 2-5 AM. Nevertheless there is no data comparing the risk of driving at the beginning or the end of the night.

Methods: A cross-over study using a balanced repeated design was planned. The study involved 2*90 minutes of simulated driving in 2 nocturnal (9.30pm-1am and 4-7.30am) and 1 diurnal (3.30-7pm) driving sessions. Simple reaction time (RT) was measured before, in the middle of and after each driving session. Twenty-five healthy young men (age=23±1.4 years, intermediate chronotype) were recruited. Standard deviation from the center of the road (driving ability) and number of lapses (RT) were analyzed. Self-perceived alertness in the morning just after awakening was assessed. This item could discriminate at-risk subjects for nocturnal tasks (Taillard et al. 2005). Taillard et al. J Sleep Res. 2006, 15:41-45.

Results: Nine participants were not able to drive between 6-7.30 am. Standard deviations from the center of the road for the 4-7.30am session

were greater (ANOVA, $p < 0.005$) than for the 3.30-5pm session for the 16 remaining subjects. Standard deviations from the center of the road for the 11.3pm-1am session tended to be greater (ANOVA, $p = 0.052$) than for the 3.30-5pm session ($n = 25$). No correlation between lapses before or after the session and driving ability was found. Between 4-5.30am, inter-individual differences were clearly observable in performance but not really in driving ability. Self-perceived alertness in the morning did not predict nocturnal performance or nocturnal driving ability.

Conclusion: This study confirms that driving ability is reduced during the night especially between 3-7 am. Simple reaction time during the stops or morning alertness just after awakening do not predict nocturnal driving ability.

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0389

POLYSOMNOGRAPHIC MEASURES IN RELATION TO PHENOTYPIC NEUROBEHAVIORAL RESPONSES TO SLEEP RESTRICTION

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Introduction: Differential vulnerability to sleep loss assayed by neurobehavioral responses has recently been demonstrated in subjects undergoing sleep restriction. This study investigated the various relationships between our neurobehavioral PVT phenotype variable and standard polysomnographic (PSG) sleep measures in response to sleep restriction.

Methods: $N = 129$ healthy adults ($M = 29.6y \pm 6.7y$; 65 women) completed 2 baseline sleep nights (TIB=10h) followed by 5 sleep restriction nights (TIB=4h) in a laboratory under carefully controlled conditions. The 10-min Psychomotor Vigilance Test (PVT) was administered every 2h during wakefulness on all days. Neurobehavioral phenotypic responses to sleep restriction were characterized using a mean difference PVT lapses/trial metric. This continuous metric is calculated as the mean deprivation lapses/trial (using all deprivation bouts) – mean baseline lapses/trial (using all baseline bouts), whereby lapses were defined as > 500 ms response time. Difference scores were also calculated between the fifth night of sleep restriction and baseline night for PSG sleep variables. Spearman's rho correlation coefficient analyses quantified the various relationships between PVT and PSG measures.

Results: Total sleep time (TST; $\rho = -0.15$, $p = 0.09$), sleep efficiency ($\rho = -0.15$, $p = 0.09$), sleep onset latency ($\rho = -0.02$, $p = 0.82$), REM latency ($\rho = -0.01$, $p = 0.93$), slow-wave sleep %TST ($\rho = 0.05$, $p = 0.57$) and REM %TST ($\rho = 0.15$, $p = 0.10$) all failed to show significant relationships to the difference lapses/trial phenotype. Only duration of wake after sleep onset showed a weak, inverse correlation to the PVT phenotype ($\rho = -0.19$, $p = 0.03$).

Conclusion: Subjects most severely affected by sleep restriction as manifested in greater increases in lapses during PVT performance failed to show the greatest changes in sleep on the last night of restriction. The aforementioned lack of significant relationships suggests that PSG-defined sleep changes in response to sleep restriction are orthogonal to changes in PVT performance and therefore may not be useful for predicting neurobehavioral deficits.

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0390**SLEEP LOSS AFFECTS SOCIAL PERCEPTION OF VOICE INTONATION, FACIAL EXPRESSIONS, AND NEGATIVE EMOTIONS***Anderson C, Webb CE, Platten CR*

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Introduction: Most laboratory research on the effects of sleep deprivation (SD) and performance tends to overlook real-world settings involving person-to-person interactions. Advances in social neuroscience reveal social behaviour is reliant on the prefrontal cortex (PFC); an area vulnerable to the effects of sleep loss. We assess the impact of sleep deprivation on social behaviours such as: interpreting non-verbal cues, and the manifestation of impulsive behaviour in the presence of positive and negative stimuli.

Methods: Thirty-two healthy, young adult (22.4y±1.6y) normal sleepers (8h±1h) without complaint of daytime sleepiness (<2naps/wk; ESS≤10) were randomly assigned to either a CONTROL (normal sleep) or SLEEP DEPRIVED (36hSD) group. Rise time was 08:00, and each group was tested at 18.00h (after normal sleep or SD). Testing consisted of a 'social cognition' test battery focussing on social performance with varying emotional stimuli: Facial Expression Recognition, Intonation Recognition, and 'go no/go' with varying emotion target stimuli.

Results: There was no effect of SD on facial recognition. However, for SD, performance improved for positive faces (i.e. happiness, surprise. $p=0.04$). For intonation, there was a significant effect of condition for both speed ($p=0.008$) and accuracy ($p=0.0005$) when intonation and content were mis-matched. For negative emotions (i.e. anger) SD subjects responded quicker for mis-match conditions ($p=0.018$). Whilst there was no effect of SD on go no/go responses to emotion-related targets, for negative-only target words SD increased hit rate and RT for no/go responses ($p=0.02$).

Conclusion: On tasks of impulsivity and non-verbal communication, SD participants were more resilient when reacting to positive emotion, but negative emotions conveyed through intonation or target words, produced more impulsive error responses. It appears that SD will have a detrimental impact on decision making and interaction in emotionally-charged environments.

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0391**INTERLEUKIN-1 MEDIATES THE EFFECTS OF SLEEP DEPRIVATION ON INTERLEUKIN-6***Guan Z, Vgontzas AN, Bixler EO, Zhang B, Fang J*

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Introduction: Elevation of interleukin-6 (IL-6) in the blood is associated with increased excessive daytime sleepiness. IL-6 levels in the blood are also increased by sleep deprivation (SD) in mice and humans. However, the mechanism by which SD induces IL-6 is unknown. Therefore, we tested the hypothesis that the effect of SD on IL-6 is mediated by interleukin-1.

Methods: Adult male C57BL/6 mice ($n=17$) and IL-1 type 1 receptor knockout (IL-1R1-KO) mice ($n=19$) were sleep-deprived for 6 hours. Control mice ($n=19$ from each strain) were undisturbed in their home cages. The animals were sacrificed immediately after SD. Trunk blood was collected to measure serum IL-6. Brain samples were collected from some mice ($n=5$ in each group) and proteins were extracted from the samples to measure brain IL-6. IL-6 levels in the samples were measured with ELISA.

Results: SD significantly altered IL-6 levels in the serum [treatment-strain interaction, $F(1,70)=11.344$, $p<0.001$]. SD increased IL-6 levels in the serum by 6 folds in C57BL/6 mice [$7.35±0.71$ (control) vs.

$44.64±9.60$ (SD), $q(2,70)=7.315$, $p<0.001$], but not in IL-1R1-KO mice. The serum IL-6 levels in C57BL/6 and IL-1R1-KO mice were not significantly different under the control condition, but significantly different after SD [Concentration (pg/ml): $44.64±9.60$ (C57BL/6) vs. $10.60±1.53$ (IL-1R1-KO), $q(2,70)=6.871$, $p<0.001$]. SD did not alter overall IL-6 levels in any brain regions tested in C57BL/6 mice [control vs. SD (pg/mg protein): cortex ($72.01±2.989$ vs. $78.10±2.624$), hippocampus ($97.50±3.64$ vs. $98.75±5.13$), hypothalamus ($190.40±9.73$ vs. $189.30±8.10$) and brainstem ($451.55±15.01$ vs. $455.90±12.59$)] and IL-1R1-KO mice [control vs. SD: cortex ($62.50±1.52$ vs. $65.40±1.20$), hippocampus ($90.90±5.35$ vs. $97.90±6.58$), hypothalamus ($178.80±4.11$ vs. $175.60±9.63$) and brainstem ($464.05±12.04$ vs. $482.70±25.16$)].

Conclusion: Our results indicate that SD induces large increases of serum IL-6 and this increase is dependent on endogenous IL-1 and IL-1R1. SD did not alter the overall levels of brain IL-6, suggesting brain-derived IL-6 is not involved in physiological sleep regulation.

Support (optional): This research was supported by NIH grant HL64415.

0392**EFFECTS OF SLEEP DEPRIVATION ON THE LATERALIZATION OF BRAIN IL-6 IN C57BL/6 AND IL-1R1-KNOCKOUT MICE***Guan Z, Zhang B, Vgontzas AN, Bixler EO, Fang J*

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Introduction: Interleukin-6 (IL-6) levels are known to be different between left and right cortices in mice, but the mechanisms for this difference are unknown. We tested the hypothesis that the lateralization of brain IL-6 could be influenced by sleep deprivation (SD) and interleukin-1 (IL-1).

Methods: Adult male C57BL/6 mice ($n=5$) and IL-1 type 1 receptor knockout (IL-1R1-KO) mice ($n=5$) were sleep-deprived for 6 hours, starting from light onset on a 12:12h light-dark cycle. The control animals ($n=5$ from each strain) were undisturbed in their home cages. The animals were sacrificed 6 hours after the light onset by decapitation to collect samples from each side of the brain. Proteins were extracted and IL-6 levels in the samples were measured with ELISA. Lateralization index [L-index=left/(left+right)] was used to determine the effects of SD and the differences between the strains. The L-index values of 1.0, 0.5 and 0.0 indicate completely left lateralization, no lateralization and completely right lateralization, respectively.

Results: C57BL/6 mice displayed significantly higher IL-6 levels on the left side of the brain compared to the right side. SD eliminated this difference in the hippocampus [L-index: $0.565±0.015$ (controls) vs. $0.495±0.026$ (SD), $p<0.025$], and tended to decrease the lateralization of IL-6 in the cortex ($0.602±0.006$ vs. $0.574±0.009$) and brainstem ($0.559±0.021$ vs. $0.517±0.008$). Compared with C57BL/6 mice, IL-1R1-KO mice had significantly reduced IL-6 lateralization in the cortex ($0.602±0.006$ vs. $0.535±0.014$, $p<0.001$) and brainstem ($0.559±0.021$ vs. $0.512±0.009$, $p<0.001$). The IL-6 lateralization in the hippocampus was significantly different between C57BL/6 and IL-1R1-KO mice under basal condition ($0.565±0.015$ vs. $0.489±0.009$, $p<0.0250$), but not after SD ($0.495±0.026$ vs. $0.532±0.022$).

Conclusion: IL-6 levels are lateralized in multiple brain regions in C57BL/6 mice. This lateralization is reduced by SD. Our data also suggest that endogenous IL-1 may play important roles in the lateralization of IL-6 and be involved in the effects of SD on this lateralization.

Support (optional): This research was supported by NIH grants HL64415 and HL084990.

0393

RELATIONSHIP OF PRE-STUDY SLEEP AND CIRCADIAN VARIABLES TO NEUROBEHAVIORAL RESPONSES TO PARTIAL SLEEP DEPRIVATION

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Introduction: Differential vulnerability to sleep loss assayed by neurobehavioral responses has recently been demonstrated in subjects undergoing sleep restriction. This study investigated whether such differential vulnerability is related to pre-study objective and subjective sleep patterns and measures of circadian phase.

Methods: N = 155 healthy adults (M=29.9y ± 7.0y; 80 women) completed 2 baseline sleep nights (TIB=10h) followed by 5 sleep restriction nights (TIB=4h) in a laboratory under carefully controlled conditions. The 10-min Psychomotor Vigilance Test (PVT) was administered every 2h on all days. Neurobehavioral phenotypic responses to sleep restriction were characterized using a mean difference PVT lapses/trial metric. This continuous metric is calculated as the mean deprivation lapses/trial (using all deprivation bouts) – mean baseline lapses/trial (using all baseline bouts), whereby lapses were defined as >500 ms response time. Sleep duration, onset, offset and midpoint were assessed for seven days before study entry using actigraphy and sleep diary logs. Chronotype was assessed via the Morningness-Eveningness Questionnaire (MEQ). Spearman's rho correlation coefficient analyses quantified the various relationships between measures.

Results: Pre-study sleep duration (range, 6.39 h-10.07 h) as measured by actigraphy ($\rho=0.04$, $p=0.6$) and sleep diary ($\rho=0.01$, $p=0.9$), showed no relationships to PVT phenotype. Similarly, actigraphic sleep onset ($\rho=0.12$, $p=0.1$) and offset ($\rho=0.14$, $p=0.1$) did not relate to the phenotype variable. Although sleep actigraphic midpoint and MEQ scores were significantly correlated ($\rho=.51$, $p<.001$), neither variable (midpoint: $\rho=0.13$, $p=0.1$; MEQ: $\rho=0.03$, $p=0.7$) associated significantly with the PVT phenotype variable.

Conclusion: Pre-study sleep (duration, onset and offset) and circadian variables (sleep midpoint and MEQ) show weak, nonsignificant relationships to the difference lapses/trial phenotype measure. Thus, these pre-study measures do not underlie differential vulnerability to partial sleep deprivation, as characterized by PVT response.

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0394

SPATIAL MEMORY IMPAIRMENTS DUE TO SLEEP FRAGMENTATION DEPEND ON RAT STRAIN AND TASK DIFFICULTY

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Introduction: The disruption of sleep has been shown to impair the formation of new memories in humans and rats. In humans, performance following sleep deprivation is dependent on both the task difficulty and on the individual's susceptibility to the effects of sleep loss. Two hippocampal dependent spatial memory tasks were used to investigate the effect of task difficulty on performance after 24h of experimental sleep fragmentation (SF). A rat strain (Fischer/Brown Norway; FBN) known to perform well in spatial memory tests was compared to a strain (Sprague Dawley; SD) known to perform more poorly.

Methods: FBN and SD rats were tested in two different versions of the water maze task following 24h of SF. SF was produced using an automated treadmill that woke the rats every 90s. The "easy" water maze task consisted of 3 sessions with 4 trials per session with a 45 min in-

ter-session interval. The "hard" water maze task consisted of 8 consecutive trials with an inter-trial interval of 1 min.

Results: Under control conditions (without SF) FBN rats performed well in both versions of the water maze task, whereas SD rats performed poorly in the "hard" task. Following 24h of sleep fragmentation, SD rats showed impaired acquisition on the "easy" task, whereas the FBN rats showed no acquisition impairment in the "easy" task. On the "hard" task, 24h SF did not impair the spatial acquisition deficits of FBN rats, but recall of the platform location 24h later was impaired.

Conclusion: SD rats are known to have poor performance abilities on the water maze task, especially in comparison to FBN rats. SD rats seem to have greater cognitive deficits following 24h of fragmented sleep compared to FBN rats. This suggests that FBN rats have a greater cognitive reserve so that deficits due to sleep disruption are not noticed unless task difficulty is increased.

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0395

OVERCOMING NORMAL DAYTIME SLEEPINESS: SLEEP LONGER AT NIGHT, TAKE AN AFTERNOON NAP, OR DRINK COFFEE?

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Introduction: People without subjective daytime sleepiness can extend usual sleep by 1-2h, which mostly reduces the mid-afternoon dip. How does this compare with a brief afternoon nap, or coffee? What happens beyond the usual 16:00h MSLT cut-off?

Methods: 20 healthy (25.9y±3.8y) adults, av.7.8h TST, non-nappers, normal MSLT sleepiness, underwent 4 counterbalanced weekly conditions: Normal night sleep; Night sleep extended upto 90min (usual bedtime); 20min afternoon nap at 14.30h; 150mg of caffeine ('blinded' with decaffeinated coffee) given at 14.00h. MSLTs were at: 15:30h, 17:00h, 19:45h, and 23:00h. Subjective sleepiness was logged two-hourly during 12:00-23:00h. Morning sleepiness was assessed by extended (30min) PVTs at 11:00h and 13:00h.

Results: Sleep was able to be extended by av. 74min [s.e. 5.2 min]. All participants napped 15-20min. The morning PVTs showed nsd between-conditions. Subsequent MSLTs were significant between conditions (ANOVA) with post-hoc significances thus: all active treatments had longer SoLs than baseline; nap and caffeine had longer SoLs than sleep extension; nsd between sleep extension and caffeine. Reduced afternoon sleepiness after caffeine did not produce rebound sleepiness that evening. Post-treatment night sleep did not differ between conditions. Subjective sleepiness showed no differences between conditions

Conclusion: Sleep extension was no better than other treatments and somewhat worse. A lengthy sleep-in is an inefficient way of reducing normal (especially afternoon) sleepiness; coffee (150mg caffeine) is equally effective, but neither is as good as a timely <20min nap. One must judge the payoff between extended sleep versus a nap in relation to the impact on one's lifestyle, including the benefits of coffee as a 'quick fix'. Seemingly, our participants only experienced nominal 'sleep debt', that was largely unnoticeable unless they were placed in experimental settings particularly sensitive to sleepiness. A 'sleep-in' can be taken for pleasure as well as need.

Support (optional): UK Economic & Social Sciences Research Council. Kate Jordan assisted with data collection.

Category G—Sleep Deprivation

0396

GENDER EFFECT ON THE SLEEP SLOW EEG FREQUENCIES AND SLEEPINESS DURING 1-WEEK MODEST SLEEP RESTRICTION

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Introduction: The effect of 1-week partial sleep restriction on the slow frequency sleep EEG, and the relationship between subjective sleepiness and spectral EEG data is not known. We hypothesized that women, due to the higher amount of slow wave sleep, will be more tolerant to sleep restriction effects on next-day sleepiness.

Methods: Twenty-two healthy, adult, normal sleepers, (twelve females), participated in a twelve consecutive nights sleep restriction protocol from eight to six hours. The EEG recorded from the central leads (C3-A2, C4-A1) was used. The FFT analysis of the whole night sleep EEG from the two post-adaptation baseline nights and from the seven sleep-restricted nights was completed. The present analysis was concentrated on the delta (0.5-3.5 Hz) and theta (3.5-7 Hz) power. The subjects reported their sleepiness in the morning and at bedtime.

Results: The slow frequency EEG spectral power was significantly increased as a response to the initial sleep restriction, without further increase. Subjective sleepiness increased significantly following initial restriction and remained significantly higher during the remainder of the restriction period. No clear linear relationship was found between chronic sleep restriction and slow frequency EEG power. Females had more slow frequency EEG power than males at baseline, and as a result of initial sleep restriction, as well as significantly higher post restriction morning sleepiness scores.

Conclusion: Post-restriction increased sleepiness and sleep EEG slow wave power appear to reflect increased homeostatic sleep pressure. Females appeared to be more sensitive in terms of slow-wave power to the initial sleep restriction than males. Increased slow-wave power in women did not protect them from the sleep restriction effects on daytime sleepiness.

0397

THE EFFECTS OF CLASS START TIME ON SLEEP PATTERNS AND ACADEMIC PERFORMANCE IN US AIR FORCE ACADEMY CADETS

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Introduction: Studies have shown that sleep quantity is the best predictor of academic performance in college students (Wolfson & Carskadon, 2003), and that sleep loss is correlated with cognitive deficits (Van Dongen et al., 2003). During adolescence, the sleep-wake cycle is marked by later sleep onset times and later wake times. However, school start times for adolescents do not shift accordingly which forces an earlier rise than that of their biological circadian pacemaker. The present study examines the effect of early vs later class start times on sleep habits and academic performance.

Methods: Experiment 1 used archival data from 56,087 cadets at the United States Air Force Academy (USAFA). Grade point average (GPA) and class start time (CST; i.e., 0700, 0730, and 0800) was used for the academic years of 1995-1998, and 2005-2006. Experiment 2 assessed sleep habits and GPA for 350 USAFA cadets, 33 of whom also wore an actigraph for 7 consecutive days and also kept sleep journal.

Results: Data from Experiment 1 were analyzed using a hierarchical linear regression. The overall model was significant with GPA predicted by CST, $F = 31.41$, $p < .001$. The two earliest CSTs elicited the lowest GPAs, and Pearson Correlations revealed CST to be significantly correlated with GPA, $.023$, $p < .001$, such that high GPAs were associated with later CSTs. Results from Experiment 2 supported those of Experi-

ment 1, while also demonstrating a significantly lower total sleep time for CSTs of 0700 ($M = 5.72$ hrs) compared to CSTs of 0750 ($M = 6.44$ hrs).

Conclusion: Concerns over disruptions in daily schedules potentially resulting from later start times must be weighed against the cognitive deficits exhibited by lower GPAs for students in early classes, who are getting substantially less sleep. Institutions of higher education pride themselves on the quality of education offered, yet with sleep deprived students, this asset is not being fully taken advantage of. Moreover, the impact of future leaders of the military and their subsequent sleep expectations of followers is a topic for potential deliberation. Future studies will incorporate other effects of sleep loss, including physiological and demographic variables.

Support (optional): Defense Advanced Research Projects Agency (DARPA)

0398

WAKE: WHAT IS IT GOOD FOR?

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Introduction: Individual deletion of arousal neuronal groups such as the LC, TMN, basal forebrain cholinergic neurons produces only minimal differences in baseline sleep/wake regulation. Arousal circuitry redundancy could be responsible for this, but it is also possible that conditions under which baseline wakefulness are recorded in rats do not behaviorally require sustained arousal. Here we expose rats to highly arousing stimuli during the rest period to examine fundamental arousal mechanisms.

Methods: Rats were exposed to highly arousing stimuli of novel social interactions with littermates and a series of novel objects presented at regular intervals (70min.) during the normal sleep phase (ZT6-11). LC lesions were performed by unilateral injection into the lateral ventricle of saporin conjugated to a dopamine-beta-hydroxylase-specific antibody (α -DBH-SAP, 0.25-1 μ g). TMN lesions were also performed using orexin-conjugated saporin.

Results: Animals spent significantly more time awake during novelty exposure ($95.1 \pm 1.3\%$, filled bar) than during the same period 24 hours prior in which no novel stimuli were present ($28.6 \pm 4.8\%$, open bar, $p = 1 \times 10^{-7}$, $n = 6$). Novel objects alone or novel social interaction alone was unable to elicit this amount of sustained wakefulness over the 5 hour period of time tested ($51.6 \pm 3\%$ and $57.3 \pm 2.5\%$, respectively, $n = 4$ each). Fos expression was increased in the cerebral cortex, LC, and other arousal areas. In LC lesioned animals, total wakefulness during novelty exposure was generally reduced, and correlated with the total LC neurons remaining ($r = 0.8$, $p < 0.01$).

Conclusion: Similar to a human presented with highly arousing stimuli during the rest phase, the natural response of a rat is to sustain wakefulness. Lesions of brain arousal regions such as the LC—which have no effect on baseline wakefulness—impair this response, and therefore this technique may have broader applicability to the study of arousal regulation.

Support (optional): NS051609

0399

THE DEVELOPMENT AND VALIDATION OF A COMPUTERIZED SLEEP DEPRIVATION MEASURE (ZZ-TEST)

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Introduction: Several tests have been developed to evaluate the change in cognitive performance associated with sleep deprivation (SD). The

aim of the present study is to investigate the construct validity of a new SD measure ZZ-Test, and to explore the relationship between the ZZ Test and the level of SD and wakefulness.

Methods: The ZZ Test is a computerized measure of vigilance, attention and visual memory designed by the first author. The test includes four trials of increasing difficulty. As advantages, it can be used on any computer, is self-administered and is shorter than many of the presently available measures of attention. In a pilot study, we administered the ZZ Test to 10 healthy subjects. In the next phase, to investigate the construct validity of the ZZ Test we are planning to administer several tests of attention (ZZ-Test, Digit Span, Trail Making Test, Stroop Color-Word Test, Wisconsin Card Sorting Test, and the Conners Continuous Performance Test) in a counterbalanced order to 50 more subjects including subjects with different levels of SD. Statistical analysis will include factor analysis and regression analysis.

Results: The pilot study included 10 subjects (F=5, M=5), age 21-51 years, mean age 34.8 (9.24). Scores ranged from 0 to 10. The time to complete the test ranged from 4 to 10 minutes depending on subject's advancement in the sequenced trials. ZZ-test scores correlated significantly with the wakefulness score ($p=0.004$), the number of hours of sleep the night before ($p=0.001$), and the average hours of sleep over the past week before the test administration ($p=0.001$).

Conclusion: The ZZ-test results correlated significantly with the other subjective SD measures. As indicated previously, we are currently evaluating the construct validity of ZZ-Test in a group of 50 healthy subjects. The final results of our study will be available by late February 2008.

Support (optional): The authors report no financial relationship with any company whose products are mentioned in this manuscript, or with companies of competing products.

0400

PVT PERFORMANCE AS A FUNCTION OF TOTAL SLEEP TIME IN A DOSE RESPONSE SLEEP RESTRICTION EXPERIMENT WITH AND WITHOUT NAPS

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Introduction: This study investigated the effect of restricted nocturnal sleep schedules with and without diurnal naps on psychomotor vigilance test (PVT) performance. Previously reported results from this study focused on the "intent-to-treat" intervention as represented by time in bed (TIB). The key result was that neurobehavioral deficits were primarily a function of total TIB per 24h—regardless of how sleep was divided among nocturnal anchor sleep and diurnal nap sleep periods. The current analysis focuses on sleep actually obtained in the TIB allowed—the "as-treated" measure of total sleep time (TST).

Methods: N=90 healthy adults (21-49y; 38 females) participated in a 10-night sleep restriction protocol (PSG recorded) where they were randomized to one of 18 sleep schedules involving restricted nocturnal anchor sleep (4.2h, 5.2h, 6.2h, 8.2h TIB) and diurnal nap (0.4h, 0.8h, 1.2h, 1.6h, 2.0h, 2.4h TIB) or no nap. PVT performance was tested at 2h intervals and lapses (RT>500ms) were averaged within each subject on each day. Response surface maps with increasing degrees of freedom were fitted to examine the build-up of performance impairment across the 10 sleep-restriction days as a function of anchor and nap sleep TST across the 18 conditions.

Results: The build-up of performance impairment over the 10 restriction days was found to be well described by a function of daily overall TST (i.e., anchor +nap), with less overall TST per 24h resulting in a more rapid build-up of PVT lapses ($\chi^2[1]=5.8$, $p=0.016$). Differentiating between anchor and nap sleep durations did not result in significantly improved goodness-of-fit ($\chi^2[1]=1.1$, $p=0.28$).

Conclusion: In agreement with results found using TIB as the independent variable, PVT performance was primarily a function of overall TST per 24h during 10-days of sleep restriction. This result suggests that total daily sleep duration, whether consolidated or split, is the primary determinant of neurobehavioral function over days.

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0401

SLEEP DEPRIVATION DECREASES POSITIVE FACIAL DISPLAYS IN RESPONSE TO AMUSING FILM CLIPS

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Introduction: Very little is known about the importance of sleep for emotional functioning. The purpose of this study was to determine the effects of sleep deprivation on facial expressiveness in response to emotionally provocative film clips.

Methods: This experiment was conducted in a controlled laboratory setting. Healthy adult volunteers (N=19, female = 6) entered the laboratory at 09:30h and completed testing throughout the day. At night, they were randomly assigned to a night of no sleep (n=11) or 9-hours sleep opportunity (23:00h to 08:00h, n=8). Subjects were shown two film clips (one sad and one amusing) on each day of the protocol between 16:00h and 18:30h. Videotape of subjects' faces as they watched the films was coded by a trained research assistant (blind to all conditions) according to a validated manual. All subjects received 10 hours of recovery sleep prior to discharge.

Results: Between groups comparisons for day 2 (deprivation vs. no deprivation) demonstrated that sleep deprived subjects showed fewer positive facial displays during the amusing film clip than control subjects ($t=3.75$, $p=0.002$). Similarly, within subjects comparisons showed that subjects who were sleep deprived showed significantly fewer positive displays after sleep deprivation relative to before sleep deprivation ($t=2.55$, $p=0.03$) while control subjects showed no such difference ($t=0.29$, $p=0.76$). No differences were found between or within groups for negative displays to the sad film clips.

Conclusion: These results suggest that sleep deprivation reduces positive facial expressions in response to amusing film clips. The study did not find that negative displays during sad film clips changed with sleep deprivation. More research is needed with larger samples and more varied emotional stimuli to further investigate how sleep deprivation influences emotional expressiveness.

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0402

ALTERED PERIPHERAL VASCULAR REACTIVITY IN HEALTHY ADULTS DURING TOTAL SLEEP DEPRIVATION

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Introduction: The mechanism by which blood pressure is increased during sleep deprivation (DEP) is not clearly understood but it may due to increased arterial vasoconstriction. We investigated the vascular reactivity of a muscular type artery.

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Methods: Twelve subjects participated (5 stayed awake continuously for up to 88 hours (5 women, 39.4±4.8 years) and 7 slept at night (3 women, 4 men, age 30.3±2.1). We performed the flow mediated dilation test (FMD) and arterial diameter and blood flow of the brachial artery were recorded with a pulsed Doppler ultrasound and analyzed from B-Mode images (HDI 5000, ATL Ultrasound). Beat-by-beat blood pressure data were recorded by photoplethysmography (Portapres, FMS) and hemodynamic parameters were calculated.

Results: During FMD test: Arterial diameter showed a decreasing trend throughout DEP and the comparison between baseline day (BL) and 34 hours was significant (diameter, cm±SE at BL: 0.32±0.01 vs. 34 hours: 0.30±0.01, $p<0.01$). Blood velocity also showed a decreasing tendency throughout DEP and the difference was significant between baseline and 58 hours SD (blood velocity, cm/s±SE at BL: 101.5±12.2 vs. 58 hours: 68.3±5.1, $p<0.05$). Peak blood flow showed a decreasing trend throughout DEP and the comparison between the BL and 58 hours was significant (peak blood flow, ml/min±SE at baseline: 490.4±41.0 vs. 58 hours: 275.3±29.4, $p<0.01$). Vascular resistance showed a tendency for an increase throughout DEP and the comparison between BL and 58 hours was significant (vascular resistance, mmHg*min/ml±SE at BL: 0.15±0.02 vs. 58 hours: 0.3±0.04, $p<0.05$). There was a tendency for an increase in the mean arterial pressure throughout DEP days.

Conclusion: Our preliminary data suggest that acute total sleep deprivation leads to alterations in the peripheral vascular response due to an increasing vasoconstriction. This may be the result of increased sympathetic outflow due to autonomic activation or altered local peripheral control mechanisms.

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0403

EMOTIONAL INTELLIGENCE PREDICTS DECLINES IN EMOTION-BASED DECISION-MAKING FOLLOWING SLEEP DEPRIVATION

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Introduction: Sleep deprivation reduces metabolic activity in emotion-related regions of the prefrontal cortex and is associated with declines in Emotional Intelligence (EQ) and advantageous decision-making as measured by the Iowa Gambling Task (IGT). According to the Cognitive Reserve hypothesis, individuals with higher EQ should be less affected by the adverse effects of sleep loss on prefrontal regions. It is also possible, however, that individuals with higher EQ may actually be more vulnerable due to the fragility of these more complex cognitive-emotive processing systems. We tested these competing hypotheses.

Methods: Twenty healthy volunteers (5 women and 15 men; Age = 20 to 35 years) were administered the BarOn Emotional Quotient Inventory (EQ-i) at rested baseline. Participants remained awake for 77 hours and completed the Iowa Gambling Task (IGT) at baseline, and after 55 and 75 hours of sleep deprivation. Nine participants also received multiple doses of caffeine (800 mg total each night). Correlation and linear regression analyses was used to predict changes in the IGT performance (i.e., the final 20 card block) from baseline as a function of EQ.

Results: Total EQ and its sub-facet scores were significantly and negatively correlated with IGT change scores. After accounting for baseline level of performance, IGT decline at 55 hours was predicted by Total EQ ($r=-.62$, $p=.01$), Adaptability ($r=-.74$, $p=.002$), and Stress Management ($r=-.51$, $p=.05$). By 75 hours, IGT decline was predicted only by Adaptability ($r=-.56$, $p=.03$). Caffeine had no effect on these relationships.

Conclusion: Higher emotional intelligence was associated with more severe decrements in emotion-based decision-making following sleep deprivation, regardless of baseline performance or caffeine administra-

tion. Sleep deprivation appears to affect critical nodes in the emotion-cognition processing system, producing greater deficits in those individuals with the most extensively developed EQ capacities. During periods of sleep deprivation, greater complexity may also mean greater vulnerability.

0404

TOTAL SLEEP TIME MEASURED BY ACTIGRAPHY PREDICTS ACADEMIC PERFORMANCE DURING MILITARY TRAINING

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Introduction: Inadequate sleep is known to impair a variety of cognitive capacities, including attention, vigilance, concentration, memory encoding, and some aspects of higher order reasoning and judgment. The ability to unobtrusively measure fatigue and predict its effects on cognitive performance is vital to successful military operations. Wrist actigraphy is one such method, but its ability to accurately measure and predict performance in militarily relevant activities is not well validated.

Methods: 108 healthy military volunteers were fit with wrist actigraphs (Actiwatch; Minimitter Inc.) while undergoing one of six military education programs lasting between 4 to 6 weeks. 64 Actiwatchs were worn consistently and yielded valid data. Actigraphic sleep data were analyzed with Actiware 3.41 using automated scoring algorithms. Indices of sleep duration, latency, and quality were used to predict academic success in these courses.

Results: Averaging across all courses and volunteers, Soldiers obtained 5.8 hours of sleep per night (SD=0.5). Sleep duration was typically reduced to 4.6 (SD=1.5) hours the night preceding an exam. Regardless of course type or test content, academic performance was significantly predicted by total sleep time (48 hours before, $r=.60$, $p<.001$; 24 hours before, $r=.54$, $p<.001$), sleep latency (48 hours before, $r=-.46$, $p=.002$; 24 hours before, $r=-.46$, $p=.002$), number of immobile minutes (48 hours before, $r=.58$, $p<.001$; 24 hours before, $r=.52$, $p=.001$), and fragmentation index (48 hours before, $r=.29$, $p=.05$; 24 hours before, $r=.28$, $p=.05$), but not total activity level (48 hours before, $r=.06$, ns; 24 hours before, $r=.07$, ns).

Conclusion: Regardless of course or exam content, academic performance was significantly related to the amount and quality of sleep obtained within the 48-hour period preceding the exams. Actigraphy appears to be a valid and unobtrusive method for predicting academic performance in military courses, although issues of participant compliance and detection of off-wrist periods need to be improved.

0405

NONVERBAL INTELLIGENCE IS INVERSELY RELATED TO THE ABILITY TO RESIST SLEEP LOSS

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Introduction: Some individuals appear to be resistant to the detrimental effects of sleep loss. Factors such as age, personality, genetics, and regional brain activity account for some variability in these effects. The Cognitive Reserve Hypothesis (CRH) suggests that individuals with greater cognitive capacity should have more reserve function to draw from to compensate for sleep loss induced decrements in cognitive functioning. To test this hypothesis, the relationship between nonverbal intelligence, measured by the Computerized Test of Nonverbal Intelligence

(C-TONI), and psychomotor vigilance speed over three nights of continuous sleep deprivation was examined.

Methods: Twenty-three healthy volunteers (4 women; 19 men; Ages 20 to 35 years) completed the C-TONI when rested and then remained awake for 77 hours while completing psychomotor vigilance testing (PVT) at 10-25 minute intervals from 0015 to 0845 each morning. 12 subjects also received caffeinated gum (200mg) every two hours. PVT speed was converted to percent of baseline (PVT%) for each subject for each night.

Results: After statistically controlling for caffeine group and subject age, Geometric Nonverbal IQ (GNIQ; a measure of fluid intelligence) emerged as significantly negatively correlated with average PVT performance by the third night without sleep (partial $r=-.49$, $p=.023$), but not for the previous two nights. This was most significant during the middle (partial $r=-.64$, $p=.002$) and last (partial $r=-.50$, $p=.022$) thirds of the third night. Pictorial Nonverbal IQ (PNIQ) and Total Nonverbal Intelligence (NIQ) were not significantly correlated with PVT.

Conclusion: Contrary to the CRH, we found that higher nonverbal intelligence was associated with greater vigilance impairment by the third night of wakefulness. More intelligent individuals showed greater decrements. These findings suggest some “vertical instability” in the ability to resist sleep deprivation, where individuals with the most complex and well developed intellectual capacities may be most vulnerable to disruption by sleep loss.

0406

EFFECT OF SLEEP INERTIA ON OBJECTIVE AND SUBJECTIVE TESTS OF SLEEPINESS BEFORE AND AFTER SLEEP RESTRICTION

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Introduction: Sleep inertia is a state characterized by a decline in performance and a subjective feeling of grogginess, immediately following an abrupt awakening from sleep. This study examined the effect of sleep inertia on both subjective and objective tests of sleepiness after a period of 5 nights of sleep restriction to 4h time in bed (TIB).

Methods: N = 95 healthy adults (30.3 ± 6.9y; 50 females), underwent 2 baseline nights (10h TIB/night, 10pm-8am), followed by 5 sleep restriction nights (4h TIB/night, 4am-8am) in a controlled laboratory setting. Every 2 hours during wakefulness (8am [directly upon awakening], 10am, 12pm, 2pm, 4pm, 6pm & 8pm) subjects completed a test bout that included a 10min Psychomotor Vigilance Test (PVT) and the Stanford Sleepiness Scale (SSS). Scores were averaged among subjects and paired t-tests were conducted to compare the test bouts at baseline day 2 (B2) and after the 5th night of sleep restriction (SR5).

Results: SSS scores and number of PVT lapses were highest at the 8am sleep inertia test bout relative to all other test bouts on B2 ($p<0.001$). Similarly, SSS scores and number of PVT lapses were highest at the 8am sleep inertia test bout relative to all other test bouts on SR5 ($p<0.001$). A comparison of SR5 and B2 revealed that the 8am sleep inertia test bout on SR5 had higher PVT lapses and SSS scores than B2 ($p<0.001$).

Conclusion: Sleep inertia adversely affected 8am PVT performance and subjective reports of sleepiness (SSS). Additionally, the effect of sleep inertia was made worse by sleep restriction. These results have implications for professions such as shift work where time for sleep is chronically reduced, but abrupt awakenings from sleep are common.

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0407

SLEEP QUALITY AND SLEEPINESS AMONG RESIDENT PHYSICIANS AND PATIENTS

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Introduction: Sleep deprivation is a common problem in both health care workers and hospitalized patients. Sleepiness in resident physicians have been associated with medical error, and increased risk of automobile accidents post call. Sleep deprivation in patients has been shown cause depression, decrease immunity and mood disturbances to name a few. We wished to objectively measure sleep quality, and sleep fragmentation among residents and hospitalized patients in telemetry unit by using wrist actigraphy.

Methods: 11 residents and 13 patients on telemetry floor were assessed by using actigraph. Residents wore the actigraph for seven days, whereas the patients wore the actigraph for their duration of stay. Subjective sleepiness was assessed by Epworth sleepiness score (ESS) administered at the end of the study period.

Results: Average resident age was 30.9 years where as an average patient age was 64.92 years ($p<0.001$). There was no statistical difference in BMI between resident and patients. There was also no difference between the total sleep time and number of awakening between residents and patients. The waking after sleep onset was significantly higher among the patients 106.4 minutes as compared to residents 38.57 minutes ($p<0.05$), even though there was no difference among the Epworth sleepiness score.

Conclusion: In contrary to the general perception both patients and residents are getting approximately seven hours of sleep. It is the quality of sleep which makes the difference, rather than quantity of sleep. Sleep time in patients tends to be severely fragmented. Measures aimed at improving sleep continuity among patients may help improve their functional status.

0408

RECOVERY SLEEP STAGE DYNAMICS FOLLOWING CHRONIC SLEEP RESTRICTION

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Introduction: Theoretical models of sleep homeostasis suggest an exponential rebound of Slow Wave Sleep (SWS) during recovery sleep from total sleep deprivation. However, there has been little systematic examination of recovery sleep stages after multiple days of sleep restriction. A sleep dose-response study was conducted to determine the nature of sleep stage rebound following chronic sleep restriction.

Methods: N=88 healthy subjects (age range 22-45y; 43 females) participated in a laboratory-controlled chronic sleep restriction protocol. Subjects underwent 2 nights of baseline sleep (10h TIB) followed by 5 nights of sleep restriction (4h TIB) and a recovery night (R1) where TIB was given in different doses (2, 4, 6, 8 & 10h TIB). Subjects were monitored during sleep polysomnographically using a standard montage (C3/A2, EOG and EMG). Sleep was scored by a trained technician according to R&K criteria. The durations of SWS, stage 2, REM, total sleep time (TST), sleep latency (SL), and the percentage sleep efficiency (EF) were calculated on R1 in each of the sleep doses.

Results: Linear and quadratic models were fit to the sleep dose functions for every sleep variable. A quadratic model best fit SWS ($R^2=0.187$), while a linear model best fit stage 2 ($R^2=0.68$), REM ($R^2=0.86$), TST ($R^2=0.89$), SL ($R^2=0.19$), and EF ($R^2=0.16$). Greater TIB at R1 re-

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sulted in more of each of the sleep stages, shorter SL, and greater SE, with the exception of SWS which was similar for all R1 doses >4h (all $p < 0.001$).

Conclusion: These data suggest that rebound of sleep stages from chronic sleep restriction is primarily linear with increases in TIB sleep doses up to 10h. Only SWS was characterized by a quadratic model, suggesting that the exponential process instantiated in theoretical models of sleep homeostasis based on total sleep deprivation studies extends to recovery sleep following chronic sleep restriction.

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0409

CHRONOTHERAPEUTIC AUGMENTATION OF ANTIDEPRESSANT MEDICATION CAN ENHANCE RAPIDITY AND MAGNITUDE OF RESPONSE AND CLOCK GENETIC FUNCTIONAL EXPRESSION

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Introduction: We have done the first study that directly compares the efficacy of a package of chronotherapeutic intervention consisting of sleep deprivation (SD), sleep phase advance (SPA), and bright light (BL) morning therapy in augmenting the response to antidepressants vs. medication only. Fifty-five bipolar depressed or major depressed disorder patients were randomly assigned to either chronobiological augmentation package of antidepressant medication (SSRI and mood stabilizer) vs. medication alone. Patients were followed for seven weeks. We found a significant group by time interaction with follow up contrasts showing that the chronotherapeutic augmentation group had greater decreases in Hamilton Rating for Depression scores beginning two days after sleep deprivation and continuing for seven weeks.

Methods: 55 depressed bipolar patients who met DSM-IV criteria were recruited and Assigned into Medication Only arm vs. Medication plus Sleep Deprivation (SD) plus Light Therapy (LT) plus Sleep phase advance (SPA). The patients were followed for seven weeks with Hamilton Rating Scale for Depression. Blood samples were drawn for Affymetrix U133 Genechip analysis before and after SD.

Results: Significant group by time interaction with follow up contrasts showed that depressed patients with chronotherapeutic augmentation (SD + LT + SPA) responded faster and showed greater magnitude antidepressant response than medication only. Twelve clock genes were studied apriori (CLOCK, PER1, PER2, NPAS2, CRY1, CRY2, BHLB2, BHLB3, CSNK1E, ARNTL, DBP, RORA) Statistical criteria was group by time ($p < .05$) Sleep dep responders showed increased gene expression for three of four significant clock genes (RORA, BHLB2, PER1) AND significant decrease gene expression for CLOCK.

Conclusion: This is the first study to show that chronotherapeutic augmentation with SD, LT, and SPA better than medication alone. This is also the first study to show that there are functional differences in clock gene expression in sleep dep responders vs. nonresponders.

0410

THREE-HOUR SLEEP LOSS IMPACTS SPEECH PERCEPTION IN ADULTS

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Introduction: Previous research demonstrates that total amount of sleep may influence cognition and behavior. Adults react slower on specific cognitive tasks and select less-challenging tasks when given a choice after sleep loss. In this study, we used a speech perception task to in-

vestigate changes in neural processes that might occur after minor sleep loss in adults.

Methods: Sixteen participants (9 males) between the ages of 30 and 45 who held a M.D., Ph.D., or equivalent terminal degree were recruited. Following an overnight polysomnography screening, participants were tested in the lab at the end of each week for two consecutive weeks. Participants were instructed to maintain their normal sleep schedules during week one. Throughout the second week they were directed to restrict their sleep by three-hours per evening. ERPs were recorded from participants using a 256-high density array electrode array while they listened to randomly ordered series of 6 different consonant-vowel sounds.

Results: A temporal principal component analysis (PCA) using a Varimax rotation identified 6 regions of the ERP that accounted for 88.23% of the total variance. A 9 (electrode) x 2 (sex) x 2 (hemisphere) x 6 (stimulus) x 2 (week) ANOVA was then applied to each region to identify potential main effects and interactions. A Greenhouse-Geisser correction was applied to all significant findings. A main effect for week occurred between 172 - 332 ms after stimulus onset, $F(1, 14)=6.53$, $p=.023$. ERP waveforms differed before and after losing three-hours of sleep, $t(15)=2.64$, $p=.019$. A week x hemisphere interaction also occurred, $F(1, 14)=7.87$, $p=.014$, indicating that left hemisphere processing changed during sleep-restriction, $t(15)=3.83$, $p=.002$.

Conclusion: Participants showed clear differences in cortical processing after losing modest amounts of sleep each night for one week. This study demonstrates that sleep loss can impact the way the brain handles simple tasks, such as speech perception.

0411

THE RELATIONSHIP BETWEEN EXCESSIVE DAYTIME SLEEPINESS AND MARKERS OF INFLAMMATION - THE MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS

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Introduction: Sleep deprivation and sleep disorders, e.g., sleep apnea, have been associated with increased levels of inflammatory markers. Furthermore, higher levels of inflammatory markers have been observed among obese individuals, independent of sleep apnea. Excessive daytime sleepiness (EDS) can result from sleep disorders, but it is also associated with chronic health conditions, including obesity and diabetes. We sought to characterize the relationship between subjective EDS and inflammatory markers, as measured by C-reactive protein (CRP) and interleukin-6 (IL-6), in a large multi-ethnic cohort.

Methods: MESA is a multicenter, longitudinal cohort study of the prevalence and correlates of subclinical cardiovascular disease and the factors that influence its progression. Individuals were included if they had no history of clinical cardiovascular disease. The cohort includes 6814 White, Black, Hispanic, or Chinese men and women between 45- 84 yr of age who were recruited from six U.S. communities. Demographics and inflammatory biomarker levels at baseline and self-reported EDS and daytime napping at 2 year follow-up were included in the analysis. Obstructive sleep apnea (OSA) was assessed by physician diagnosis or patient reported symptoms.

Results: Complete data were available from 5,841 participants. Using multivariable logistic model to adjust for age, race, gender, and baseline status of BMI, smoking, alcohol use, hyperlipidemia, hypertension, diabetes, depression, and OSA, the odds of reporting EDS at follow-up was significantly associated with higher levels of baseline CRP (OR tertile 3 ≥ 3.19 mg/dl] = 1.21; p trend = 0.034). Similarly, regular napping was associated with higher levels of baseline IL-6 (OR tertile 3 ≥ 1.58 pg/ml] = 1.17; p trend = 0.046).

Conclusion: These data indicate that higher levels of inflammatory markers are associated with EDS and napping independently of BMI and OSA. Future studies are needed to address mechanisms of this relationship.

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0412

EFFECTS OF SLEEP DEPRIVATION ON BLOOD PRESSURE AND VASCULAR CELLULAR ADHESION MOLECULES

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Introduction: Epidemiological studies link short sleep with increased relative risk for developing diabetes and cardiovascular disease. Experimental sleep deprivation leads to a small elevation in inflammatory mediators and BP. The mechanisms by which these changes occur, and their overall effects on long-term health, are not fully understood. We investigated the changes in BP and soluble vascular cellular adhesion molecule-1 over the course of prolonged total sleep deprivation (TSD) and recovery sleep.

Methods: Subjects were 22 healthy participants (7 females, 15 males, mean age 34.4 ± 1.7 yrs, no current history of any medical disorders, habitual sleep duration between 6.5 and 9.0 hrs). Systolic blood pressure (SBP) was analyzed for 21 and plasma sVCAM-1 levels analyzed for 22 participants. Starting on the 2nd baseline day, participants were equipped with recording devices to monitor blood pressure, temperature, EEG; blood and urine were also sampled. On the 3rd day participants were randomized to sleep or sleep deprivation conditions. Lights and posture were controlled during the 7 day in-hospital stay, and participants were closely monitored by an experimenter throughout the waking periods of the study to prevent any non-scheduled sleep episodes. Nocturnal blood pressure was measured using the Portapres System (continually measures blood pressure on a beat to beat basis). sVCAM-1 was measured in serum using Enzyme-Linked Immunosorbent Assay (ELISA) methodology (R&D Systems). sVCAM-1 was assayed from the 05:30 am fasting blood sample taken during sleep/sleep deprivation at baseline and through the 3 deprivation nights and during recovery sleep. Mixed models analysis of variance was used to statistically analyze the systolic blood pressure (SBP) and the sVCAM-1 data.

Results: Systolic blood pressure increased significantly during deprivation at night for all sleep deprived subjects (on average from 112 to 135 mmHg for sleep deprivation, compared with 111 to 110 mmHg for the sleep condition) ($p < 0.05$). sVCAM-1 levels significantly increased during the three nights of sleep deprivation by > 90 ng/ml over the normal sleep control ($p < 0.05$) and remained elevated during the recovery sleep. sVCAM-1 increases were correlated with increased SBP levels on the second night of sleep deprivation ($r = 0.40$; $p < 0.05$).

Conclusion: Sleep deprivation increases SBP and sVCAM-1. This elevation in blood pressure observed during sleep deprivation may lead to the increase seen in sVCAM-1.

Support (optional): HL 075501 and GCRC RR01032

0413

ELECTROENCEPHALOGRAPHIC CORRELATES OF HABITUAL SLEEP DURATION PATTERNS IN A COMMUNITY SAMPLE: THE SLEEP HEART HEALTH STUDY

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Introduction: Self-reported habitual sleep duration is associated with increased risk of poor health outcomes, although little is known about

objective measures of sleep associated with self-reported patterns. The purpose of this study was to describe the association between EEG spectral power indices and habitual sleep duration patterns, and to assess the impact of sleep-related conditions in a community-based sample.

Methods: Data from the Sleep Heart Health Study ($n = 6,369$) were analyzed. A questionnaire administered to participants provided data on self-reported habitual sleep duration patterns on weekdays and weekends. Electroencephalographic data from C4 and C3 leads were collected from one night of at-home polysomnography. Spectral power in delta (0.8-4.0 Hz), theta (4.1-8.0 Hz), alpha (8.1-12.0 Hz), sigma (12.1-16.0 Hz) and beta (16.1-32.0 Hz) frequency bands (both absolute and percent power) was calculated for each 30-s epoch of sleep using the fast Fourier transform. Generalized linear models were used to estimate differences in median spectral power indices across categories of usual sleep duration (< 6 , 6 to < 7 , 7 to < 8 , 8 to < 9 , and > 9 hours), with adjustment for age, sex, race/ethnicity, body mass index, smoking, sleep-disordered breathing (SDB), excessive daytime sleepiness (EDS), and insomnia.

Results: Median absolute delta power was increased for habitual sleep duration of < 7 hours relative to those sleeping 8 to < 9 hours per night ($p < 0.05$). The pattern persisted after covariate adjustment. Similar results were found after excluding wake epochs. Findings differed slightly for median percent delta power, with decreased percent delta among weekend sleep extenders ($p < 0.05$). Further spectral power analyses were conducted for other frequency bands.

Conclusion: Differences in spectral power indices across usual sleep duration found in these data were not explained by other conditions associated with sleep duration. Assessment of electroencephalographic (EEG) features associated with habitual sleep behaviors could improve understanding of mechanisms or mediators underlying the association with poor health.

0414

EXPRESSION OF GENES RELATED TO BRAIN ENERGY METABOLISM FOLLOWING PHARMACOLOGICAL AND INSTRUMENTAL SHORT SLEEP DEPRIVATION

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Introduction: It has been hypothesized that sleep could serve to restore the brain glycogen levels used during wakefulness. We have previously shown that enzyme activity and expression of genes related to glycogen synthesis were up-regulated after a 6hour sleep deprivation in the cerebral cortex of mice. Here, we investigated the effects of a shorter sleep deprivation period (3-4h), on the expression of genes related to glycogen metabolism (GlycMet), glucose transport and phosphorylation (GluTP) and genes involved in the pentose phosphate pathway (PPP), in the anterior and posterior parts of the cerebral cortex (antCx, postCx), the cerebellum (Crb) and the hippocampus (Hip).

Methods: Prolonged wakefulness was induced by "gentle sleep deprivation" (GSD) or by a pharmacological method using Ritaline (40mg/Kg) and Modafinil (150mg/Kg) in adult C57BL/6j mice. The gene expression was determined by qRT-PCR.

Results: Ritaline induced a significant increase in PTG mRNA levels in the aCx whereas the GSD induced a increase in PTG mRNA levels in the pCx. Ritaline, Modafinil or GSD failed to induce significant variations of the other genes related to GlyMet. The levels of GLUT1 mRNA were significantly induced in the Crb by GSD and Ritaline whereas Modafinil failed to induce the expression of the GLUTs mRNA in this structure. Ritaline exhibited a specific action on PPP, an effect that do not seems to be related to sleep deprivation since GSD or MOD have no action on these genes. No significant variation of gene expression was observed in the Hip.

Conclusion: This study shows that short period of forced wakefulness induced by GSD or by psychostimulant drugs exerts a stimulating action on the expression of specific genes related to glucose transport and metabolism. Finally, the lack of action of Modafinil on the expression of

Category G—Sleep Deprivation

gene related to energy metabolism stress on the specific features of this wake-promoting drug.

0415

SLEEP RESTRICTION CAUSES PHONEMIC DECODING DIFFERENCES IN ADULTS

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Introduction: Myriad studies investigating sleep deprivation and minor sleep loss have shown negative effects on cognitive performance. Reduced functioning, including slower reaction and decreased alertness have adverse effects on speech processing. An underlying component of speech processing and thereafter receptive language is phonemic decoding. Event-Related-Potentials (ERPs) examine auditory perception and information processing. The present study used ERPs to investigate differences of various speech sounds as a function of sleep loss in adults.

Methods: Forty-two participants (21 males) holding a doctorate between the ages of 30 and 45 were recruited for two weeks and tested at the end of each week. They were assigned to a control, one-hour, or three-hour sleep restriction per evening during the second week of study. A 256-electrode net recorded participants' ERPs while attending to six different speech sounds. Sounds (/ba/, /da/, /ga/, /bu/, /du/, /gu/) varied by vowel (/a/ and /u/) and place of articulation (bilabial, alveolar, velar). After hearing the speech sound, participants responded using a pre-designated number value (i.e. "ba" or "bu" = 1, "da" or "du" = 2, "ga" or "gu" = 3) on a response pad.

Results: Factor 1 (272- 776 ms) A week x condition x electrode x sleep group interaction existed, $F(32, 608) = 1.903$, $p = .002$, obs. power = .999. Analysis also revealed a week x condition x hemisphere x sleep group interaction existed, $F(4, 76) = 3.417$, $p = .013$, obs. power = .832.

Conclusion: Mild sleep loss has shown to have an adverse effect on phonemic decoding. This study demonstrates that there is a significant difference during the passive response to phoneme cognates between the control group and the sleep restricted participants. These findings suggest that sleep deprivation negatively effects speech processing, which is critical to the larger scope of receptive language.

0416

PAT HYPNOGRAM: SLEEP STAGES ASSESSMENT USING PERIPHERAL ARTERIAL TONE AND ACTIGRAPHY

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Introduction: We previously described algorithms to detect REM sleep stage using Peripheral Arterial Tone (PAT) and actigraphy. We further developed the algorithms using same frequency domain derivatives of the PAT signal for full sleep stages stratification that can now differentiate between light, deep, REM and wake stages.

Methods: AA set of 49 (40 males) OSA patients and normal volunteers undergoing simultaneous standard full PSG and PAT recording were used as a training set for the algorithms development. A separate set of 44 OSA suspected patients (30 males) and 10 healthy volunteers (8 males) was used to validate the algorithms. Different characteristics of the PAT amplitude and the Pulse rate in the time and frequency domains were extracted. The main characteristics in the frequency domain were derived for frequency ranges corresponding to respiratory, baro-receptor, thermoregulation and hormonal ranges: 0.4 -- 0.15 Hz (HF), 0.15 -- 0.04 Hz (LF), 0.04 -- 0.015 Hz (VLF) and 0.015 -- 0.005 Hz (ULF) respectively.

Results: Overall sensitivity, specificity and agreement of the automatic algorithm to identify standard 30sec epochs of light and deep sleep stages were 66%, 89%, 82% and 65%, 87%, 80% for the training and validation sets respectively. The validation set showed a very little degradation compared to the training set. Together with the already existing algorithms for REM and wake detection we propose a near-full sleep stages detection based on the PAT and Actigraphy signals only. The total agreement of detecting the 4 stages (wake, light, deep, REM sleep) is 68% which is slightly below the reported inter-scoring variability of 69.3%. The correlation of percent deep sleep over the night compared to PSG was 52% ($P < 0.05$).

Conclusion: The PAT signal coupled with actigraphy signal gives a reasonable accuracy in detecting sleep stages. We propose it can thus offer a new tool for ambulatory studies.

Support (optional): Itamar Medical Ltd. Cesarea, Israel; ²Sleep Lab, Rambam Medical Center, Technion, Haifa, Israel

0417

AIR LEAK IS ASSOCIATED WITH POOR ADHERENCE TO AUTO-PAP THERAPY

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Introduction: In bench studies, performance of automatic positive airway pressure (autoPAP) devices may deteriorate in the presence of air leak. To our knowledge, there is lack of clinical evidence regarding the effect of air-leak on adherence to autoPAP therapy. We wanted to examine whether air-leak as quantified by the autoPAP device correlates with adherence to such therapy. We tested the hypothesis that greater levels of air-leak are associated with poor adherence to autoPAP therapy.

Methods: Ninety-six consecutive patients with obstructive sleep apnea received 1-week of autoPAP therapy following which both adherence data and air-leak information (due to poor mask-fit or mouth opening) were downloaded from the device microchip. Continuous positive airway pressure (CPAP) therapy was then issued for 5-weeks with pressure set at 90th percentile of that delivered during autoPAP therapy. Adequate adherence was defined as average usage greater than 240 min/night.

Results: Forty-three patients were adherent to autoPAP therapy (350 ± 67 [SD] min/night), whereas 53 patients were not (122 ± 65 min/night; $P < 0.0001$). Average pressure delivered by autoPAP in non-adherent patients (7.4 ± 2.1 cm H₂O) was lower than that of adherent patients (8.4 ± 2.6 cm H₂O; $P = 0.04$). However, average air-leak experienced by non-adherent patients (48 ± 21 liters/min) was greater than that of adherent patients (39 ± 16 liters/min; $P = 0.02$). When air-leak was adjusted for pressure delivered, the leak levels in non-adherent patients (7.0 ± 3.5 L/min/cmH₂O) was still greater than that of adherent patients (4.9 ± 1.7 L/min/cmH₂O; $P < 0.0001$). Logistic regression analysis revealed that higher levels of air-leak was associated with non-adherence to autoPAP therapy (Hazard [Odds] ratio 1.43; 95% CI, 1.1, 1.8; $P = 0.003$). Moreover, adherence to autoPAP therapy was strongly correlated with subsequent adherence to CPAP therapy ($R^2 = 0.74$; $P < 0.0001$).

Conclusion: Air-leak was associated with poor adherence to autoPAP therapy. Adherence to autoPAP therapy was strongly correlated with subsequent adherence to CPAP therapy.

0418

APNEA POSITIVE PRESSURE LONG-TERM EFFICACY CARDIOVASCULAR OUTCOMES RESEARCH STUDY (APPLE CORS): PRELIMINARY STUDY

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Introduction: Multimodality noninvasive imaging and serum biomarkers in detection of early, subclinical manifestation of cardiovascular disease may present an alternative strategy for early intervention and prevention of cardiovascular morbidity and mortality. APPLE CORS is a randomized, double-blinded, sham-controlled trial of CPAP therapy designed to study the biomarkers and early structural/functional outcomes of the major pathogenetic mechanisms of heart dysfunction and cardiovascular disease associated with OSA and to investigate if they are reversible with CPAP.

Methods: Eighteen subjects with moderate-to-severe OSA were randomized to either active or sham CPAP and evaluated at baseline and after 3 months. The subjects were assessed with cardiac MRI, echocardiography, and vascular ultrasound; these tests were performed to assess flow-mediated vasodilatation (FMD) of the brachial artery, adenosine stress myocardial perfusion reserve (MPR), LV mass, LV and RV ejection fraction (EF), and nitroglycerin-mediated coronary vasoreactivity. Fasting blood tests assessed C-reactive protein, asymmetric dimethylarginine, epinephrine, norepinephrine, hemoglobin, hematocrit, lipid profile, aldosterone, plasma renin activity, apolipoprotein Eε4, atrial natriuretic peptide, B-type natriuretic peptide, D-dimer, fibrinogen, homocysteine, ghrelin, and leptin. Twenty-four hour ambulatory blood pressure (ABP) measures, 2-hr glucose tolerance tests plus insulin, and sleep parameters were also evaluated. Group means were compared using unpaired t-tests or Mann-Whitney-Wilcoxon two-sample tests, as appropriate; and nominal p-values are reported.

Results: Both FMD of the brachial artery and MPR improved significantly from baseline ($p = 0.01$) for patients in the active CPAP group compared to those in the sham CPAP group. No significant differences were observed in LV mass, LV or RV EF, and coronary vasoreactivity between the two groups. For the biomarkers and blood measures, there were no significant differences between groups, except for leptin levels, which showed a significant decrease for patients in the active CPAP group vs. those in the sham group. For the ABP measures and sleep parameters, only the total sleep time was significantly different (i.e., lower in the sham group).

Conclusion: Preliminary study results indicate that subclinical cardiovascular disease, as assessed by markers of microvascular function

Category H—Sleep Disorders – Breathing

(FMD, MPR), may be reversed with 3 months of CPAP use in moderate-to-severe OSA patients.

Support (optional): Respironics, Inc. provided funding and loaned equipment (active and sham CPAPs) for this study.

0419

ASSOCIATION BETWEEN EXCESSIVE DAYTIME SLEEPINESS AND OXYGEN DESATURATION IN OBSTRUCTIVE SLEEP APNEA SYNDROME: WHAT IS IMPORTANT? NADIR OXYGEN SATURATION OR MEAN OXYGEN SATURATION OR TIME SPENT BELOW 90% OXYGEN SATURATION

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Introduction: Excessive daytime sleepiness (EDS), a common symptom associated with obstructive sleep apnea syndrome (OSAS), is thought to result from sleep fragmentation and/or hypoxemia during sleep. Multiple parameters are used to indicate the severity of hypoxemia. Previous studies have shown some association between nadir/mean oxygen saturation and EDS but the evidence is not robust. To-date no studies have investigated the importance of time spent below 90% oxygen saturation and also none of the studies have compared the relative value of each of these three measures in relation to EDS.

Methods: 300 polysomnograms of OSAS patients (AHI > 5) were reviewed (150 with > 5% of total sleep time spent below 90% oxygen saturation and 150 with nadir oxygen saturation of >90%). Information was collected on various parameters including age, sex, neck circumference, arousal index, etc. EDS was considered significant if Epworth sleepiness scale (ESS) score was > 10.

Results: Statistically significant negative correlation was noted between ESS score of > 10 and mean oxygen saturation ($r: -0.293, p < 0.01$), nadir oxygen saturation ($r: -0.491, p < 0.01$), and time spent below 90% oxygen saturation for > 5% of total sleep time ($r: -0.615, p < 0.01$). Significant correlation was also noted between EDS and neck circumference, BMI, AHI, and the arousal index. Logistic regression analysis showed that after adjustment of other variables, only time spent > 5% of total sleep time below 90% oxygen saturation was statistically significant ($p < 0.001$).

Conclusion: Although the mean and the nadir oxygen desaturations can predict EDS, it is the time spent below 90% oxygen saturation for > 5% of total sleep time, that is most important in predicting EDS in patients with OSAS. This is the first study that has systematically analyzed this parameter and compared the relative importance of each of the three different oxygen desaturation parameters.

0420

PHOX2B MUTATION-CONFIRMED CONGENITAL CENTRAL HYPOVENTILATION SYNDROME IN A CHINESE FAMILY: PRESENTATIONS FROM NEWBORN TO ADULTHOOD

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Introduction: Congenital central hypoventilation syndrome (CCHS), usually develops in the newborn, is characterized with compromised chemoreflexes, which results in hypoventilation mainly at sleep. CCHS may have central hypoventilation in isolation or associated with neurocristopathy. Recently, heterozygous PHOX2B gene mutation was identified in CCHS. This study reports a Chinese family of CCHS with pre-

sentations from newborn to adulthood, with genetic analysis confirming the presence of PHOX2B mutation.

Methods: Following identifying central hypoventilation in one adult man, clinical evaluation was performed to the complete family, consisting of parents, five siblings, and five offspring. In addition, pulmonary function test, overnight polysomnography, arterial blood gas, and hypercapnia ventilatory response, and genetic screening for PHOX2B gene mutations were performed in alive family members.

Results: The index patient and four offspring demonstrated features of central hypoventilation. The index patients had hypoxia and hypercapnia while awake breathing room air; nocturnal hypoventilation with nadir SpO₂ of 50%; and polycythemia with hematocrit of 70%. The first and fourth children had frequent cyanotic spells after birth died of respiratory failure. The fourth child had been diagnosed as CCHS. The second and third children remained asymptomatic till adulthood but had decreased hypercapnia ventilatory response. The third child had nocturnal hypoventilation with nadir SpO₂ of 59%. PHOX2B gene five alanine expansions were detected in all affected alive subjects including the index patient and two (second and third) children.

Conclusion: Our study confirms that transmission of late-onset CCHS is autosomal-dominant and genetic screening of family members of CCHS probands allows early diagnosis and treatment.

0421

ATHEROSCLEROTIC PHENOTYPE OF MONOCYTES IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA), characterized by Intermittent Hypoxia/Reoxygenation (IHR), is associated with cardiovascular morbidity preceded by atherosclerosis. Atherosclerosis is multifactorial, composing of elements of oxidative stress, inflammation and lipid deposition. Exposure of monocytes/macrophages to oxidized low density lipoprotein (oxLDL), promotes inflammation, intracellular cholesterol deposition and lipid-laden foam cell formation. We hypothesized that OSA alters monocyte function towards an atherogenic phenotype via increased production of cytokines, adhesion molecules, oxLDL uptake and its scavenger receptor CD36, all facilitating increased foam cell formation.

Methods: Monocytes were isolated from co-morbidity free OSA patients (n=11) and controls (n=11) closely matched by age (38.6±9.6 vs. 37.6±8.9 years), gender (in both 1f/10) and BMI (28.3±4.6 vs. 28.1±5.1 Kg/m²). Membrane expression of CD11b, oxLDL and CD36, and intracellular TNF-alpha and IL-10 levels were analyzed by flow-cytometry. Foam cell formation was followed microscopically by Oil-Red-O staining.

Results: The percentage of monocytes expressing TNF-alpha and IL-10 was significantly higher in OSA as compared to controls (23.1±12.6, vs. 12.3±7.6%, $p < 0.01$; 37.81±12.9, vs. 26.2±10.1%, $p < 0.01$, respectively). TNF-alpha positively correlated with IL-10 ($r = 0.75, p < 0.01$). Expressions of CD11b, oxLDL and CD36, determined by mean fluorescent intensity (MFI), were significantly higher in OSA than in controls (219±86, vs. 141±57, $p < 0.05$; 94±42 vs. 62±25, $p < 0.05$; 229±116 vs. 139±63, $p < 0.05$, respectively), and were positively correlated with each other (oxLDL/CD36 $r = 0.57, p < 0.01$; oxLDL/CD11b $r = 0.45, p < 0.05$; CD36/CD11b $r = 0.44, p < 0.05$). Plasma oxLDL was higher as well (75.8±21 vs. 53.3±27 U/L, $p < 0.05$). Also, spontaneous foam cell formation in culture was higher in OSA than in controls (17.9 ±10.0 vs. 6.3±2.2%, $p < 0.009$).

Conclusion: A pro-atherogenic monocyte phenotype is evident in OSA via increase in inflammatory cytokines, expression of adhesion molecules and oxLDL scavenger-receptor CD36, oxLDL uptake and increased foam cell formation. These atherogenic sequela most likely contribute to the development of cardiovascular morbidity in OSA.

0422

PLATELET PROTHROMBOTIC PHENOTYPE IN OBSTRUCTIVE SLEEP APNEA IS NORMALIZED WITH TREATMENT

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Introduction: Obstructive sleep apnea (OSA) constitutes an independent risk factor for cardiovascular morbidity. Platelets maintain vascular homeostasis by clot formation and wound healing, but also participate in atherosclerosis. We hypothesized that the apnea-induced intermittent hypoxia promotes a prothrombotic phenotype in platelets, resulting in increased platelets/platelets and platelets/leukocytes aggregates promoting cardiovascular risk.

Methods: Platelet interactions with monocytes and polymorphonuclear leukocytes (PMNs) were determined in polysomnographically diagnosed, co-morbidity free 16 OSA and 16 matched controls (OSA: age=45±10 years, BMI= 30±5 kg/m², AHI= 44±24 events/h; control: age=44±9 years, BMI=28±3 kg/m², AHI=5±3 events/h), in 7 OSA patients at baseline and after 3 months of dental device treatment, and in 5 additional nCPAP treated OSA patients tested on two consecutive nights with and without nCPAP. Also, expression of platelet receptors CD41/CD61 and CD62P, fibrinogen levels in plasma, and reactive oxygen species (ROS) generated by PMA activated platelets were determined. Percentage of cells expressing receptors (%) and their density of expression determined by mean fluorescence intensity (MFI) were determined for all measures using flow cytometry.

Results: Platelets/monocytes and platelets/PMNs aggregates were increased in OSA patients (296±177 vs. 177±106 MFI, p<0.03; 219±158 vs. 103±5 4MFI, p<0.06 respectively), while treatment with dental device significantly decreased both types of aggregates (168±68 vs. 100±23 MFI, p<0.03; 168±61 vs. 79±16 MFI, p<0.003). Only platelets/PMNs interactions were significantly increased by removing nCPAP for one night (from 71±14 to. 243±77 MFI, p<0.01). Platelets/PMNs aggregates correlated with apnea/hypopnea index (r=0.37, p<0.04). Platelet/platelet aggregates were increased in OSA (680±416 vs. 375±253 MFI, p<0.02), as well as CD62P expression (48±14 vs. 29±9, p<0.002). Also fibrinogen levels in plasma (402±64 vs. 360±25 mg/dl, p<0.03) and ROS generation by PMA stimulated platelets (242±141 vs. 126±82 MFI, p<0.05) were higher in OSA patients than in controls.

Conclusion: A pro-atherogenic platelet phenotype is evident in OSA via increase in adhesion molecules, fibrinogen receptors, platelets/platelets and platelets/leukocytes aggregates and ROS generation. Effective treatment attenuated platelet/leukocyte aggregates. These atherogenic sequela most likely contribute to the development of cardiovascular morbidity in OSA.

0423

EXAGGERATED NEUTROPHIL FUNCTION IN RESPONSE TO INTERMITTENT HYPOXIA/REOXYGENATION IN-VITRO

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Introduction: Obstructive sleep apnea (OSA), characterized by Intermittent Hypoxia/Reoxygenation (IHR), is associated with atherosclerosis. Neutrophils are implicated in atherogenesis by producing oxidizing molecules, proteolytic enzymes and leukotrienes during neutrophils/endothelium interactions. Neutrophil apoptosis is an injury-limiting mechanism and its suppression may exacerbate inflammation and induce vascular damage. OSA as well as IHR in-vitro, profoundly suppress neutrophil apoptosis (NA), whereas TNF- α has bi-modal effects, causing early acceleration and late inhibition of NA. The effects of TNF- α and

the expression of the survival neutrophil regulator interleukin-8 (IL-8) on NA were investigated under IHR in-vitro.

Methods: Whole blood or purified neutrophils from 8 healthy subjects (AHI=2.7±2.4; BMI=24.9±4.2; age=34.3±11.5) were exposed to IHR, to sustained hypoxia (SH) or to normoxia (NOX) in-vitro using BioSpherix OxyCycler C42 system (3 or 6 IHR periods, O₂ saturation at 2%, for 6.6±3.6 min/hour, followed by reoxygenation). NOX and SH were employed for the same durations. NA was determined by nuclear and chromatin condensation by Giemsa and Hoechst 33342 staining and flow cytometry of "low-CD16" appearance, and caspase-3 activity. Intracellular IL-8 was assessed by flow cytometry.

Results: By nuclear morphology, NA was attenuated by 73% under IHR as compared to NOX. The suppression of NA by IHR depended on the intensity of the hypoxia and was more effective than SH (4.97±1.7% at IHR vs. 8.5±3.1% at SH, p<0.05, compared with 11.45±3.3% at NOX, NOX vs. SH p<0.01, and vs. IHR, p<0.005). Treatment with TNF- α (0.1-50 ng/ml) attenuated NA in dose- and time-dependent manner in NOX, IHR and SH (more than 50% at 10 ng/ml for all treatments). IHR suppressed NA via a decreased caspase-3 activity from 42.05±11.3% at NOX to 16.04±8.9% at IHR (p<0.0001), and increased IL-8 from 17.9±11.5% at NOX to 28.2±17.6% at IHR (p<0.01).

Conclusion: IHR in-vitro profoundly inhibited NA in healthy subjects as previously seen in OSA patients undergoing IHR in-vivo. Suppression of NA under IHR conditions was amplified by TNF- α and was mediated by caspase-3 and upregulation of the survival neutrophil regulator IL-8, thus supporting exaggerated inflammation under IHR. These data further support suppressed NA in OSA, and possibly delineate some of the mechanisms responsible for the suppressed NA and exaggerated inflammation in OSA.

0424

CLINICAL CORRELATES OF SLEEP DISORDERED BREATHING IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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Introduction: Sleep disordered breathing (SDB) is a well established risk factor for cardiovascular morbidity. SDB is more common in patients with ischemic heart disease and may be associated with worse outcome after myocardial infarction. Therefore, it is important to identify SDB in patients with acute myocardial infarction.

Methods: We studied patients without a previous diagnosis of SDB who were admitted for acute myocardial infarction. Sleep studies were done in the intermediate care unit when the patients were clinically stable. For the sleep studies we used the Watch-PAT 100 which uses peripheral arterial tonometry, oxymetry and actigraphy in order to detect respiratory events. Patients were divided into 3 groups with no or mild (AHI<20), moderate (40>AHI>20) or severe (AHI>40) SDB. Demographic and clinical data were compared among the three groups.

Results: Eighty four patients (21% female) with a recent myocardial infarction were studied. Forty four (52.4%) had no or mild SDB, 21 (25%) had moderate and 19 (22.6%) had severe. Age (no-mild: 55.6±1.4, moderate: 61.2±2.0 and severe: 60.8±2.2 yrs, ns), BMI (28.5±0.8, 26.9±1.1, 29.4±1.4 Kg/m², ns), and % males (76.2%, 81.8%, 78.9%, ns) were comparable among groups. Likewise, there were no significant differences in the rates of hypertension (43.2%, 47.6%, 63.2%) and diabetes (34.1%, 28.6%, 36.8%). the group with severe SDB however had significantly higher rate of CHF (11.4%, 19%, 42.1% p<.02) and previous MIs (9.1%, 28.6%, 31.6%, p<.05). In addition, a high AHI significantly correlated with elevated C-reactive protein levels (21.9, 21.2, and 42.8 mg/L in patients with AHI < 20, AHI 20-40 and AHI > 40, respectively; P = 0.03).

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Conclusion: SDB is common among patients with recent acute myocardial infarction. The significant association between CRP levels and SDB may have an effect on recovery from MI and on future prognosis.

0425

HIGH PREVALENCE OF SLEEP DISORDERED BREATHING AMONG HIV SERONEGATIVE AND SEROPOSITIVE MEN IN THE MULTICENTER AIDS COHORT STUDY (MACS)

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Introduction: Sleep disordered breathing (SDB), is present in 24% of men in the general population and leads to daytime fatigue and impacts quality-of-life and physical health. Highly active anti-retroviral therapy (HAART) is associated with metabolic changes, including weight gain, increased visceral adiposity, and subcutaneous lipotrophy, which are known risk factors for SDB. Therefore, we hypothesized that HAART would be associated with an increased prevalence of SDB.

Methods: A cross-sectional study was nested within the Baltimore site of the MACS. All HIV infected men who were not on HAART and random samples of HAART users (HAART) and seronegative men (HIV-) of similar age and race were invited to participate in nocturnal sleep studies: 49 HIV+ using HAART (median CD4 cell count 566 / μ l and viral load < 40 c/ml), 29 HIV+ not using HAART (median CD4 476 cells/ μ l and viral load 14,940 c/ml) and 55 HIV- , of similar ages and races. SDB was defined as an apnea-hypopnea index \geq 5 events/hour (mild: 5.0 - 14.9 events/hr, moderate: 15.0 - 29.9 events/hr, severe: \geq 30 events/hr). Categorical data were assessed for statistical significance with chi-square analyses and logistic regression where appropriate.

Results: Overall, the median age and body-mass index (BMI) were 50.3 yrs and 25.9 kg/m² ; 57.1% were African-American, 41.4% Caucasian, and 1.5% Hispanic. The prevalence of SDB was 74.4% (29.3% mild, 30.8% moderate, and 14.3% severe). The odds ratios (95% confidence interval) for SDB were 1.2 (1.0, 1.3) for each kg/m² increase in BMI and 1.7 (1.0, 2.7) for each 10 year increase in age. The prevalence of SDB in HIV+ men, whether using HAART (71.4%) or not (65.5%) did not differ significantly from that in HIV- men (81.8%) even after adjustments for BMI and age and this was also true in a sub-analysis restricted to participants of BMI < 25 kg/m².

Conclusion: Neither HAART nor HIV infection was associated with an elevated prevalence of SDB compared to HIV- men. The unexpectedly high rates of SDB in all groups compared to the general population are unexplained but may be due to other underlying comorbidities or to increased participation of individuals with perceived sleep problems. The results emphasize the importance of internal controls similar to exposure groups in risks and demographics, and suggest that screening for SDB in HIV risk groups should be considered.

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0426

HIGH PREVALENCE OF SLEEP DISORDERED BREATHING AMONG HIV SERONEGATIVE AND SEROPOSITIVE WOMEN IN THE WOMEN'S INTERAGENCY HIV STUDY

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Introduction: Sleep disordered breathing (SDB), is present in 9% of predominantly Caucasian women in the general US population and leads to daytime fatigue and impacts quality-of-life and physical health. High-

ly active anti-retroviral therapy (HAART) is associated with metabolic changes, including weight gain, increased visceral adiposity, and subcutaneous lipotrophy, which are known risk factors for SDB. Therefore, we hypothesized that HAART would be associated with an increased prevalence of SDB.

Methods: A cross-sectional study of a random sample of women selected after stratification for HIV status and HAART use was nested within the Washington D.C. site of the Women's Interagency HIV Study (WIHS): 16 with HIV infection using HAART (HIV/HAART+, median CD4: 594 cells/mm³ and viral load: 80 copies/ μ l) and 14 HIV+ not using HAART (HIV/HAART -, median CD4: 502 cells/mm³ and viral load: 1,250 copies/ μ l), and 16 HIV-, of similar ages and race. All participants had nocturnal sleep studies for the assessment of SDB, defined as an apnea-hypopnea index \geq 5 events/hour (mild: 5.0 - 14.9, moderate: 15.0 - 29.9, severe: \geq 30). Categorical data were assessed for statistical significance with chi-square analyses and logistical regression where appropriate.

Results: WIHS participants in this study had a median BMI of 30.2 kg/m² and age of 41.1 years, with 91.3% described as being African-American, 6.5% Hispanic, and 2.2% other. The prevalence of SDB was 34.8% (19.6% mild, 10.9% moderate, and 4.4% severe). The odds ratios (95% confidence interval) for SDB were 1.1 (1.0, 1.3) for each kg/m² increase in BMI and 1.25 (0.5, 3.0) for each 10 year increase in age. The prevalence of SDB in HIV+ women, whether using HAART (31.3%) or not (42.9%) did not differ significantly from that in HIV- women (31.3%) even after adjustments for BMI and age.

Conclusion: Neither HAART nor HIV status was associated with an increased prevalence of SDB compared to HIV- women in this pre-menopausal, African-American cohort. The unexpectedly high rates of mild to moderate SDB in all groups compared to the general population are unexplained but may be due to other underlying comorbidities, or to increased participation of individuals with perceived sleep problems. The results emphasize the importance of internal controls similar to exposure groups in risks and demographics, and suggest the need for further studies in these populations.

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0427

SELF-EFFICACY, ADHERENCE, AND SUBJECTIVE IMPROVEMENT: A DAILY DIARY STUDY

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Introduction: Social cognitive factors, including CPAP self-efficacy are predictive of adherence and interventions to increase self efficacy have been successful at increasing CPAP adherence. The purpose of this study was to test the impact of CPAP self efficacy on nightly CPAP use and mood during the first week of treatment.

Methods: Thirty CPAP naive male patients with OSA completed pre-treatment questionnaires and a daily assessment of mood and adherence for 10 days beginning the first week of treatment. Data were analyzed using multilevel modeling to test effects within and between subjects.

Results: As expected, nightly CPAP adherence predicted decreased sleepiness (p<.01), decreased negative mood (p<.01), and increased positive mood (p<.01) during the next day. Daily mood was not predictive of adherence during the following night. CPAP self-efficacy, in particular determination to use treatment despite side effects, was a moderator of these effects. Patients with stronger pre-treatment CPAP determination reported a stronger positive correlation between adherence and next day improvements in mood and subjective sleepiness(p<.05).

Conclusion: These results provide further support to the importance of social cognitive factors in CPAP adherence. The findings suggest that patients with greater pre-treatment commitment to CPAP experience stronger daily benefits from treatment. For patients with stronger com-

mitment to CPAP before beginning treatment, treatment adherence may be reinforced by greater subjective improvement on a daily basis.

0428

CARDIAC AUTONOMIC EFFECTS OF SLEEP-DISORDERED BREATHING IN CHILDREN: PENN STATE CHILD COHORT

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Introduction: Studies in adults have demonstrated significant adverse cardiovascular effects of sleep-disordered breathing (SDB). However, such effects have not been systematically investigated in children. The goal of this study was to assess the influence of SDB on the cardiac autonomic balance in a population-based sample of children.

Methods: A random sample of local elementary school children (K-5) was assessed using a two-phased strategy. Phase I was a brief questionnaire completed by a parent of all of the children in a specified elementary school (N=5,740) with a response rate of 78.5%. Phase II randomly selected children and their parent to spend a night in our sleep laboratory (N=700) with a response rate of 70.0%. Cardiac autonomic control (CAC) was measured by heart rate variability analysis of the beat-to-beat RR interval data from the ECG recorded during the one night PSG.

Results: The sample included 616 children with a mean (SD) age of 9.12 (20.2) months, with 47% females. The average AHI (SD) was 0.79 (1.03) during the entire sleep, with 73.1% having AHI < 1 (No SDB group), 25.8% having AHI 1-5 (mild SDB group), and 1.1% having AHI > 5 (Moderate SDB group). After adjusting for age, sex, BMI, snore status, and sleep efficiency, across all children during NREM compared to awake there was a significant shift of CAC balance towards parasympathetic dominance and lower sympathetic outflow. REM was associated with a shift towards sympathetic overflow not opposed by parasympathetic modulation. However, among those children with moderate SDB the shift towards parasympathetic dominance and lower sympathetic outflow during NREM was diminished to a CAC pattern that was very similar to REM.

Conclusion: These data suggest that in children similar to adults significant adverse cardiovascular effects are associated with moderate SDB.

0429

THE RELATIVE CLINICAL SIGNIFICANCE OF REM AHI IN A POPULATION SAMPLE OF CHILDREN

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Introduction: It has been reported that in children the AHI observed during REM sleep is clinically a better indicator of sleep-disordered breathing (SDB) than the overall AHI, which is commonly used in adults. We used blood pressure as our indicator of clinical significance and assessed its association with AHI quantified based on REM and NREM sleep as well as the total sleep period in a representative sample of elementary school children.

Methods: A random sample of local elementary school children (K-5) was assessed using a two-phased strategy. Phase I was a brief questionnaire completed by a parent of all of the children in a specified elementary school (N=5,740) with a response rate of 78.5%. Phase II randomly selected children and a parent to spend a night in our sleep laboratory (N=700) with a response rate of 70.0%. As part of the physical evaluation blood pressure was measured in the evening.

Results: The average AHI observed in our sample during REM sleep was 1.11±0.07 compared to 0.74±0.07 during NREM sleep (P<0.001), which supports the hypothesis that in children the REM AHI is greater than the NREM AHI. To assess the clinical significance of SDB based on the different methods of quantifying the AHI we evaluated their re-

spective association with blood pressure. The NREM AHI was significantly associated with elevated systolic (P<0.002) with a trend for elevated diastolic blood pressure (P=0.080). In contrast, the REM AHI was not associated with either systolic (P=0.128) or diastolic blood pressure (P=0.452). Further, the overall AHI was also associated with systolic (P=0.001) but not with diastolic blood pressure (P=0.136).

Conclusion: Using elevated systolic blood pressure as an indicator of clinical significance of AHI it appears that the REM AHI is not a better clinical marker of SDB than the overall AHI.

0430

SALIVARY CORTISOL CONCENTRATIONS ARE LOW IN CHILDREN WITH SLEEP DISORDERED BREATHING: SELECTION OF SUBJECTS WITH DECREASED STRESS SYSTEM ACTIVITY AND DEFICIENT AROUSAL MECHANISMS?

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Introduction: In adults, sleep-disordered Breathing (SDB) has been associated with mild activation of the stress system, compared to obese controls i.e. the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system, presumably as a result of intermittent hypoxia and sleep fragmentation. In this study we examined the association of cortisol levels with the presence of SDB in children.

Methods: 393 young subjects from a subset of a community sample assessing the prevalence of SDB in children were evaluated in our GCRC for one night in sound-attenuated and temperature-controlled rooms. Every child had a thorough clinical history and physical examination, completed subjective questionnaires and had a 9-hour complete polysomnographic study. In addition, an evening saliva sample (6:00-7:00pm) before dinner and a morning saliva sample (6:30-7:30) before breakfast were obtained for the assessment of cortisol concentration.

Results: A stepwise multivariate regression analysis was performed that included as predictors age, gender, percentile for Body Mass Index (BMI), and apnea hypopnea index (AHI). Both evening and morning salivary cortisol levels were predicted by AHI (p<0.001 and p=0.014, respectively) and at both time points the association was negative.

Conclusion: These data suggest that in a general random population of elementary school age children, SDB was associated with decreased cortisol secretion and may reflect low activity of the stress system associated with low arousal mechanisms in these children. The low cortisol as well as SDB may both be related to genetic or developmental predisposition, the latter because of exposure to adverse events during the pre-/perinatal period, such as deficient nutrition, maternal stress, resulting in intrauterine growth restriction or brain hypoxia. Further studies are indicated to explore these testable hypotheses.

0431

CHRONIC INTERMITTENT HYPOXIA INCREASES CARDIAC CONTRACTILITY IN C57BL/6J MICE

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Introduction: Animal models that use chronic intermittent hypoxia (IH) to simulate the hypoxic stress of obstructive sleep apnea exhibit sustained hypertension. However, the effects of chronic IH on cardiac function are less clear with studies in rats suggesting a gradual impairment of contractility. In mice, however, four weeks exposure to IH did not exacerbate experimentally-induced myocardial injury, which was evident during a shorter two-week of exposure. We, therefore, hypoth-

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esized that four weeks exposure to chronic IH in mice would either decrease or have no effect on cardiac contractility.

Methods: 28 adult male C57BL/6J mice were exposed to 4 weeks of IH (n=15; nadir FIO₂=0.05-0.06 at 60 cycles/hr for 12 hr during the light period only), or IA (n=13; intermittent air for 12 hr). At the end of 4 weeks, mice were anesthetized, ventilated, and underwent pressure-volume loop analysis using a Millar conductance catheter inserted into the left ventricle (LV). Western Blot analysis was performed on the LV tissue at sacrifice.

Results: The LV maximum systolic pressure trended higher in the IH group (97±2 mmHg) compared to the control group (91±3 mmHg; p = 0.054). There was a significant increase in both LV ejection fraction (IH:63.4±3.5%; IA:50.5±2.6%; p=0.008) and dP/dtmax (IH:8698±485 mmHg/sec; IA:6951±524 mmHg/sec; p=0.021) in the hypoxic group compared to the control group. Furthermore, the LV preload independent maximum power (mWatts/μL2) was greater in the hypoxic group compared to the control group (IH:229±30; IA:136±16; p=0.02). The ratio of phosphorylated to total JNK/SAP and p-38 was not different between groups, whereas this ratio for ERK1+ERK2 was almost 3 fold higher (p=0.014) in the hypoxic group compared to the control group.

Conclusion: In contrast to our hypothesis, chronic exposure to IH increased cardiac contractility in mice and was associated with upregulation of the contractile-modulating ERK signaling pathway.

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0432

OCCUPATIONAL INJURIES IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: The association between OSA and rates of occupational injuries is unclear. We sought to: 1) determine whether patients with OSA are at increased risk of occupational injury, and 2) identify types of injuries associated with OSA.

Methods: We recruited patients referred to the University of British Columbia Hospital Sleep Laboratory for suspected OSA (May 2003 to April 2006). Rates and types of validated occupational injuries (that caused at least one day of disability) in the five years prior to their polysomnogram were calculated by linking to claim data from the Workers Compensation Board. Only adult patients who reported working at least 10 hours per week were included in the analysis.

Results: There were 706 patients; 73% were male, mean age=47±(SD)9.9 yrs, mean AHI=22.6±23/hr, 81% had OSA (AHI>5), and mean ESS score=10±5.3. There were a total of 95 occupational injuries. When compared to patients without OSA, patients with OSA had 75% more injuries (0.029 injuries/yr vs. 0.017/yr; p=0.04 unadjusted Poisson regression). However, after adjustment for potential confounders (ESS, hours worked, BMI, age, gender, alcohol use, blue collar occupation) OSA was no longer a significant factor (p=0.15). However, when only falls and motor vehicle crashes were considered (i.e. injuries more likely affected by sleepiness), rates were 5.1 times greater in patients with OSA (0.0077/yr vs. 0.0015/yr); the effect of OSA persisted even after controlling for confounders (p=0.009). The mean claim costs of injuries did not differ significantly between patients with and without OSA (i.e. 6,255 vs. 2,264 \$CAD, p>0.1). There was no consistent relationship between OSA severity and occupational injuries.

Conclusion: Patients with OSA have increased rates of occupational injuries; the effect appears greater for certain types of injuries (e.g. falls,

motor vehicle crashes). Screening and treatment of workers with OSA may reduce rates of injury.

Support (optional): Michael Smith Foundation for Health Research (Sleep Disordered Breathing Infrastructure Grant; Scholar Award), BC Lung Association Operating Grant

0433

INFLAMMATORY CYTOKINE PROFILE OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: Systemic inflammation is important in the pathogenesis of cardiovascular disease but the role of circulating pro-inflammatory mediators in OSA induced vascular disease is still unclear. Using a relatively large patient sample, we sought to characterize the systemic inflammatory profile (phenotype) associated with OSA.

Methods: We recruited adult patients referred to the University of British Columbia Hospital Sleep Laboratory for suspected OSA (2005 to 2007). Fasting serum samples were obtained the morning after their diagnostic polysomnograms. Samples were tested for the following circulating inflammatory mediators: interferon gamma; interleukins 1B, 6, and 8; intercellular and vascular cell adhesion molecules (sICAM1 and sVCAM1); and leptin using a multiplex Luminex System. Patients using statins were excluded.

Results: There were 181 patients; 67% were male, mean age=50+/- (SD)11 yrs, mean AHI=22.8+/-22/hr, mean desaturation (i.e. % of time spent below an oxyhemoglobin saturation of 90%)=5.3%+/-15, mean BMI=32.3+/-8.3 kg/m², and mean ESS score=10.6+/-5.1. In univariate analyses, only leptin, sVCAM1, and sICAM1 were significantly associated with indices of OSA severity (i.e. AHI and/or desaturation). In multivariate linear regression analyses that included BMI, gender, and age; desaturation persisted as a significant independent predictor for elevated sVCAM1 (p=0.0003) and leptin (p=0.003). AHI (p=0.03) and BMI (p=0.009) were independent predictors for elevated sICAM1 and BMI was an independent predictor of elevated leptin (p<0.0001).

Conclusion: In contrast to previous reports, we did not find significant associations between OSA and markers of activated innate immunity (IL-1B, 6, and 8). OSA severity was independently associated with elevated levels of soluble adhesion molecules and leptin, mediators that may represent pathogenic mechanisms involved in the cardiovascular disease associated with OSA. These mediators may represent potential future targets for therapy.

Support (optional): Michael Smith Foundation for Health Research (Sleep Disordered Breathing Infrastructure Grant; Scholar Award), BC Lung Association Operating Grant

0434

SLEEP APNEA IS AN INDEPENDENT RISK FACTOR FOR ALL-CAUSE MORTALITY: THE BUSSELTON HEALTH STUDY

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Introduction: Previously published clinical cohort studies have suggested that obstructive sleep apnea (OSA) is a risk factor for cardiovascular disease associated mortality. However, it is unknown whether sleep apnea is an independent risk factor for all-cause mortality in a community-based sample free from clinical referral bias.

Methods: Residents of the Western Australian town of Busselton were investigated with a home sleep apnea monitoring device (MESAM IV) in 1990. OSA was quantified via the respiratory disturbance index (RDI). Data matching from the Australian National Death Index and the Western Australian Death Register were used to ascertain mortality in 397/400 participants (99.3%) after up to 14 years (mean follow-up 13.4 years). Univariate analyses and multivariate Cox proportional hazards modelling was used to ascertain the association between sleep apnea and mortality after adjustment for age, gender, body mass, mean arterial pressure, total cholesterol, high-density lipoprotein cholesterol, diabetes and doctor diagnosed angina in those free from heart attack or stroke at baseline (n=380).

Results: Among the 380 participants, 18 had moderate-severe OSA (RDI \geq 15/hr, 6 deaths) and 77 had mild OSA (RDI <5/hr, 5 deaths). Moderate-to-severe OSA was independently associated with greater risk of all-cause mortality (Fully adjusted Hazard Ratio= 6.24, 95% CL 2.01, 19.39) than no-OSA (n=285, 22 deaths). Mild OSA (RDI 5-<15/hr) was not an independent risk factor for higher mortality (HR=0.47, 95% CL 0.17, 1.29).

Conclusion: Moderate-severe sleep apnea is independently associated with a large increased risk of all-cause mortality in this community-based sample.

0435

MAINTENANCE OF WAKEFULNESS TEST PREDICTS REAL DRIVING PERFORMANCE IN UNTREATED OBSTRUCTIVE SLEEP APNEA PATIENTS

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Introduction: Obstructive sleep apnea syndrome (OSAS) is associated with a risk of traffic accidents. We evaluated the ability of the Maintenance of Wakefulness Test to predict real driving performance in untreated sleep apnea patients.

Methods: Thirty eight apneic patients (mean age [\pm SD]=51 \pm 9 years, mean apnea/hypopnea index (AHI) [\pm SD]=41 \pm 25), and 14 healthy controls (mean age [\pm SD]=46 \pm 9 years) were included in the study. Nocturnal polysomnography, mean sleep latency at 4x40-minute Maintenance of Wakefulness trials, Epworth Sleepiness Scale, Karolinska Sleepiness Scale, Body Mass Index and number of inappropriate line crossings during a 90 minutes real driving session were analyzed.

Results: As defined by Maintenance of Wakefulness Test scores, 21% of the patients were very sleepy (0-19 min), 39.5% were sleepy (20-33 min), and 39.5% were alert (34-40 min). We found a significant difference of number of inappropriate line crossings between the 4 drivers groups (very sleepy, sleepy, alert and controls) (Kruskal-Wallis test, H = 11.319, P<0.01). Post hoc tests revealed that the very sleepy group (0-19 min) and the sleepy group (20-33 min) had more ILC than the control group (P<0.05). Moreover, very sleepy (0-19 min) and sleepy (20-33 min) groups had more ILC than the alert group (34-40 min) (P<0.05). We found no difference between the alert (34-40 min) and the control group. Number of inappropriate line crossings correlated with Karolinska Sleepiness Scale scores measured at half-way driving (Rho, r = 0.453, P<0.01), Body Mass Index and microarousal index (Rho, r = 0.383, P<0.05 and r = 0.439, P<0.01).

Conclusion: We confirm that reduced sleep latencies at the Maintenance of Wakefulness Test predict driving impairment. Only alert apneics (33-40 minutes) match performances of non apneic drivers. Maintenance of Wakefulness Test could be used to assess driving ability of untreated apneic patients.

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0436

VALIDATION OF COMPUTATIONAL SIMULATIONS OF UPPER AIRWAY AERODYNAMICS IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Computational simulations of biological processes are being increasingly applied to understand disease mechanisms. The objective of the current study is to validate 3-dimensional flow computations using a physical model of a subject with sleep apnea.

Methods: Cross-sectional and sagittal upper airway MR data from a subject with sleep apnea was acquired on a 1.5 T scanner. Edge detection software was used to identify the airway boundaries from the sagittal and transverse MR's. Three dimensional shape of the airway was reconstructed by refining and smoothing the airway coordinates in commercial grid generation software (GAMBIT). This was then meshed and used as an input to the flow solver FLUENT. The same geometry was converted into a CAD source file which was used to fabricate the transparent physical model. Computational and Experimental Studies of the upper airway were conducted at an inlet mass flow of 10 liters /min.

Results: Numerical Simulations indicated a highly unsteady three dimensional flow and pressure distribution. Flow velocities were found to reach a maximum of 5m/sec at the location of minimum cross section. This was accompanied by an increased negative pressure (-21 pascal) in the static pressure at the same location making the airway wall more compliant. Non-invasive laser flow diagnostic (PIV-Particle Image velocimetry) and Static Pressure measurements were used to acquire the 3 dimensional flow field & Static and Dynamic pressure inside the transparent physical model. Comparisons between the computations and experiments of the flow field and airway lumen pressure strongly agree over the entire upper airway.

Conclusion: Our results support the use of Computational simulations of upper airway as a non-invasive tool to better understand the pathophysiology of OSA.

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0437

THE IMPACT OF CPAP ON CARDIOVASCULAR BIOMARKERS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA: A RANDOMIZED CROSSOVER TRIAL

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Introduction: Previous, largely uncontrolled studies, have demonstrated fairly substantial effects of CPAP on a variety of physiological and biochemical markers known to be risk factors for cardiovascular disease (cardiovascular biomarkers). In this pilot study, we assessed CPAP therapy's effect on biomarkers using a randomized controlled crossover design.

Methods: We recruited patients referred to the University of British Columbia Hospital Sleep Laboratory with an AHI>15 by overnight polysomnography. Patients were randomized to either CPAP or no therapy for 4 weeks followed by a washout of 4 weeks, and then the other arm. Fasting morning blood and urine, 24-hr blood pressure (BP) measurements, and endothelial function (peak flow-mediated dilation to nitroglycerin-mediated dilation ratio assessed by brachial ultrasound) were assessed before and after each study intervention.

Results: 9 adult male and 4 female patients were studied. Mean age=55+/- (SD) 7 years, mean AHI=27.9/hr, mean Epworth Score=6.8 (11/13 had a score <10), and mean BMI=30.4kg/m². Mean compliance with CPAP therapy was 5.53 hours/night. Compared to no therapy, improvements were observed with CPAP for triglyceride levels (decreased by 0.52mmol/L), urinary microalbumin/norepinephrine/epinephrine to creatinine ratios (decreased by 3.51mg/mmol, 1.70nmol/mmol, 0.95nmol/mmol respectively), 24-hr BP (systolic decreased by 3.60mmHg, diastolic 0.70mmHg), homeostasis model for insulin resistance score (decreased by 1.11), and endothelial function (increased by 7.4%). However, none of the above differences were significant (p>0.10). In subgroup analysis of patients with more substantial OSA (AHI>25), systolic BP was substantially reduced (by 10.8 mm hg) which trended to significance (p=0.06).

Conclusion: In this pilot study, there were potential improvements in a variety of cardiovascular biomarkers with CPAP. However, for many outcomes, the magnitude of changes was smaller than that seen in other studies. Given that CPAP compliance was reasonable (despite the fact that the patients were not particularly sleepy), large randomized controlled trials to assess the potential cardiovascular benefits of CPAP are feasible and warranted.

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0438

NASAL SURGERY FOR OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: To investigate how nasal surgery affects obstructive sleep apnea syndrome (OSAS) patients using subjective and objective measures, and to assess whether any preoperative factors are predictive of surgical outcomes.

Methods: We performed the prospective, comparative study in a tertiary-care, sleep disorder referral center. Forty-four OSAS patients (42 men, 2 women; mean age 38 years; apnea/hypopnea index (AHI), 35.1±27.9 events/hr, body mass index (BMI), 26.2± 3.5 kg/m²) with nasal obstruction secondary to a deviated nasal septum were enrolled for nasal surgery (Septomeatoplasty) as study group. A match set of 22 OSAS patients who were unwilling to receive nasal continuous positive

airway pressure (CPAP) therapy or surgery was used as control group. Outcome measures including Snore Outcome Survey (SOS) and Epworth Sleepiness Scale (ESS), measurements of nasal resistance (NR) and polysomnographic data were compared between baseline and outcome after an interval of 3 months in two groups.

Results: BMI revealed no change (P>0.05) after operation. Analysis of clinical measures showed significantly improved SOS (P<0.001), ESS (P<0.001) and total NR (P=0.003) in nasal surgery group. However, no significant change (P>0.05) was noted postoperatively in AHI, minimal oxygen saturation, and sleep architecture postoperatively in both nasal surgery and control groups. According to Sher's criteria (reduction of AHI>50% and postoperative AHI<20), seven (16%) patients were classified as "success" following nasal surgery for OSA. No patient achieved "success" in the control group. Significant differences were observed in the changes of AHI scores after nasal surgery between Friedman tongue position (FTP) I/II and FTP III/IV groups (P=0.007).

Conclusion: Surgical correction of obstructed nasal airway ameliorated symptoms of nasal impediment, snoring, and daytime sleepiness in OSAS patients. Despite improved subjective quality-of-life, the data revealed no clinically meaningful improvement in sleep respiratory events. Palate/tongue relationship may affect response to nasal surgery for OSAS.

0439

RENAL SYMPATHETIC ACTIVATION INDUCED BY CHRONIC INTERMITTENT HYPOXIA AND SLEEP RESTRICTION IN RATS: ACTIONS OF ANGIOTENSIN (1-7)

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Introduction: Clinical studies demonstrated a relationship between obstructive sleep apnea and hypertension, although the mechanisms by which nocturnal upper airway obstructions lead to daytime hypertension are not well established. Our group showed that sleep restriction (SR - for 21 days) induced an increase in renal sympathetic nerve activity and decrease in plasma angiotensin (1-7), a potent vasodilator that counters the effects of angiotensin II. The present study was designed to determine the isolated effects of chronic intermittent hypoxia (CIH) and combined effects of SR and CIH in heart rate, blood pressure, splanchnic and renal sympathetic nerve activity in rats. The study also assessed the effects of both conditions on plasma renin-angiotensin system as well as serum creatinine, sodium and potassium concentrations.

Methods: Wistar male rats (n=9/group) were submitted to CIH exposure (room air - 10% O₂ for 1000-1600h) followed by a SR period of 18h (1600-1000h) for 21 days using the single platform method. Rats were randomly assigned to three experimental groups: 1) control, 2) CIH, and 3) CIH-SR.

Results: CIH group showed a selective increase in renal sympathetic nerve activity associated to a reduction in plasma angiotensin (1-7) concentrations. However, the CIH-SR rats did not modify sympathetic nerve activity when compared to controls, but showed a higher angiotensin (1-7) concentration when compared to CIH.

Conclusion: The observed decrease of angiotensin (1-7) concentrations after CIH exposure could be interpreted as a reduction of protective effect in the cardiovascular system. Most likely, the net effect of renal sympathetic nerve activity in the CIH-SR group depends on the concentrations of circulating angiotensin (1-7). Thus, the results suggest that changes in the sympathetic and angiotensinergic system in response to hypoxia may be an important mechanism through which hypertension develops.

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0440

PERIPHERAL RECRUITMENT OF MARROW-DERIVED VERY SMALL EMBRYONIC-LIKE (VSEL) STEM CELLS FOLLOWING INTERMITTENT HYPOXIA DURING SLEEP

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Introduction: The concept that bone marrow (BM)-derived cells participate in neural regeneration remains highly controversial and the identity of the specific cell types involved remains unknown. Recently we identified in murine BM a homogenous population of rare (~0.01% of BMMNC) Sca-1+ lin- CD45- cells that express by RQ-PCR and immunohistochemistry markers of pluripotent stem cells (PSC) such as SSEA-1, Oct-4, Nanog and Rex-1 and highly express Rif-1 telomerase protein (Leukemia 2006;20,857-869). Furthermore, VSELS not only express neural lineage markers, but more importantly form neurospheres in vitro and can differentiate into neuronal and microglial lineages. It is now clearly established that time-dependent cognitive and cardiovascular deficits are induced by intermittent hypoxia (IH) during sleep, a surrogate murine model of sleep apnea. We hypothesized that the magnitude of such deficits may reflect, at least in part, the ability to recruit VSELS.

Methods: To examine the effect of IH exposures during sleep on BM and peripheral blood (PB) VSEL populations, C57Bl6 mice were exposed to IH (8% O₂ alternating with 21% O₂ every 90 sec for 48 hours) or room air (RA). Subsequently VSELS were isolated and counted using flow cytometry from BM and PB. Stromal derived factor-1 (SDF-1) levels were assayed in plasma using ELISA. (p<0.001).

Results: IH-exposed mice showed significant decreases in BM and reciprocal increases in PB when compared to RA mice. Additionally, IH-exposed mice had significantly higher SDF-1 levels compared to normoxic controls (p<0.001).

Conclusion: A pool of CXCR4+ epiblast derived VSELS that is deposited in the bone marrow (BM) during embryogenesis and may subsequently serve as a reserve pool is mobilized into peripheral blood during IH, and may play an important role in end-organ regeneration.

Support (optional): Children's Foundation Endowment for Sleep and Neurobiology Research.

0441

RIGHT VENTRICLE DIASTOLIC DYSFUNCTION IS ASSOCIATED TO OBSTRUCTIVE SLEEP APNEA

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Introduction: Diastolic may precede systolic cardiac dysfunction in OSA patients. Right Ventricle (RV) dysfunction might be seen in some patients with OSA, usually assessed by two-dimensional echocardiogram with tissue Doppler image (TDI). Literature on RV function in OSA subjects is scant. Aim: To analyze RV diastolic function alterations in OSA patients with normal systolic function using TDI.

Methods: Fifty six mild to severe OSA and 50 controls matched by gender, age, BMI, and presence of hypertension were studied. They had no cardiac or pulmonary diseases. All patients and subjects underwent full polysomnography (PSG) and real-time three-dimensional echocardiogram with conventional and tissue Doppler using Philips IE33®, equipment. All images were collected in the lateral wall of both ventricles

and were digitally stored for off-line analysis (mean of three successive measurements). Statistics: One-Way ANOVA was used to compare PSG and 3D Echo variables between groups. Multiple Regression model was built including the E/A RV as dependent variable, and Apnea Hypopnea Index (AHI), presence of hypertension, SaO₂ sleep time spent below 90%, and SaO₂ nadir as predictive variables.

Results: E/A RV and Em lateral tricuspid annulus were lower in OSA group compared to controls (0.81 ± 0.31 vs 1.49 ± 0.31 m/sec; 9.22 ± 2.52 vs 13.83 ± 3.65 cm/sec, respectively, p<0.0001, all) While A RV and E tricuspid deceleration time were higher in OSA group (12.23 ± 3.47 vs 10.65 ± 3.34 cm/sec, p=0.04; 238.9 ± 51.4 vs 133.84 ± 42.6 msec, p<0.0001, respectively) AHI was an independent predictor of E/A RV (p=0.02) in this sample.

Conclusion: We found a diastolic RV dysfunction in OSA patients compared to non-OSA controls. AHI was the only independent predictor of this dysfunction, as shown by E/A RV in our population.

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0442

POSTOPERATIVE COMPLICATIONS IN SURGICAL PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive Sleep Apnea (OSA) is presumed to be a risk factor for perioperative morbidity and mortality. However, currently the data on perioperative complications in patients with OSA are very limited to make any major correlations. This study attempts to explore the association between OSA and postoperative complications.

Methods: After hospital ethics approval, preoperative patient over 18 years old were recruited. The patients were invited for an overnight in-laboratory polysomnography (PSG) study and followed up until one month after surgery. If a patient had an AHI > 30 during their PSG, the anesthesiologist of the patient was notified. Clinical data on postoperative complications and treatment were documented and analyzed.

Results: A total of 211 patients completed the study. 147 patients were classified as OSA (AHI>5). Compared to the Non-OSA group, the OSA patients were older (59.12 vs 50.14, p<0.001), more obese (BMI: 30.6 vs 28.6, p=0.0006), higher percentage of males (57% vs 36%, p=0.004) and a higher prevalence of hypertension (49% vs 31%, p=0.017). The patients with OSA had a significantly increased incidence of postoperative complications (27% vs 12%, p<0.05). There was no death or life threatening complication in either group. Respiratory complications were most common (23% vs 9%, p=0.02). However, there was no statistically significant difference between the two groups in the incidence of cardiac complications (7% vs 3%, p=0.350) and neurological complications (1% vs 0%, p=0.99). The most common respiratory complication was desaturation (SaO₂ 93%, 21% vs 9%, p=0.04). OSA patients tended to require more treatment, such as: prolonged oxygen therapy (14% vs 5%, p=0.06).

Conclusion: Compared to non-OSA surgical patients, OSA surgical patients had a higher incidence of postoperative complications. Desaturation was the most common complication and extra treatment was required.

0443

SCREENING FOR OBSTRUCTIVE SLEEP APNEA IN SURGICAL PATIENTS

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Introduction: In response to the need for a concise and easy-to-use screening tool for OSA in surgical patients, we have developed and validated the STOP questionnaire. In the current report, we analyzed the predictive capacity of STOP-Bang, an alternative scoring model for the STOP questionnaire which incorporates BMI, age, neck circumference and gender into the scoring method.

Methods: After hospital ethics approval, preoperative patients over 18 years and without previously diagnosed OSA were recruited. The STOP questionnaire, which consists of four 'yes/no' questions, related to snoring, tiredness during the daytime, obstruction of breathing during sleep and high blood pressure, was answered by patients. The BMI, age, neck circumference and gender (Bang) were documented by research staff. The STOP-Bang score includes 8 yes/no items: four questions from STOP questionnaire, BMI > 35 kg/m², age > 50, neck circumference > 40 cm, male gender. Patients responding 'yes' to 3 or more of the 8 items were classified as being at high risk of having OSA. The score from the STOP-Bang was validated against the apnea hypopnea index (AHI) from overnight laboratory polysomnography (PSG).

Results: A total of 177 who completed PSG were analyzed. The mean age of patients was 55 ± 13 years; 49.7% males; BMI 30 ± 6 kg/m². 41% patients had hypertension and 23% GERD. The average AHI was 20 ± 6. The sensitivity of STOP-Bang at AHI > 5, > 15 and > 30 as cut-off was 83.6% (CI: 75.8-89.7), 92.9% (CI: 84.1-97.6) and 100% (CI: 91.0-100.0), respectively. The corresponding negative predictive value was 60.8% (CI: 46.1-74.2), 90.2% (CI: 78.6-96.7) and 100% (CI: 93.0-100.0). The odds ratio was 6.6 (CI: 3.2-13.5), 9.8 (3.7-26.30) at AHI > 5 and > 15 as cutoff.

Conclusion: The STOP-Bang demonstrated a high sensitivity and negative predictive value in screening the surgical patients for OSA. It was especially sensitive in detecting surgical patients with moderate to severe OSA.

0444

CHRONIC INTERMITTENT HYPOXIA INDUCES SEVERE HEPATITIS IN MICE TREATED WITH ACETAMINOPHEN

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Introduction: Obstructive sleep apnea (OSA) leads to chronic intermittent hypoxia (CIH) during sleep. OSA has been associated with liver injury. We have previously shown that CIH leads to liver injury in C57BL/6J mice and that CIH exacerbates the toxicity of a single dose of acetaminophen (APAP). The goal of the present study was to examine whether CIH aggravates hepatic toxicity of chronic APAP treatment and to explore the mechanisms of CIH-APAP interactions.

Methods: C57BL/6J mice were exposed to CIH or intermittent air (IA) for 4 weeks. Mice in both groups were treated with i.p. injections of either APAP (200 mg/kg) or normal saline daily.

Results: A combination of CIH and APAP caused liver injury with marked increases in serum alanine aminotransferase, aspartate aminotransferase, gamma glutamyl transferase and total bilirubin levels, whereas CIH alone induced only elevation in serum aspartate aminotransferase levels. APAP alone did not affect serum levels of liver enzymes. Histopathology revealed necrosis of zone 3 hepatocytes in mice exposed to CIH and APAP, whereas the liver remained intact in all other groups. Mice exposed to CIH and APAP demonstrated glutathione depletion and a five-fold increase in nitrotyrosine levels, suggesting formation

of toxic peroxynitrite in hepatocytes. APAP or CIH alone had no effect on either glutathione or nitrotyrosine. A combination of CIH and APAP caused marked increases in pro-inflammatory chemokines, MCP-1 (6 fold) and MIP-2 (40%), in liver tissue. APAP raised liver levels of IL-6 and resulted in a trend to increase TNF- α levels, regardless of the presence of CIH. CIH alone did not affect cytokine and chemokine levels.

Conclusion: Our data suggest that CIH exacerbates hepatotoxicity of APAP via oxidative stress mechanisms, specifically, depletion of glutathione and accumulation of peroxynitrite in the liver.

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0445

UP-REGULATION OF HEPATIC STEAROYL COENZYME A DESATURASE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) is associated with dyslipidemia and atherosclerosis. We have previously developed a mouse model of chronic intermittent hypoxia, which mimics the oxygen profile in patients with OSA, and have shown that chronic intermittent hypoxia induces atherosclerosis in association with dyslipidemia and up-regulation of a key hepatic enzyme of lipoprotein secretion, stearoyl coenzyme desaturase (SCD).

Methods: The objective of the current study was to examine expression of hepatic SCD in patients with OSA. We enrolled nineteen consecutive patients from the Johns Hopkins Bariatric Cohort without significant comorbidity. Overnight polysomnogram was performed prior to bariatric surgery with liver biopsy. SCD mRNA levels in the liver were measured in real time PCR and expressed as a difference in critical threshold value (Δ Ct) between SCD and a house-keeping gene 18S. SCD protein levels were semiquantitatively assessed in Western blot and normalized to α -actin.

Results: There was no association between BMI, apnea-hypopnea index and SCD expression. Hepatic SCD mRNA and protein levels were significantly higher in patients with severe oxyhemoglobin desaturation during apneic events, Δ SaO₂ \geq 5%, vs individuals with mild hypoxemia, Δ SaO₂ < 5% (mRNA Δ Ct -11.3 ± 0.7 vs. -14.8 ± 0.4, respectively, p < 0.05; protein SCD/actin ratio 1.9 ± 0.01 vs. 1.3 ± 0.2, respectively, p = 0.01). There was a strong correlation between Δ SaO₂ and SCD mRNA levels (r = 0.68, p = 0.001). The patients with Δ SaO₂ \geq 5% also exhibited higher fasting serum triglyceride (TG) and cholesterol (CL) levels than patients with mild hypoxemia (125 ± 18 mg/dl vs. 66.6 ± 4.5 mg/dl respectively for TG, p < 0.05; 204 ± 8 mg/dl vs. 175 ± 10 mg/dl respectively for CL, p < 0.05), which was consistent with up-regulation of SCD.

Conclusion: Hypoxic stress of OSA may cause dyslipidemia inducing SCD expression in the liver.

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0446

DIFFERENTIATING DAYTIME SLEEPINESS FROM FATIGUE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: Daytime sleepiness and fatigue are common in OSA patients. While often used interchangeably, these constructs are thought

to be related, but not identical. We compared predictors of fatigue and daytime sleepiness in OSA patients.

Methods: 113 treatment-naïve OSA patients (apnea/hypopnea index ≥ 10) were studied with overnight polysomnography (PSG) and completed standard psychological instruments, including the Epworth Sleepiness Scale (ESS) and the Profile of Mood States, which includes a widely-used fatigue subscale (POMS-Fatigue). Candidate predictors (personal characteristics, PSG, and psychological variables) having a simple correlation with ESS or POMS-F that was significant at $p < .10$ were included in subsequent hierarchical regression analyses. Significance was set at $p < .05$ for the hierarchical regression analyses.

Results: ESS and POMS-Fatigue showed a trend toward significant correlation ($r = .23$, $p = .06$). The following were significant ($p < .10$) univariate correlates of POMS-Fatigue: time in bed ($r = -.53$); % REM ($r = .27$); Stage 1 ($r = .33$), Stage 2 ($r = .25$), and Stage 3 ($r = .19$) sleep; ESS ($r = .23$); and, POMS vigor ($r = -.65$), tension ($r = .33$), depression ($r = .17$), anger ($r = .28$), and confusion ($r = .21$). The following were significant ($p < .10$) univariate correlates of ESS: diastolic BP (DBP; $r = -.21$); sleep onset latency ($r = -.29$); total sleep time (TST; $r = .19$); Stage 1 sleep ($r = .21$); and, POMS vigor ($r = -.20$), fatigue ($r = .23$), tension ($r = .23$), depression ($r = .21$), and confusion ($r = .32$). With POMS-Fatigue as the dependent variable, the overall hierarchical regression model was significant ($R^2 = .53$, $p < .001$). Sleep variables explained 30% of variance in fatigue ($p < .001$); psychological variables added another 23% ($p < .001$). Significant individual predictors were less time in bed ($p = .004$), less POMS vigor ($p < .001$) and more POMS tension ($p = .04$). With ESS as the dependent variable, the model was n.s. overall ($p = .10$) and at each step ($p = .12-.27$).

Conclusion: Fatigue and daytime sleepiness are overlapping but not redundant constructs in OSA patients. PSG and psychological variables explained half the variance in fatigue. However, in multivariate analysis, these predictors did not explain a significant portion of variance in daytime sleepiness. Thus, predictors of daytime sleepiness remain elusive in this group of OSA patients.

Support (optional): Lance Armstrong Foundation; Susan G. Komen Foundation POP0504026; NIH HL44915, HL36005, CA23100, AG08415

0447

SLEEP-DISORDERED BREATHING AND VERBAL ABILITIES IN OBESE AND NON-OBESE CHILDREN

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Introduction: Studies examining the effects of sleep-disordered breathing on verbal abilities have yielded mixed results, with some but not all studies reporting significant differences. Most of these studies have examined cluster verbal scores rather than focus on specific subtests or tasks, which may measure different types of verbal abilities. In addition, the relative role played by obesity in this context has not been specifically sought.

Methods: 865 children, ages 5-9 (mean age \pm SD = 6.8 ± 0.7 years; 44% female; 39% non-Caucasian) were recruited from the community, and underwent an overnight polysomnography followed by neurocognitive testing. Verbal abilities were measured by the Differential Abilities Scale (DAS) Verbal Abilities cluster score, which is derived from the scores of two subtests: Word Definitions, which measures expressive verbal knowledge, and Similarities, which measures verbal knowledge and reasoning. Participants were grouped according to their obstructive apnea hypopnea index (AHI < 1 ; $1 < \text{AHI} < 5$; AHI $> 5/\text{hrTST}$), respiratory arousal index (RAI < 1 ; $1 < \text{RAI} < 5$; RAI $> 5/\text{hrTST}$), and oxygen saturation nadir (nSPO2 $> 90\%$; $80 < \text{nSPO2} < 90\%$; nSPO2 $< 80\%$).

Results: Significant differences were found in the DAS Verbal Abilities cluster score for AHI ($F(2,861) = 9.35$, $p < .01$), RAI ($F(2,844) = 5.81$,

$p < .01$) and for nSPO2 ($F(2,846) = 12.40$, $p < .01$), with higher mean scores associated with normal sleep patterns. Differences in performance on the Similarities (significant differences for all three variables) but not on the Word Definition (no significant differences) subtests emerged. Separate analyses for obese ($n = 180$) and non-obese ($n = 523$) children yielded similar effects.

Conclusion: Verbal abilities are adversely affected in both obese and non-obese children with sleep-disordered breathing. Interestingly, the deficits in verbal abilities associated with sleep-disordered breathing occurred in more complex tasks requiring both verbal reasoning and knowledge, as opposed to a less demanding task requiring prior verbal knowledge only. Thus, it is likely that the main effect of sleep-disordered breathing may involve higher cognitive processing brain regions.

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0448

CHRONIC INTERMITTENT HYPOXIA INDUCES HYPOTHERMIA, AND INCREASES FREQUENCY OF SLEEP BOUTS AND SLEEP PROPENSITY IN HUMAN APOLIPOPROTEIN E4 TRANSGENIC MICE

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Introduction: Significant disruption in sleep/wake patterns are observed in patients even during early stages of Alzheimer disease (AD). In AD patients, the presence of obstructive sleep apnea, i.e., cyclic intermittent hypoxia (IH), accelerates neurodegenerative processes. While epidemiological associations have emerged between apolipoprotein E4 (ApoE4), AD, and sleep apnea, no studies have specifically assessed sleep phenotype or core body temperature (Tb) and gross motor activity (Ag) regulation under chronic IH conditions in transgenic mice expressing human ApoE4.

Methods: ApoE4-targeted replacement transgenic mice ($n = 4$) were chronically implanted at age 7 months with a telemetric transponder to measure EEG, EMG, Tb and Ag. After the baseline recording for 24h, animals were subjected to either IH (cycling of 5.7% or 21% oxygen every 3 min) starting from 7.00 am to 7.00 pm (light period) followed by room air (RA) until 7.00 am next day, or RA (21% oxygen throughout) in 2 identical commercially designed chambers (Oxycycler model A44XO, Bio-Spherix, NY) operated under a 12-hour light-dark cycle. Sleep-wakefulness, Tb, and Ag were recorded for 24 h at ages 7, 7.5, 8, 8.5, 9 and 9.5 months.

Results: Our preliminary results indicate a dramatic decrease in Tb in IH-exposed mice during the light period versus controls. However, during the dark period, Tb returned to values within the range of RA mice. The number of sleep bouts during the light period was markedly increased in IH mice, and Ag was lower during the light period and markedly higher during dark period as compared to RA mice. Modified sleep latency tests showed IH mice had shorter sleep latency compared to RA, indicating increased sleepiness.

Conclusion: Using a combination of sleep-wake, Tb, and Ag recordings, the preliminary results support the hypothesis that chronic IH imposes global temporal effects on multiple physiological functions, and suggest unique vulnerability among transgenic mice aiming to reproduce human neurodegenerative disorders.

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0449

EFFECTS OF FIXED- AND AUTOADJUSTING-CONTINUOUS POSITIVE AIRWAY PRESSURE ON CARDIAC SYMPATHOVAGAL BALANCE DURING SLEEP IN OBSTRUCTIVE SLEEP APNEA PATIENTS

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Introduction: We have recently reported that fixed-continuous positive airway pressure (CPAP), but not autoadjusting-CPAP (APAP) treatment, was associated with a decrease in arterial pressure and insulin-resistance (Patruno et al, Chest 2007) in OSA patients, and that CPAP and APAP may be differently capable of normalizing the sympathovagal balance during sleep. Aim of this study was to compare the effects of CPAP and a last-generation APAP device on the cardiac sympathovagal balance during sleep using a randomized cross-over study.

Methods: Twelve consecutive patients with severe OSA (AHI >30) after standard CPAP titration were randomly assigned. Group A received one-month (T1) treatment with APAP followed by one-month fixed CPAP (T2), while Group B undertook the same treatments but in the opposite order (RemStar Auto CPAP device, Respiromics Inc., set in APAP or CPAP mode). All patients underwent polysomnography before treatment, at titration and at T1 and T2. We applied heart rate variability (HRV) spectral analysis to polysomnographic ECG and respiratory signals. HRV was performed considering the typical Wake (W), 2, 4 and REM sleep stages (S). LF/HF ratio was considered as an index of the cardiac sympathovagal balance.

Results: Eleven patients (9M, 2F; age 52.4±9.9; BMI 31.6 ± 4.4) completed the study. Four were hypertensive without any treatment change during the study. All patients showed good objectively measured adherence to PAP therapy. AHI, ODI, Mean SaO₂, SaO₂ nadir, time with SaO₂<90% and ESS were significantly reduced in both groups from BL by both treatment conditions. In both groups, systolic and diastolic blood pressure were similarly affected by the two treatments. As to HRV, the mean HR as well as the LF/HF ratio progressively decreased from W to 4S and went back to W levels during REM, similarly during CPAP and APAP treatments, without any significant differences between groups. Coherence levels between HRV and respiration were highest with both treatments through all sleep stages.

Conclusion: Our results suggest that treatment with CPAP or last-generation APAP devices are associated with a similar effects on sleep, respiratory, cardiovascular and autonomic variables during sleep. This suggests that different APAP devices may distinctively affect sympathovagal balance. These differences are likely to be due to the specific efficiency of each algorithm implemented on the devices in maintaining the highest level of cardiorespiratory coupling.

0450

LEFT ATRIAL ALTERATIONS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA ASSESSED BY REAL TIME THREE DIMENSIONAL ECHOCARDIOGRAPHY

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Introduction: Several studies have been suggesting that Obstructive Sleep Apnea (OSA) contributes to deterioration of left ventricular diastolic function (LVDF). It may lead to atrial myocardium stretching and enlargement which may be associated to increased risk of cardiovascular events. We sought to evaluate: Geometric and functional abnormalities of left atrium (LA) through three-dimensional real time echocardiogra-

phy (3DRT echo) in OSA patients and control group; the influence of LVDF over these abnormalities.

Methods: Fifty six mild to severe OSA patients and 50 controls matched by gender, age, BMI, and hypertension were studied. All subjects underwent full polysomnography and 3DRT echo.

Results: BMI and diabetes were similar in both groups. 3DRT echo showed larger 3D maximum LA volume/Body surface area (3DLAVmax/m²), volume before atrial contraction, and higher active atrial ejection fraction in OSA patients versus controls (24.88ml±12.32 versus 18.55 ml±5.52, 31.52ml±20.44 versus 21.68ml±6.93, and 39.40ml±12.96 versus 32.92ml±12.11, p<0,01 for all). Mitral annular early diastolic velocity (e) was significantly reduced in patients with OSA (7.01cm/s±1.85 versus 7.87cm/s±2.24, p=0.032) while late diastolic velocity (a) and mitral valve early diastolic velocity/mitral annular early diastolic velocity ratio (E/e) were increased in the same group (7.11cm/s±1.89 versus 6.24cm/s±1.99 and 10.64cm/s±2.97 versus 9.39 cm/s±2.86, p<0.05 for both). It was shown a linear increase in 3DLAVmax/m² according to OSA severity. Apnea-hypopnea index and E/e were independent predictors of increase 3DLAVmax/m² in multiple regression model.

Conclusion: We found a significant increase in 3DLAVmax/m², volume before atrial contraction, and higher active atrial ejection fraction in OSA patients by 3DRT echo. These findings may be associated to impaired diastolic function in this population.

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0451

DOES ADHERENCE TO LIPID-LOWERING MEDICATIONS PREDICT CPAP ADHERENCE?

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Introduction: Observational research reports suggest that patients with obstructive sleep apnea (OSA) who are poor adherers to continuous positive airway pressure (CPAP) therapy have higher cardiovascular morbidity when compared to CPAP adherent patients. However, this association may be confounded, and falsely suggest causation, if adherent CPAP users are also healthier than nonusers in ways not captured by traditional methods.

Methods: Retrospective cohort study at the Philadelphia VA Sleep Center, 2005-2006, of consecutive adults prescribed a lipid-lowering medication (HMG-CoA reductase inhibitors, fenofibrate, or cholestyramine) via the VA closed pharmacy system. We defined pharmacy refill adherence as the percent of days a patient had a lipid-lowering medication available during the 365 days prior to CPAP ordering. We performed multivariable logistic regression with the outcome defined as 4 or more hours/day of CPAP “on-mask” time in the first seven days of CPAP treatment, as measured objectively by an electronic meter in the CPAP unit.

Results: Complete clinical and CPAP adherence data were available for 131 of the 169 (77.5%) subjects on lipid-lowering medication. Pharmacy refill adherence averaged 74.8 ±24.6% in the year before CPAP initiation. Median apnea hypopnea index (AHI) equaled 38.1 events/hour (inter-quartile range 19.5-53.7). CPAP adherence averaged 3.6 ±2.4 hours/day in the first 7 days. Adjusting for age, AHI, body mass index (BMI), and Epworth Sleepiness Scale (ESS), subjects in the second (OR= 2.5, CI 0.9-7.0), third (OR=3.7, CI 1.2-11.5) and top quartiles (OR=4.0, CI 1.4-11.6) of pharmacy refill adherence demonstrated significantly better CPAP adherence when compared to those in the lowest quartile of medication adherence (p=0.04). AHI, BMI, and ESS did not predict CPAP adherence.

Conclusion: Consistent refilling of lipid-lowering medications predicts higher initial CPAP adherence. This finding suggests that a “healthy user

bias” might confound observational reports ascribing a causal link between poor CPAP adherence and cardiovascular morbidity.

Support (optional): Competitive Pilot Research Program Grant, Center for Health Equity Research and Promotion (CHERP), Philadelphia Veterans Affairs Medical Center

0452

NEIGHBORHOOD SOCIOECONOMIC FACTORS PREDICT INITIAL CPAP ADHERENCE BETTER THAN DISEASE OR PATIENT-LEVEL CHARACTERISTICS

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Introduction: Adherence to continuous positive airway pressure (CPAP) therapy, the primary treatment for obstructive sleep apnea (OSA), is poor. Risk factors are not well understood but might reflect individual clinical and demographic factors or socioeconomic factors as measured by the characteristics of patient neighborhoods.

Methods: Retrospective cohort study of consecutive adults initiating CPAP at the Philadelphia VA Sleep Center, 2005-2006. We obtained demographic and clinical data from the electronic medical record and neighborhood socioeconomic data at the census block level from the 2000 Census. We performed multivariable logistic regression with an outcome of “adequate” CPAP use defined as 4 or more hours/day of CPAP “on-mask” time during the first seven days of therapy, as measured objectively by the CPAP unit’s electronic meter.

Results: Complete demographic and outcome data were available for 275 of the 379 (72.6%) subjects. CPAP adherence averaged 3.6 ±2.3 hours/day. In bivariable analyses, the following neighborhood socioeconomic factors were associated with “adequate” CPAP use: female employment [OR=1.3 (CI 1.1-1.6) for every 10% increase]; male employment [OR=1.2 (1.0-1.4) for every 10% increase]; married households [OR=1.3 (1.1-1.5) for every 10% increase]; adult completion of a high school degree [OR=1.3 (1.1-1.6) for every 10% increase]; and median household income [OR=1.2 (1.0-1.4) for every \$10,000 increase]. In multivariable analyses, female employment [OR=1.2 (1.0-1.5) for every 10% increase], married households [OR=1.3 (1.0-1.7) for every 10% increase], and individual patient marital status [married OR=2.0, (1.1-3.8) versus separated/divorced] were independently associated with “adequate” CPAP adherence. Age, occupation, race, neighborhood racial composition, apnea hypopnea index, body mass index, and Epworth Sleepiness Scale were not associated with adherence.

Conclusion: Higher neighborhood socioeconomic factors and social support are independently related to improved CPAP adherence, whereas most individual characteristics are not. A better understanding of the patient’s environment and co-existent socioeconomic barriers may help in developing and targeting interventions to promote CPAP adherence.

Support (optional): Competitive Pilot Research Program Grant, Center for Health Equity Research and Promotion (CHERP), Philadelphia Veterans Affairs Medical Center.

0453

NOCTURIA AND SNORING: EQUIVALENT PREDICTORS FOR SLEEP-DISORDERED BREATHING

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Introduction: No robust screening process for SDB exists to determine the need for PSG testing, and most clinicians rely on patient reports of snoring, cessation of breath, and other breathing symptoms. This para-

digram falls short; many people are unaware of snoring and breathing difficulties because they are asleep when these signs manifest. In contrast, patients are consciously aware of nocturia, a symptom pathophysiologically linked to SDB via increased production of atrial natriuretic peptide (ANP). We hypothesize that patient reported nocturia will be equivalent to snoring as a predictor for clinically significant SDB (AASM: RDI ≥ 15).

Methods: At intake, patients seeking treatment at Maimonides Sleep Arts & Sciences were questioned on the presence of snoring and nocturia. All patients underwent diagnostic PSG testing. Data presented includes demographics, reported presence of nocturia and snoring, and objective RDI.

Results: A total of 1129 patients (mean: age 46.4, SD=17.6; BMI 29.8, SD=7.7; 46.7% female) were tested. Of the 1129 patients, 1088 had clinical SDB, RDI ≥ 15. The positive predictive value (PPV) of snoring was 96.92%. PPV of nocturia was 97.10%. Negative predictive value (NPV) of snoring was 5.58%. NPV of nocturia was 7.98%. Sensitivity of snoring is 78.21%, while nocturia is 86.21%.

Conclusion: Nocturia was equivalent to snoring as a predictor for the presence of SDB in this population as indicated by test sensitivities and PPVs, however PPV significance is limited due to the low number of SDB-negative individuals. Nocturia is a symptom of SDB that is conspicuous and known to patients. It can be helpful for clinicians to screen patients for nocturia when determining diagnostic PSG necessity, especially among those who are uncertain about their breathing symptoms. We also speculate that the prospect of eliminating nocturia is a stronger motivator than the prospect of snoring cessation in patient adherence to PAP therapy.

Support (optional): Maimonides Sleep Arts and Sciences, and Sleep and Human Health Institute

0454

IMPACT OF CLINICAL ASSESSMENT ON THE DIFFERENCE BETWEEN UNATTENDED LIMITED MONITORING AND FULL IN-LAB PSG

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Introduction: Indices of SDB have been shown to be similar when obtained by unattended limited monitoring (LM) and by in-lab PSG. We examined the interaction between clinical evaluation by a sleep specialist and the method of obtaining the SDB index.

Methods: 30 patients (23M/7F, 30-67 yrs, BMI 23-43 kg/m²) presenting to the NYU Sleep Disorders Center with a high clinical suspicion of SDB, one patient with isolated EDS and no suspicion of SDB and 11 volunteers recruited as research subjects (8M/3F, 21-73 yrs, BMI 19-27 kg/m²) underwent 2 nights of LM at home with the ARES™ Unicorn, followed by a full in-lab PSG. Clinical data from the medical chart were de-identified and then combined with the raw/tabulated data from either the PSG (C+PSG) or from the LM (C+LM). Diagnosis and treatment recommendations were established separately by two trained sleep specialists who were presented C+PSG and C+LM >2 weeks apart. Comparisons were made across presentations and between readers. Agreement between the AHI and RDI from LM and PSG has been previously presented (ICC=0.8, Ayappa et al www.aasmnet.org/jcsm/JCSM AcceptedPapers).

Results: Using C+PSG (42 subjects), Reader 1 made a diagnosis of SDB in 30/30 patients with suspected SDB and 2/12 of the others. 3 additional subjects were diagnosed with primary snoring. Treatment recommendations were for CPAP treatment or trial in 25 subjects, non-CPAP treatment in 8 and no treatment in 9. For Reader 1 agreement between decisions based on C+PSG and C+LM was 98% for diagnosis and 93% for treatment. For Reader 2 (31 subjects) agreement between decisions based on C+PSG and C+LM was 74% for diagnosis and 77% for treatment. Reader 2 found 5/31 LM studies to be inconclusive due

Category H—Sleep Disorders – Breathing

to insufficient supine time. Using C+PSG (31 subjects) Reader 2 agreed with Reader 1 on the diagnosis in 87% and treatment in 84%. Using C+LM Reader 2 agreed with Reader 1 on the diagnosis in 77% and treatment in 74%.

Conclusion: When provided with the clinical plus PSG data there was good agreement between readers on diagnosis and treatment recommendations. Whereas Reader 1 arrived at the same diagnosis and therapeutic recommendations using C+PSG or C+LM in nearly every case, Reader 2 had a lower level of agreement between C+PSG and C+LM. The primary reason for this difference between the physicians was the importance one placed on finding insufficient supine time during the LM. These data highlight the importance the clinical algorithm plays in comparisons between the use of PSG and LM.

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0455

THE RESPIRATORY AROUSAL THRESHOLD IN HEALTHY INDIVIDUALS AND CPAP-TREATED OBSTRUCTIVE SLEEP APNEA PATIENTS

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Introduction: In OSA, termination of respiratory events occurs either by arousal from sleep or sufficient recruitment of pharyngeal dilator muscles to restore ventilation and preserve sleep. Pharmacologically increasing the respiratory arousal threshold (AT) to allow sufficient time to recruit pharyngeal dilator muscles during respiratory events may be a therapeutic option for certain patients (i.e. those with a low AT and recruitable dilator muscles). The AT is high in severe OSA patients, but has been minimally studied in less severe OSA. Thus, we sought to determine the AT across the spectrum of OSA severity and compare the result to that in healthy subjects with a view towards defining which patients may be amenable to pharmacological manipulation to treat OSA.

Methods: 13 CPAP-treated (≥ 3 months) OSA patients of varying severity (AHI 12-148/h) and 14 healthy age-matched controls were studied overnight on CPAP. During NREM sleep, transient CPAP reductions were performed to induce flow limitation and provide ≥ 3 (mean 6 ± 0.5) respiratory load-induced arousals. AT was quantified as the nadir epiglottic pressure (Pepi) on the breath prior to load-induced arousal for each CPAP drop.

Results: AT was higher (more negative Pepi) in OSA patients than controls (-16.4 ± 1.4 vs. -11.6 ± 1.3 cmH₂O, $p = 0.02$). However, AT values varied substantially between subjects (-6.3 to -25.6 cmH₂O). When grouped according to disease severity, only severe patients (AHI > 40 /h) had an AT (-18.2 ± 1.6 cmH₂O) higher than controls, with less severe (AHI < 40 /h) patients having a similar AT (-12.4 ± 1.6 cmH₂O) to controls. Further, AT correlated with AHI in the OSA patients ($r^2 = 0.46$, $p = 0.01$) indicating higher AT with increasing disease severity even in treated OSA.

Conclusion: While sub-optimal CPAP adherence or incomplete treatment efficacy remain potential contributing factors, these data suggest an underlying difference or long-term adaptation of AT neural mechanisms may occur in severe OSA. Furthermore, mild OSA patients may be more likely to benefit from sedatives than patients with severe OSA.

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0456

PARAMETRIC FMRI STUDY OF WORKING MEMORY IN OBSTRUCTIVE SLEEP APNEA PATIENTS

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Introduction: Functional magnetic resonance imaging (fMRI) studies enable the investigation of neural correlates underlying behavioral performance. In the present study we investigate the working memory (WM) function of patients with untreated obstructive sleep apnea (OSA) and compare the results to previous fMRI studies of healthy subjects as well as the only previous fMRI study of WM in OSA patients.

Methods: A parametric fMRI experiment with four levels of a spatial N-back task was used to investigate the pattern of cortical activations across the various degrees of load in 14 patients with moderate or severe OSA.

Results: We found activations in a similar cortical network in patients as the one previously described in healthy subjects, involving among others the supplementary motor area, dorsolateral prefrontal cortex (DLPFC), precentral and parietal regions. The activity in these regions increased linearly with increasing load, whereas a linear decrease was observed in the medial PFC, posterior cingulum and both hippocampi; this decrease pattern being consistent with previously described "default network" regions. Moreover, an inverted-U shape trend of activation was observed in posterior cingulum, thalamic and occipital regions, as well as right insula and left parietal and left DLPFC. The latter observation may represent a reflection of the observed decrease of behavioral performance at maximal load.

Conclusion: Our results indicate that the same cortical regions are involved in WM function in OSA patients as in healthy subjects and that, similarly, some components of this network demonstrate a capacity-constrained response. This is in contrast with the results of the prior WM fMRI study (Thomas et al.), which revealed an absence of activation in the DLPFC of OSA patients.

0457

INFLUENCE OF SLEEP-DISORDERED BREATHING ON NEUROCOGNITIVE FUNCTIONS PRE- AND POST-TREATMENT WITH ORAL APPLIANCE THERAPY

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Introduction: Mandibular Advancing Devices (MADs) are increasingly accepted for treatment of Obstructive Sleep Apnea (OSA), particularly for patients with mild to moderate OSA. In contrast to the extensive literature documenting CPAP effects on neurocognitive function, surprisingly few studies report objective outcome measures of alertness and cognitive function as result of MAD therapy.

Methods: The Alertness and Memory Profiler (AMP) quantified EEG/performance during: 3-Choice-Vigilance-Test (3C-VT), Image-Recognition (IR), IR with Interference (I-IR), Verbal/Number-Image Paired-Associate-Learning (VPAL/NUM-PAL), and Sternberg-Verbal-Memory-Scan (VMS). Subjective sleepiness and depression measures included Epworth and Beck Depression Inventory (BDI). OSA patients referred for MAD therapy ($n=30$, mean RDI=18.3, SD=10.2, range 5-54) were evaluated with AMP pre-treatment and 4-weeks post-treatment with MAD and compared to OSA patients treated with CPAP ($n=30$, mean RDI=23.4, SD=10.7, range 5-39) and healthy controls ($n=46$).

Results: 3(group) X 2(time) RMANOVA showed pre-treatment OSA patients in MAD and CPAP groups had significantly slower reaction times (RT) and decreased accuracy (%correct) on 3C-VT ($F=15.25, p < .0001$;

F=18.96, $p<.0001$), VMS(F= 40.62, $p<.0001$; F=17.73, $p<.0001$), IR(F= 8.43, $p<.01$; F= 4.66, $p<.05$) and I-IR(F=12.67, $p<.001$; F=26.64, $p<.0001$) and showed higher risk for OSA in an EEG composite evaluation score (F=19.92, $p<.0001$) compared to healthy controls at both baseline and 1-month. Both MAD and CPAP groups evidenced significantly faster RT and increased %correct on 3C-VT(F=13.10, $p<.001$; F= 13.79, $p<.0001$), VMS(F=22.10, $p<.0001$; F=8.93, $p<.01$) and IR-I(F= 5.12, $p<.05$; F=19.32, $p<.0001$) and improved EEG scores (F=42.06, $p<.0001$) after 1-month of therapy. BDI and Epworth scores were significantly decreased after 1-month (BDI: F=8.25, $p<.01$, Epworth (F=11.05, $p<.01$).

Conclusion: Pre-treatment, OSA patients evidenced impaired alertness and memory in comparison to healthy controls. Significant and equivalent improvements in objective measures of alertness/memory and self-reported sleepiness and depression were observed following one-month of treatment with MAD and CPAP therapy; however, OSA patients in both treatment groups remained impaired relative to healthy controls. The AMP is an easy-to-administer method for quantifying OSA-related cognitive impairments and verifying treatment efficacy.

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0458

EFFECT OF TREATMENT WITH MANDIBULAR ADVANCING DEVICE (MAD) ON AUTONOMIC NERVOUS SYSTEM ACTIVITY AS MEASURED BY HEART RATE VARIABILITY (HRV)

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Introduction: Increased activity of the sympathetic nervous system (SNS) as measured by catecholamine blood levels, muscle sympathetic nerve activity or heart rate variability (HRV) has been reported in patients with obstructive sleep apnea (OSA). Continuous positive airway pressure (CPAP) therapy reduces the activity of the SNS but its use in treating OSA is still limited due to patient non-compliance. Mandibular advancing devices (MAD) have proven efficient in reducing the number of abnormal respiratory events in mild and moderate OSA. However, little is known regarding MADs efficacy in restoring the balance in the autonomic nervous system. This study investigated the effects of MAD treatment upon the activity of SNS and parasympathetic nervous system (PNS) using HRV.

Methods: Spectral analysis of HRV was performed prior to (Session 1) and after one month of MAD treatment (Session 2) in 24 subjects with mild to moderate OSA (pre-treatment AHI=18±11) and 10 healthy individuals (session 1 only) from 5-minute segments of EKG. Differences in Low Frequency (LF), High Frequency (HF) and LF/HF ratio between OSA patients and healthy controls, and before and after treatment in OSA subjects were tested with t-test for independent and paired samples respectively.

Results: OSA patients had higher pre-treatment LF and LF/HF ratio compared to healthy controls (LF:t=3.27, $p<.01$; HF/LF:t=3.08, $p<.01$). A significant decrease in LF/HF ratio was found between the two sessions (t=2.71, $p<.01$), accompanied with a decrease in LF(t=2.24, $p<.05$) and AHI(10.5±6.9, t=2.51, $p<.01$). Post-treatment LF/HF ratio was still higher in OSA patients compared to healthy controls (t=2.18, $p<.05$). HF did not change significantly.

Conclusion: Though preliminary, these findings suggest that the MAD successfully ameliorates the increased activity of the SNS in OSA patients, and provide additional support for MAD therapy as important alternative to CPAP.

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0459

REPEAT STUDY OF 149 PATIENTS SUSPECTED OF HAVING SLEEP APNEA BUT WITH AN AHI < 5

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Introduction: The literature indicates a night-to-night variation in apnea rates that may have a significant impact on the diagnosis of patients in borderline ranges. Performing a repeat study has financial implications and it raises questions of inappropriate utilization of scarce resources. Not doing it, however, may impair quality of life, social and occupational functioning, and even lifespan, if sleep apnea is missed.

Methods: Patient selection - consecutively seen patients referred for sleep apnea, meeting daytime sleepiness criteria for an initial polysomnogram that then showed an AHI of < 5. All patients had a repeat PSG. The data was assessed (clinically and statistically) to identify the value of performing the second study and to attempt to differentiate sleep apnea patients from those without it.

Results: One hundred and forty nine (149) patients were assessed. Forty eight percent (48%) were found to meet PSG criteria for sleep apnea (AHI \geq 5) on the second study. No parameters were able to clinically discriminate between the patients who had AHI's \geq 5 on the repeat study and those who did not.

Conclusion: This study confirms the high rate of sleep apnea in patients suspected of having OSA clinically but whose first study is negative. The mounting evidence is probably now sufficient to indicate that patients should not be informed that they do not have sleep apnea on the basis of one PSG. Funding agencies need to be made aware of these data so they do not have justification to deny further studies. More research is needed to identify patients who do not require second studies. At present, there does not seem to be a clinical profile that is satisfactory. All patients should, therefore, probably be studied again, notwithstanding the burden this will impose on our facilities.

0460

DAY-NIGHT PATTERN OF HEART RATE VARIABILITY AND BAROREFLEX SENSITIVITY IN HEART FAILURE PATIENTS WITH SLEEP APNEA

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Introduction: Abnormal heart rate variability (HRV) and reduced baroreflex sensitivity (BS) are markers of poor prognosis in heart failure (HF). Sleep apnea is highly prevalent in HF patients, but the relative role of sleep apnea on autonomic modulation is poorly understood. We tested the hypothesis that patients with HF and sleep apnea present a damped HRV and BS as compared with HF patients without sleep apnea.

Methods: Twenty-five HF patients (left ventricular ejection fraction \leq 45%), age 42-70 yrs, were divided into three groups: obstructive sleep apnea (OSA, n=8), central sleep apnea (CSA, n=9) and no sleep apnea (NoSA, n=8). A normal control group, matched for age and body mass index was also studied (NC, n=8). All participants were submitted to a standard overnight polysomnography, with simultaneous electrocardiography and beat-to-beat blood pressure monitoring (Portapres). HRV (autoregressive power spectral analysis) and BS (sequence method) were evaluated during sleep (stage 2 of NREM sleep in periods without respiratory events) as well as while awake at ~6 AM, ~10 AM and ~10 PM.

Results: During all periods, low frequency of RR intervals and RR variance were depressed in OSA and CSA as compared to NoSA and NC groups ($P<.05$). In addition, we found that BS and total power were markedly lower in OSA as compared to NC group. There was a trend for lower high frequency in OSA as compared to NC group. In all groups,

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the sympatho-vagal balance (low frequency/high frequency of RR intervals) was significantly increased during early morning period (~6 AM) as compared to sleep ($P < 0.05$).

Conclusion: Patients with HF and sleep apnea present a decreased HRV and BS as compared to patients without sleep apnea and normal controls. This pattern seems to be similar over the 24 hours and may contribute to increase cardiac risk in this subset of patients even in periods of relative quiescence, such as sleep.

Support (optional): FAPESP and CNPq

0461

STEREOTYPED PATTERNS DURING CARDIO-RESPIRATORY MONITORING CAN REFLECT NOCTURNAL FRONTAL LOBE EPILEPSY IN PATIENTS INVESTIGATED FOR SLEEP APNEA SYNDROME

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Introduction: To evaluate the potential ictal nature of stereotyped cardio-respiratory and motor patterns in patients polygraphically investigated for sleep disorder breathing.

Methods: Over 1000 cardio-respiratory ambulatory recordings were analyzed. Monitoring was carried out for diagnosis of sleep apnea syndrome. Snoring, airflow, toracic effort, pulse rate, body position, oxygen saturation and activity of the anterior tibialis muscles were quantified. Recordings showing stereotyped polygraphic patterns recurring throughout the night, but without the features of repetitive breathing events peculiar to sleep apnea ($AHI \geq 5$), were selected for investigation. Once included in the study, patients underwent an attended nocturnal video-polysomnography.

Results: A total of 10 recordings met the inclusive criteria. They all showed recurrent polygraphic patterns characterized by a stereotyped sequence of limb movements, heart rate acceleration and artifact on the breathing sensor similar to a vocalism, followed by body position change. The sequence was never accompanied by a desaturation event. Recordings belonged to patients (4 males and 6 females; mean age: 32 ± 8 years) who referred to our Sleep Disorders Center complaining of irregular snoring, sudden nocturnal arousals associated with respiratory pauses, choking gasps or tachycardia. Sleep-related limb movements and sleep talking were often reported. In the nocturnal video-polysomnography, periodic EEG arousals were often triggered by epileptic discharges and correlated with autonomic activation and stereotyped events, involving the limbs, the axial muscles and/or the head. A diagnosis of nocturnal frontal lobe epilepsy was established for all patients.

Conclusion: The typical cardio-respiratory profile of sleep apnea syndrome is the repetitive occurrence of respiratory events and oxygen desaturations. In the absence of abnormal breathing features, identification of stereotyped and recurrent patterns during cardio-respiratory monitoring should be explored. Nocturnal Frontal Lobe Epilepsy should be taken into consideration in patients with sleep related events which may simulate sleep disordered breathing. In these cases a video-polysomnography is recommended.

0462

A FUNCTIONAL MRI STUDY OF WORKING MEMORY IN OBSTRUCTIVE SLEEP APNEA (OSA) PATIENTS

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Introduction: Obstructive Sleep Apnea syndrome (OSAs) is associated with cognitive (attention, memory and executive-functions) and functional (work performance, daytime sleepiness and quality-of-life) deficits. Their pathophysiology is controversial. The main contributing factors proposed are daytime-somnolence caused by sleep fragmentation and intermittent hypoxemia that may affect brain functioning. We assessed cognitive performance and cerebral activity during cognitive challenge in OSA, using neuropsychological tests and functional-magnetic-resonance-imaging (fMRI).

Methods: 15 male untreated severe OSA patients (mean age 43.7 ± 7.5) and 15 age-education matched healthy controls. OSA diagnosis was made with polysomnography ($AHI > 30h$). They were assessed with neuropsychological tests, rating scales (ESS, BDI) and quality-of-life questionnaires. During fMRI-scanning participants performed a 2-back working-memory task.

Results: Patients scored significantly below controls in short and long-term-memory, executive-functioning. Behavioral results during fMRI-scanning did not show significant differences between groups. Imaging results showed bilateral activations related to task difficulty in both groups in the posterior parietal cortex, insula, pre-supplementary motor area, left ventro-lateral and dorso-lateral frontal cortex and cerebellum. Significant differences were also observed. Increased activations in patients, compared to controls, were observed in the left superior, middle and inferior frontal gyri, dorsal medial precuneus, putamen and cerebellum. Decreased activations in patients were observed in the middle-occipital-gyrus and in the pontine reticular formation.

Conclusion: Neuropsychological tests confirmed the cognitive impairments already shown in OSA. Stronger activations in patients were observed in frontal regions associated with sub-vocal verbal rehearsal and strategic organization of information, suggesting a compensatory-recruitment response to support normal performance. The normal behavioral performance during scanning fits with this interpretation, which is also supported by differential fMRI activations in the two groups. Weaker activations in patients were observed in pontine structures involved in respiratory control. The results extend previous reports on the cognitive impairments and the altered functional neurocircuitry associated with OSAs.

Support (optional): Research supported by Respiration Foundation

0463

AIRFLOW THROUGH AN OPEN NASAL CANNULA TREATS CHILDREN WITH RESIDUAL OBSTRUCTIVE SLEEP APNEA AFTER ADENOTONSILLECTOMY

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Introduction: Few treatment options are available for children with obstructive sleep apnea (OSA). For children with residual OSA after upper airway surgery, continuous positive airway pressure (CPAP) is the treatment of choice but compliance is low. Recently, we demonstrated that an open nasal cannula can be used to increase pharyngeal pressure and

improve inspiratory airflow in adults with OSA. We hypothesized that this open CPAP system would have a greater effect on treating OSA in children because the majority of children with OSA have milder degrees of upper airway obstruction during sleep.

Methods: In ten children, with residual sleep apnea after adenotonsillectomy who were treated with CPAP of 8 ± 5 (Range 5-20)cmH₂O, standard polysomnography was performed on and off treatment with a nasal cannula which delivered room air at a rate of 20 L/min. Apnea Hypopnea Indices (AHI) were compared between nights on and off treatment.

Results: Ten children (Age 11 ± 2 years, BMI 34 ± 12) with mild to severe degrees of OSA were studied. On treatment the total AHI decreased from 12 ± 11 to 4 ± 5 events/hr, $p < 0.01$, and decreased below 2 events/hour in all but two subjects. The NREM AHI decreased from 6 ± 7 to 3 ± 4 , $p < 0.01$, and the REM AHI decreased from 21 ± 22 to 9 ± 15 , $p = 0.05$.

Conclusion: The majority of children with residual OSA can be effectively treated with an open CPAP system by delivering air via nasal cannula. Our data indicate for the majority of children, this is an alternative treatment to standard CPAP. Further studies are required to compare the effectiveness of these two treatment options.

0464

AUTONOMIC DIFFERENCES BETWEEN GENDERS IN OSA AND CONTROLS

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Introduction: Previous reports suggest gender differences in OSA consequences. We hypothesize that autonomic function differs between genders in obese individuals with and without OSA.

Methods: Obese subjects, without known co-morbidities, with and without OSA were studied. Autonomic function was measured with heart rate variability (HRV), pre-ejection period (PEP, measure of isovolumic contraction time estimating cardiac sympathetic activity), urine catecholamines (UC), and radial arterial tonometry (RAT).

Results: 33 females, 13 with OSA, median AHI 22.3 (12.1-122.3 events/hr), and 22 males, 15 with OSA, median AHI 27.6 (13-105 events/hr) were included in the analysis. The female OSA group had a higher median BMI compared to the female control group (43.4 vs 38.0 m/kg², $p = .01$). Male OSA subjects had similar BMI to controls. HRV analysis showed decreased overall variability (SDNN, standard deviation of normal-to-normal sinus intervals) in the OSA group compared to control ($.037 \pm .014$ msec vs $.065 \pm .038$ msec respectively, $p = .002$) but was not influenced by gender. Urine catecholamines (epinephrine and norepinephrine) were increased in the OSA group compared to controls (20.8 ± 9.6 vs 14.9 ± 8.4 mg/8hrs, $p < 0.05$) but was also not affected by gender. Augmentation index measured by RAT and controlled for heart rate (AI @ 75 bpm) was higher in male OSA subjects vs male control subjects (2.5% vs. 13.7%, $p = .001$) but there was no difference in the female groups. The female OSA group had decreased median PEP during standing compared to the female control group (142.8 vs. 134.8, $p = .03$).

Conclusion: Our results confirm prior reports of increased global sympathetic activity and suppressed parasympathetic activity in OSA. Further, our data suggest OSA manifests in women with increased cardiac sympathetic activity whereas men have increased vascular stiffness.

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0465

SLEEP DISORDERED BREATHING IS ASSOCIATED WITH WHITE MATTER LESIONS BUT NOT HIPPOCAMPAL VOLUME IN COMMUNITY-DWELLING OLDER ADULTS

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Introduction: Obstructive Sleep Apnea Syndrome (OSAS) is characterized by sleep-related decreases (hypopneas) or pauses (apneas) in respiration. Investigators suggest OSA-associated hypoxia leads to cerebral vascular changes including white matter lesions (WML). Robbins (2005) found increased WML associated with increased OSA severity. Others suggest OSA negatively impacts brain regions such as the hippocampus. Morrell (2003) found lower hippocampal volumes in patients with OSA. O'Donoghue (2005) found no significant decrease in hippocampal volume or any brain region as related to OSAS. Neither study investigated WML. We investigated the association of OSA with WML and hippocampal volume in older adults.

Methods: 35 non-depressed, community-dwelling older adults participated, range 55-92 years, mean age 70.28 years. MRIs were acquired on a GE Signa 1.5 Tesla MRI and hippocampal volume measured with Medtronic Surgical Navigation Technologies. Prevalence of WMLs was determined through T2 images. Subjects underwent ambulatory polysomnography, and the Apnea-Hypopnea Index (AHI; the average number of apneas and hypopneas per hour of total sleep time (TST), was our measure of OSA severity. We assessed mean oxygen saturation during TST, minimum SaO₂ level, and time spent below 90% of oxygen saturation.

Results: Higher AHI and greater duration of time spent below 90% of oxygen saturation were significantly associated with increased numbers of WMLs, after controlling for total white matter, age and BMI ($R^2 = .32$; $p < .01$). There was no significant association of OSA severity and hippocampal volume. Neither OSA severity nor any of our measures of hypoxia were significantly associated with total gray matter, or our measures of frontal, temporal and occipital lobes.

Conclusion: The association of increased WMLs with increased severity of OSA and greater duration of hypoxia lends support to the perspective that OSAS results in significant cerebral vascular changes. Future work should examine whether the negative impact of OSAS on brain function and cognition is mediated by such changes.

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0466

OBSTRUCTIVE SLEEP APNEA AS A MARKER OF INCREASED HOSPITALIZED MORBIDITY

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Introduction: The morbidity associated with obstructive sleep apnea (OSA) has been well defined in the outpatient population. The impact of OSA on the morbidity of hospitalized patients has not been well examined. The levels of monitoring and resource utilization for patients with OSA are not clearly defined. The aim of this study was to characterize the frequency with which OSA patients require utilization of acute care resources.

Methods: Retrospective analysis was performed on all hospitalized patients at the Northwestern Memorial Hospital from 9/2005 to 5/2007. Acute care management, defined as rapid response team (RRT) calls,

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code calls, or unplanned ICU transfers were identified. OSA was identified by reviewing discharge diagnoses. Proportions were compared with Chi-square test.

Results: 800 of 59,030 patients without OSA (1.4%) required a RRT call, whereas a RRT call was made in 56 of 1,377 patients with OSA (4.1%, $\chi^2 = 70.8$, $p < 0.01$). Likewise, 2.9% of patients with OSA and 1.7% of patients without OSA required a code to be called ($\chi^2 = 13.1$, $p < 0.01$). In those patient with OSA, 4.1% of surgical patients and 7.5% of non-surgical patients required an acute care management call ($\chi^2 = 10.9$, $p < 0.01$). On average, 1 OSA patient underwent acute care management every 4.5 days.

Conclusion: OSA causes significant morbidity in the inpatient setting, and non-surgical patients may be at greater risk than surgical patients. The results of this study support enhanced monitoring of patients with OSA in the hospital to reduce the need for acute care resources. The implications of an improved monitoring strategy need to be examined in future studies.

Support (optional): None

0467

PRESSURE PROFILES IN HEAVY ADULT SNORERS USING VARIABLE POSITIVE AIRWAY PRESSURE DEVICES

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Introduction: Upper airway resistance during sleep has been found to be in excess of five times greater in nonapneic heavy snorers compared to normals. The resultant increase in work of breathing may produce sleep fragmentation. Patients often present with frequent nocturnal awakenings, nonrestorative sleep, or hypersomnolence. The purpose of this study is to assess pressures to normalize upper airway resistance as measured by outpatient auto-titrating CPAP devices as well as treatment outcomes.

Methods: This is a retrospective review of 39 subjects with heavy snoring and sleep complaints who underwent baseline PSG followed by auto-CPAP titration. Only those with a respiratory disturbance index of < 10 were included. All underwent pre and post treatment assessment using the SleepMed Insomnia Index (SMI) to assess the insomnia complaint and the Epworth Sleepiness Scale (ESS) to assess daytime sleepiness. Means, standard deviations, and t-tests are assessed.

Results: There were 12 males (31%) and 27 females (69%). Mean age was 50 (14) and BMI was 31(6). Means for the baseline PSG were: RDI 5(3), AHI 4(3), and nadir oxygen saturation 86(4). Patients were studied on auto titrating devices: 15 were studied on ResMed and 24 on Respironics devices. For the 23 patients (59%) who used the device more than 4 hours/night the peak pressure at the 90-95 percentile was 9cm with an average peak pressure of 11cm. The median days of use were 18 with a minimum of 6 days. For those with > 4 hours on the device, pre therapy SMI scores were 20/40(8) and post therapy SMI scores were 15/40(9) with t-tests significant $p=0.01$. An SMI score of 10 or less is considered normal. The SMI has been found to identify a high likelihood of significant sleep disruption or sleep process abnormality in patients with SMI scores greater than 20. Pre therapy ESS scores were 12/24(5) and post ESS scores were 10/24(6) with t-test not significant. ESS scores < 10 are considered normal. Mean number of months at follow-up was 5 with 25 (65%) remaining on CPAP.

Conclusion: Our results demonstrate that variable CPAP devices titrate to comparable pressures as is seen in many patients with obstructive sleep apnea. The average pressure at the 90-95 percentile achieved with auto-CPAP was 9cm. Heavy snorers showed improvement with auto titrating CPAP therapy as measured by the SMI and resulted in 65% remaining on CPAP at follow-up. The SMI can be useful to assist the clinician to quantify the sleep complaint and assess the efficacy of therapy.

0468

DATABASE ANALYSIS OF THE EPWORTH SLEEPINESS SCALE SCORE AND THE RESPIRATORY DISTURBANCE INDEX (RDI) BASED ON BODY MASS INDEX (BMI) IN ADULTS PRESENTING FOR POLYSOMNOGRAPHY (PSG) IN ONE OUT-PATIENT SLEEP CLINIC IN SOUTH CAROLINA: A RETROSPECTIVE ANALYSIS OF 1932 CONSECUTIVE PATIENTS

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Introduction: Individuals present to a sleep clinic with a variety of sleep complaints. One of the more common presenting complaints is excessive daytime sleepiness. Sleep apnea constitutes 70% of diagnoses made at sleep clinics. The Epworth Sleepiness Scale (ESS) is an accepted measure of daytime sleepiness. Research studies have documented the correlation of severity of sleep apnea with excessive daytime sleepiness and obesity. The present study examines characteristics of a population of patients undergoing a baseline PSG evaluation of a sleep complaint at one sleep clinic location in South Carolina.

Methods: 1932 consecutive patients at SleepMed in Columbia, SC who underwent baseline polysomnography between 2004 and 2007 were studied retrospectively. ESS scores were collected on each patient prior to PSG. The relative frequency of patients with BMI < 26 , BMI 27-35, and BMI > 36 who had either RDI < 5 or RDI > 15 events/hour is reported. The relative frequency of patients with ESS scores > 10 is also reported for the various groups analyzed.

Results: There were 53% females and 47% males. The relative frequencies are reported for each BMI group. For those with RDI > 5 and BMI $< 26 = 44\%$; BMI 27-35 = 67%; and BMI $> 36 = 74\%$. For those with RDI > 5 and ESS > 10 and BMI $< 26 = 43\%$; BMI 27-35 = 50%; and BMI $> 36 = 51\%$. Of those with RDI < 5 and ESS score of > 10 and BMI $< 26 = 48\%$; BMI 27-35 = 51%; and BMI $> 36 = 50\%$. For those with RDI > 15 and BMI $< 26 = 15\%$; BMI 27-35 = 31%; and BMI $> 36 = 37\%$. Of those with RDI > 15 , ESS score of > 10 and BMI $< 26 = 48\%$; BMI 27-35 = 52%; and BMI $> 36 = 50\%$. For the entire group studied there were 49% 955/1932 with ESS scores > 10 .

Conclusion: The prevalence of non-obese patients with sleep apnea may be underestimated. In our clinic the prevalence of OSA in non-obese patients presenting to the sleep clinic for a sleep complaint is significantly higher than the general population. There is an increase in RDI with increasing BMI. Interestingly the prevalence of hypersomnolence as measured by the ESS score is about 50%. Patients with OSA may have sleep complaints other than hypersomnolence.

0469

PAP (POSITIVE AIRWAY PRESSURE) TITRATION VIA SPLIT-NIGHT POLYSOMNOGRAPHY (SNP) VS FULL NIGHT PAP TITRATION (FNT) IN OSA PTS

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Introduction: Two nights are standard for diagnosing OSA & FNT; to prevent delays SNP may be used. Seemingly cost/time saving, SNP limits time to achieve most effective pressure (pres.) & observe pt at ending pres. in supine position & REM, resulting in only partial clinical improvement, more follow-up, diminishing cost effectiveness.

Methods: Retrospective chart review for 100 consecutive OSA pts who underwent PAP titration (50 SNP/50 FNT) noted age, sex, BMI, AHI, lowest SaO₂, optimal & highest pres. achieved, time on optimal pres., REM & supine REM on optimal pres., post-study sleepiness, pt's perception of CPAP effectiveness, likelihood to choose CPAP or other options, likelihood to use CPAP on long-term basis, clinical improvement at follow-up & need for changes in PAP. Variables were compared using Chi-Square analysis & t-test for equality of means.

Results: FNT group PAP pres. tended to be higher ($p < 0.07$). Split-night group achieved optimal pres. more frequently than CPAP group ($p < 0.04$). There was no difference in achievement of REM or supine REM on optimal pres. Independent variables including age, AHI, lowest SaO₂, highest pres. & time in REM at optimal pres. didn't predict pts' likelihood to use CPAP. Post-study FNT pts reported less sleepiness ($p < 0.04$), more CPAP effectiveness ($p < 0.02$), choose CPAP as treatment ($p < 0.03$) & as long-term treatment ($p < 0.03$). At follow-up, SNP pts were more likely to require changes in CPAP pres. ($p < 0.03$).

Conclusion: FNT pts were more likely to report CPAP as effective & choose CPAP treatment. Although optimal pres. was achieved more frequently in SNP pts, this group was more likely to require pres. changes during the follow-up period.

0470

AFFECTIVE AND COGNITIVE SYMPTOMS IN REM-RELATED OSA (ROSA) VS NREM-RELATED OSA (NOSA)

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Introduction: Attempts to describe relationships between OSA & daytime symptoms are numerous, with a noted weak correlation between the number of respiratory events and daytime sleepiness. In comparing ROSA to NOSA patients, there is little data to suggest that the two groups have different symptom clusters within the affective or cognitive realms.

Methods: A retrospective review of pts. who underwent polysomnography was performed; pts. with an AHI of 5-40 were selected and stratified by an AHI in NREM that was two-times greater than REM (Group A) and an AHI that was two-times greater in REM than NREM (Group B). Patients with psychiatric histories were excluded. Demographic data included age, gender, BMI, & history of pulmonary/cardiac/neurological co-morbidities. As part of standard clinical procedure, all pts. completed a Sleep Disorders Inventory (SDI), which includes four dichotomous (y/n) questions related to affective & cognitive symptomatology: "Are you bothered by low mood, irritability, or anxiety during the day?"; "Are you bothered by problems with attention, concentration, or memory during the day?"; "Do you find it hard to persist at things you are doing, even simple things?"; and "Do you feel that you have lost motivation to do things, or that you have lost interest or pleasure in activities that you used to enjoy?" The number of "yes" responses was converted to a percentage endorsed. Groups were compared by t-test to see if they differed in frequency of endorsement to the cognitive/affective symptom cluster.

Results: A total of 74 subjects were included in the final analyses (Group A; n=31 and Group B; n=43). Results indicated that gender was not equally distributed between groups (Group A M/F ratio: 5.2:1, whereas Group B M/F ratio: 1:1.2) [Chi-square, $p < 0.001$]. Group B had a significantly greater BMI than Group A ($t = -3.54$, $p < 0.001$, 2-tailed). Groups were equivalent in terms of age. There were no significant differences between groups in terms of positive responses to the cognitive/affective symptom cluster in the SDI (Group A = 45%, Group B = 40%).

Conclusion: Although findings do not support a difference in symptom presentation between ROSA and NOSA pts., the unequal gender and weight distributions, and the possible insufficiency of the 4 questions utilized may have contributed to the failure to elucidate differences between the groups.

0471

TOLERABILITY AND SAFETY OF A NOVEL TONGUE ADVANCEMENT DEVICE FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: Many sleep surgeries for obstructive sleep apnea (OSA) result in high patient morbidity with only limited clinical efficacy. This study evaluates tolerability and safety of a new adjustable minimally invasive surgical procedure for tongue advancement for the treatment of OSA.

Methods: Patients with an apnea hypopnea index (AHI) between 15 and 50 underwent a minimally invasive surgical procedure to implant the Advance™ System. The procedure consisted of connecting a tongue based tissue anchor to a mandibular titration spool that is adjustable. Patients returned for titration of tongue advancement under local anesthesia. Complications and postoperative morbidity were assessed.

Results: 26 patients underwent implantation. No functional impairment in speech, swallowing, sense of taste and pharyngeal irritation were detected. Postoperative pain on a VAS was moderate 4.8 ± 2.8 on day one decreasing rapidly to 0.9 ± 1.1 on day five. Removal and re-implantation of the device was necessary in 3 patients due to a detachment of tetherline at the titration spool. The fixation knot was modified with no further detachments. No wound infection, abscess or tongue hematoma occurred. One patient experienced a transient unilateral tongue weakness after implant retrieval and one patient suffered ecchymosis of the floor of mouth with no sequelae. One patient undergoing post implant titration had excessive pain which was immediately relieved by loosening the tension.

Conclusion: Adjustable tongue advancement with the Advance System is a well tolerated technique. The opportunity of titration under local anesthesia offers the potential to adjust tongue advancement according to clinical efficacy and postoperative morbidity.

Support (optional): This study was supported by Aspire Medical, Inc.

0472

DECREASED ARTERIAL STIFFNESS IN LONG-TERM CPAP TREATED MALE OBSTRUCTIVE SLEEP APNEA PATIENTS AS MEASURED BY OVERNIGHT DIGITAL ARTERIAL TONOMETRY MONITORING

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Introduction: Obstructive sleep apnea (OSA) is associated with increased risk for cardiovascular disease. CPAP treatment has been shown to reduce apnea events and improve cardiovascular outcome. Peripheral Arterial Tonometry (PAT) is derived from the finger tip arterial pulse wave amplitude. We have previously shown that OSA patients have increased arterial stiffness as measured by PAT derived augmentation index (PAT-AI). This study investigated the effect of long term treatment with CPAP on PAT-AI.

Methods: Study population: PAT-AI was compared between chronic CPAP treated and non treated OSA patients. CPAP group comprised ten male OSA patients treated with CPAP for at least 3 months who had RDI > 20 at the initiation of treatment and RDI < 5 during the night of measurement. OSA group comprised ten age, height and BMI matched males with RDI > 20. Mean age was 55 ± 15 and 54 ± 16 y, height 175 ± 6 and 173 ± 8 cm and BMI 30 ± 5 and 30 ± 6 in the CPAP and OSA groups respectively (all $p = ns$). All subjects underwent a single night full PSG study in the sleep laboratory with concurrent monitoring using a portable device to record the PAT signal (Watch_PAT 100, Itamar Medical,

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Caesarea, Israel). The AI, an established measure of arterial stiffness, was calculated from the PAT waveform.

Results: Mean all night PAT-AI was significantly lower in the CPAP treated group as compared to the OSA group (25 ± 25 vs. 39 ± 20 %; $p=0.023$). Adjustment of PAT-AI for age and heart rate slightly increased the significance (25 ± 18 vs. 39 ± 13 %; $p=0.013$).

Conclusion: Arterial stiffness assessed by calculation of the augmentation index from the PAT signal is decreased in male OSA patients receiving effective long term treatment with CPAP as compared to non treated OSA patients of similar body habitus and similar intrinsic OSA severity.

0473

DETERMINANTS OF CPAP COMPLIANCE IN NEWLY DIAGNOSED PREVIOUSLY UNTREATED OBSTRUCTIVE SLEEP APNEA PATIENTS

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Introduction: Nasal continuous positive airway pressure (CPAP) is the gold standard in the treatment of obstructive sleep apnea syndrome (OSAS). However, the benefits of CPAP rely on its regular use by the patient, which in turn depends on several social, mechanical, economical and demographical factors. The aim of this study is to 1) assess CPAP compliance in Buffalo Metropolitan area and 2) investigate any possible association of the polysomnogram (PSG) variables with objective CPAP compliance.

Methods: A retrospective chart review was performed on 141 random patients whose short term (2.5 month) CPAP compliance data were available. The final sample consisted of 80 patients with newly diagnosed and previously untreated OSA (rest excluded due to history of previous diagnosis of OSA and/or treatment CPAP).

Results: Among these 80 newly diagnosed OSAS patients (43 men and 37 women), mean age was 51.14 ± 12.4 years and mean weight was 213.44 ± 47.07 lbs. The CPAP compliance was an average of 5.95 hours/night (h/n). Comparison between non compliant group (NCG) of 26 patients (who used CPAP for >4 h/n for $\leq 50\%$ of the nights) and compliant group (CG) of 54 patients (who used the CPAP >4 h/n for $>50\%$ of the nights) showed that NCG had a trend toward lower Epworth Sleepiness Scale [$p=0.15$], higher sleep efficiency [$p=0.18$], and lower Respiratory Distress Index [$p=0.08$] as compared to the CG. A significant difference was found between the two groups in respiratory arousal index (RAI) [$p=0.008$]. Mild, but significant positive correlation was found between CPAP compliance and RAI on Pearson's scale ($r=0.295$, $p=0.008$).

Conclusion: In newly diagnosed patients with OSAS, 1) short term compliance to CPAP was an average of 5.95 h/n and 2) higher RAI was indicative of higher CPAP compliance. Respiratory arousal index may be an important overlooked predictor of CPAP compliance.

Support (optional): None

0474

DIFFERENTIAL EFFECTS OF ETHNICITY AND BMI ON SLEEP APNEA SEVERITY

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Introduction: Sleep Apnea affects up to 20% of all Americans. This disease has been associated with several cardiovascular risk factors leading to coronary heart disease, stroke and death. These risk factors include diabetes, hypertension and especially obesity. Research has found ethnic differences in prevalence and severity of diabetes and hypertension and has found African American (AA) and Latino American (LA) populations to suffer from higher rates of obesity than Caucasian Americans (CA). These findings are consistent in sleep research—African Ameri-

can and Latino American patients have been found to have higher apnea hypopnea indices (AHI) than their Caucasian counterparts. Pilot studies show that while Asian Americans (AsA) have lower BMIs than CA, they have similar levels of OSA. The purpose of our study was to replicate these findings using a larger sample and to expand the findings regarding the impact of ethnicity on AHI. We hypothesized that AsA would have lower BMIs than AA, CA, and LA but would have similar OSA severity

Methods: Using retrospective chart review, we collected data from 196 patients seen at Clinilabs/Sleep Disorders Institute in New York, NY. Subjects were classified into four ethnic groups based on self-report: Caucasian Americans (CA), African Americans (AA), Latino Americans (LA) and Asian Americans (AsA). A One-Way ANOVA with Bonferroni corrections were used to compare the AHI across age, BMI, gender and race. Regression plots were calculated for all subjects by BMI and AHI and for each ethnic group.

Results: There were no significant differences in AHI amongst the four ethnic groups (Mean AHI = 43.7). In contrast, AsA had significantly lower BMIs when compared to the other three groups ($p<.05$). Further analysis indicated that AA and CA patients had AHIs that were moderately associated with their BMIs. LA patients had AHI's that were poorly predicted by BMI. Regression analysis demonstrated that when all ethnic groups were considered together, BMI was weakly associated with AHI. When individual ethnic groups were considered, BMI predicted AHI differentially with predictions being strongest for CA (R square = .36) and AA (R square = .24) groups and weakest for LA (R square = .01) and AsA (R square = .12) groups.

Conclusion: Findings suggest that BMI is differentially related to apnea severity in different ethnic groups. One possibility is that factors other than BMI may contribute to the development of OSA.

0475

ANTHROPOMETRIC AND EXERCISE MARKERS OF RISK FOR OBSTRUCTIVE SLEEP APNEA IN YOUNG MEN

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Introduction: Obstructive sleep apnea (OSA) is a disorder that contributes to the development of several chronic diseases, including hypertension (HTN). It often goes unrecognized in routine clinical evaluation. Exercise testing has been a useful tool for identifying those at risk for HTN and coronary artery disease, but its utility in identifying OSA risk has been given limited attention. The purpose of this study was to determine whether simple anthropometric measures in conjunction with ramp exercise test (RXT) responses might serve to discriminate between young men with and without OSA.

Methods: Ninety-one men (age = 21.6 ± 0.30 yr) were screened for OSA using an at-home, simplified somnographic device. Subjects underwent fasting blood lipid analysis, were evaluated for neck and trunk girths, body composition via dual-energy x-ray absorptiometry, and cardiorespiratory responses to maximal RXT via cycle ergometer. Exercise measures included oxygen consumption, heart rate (HR), and blood pressure (BP). HR and BP data also were expressed in recovery as rates of change in the early post-exercise period, i.e. HR difference (HR_{diff}) calculation ($HR_{peak} - HR_{1-min\ recovery}$), and BP was converted to a

recovery ratio (systolic BP_{1-min recovery} / systolic BP_{peak}) for each minute of recovery.

Results: Stepwise linear regression revealed that hip-to-height ratio (HHR), hip circumference, serum triglycerides, and recovery systolic BP ratio at 2 and 4 minutes were independent predictors of AHI (model fit: $R^2 = 0.68$, $p < 0.0001$). ROC curve analysis showed that percent body fat, HHR, and HR_{diff} at 2 and 4 minutes were the best univariate predictors of OSA risk (AUC = 0.77 for each measure, $p = 0.003$).

Conclusion: For young adult men, simple anthropometric measures and cardiovascular responses from routine clinical exercise testing were more effective in discriminating those at increased risk for OSA than were several of the more established clinical screening variables.

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0476

THE EFFECTS OF NASAL CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) ON THE SYMPTOMS OF GULF WAR SYNDROME (GWS)

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Introduction: Veterans with GWS complain of symptoms including pain, fatigue, cognitive impairment and sleep disturbance. These symptoms resemble those of fibromyalgia patients. In a previous clinical trial, nasal CPAP produced a significant improvement of the symptoms of fibromyalgia patients. Therefore, we performed a controlled trial of nasal CPAP upon the symptoms of GWS.

Methods: We recruited 12 veterans with GWS and IFL during sleep. GWS was defined as unexplained pain, fatigue and cognitive dysfunction in a Persian Gulf veteran deployed between 8/90 & 8/91. IFL was identified during a polysomnogram and the CPAP needed to overcome IFL, therapeutic pressure (P_{therapeutic}) was determined. All participants underwent a baseline questionnaire assessment of symptoms. Pain was assessed by a visual analogue scale (VAS) administered daily for 1 week. Fatigue during 2 weeks was assessed retrospectively using the Fatigue Severity Scale. Cognition during 1 week was assessed retrospectively with a cognitive VAS. Sleep quality during 1 month was assessed retrospectively with the Pittsburgh Sleep Quality Index (PSQI). Equal numbers of participants were randomized to either P_{therapeutic} or sham CPAP for 3 weeks of treatment. Compliance was monitored with compliance software. During the 3rd week of treatment, all participants repeated their symptom assessments.

Results: The two groups were equally compliant with treatment. Participants receiving P_{therapeutic} experienced: A 37 % improvement of pain VAS score ($p=0.002$) A 49 % improvement of Fatigue Severity Scale score ($p=0.0002$) A 44% improvement of cognitive VAS score ($p=0.014$) A 43% improvement of PSQI score ($p=0.007$) The p-values are compared to the sham group who generally experienced mild worsening of symptoms.

Conclusion: Our findings suggest that pharyngeal collapse during sleep plays a role in the development of pain, fatigue, cognitive dysfunction and sleep disturbance among GWS patients. These findings are similar to our previous findings among fibromyalgia patients.

Support (optional): Department of Veterans Affairs, Career Development Award. Respiroics Inc. supplied the CPAP and sham units

0477

MEASUREMENT OF INSPIRATORY AIRFLOW DYNAMICS DURING SLEEP IN VETERANS WITH GULF WAR SYNDROME (GWS)

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Introduction: Veterans with GWS complain of symptoms including fatigue, cognitive impairment, pain and sleep disturbance. These symptoms of GWS are similar to those found in upper airway resistance syndrome (UARS). Inspiratory airflow limitation (IFL) during sleep characterizes UARS and may account for its symptoms. Therefore, we studied the inspiratory airflow dynamics during sleep of veterans with GWS to determine whether they demonstrate IFL.

Methods: We recruited 12 veterans with GWS, defined as unexplained pain, fatigue and cognitive dysfunction in Persian Gulf veterans deployed between 8/90 & 8/91. Each participant underwent a full-night polysomnogram while sleeping supine. Sleep was assessed using standard methods. Airflow was measured with a pneumotachograph in series with a nasal mask and respiratory effort with a supraglottic pressure (P_{sg}) catheter. For each participant, we identified the first two 2-minute samples of continuous stage 2 sleep and exported the flow and effort signals into an analysis program. For each breath, we plotted inspiratory airflow against P_{sg} and determined the presence of IFL defined as a plateau of airflow despite a decrease in P_{sg} of at least 1 cmH₂O. For each participant, the total number of flow-limited breaths divided by the total of sampled breaths determined the percentage of flow limited breaths.

Results: Our GWS participants were all males with mean age of 43 years and mean BMI of 33kg/m². Nine of our 12 participants snored. Four of our 12 participants had apnea with frequent arousals and no 2-minute periods of continuous stage 2 sleep. Among the remaining 8 participants, 94 % of the inspiratory efforts during continuous stage 2 sleep demonstrated IFL.

Conclusion: As in UARS, veterans with GWS experience pharyngeal collapse with a high prevalence of IFL during sleep. How this finding compares with healthy Gulf War veterans remains to be determined.

Support (optional): Department of Veterans Affairs, Career Development Award.

0478

CPAP ADHERENCE IN VETERANS WITH PSYCHIATRIC DISORDERS - AN UPDATE

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Introduction: Despite an increased prevalence of psychiatric disorders such as depression and PTSD in individuals with sleep apnea, little is known about whether such conditions affect adherence to CPAP treatment. The present study examined rates of CPAP adherence in veterans with and without co-morbid psychiatric diagnoses (PD) and updates our 2007 APSS poster.

Methods: Data were obtained from the Respiroics Encore Pro® database of veterans receiving CPAP treatment for sleep apnea between 2000-2007. Investigation of VA medical records was used to determine presence or absence of PD. Patients with PD other than PTSD or mood disorders were excluded.

Results: The first 500 qualifying patients in the database were analyzed (484 males; mean age = 56.8 years, SD = 10.9, mean RDI = 40.4, SD = 29.0). Two hundred seventy two (54%) patients had co-morbid PD.

Category H—Sleep Disorders – Breathing

At one month post-CPAP, those with PD used CPAP an average of 4.37 hrs/night on 65.6% of nights, whereas those with no psychiatric disorders used CPAP 4.70 hrs/night on 71.5% of nights. The difference in amount of CPAP use between groups (20 min/night) was not significant. Although the percentage of nights was significantly lower in patients with PD, this translated into a clinical difference of only .4 nights/week. There were no significant group differences in CPAP use at 3 months post-CPAP. Veterans were classified into “good” and “poor” adherence based on whether they used CPAP > 4 hrs/night and > 70% of nights at 1 month. Although a higher percentage of “good” adherers did not have PD (53% vs. 46%), chi-square analysis was not significant.

Conclusion: Veterans with PTSD and/or mood disorders used CPAP slightly less consistently but for a similar amount of time each night compared to those without psychiatric disorders. The presence of comorbid psychiatric disorders in veterans does not seem to greatly impact adherence to CPAP treatment.

0479

EEG AROUSALS AND DISTRIBUTION IN PATIENTS WITH SLEEP APNEA COMPARED WITH CPAP AND NORMS

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Introduction: Decade specific norms for EEG arousals have been published recently. The current study compared arousals in moderate and severe apnea patients before and with effective cpap treatment (i.e., no snoring) to determine the degree of sleep disturbance compared with the norms.

Methods: Seventeen patients with severe obstructive sleep apnea and 14 patients with moderate obstructive sleep apnea with data from separate baseline and cpap nights were identified based on RDI. Patients with other significant sleep disorders or medical illness were excluded. Sleep studies were rescored by the same scorer who had scored recordings for the construction of arousal norms.

Results: RDI for the patient groups (selection factor) was 89 ± 29 and 28 ± 14 respectively. Groups did not differ in age (49 years) or BMI (38.1 vs 36.4) but did differ in effective cpap pressure (11.5 vs 8.7 cm H₂O; $t_{29}=2.722$, $p<.05$). Arousal index at baseline was significantly greater in severe apnea patients (77 ± 42 vs 42 ± 14). However, at effective cpap, arousal index was significantly lower in the severe patients (12.7 ± 6 and 22.2 ± 8 , $t_{29}=3.69$, $P<.001$). Both apnea groups had increased arousals compared to norms prior to cpap therapy. On effective therapy, the apnea groups did not differ from the 40-year-old age norm (16.5 ± 6.3) with severe patients trending lower and mild patients trending higher.

Conclusion: Expected elevations in arousals in patients at baseline and reduction with cpap were found. Arousal index with cpap was reduced in severe apnea patients below levels in moderate apnea patients and normals. This suggests that severe but not moderate apnea patients are recovering from sleep deprivation during their initial cpap use. The similarity of reduced arousals with cpap and after sleep deprivation could be used as a measure of sleep disturbance associated with sleep apnea.

Support (optional): Dayton Department of Veterans Affairs Medical Center, Wright State University, Kettering Medical Center and the Sleep-Wake Disorders Research Institute

0480

DOES REDUCTION IN DEPRESSION DUE TO CPAP INFLUENCE PERSONALITY CHANGE IN OSAS PATIENTS?

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Introduction: Clinicians describe patients who are diagnosed with the obstructive sleep apnoea syndrome (OSAS) as having impulsive reactions and a quick temper. Personality of OSAS patients seem to change due to Continuous Positive Airway Pressure (CPAP) treatment. However, the relationship between OSAS and personality change has rarely been studied. Research has shown that OSAS can cause depression. Aim of the present study was twofold: to examine 1) whether personality of OSAS-patients changes due to treatment and 2) whether depression influences change in personality.

Methods: In total, 71 diagnosed OSAS patients (AHI>15; mean \pm SD, 38.4 ± 16.7), of which 57 were men and 14 women (mean \pm SD, 56 ± 8.9 years) filled out both a depression scale, the Beck Depression Inventory (BDI), and a personality measure, the NEO-FFI, before the start of their treatment and again after four months of treatment with CPAP. The control group that consisted of 82 sleep patients without OSAS of which 69 were women and 13 were men (mean \pm SD, 50.7 ± 9.8 years) also filled out both inventories at both times of measurement. The total score of the BDI was used to measure depression. Five basic personality factors were examined: neuroticism, extraversion, openness, agreeableness and conscientiousness.

Results: Paired sample t-tests showed a higher score in altruism ($t(86)=-2.17$, $p<.05$) and lower scores on neuroticism ($t(83)=3.01$, $p<.05$) and depression ($t(76)=2.67$, $p<.01$) after treatment. When compared with untreated sleep patients no significant time effect was found. Controlling for depression does not reduce the correlations between measurements before and after treatment of each personality factor.

Conclusion: Personality of OSAS patients appears to change after four months of CPAP treatment. Depression is not the cause of this change. Future studies could explore which factors do contribute to this personality change and whether the change is permanent.

0481

REM RELATED OBSTRUCTIVE SLEEP APNEA (REM OSA): PREVALENCE AND GENDER DISTRIBUTION

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Introduction: Although characteristics of REM OSA (clustered and longer apnea/hypopnea events with significant desaturations predominantly during REM) are well described, clinical significance is still not clear. Treatment necessity of REM OSA has been discussed in recent publications even though other risk factors such as sinus pauses associated with REM OSA maybe present. The goal of this study was to investigate the prevalence and severity of REM OSA among patients with OSA and to find out the influence of gender on REM OSA.

Methods: We reviewed 21586 standard PSGs acquired from November 2004 through November 2007. 20729 PSGs (12563 male, 8166 female) were selected based on the following age criteria (>16 years old). The inclusion criteria for the REM OSA group (2288) was: AHI > 5, REM duration greater 30 min, REM AHI>20/h and non-REM AHI<10/h. The remaining were considered the non-REM OSA group (18441).

Results: 2288 (11%) met defined criteria for REM OSA. No differences were found between REM and non-REM OSA by age (49.63 and 49.66), BMI (34.9 and 32.44) and Epworth Sleepiness Scale (ESS) (9.52 and 9.30). Significant differences ($p<.001$) were observed in male/female ratio in 2 groups: 1:1.26 in REM OSA and 1.68:1 in non-REM OSA. AHI was significantly higher in non-REM OSA group (24.91/h) than in REM OSA group (11.35/h). Non-REM AHI was higher in males of non-

REM OSA (male 29.29/h and female 15.23/h) group with no differences between male and female in REM OSA (5.57 and 4.80 respectively).

Conclusion: These results suggest that REM OSA is a typical characteristic of about 1/10th of patients with OSA. REM OSA also appears to be more prevalent in female patients. Follow-up studies (including MSLT) are needed to adequately solve the question regarding treatment necessity as no differences were found in ESS between REM OSA and non-REM OSA groups.

0482

IMPACT OF WIND-INSTRUMENT PRACTICE ON OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Obstructive sleep apnea syndrome (OSAS) is a condition characterized by reduction or cessation in airflow with resultant oxygen desaturation and arousals. Treatment of obstructive sleep apnea is heavily reliant on physical manipulation of the upper airway. With the exception of weight loss, the role for self-directed care or “physical therapy” in this condition has been limited. In this case series, we describe a phenomenon of musicians with severe OSA who demonstrated minimal sleepiness and oxygen desaturation.

Methods: A series of 3 wind-instrument musicians is described including sleep history, degree of sleepiness, and features/statistics regarding their musical ability. Average apnea-hypopnea index (AHI), oxygen saturation, time spent below an oxygen saturation of 90%, respiratory event length, and minimum oxygen saturation were calculated from polysomnographic testing.

Results: The subjects had an average AHI of 37.1 seconds, average oxygen saturation of 94.7%, average minimum oxygen saturation of 87.3%, average respiratory disturbance length of 30.1 seconds, and spent an average of 6.7 minutes at an oxygen saturation less than 90% (2.3 % of the total sleep time). This case series demonstrates a rarely described phenomenon of minimal oxygen desaturation despite significantly elevated apnea-hypopnea indices and apnea/hypopnea duration.

Conclusion: In addition to improving current positive airway ventilation techniques, there is a need to explore novel therapeutic approaches to OSAS. We propose that some musicians with OSAS are conditioned from a cardiopulmonary standpoint, through playing wind instruments, to minimize the impact of even lengthy apneas on oxygen saturation. Many years of such training seems to have altered their physiologic ability to extract and carry oxygen. This case series suggests possible therapeutic benefit from wind-instrument playing (music therapy) on sleep disordered breathing. Further research into the efficacy and practicality of this type of treatment for OSAS should be considered.

Support (optional): None

0483

RISK FOR SLEEP APNEA SYNDROME IN PAKISTAN: CROSS-SECTIONAL SURVEY UTILIZING THE BERLIN QUESTIONNAIRE

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Introduction: In developed world raised apnea index with symptoms of Obstructive Sleep Apnea (OSA) ranges between 2-4%. Asian data is scarce; however studies report 2.1-7.5% prevalence. OSA prevalence studies in Pakistani population are lacking. We used standardized Berlin-Questionnaire, to survey a representative Pakistani population; and estimate prevalence of individuals high-risk for OSA.

Methods: The survey was conducted at Aga Khan University Hospital, Pakistan. Individuals, above eighteen years of age who had come

to attend a public health education seminar were included. Berlin-questionnaire was administered by a group of medical students. Based on responses to Berlin Questionnaire, participants were grouped into high or low-risk for OSA.

Results: In our study total sample size was 156 (n). 124 were male, with most (59%) in the 18-30 years age group. Mean BMI was 23 +/- 3. 33% reported snoring which was significantly more prevalent in the high-risk group (p<0.0001). Daytime sleepiness (p< 0.001) and tiredness (p=0.002) were more significantly common among high-risk group. More women reported tiredness upon waking compared to men (p= 0.03). 15% reported that they had nodded off to sleep while driving at least once in life. 15% reported hypertension, which was significantly more prevalent in the high-risk group (p<0.001). Most high-risk individuals were among 55-65 years age group. The overall prevalence of individuals who were high risk for OSA was 15%.

Conclusion: A significant proportion of the population is at high-risk for OSA. However, risk of OSA in our study population is lower compared to US population; a finding consistent with previously published data from the studies examining the prevalence of OSA in Asian populations. Further studies, with larger sample size, will allow estimate of the true OSA prevalence in Pakistan that may result in better public health planning and yield benefits.

0484

MMA COMBINED UP3 FOR THE ORIENTAL OBESE PATIENTS WITH SEVERE OSAS

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Introduction: For oriental obese patients with severe obstructive sleep apnea syndrome (OSAS), Maxillomandibular advancement (MMA) procedures may cause craniomaxillofacial deformities after their jaws advance in large distance though these procedures can resolve the upper airway problem. What we want is to resolve the problem by means of combined uvulopalatopharyngoplasty (UP3/UPPP) and MMA in same term.

Methods: 12 cases of obese patients with severe OSAS, their age 45.6±16.5, BMI 35.23±3.52, AHI 85.36±5.47 preoperatively. All patients underwent cephalometric analysis, PSG and estimate of velopharyngeal closure and speech function over 12 months preoperatively and postoperatively. All patients underwent UPPP and MMA in same term. Their maxilla advanced 8.5±2.4mm by Lefort I osteotomy, and their mandible moved forward 10.4±3.3mm by bilateral sagittal split ramus osteotomy and their menton advanced 15.3±2.2 by genioplasty.

Results: All patients' sleep-related breathing disorders was cured successively estimating by Stanford successful criteria, their AHI 10.36±7.24 postoperatively, mean follow-up duration is 15.3 months. All patients have no speech/swallow problems and have good teeth occlusion and good appearances.

Conclusion: VPI can be avoided by means of computer-aided designed UP3 and MMA. Patient's maxillary bone and wound can also get to heal smoothly and well after underwent combined UPPP and MMA in same term. The surgical procedures have good responds for the oriental obese patients with severe OSAS. Long term results need to be followed.

0485

COMPUTER-AID DESIGNED UVULOPALATOPHARYNGOPLASTY(UPPP) FOR OBESE PATIENTS WITH OSAS

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Introduction: There are only 40% to 50% OSAS patients who have a good response to uvulopalatopharyngoplasty(UPPP). The main reasons are that there are multipoint narrow at patients' upper airway, while UPPP can only relieve the narrow at the region behind the soft palate, and how much tissue at soft palate and lateral pharynx to be removed is difficult to determined. UPPP treatment may cause the velopharyngeal incompetence and patients may choke while they are eating something and may have exorbitant rhinolalia while they speak. To reduce or eliminate these complications we applied the computer-aided designed UPPP for these patients.

Methods: 16 cases obese patients with OSAS, age 40.5±10.7, AHI 32.56±7.32, we analyzed and determined the narrow and occlusive site by using computer cephalometric analysis system, meanwhile we took the lateral roentgenograms for these patients while they continuously sound /i/. we found the velopharyngeal closure point and measured the distance from velopharyngeal closure point to the top of uvula, then we cut the 90% of soft tissue measured from uvula top forward to soft palate, so that the excessive soft tissue in this region could be resected safely. We evaluated the results by PSG, cephalometric analysis and speech examination been performed both pre- and post- operation.

Results: there are 75% of the patients who had good response to this kind of UPPP, sleep disorder breathing in 16 cases were remarkably relieved with mean AHI 17.37±8.51, and all patients had a good velopharyngeal closure while they eat or speak, there are no problem with speech or swallowing. the mean follow-up duration is 15.3 months.

Conclusion: It is the key to select correctly surgical indication and to measure and remove excessive soft tissue accurately for UPPP. Computer-aided designed UPPP increases the achievement ratio and decrease the complications remarkably.

0486

POOR SLEEP AND CO-MORBIDITIES PREDICT MORTALITY IN ELDERLY PATIENTS WITH SLEEP APNEA

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Introduction: Sleep disordered breathing is particularly prevalent in the elderly population. Therefore, the question if sleep apnea constitutes an independent risk for mortality in the elderly is clinically important. The purpose of this study was to investigate all cause mortality in a sleep clinic population of elderly patients investigated by whole night polysomnography (PSG) because of suspected sleep apnea syndrome.

Methods: During January 1st 2000 - 31st December 2005, 633 elderly (age> 65 yrs, 461 men and 172 women) were referred to the Technion Sleep Medicine Center because of suspected sleep apnea. Participants' personal identification (ID) number was used to collect mortality information from the computerized files of the Ministry of the Interior. Demographic, sleep and clinical data were compared between alive and dead patients.

Results: Fifty six patients (8.84%; 42 men and 14 women) died during the follow-up period (Median=4 yrs). Patients who died were significantly older (73.1±6.1 vs. 69.5±4.4, p<.000001) and had higher RDI (33.8±24.4 vs. 28.4±19.5, p<.053) than alive patients. They also had higher rates of asthma (12.5 vs 5.7%, p<.04), COPD (35.7 vs 9.0%, p<.000001), s/p myocardial infarction (17.9 vs 4.5%, p<.00003), chronic heart failure (17.9 vs 2.6%, p<.000001), diabetes (42.9 vs 21.0%,

p<.0001), peripheral vascular disease (5.4 vs 1.2%, p<.01), other cardiovascular disease (25.0 vs 9.4%, p<.0003), ischemic heart disease (46.4 vs. 23.6%, p<.0001), and stroke (12.5 vs. 3.6%, .002). PSG data revealed that patients who died had significantly longer sleep latency (41.5±58.3 vs. 28.5±32.5 min, p<.009), lower sleep efficiency (60.9±22.1 vs.71.6±16.5%, p<.000009), less stage 3-4 (9.4±8.4 vs. 14.2±9.6, p<.0003) and REM sleep (10.5±6.6 vs. 14.9±6.8%, p<.000003). Multivariate analysis revealed that age, sleep efficiency, asthma, COPD, s/p MI, CHF, diabetes, other cardiovascular diseases, IHD and stroke, were independent predictors of mortality.

Conclusion: Poor sleep and co-morbidities but not apnea severity predict mortality in elderly sleep apnea patients.

0487

VALIDATION OF INSOMNIA COMPLAINTS IN PATIENTS WITH SEVERE SLEEP APNEA

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Introduction: It is widely accepted that complaints about excessive sleepiness, non-refreshing sleep, and chronic fatigue, are the hallmark symptoms of sleep apnea syndrome. There is evidence that co-morbid insomnia is also prevalent in sleep apnea patients. Previous studies investigating insomnia in sleep apnea however did not control for confounding variables. The present study compared polysomnographic (PSG) data of patients with severe sleep apnea with and without complaints about insomnia controlling for confounding variables.

Methods: Thirty one patients diagnosed with severe sleep apnea (apnea hypopnea index (AHI)>30) who complained about sleep onset insomnia and sleep maintenance insomnia were individually matched for age, BMI and AHI with 31 patients with severe sleep apnea who did not have any complaint about insomnia. PSG sleep data were compared between the two groups.

Results: Sleep apnea patients with and without insomnia had comparable age (Insomnia: 51.4±5.9; without-insomnia 50.6±5.1 yrs), BMI (Insomnia: 34.1±5.7; without-insomnia: 33.6±5.2 Kg/m2) and AHI (Insomnia: 54.9±16.6; without-insomnia: 55.6±16.7 events/hour). PSG recordings revealed that the insomnia group had significantly less total sleep time (297.5±91.6 vs. 364.9±53.8 min, p<0.0008), lower sleep efficiency (69.6±6.0% vs. 84.1±10.8%, p<0.001), and lower percent of REM sleep (13.2±7.0 vs. 16.8±5.7%, p<.03). Sleep latency was non-significantly longer in patients with insomnia (37.9±54.4 vs. 21.7±27.2, p<.12).

Conclusion: The present results demonstrate the validity of complaints about insomnia in patients with severe sleep apnea. Insomnia, particularly of the sleep onset type, is not considered a typical complaint of sleep apnea syndrome and is often explained as secondary to sleep fragmentation caused by the respiratory events, or as a nonspecific complaint because of patients' general dissatisfaction with their sleep. In view of the validity of the complaints and the potential detrimental effects of co-morbid insomnia on compliance with nCPAP treatment, careful attention should be paid to the diagnosis and treatment of co-morbid insomnia in sleep apnea patients.

0488

DETERMINANTS OF CPAP-EMERGENT (COMPLEX SLEEP APNEA) IN THE VETERAN POPULATION

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Introduction: Sleep apnea in the veteran population has been associated with increased morbidity and mortality. While central sleep apneas (CSA) have been commonly reported in veterans, the determinants of CPAP-emergent CSA (also termed as complex sleep apnea) are not

known. A retrospective study was conducted to assess the predictors of complex sleep apnea in the veteran population.

Methods: A retrospective chart review, from 9/2006 to 5/2007, of veterans undergoing polysomnography (PSG) for evaluation of sleep apnea was done. 200 charts were reviewed. Apnea hypopnea index (AHI) was defined as the total number of respiratory events (apneas and hyponeas) divided by the total sleep time. Central apnea index (CAI) was defined as the total number of central apneas divided by the total sleep time. CSA was defined as a CAI of >5/hr. CPAP-emergent CSA was defined when central sleep apnea appeared during CPAP or bi-level titration study. We analyzed the clinical data on all patients who were identified as having central sleep apnea or CPAP-emergent CSA on their sleep study report. Patients who underwent split-night PSG and PSG and positive airway pressure titration on separate nights were included. The following data were extracted: gender, age, BMI, Epworth Sleepiness Scale, AHI, CAI, past medical history, past surgical history, social history-opiate use, medication use, and when available PFT and 2D-echo results.

Results: All subjects were males, with an average age of 60.0±12.3 years and BMI 34.2±6.5 kg/m². The AHI was 52.6±36.9/hr, the CAI was 16.6±24.6/hr. 200 patients underwent PAP titration. Of these, 80 were found to have CSA. Eighteen (37.5%) patients were also classified as having CPAP-emergent CSA, as defined above. 160 patients underwent split-night studies. The relative risk of CPAP-emergent CSA following a split-night study vs a separate night of titration was 7.7 (p=0.002). Age, BMI, ESS, HTN and other comorbid factors were not significant risk factors for the absence or presence of CPAP-emergent CSA in this small population.

Conclusion: A split-night study protocol seemed to be a predictor of CPAP-emergent CSA in this population. Further investigations in a larger population are warranted.

0489

MALLAMPATI SCORE AND OBESITY AS SIMPLE PREDICTORS OF ORAL APPLIANCE EFFICACY IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Mandibular advancement often fails to improve passive upper airway patency in persons with redundant oropharyngeal soft tissue including obese patients with obstructive sleep apnea (OSA) (Isono et al. Anesthesiology 1997). This suggests that oral appliances for the treatment of OSA may not be efficacious for obese OSA patients. Since Mallampati score (MS) reflects the amount of soft tissue in the oral cavity to some extent, we hypothesized that OSA patients with higher MS would not respond well to oral appliance.

Methods: A total of 77 OSA patients [Apnea Hypopnea Index (AHI)=19.5±12.3/hr, Body Mass Index (BMI)=24.9±4.5 kg/m², MS=3±1] were recruited. Patients were divided into lower (i.e., Class 1 to 3, N=41) and higher (i.e., Class 4, N=36) MS groups. Follow-up polysomnography was completed with the ventrally-adjusted oral appliance in place. Responders were defined as patients having an absolute reduction in AHI to <5/hr and/or a relative reduction in AHI of >50% from baseline.

Results: Forty-seven patients were regarded as responders. MS did not satisfactorily predict treatment outcome: the positive and negative predictive values (PPV/NPV) of MS were 0.68/0.33. When the optimum cut-off value for BMI was set at 24 kg/m² determined by a receiver operating characteristic (ROC) curve, the higher BMI (>24) group tended to possess higher MS compared with the lower BMI (≤24) group (p<0.05). Area under the ROC curve was 0.72. Lower (PPV/NPV=0.77/0.47) and

higher (PPV/NPV=0.94/0.55) MS groups could individually predict treatment success when both groups were divided into the lower and higher BMI subgroups, respectively (p<0.05).

Conclusion: We conclude that MS alone is insufficient to predict the efficacy of oral appliances for OSA but becomes effective when BMI is used simultaneously. A better response to oral appliances is expected regardless of MS when BMI is ≤24, whereas a greater chance of treatment failure occurs when the Class 4 MS is combined with a BMI >24.

0490

NO DIFFERENCES, ASSOCIATION OR TREND BETWEEN NEUROCOGNITIVE FUNCTIONING AND SLEEP DISORDERED BREATHING IN A COMMUNITY SAMPLE OF YOUNG SCHOOL AGE CHILDREN

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Introduction: Only two previously conducted studies have compared children with sleep disordered breathing (SDB) and controls on neurocognitive measures within the general population, and the results were mixed. The goal of this study was to examine the difference, association and trend between neurocognitive functioning and both SDB and snoring in a large general population sample of children who underwent a full overnight polysomnogram and comprehensive neurocognitive test battery.

Methods: 594 children age 6-12 from a general population sample assessing the prevalence of SDB, underwent a full night polysomnography and comprehensive neuropsychological testing (intelligence, attention, memory, processing speed, and visual-motor skill) in our sleep laboratory.

Results: A one way analysis of variance (ANOVA) with Bonferroni t-tests demonstrated no significant differences between children grouped by apnea/hyponea index severity (AHI<1, >1AHI<5 and AHI>5) on any measure of neurocognitive functioning. Likewise, no differences in neurocognitive functioning were found between children who snore versus those that do not. Correlations (Pearson r) between AHI and neurocognitive test scores were all nonsignificant. Further, trend analysis revealed no significant trend on any neurocognitive measures between the three AHI groups.

Conclusion: The main finding of this study is that young children with full PSG defined SDB showed no significant neurocognitive impairment compared to children without SDB. No difference, association or trend was found between any combination of SDB and snoring groups on any measure of neurocognitive functioning including IQ, attention, executive functioning, memory, processing speed, or visual-motor skill.

0491

USING CYCLIC ALTERNATING PATTERN AS A PREDICTOR OF AN OPTIMAL CPAP TITRATION. D. YADGAROV, MD, S. LUND, MD, J. FREEMAN, PHD, L. LIANG, RPSGT SLEEP DISORDERS INSTITUTE, NEW YORK, NY

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Introduction: Continuous Positive Airway Pressure (CPAP) therapy is the standard treatment for symptomatic Obstructive Sleep Apnea (OSA) in adults. The goal of in-laboratory CPAP titration is to establish an optimal pressure. Determination of optimal pressure is typically a clinical judgment that takes into account factors such as refractory respiratory events, EEG arousals, patient comfort, etc. The Cyclic Alternating Pattern (CAP) is a microstructural framework that ties together both sleep disrupting and sleep preserving EEG features. CAP presence is a marker of unstable sleep, while the absence of CAP reflects a condition of sustained stability. The purpose of this study is to determine if CAP analysis support clinical decision of optimal pressure. We would predict that pa-

Category H—Sleep Disorders – Breathing

tients achieving optimal CPAP pressure would have lower CAP rate than patients not achieving optimal pressures.

Methods: Retrospective data were utilized in this study. Two groups of subjects were determined: those who received optimal CPAP pressure (optCPAP) (n3) and those who did not (nonoptCPAP) (n3). Optimal CPAP pressure was determined by physician review of the data and documented in the patient's report. Once groups were identified, respiratory signals were deleted from the PSG record. Scorers blind to patient group membership manually determined the CAP rate for each study. CAP was analyzed using Somnologica software version 3.2.1.

Results: Both groups were equivalent in terms of age, BMI, and gender distribution. Groups were compared by a t-test. The nonoptCPAP group had significantly greater AHI(p<0.003) and significantly greater mean CAP rates. (optCPAP 33.8; nonoptCPAP 55.8; p<0.01)

Conclusion: The results suggest that CAP may be useful index for determining adequate CPAP titration. Larger studies are to be conducted.

0492

THE INFLUENCE OF OCCULT DEPRESSION ON CPAP COMPLIANCE IN PATIENTS WITH OSAS IN AN AASM ACCREDITED CENTER

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Introduction: A high prevalence of depression has been reported in individuals with a clinical suspicion for obstructive sleep apnea syndrome. However the impact of residual depression on CPAP compliance in a structured CPAP compliance program in an AASM accredited sleep center has not been previously reported. QIDS-SR16 depression scale was used to assess the impact of occult depression on CPAP compliance.

Methods: 112 patients were selected randomly from the total OSAS patients on nasal CPAP at an accredited sleep center with access to multidisciplinary team. All subjects initially were divided into three groups based on objective CPAP usage < 2 hours, 2 to 4 hours and > 4 hours. For the study, all subjects in the < 2 hours group, every other patient in the 2-4 hours group and every 10th subject in the >4 hours group were selected. Subjective depressive symptoms were assessed by mailing out the self reported QIDS-SR16 scale to each participant individually.

Results: Response rates in the <2hrs group was 48.27% (14/29), 2-4 hrs 37.14 % (13/35) and >4 hrs was 70.8% (34/48) with an overall rate of 55.36 % (62/112). Point prevalence of occult depression was 38% and was higher in the group with a psychiatric diagnosis (58% vs 24%). Mean QIDS score was 5.23(+/- 3.75). PSQI (r=-0.460, p=0.002) and not compliance (r= -0.141, p=0.27) had a significant correlation with QIDS score. PSQI was shown to significantly influence depression scores independently after logistic regression controlling for age, BMI, AHI, ESS, CPAP Compliance, Min SpO₂, Sleep efficiency, REM Latency, REM percentage and CPAP pressure (p=0.029).

Conclusion: Depression does affect the quality of sleep significantly as measured by PSQI. However, in a multidisciplinary CPAP program with close follow up in an AASM accredited sleep center objective CPAP compliance is not dependent on depression scores as measured by QIDS.

Support (optional): This was not an industry sponsored study and there are no financial conflicts of interest.

0493

IMPAIRED SUBJECTIVE SLEEP PERCEPTION IN COPD PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Subjective sleep perception, based on our post-test sleep questionnaire, has been shown to correlate with apnea/hypopnea index

(AHI) and arousal index (AI) in patients with obstructive sleep apnea (OSA). In COPD patients, the blunted hypoxic and arousal response and reduced perception of the magnitude of resistive loads may impair their sleep perception. We conducted a study to prove this hypothesis.

Methods: This was a retrospective chart review of patients with OSA at a university-based teaching hospital. All the patients filled out a post-test sleep questionnaire at the completion of their overnight polysomnogram (PSG). Patient's demographic, pulmonary function and PSG variables were reviewed and analyzed to determine correlations between sleep perception and PSG variables.

Results: A total of 246 patients were included in the study. Forty two patients have clinical diagnosis of COPD (mean FEV₁ of 1.48 ± 0.13 liters). The average age was 53.32 ± 0.76. The mean AHI was 34.86 ± 2.56 events/hour. Comparing COPD and non-COPD groups, there was no differences in gender, BMI, sleep efficiency, sleep stage distribution and AHI. Overall, the subjective feeling upon awakening (Q15; scale 1-6) correlated with AHI (Pearson correlation coefficient, r = 0.18, P<0.05). The subjective sleep quality (Q7, scale 1-4) correlated with both AHI (r = 0.25, P<0.05) and apnea/hypopnea AI (r = 0.21, P<0.05). The subjective awake time (Q4) correlated with both AHI (r=0.28, P<0.05) and apnea/hypopnea AI (r = 0.22, P<0.05). In subgroup analysis, non-COPD group revealed significant correlations between Q15 and AHI (r = 0.20, P<0.05), Q4 and AHI (r = 0.33, P<0.05) and Q4 and apnea/hypopnea AI (r = 0.22, P<0.05). No significant correlation between sleep perception (Q15 and Q4) and AHI in COPD group was observed.

Conclusion: Subjective sleep perception based on post-test sleep questionnaire does not correlate with the severity of apnea and frequency of arousal in COPD patients. The modulation of hypoxic and arousal response in COPD patients may impair their sleep perception.

0494

ADJUSTABLE TONGUE ADVANCEMENT PROCEDURE FOR OBSTRUCTIVE SLEEP APNEA: 6 MONTHS RESULTS OF INITIAL HUMAN EXPERIENCE

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Introduction: Obstructive sleep apnea (OSA) is caused by partial or complete collapse of the upper airway during sleep. Hypopharyngeal (Fujita Type III) collapse plays an important role in moderate to severe OSA and may cause failure of palatal procedures. Poor CPAP compliance and limited efficacy and high morbidity of existing hypopharyngeal procedures justify innovative research for new procedures with minimal morbidity that addresses the hypopharynx.

Methods: In a prospective, phase 1, non-randomized, multicenter study, the feasibility, safety and efficacy of a novel implantable device (Advance System™) is evaluated in patients with OSA due to tongue base collapse and intolerance for CPAP. Apnea Hypopnea Index (AHI) measured with polysomnography was used for baseline and 6 month follow-up. Daytime sleepiness was scored with the Epworth Sleepiness Scale (ESS). Snoring was scored with a bedpartner visual analogue scale and with the Functional Outcomes of Sleep Questionnaires (FOSQ) at baseline and 6 month follow-up.

Results: 26 patients have been enrolled in the study and 21 patients were evaluated at 6 months post implantation. The average AHI was reduced from 23.3 to 18.6 (p=0.114) where 43% of patients had >50% reduction in AHI and 58% of patients had >30% reduction. ESS was reduced from 12.5 to 7.6 (p=0.001). Snoring was reduced from 7.9 to 4.3 (p=0.001) and FOSQ showed an improvement from 14.9 to 17.4 (p=0.001). The procedure was well tolerated with Pain VAS of 5 on the first day post-implant dropping to 1 five days post implant. At six months pain levels remain minimal.

Conclusion: The Advance™ System is a novel low morbidity procedure for treatment of OSA in patients with type III collapse and poor compliance to CPAP resulting in good surgical success and a reduction of AHI, daytime sleepiness and snoring.

Support (optional): This study was sponsored by Aspire Medical, Sunnyvale, California, USA

0495

CPAP PRESSURE REQUIREMENT AT VARYING ALTITUDES IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Many CPAP machines are built currently with either manual or automatic adjustments for when OSA patients travel to different altitudes, based on the need for higher fan speeds in order to generate the same CPAP pressure at higher altitude. These adjustments have only been tested in a mannequin with simulated altitude changes. The question addressed in this investigation is: Does a living breathing sleep apnea patient need the same CPAP pressure at various altitudes, or might his/her CPAP pressure requirement change at varying altitudes. Two factors suggest that an OSA patient may require less CPAP pressure at higher elevation. 1.) greater central apnea component at higher elevation. 2.) thinner, less viscous air. On the other hand, severity of OSA decreases with descent, perhaps suggesting a lower CPAP pressure requirement at lower elevation.

Methods: Six OSA patients living between 7400 ft. and 10,100 ft. participated. They had planned trips descending over 6000 feet in elevation for three or more days. Each patient used a ResMed auto CPAP unit at his/her home, and at his/her lower travel destination.

Results: In total, these 6 patients spent 51 nights at high altitude, and 50 nights at low elevation on the auto-CPAP. Only 1 patient had a change of over 1cm. in either Pressure-95th percentile, or Median pressure with descent. At high elevation, average CPAP Pressure-95th percentile was 9.41cm (+/- 1.37) vs. 9.68 cm (+/- 0.90) at low elevation. At high elevation median required CPAP pressure was 7.03 cm. (+/- 1.47), vs. 7.39 cm. (+/- 1.28) at low elevation.

Conclusion: For OSA patients, descent 6,000 - 10,000 ft. in altitude does not significantly alter CPAP pressure requirements. The change in fan speed currently utilized by most CPAP machines to adjust for barometric pressure changes at different altitudes is all that is necessary.

0496

OBSTRUCTIVE SLEEP APNEA: ITS RELATION TO INSULIN RESISTANCE, SERUM ADIPONECTIN, AND VISFATIN

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Introduction: Visceral obesity has been observed to be closely related to insulin resistance and obstructive sleep apnea (OSA). Adipocytokines, adiponectin and visfatin may have an impact on the development of insulin resistance in the OSA subjects. Therefore, the aim of this study is to investigate the relation between OSA and insulin resistance or adiponectin or visfatin in Korean subjects.

Methods: Eighty one adult habitual snorers who took polysomnographs on two consecutive nights, were divided into the following groups: simple snorers (apnea-hypopnea index [AHI] <5), mild OSA subjects (5 ≤ AHI < 15), and moderate and severe OSA subjects (AHI ≥ 15). The anthropometric data were measured. The serum adiponectin, visfatin, and insulin levels were measured by the ELISA method. The value of insulin resistance is expressed as homeostasis model assessment (HOMA).

Results: The results of comparisons for anthropometric data between subgroups based on AHI, waist circumference and waist to hip ratio (WHR) were significantly different. On the other hand, insulin, HOMA, and adipocytokines, after adjustments for waist and WHR, were not different among the subgroups. AHI, waist circumference, and WHR were negatively correlated with serum adiponectin, but positively correlated with insulin and HOMA. There is a significant positive correlation between the body mass index and hip circumference with the insulin and HOMA. No statistically significant correlation variables with serum visfatin were found. Stepwise multiple regression analysis indicated that AHI and waist circumference were independently related to HOMA. Waist circumference was shown to be a predictor of insulin and WHR was shown to be a predictor of adiponectin.

Conclusion: We found the AHI and waist circumference were independently associated with insulin resistance in OSA subjects. However, the AHI was not a variable as predictor of adiponectin and visfatin.

0497

SLEEP DISORDERED BREATHING IN LIVER CIRRHOSIS: A CROSS SECTIONAL STUDY BASED ON CHILD CLASSIFICATION

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Introduction: Sleep disordered breathing (SDB) is common in liver cirrhosis with ascites. Moreover, the severity of SDB tends to be higher with increasing volume of ascites. Thus, a relationship between ascites and upper airway dynamics during sleep appears to exist in patients with cirrhosis (Ogata et al.). Analysis of sleep architecture in cirrhotic patients with sleep disturbance indicated that these subjects had delayed sleep latency, increase wake after sleep onset, and insomnia with preference for evening activities as compared with those with normal sleep. Moreover, Patients with liver cirrhosis report un-refreshing sleep and a study with actigraphy showed a shift of activity toward later hours (Juan et al., 1998). Hepatopulmonary syndrome which is a complication of chronic cirrhosis lead to abnormal gas exchanges (Gastro and Krowka, 1996). Obstructive sleep apnea syndrome (OSAS) was recently reported to also be common in liver cirrhosis. Few literatures evaluate the relationship between the stage of liver cirrhosis and the frequency of sleep or hypopnea (Ogata et al., 2006). Aim of the study: Evaluation of obstructive sleep apnea in patients with liver cirrhosis and relation between apnea hypopnea index and grading of liver cirrhosis.

Methods: We recruited 30 subjects with liver cirrhosis, 10 subjects met criteria of child A, 10 with child B and 10 with child C, also we recruited an additional 10 healthy non cirrhotic control subjects. After signing a consent form their demographic, laboratory, abdominal ultrasound, pulmonary function, ABGs and polysomnographic study data were collected and analyzed.

Results: There was a statistically significant difference among Child classes and healthy control in regard to different parameters of sleep architecture. There was positive correlation between Child score and AHI but negative correlation between albumin and AHI. Also, there was significant increase in AHI in cirrhotic patients with ascites compared to those without ascites.

Conclusion: Sleep disordered breathing more prevalent in cirrhotic compared to normal control. The severity tends to correlate with the stage of cirrhosis. Serum albumin and serum bilirubin are correlate with severity of SDB.

0498

CASE SERIES OF EFFECT OF BILEVEL POSITIVE AIRWAY PRESSURE VENTILATION ON OPIOID INDUCED CENTRAL SLEEP APNEA IN PATIENTS WITH CHRONIC PAIN.

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Introduction: Thirty percent of subjects on methadone maintenance have central sleep apnea (CSA). There are few reports of disordered breathing in patients receiving opioids for chronic pain. We report the effects of bilevel positive airway pressure ventilation (BLV) in a series of patients receiving chronic opioids with CSA.

Methods: Six patients referred to our sleep center, on sustained release opioid for treatment of chronic pain for more than six months with excessive daytime sleepiness were evaluated. Polysomnography (PSG) showed Apnea-Hypopnea Index (AHI) more than 20 with 40% and higher central events, BLV titration was done and patients were followed for at least 6 months on nocturnal BLV.

Results: Age 41-68, 2 females and 4 males, BMI 27 - 34, 5 smokers, morphine equivalent doses were 120 - 420 mg per day, Epworth Sleepiness Scales (ESS) 7 to 21, AHI 28.4 - 106, central events 44-84% of total. Time less than 90% O₂ saturation (T90) was 1.8 minutes to 6.4 hours. Respiratory Arousal Index (RAI) ranged 6.6- 41.6. One patient refused titration. In the others a level of BLV that successfully treated CSA was found, and returned AHI to normal with elimination of hypoxemia and respiratory arousals. BLV pressure settings ranged from 12 - 17 cm H₂O (IPAP)/8 - 9 cm H₂O (EPAP) with back-up rate 12 - 16. Three patients required oxygen supplementation. Among four patients using BLV treatment for at least 6 months ESS improved (by 4, 12, 5 and 9 respectively). No clinical improvement was noted in the 2 not using BLV ventilation.

Conclusion: Treatment of opioid associated CSA with BLV restored nocturnal ventilation, reversed hypoxemia and reduced sleep fragmentation. Randomized controlled trials, with objective measures of daytime function are recommended in opioid induced CSA.

0499

NEUROCOGNITIVE OUTCOMES OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA TREATED WITH CONTINUOUS POSITIVE AIRWAY PRESSURE

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Introduction: Obstructive sleep apnea (OSA) is characterized by nighttime disrupted breathing and hypoxemia, daytime sleepiness and changes in cognition and mood. The reversibility of cognitive deficits after treatment with continuous positive airway pressure (CPAP) is controversial.

Methods: We report analyses of an ongoing study of the outcomes of CPAP treatment on attention and executive function. Thirty-two patients with moderate to severe OSA and compliant on CPAP treatment for at least three months were studied with working memory tasks, neuropsychological testing, and overnight polysomnographic sleep study (PSG), and compared to 20 age- and education-matched healthy controls.

Results: After CPAP treatment, patients showed improved nighttime respiratory disturbance index (RDI), minimum and mean oxygen saturation, and daytime sleepiness ratings as measured by the Epworth Sleepiness Scale (ESS). In terms of neurocognitive function, treated patients performed at a comparable level to controls on basic working memory

storage functions as measured by the verbal and spatial item recognition tasks, 0-back condition of the verbal and spatial n-back tasks, digit span and word span, psychomotor tracking and sentence verification span. However, treated patients still showed a significant reduction on tests of working memory requiring the central executive (2-back condition of spatial n-back tasks, and dual condition of the working memory span), as compared to controls. Patients also performed worse on neuropsychological measures of attention (digit symbol, D2 Test of Attention), executive function (Trail B, Wisconsin Card Sorting Test), and psychomotor speed (Grooved Pegboard).

Conclusion: While CPAP is an effective treatment for sleep disturbances and daytime sleepiness, cognitive deficits, especially executive function may be more resistant to treatment in OSA. These results have implications for current treatment protocols and patient education strategies.

Support (optional): Nova Scotia Health Research Foundation (Project Grant), Sir Edward Youde Memorial Overseas Fellowship (EYYL)

0500

EFFECTS OF CONTINUOUS POSITIVE AIRWAY PRESSURE TREATMENT OF OBSTRUCTIVE SLEEP APNEA ON DAILY FUNCTIONS, MOOD, AND QUALITY OF LIFE

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Introduction: Obstructive sleep apnea (OSA) is characterized by disrupted breathing during sleep, leading to hypoxemia and fragmented sleep, daytime sleepiness, and functional deficits. Here, we report the outcomes of CPAP treatment on hypoxemic indices, sleepiness, and psychosocial variables.

Methods: Thirty patients with moderate to severe OSA and compliant on CPAP for at least three months were studied with an overnight polysomnographic sleep study (PSG), self-reported measures of sleep quality (Pittsburg Sleep Quality Index, PSQI), daytime sleepiness (Epworth Sleepiness Scale, ESS), mood (Beck Depression Inventory, BDI), affective states (Profile of Mood States, POMS), functional outcomes (Functional Outcomes of Sleep Questionnaire, FOSQ), and quality of life (QoL) as measured by a visual analogue scale (VAS), and the Quebec Sleep Questionnaire (QSQ).

Results: CPAP treatment significantly improved respiratory disturbance index (RDI), minimum and mean oxygen saturation, daytime sleepiness, sleep quality, functional outcomes, and QoL. The number of patients with clinically abnormal scores fell from 71% to 28% for sleepiness, from 83% to 28% for subjective sleep quality, and from 79% to 38% for functional outcomes after treatment. Sleepiness was found to be a significant predictor of mood, affective states, functional outcomes, and QoL, while subjective sleep quality predicted functional outcomes and QoL.

Conclusion: CPAP appears to be effective in improving nighttime breathing, sleep, and daytime outcomes, although it does not appear to be consistently effective for all patients. Residual sleepiness and issues in sleep quality continue to affect psychosocial domains of patients with OSA. These might be important indexes to consider in evaluating treatment effectiveness and adjunctive therapies targeting sleepiness and sleep quality might be beneficial.

Support (optional): Nova Scotia Health Research Foundation (Project Grant), Sir Edward Youde Memorial Overseas Fellowship (EYYL)

0501

EPWORTH SLEEPINESS SCALE SCORE STABILITY OVER TIME IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: The Epworth Sleepiness Scale (ESS) score is commonly used at sleep disorders centers to assess subjective sleepiness. Results have been shown to be consistent over time, but reliability data remain limited for patients with untreated obstructive sleep apnea (OSA).

Methods: A retrospective chart review of all polysomnograms (PSGs) performed between April 2006 and November 2007 was performed. Subjects were included if they were at least 18 years of age and had a routine diagnostic PSG showing OSA followed by a subsequent CPAP titration study. An ESS was completed just prior to the PSG and again just prior to the CPAP titration. An ESS score of 10 or more, on a scale that ranges from 0 to 24, was considered to reflect excessive sleepiness.

Results: A total of 1470 subjects were included in the study: mean age was 49.8 years, mean BMI was 34.3 kg/m², mean apnea/hypopnea index (AHI) was 31.6, and 59.3% were male. There were significant initial differences in ESS scores between men and women, even after accounting for body mass index (BMI) (9.6 vs. 10.3 respectively; $p=0.007$). There was a mean of 5.4±8.2 weeks, with a median of 2.6 weeks, between ESS scores. The mean change in ESS scores between the two time points was only 0.2±3.5, but the mean absolute change in ESS scores was 2.3±2.6. Neither gender, BMI, AHI, or age was significantly predictive of the latter difference. However, length of time between the two ESS administrations was weakly correlated with the absolute difference between ESS scores ($r=0.14$, $p<0.001$). Over time, 7.1% of the subjects moved out of the excessive sleepiness range and 9.0% moved into the excessive sleepiness range.

Conclusion: Among patients with untreated OSA, the ESS remains relatively stable over time and changes are not associated with gender, age, or BMI. However, some patients change their sleepiness classification spontaneously if a specific ESS score is applied as a cutoff.

0502

RAPID EYE MOVEMENT-RELATED SLEEP DISORDERED BREATHING: EFFECTS OF AGE & GENDER

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Introduction: REM-related sleep disordered breathing (REM SDB) accounts for 14 to 36% of obstructive sleep apnea and demonstrates a female predominance. This gender difference suggests that female hormones may affect the expression of REM SDB, possibly protecting women from disordered breathing in NREM but not REM sleep, thus resulting in REM SDB. As increasing age in women is associated with decreasing levels of estrogen and progesterone and levels are low in men, we hypothesized that REM SDB prevalence decreases with age in women but not in men.

Methods: Included were 2,489 subjects who met these criteria: 1) age≥18, 2) AHI≥5, 3) TST≥100 min and 4) REM≥10 min. REM SDB was defined as follows: 1) AHI≥5, 2) NREM AHI≤15 and 3) REM AHI:NREM AHI (R:N)≥2. Men and women were separately stratified by age groups 18-29, 30-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69 and ≥70; prevalence and mean R:N were calculated. Chi-squared and

Pearson's rank sum testing were performed to determine if REM SDB or R:N correlated with age group or age respectively.

Results: Of the 817 women and 1,672 men included in the analysis, 333 women and 351 men had REM SDB, yielding prevalence data for all subjects, women and men of 27.5%, 40.8% and 21.0% respectively. In women, REM SDB prevalence and R:N for the aforementioned age categories totaled 54.1%, 54.3%, 50.7%, 44.2%, 44.1%, 35.9%, 33.3%, 31.7% and 26.4% respectively for prevalence and 5.2±0.9, 4.6±0.5, 4.3±0.5, 3.8±0.4, 4.5±0.4, 3.6±0.3, 3.2±0.4, 2.9±0.4 and 2.7±0.3 (mean±SE) for R:N. In women, the presence of REM SDB correlated significantly with age group ($\chi^2=25.9$, $p=0.001$), while R:N correlated negatively with age ($r=-0.16$, $p<0.001$). In men, neither REM SDB prevalence nor R:N were significantly correlated with age.

Conclusion: Both REM SDB expression and R:N ratio are significantly correlated with age in women but not in men. These gender specific relationships suggest that female hormones may explain the differential expression of SDB in REM and NREM sleep as defined by REM SDB prevalence and R:N ratio.

0503

EFFECT OF LYING ON THE FACE FOR OSAS PATIENTS

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Introduction: Subsidence of tongue with supine position during sleep is known to cause obstructive sleep apnea syndrome (OSAS). Because it receives less subsidence to press the airway, sleep with lying on the face may be able to prevent OSAS. However, there is no polysomnography (PSG) study, which is a gold standard to diagnose OSAS, has been reported. The goal of this study is to confirm whether sleep by lying on the face is effect to prevent OSAS, using a special bed (The Prone Positioning Bed) created the France Bed Medical Service Co.,Ltd. with a hole allowing examiner to sleep with facing downward.

Methods: Thirty three male cases and one female case (sixteen OSAS patients and eighteen healthy control cases) were investigated, average age was 45.8±13.5, and average body mass index was 24.9±4.6kg/m². PSG was done with lying on the face of OSAS patients. To exclude the first night effect, PSG was record three nights continuously for the control group, and data was analyzed from either second or third night with lying on the faces.

Results: There is no difference between sleep structure or sleep depth compared to different sleep position, however, total sleep time and sleep efficiency were significantly decreased in lying on the face group. Apnea hypopnea index (AHI) above 5 was found in twenty five from thirty four cases, and lying on the face group was significantly lower (AHI = 21.9±20.0) in comparison to supine position group (AHI = 34.1±24.7). Although total sleep time and sleep efficiency were decreased in lying on the face group, it may due to the inexperienced sleep position. Furthermore, AHI was remarkable improved in lying on the face group. Sleep with lying on the face is effective for OSAS patients with economic effect and without risk in comparison to other therapy, such as continuous positive airway pressure (CPAP), oral appliance or surgery. About thirty percent of total OSAS patients were failed in any treatment. In addition, numerous patients are failed in CPAP therapy.

Conclusion: Sleep with lying on the face may be the fourth treatment for those patients who are failed from CPAP, oral appliance, or surgery.

Support (optional): This study was supported by the France Bed Medical Home Care Research Subsidy Foundation.

0504

REM APNEA: SEARCHING FOR CLINICAL AND POLYSOMNOGRAPHIC CORRELATES

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Introduction: Rapid eye movement (REM)-related sleep apnea is becoming a recognized pattern of sleep disordered breathing (SDB), the significance of which is not well understood. This study seeks to identify clinical and polysomnographic features that occur with significantly greater frequency to help clinicians identify this disorder.

Methods: This retrospective chart review was conducted over a 4 week period. Patients age >18 undergoing routine 16 channel polysomnography (PSG) for presumed SDB were included. Exclusion criteria were: age <18, total sleep time <120 minutes, total REM sleep <30 minutes, and those patients on treatment. Demographics and Epworth Sleepiness Scale (ESS) were reviewed and the characteristics of snoring, morning headaches, use of tobacco/caffeine/alcohol and of antidepressant and oral contraceptive pills (OCP) were recorded. PSG parameters recorded were: total sleep time (TST), sleep in each stage (N1, N2, N3 and REM), sleep latency (SL), sleep efficiency (SE), sleep maintenance (SM), arousal index (AI), apnea-hypopnea index (AHI), AHI in REM sleep, AHI in non-REM sleep and minimum oxygen saturation. Subjects whose AHI REM to AHI non-REM ratio was >2 were designated as the REM specific sleep-apnea group (REMo). The remainder of the subjects were assigned to the non-REM sleep apnea group (NREMo). Statistical analysis was performed using unpaired t-test.

Results: There were 65 total patients included. 36 patients (55%) had NREMo and 29 patients (45%) had REMo. The average age was 50 in both groups and there were more females in the REMo group (55%). BMI was 32.3±23(NREMo) vs. 35.9±30.2(REMo); p=0.003. ESS was 11.9±29.7(NREMo) vs. 9.4±26.8(REMo); p=0.048. AI was 23.6±257.29(NREMo) vs. 10.74±69.71(REMo); p=0.0001. No statistical difference in TST, SL, SM, SE or minimum oxygen saturation was noted. A trend was seen with stage N1 (increased in NREMo; p=0.06); stage N2 (increased in REMo; p=0.06); stage N3 (increased in REMo; p=0.08); stage R (increased in NREMo; p=0.08) but this was not statistically significant. Patients with REMo had primary complaints of HA, sleep paralysis, and hypnagogic hallucinations. More patients with NREMo had endorsed smoking, ETOH and caffeine use. None of the patients were on OCPs.

Conclusion: REMo patients are likely to be female, less drowsy (ESS), have narcolepsy like symptoms and complain of HA. These features can help the clinician identify this group of SDB patients. This study supports that REMo is a separate clinical entity from other forms of SDB.

0505

OBSTRUCTIVE SLEEP APNEA AND DEPRESSION IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction: Depression has been repeatedly shown to be associated with obstructive sleep apnea syndrome (OSAS) in various patient populations. Recently this has been demonstrated in the DOPPS study for hemodialysis patients. Although both conditions are very frequent in chronic kidney disease (CKD) patients not yet on dialysis, the association between OSAS and depression has not been investigated in chronic

kidney/predialysis patients. Here we assess the association between depressive symptoms and OSAS in a predialysis patient population.

Methods: 421 patients with varying degree of chronic renal failure followed at two predialysis clinics were enrolled to participate in this cross-sectional study. The Berlin Sleep Apnea Questionnaire and the Centre for Epidemiological Studies - Depression (CES-D) scale were utilized to assess the risk of OSAS and depression, respectively. Socio-demographic variables, etiology of kidney disease and laboratory parameters were also recorded.

Results: Mean age was 61±18 years, 55% of the patients were female, 35% had diabetes. 48% of the patients were at CKD stage 2 or 3, 40% of them had stage four CKD (eGFR between 15 and 30 ml/min/1.73m²) and 11% had an eGFR less than 15 ml/min/1.73m². Forty one percent of the patients had high risk of OSAS; these patients were older, had higher BMI, rate of diabetes, and the prevalence of depressive symptoms was also greater than among those without OSAS risk. In a multivariate regression model the high risk of OSAS demonstrated an independent, significant association with the presence of depressive symptoms (OR=3.7; CI: 1.6-8.6; p=0.003) following an adjustment for several covariables (gender, age, diabetes, hemoglobin, eGFR, serum albumin and other sleep disorders).

Conclusion: OSAS is independently associated with depressive symptoms among patients with chronic kidney disease. As both conditions are very frequent in CKD patients, the presence of one of these conditions should prompt screening to rule out the presence of the other.

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0506

THE DIFFERENCE OF SLEEP ARCHITECTURE BETWEEN HYPERCAPNIC AND NON-HYPERCAPNIC PATIENTS FOR CHRONIC RESPIRATORY FAILURE

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Introduction: Sleep disturbance related symptoms are common in patients with long-term oxygen therapy (LTOT). Essentially, there were only few previous reports about the sleep architecture and disturbance in patients with respiratory disease, such as chronic obstructive pulmonary disease (COPD). However, the purposes of those studies were only part of the evaluation for the efficiency of oxygen inhalation during sleep. Aim: The aim of this study was to examine the sleep architecture of the patients under LTOT with or without hypercapnia.

Methods: 19 subjects with chronic respiratory failure were enrolled to the study. All the subjects were pre-evaluated by pulmonary function test and blood gas analysis (ABG) including exercise testing. After enroll, overnight polysomnography (PSG) test were performed in each subject with supplemental oxygen. PSG test was performed during 20:00h-06:00h by using digital PSG system. Arterial blood sample was collected from radial artery at upright position and oxygen supplementation in “usual amount” before one hour of the PSG test. The estimated base line PCO₂ value that reflects overall PaCO₂ including sleep period was calculated using equation of PaCO₂ [2.4 x (HCO₃⁻) - 22] from obtained ABG value just before PSG test. Statistical analysis: Data are shown as mean + SE unless otherwise stated. Statistical analyses were performed by using the commercially available software (StatView 5.0, Abacus Concepts, Lnc., CA). Data between groups were compared by one-way ANOVA.

Results: Seven subjects were classified as hypercapnic group (base line PCO₂ ≥ 45mmHg) and twelve subjects were non-hypercapnic group (base line PCO₂ < 45mmHg). There are no hypoxic episodes during sleep period in all patients. Latency persistent sleep of PSG data was significant higher in patients with hypercapnic than non-hypercapnic (p<0.01). Periodic Limb Movement was seen in 23.6% of the subjects however no contribution for arousals. Other PSG data include mean SpO₂ were no significant difference. Also, we will present the PSG data

from one of the typical case of COPD patient with LTOT and bi-level PAP for farther discussion.

Conclusion: This study suggests that patients with estimated hypercapnia was more disturbed sleep architecture especially significant loss of sleep latency than non-hypercapnic patient with chronic respiratory failure under LTOT. Nocturnal PCO₂ level or ventilatory function may contribute to sleep disturbance in patients with estimated hypercapnia during LTOT.

0507

A SIMPLE TECHNIQUE FOR EVALUATING VENTILATORY CONTROL STABILITY (LOOP GAIN)

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Introduction: Loop gain (LG), a measure of ventilatory control stability, may be important in the pathogenesis of obstructive sleep apnea. However, current techniques for measuring loop gain are difficult and not always achievable. We present a new method that overcomes many of these difficulties.

Methods: 21 individuals were studied during sleep on enough CPAP to eliminate flow limitation. Pressure support ventilation (PSV) was increased over 1 minute to ~6 cm H₂O. After 3 minutes at 6 cm H₂O, PSV was abruptly decreased to zero for 3 minutes. This produced a step reduction in ventilation followed by a gradual recovery to baseline. From these ventilatory changes, the gain, time constants, and delay parameters of the ventilatory control system were estimated by fitting the data to a mathematical model of breathing (parameter estimation). The resulting model (with the estimated parameters) was used to calculate the LG at the frequency associated with a phase angle of 180 degrees. The LG from this new technique was compared to the LG from an existing technique that uses proportional assist ventilation (PAV).

Results: Mean LG measured with PSV was 0.29 ± 0.09 . LG could be measured in all 21 subjects with PSV. However, LG could be determined in only 10 subjects with PAV (the other 11 subjects had “less than” LG values). Mean LG measured with PAV (in the 10 successful measurements) was 0.29 ± 0.07 . In these 10 individuals, there was a trend towards a relationship between the two measurements, but the correlation was not statistically significant due primarily to two outliers ($r = -2.06$, $p = 0.54$). In the 11 subjects with a less than PAV value, 10 had a PSV measurement that was less than the PAV measurement, suggesting a reasonable agreement in these individuals. Of note, we were able to perform multiple PSV determinations in each subject. However, only a single PAV measurement was achievable in each subject.

Conclusion: PSV overcomes many of the existing difficulties associated with measuring LG and can be used to quantify ventilatory control stability during sleep. The method is simple and takes ~7 minutes to perform, allowing for multiple measurements in a single night.

0508

SLEEP FRAGMENTATION DECREASES EVEN DURING NCPAP TITRATION IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Obstructive sleep apnea syndrome (OSAS) not only causes respiratory disturbances during sleep but also decreases the quality of nocturnal sleep through sleep fragmentation and change in sleep structure. It might be assumed that titration process of nCPAP per se might make nocturnal sleep further fragmented. No studies, to our knowledge, have looked into sleep fragmentation change induced by nCPAP titration quantitatively. We aimed at comparing the changes in sleep fragmentation and structure between baseline (diagnostic) nocturnal polysomnography (NPSG) and nCPAP titration nights.

Methods: Patients with a baseline RDI (respiratory disturbance index) of 5 or greater and reduced RDI during nCPAP titration were selected retrospectively. Then, the baseline NPSG and the NPSG during nCPAP titration were compared. Sleep fragmentation index (SFI) was defined as the total number of awakenings and shifts to stage 1 sleep divided by the total sleep time in hour. SFI and other polysomnographic parameters were statistically analyzed.

Results: Data of 97 men (84.3%) and 15 women (13.0%) patients were analyzed. The average age was 53.8 ± 11.4 years. SFI on the baseline NPSG and the nCPAP titration nights were 28.91 ± 13.95 and 15.42 ± 8.87 , respectively, with significant decrease on the nCPAP titration night ($t = 10.01$, $p < 0.001$). Total sleep time and sleep efficiency did not differ significantly between the two nights. SFI showed negative correlations with sleep efficiency and total sleep time on both nights. SFI showed a positive correlation with RDI on both nights. SFI had no significant correlations with PSQI (Pittsburgh Sleep Quality Index), ESS (Epworth Sleepiness Scale), or BDI (Beck Depression Inventory) on both nights. nCPAP titration were found to improve sleep structure by increasing stage 2 sleep(%), slow wave sleep(%), and REM sleep(%) and by decreasing stage 1 sleep(%), all significantly ($p < 0.05$).

Conclusion: nCPAP even during titration decreased sleep fragmentation and improved sleep structure in patients with OSAS. We suggest that SFI may be useful as an index in the assessment of OSAS severity and nCPAP efficacy.

0509

HIGHER PREVALENCE OF GLAUCOMA IN PATIENTS WITH MODERATE TO SEVERE OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME

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Introduction: Obstructive sleep apnea/hypopnea syndrome (OSAHS) creates transient hypoxemia and increased vascular resistance, which may compromise optic head perfusion and oxygenation and may cause glaucomatous optic neuropathy. The purpose of this study is to determine the prevalence of glaucoma in Taiwanese patients with OSAHS.

Methods: One hundred and twenty-six patients with loud snoring and excessive daytime sleepiness underwent an overnight polysomnography for evaluation. All patients received a complete ophthalmological examination which included best-corrected visual acuity, intraocular pressure measurement, silt lamp exam, optic disc evaluation, Humphrey 30-2 visual field and a retinal nerve fiber layer exam by optic coherence tomography.

Results: Ninety-eight (77.8%) of the 126 patients had an apnea/hypopnea index (AHI) > 5, which indicates OSHAS. Twenty-five patients (19.8%) had mild OSAHS with an AHI between 5 and 15, 24 patients (19.0%) had moderate OSAHS with an AHI between 15 and 30, and 49 patients (38.8%) had severe OSAHS with an AHI greater than 30. Among the OSAHS patients, glaucoma was found in 6 patients with a prevalence of 6.1% (6/98), which was higher than that of the general Chinese population (3.2%). In the glaucoma patients, 3 were in the moderate OSAHS group and 3 were in the severe OSAHS group. There were no glaucoma patients in the normal (AHI < 5) and mild OSAHS groups.

Conclusion: Patients with OSAHS had a higher prevalence of glaucoma in Taiwan, especially in patients with moderate and severe OSAHS. Therefore, patients with moderate to severe OSAHS, who had decreased ocular perfusion with subsequent hypoxia of the optic disc, should be screened for glaucoma.

Support (optional): None.

0510

ONE NEGATIVE POLYSOMNOGRAPHY DOES NOT EXCLUDE OBSTRUCTIVE SLEEP APNEA

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Introduction: A negative polysomnographic study (PSG) may not rule out obstructive sleep apnea syndrome (OSA). It is not clear which subpopulations of patients with clinically suggestive symptoms, but a negative first PSG, are most likely to be identified as having OSA on a second PSG (“converters”).

Methods: We retrospectively examined PSG data on patients who presented with symptoms suggestive of OSA, had a negative first PSG based on an Apnea-Hypopnea Index (AHI) of less than 5.0, and went on to have a second PSG. Changes in PSG variables between the first and second PSG were tested using a paired t test and predictors of being a “converter” were evaluated using logistic regression.

Results: Mean age was 42.9 years (range 11-91) for the 266 patients included and 70.7% were female. Mean body mass index (BMI) was 28 (SD 7.9). An AHI ≥ 5 on the second PSG was found in 40 (15.3%) patients (“converters”). An increase from the first to second PSG was found in total sleep time, stage REM, sleep efficiency, and AHI ($p < .05$ for each). However, none of these PSG variables differed significantly between “converters” and “non-converters”. Patients with a BMI ≥ 25 were more likely to be converters (odds ratio 4.4, 95% CI 1.65-11.60, $p=0.003$), even when controlling for sleep efficiency on the first PSG.

Conclusion: A clinically relevant proportion (15%) of patients with clinical symptoms but a negative first PSG may be found to have OSA on a second PSG. Even though PSG variables vary from the first to second PSG (“first night effect”), none of them predicted which patients were more likely to be “converters”. Patients with a BMI ≥ 25 were more likely to be “converters” and a second PSG should be recommended for these patients when clinical symptoms of OSA are present.

0511

IDENTIFICATION OF AROUSALS BY MEASUREMENT OF RR INTERVAL VARIABILITY

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Introduction: The identification of arousals is critical in interpreting polysomnograms. Arousals can signal respiratory events and arousal indices serve as measures of sleep fragmentation. Arousals are inevitably accompanied by autonomic changes. We propose a method of identifying arousals on polysomnograms by measuring the increased variability in R-R intervals seen with arousals.

Methods: Polysomnograms were selected at random from all studies done after September 2007. Patients with cardiac co-morbidities/medications were excluded. Polysomnograms were acquired with standard derivations (6 channel EEG), airflow thermistor, nasal pressure transducer and thoracic/abdominal belts. Patients were selected if one hundred contiguous epochs could be identified with relatively stable NREM sleep with wake time <5 minutes. These epochs were re-scored by investigators per current guidelines. Two patients with arousal index <20 were selected. RR intervals were extracted by open source software (Physionet-NIH funded resource). The variance of RR intervals in each 30 seconds epoch was calculated. Variances were then classified into two groups—those from stable sleep epochs (no arousals) and arousal epochs (arousals present). A receiver operating characteristic (ROC) curve was constructed for RR interval variances to establish optimal cutoff values for sleep versus arousal groups. The sensitivity and specificity of the cutoff value was calculated.

Results: A total of 200 epochs from 2 patients were analyzed. All indices below are from the selected epochs and not the complete record it was derived from. There were a total of 6909 RR intervals. The arousal index was 7.1 in subject 1 and 22.8 in subject 2. The results of the ROC analysis indicate that heart rate variability, as measured by the variance of RR intervals within epochs, is a predictor of arousals with area under the curve (AUC) of 0.88 and 0.84 for subject 1 and 2, respectively (p -values 0.004 and <0.001 , respectively). The optimal cutoff value for variances, as identified from the ROC curves, resulted in a sensitivity and specificity of 100% and 75% in subject 1 and 93% and 77%, respectively in subject 2 for identifying arousals.

Conclusion: Variability in RR intervals is highly sensitive in identifying arousal containing epochs in this select population.

0512

ELEVATED PLASMA FIBRINOGEN IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) has been implicated in cardiovascular and cerebrovascular diseases. Systemic inflammation and the coagulation process may be an important mechanism related to cardiac and vascular diseases in patients with OSA. Fibrinogen is the major coagulation protein and closely associated with inflammation. According to the Fibrinogen Studies Collaboration (FSC), a long-term increase of 100 mg/dL in fibrinogen level is associated with an approximate doubling in risk of major cardiovascular diseases. Elevated fibrinogen has been reported in OSA patients with cerebrovascular diseases and with hypertension. We tested the hypothesis that OSA patients who are newly diagnosed, untreated and otherwise healthy have increased plasma fibrinogen compared to matched healthy controls.

Methods: We studied 20 newly diagnosed patients (18 males and 2 females) with mild OSA (apnea-hypopnea index, AHI $\geq 5 < 20$ events/hour) and 20 patients (18 males and 2 females) with moderate to severe OSA (AHI ≥ 20 events/hour). The OSA patients were free of other diseases, had never been treated for OSA and were on no medications. We compared fibrinogen measurements in these patients to measurements obtained in 20 (18 males and 2 females) control subjects matched for age, sex, body mass index (BMI), waist to hip ratio, and in whom occult OSA was excluded by overnight sleep study (AHI <5 events/hour).

Results: Plasma fibrinogen levels were significantly higher in patients with moderate to severe OSA than either controls (426 \pm 13 vs. 320 \pm 18 mg/dL, $P < 0.001$) or patients with mild OSA (426 \pm 13 vs. 355 \pm 20 mg/dL, $P < 0.001$). Although the difference in plasma fibrinogen levels between mild OSA and controls (355 \pm 20 vs. 320 \pm 18 mg/dL) was not statistically significant, elevated fibrinogen in severe OSA patients may be a potential risk factor for cardiovascular diseases.

Conclusion: Severe OSA is associated with elevated levels of plasma fibrinogen, which may contribute to cardiac and vascular disease in OSA patients.

0513

CURRENT MAJOR DEPRESSION IN OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS) RATIONALE, DESIGN AND PRELIMINARY RESULTS OF A NORWEGIAN, POPULATION-BASED STUDY*Hrubos-Strøm H^{1,2}, Dammen T³, Nordhus P⁴*

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Introduction: OSAS is a prevalent disorder in the community associated with depression. The latest review of research concerning this association recommend further emphasis to subject selection and quality of diagnostic tools in future research. The aims of the study are: 1: To estimate the prevalence of current major depression in subjects derived from the general population with high risk of having OSAS. 2: To assess how current major depression is associated to severity of OSAS measured by the Apnea Hypopnea Index (AHI).

Methods: Phase-I: The Berlin Questionnaire (BQ) is designed to identify persons with high risk of OSAS based on self-reported snoring, daytime sleepiness and hypertension or obesity. A questionnaire consisting of the Norwegian version of the BQ and additional questions was mailed to 30 000 subjects. The draw was stratified in gender and age from 30 to 65 years in subjects residing in Akershus, Hedmark or Oppland counties, registered in the Norwegian National Register. Phase-II: A random sample of 292 subjects with high risk of having OSAS were interviewed with the Structured Clinical Interview for DSM-IV, axis-I disorders (SCID-I) and completed a full night polysomnography after the interview. OSAS diagnosis was based on AHI > 5 plus self-reported excessive daytime sleepiness or AHI >15 alone.

Results: The phase-I response-rate was 54%. Among subjects eligible for further investigations, 23% had high risk and 77% low risk for OSAS. Preliminary results indicated a point prevalence of current major depression of 12%. This estimate is 3-4 times higher than estimates for published for current major depression in the general population. Current major depression was not associated with severity of OSAS measured by AHI.

Conclusion: In a population based sample of subjects with high risk of having OSAS, current major depression was highly prevalent, but not associated with severity of AHI.

0514

THE SLEEP SYMPTOMS CHECKLIST: USEFUL FOR SCREENING BUT NOT DIAGNOSIS*Bailes S¹, Baltzan M^{2,4}, Dorrie R¹, Fichten C^{1,5}, Grad R^{2,4}, Libman E^{1,4}*

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Introduction: We have demonstrated that the Sleep Symptoms Checklist (SSC) can identify some primary care patients at risk for sleep apnea. The present study seeks to determine if the SSC can distinguish patients with and without apnea in (a) a sample of physician-referred sleep clinic patients, and (b) using a conceptually similar questionnaire format, an older community sample of sleepy/tired individuals with sleep problems.

Methods: Participants included the Sleep Clinic (N=95, Mean Age=52), Sleepy/Tired Older Community (N=107, Mean Age=62), and Control (N=21, Mean Age=42) samples. The Sleep Clinic and Control samples were administered the SSC, a 21-item screening instrument including signs and symptoms of sleep disorders reduced to 4 factors: SSCSleep-Disorder, SSCDaytimeDistress, SSCInsomnia, SSCPsychological. The

Older Community and Control samples completed an extensive questionnaire battery (Q). A subset of 21 Q items, selected to match items of the SSC, have a similar, 5-factor structure: QSleepDisorder, QFatigue, QSleepiness, QInsomnia, QPsychological. All participants underwent nocturnal screening for sleep apnea.

Results: In the Sleep Clinic sample, all referred patients (with and without diagnosed apnea) had significantly higher scores on the SSCSleep-Disorder, SSCDaytime and SSCInsomnia subscales than healthy Controls. No differences were found between those with and without apnea. Similarly, in the Older Community sample, no significant differences were obtained between those with and without apnea, but both groups were significantly more symptomatic on 4 of the 5 Q factors than the healthy controls.

Conclusion: The SSC can identify those individuals at risk for sleep apnea, who should be evaluated with polysomnography. It cannot be used to definitively diagnose sleep apnea. A similar pattern of results was obtained in the physician-referred Sleep Clinic and the Community samples using a different questionnaire format. This indicates that it is the symptom profiles themselves, independent of questionnaire format, that identify individuals at high risk for sleep apnea.

Support (optional): Canadian Institutes of Health Research

0515

URINE PH DOES NOT DECREASE IN RESPONSE TO OBSTRUCTIVE SLEEP APNEA*Watenpaugh DE^{1,2}, Dao D¹, Burk JR¹*

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Introduction: Nightlong compromised ventilation associated with obstructive sleep apnea (OSA) leads to sustained nocturnal hypercapnia and possibly respiratory acidosis. Such acidosis should in turn elicit renal compensation with reduced morning urine pH relative to pH at bedtime. Because positive airway pressure (PAP) normalizes nocturnal respiration in OSA, one would expect PAP treatment to counteract any OSA-induced nocturnal urine pH reduction. We hypothesized that: 1) morning urine pH would decrease relative to urine pH measured prior to bedtime in untreated OSA patients, and 2) treatment with PAP prevents this nocturnal urine pH reduction.

Methods: Patients (137 total) had mild to severe OSA. Urine samples were collected before and after full-night diagnostic nocturnal polysomnography (NPSG) and full-night PAP titration. Patients provided a urine sample prior to bedtime and from the first morning void. NPSG always occurred before PAP titration, but studies did not occur on consecutive nights. Color-indicator dipsticks quantified urine pH to +/- 0.5 units. There was no control or monitoring of diet, electrolyte metabolism, or fluid balance.

Results: No evening-to-morning change in urine pH occurred during NPSG or PAP titration. Urine pH averaged (SD): 5.8 (0.8) before NPSG, 5.9 (0.8) after NPSG, 5.6 (0.7) before PAP, and 5.7 (0.7) after PAP.

Conclusion: The data refuted our hypotheses: urine pH failed to decrease after a night with untreated OSA, and PAP treatment had no affect on this finding. These results suggest that no significant respiratory acidosis occurs during a night with untreated OSA, or that no renal compensation occurs in response to such acidosis. Furthermore, the findings do not support use of urine pH as an indirect indicator of the hypercapnia associated with OSA.

0516

AN EXTERNAL VALIDATION OF THE SLEEP APNEA SUBSCALE (SA) OF THE SLEEP DISORDERS QUESTIONNAIRE (SDQ)

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Introduction: The internal consistency and diagnostic validity of the SA scale is based on the polysomnography results of the 519 subjects from the original 1994 study by Douglass et al. However, the SA scale has not yet been externally validated in a second population of apnea patients diagnosed using polysomnography. Therefore the main aim of this present study is to perform that external validation using a sample of apnea patients from the Royal Ottawa Mental Centre Sleep Disorders Clinic.

Methods: The patient files of 240 patients from the sleep laboratory were analysed and the following variables were entered into a stepwise multiple regression: age, sleep efficiency, number of shifts to stage 1 sleep, number of awakenings during sleep, percent of time spent in REM sleep, mean duration of apneas, sleep onset latency (SOL), Wake After Sleep Onset (WASO), Respiratory Disturbance Index (RDI), Apnea-Hypopnea Index (AHI), apnea index in REM, minimum oxygen saturation in REM (minO₂), percent time spent with oxygen saturation of 90-100%, sleep state perception score, and positional AHI. Before regression, variables were examined for non-normality of statistical distribution and transformed as required by log, square root, or logit. The SDQ-SA score was used as the dependent variable.

Results: Nine variables were dropped from the analysis. The final model ($F = 16.78$, $p < 0.0001$, $R^2 = 0.303$) contained age ($p = 0.100$), shifts to stage 1 ($p = 0.024$), SOL ($p = 0.106$), WASO ($p = 0.024$), RDI ($p < 0.0001$) and minO₂ ($p < 0.0001$).

Conclusion: Higher scores on the Sleep Apnea scale are predicted by more frequent shifts to Stage 1, higher sleep efficiency (lower WASO), higher RDI and lower minimum oxygen saturation levels.

0517

A NOVEL PHYSICAL EXAM TECHNIQUE TO SCREEN FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: With the high cost of polysomnography, simple screening tests to predict apnea are needed. Currently clinicians rely on risk factors such as waist circumference, body mass index, and clinical signs of the disorder. Measures of oropharyngeal crowding such as the Friedman palate score (modified Mallampati), Friedman tonsil score, and other more complex calculations have been used. We propose a technique for assessing collapsibility of the pharynx near the root of the tongue. Sitting vertically and looking straight ahead, the patient breathes through the nose while the clinician places a thumb above the cricoid cartilage. Pressure is applied towards the occiput and any change in breath sounds noted (“Douglass gag test”).

Methods: We completed a retrospective chart review of 223 patients who had a sleep consultation that included the gag test plus Friedman palate and tonsil scores. The latter were determined from a clinical drawing of the oropharynx done during consultation. The Douglass technique was scored from 0 through 4 (no change in airflow, minimal change, noticeable change, almost complete occlusion, and complete occlusion of breathing). Patients then underwent polysomnography. The apnea hypopnea index (AHI) was divided into quartiles (Less than 5, 5--14.9, 15--29.9, 30+), then entered into a log-linear analysis with the Friedman palate score and the Friedman tonsil score.

Results: The Douglass gag score (OR 1.46, CI = 1.19 -- 1.80) and Friedman palate score (OR 1.50, CI = 1.16 -- 1.94) were significantly associated with higher AHI quartiles. The Friedman tonsil score was not significantly associated with AHI quartile (OR 0.93, CI = 0.72 -- 1.20)

Conclusion: The Douglass gag test significantly predicted sleep disordered breathing. The degree of association, while modest, is equivalent to well established risk factors in the literature. It therefore provides a novel and easy to screening tool for the clinician.

Support (optional): Royal Ottawa Foundation for Mental Health

0518

THE USE OF A NASAL RESISTANCE VALVE TO TREAT SLEEP DISORDERED BREATHING

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Introduction: A recent evaluation of a nasal expiratory resistance valve device (Provent™ Ventus Medical Inc) in obstructive sleep apnea reported significant improvements in apnea hypopnea (AHI) and oxygen desaturation (O₂DI) indices. Limitations of the study included one night of device evaluation, a single resistance level and no sham control. In order to further evaluate the device a second study was conducted where sleep parameters as well as intranasal pressure (Pin) was monitored using 8 of the original participants and an additional subject.

Methods: Five different conditions were evaluated on non-consecutive nights: control (no device), sham (a device with no valve) and one of three different resistance levels calibrated to approximately 40, 80 and 150 cmH₂O*sec/liter flow. The order of conditions was randomized across subjects using a modified Latin square design. All studies were scored blind to the condition. Output variables included Pin, AHI and O₂DI. Analysis was conducted on the 7 subjects (5 men) (aged 56.4 ± 7.8, BMI 29.9 ± 5.2) with data from all conditions, using repeated measures ANOVA. Planned contrasts compared each of the device conditions to the control condition.

Results: AHI showed a main effect of device use ($F(1,24)=6.9$, $p < 0.001$), with no difference between the control (34.17 ± 2.0) and sham (29.32 ± 25.4) conditions, but significant decreases for each of the 40 (13.4 ± 10.5 , $p < .05$), 80 (11.6 ± 13.2 , $p < .01$) and 150 cmH₂O resistance (14.0 ± 11.8 , $p < .01$) conditions compared to control. O₂DI had the same pattern of results with a significant main effect ($F(1,24)=6.9$, $p < 0.001$), no improvement from control (35.8 ± 18.6) with sham (23.5 ± 23.4), and significant improvements with the 40 (15.3 ± 12.1 , $p < .05$), 80 (19.4 ± 25.7 , $p < .05$) and 150 cmH₂O (17.0 ± 20.1 , $p < .05$) devices. Pin was significantly increased in the three active devices ($p < .001$ in all cases) relative to the sham device.

Conclusion: The data indicate that the improvement in sleep disordered breathing seen with device use is due to elevated expiratory pressure not nasal dilation from device insertion. Improvements are also independent of the strength of resistance within the tested range.

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0519

FUNCTIONAL CAPACITY IN OSA PATIENTS AND CONTROLS ACCORDING TO BMI

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Introduction: There are some evidence in the literature that OSA patients have impaired functional capacity compared to controls. It is also known that obesity may impair exercise capacity. Previous studies did

not control for BMI. We sought to evaluate the influence of BMI in functional capacity in OSA and non-OSA matched controls.

Methods: Seventy-five OSA patients (AHI > 5/hour of sleep, mean of 27.7 ± 22.7) and 64 controls (mean AHI = 3.6 ± 4.0) were included in this study, mean age of (52.2 ± 8.5 , 50.0 ± 6.7 ; ns). Patients underwent full polysomnography, spirometry, cardiopulmonary exercise test (ramp protocol), echocardiography, ECG, and ambulatorial evaluation in order to exclude respiratory and cardiac diseases. Patients with BMI > 40 were also excluded. Thirty-one OSA patients had BMI < than 27kg/m^2 , and 38, in the control group. One-Way ANOVA, factorial ANOVA, and factorial ANOVA for repeated measures were used to analyze differences between groups.

Results: OSAS vs Controls : Neck and abdominal circumferences were higher in OSA group. Baseline and peak heart rate (HR), blood pressure (BP), and VO₂ were similar between groups. Factorial ANOVA results (OSA vs Controls; BMI > 27kg/m^2 vs < 27kg/m^2): Neck circumference was similar for all conditions analyzed, but the abdominal differentiate obese from non-obese subjects. Peak exercise systolic and diastolic BP were significantly higher in obese subjects ($191.87\text{ mmHg} \pm 28.79$; 177.46 ± 31.50 , $p = 0.01$). All HR measures did not change according to the conditions analyzed. A lower VO₂ ($26.22 \pm 7.44\text{ ml/kg/min}$; 30.80 ± 7.90 , $p = 0.0006$) and anaerobic threshold ($22.08\text{ ml/kg/min} \pm 5.57$; 27.30 ± 7.29 , $p = 0.0001$) were found in obese subjects. All the above significant results for obese subjects occurred independently of OSA diagnosis.

Conclusion: 1-Obesity, but not OSA, was responsible for the alterations found in blood pressure and VO₂ responses to exercise test. 2-Abdominal, but not neck circumference, differentiate non-obese from obese subjects in the present sample of OSA and non-OSA controls.

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0520

CARDIORESPIRATORY RESPONSE TO EXERCISE IN MEN AND WOMEN WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: OSA severity has been associated with self-reported sedentarism. Most of the research has been done with men recruited from sleep clinics. There is limited data on the exercise performance of women with OSA. Therefore, the aim of this study was to assess exercise performance in a prospective, consecutive sample of men and women with OSA to compare their arterial blood pressure and heart rate responses during and after exercise.

Methods: Sixty-two subjects (32 men) completed the protocol. Men had a higher peak VO₂, % predicted peak VO₂, VCO₂, heart rate, systolic BP, and oxygen pulse than women.

Results: There were no differences between men and women for peak oxygen saturation, peak Borg scales for dyspnea and leg fatigue and diastolic BP. A significant negative correlation was found between severity of OSA as measured by AHI, and peak VO₂ ($r = -0.44$) in women, but not in men. Men with OSA had higher: peak VO₂ ($33.3 \pm 10.2\text{ ml/kg/min}$; 23.3 ± 7.0 , $p < 0.0001$), peak exercise heart rate $157 \pm 23\text{ bpm}$; 141 ± 20 , $p = 0.007$), end-exercise systolic BP ($193.8 \pm 22.4\text{ mmHg}$; 173.2 ± 22.8 , $p < 0.0001$) than women. SBP during recovery from exercise was also higher in men compared to women; although this difference is not significant when adjusted for peak systolic BP.

Conclusion: 1-Both men and women with OSA have normal cardiorespiratory fitness in the absence of cardiac or respiratory disease; 2- Men responded to exercise with higher heart rate, systolic BP, and VO₂ at peak than women did; 3- The negative correlation between VO₂ and AHI was found only among women.

Support (optional): AFIP, FAPESP (CEPID 98/14303-3)

0521

USE OF A SNORING SEVERITY SCORE (SSS) BASED EQUATION TO PREDICT CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) AMONG PATIENTS WITH SUSPECTED OBSTRUCTIVE SLEEP APNEA (OSA) WHILE THEY AWAIT OVERNIGHT POLYSOMNOGRAPHY: A PROSPECTIVE PILOT STUDY

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Introduction: Retrospectively, we demonstrated that technologist observed snoring severity during nocturnal polysomnography (NPSG) could be used to accurately predict effective CPAP (Pe-CPAP = $0.086 \times \text{BMI} + 0.029 \times \text{SSS} + 5.989$ with SSS: none=5, mild=15, moderate=30, severe=75) 1. Now we report our prospective pilot study to validate our equation and to determine the consequences of prescribing Pe-CPAP prior to NPSG.

Methods: Randomly, we assigned to Groups 1 and 2 patients with suspected OSA waiting for NPSG and saw them one month before NPSG (Visit 1), at NPSG (Visit 2) and one month following NPSG (Visit 3). Group 1 began CPAP at Visit 1 using Pe-CPAP determined from our equation but using patient reported snoring severity. Group 2 began CPAP after NPSG-titrated-CPAP (Te-CPAP) was determined at Visit 2. CPAP among Group 1 was adjusted when Te-CPAP \neq Pe-CPAP. For all patients, Pe-CPAP and Te-CPAP were compared and AHI at Pe-CPAP were determined using both patient reported and technologist observed snoring severity. Patient reported sleep time, nocturnal awakenings, sleep quality (score 0-5) and sleepiness (Epworth Score) were determined at all visits. CPAP-compliance was determined at Visit 3. Mann-Whitney-U and Chi-Square tests were used to compare data differences among the two groups.

Results: Eight and six patients comprised Group 1 and Group 2 respectively. Based on patient reported and technologist observed snoring severity, Pe-CPAP = Te-CPAP \pm $-2.5\text{cmH}_2\text{O}$ respectively in 62% and 69% of the 14 patients and AHI < 5 events per hour in all 14. For Groups 1 and 2 respectively, mean sleep time were 7.3, 4.8 hours and mean sleep quality were 4.4, 0.5 at Visit 2, mean Epworth Score were 13, 7, 6 and 14, 12, 6, across the three visits, and mean CPAP use was 4.2 and 4.1 hours per day (Visit 3).

Conclusion: Patient-reported snoring severity reliably predicted e-CPAP associated with AHI < 5 events/hour. Prescribing Pe-CPAP was effective without deterring compliance with CPAP use. Our study continues.

0522

ROLE OF OBSTRUCTIVE SLEEP APNEA IN THE ACUTE DECOMPENSATION OF HEART FAILURE

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Introduction: Obstructive Sleep Apnea (OSA) is present in up to 53% of patients with chronic heart failure. OSA is associated with worse outcomes of hypertension, atrial fibrillation, coronary disease, and ventricular arrhythmia. Therefore OSA may be involved in the acute decompensation of heart failure (ADHF).

Methods: Patients admitted with ADHF symptoms were systematically evaluated with an inpatient sleep study (Stardust®, Respiromics). Patients with ADHF and OSA (AHI > 15, 50% events obstructive) were randomized to inpatient Auto-titrating PAP vs. Out patient standard of care PSG and subsequent CPAP initiation. Measurements were obtained at baseline and 4 days post-randomization. These included: left ventricu-

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lar ejection fraction, 24 hr urinary norepinephrine, and a profile of acute heart failure recovery (6 minute walk test, BNP, BUN, and questionnaires).

Results: The prevalence of OSA (AHI>15) was 62% in patients with ADHF (145 /322 consecutive unscreened patients). So far, a total of 32 subjects are enrolled in the intervention protocol, with 17 subjects in the intervention group (14 male, age 54±17, BMI 34±11, and AHI 40±10), and 15 in the control arm (14 male, age 58±14, BMI 32±7, and AHI 38±16). In the intervention arm, LVEF increased by 2.5±5.0 (22.8±7.3 to 24.5±7.6). In the control group LVEF increased by 1.5±7.7 (21.3±9.3 to 23.0±12.5) (NS). Urinary norepinephrine levels in the device group decreased by 31.8±47.5 µg/24h from baseline of 72.4±62.8 to conclusion of 51.9±37.5 µg/24h, while control group showed a mean decrease of 6.7±17.4 µg/24h (baseline of 83.5±48.9 and conclusion 90.2±69.2 µg/24h) (NS).

Conclusion: OSA is prevalent in patients with ADHF and may play a role in the acute decompensation of heart failure. Early identification and inpatient treatment of underlying previously unrecognized OSA may improve the outcomes in patients hospitalized with ADHF.

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0523

ENDOTHELIAL DYSFUNCTION IN OBSTRUCTIVE SLEEP APNEA IS DUE TO INCREASED ENDOGENOUS INHIBITORS OF NITRIC OXIDE

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Introduction: Patients with Obstructive Sleep Apnea (OSA) have endothelial dysfunction and reduced nitric oxide (NO) bioavailability. A potential mechanism for the reduced NO function in these patients is increased endogenous inhibitors of NO such as asymmetrical dimethylarginine (ADMA), a circulating endogenous inhibitor of NO synthase that competes with L-Arginine for NO synthesis.

Methods: Patients with OSA (AHI >10) and no coexisting cardiovascular disorders (specifically no hypertension, diabetes, coronary heart disease, smoking, or dyslipidemia) and healthy controls were enrolled. Participants underwent evaluation of flow mediated dilation (FMD) of the brachial artery and blood draw. Experiments were performed before 8 AM in the fasting state. Patients returned 6-8 weeks after initiation of CPAP. ADMA levels were measured by HPLC analysis of serum.

Results: Nine patients with OSA and seven healthy controls are enrolled so far. Five patients returned after treatment. Average FMD in controls was 6% of baseline diameter and 14% with Nitroglycerin (NTG). In OSA patients, FMD was 2% of baseline and NTG induced dilation was 4%. Post Treatment FMD was 4% of baseline and NTG induced dilation was 15%. The average serum level of ADMA was higher in OSA patients than healthy controls (average± SE) 0.379± 0.228 in patients vs 0.158± 0.075 µM in controls). After CPAP, ADMA levels decreased in patients to 0.136± 0.025 (a 64% decrease from baseline). The serum levels of homoarginine in patients was 2.08 ± 0.9 vs. 1.545± 0.278 µM in controls. In patients, post treatment homo-arginine dropped to 1.260± 0.020 µM (drop of 39%).

Conclusion: These findings suggest that endothelial dysfunction is present in patients with OSA and no cardiovascular disease. OSA causes endothelial dysfunction by increasing levels of ADMA resulting in reduced NO bioavailability, an effect that is reversible with CPAP.

0524

A NEW INSTRUMENT FOR RAPID CLINICAL SCREENING OF OBSTRUCTIVE SLEEP APNEA

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Introduction: Sleep problems are a common complaint in a primary care practice and the need for efficient use of physician time makes a rapid, accurate screening device a potentially important tool for evaluating patients with sleep disorders. The Glidewell Rapid Sleep Screen (GRSS) is a brief semi-structured interview developed to enable primary care clinicians to quickly and reliably detect and distinguish various sleep disorders.

Methods: 60 new patients presenting to a private AASM accredited sleep center were administered the interview by a staff nurse prior to clinical consultation with a board certified sleep physician whose practice is limited to sleep disorders. Following consultation the physician completed a locally developed checklist indicating their initial diagnostic impressions. The patient and sleep physician were blind to the results of the interview. Using the physician's initial diagnostic impression as the reference, sensitivity and specificity analysis was completed to determine the ability of the interview to correctly classify obstructive sleep apnea (OSA) patients.

Results: The original 6-item decision rule of the interview resulted in sensitivity of .75 and specificity of .67. Analysis of response patterns in the 16 patients incorrectly classified by the original rule revealed (a) excessive daytime sleepiness and signs of obstruction other than snoring are unreliable predictors of OSA in this subgroup and (b) poor sleep quality was a reliable predictor of OSA in this subgroup. The data was reanalyzed using a modified 3-item decision rule: (snoring plus either EDS or poor sleep quality) that resulted in sensitivity of .88 and specificity of 1.

Conclusion: Using the modified rule, clinicians can make a rapid and reliable initial diagnosis of OSA with excellent sensitivity and specificity. This can aid in the selection of patients to be referred for polysomnographic evaluation. Investigation of this instrument within a primary care practice is warranted.

0525

EPIDEMIOLOGY OF SLEEP DISORDERED BREATHING (SDB) IN BANGKOK (THAILAND)

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Introduction: A representative sample of the Bangkok population was pre-selected by the National Statistics Office of Thailand based on results of the 2000 Census (population 6,320,174). A total of 4680 participants underwent a face-to-face interview to investigate a frequency of SDB.

Methods: The sleep inventory included 49 questions. SDB was defined as habitual snoring (at least 3 nights/week) with excessive daytime sleepiness at least 3 days/week.

Results: Four percent of the total sampled Thai population had SDB: 5.3% of men, and 3.5% of women. SDB subjects were older (41.4 versus 36.7 yrs, p<0.0001), had greater BMI (26.0 versus 22.8 kgm², p<0.0001), larger necks (34.7 versus 32.5 cm, p<0.0001), and larger waist circumference (88.0 versus 78.7 cm, p<0.0001). SDB subjects reported shorter total nocturnal sleep time (7.0 versus 7.7 hours, p<0.0001), and greater frequency of choking during sleep, sleep disturbance and awakenings, night

sweats, nocturia, daytime naps, cardiovascular disease, endocrine disease, uncomfortable feelings or sensations in legs with recurrent need or urge to move while sitting or lying down, and bruxism. They were more likely to report poor quality and unrefreshing sleep. Multivariate analysis showed male gender, BMI, and waist size were significant predictors of SDB. Age and neck circumference were not predictive of SDB. Multivariate analysis of complaints associated with SDB showed awakenings in the middle of night, witnessed apneas, unrefreshing sleep and uncomfortable feelings or sensations in legs with recurrent need or urge to move while sitting or lying down, to be the significant variables associated with SDB.

Conclusion: This is the first epidemiological study performed on a representative sample of the Thai population, an ethnic group with a more brachiocephalic craniofacial presentation compared to Caucasians. Similar factors predicted SDB in this population, with the exception of neck circumference which had no predictive relationship with SDB.

Support (optional): The Thailand Research Fund

0526

EPIDEMIOLOGIC BANGKOK (THAILAND) STUDY: GENDER DIFFERENCES IN SLEEP DISORDERED BREATHING (SDB)

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Introduction: Systematic sampling of the Bangkok population was performed to demographically represent the population from the 2000 national census. Gender comparisons in the demographics and clinical presentation of sleep disordered breathing (SDB) were performed.

Methods: A face-to-face interview using a 49-question sleep inventory was conducted in 4680 subjects. SDB was defined as habitual snoring (>3 nights/week) and excessive daytime sleepiness occurring at least 3 days a week.

Results: Among 4680 subjects sampled, 202 (4.3%) had SDB. Among 2118 men, 112 (5.3%) had SDB compared to 90 (3.5%) of 2562 women ($p<0.0001$). The prevalence of SDB in men younger than 45 years of age was 5.0%, which was twice that of women in the same age group (2.5%, $p<0.0001$). The prevalence of SDB increased in both men and women after the age of 45 to 6.1%, although this increase was statistically significant only for women. Men and women with SDB had significantly greater BMI, neck and waist size compared to men and women without SDB (Men: BMI 25.4 vs 22.7 kgm², neck 36.1 vs 34.1 cm, waist 88.0 vs 80.7 cm; Women: BMI 26.8 vs 22.8 kgm²; neck 32.8 vs 31.2 cm; waist 87.9 vs 77.1 cm ($p<0.0001$)). BMI, neck and waist size did not differ significantly by age-group in either men or women with SDB. With respect to symptoms, SDB women did not differ from SDB men in the report of insomnia, choking, night sweats, bruxism, urge to move legs with unpleasant feelings when seated or lying in bed, or parasomnias; but women with SDB reported more nocturia (48.9% vs 32.1%), less alcohol intake (4.4% vs 19.6%), and less witnessed apneas (7.8% vs 22.3%).

Conclusion: SDB is least prevalent in younger women. Risk factors and symptoms of SDB were generally similar in both men and women regardless of age group.

Support (optional): The Thailand Research Fund

0527

HIGH PREVALENCE OF MODERATE TO SEVERE SLEEP DISORDERED BREATHING WITHOUT DAYTIME HYPERSOMNOLENCE IN JAPANESE MALE TRUCK DRIVERS

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Introduction: In Japan, the daytime hypersomnolence is often used for screening of the sleep apnea syndrome (SAS) in professional drivers. However, there were several cases of professional drivers who had not perceived daytime hypersomnolence and showed severe sleep disordered breathing (SDB) by polysomnography after traffic accidents. We conducted the present study to estimate the prevalence of the SDB without daytime hypersomnolence in truck drivers.

Methods: Data of 11,736 male truck drivers (aged 18 to 69) who underwent a home sleep study using a single-channel portable respiratory monitor, were used to estimate the prevalence of the SDB. The monitor used a polyvinylidene fluoride film as a thermal sensor to detect airflow. The flow signal was analyzed using short time power-spectral analysis which yield respiratory disturbance index (flow-RDI). The flow-RDI was demonstrated to correlate highly with AHI obtained by full-polysomnography (Eur Respir J 29:728-736; 2007). The Epworth Sleepiness Scale (ESS) was distributed to all the subjects. We defined daytime hypersomnolence as those who had ESS score of 11 or higher.

Results: The prevalence of SDB categorized by the flow-RDI level was 44.2 % (flow-RDI level of 5 to 19.9), 6.0 % (flow-RDI level of 20 to 39.9) and 1.3 % (flow RDI of 40 or higher). Daytime hypersomnolence was not found in 91.2 % and 91.6 % of drivers with flow-RDI level of 20 to 39.9 and 40 or higher, respectively.

Conclusion: When we use the subjective sleepiness to detect the SAS among truck drivers, fairly high proportion of them with moderate to severe SDB are overlooked, suggesting the usefulness of the home sleep monitoring of airflow for screening of the undiagnosed SAS in truck drivers.

0528

COGNITIVE AND MOOD DISTURBANCES IN OBSTRUCTIVE SLEEP APNEA AND OTHER SLEEP DISORDERS

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Introduction: Sleep disorders (SD) lead to daytime consequences. Among them cognitive and mood disturbances are described. Cognitive dysfunction is also associated to psychiatric conditions. OSA's consequences have extensively been described. We hypothesize that OSA's impairments are different from other SDs. Aim: We sought to evaluate cognitive, mood, anxiety, and level of stress in OSA patient compared to other SDs.

Methods: One hundred and sixty patients diagnosed as having OSAS and ninety having others SDs including insomnia, parasomnias, and disorders of movements during sleep. They all completed the Epworth Sleepiness Scale (ESS), Geriatric Depression Scale (GDS), self-concept scale (SCS), Lipp Inventory for Stress Symptoms (LISS), State Trait Anxiety Examination Inventory (STAI) and Mini-mental state examination (MMSE) to assess mood and cognitive disorders.

Results: There were no differences in the MMSE, GDS, and STAI for OSA group compared to other SDs. However, when the attention and calculation domains of MMSE are concerned, OSA subjects exhibited lower performance than other SDs group ($2,94 \pm 2,32$ vs $3,79 \pm 2,01$, $p=0.02$). LISS and SCS did not differentiate both groups, but when the scores are analyzed all subjects showed high values of stress, LISS score

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[3,34 ± 2,66 vs 4,10 ± 3,03 (normal scores < 3,00)]; and low self-concept, SCS score [83,21 ± 14,82 vs 87,90 ± 15,25 (normal scores > 125)].

Conclusion: OSA's subjects presented higher deficit in attention and calculation reflecting some impairment of mentally manipulate information. OSA and other SD groups similarly affected stress and self-concept scoring. Comparison with a healthy control group is under investigation.

Support (optional): AFIP, FAPESP (CEPID 98/14303-3)

0529

INTERMITTENT HYPOXIA-INDUCED FOAM CELL FORMATION AND ATHEROGENESIS: POTENTIAL INVOLVEMENT OF FATTY ACID BINDING PROTEIN

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Introduction: Obstructive sleep apnea (OSA) which is characterized by intermittent hypoxia (IH) during sleep, has emerged as an independent risk factor for cardiovascular disease, and more specifically coronary heart disease. IH is associated with disruption of lipid metabolism, activation of inflammatory pathways, and endothelial cell injury through oxidative stress mechanisms. However, the causal relationship between IH and atherosclerosis has not yet been fully established. Recently, it has been reported that adipocyte fatty acid binding protein (FABP) plays a critical role in the process of atherosclerosis and inhibition of FABP effectively reduces atherosclerotic lesion formation.

Methods: To further explore the effect of IH on FABP expression and IH-induced atherosclerosis, we used in vitro monocyte cell line model to test macrophage transformation, activation of inflammatory pathways, and foam cell formation under carefully controlled IH exposures. The THP-1 cell line was exposed to IH for 3, 6, 12, 18, and 24 hours. FABP mRNA and protein expression were assessed by real-time RT-PCR and Western-blotting, respectively. Macrophage transformation was assessed by flow cytometry using specific cell lineage markers. Induction of inflammation was examined by measuring TNF- α , IL-1, and IL-6. Foam cell formation was determined by oil red O staining before and after exposure to oxidized LDL.

Results: IH induced increased expression of FABP and increased nuclear factor kappa B nuclear binding. IH was associated with transformation of monocytes to activated macrophages, as evidenced by increased expression of CD1a, CD68, and CD36. In addition, IH increased foam cell formation in the presence of oxidized LDL. Furthermore, down regulation of FABP through specific siRNAs markedly decreased IH-induced macrophage activation, inflammation, and foam cell formation.

Conclusion: FABP plays an important role in IH-induced atherogenesis and may become a viable therapeutic target aiming to prevent and potentially reverse OSA-associated atherosclerosis.

Support (optional): SCOR 2P50HL60296, HL 69932 and HL65270, and the Children's Foundation for Sleep and Neurobiology Research

0530

OSA SCREENING TOOLS IDENTIFIED THE PATIENTS AT RISK OF OSA RELATED POSTOPERATIVE COMPLICATIONS

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Introduction: Patients with obstructive sleep apnea (OSA) have more postop complications. Identifying patients susceptible to OSA related postop complications are an important step towards preventing them. The purpose of the study is to explore the validity of three screening tools, the STOP questionnaire (4-items assessing snoring, tiredness, breathing obstruction and hypertension), the American Society of An-

esthesiologists (ASA) checklist and the Berlin questionnaire (BQ), in predicting the occurrence of postop complications.

Methods: Following hospital ethics approval, preop patients (18+ years) were asked to complete the STOP and Berlin questionnaire, and prior to scoring, the ASA checklist was administered. All patients were invited to undergo preoperative laboratory polysomnographic testing. Postop complication data were collected by chart review.

Results: Data from 211 patients were analyzed. The average age was 51 ± 13; 50.2% male, BMI 30 ± 6 kg/m². The incidence of hypertension: 43.6%, gastroesophageal reflux : 30.8% and diabetes: 18.0%. The incidence of overall postoperative complication was 22.8%, primarily oxygen desaturation (SaO₂<95%) (17.1%). There were no deaths or life threatening complications. Patients ranked as high risk of OSA by the STOP questionnaire had a significantly higher incidence of respiratory complications (23.8% vs 10.6%, p<0.05), desaturation (22.2 % vs 9.4%, p<0.05), and severe desaturation (SaO₂<93%) (15.1% vs 4.7%, p<0.05). A higher incidence of postoperative respiratory complications (25.7 % vs 9.9%, p<0.05) and oxygen desaturation (21.4 % vs 8.5%, p<0.05) was also found in the patients identified as high risk of OSA by the ASA checklist. There was no significant difference in postop complications between patients classified as high or low risk of OSA by the BQ.

Conclusion: The patients recognized as being at high risk of having OSA by the STOP questionnaire or the ASA checklist demonstrated a significantly higher incidence of postoperative respiratory complications, mainly due to oxygen desaturation. The BQ was not able to identify patients with OSA-related postop complications.

0531

THE EFFECT OF SURGERY ON THE SLEEP ARCHITECTURE OF PATIENTS AT RISK OF OBSTRUCTIVE SLEEP APNEA - A PILOT STUDY

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Introduction: Anesthetics, analgesics and surgery may have a tremendous impact on the sleep architecture of patients in the postop period. This is a preliminary report of an on-going study designed to investigate the effect of surgery and anesthesia on the sleep of surgical patients.

Methods: After hospital ethics approval, preoperative patient over 18 years old were recruited. The patients were screened with STOP questionnaire (4-items assessing snoring, tiredness, breathing obstruction and hypertension). Patients classified as having a high risk of having OSA were invited to undergo polysomnography (PSG) with a portable device (Embletta x100) preop at home, first and third night postop in the hospital. The PSG was scored by a certified sleep technologist. The data were input into a specifically designed MS Access database and analyzed by SAS 9.1.

Results: A total of 16 patients completed all three nights of sleep study. The average age was 65 ± 9; 11 male, 5 female; BMI 32.8 ± 6 kg/m²; neck circumference 39.5 ± 7.5cm. The average preoperative apnea hypopnea index (AHI) was 22.4 ± 15 and 15 patients (93.8%) had an AHI>5. Compared with preop PSG, the sleep efficiency, percentage of REM and slow wave sleep (stage 3 and 4) on first and third postop night were significantly decreased. The stage 3 sleep was significantly increased. On the third postop night AHI was significantly increased vs preop, (50.1 ± 38 vs 22.4 ± 15, p<0.05). The oxygen desaturation index was significantly increased vs preop (41.2 ± 34. vs 15.8 ± 14 p<0.05 and first night 41.2 + 34 vs 15.1 ± 18 first night, p<0.05). Average SaO₂ and lowest SaO₂ were also significantly lower in third vs first postop night.

Conclusion: Following surgery, the patients at high risk of OSA had significantly lower sleep efficiency. REM and slow wave sleep was signifi-

cantly reduced. On the third postop night, AHI and oxygen desaturation index were significantly increased vs preop or first postop night.

0532

PLASMA CYSTEINE CONCENTRATION IN OSA PATIENTS AFTER CPAP THERAPY

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Introduction: Plasma cysteine (Cys) levels has been reported to be risk factor for coronary heart disease as homocysteine is. The role of homocysteine and cysteine in the pathophysiology of cardiovascular consequences of Obstructive Sleep Apnea (OSA) is less understood. We sought to evaluate changes in plasma Cys and homocysteine concentration and the related vitamin in patients with stratified OSA severity levels, before and after CPAP therapy.

Methods: All OSAS patients with AHI > 6 were consecutively recruited from Sleep Disorders Ambulatory of Federal University of Sao Paulo during three-month period. Patients were divided into three groups: mild OSA (n= 27, mean age 50.9±12.5), moderate OSA (n= 37, mean age 57.7±9.8), and severe ones (n= 51, mean age 57.7±11.5). Patients underwent clinical evaluation, echocardiogram, and 12-lead ECG. Blood sample were obtained in the morning, and Cys, homocysteine, Cholesterol, Uric Acid, vitamins B6, B12, E, C, folato, and many other blood parameters were analyzed. Twenty patients were consecutively selected to receive CPAP therapy. Blood samples were again collected after 1 month. Statistics: One-way ANOVA and Chi-Square test were performed.

Results: Cys level, Vitamin B6, and Uric Acid significantly increased according to OSA severity [495.7±20.2; 547.4±16.0; 565.3±13.4; (p=0.02)]; [32.2±2.1, 34.3±1.9, 38.7±1.5; p=0.03]; [5.6±0.3, 5.6±0.2, 6.4±6.4; (p=0.03)], respectively, as previously shown. Arterial hypertension was significantly more frequent in severe OSAS patients (65.3%, p=0.01). Groups had similar BMI, age, left ventricular ejection fraction, ECG, homocysteine, and other blood parameters. Cysteine concentration before and after CPAP therapy were respectively, [465,51±80,36; 426,43±47,40, p=0,10]. BMI, vitamin B6 and B12 did not change after CPAP treatment.

Conclusion: Cysteine has been shown to be associated to OSA severity. One-month of CPAP therapy did not normalize cysteine concentrations. Long-term CPAP therapy should be tested.

Support (optional): AFIP, FAPESP (CEPID 98/14303-3)

0533

COMPARISON OF A NEW POSITIONAL DEVICE TO CPAP THERAPY IN PATIENTS WITH POSITIONAL OBSTRUCTIVE SLEEP APNEA

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Introduction: The ability of positional therapy to normalize the apnea-hypopnea index (AHI) (AHI < 5 events/hr) has not been adequately evaluated. We evaluated a new positional device (PD)(ZZOMA) to treat positional OSA and compared it to CPAP.

Methods: We identified 12 patients (10 males, 47±13 yrs, BMI=31±6) with positional OSA (AHI 13±8, nonsupine index 3±1 events/hr). Patients were then randomized to a night with CPAP (9±2 cm H20) or the PD. A third study night consisted of the opposite therapy.

Results: Compared to baseline, both the PD and CPAP decreased the AHI, from 13±8 to 3±2 and 3±6 events/hr, respectively (p<0.001), with no significant difference between the two. % total sleep time (TST) spent supine, compared to baseline, was eliminated with the PD, but

unchanged with CPAP, from 45±27 to 0±0 and 61±25%, respectively (p<0.001 for the PD). Compared to baseline, the mean and lowest oxygen saturations were unchanged with both the PD and CPAP, from 96±4 to 96.3±1.3 and 96.4±2% (p=0.8), and 85.3±5.6 to 88.6±3.6 and 88.5±2.9% (p=0.3), respectively. TST and sleep efficiency, compared to baseline, were unchanged with both the PD and CPAP therapy, from 332±70 to 333±71 and 305±71 minutes (p=0.3), and 87±9 to 87±15 and 82±16% (p=0.4), respectively, as was the arousal index from 25±14 to 24±18 and 24±19 arousals/hr (p=0.8), respectively. Finally, compared to baseline, %TST in stage N3 and REM was unchanged with both the PD and CPAP, from 8±9 to 10±10 and 15±13% (p=0.5), and 17±7 to 16±6 and 15±8% (p=0.7), respectively.

Conclusion: In patients with positional OSA, a new positional device: 1) is as effective as CPAP at decreasing the AHI; 2) normalizes the AHI to < 5 events/hr; 3) eliminates supine sleep during the night; and 4) is similar to CPAP in regards to effects on sleep quality and nocturnal oxygenation.

0534

POSTOPERATIVE MANAGEMENT STRATEGIES AND OUTCOMES IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA WHEN UNDERGOING TRANSSPHEOIDAL SURGERY

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Introduction: Patients with OSA who are undergoing transsphenoidal surgery for pituitary adenomas present management dilemmas since postoperative nasal packing precludes the use of standard nasal CPAP. The development of pneumocephalus with the application of positive pressure into the nasal cavity presents an additional concern. In this retrospective observational study, we evaluated our experience in managing these complex cases.

Methods: We searched our institution's medical record database to identify patients with a diagnosis of OSA who had undergone transsphenoidal surgery between January 1997 and November 2007. Information gathered included demographics, diagnostic parameters of OSA, postoperative management strategies, postoperative complications, ventilator days, ICU days, and hospital days.

Results: Our search identified 8 patients that met our inclusion criteria. Six of the patients were male (75%) with a median age of 60.5 (range 32-81). Three patients had polysomnographic data available with a mean apnea and hypopnea index of 25.2 (7-57.4). Five of the patients had been previously diagnosed with OSA outside of our institution. Preoperatively, five of the patients were using CPAP, 2 patients were noncompliant with CPAP, and 1 patient was being managed with position therapy. Management strategies for sleep apnea postoperatively included head of bed elevation and position restriction in 2, temporary tracheostomy in 1, and uvulectomy in 1. Four patients received no specific therapy other than close monitoring, anesthesia notification, and the usual conservative measures. Two patients (25%) experienced complications postoperatively. Mean ventilator days, ICU days, and hospital days were 0.75 (0-5), 1.5(0-7), 3.5 (2-8) days, respectively. Ventilator, ICU and hospital days for patients with specific management strategies were 0.25 (0-1), 0.5 (0-1), and 3 (2-4), respectively, compared with 1.25 (0-5), 2.5 (1-7), and 4 (2-8), respectively, for those without any specific management strategy. The normal expected ventilator, ICU and hospital days for transsphenoidal surgery are 0, 1, and 2, respectively.

Conclusion: The presence of sleep apnea appears to increase the risk for complications and prolong ICU and hospital stay following surgery. Preoperative assessment for patients with OSA who undergo transsphenoidal surgery may significantly reduce morbidity following surgery. A larger prospective study is needed to clarify the risk and help guide management strategies in this setting.

0535

A CORRECTION INDEX FOR THE ADJUSTMENT OF THE APNEA-HYPOPNEA INDEX VARIABILITY

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Introduction: A previous study from our group assessed the variability of apnea-hypopnea index (AHI) by polysomnography (PSG) throughout 4 consecutive nights in 20 patients with obstructive sleep apnea syndrome (OSAS). The results of this study showed that AHI in OSAS patients presented a good correlation among the 4 nights, but a significant individual variability should be considered. The aim of the present study was to develop a correction index that could be used by physicians to adjust their patients' AHI who had been submitted to only one night of PSG recording.

Methods: Based on the first PSG (PSG 1), the 20 patients were distributed in three groups, according to severity of AHI, in mild (AHI between 6 to 15), moderate (AHI between 16 to 30) and severe (AHI higher than 30). The correction index was calculated for each patient by the following formula: $((PSG2/PSG1)+(PSG3/PSG1)+(PSG4/PSG1))/(PSG1+PSG2+PSG3+PSG4) \times 10$. Afterward, we developed a mean index for each group of patients.

Results: Five patients were included into the mild group, 3 into moderate group and 12 into severe group. The correction index for the mild group was 0.63 ± 0.08 , for the moderate group was 0.36 ± 0.06 , and for the severe group, 0.15 ± 0.04 . Statistical analysis of these values was performed by a one-way ANOVA, which showed a significant difference ($F(2,17) = 121.35$; $p < 0.00001$). Post-hoc analysis revealed that index of mild group > moderate > severe ($p < 0.0005$).

Conclusion: Considering the night to night variability of the AHI, these correction indexes, developed according severity of AHI, could help physicians to manage their OSAS patients. This possibility will be tested in the near future.

Support (optional): AFIP, FAPESP (CEPID 98/14303-3), CNPq

0536

THE EFFECT OF DECOMPRESSION SURGERY OF THE POSTERIOR CRANIAL FOSSA UPON SLEEP PARAMETERS IN ADULT PATIENTS WITH CHIARI MALFORMATION

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Introduction: Adult Chiari Malformation (CM) is characterized by herniation of the cerebellar tonsils through the foramen magnum. Compression of the brainstem, high cervical medulla, and of characteristic components of CM may generate several neurological deficits. As the central respiratory controlling system is located in the affected region, CM patients are under higher risk of developing sleep central and/or obstructive apnea, and hypoventilation. The aim of this study was to assess the effect upon sleep parameters of CM patients who have undergone decompression surgery of the posterior cranial fossa.

Methods: All the patients referred to the Instituto do Sono/AFIP by the neurosurgery service of the Hospital Servidor Público Estadual (HSPE) were sequentially evaluated. CM was clinically diagnosed and confirmed by magnetic resonance imaging (MRI). Two full night polysomnographies were performed: basal and after intervention. Surgical decompression of the posterior cranial fossa was performed by the same neurosurgeon of the HPSE. The clinical and polysomnographic analyses were blinded and randomized performed.

Results: 22 patients (8 men, 41 ± 13 years, body mass index 25 ± 4 kg/m²) were evaluated. Prior to the surgery, 13 patients (59%) presented AHI > 5, with a mean value of 29 ± 34 , and after surgery the AHI of that group was 9.9 ± 8.7 ($P = 0.015$). 10 patients (45%), from the total number of subjects with CM, presented periodic leg movements (PLM) index > 5

movements per hour. The PLM index and after surgery was 17.3 ± 29 and 10.6 ± 25 ($p = 0.14$), respectively. In the group of patients whose AHI before the surgery was $IAH > 5$, the PLM index before and after the surgery was 21.1 ± 25 and 3.8 ± 5.8 ($p = 0.02$), respectively.

Conclusion: Surgical decompression of the posterior cranial fossa in CM patients may be helpful in the reduction of adverse respiratory events as well as of PLM during sleep.

Support (optional): AFIP, FAPESP (CEPID 98/14303-3), CNPq

0537

PREVALENCE OF PERIODIC LEG MOVEMENTS DURING THE POSITIVE AIRWAY PRESSURE TITRATION NIGHT IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Prevalence of periodic leg movement (PLM) is estimated to include 5 to 44% of the general population, and there is often a temporal association between leg movements and sleep apneas in patients with Obstructive Sleep Apnea (OSA). Thus, once PLM and OSA might coexist, it becomes important to differentiate whether leg movement is part of the behavior of OSA syndrome or if it is part of PLM disorder. Besides, the treatment of OSA patients with CPAP remains controversial since it could unmask or exacerbate PLM. The aim of the present study was to evaluate the PLM prevalence in OSA patients during the OSA diagnostic night and CPAP titration night.

Methods: Data from polysomnography (PSG) and Sleepiness Epworth Scale (SES) from patients referred to the Sleep Institute/AFIP for OSA diagnosis (PSG1) and CPAP titration (PSG2), in two different nights, were compared. The criteria for PLM scoring were based on the ASDA Task Force (1993), and leg movements associated with abnormal respiratory events were excluded.

Results: Data from 142 patients (29 females), aged 53 ± 10 years, body mass index (BMI) of 31 ± 7 kg/m², and SES score of 12 ± 6 , were evaluated. Thirteen patients (9%) presented PLM index (PLMi) > 5 during PSG1, and 18 (13%) during PSG2. 5 patients with PLMi > 5 during PSG1 remain during PSG2 (3 patients presented decrease and 2 presented increase of the PLMi). Comparing data from patients with PLMi < 5 vs. patients with PLMi > 5, during PSG1 there were no differences among age, BMI, SES score, and PSG data, except for the arousal index (24 ± 16 vs. 37 ± 26 , $p = 0.008$), and during PSG2, all data were similar.

Conclusion: We suggest that, in the OSA population evaluated, the prevalence of PLM was similar to the general population and one night of CPAP treatment unmasked, but did not exacerbate, PLM.

Support (optional): AFIP, FAPESP (CEPID 98/14303-3), CNPq

0538

COMPARISON OF AUTOSCORING VERSUS MANUAL SCORING IN EVALUATION OF SLEEP DISORDERED BREATHING WITH A PORTABLE SLEEP MONITORING DEVICE

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Introduction: Current AASM guidelines recommend data obtained from portable monitoring (PM) devices be manually scored and clinically evaluated by a sleep physician for assessment of sleep disordered breathing (SDB). This study compared automatically and manually scored apnea-hypopnea index (AHI) and oxygen desaturation index (ODI) in evaluation of the presence of SDB in patients following elective surgery.

Methods: During the first postoperative night, 96 patients were monitored and AHI and ODI autoscored with a class 4 PM device (Medcare

Compass®, Somnologica® software, Reykjavik, Iceland). A sleep physician manually scored the raw data using standard AASM criteria.

Results: Autoscoring identified 38/96 patients (39%) with $AHI \geq 5$ and 17/96 (17%) with $AHI \geq 15$; there were 45/96 (46%) with $ODI \geq 5$ and 17/96 (17%) with $ODI \geq 15$. Autoscoring falsely identified an $AHI > 5$ in 4/96 patients (4.1%). Manual scoring identified 51/96 patients (53%) with $AHI \geq 5$, and 18/96 (18%) with $AHI \geq 15$; 42/96 patients (43%) with $ODI \geq 5$ and 19/96 (19%) with $ODI \geq 15$. AHI and ODI by manual and autoscoring were highly correlated ($r = 0.90$, $p < 0.001$, $r = 0.80$, $p < 0.001$, respectively). Sensitivity and specificity of autoscoring for $AHI \geq 5$ were 71 and 96%; for $AHI \geq 15$ were 78 and 96%; for $ODI \geq 5$ were 95 and 91%, for $ODI \geq 15$ were 89 and 100%. There was substantial agreement between manual and autoscoring for $AHI \geq 5$ and ≥ 15 (kappa score 0.65 and 0.75) and almost perfect agreement between manual and autoscoring for $ODI \geq 5$ and ≥ 15 (kappa score 0.85 and 0.93).

Conclusion: Despite overall good correlation with manual scoring, AHI autoscoring was less sensitive and while both AHI and ODI occasionally resulted in false-positive readings, autoscoring is comparable to manual scoring for ODI .

0539

PREDICTING CPAP ADHERENCE BEFORE EXPERIENCE WITH CPAP

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Introduction: Adherence to Continuous Positive Airway Pressure (CPAP) therapy for Obstructive Sleep Apnoea (OSA) is often poor despite the efficacy of the therapy. Biomedical indices explain little of the variance in CPAP use. This study tested a Health Beliefs model of adherence to CPAP.

Methods: 77 consecutive patients newly diagnosed with OSA (61% male, Mean age=55.25, Mean $AHI=38.36$) and had never tried CPAP before completed questionnaires at baseline (prior to CPAP treatment). Questionnaires assessed; outcome expectancy with treatment, self-efficacy, functional outcomes of sleepiness, and perceived risk of negative health outcomes. Physiological data from standard clinical diagnostic sleep study (PSG) was obtained. CPAP adherence was assessed at 3 months post-treatment initiation.

Results: The Health Beliefs Model measures alone explained 21.8% of the variance in CPAP adherence ($p < .01$). The Health Beliefs Model measures plus biomedical indices together explained 31.8% of the variance in CPAP adherence ($p = .01$). The greatest proportion of CPAP adherence was explained by higher outcome expectancies with treatment, greater functional limitations as a result of sleepiness, and lower risk perception.

Conclusion: These results suggest that functional outcomes of sleepiness, and outcome expectancies before CPAP is first tried, uniquely predict adherence. Psychological factors, rather than disease severity and objective physiological indices, are most important in a patients' decision to adherence to CPAP therapy. Efforts should be made to measure and address these factors in patients with obstructive sleep apnoea.

0540

GENDER AND AIRWAY LENGTH IN OBESE ADOLESCENTS

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Introduction: Although airway length has been implicated in the increased male predisposition for obstructive sleep apnea (OSA) in adults, data in obese children and adolescents are lacking. Given the high prevalence of OSA in obese children and adolescents it is important to confirm that findings from adults can be extrapolated to this high risk group. The goal of this study was thus to determine the effect of gender on airway length in obese adolescents.

Methods: All obese adolescents seeking treatment at Cincinnati Children's Sleep center with $AHI < 1$ on overnight polysomnogram were eligible for recruitment. The midline sagittal T2 weighted image obtained on a 1.5 Tesla scanner was used for airway measurements. Airway length was determined by the distance between the hard palate and base of epiglottis. The effect of height on airway length was controlled by using the standardized airway length (airway length/ subject's height). The gender groups were compared using unpaired student's t test.

Results: The mean age of the 16 subjects was 14.8 years \pm 2.1, mean BMI 37.9 kg/m² \pm 7.3, and 62% were African American. Male obese subjects (n=7) did not differ from female obese subjects (n=9) in their age (14.5 years \pm 1.9 vs 14.9 years \pm 2.3, $p = 0.5$) or standardized airway length (0.43 cm \pm 0.06 vs 0.44 cm \pm 0.06, $p = 0.9$) but had a lower BMI (33.6 \pm 4.4 vs 41.3 \pm 7.5, $p = 0.02$) than females. Subgroup analysis of groups that did not statistically differ by BMI also revealed no difference in standardized airway length between male obese subjects (n=6) and female obese subjects (n=7) (0.43 cm \pm 0.06 vs 0.43 cm \pm 0.07, $p = 0.7$).

Conclusion: Our results indicate no effect of gender on airway length in obese adolescents suggesting that airway length may not explain the increased male gender predisposition for OSA in this group.

Support (optional): AASM/Pfizer Scholars grant in Sleep Medicine (Kalra) Cincinnati Children's Research Foundation Trustee grant (Kalra)

0541

PREVALENCE OF CHRONIC KIDNEY DISEASE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive Sleep Apnea (OSA) highly cause cardio-cerebro-vascular events. However, little is known about the comorbidity of the kidney lesion. Recently, in Japan, it has become clear that chronic kidney disease (CKD) is a far more common disease (18.7% of all population of 20 or more years old and about 18 million people) than U.S. frequency (4.3%), and is the important dangerous factor of cardiovascular disease or end stage renal disease.

Methods: We investigated the prevalence of CKD in patients with OSA ($AHI \geq 5$). A cross-sectional study of patients with a definite diagnosis of CKD was performed using new diagnostic criteria for estimated glomerular filtration rate (eGFR) value that were designed for the Japanese population.

Results: There was a significantly increased prevalence of CKD (eGFR < 60 mL/min/1.73 m²) in patients with OSA (n=411, Age 57.5 \pm 14.0, Men 77.4%, BMI 27.8 \pm 2.7, AHI 45.8 \pm 29.1) compared to the general population who participated in annual health check programs in our hospital (n=2,667, Age 50.0 \pm 10.1, Men 64.1%, BMI 22.9 \pm 3.3) (19.5% vs. 9.0%, $p < 0.01$). Furthermore, difference was greater in prevalence of CKD (eGFR < 50 mL/min/1.73 m²) (6.8% vs. 1.5%, $p < 0.01$). There was no difference about prevalence of CKD in OSA patients

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with metabolic syndrome (MetS) and in those without MetS (33.4% vs. 23.2%, $p=0.07$). But, when satisfying four composition factors (waist circumference, hypertensive status, dyslipidemia, and impaired glucose tolerance), prevalence of CKD was higher than those who do not have a composition factor (29.7% vs. 16.7%, $p<0.05$). In the logistic regression analysis which makes CKD the purpose variable, a significant correlation with age was shown but a correlation with BMI was not proved. There was weak correlation with gender (male) and AHI.

Conclusion: Additionally to aging, male, severe sleep-related breathing disorder and all the composition factors of a MetS is related as a reason of the high CKD prevalence in an OSA. As a whole body complication of severe OSAS, more attention should be paid to CKD.

0542

PREDICTORS OF SUCCESSFUL IN-LABORATORY CPAP TITRATION

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Introduction: To ensure the effective CPAP delivery, optimal CPAP titration is essential. We documented the efficacy and the predictors of successful in-lab manual titration to predict the titration failure group.

Methods: We included 108 consecutive patients (108 male; age, 43.7 ± 10.8 years old; BMI, 27.1 ± 3.2 ; AHI, 44.1 ± 24.4) who accepted CPAP therapy without significant central apneas, central apnea index less than 5 on the diagnostic PSG and history of cardiopulmonary and neurological diseases from March 2005 to December 2006. CPAP titration procedure followed a general method (Thomas RJ, 2005). Successful CPAP titration was defined when at certain pressure RDI is less than 5 and total arousal index less than 20 with normalization of oxygen saturation ($>90\%$). With that pressure, patient should be in REM-sleep with supine position during at least 10 min. We analyzed the rate of successful titration and its predictors.

Results: Overall success rate was 73.0% ($N=81$). BMI and ESS did not predict the successful CPAP titration. Characteristics from diagnostic PSG neither predicted such as OSA severity, presence of any degree of central apneas, CAP-dominant OSA, REM-dependency, or positional OSA. Level of prescribed CPAP pressure was not different between titration success or failure group. However, titration failure group was older than success group (47.2 ± 10.8 vs. 42.5 ± 10.6 , $p=0.04$). Presence of significant nasal obstruction was higher in the failure group without statistical significance (4.9% vs. 3.7%, $p=0.07$).

Conclusion: Overall success rate of CPAP titration is not satisfactory. Success was significantly associated with age and marginally with nasal airway obstruction. Titration method should be standardized and improved. Alternatives to in-lab titration might be necessary.

0543

ENDOTHELIAL DYSFUNCTION AND ARTERIAL STIFFNESS IN RELATION WITH THE SEVERITY OF OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Early signs of atherosclerosis, such as endothelial dysfunction and arterial stiffness, have been reported in obstructive sleep apnea syndrome (OSAS). To corroborate previous findings, we investigated flow-mediated dilatation (FMD) and carotid-femoral pulse wave velocity (cfPWV) in patients with OSAS in relation with the severity of respiratory disturbances and hypoxemia.

Methods: This study enrolled 107 male subjects who were referred to sleep laboratory to undergo nocturnal polysomnography (NPSG). After they finished NPSG, FMD was measured on the brachial artery and

cfPWV was measured using a noninvasive automatic device. All the subjects fasted at least 8 hours. Subjects aged older than 60 years, taking antihypertensives, antihyperlipidemic drug, diabetes medication or suffering from inflammatory diseases were excluded.

Results: Based on the apnea hypopnea index (AHI), we classified the subjects into three groups; severe OSAS group with $AHI \geq 30$ ($N=41$), mild to moderate OSAS group with $AHI \geq 5$ and < 30 ($N=40$), and normal control group ($AHI < 5$; $N=26$). There were significant differences in FMD ($p<0.01$) and cfPWV ($p<0.05$) among three groups, although there were no significant differences in age, body mass index (BMI), neck circumference, and waist-to-hip ratio. Stepwise multiple regression showed that lowest O₂ saturation was significant determinant of FMD (beta = 0.23, adjusted $R^2=4.5\%$, $p<0.05$), and age (beta=0.27, $p<0.01$) and percentage of time below 90% O₂ saturation (beta=0.31, $p<0.01$) were significant determinants of cfPWV (adjusted $R^2=15\%$, $p<0.01$). FMD was significantly correlated with cfPWV ($r=-0.24$, $p<0.05$).

Conclusion: FMD and cfPWV were impaired in OSAS, which could be implicated in the pathogenesis of cardiovascular complications of OSAS. Nocturnal hypoxemia rather than AHI might better explain the detrimental changes of FMD and cfPWV in OSAS.

0544

EFFECTS OF AGE ON THE CLINICAL FEATURES OF OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: The prevalence of obstructive sleep apnea syndrome (OSAS) was reported to be higher in elderly population than young or middle-aged population. However, the differences in clinical characteristics of OSAS between these age groups were not fully explained. The aim of this study was to elucidate the characteristics of elderly patients compared to young or middle-aged patients with OSAS.

Methods: We enrolled 757 male subjects who were referred to undergo nocturnal polysomnography (NPSG) during 2003-2007. The patients who were diagnosed as OSAS (apnea hypopnea index; $AHI \geq 5$) were divided into three groups: 20-44 aged ($N=254$, group 1), 45-64 aged ($N=373$, group 2), and 65-86 aged group ($N=130$, group 3). They also completed the Epworth Sleepiness Scale (ESS) and Pittsburgh Sleep Quality Index (PSQI).

Results: There were no differences in AHI, average O₂ desaturation or oxygen desaturation index among three age groups. However, body mass index (BMI) and the proportion of over-weighted patients ($BMI \geq 25$) were lower in the group 3 compared to the other age groups (all $p<0.01$). With severe OSAS patients only, similar results were observed. Patients in the group 3 also showed lower ESS scores, higher PSQI scores, lower sleep efficiency, and increased number of awakenings (all $p<0.01$) than the other aged groups. In addition, high % of apnea among apnea and hypopnea (apnea%; $p<0.05$), increased duration of apnea ($p<0.01$), and increased longest apnea duration ($p<0.01$) were observed in the group 3.

Conclusion: The influence of body weight on the occurrence of OSAS was decreased in elderly patients with OSAS. Because of higher collapsibility of upper airway, elderly patients with OSAS showed higher apnea% and longer duration of apnea compared to young and middle-aged OSAS patients. In the elderly patients with OSAS, subjective and objective sleep qualities were more impaired, but daytime sleepiness was less common than in young or middle-aged patients with OSAS.

0545

INFLAMMATORY CYTOKINES AND INSULIN RESISTANCE IN OBESE PATIENTS WITH OSAS: EFFECTS OF CONTINUOUS POSITIVE AIRWAY PRESSURE

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Introduction: Adiponectin is a protein with anti-inflammatory, anti-atherosclerosis and insulin sensitizing effects. Reduced adiponectin concentrations are risk factor for cardiovascular and metabolic disorder. Conflicting data show controversies in adiponectin levels and insulin resistance in OSAS. CPAP effects in metabolic statuses are not well demonstrated. The aim of this study is to evaluate inflammatory cytokines and insulin resistance in OSAS and determine if CPAP therapy influenced responses.

Methods: Adiponectin, TNF α and insulin resistance by HOMA were collected in 23 controls (GI) and 22 patients with OSAS (GII). Nine patients with severe OSAS were re-evaluated three months after nCPAP.

Results: Age, BMI, abdominal circumference, blood pressure, insulin resistance and IL-6 of GI and GII were similar. The mean value + SD of AHI was 59.1 + 8.3 in GII compared to 3.1 + 0.41 in GI ($p < 0.001$). Adiponectin was lower (10.3 + 1.2 ng/ml) in GII compared to GI (17.6 + 2.3 ng/ml; $p = 0.009$) and TNF α was higher (10.9 + 2.0 pg/ml) in GII compared to GI (6.6 + 0.4 pg/ml; $p = 0.04$). CPAP increased adiponectin level in 6.4 + 3.7 ng/dl ($p = 0.12$); decreased TNF α in 2.3 + 1.2 pg/ml ($p = 0.10$) and HOMA in 1.9 + 1.1 ($p = 0.13$), however not significantly. When we excluded of this analysis 2 patients that with CPAP got 50% decrease of AHI, significant increase in adiponectin ($p = 0.05$) and lower TNF α ($p = 0.09$) were obtained.

Conclusion: OSAS patients have higher inflammation and hypoadiponectinemia independent of BMI. CPAP tended to improve insulin resistance and adiponectin levels.

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0546

RELATION OF OSAS SEVERITY WITH INSULIN RESISTANCE

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Introduction: Studies show relation between Metabolic Syndrome (MS) and OSAS since higher sympathetic activation linked to the respiratory sleep events is associated with insulin resistance, systemic hypertension and dyslipidemia. However, is not clear if the severity of OSAS has impact in the severity of MS. The aim of this study is to evaluate: a) Prevalence of MS in patients screened for OSAS; b) The relation between the OSAS severity with the level of insulin resistance.

Methods: Patients referred from sleep laboratory of Sleep Medicine Division- UNIFESP, were evaluated for MS according to NCEP-ATPIII criteria and OSAS by ASDA criteria.

Results: 68 patients were evaluated with X/SD of age 51.6 + 10.1 years; BMI 30.1 + 5.3 kg/m² and waist circumference 98.3 + 12.3 cm. Patients with AHI > 30 was 39.7% and AHI < 10, 35.3%, with MS prevalence of 55.6% e 20.8%, respectively. We also analyzed patients with BMI < 30 Kg/m² and AHI lower 10 (GI: 55.5%) and higher 30 (GII: 44.5%): MS occurred in 12.5% and 30% of them respectively. The fast plasma glucose was not different between groups, however 2 hs plasma glucose were lower in Group I (112 + 36.8 mg) compared to group II (162.3 + 73.6 mg, $p < 0.05$) as well as 2 hs plasma insulin (54.5 + 34.3 vs 117.4 + 93.2 mg; $p < 0.05$). The regression analyses showed that both BMI and AHI were independent factors for 2h plasma glucose.

Conclusion: The prevalence of Metabolic Syndrome is high in OSAS population. Insulin resistance is related with the severity of OSAS.

Support (optional): AFIP, FAPESP (CEPID 98/14303-3)

0547

EVALUATION OF LONG-TERM CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY IN OBSTRUCTIVE SLEEP APNEA PATIENTS ON EXCESSIVE DAYTIME SLEEPINESS, FATIGUE AND DEPRESSION

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Introduction: Continuous positive airway pressure (CPAP) provides an effective treatment for patients with obstructive sleep apnea syndrome (OSAS). In this study, we assessed the effect of long-term CPAP therapy on excessive daytime sleepiness (EDS), fatigue and depression in OSAS patients.

Methods: A prospective investigation in which we measured EDS, fatigue, depression (all by means of standardized questionnaires) and compliance in patients using CPAP. Epworth Sleepiness scale (ESS), Beck Depression Inventory (BDI) and the multidimensional fatigue inventory (MVI-20) were used.

Results: Of 151 patients, who were identified in the outpatient clinic's database, 116 filled out the questionnaires and 100 also underwent a full-night polysomnography. CPAP was used during median 28 months (range 1 to 10 years). Median apnea/hypopnea index was 38 (range 6-182) and mean CPAP pressure level was 7.3 (SD 1.8) cm H₂O. CPAP was used mean 6.5 (SD 1.4) nights per week for more than 3 nights per week by 78% of patients. CPAP-treatment had a statistically significant favourable effect on subjective headache, dry mouth, snoring and sleepiness. After CPAP treatment, scores on ESS (12.3 before and 6.6 after treatment), MVI-20 (13.9 before and 10.1 after) and BDI (10.3 before and 7.3 after) normalized.

Conclusion: CPAP treatment had a significant effect on EDS, fatigue and depression in OSAS patients frequently using CPAP.

0548

COMPARISON OF OXYGEN DESATURATION INDEX, EPWORTH SLEEPINESS SCALE, BERLIN QUESTIONNAIRE AND MODIFIED BERLIN QUESTIONNAIRE IN POSTOPERATIVE PATIENTS WITH SLEEP DISORDERED BREATHING

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Introduction: Adverse outcomes are more likely in post-operative patients who experience sleep disordered breathing (SDB). Currently there are no standards for identifying patients at risk of SDB in the post-operative setting although tools such as questionnaire, clinical impression, and monitoring oxygen desaturation index (ODI) are being used. This study compared Berlin Questionnaire (BQ), Modified Berlin Questionnaire (MBQ), anesthesiologist's clinical impression, ODI and Epworth Sleepiness Scale (ESS) for identification of SDB in post-operative patients using a portable sleep monitoring (PM) device.

Methods: 116 adult elective surgery patients were clinically assessed pre-operatively by their anesthesiologist, and post-operatively completed the BQ, MBQ and ESS questionnaires. Nasal flow and pulse oximetry were monitored during the first post-operative night using the Medcare Compass® (Reykjavik, Iceland, Class IV portable monitoring device). 100 patients had interpretable data, scored by a sleep physician using standard AASM criteria.

Results: AHI ≥ 5 occurred in 51/100 (51%) patients. Among patients with an elevated AHI, anesthesiologist's pre-operative clinical impression of SDB identified 2/51 patients (3.9%). 34/51 (66.6%) were identified as "low risk" on BQ, 32/51 (62.7%) were rated "low probability"

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on MBQ and 8/51 (16%) had a significant ESS score (≥ 10). An ODI ≥ 5 identified 41/51 patients (80.3%). The best predictive tests were the BQ with a positive predictive value (PPV) of 70.8% and a negative predictive value (NPV) of 55.2%, the MBQ with a PPV of 61.2% and a NPV of 53.6% and the ODI identified with a PPV of 97.6% and NPV 82.7%. The anesthesiologist's pre-operative clinical impression and the ESS performed too poorly to be clinically useful.

Conclusion: Compared to objective measurement of SDB in post-operative patients, anesthesiologist's pre-operative clinical impression was the poorest predictor of SDB. None of the questionnaires performed well. The ODI appears to be the best predictor of SDB among these tests in the post-operative surgical population.

0549

DO INCREASED GENIOGLOSSUS ACTIVITY AND END EXPIRATORY LUNG VOLUME ACT SYNERGISTICALLY TO DILATE THE UPPER AIRWAY?

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Introduction: Both increased genioglossus muscle activity (GG) and increased end-expiratory lung volume (EELV) improve airway patency in humans. However, these effects likely occur through different mechanisms with increased GG primarily causing airway dilation whereas increased EELV likely stiffens the pharyngeal airway walls. The ability of the GG to dilate the airway may be enhanced when the EELV is increased and airway walls stiffened. The aim of this study was to determine whether increased GG and EELV have an additive or synergistic effect on airway patency.

Methods: Patients with CPAP treated obstructive sleep apnea were instrumented with an epiglottic catheter (respiratory drive), intramuscular GG electrodes (GG electromyogram, EMG_{GG}), magnetometers (lung volume) and a nasal mask/pneumotachograph (CPAP delivery, airflow and mask pressure measurement). Subjects slept supine in a head-out plastic chamber in which the extra-thoracic pressure could be manipulated (to raise EELV) in combination with nasal CPAP and a variable deadspace for episodic re-breathing (to elevate PCO₂ and activate EMG_{GG}). The pharyngeal critical closing pressure (P_{CRIT}) was measured in 4 conditions: a) at baseline, b) with ~500cc increased EELV, c) with ~50% increased EMG_{GG} and d) with combined ~500cc increased EELV and ~50% increased EMG_{GG}.

Results: Adequate data have been obtained in 3 patients to date (2 men, aged 52±5yrs, AHI 66±19 events/hr). Actual increases in GG/EELV for conditions b-d were 593cc, 110% and 563cc + 58% respectively. P_{CRIT} was 3.7±1.0 cmH₂O at baseline and was reduced to -0.6±1.1, 1.5±1.3 and -1.0±1.3cmH₂O in conditions b-d respectively.

Conclusion: These preliminary data indicate that increasing EELV by ~600cc reduces P_{CRIT} to a greater degree than doubling EMG_{GG}. Increased GG and EELV appear to act in an additive fashion to reduce P_{CRIT}.

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0550

SHORT TERM CHRONIC INTERMITTENT HYPOXIA LEADS TO CARDIAC DYSFUNCTION AND OXIDATIVE STRESS

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Introduction: Obstructive sleep apnea (OSA) is a major health problem leading to increase incidence of cardiovascular disease including hypertension and myocardial infarction. Chronic intermittent hypoxia (CIH) is an experimental model mimicking many of the clinical features

of OSA including myocardial deterioration and oxidant stress. In most studies CIH has been given for at least 5 weeks. We hypothesize that even short exposure to CIH leads to adverse effects.

Methods: Rats were exposed to either 10 days of CIH (N=10: O₂ nadir 6%, 8 hours/day) or similarly handled normoxic controls (HC: N=9). At the end of exposure echocardiography and catheterization were performed. As an index of oxidant stress, myocardial lipid peroxides (LPO) were measured.

Results: Compared to HC, animals exposed to CIH showed increased mean blood pressure (CIH: 143.5±/54.3; HC: 94.0±/6.8 torr; p=.015), heart rate (CIH: 379±/73; HC: 310±/40 bpm; p=.025), decreased ejection fraction (CIH: 73.7±/4.5; HC 86.9±/3.9%; p<.0001), fraction shortening (CIH: 38.0 ±/3.7; HC: 51.5 ±/5.2%; p<.0001), and larger left ventricular (LV) end-systolic diameter (CIH: 0.43 ±/0.03 cm; HC 0.34 ±/0.05 cm; p<.0001) and LV end-systolic volume (CIH 0.20 ±/0.04 cm³; HC 0.1 ±/0.04 cm³ p<.0001). Myocardial LPO levels were greater in the CIH than HC (CIH: 589.6±/307.8 HC: 322.0 ±/105.4 micron/mg protein; p=0.025). Calculated LV mass was also greater in CIH than HC (CIH: 60.8±/14.2; HC 48.7±/10.2 mg; p<.05).

Conclusion: Even short-term exposure to CIH leads to increased blood pressure and heart rate, associated with myocardial deterioration and oxidant stress.

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0551

CAN COPING STYLES PREDICT CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) ADHERENCE?

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Introduction: Continuous positive airway pressure (CPAP) therapy remains the most effective treatment option for patients with obstructive sleep apnea (OSA). Despite its effectiveness however, many patients do not use the CPAP as prescribed, limiting the beneficial effects of the therapy. Despite numerous studies, consistent predictors of adherence to CPAP have not been identified. Previous studies have evaluated psychological determinants of adherence. One study reported that patients who engage in active coping strategies had higher CPAP adherence. The goal of this study was to evaluate factors which may be associated with enhanced CPAP adherence, including assessing whether a patient's methods of coping with stressful situations could predict adherence to CPAP therapy.

Methods: This was a prospective study during which objective adherence data was obtained from consecutive patients diagnosed with OSA (AHI ≥ 15). Complete objective monitoring data from the CPAP as well as subjective information from a subsequent follow-up visit with the sleep physician was available for 59 of the 148 enrolled patients. All patients were administered the Brief COPE questionnaire at the time of their initial polysomnogram. Other domains evaluated for correlation with adherence included those pertaining to the mask interface, patient comfort and symptom improvement.

Results: No correlations were identified between adherence rates and any of the coping domains measured on the Brief COPE. Statistically significant correlations were identified with 2 other domains: Adherence was higher with patients using standard nasal masks compared with nasal pillows or full face masks and was negatively correlated with CPAP pressure intolerance. Trends toward improved adherence were identified in patients who reported nocturnal or daytime symptom improvement, although the results did not reach statistical significance. Conversely, there were no differences in adherence in patients reporting nasal congestion or oral/nasal dryness.

Conclusion: This study did not confirm a previous report that CPAP adherence can be predicted by a patient's coping style. Although overt

discomfort with the CPAP will limit adherence, it remains difficult to prospectively identify the factors which predict adherence.

0552

COMPLIANCE TO THE CONTINUOUS POSITIVE AIRWAY PRESSURE AND ORAL APPLIANCE IN THE SAME SAMPLE OF OBSTRUCTIVE SLEEP APNEA SYNDROME PATIENTS

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Introduction: Objective compliance to the Continuous Positive Airway Pressure (CPAP) is relatively low (40-46%) when compared to subjective compliance (60-90%). An alternative treatment that yields positive results is the Oral Appliance (OA). Studies examining different patients' groups who resort to the OA and CPAP reveal higher compliance to the OA, although the CPAP is more efficient. The aim of this study was to compare compliance to the OA and CPAP and establish the factors that determine adherence in the same sample of moderate to severe Obstructive Sleep Apnea Syndrome (OSAS) patients.

Methods: Patients with moderate to severe OSAS, aged 21 to 65 years, BMI<35Kg/m², in appropriate dental health for the use of the OA, participated in the study. In a randomized and cross-over manner, the patients used the CPAP for one month and the OA for an equal period. By the end of each treatment, the Epworth Sleepiness Scale (ESS), polysomnography, the Sleep and OA Diary and the built-in compliance meter of CPAP use was analyzed.

Results: The CPAP was more efficient in reducing the AHI than the OA was (basal:40.3; CPAP:9.8; OA:24.3; p<0.002). There occurred an increase in the percentage of use of the OA compared to the CPAP (86±17%×67±26%, p=0.02). There was also a closer correlation (r=0.62) between age and compliance to the OA but such correlation was lower with the CPAP (r=0.21). There was lower correlation when we analyzed ESS with compliance to OA (r=0.39) and a higher correlation to the compliance of the CPAP (r=0.56).

Conclusion: Although the CPAP is more efficacious in reducing AHI in patients with moderate and severe cases of OSA, the OA is more effective in such patients due to better acceptance. Excessive somnolence was found to be a determining factor in CPAP compliance while age determined compliance to the OA.

Support (optional): AFIP, FAPESP (CEPID 98/14303-3), CNPq

0553

EFFECTS OF EXERCISE TRAINING ASSOCIATED WITH CPAP IN MODERATE TO SEVERE OBSTRUCTIVE SLEEP APNEA PATIENTS

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Introduction: The aim of this study was to evaluate the effects of a 2-month chronic exercise training program associated with CPAP on the subjective and objective sleep measurements, quality of life and mood state in moderate to severe OSA patients.

Methods: Thirty-two male patients (25-65 years, sedentary, BMI<35kg/m², AHI>15/h, Epworth Sleepiness Scale >9) were randomized into two treatment groups: CPAP (n=19) and CPAP+exercise (n=13). All patients in both groups completed one month of sleep hygiene, two months of treatment (CPAP or CPAP+exercise) and one week of washout (no treatment). Subjective (sleep disturbances questionnaire, Epworth Sleepiness Scale, sleep diaries) and objective (polysomnography) sleep parameters, quality of life (SF-36), mood state (POMS) and anthropometric measurements (neck circumference and body composition) were evaluated. CPAP+exercise group also underwent cardiopulmonary exercise test before and after treatment.

Results: Both treatments were effective in improving subjective sleepiness. No significant differences were found in most of the sleep parameters studied. CPAP+exercise group showed lower values of tension and fatigue on POMS after treatment compared to baseline. Depression was lower after treatment only in the CPAP group. CPAP+exercise group showed higher values of physical functioning, general health perception and vitality in SF36 after treatment. Vitality also improved for CPAP group after treatment. Mental health improved only after washout in the CPAP group. In regards to neck circumference and percentage of body fat, no significant differences were found in neither groups. In the CPAP+exercise group, no differences were found after treatment in oxygen consumption and heart rate but the speed reached on the treadmill was higher after treatment at maximum exercise and at the anaerobic threshold.

Conclusion: 2 months of chronic exercise training associated with CPAP for moderate to severe OSAS patients has positive impact on subjective daytime sleepiness, quality of life (physical functioning and general health perception) and mood state (tension and fatigue).

Support (optional): AFIP, FAPESP (CEPID # 98/14303-3)

0554

A PRELIMINARY EVALUATION OF SLEEP, COGNITION, AND RESPIRATION UNDER FOUR WEEKS OF INTERMITTENT NOCTURNAL HYPOXIA IN ADULT HUMANS

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Introduction: A pilot study was conducted to examine the effects of intermittent nocturnal hypoxia on sleep, respiration and cognition in healthy adult humans via prospective experimental physiological assessment in a General Clinical Research Center.

Methods: Eight healthy, non-smoking, subjects (four male, four female), mean age of 27 ± 1.5 years, and BMI 23 +/- 0.9 Kg/m² were exposed to nine hours of intermittent hypoxia between the hours of 10 P.M. and 7 A.M. for 28 consecutive nights. Two nights of graded acclimatization were followed by exposure to a simulated altitude of 13,000 feet (FIO₂ 0.13). Intermittent hypoxia was achieved by administering a brief (approximately five seconds) bolus of nasal oxygen alternating with nitrogen, delivered via nasal prongs, every three minutes.

Results: Overall sleep quality showed worsening trends but no statistically significant change following exposure. There was no difference after hypoxia in sleepiness, encoding, attention or working memory. Hyperoxic central apneas and post-hyperoxic respiratory instability were noted as special features of respiratory dyscontrol induced by intermittent nocturnal hypoxia.

Conclusion: In this model, exposure to nocturnal intermittent hypoxia for 4-weeks caused no significant deficits in subjective or objective alertness, vigilance, or working memory.

0555

SUBJECTIVE EFFECTS OF SELF-GUIDED IMAGERY ON PAP THERAPY ADAPTATION

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Introduction: Adapting to PAP therapy is difficult for many sleep-disordered breathing (SDB) patients. We hypothesized that self-guided imagery could be taught to patients in the sleep lab environment prior to a PSG titration to help them acclimate to the mask and pressurized air.

Methods: On the night of their titration PSG at Maimonides Sleep Arts & Sciences, SDB patients were provided a handout explaining mental

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imagery concepts and asked to rate their ability to see images in their mind's eye. Sleep technicians then discussed with patients how to use self-guided imagery to relax while wearing the mask and adapt to pressurized air. Specifically, patients learn that imagery distracts the PAP therapy user from attempting to over control their breathing, and imagery diminishes anxiety caused by exhaling against pressurized air. In the morning, patients report on the use of imagery and rate it as "helpful, no impact, or a hindrance."

Results: A total of 77 patients, (57% female), with a Mean (SD) age = 50.82 (12.20) and Mean (SD) BMI = 30.17 (7.01) underwent PSG titrations and the protocol for self-guided imagery. Of these 77, 72 (94%) reported using imagery during the titration and rated it as follows: 45 (63%) helpful; 26 (36%) no impact; and 1 (1%) a hindrance in facilitating adaptation to PAP therapy. Sleep technicians observed that among those in the "helpful" category, imagery appeared to decrease anxiety about the initiation of PAP therapy.

Conclusion: In this small pilot study, an overwhelming majority of patients used self-guided imagery on the night of their titrations following instructions from sleep technicians. Most users reported imagery as "helpful" in PAP therapy adaptation. Self-guided imagery may be a hindrance in rare cases. Randomized control studies must assess self-guided imagery on PAP therapy adaptation over a longer follow-up period, using more precise outcomes.

Support (optional): Maimonides Sleep Arts & Sciences, and the Sleep and Human Health Institute

0556

DEMOGRAPHIC PREDICTORS OF CPAP ADHERENCE AMONG VETERANS

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Introduction: Previous studies have indicated that only 50% of Veterans prescribed CPAP are adherent treatment. As behavioral interventions aimed at increasing adherence are being developed, knowledge of demographic differences in adherence may better help refine and target these interventions.

Methods: Fourteen-hundred-and-eighty-six patients who were prescribed and tried CPAP between April 2003 and April 2007 were included. Adherence information was captured on a data card by a CPAP micro-recording device. Patients were asked to return cards by mail at one month, one year and two years. Adherence was assessed through the first two weeks and during 31 day intervals corresponding to month 5, month 10, and month 15. Adherence was defined as percentage of days that the device was used for four or more hours. We assessed both response (return of a used card) and the average adherence by ANOVA. Potential predictors included age, gender, race, Hispanic-ethnicity, marital status, Veteran means (requirement of co-pay), and BMI.

Results: Average adherence at week 2, and at months 5, 10 and 15 were 56%, 60%, 64% and 65%, respectively. The most striking finding was that Blacks were significantly less likely to use CPAP than Whites at all time points (eg, average compliance = 44% versus 67% at 10 months, $p < 0.0001$). Blacks were also significantly less likely to use CPAP than Asians ($p < 0.05$), despite the small sample size for Asians ($N=44$). These findings remained highly significant following multivariate adjustment. The only other finding that remained significant after multivariate adjustment was that women were slightly less adherent than men (eg 61% versus 54% at month 5).

Conclusion: Black Veterans are significantly less likely to adhere to CPAP than White or Asian Veterans. Given the importance of CPAP adherence, research into physical characteristics (eg anatomical versus

obese etiology) or cultural differences may be warranted to explain the disparity.

0557

THE ROLE OF TONSILLECTOMY AND ADENOIDECTOMY AS TREATMENT OF OBSTRUCTIVE SLEEP APNEA IN CHILDREN

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Introduction: Tonsillar and adenoidal hypertrophy is one of the risk factors for the development of Obstructive Sleep Apnea (OSA) in children. We review the success rate of tonsillectomy and adenoidectomy (T & A) as a treatment of choice in these patients.

Methods: We retrospectively reviewed the charts of 18 pediatric patients with Tonsillar Hypertrophy and OSA from 2006-2007, (14 males, 4 females, age range 3-10 yrs). All patients underwent overnight Standard Polysomnography (PSG) before and after undergoing tonsillectomy and adenoidectomy.

Results: The most common manifestation was snoring (100%), followed by excessive daytime sleepiness (61%), witnessed apneas (16%), enuresis (16%), ADHD (11%), hyperactivity and poor school performance (15%). Most patients were ideal body weight, with Median BMI in the 80th percentile. Their tonsillar hypertrophy ranged from moderate to severe. (two to four plus tonsils). All patients underwent overnight Standard Polysomnography (PSG) before and after the T & A. Before the procedure, 6 patients had Severe OSA (33%), 2 patients had Moderate OSA (11%) and 10 patients had Mild OSA (55%), with RDI ranging from 4.6-42.1 events per hour. All patients underwent tonsillectomy and adenoidectomy. Post procedure, only 1 patient with Moderate OSA (RDI 5.3events/hr) continued to demonstrate OSA and it was still Moderate (RDI 9.8 events /hr). Our literature review indicated that T&A may not cure all OSA cases. Our patient, however, also had excess weight gain as a confounding post-operative risk factor for OSA as her BMI went from 18 to 28. The remainder of the 17 patients (94%), including the 6 patients with Severe OSA (RDI 10.7-42.1 events /hr) did not have any evidence of OSA in their post procedure PSG (RDI < 1.2). Using the Fisher Exact Test, the p Value was <0.0001.

Conclusion: Tonsillectomy and adenoidectomy is a highly successful treatment for children with OSA and tonsillar hypertrophy. Pediatric patients with tonsillar hypertrophy should be referred to otorhinolaryngologists for tonsillectomy and adenoidectomy as a first line of treatment for Obstructive Sleep Apnea.

0558

INFLUENCE OF CHANGE IN BODY MASS INDEX (BMI) TO OPTIMAL PRESSURE OF CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) TREATMENT

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Introduction: Obesity has been recognized as one of the most common risk factors for obstructive sleep apnea (OSA). Weather BMI change influences optimal pressure of CPAP after initial titration is unclear.

Methods: We performed retrospective review of medical charts of all patients diagnosed as moderate or severe OSA who underwent CPAP titration in Sleep Disorders Center, Toyohashi Mates Clinic, Toyohashi, Japan from December, 2005 to November, 2007. Follow-up titration was offered in 3 months and every 12 months. Optimal pressure was determined by the 95th centile pressure from autotitration. Those who underwent titration at least twice were involved and BMI was recorded

with every titration. A change in BMI and optimal pressure was analyzed.

Results: We identified total of 215 patients (177 men and 38 women). Average age, BMI, average follow-up period, average initial apnea hypopnea index (AHI) were 49.7 years (ranging 12 to 77), 27.5 kg/m² (ranging from 17.9 to 48.7), 243 days (ranging from 28 to 654) and 54.3 (ranging from 20 to 117.5) respectively. Average change in BMI was 0.08 (ranging from -9.7 to 4.9) and average optimal pressure change was 0.35 (ranging from -7.8 to 6.8). For those patients with initial BMI more than or equal to 30, there is positive correlation with statistical significance (correlation coefficient and p-value was 0.39 and 0.0079). No statistical significant correlation was found for the patient with BMI between 25 and 30 or less than 25 (correlation coefficient was -0.0026, 0.03 and p-value was 0.8, 0.76).

Conclusion: BMI change had correlation with CPAP optimal pressure in the patients with BMI of more than or equal to 30. This result may support more aggressive weight reduction program for these patients. On the other hand, for the patients with BMI of less than 30, body weight reduction may not help.

0559

WHICH FACTOR INFLUENCES THE IMPROVEMENT OF EXCESSIVE DAYTIME SLEEPINESS (EDS) IN OBSTRUCTIVE SLEEP APNEA (OSA) WITH CONTINUOUS AIRWAY PRESSURE (CPAP)?

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Introduction: Excessive daytime sleepiness (EDS) is one of the most common and serious symptoms of OSA. Which factor influences the improvement of EDS with CPAP treatment is still unclear.

Methods: We performed retrospective review of medical charts of all patients diagnosed as moderate or severe OSA who received CPAP treatment in Sleep Disorders Center, Toyohashi Mates clinic, Toyohashi, Japan from January, 2006 to November, 2007. Those patients who were evaluated for CPAP treatment and seen at least once in our clinic after initial titration were involved. Epworth sleepiness scale (ESS) was recorded in every clinic visit. Correlation of improvement of ESS and age, body mass index and pretreatment apnea hypopnea index (AHI) were analyzed.

Results: We identified total of 169 patients (139 men and 30 women). Average age, BMI, average follow-up period and average initial apnea hypopnea index (AHI) were 49.9 years (ranging 15 to 76), 27.4 kg/m² (ranging from 17.9 to 48.7), 207 days (ranging from 31 to 546) and 55.1 (ranging from 20 to 126.9) respectively. Average improvement in ESS was 4.7 (ranging from -7 to 18, positive number=improvement). Correlation coefficient of improvement of ESS and age, BMI and AHI were -0.32 (p-value=0.000028), 0.21 (p-value=0.005) and 0.19 (p-value=0.01).

Conclusion: Improvement of ESS had negative correlation with age with statistical significance. Weak positive correlation with BMI and no correlation with AHI were found. With this study, it seems younger patients are expected to have more improvement of EDS than older patients.

0560

POSTURAL CHANGE IN PULMONARY FUNCTION TEST AS A PREDICTOR OF SLEEP DISORDERED BREATHING IN OBESE CHILDREN

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Introduction: The current epidemic of childhood obesity has increased the risk of sleep disordered breathing (SDB). Optimal timing for testing

of children with suspected SDB has not been adequately defined. Since it is known that sleep position may have an impact on the presence and severity of SDB, we hypothesized that postural change in pulmonary function test (PFT) may help to identify obese children at risk of SDB.

Methods: A cross-sectional study of children referred to our pediatric sleep laboratory from 2000-2004 was undertaken to correlate PSG results with upright vs supine PFTs. Children were included if they underwent overnight polysomnography as well as upright and supine PFTs. Children with neuromuscular weakness or skeletal deformities were excluded. Children were considered obese if body mass index was >95% for age and gender. The PSG was considered abnormal if it identified OSA, UARS, or hypoventilation.

Results: Complete data were available for 37 children (23 males) with a mean age of 12.7 yrs + 3.6 yrs. Approximately half of the children were obese. The average Δ FEV1 upright vs. supine was -10.2 + 6.8 % in the obese children vs -7.6 + 4.6 % in the nonobese children. Twenty-two children (59%) had an abnormal PSG. The majority of children with an abnormal PSG were obese. Subgroup analysis of the 18 obese children revealed 16 with an abnormal PSG. In retrospect, obese children with an abnormal PSG, had a larger Δ FEV1 from upright to supine (10.8 % vs. 5.0 %).

Conclusion: There is a sense that Δ FEV1 upright vs. supine may help identify obese children at greater risk for SDB. Further prospective and well-powered studies are needed.

0561

THE RELATIONSHIP BETWEEN CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND OBSTRUCTIVE SLEEP APNEA

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Introduction: The relationship between Chronic Obstructive Pulmonary Disease (COPD) and Obstructive Sleep Apnea (OSA) has yet to be well defined. The objective of our study is to examine a possible correlation between COPD and OSA.

Methods: We performed a retrospective chart review of all patients who underwent both pulmonary function testing (PFT) and polysomnography (PSG) at a tertiary medical center during a seven year time period (2000-2007). Data collected included patient demographics, smoking history, body mass index (BMI), PFT and PSG results.

Results: Data from 457 patients in this ongoing study were analyzed for the purpose of this abstract. 167 (36.5%) had COPD, 279 (61.1%) had OSA and 101 patients (60.5%) had both disorders. We found no significant correlation between COPD and OSA (P=0.92). There was no statistically significant correlation between Forced Expiratory Volume in One Second (FEV1) and apnea Hypopnea index (r=-0.068). Independent analysis of COPD patients revealed that compared to patients without concomitant OSA, patients with overlap syndrome demonstrated a lower percentage of total lung capacity (TLC) (91.36 ± 22.17 vs. 101.18±16.45; P=0.009). They also had a higher FEV1/FVC ratio (61.03±10.7 vs. 54.61 ±12.3; p=0.001) and a predominance of males (58.4%; p=0.018). All other studied variables were not statistically significant between the 2 groups including snoring, day time sleepiness, age, BMI and smoking history. It was noted that despite a significantly lower nadir during sleep in patients with overlap syndrome (77.93± 10.8 vs. 85.18±6.3; p<0.00001), resting oxygen saturation did not differ.

Conclusion: Although COPD and OSA commonly occur concomitantly we did not find any correlation between the severity of COPD and OSA. We found that COPD patients with OSA had a lower TLC and a higher FEV1/FVC ratio. This indicates that those values may bear clinical importance in predicting the presence of OSA.

0562

TRIDIMENSIONAL ASSESSMENT REPRODUTIBILITY OF PHARYNGEAL AIRWAYS IN CHILDREN

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Introduction: Three-dimensional instruments as cone beam computerized tomography (CBCT), with high resolution and low radiation dose, have been used to study craniofacial structures. Our objective was to compare the inter-observer data from three-dimensional models of airway assessment.

Methods: In this cross-sectional study, CBCT images from CenPRA (Centro de Pesquisa Renato Archer -Brazil) database of ten children were used with specific protocol to get the images: width and space among slices not exceeding 1mm and gantry with inclination of zero degrees. Area of PAS (pharyngeal transversal section of B-Go line extended to airway) was used as reference. Data from two areas: SPAS (smaller pharyngeal transversal section above PAS) and IPAS (smaller pharyngeal transversal section below PAS), obtained by two independent searchers, were compared. The two softwares used were: InVesalius - a free software developed by CemPRA- (to generate stl. files) and Magics 9.51 - from Materialize (to manipulate stl. files). After getting the images, each searcher moved it through the cursor and chose the smaller area. T-test for dependent sample was used to compare intra-observer measure, the intraclass correlation coefficient (ICC) was used to assess agreement between observer, and 95% confidence interval for difference between measure was calculated for evaluating the precision of differences. The significance level was 0.05.

Results: The mean difference on SPAS1-SPAS2 was 5.7±16.9 (95%CI 11.6 - 30.8) and on IPAS1-IPAS2 was 12.2 ± 17.7 (95%CI 17.0 - 45.3). The ICC associated with the SPAS measure was 0.85 (95%CI 0.50 - 0.96) and associate with the IPAS was 0.96 (95%CI 0.86 - 0.99). No significant difference was found in SPAS (P=0,314) or IPAS (P=0,154) measurements between observers.

Conclusion: This study suggests good (and significant) agreement between observers in SPAS or IPAS measure.

0563

ASSOCIATION BETWEEN OBSTRUCTIVE SLEEP APNEA AND HYPERTENSION

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Introduction: Obstructive sleep apnea (OSA) has been known as an independent risk factor for systemic hypertension. We defined the prevalence of hypertension in OSA and compared with general population data. To investigate causal relationship between OSA and hypertension, we documented a correlation between OSA severity and hypertension prevalence.

Methods: Seven hundred eighteen OSA patients (male, 611) diagnosed with polysomnography were included. Hypertension was defined as systolic blood pressure over 140mmHg or diastolic blood pressure over 90mmHg, or the use of antihypertensive medications. We compared the prevalence with the Third Korea National Health and Nutritional Examination Survey (KNHANES III, 2005) data. Correlation between the OSA severity and the prevalence was analyzed. Other vascular risk factors such as age, sex, body weight, smoking and alcohol-drinking were adjusted.

Results: Prevalence of hypertension was higher in OSA group (39.0%) than general population (13.0% from KHANES III). Univariate analysis showed that age (p<0.01), body mass index (BMI) (p<0.01), apnea-hypopnea index (AHI) (p<0.01), and degree of oxygen desaturation (p<0.01) were significantly associated with hypertension. When adjusted

with other risk factors, age, BMI, and AHI was significantly associated with hypertension (p<0.01). For one increase in AHI, prevalence of hypertension was increased by 1.3% (OR=1.013; 95% CI, 1.005-1.020).

Conclusion: Hypertension was much more prevalent in OSA group. Severity of OSA was independently associated with prevalence of hypertension.

0564

PREDICTABILITY OF CPAP COMPLIANCE USING A DETAILED FOLLOW-UP PROGRAM

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Introduction: As health related consequences related to sleep apnea are better understood and stricter treatment usage guidelines are outlined by managed care, the ability to identify predictors of CPAP compliance therapy gains significance. Previous data suggest that a thorough follow-up program can yield improved therapy compliance, although maintenance of such a program can require considerable resources. This study utilized a structured follow-up assessment with downloaded compliance to better predict outcomes.

Methods: Patients who were diagnosed with sleep apnea and subsequently treated on nasal CPAP at a Midwest metropolitan sleep center were followed-up by phone at 3 weeks and 8 weeks to assess CPAP compliance using a structured data driven scale. The scale includes questions regarding subjective interpretation of sleep quality, treatment benefit, mask or pressure problems, and various nasal symptoms rated on either a 4-point or 10-point scale. Download of the CPAP machine compliance data for each interval was used for comparison. In addition, variables from the baseline and CPAP titration polysomnography, as well as subjective estimates of sleep quality and daytime functioning were also used to determine predictability.

Results: Significant correlations (p<.05) were found between 3-week compliance and subjective interpretation of improvement in sleep quality, hours/night use, feeling better, and an inverse relationship with Stage 3% from the baseline polysomnogram. Correlations at 8-weeks include improvement in sleep quality and feeling better at 3-weeks. Path analysis regression reveals that baseline Stage 3% fully mediates the relationship between 3 week compliance and reporting one feels better, accounting for 31% of the variance. Linear regression demonstrates that improvement in symptoms at 3 weeks significantly predicts compliance at 8 weeks and accounts for 30% of the variance.

Conclusion: Simple structured follow-up assessment, especially at 3 weeks, can provide valuable predictable information into compliance with CPAP therapy, and be employed with minimal resources.

0565

THE ROLE OF THE PATIENT HEALTH QUESTIONNAIRE-9 IN OUTCOME MEASURES OF OBSTRUCTIVE SLEEP APNEA AFTER TREATMENT WITH CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)

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Introduction: Depressive symptoms are common in patients with Obstructive Sleep Apnea (OSA). Studies suggest depression scales improve after treatment of OSA. The Patient Health Questionnaire-9 (PHQ-9) is a validated tool to screen and monitor patients with depression. However, its role in depressive symptoms associated with sleep disorders has not been fully evaluated. This study examines the change in PHQ-9 scores before and after treatment of OSA with CPAP and the utility of the PHQ-9 as an outcome measure in OSA.

Methods: Retrospective chart review between July and September 2007 of 41 patients diagnosed with OSA by polysomnogram and treated with

CPAP. Initial and follow-up visits were reviewed for completed pre- and post-treatment questionnaires and CPAP compliance. Patients were divided by OSA severity using the Apnea-Hypopnea Index (AHI); mild (AHI=5-14), moderate (AHI=15-29), severe (AHI≥30), and by questionnaire scores. Normal Epworth Sleepiness Scale (ESS) scores were <10. PHQ<10 (normal/mild depression) was compared with PHQ≥10 (moderate/severe depression).

Results: Group characteristics: 65% male; average age 53.7 (+/-10.8); average Body Mass Index 35.5 +/- 11.5. OSA severity: 25% mild, 24% moderate, and 51% severe. 26% were previously diagnosed with depression. In patients with normal and abnormal ESS scores, the change in PHQ-9 scores after CPAP was -2.8[-0.96 to -4.69, p=0.006] and -3.4 [-1.9 to -4.8, p<0.001] respectively. In patients with normal and abnormal initial PHQ-9 scores, the change in PHQ-9 scores was -2.1[-1.04 to -3.1, p<0.001] and -1.2 [-3.48 to -0.72, p<0.001] respectively, with an overall change by -3.1 [-2.01 to -4.3, p<0.0001]. Change in PHQ-9 scores in mild, moderate and severe OSA were -4.8 [-2.48 to -7.12], -1.9 [-0.53 to -3.24], and -2.8 [-1.7 to -4.61] respectively, all having p<0.01.

Conclusion: Depressive symptoms as measured by the PHQ-9 improved in patients treated with CPAP, independent of sleepiness and apnea severity. The PHQ-9 may be a valuable tool in evaluating depressive symptoms associated with untreated OSA and to measure treatment effect after CPAP therapy.

0566

EFFECT OF INCREASED AIRWAY LENGTH ON AIRWAY COLLAPSIBILITY: COMPUTATIONAL FLUID DYNAMICS ANALYSIS

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Introduction: Increased airway collapsibility has been implicated in the pathogenesis of Obstructive Sleep Apnea (OSA). The objective of this study is to analyze the effect of increased pharyngeal airway length on airway collapsibility by performing three-dimensional Computational Fluid Dynamics (CFD) analysis of the airway.

Methods: Three obese subjects with OSA underwent airway MR imaging. Traverse MR sequences were acquired to cover the pharyngeal airway from the nasopharynx to the base of the epiglottis. A 3D computational airway model was reconstructed from these MRI data. The baseline model was then modified by adding 5mm slice(s) in the retro palatal or retro glossal region to increase airway length. 3D steady Reynolds Averaged Navier Stokes (RANS) flow simulations were performed using commercial FLUENT software. The flow pattern inside the airway was computed for an inlet flow rate of 10 liters per minute for all the virtual cases assuming rigid boundary conditions. The results were analyzed to determine any change in velocity, static pressure and wall shear stress distributions.

Results: Under similar flow rate of 10 liters per minute, an increase in the length of airway up to 1cm in the retro palatal or the retro glossal region did not result in any change in the velocity, static pressure or the wall shear stress distributions.

Conclusion: Our results indicate that increase in airway length in either the retopalatal or retroglossal regions by itself does not increase the airway predisposition to collapse. These findings need to be replicated with fluid structure interaction included in the computational simulations.

0567

TITRATION OF CONTINUOUS POSITIVE AIRWAY PRESSURE BY PROPOFOL-INDUCED ANESTHESIA FOR SLEEP-DISORDERED BREATHING IN MULTIPLE SYSTEM ATROPHY

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Introduction: Some researchers have reported the usefulness of continuous positive airway pressure (CPAP) and/or non-invasive positive pressure ventilation in the management of sleep-disordered breathing (SDB) with or without nocturnal laryngeal stridor associated with vocal cord dysfunction in multiple system atrophy (MSA). We examined how CPAP affected the upper airway, especially the larynx, in MSA patients.

Methods: 6 probable MSA patients (M/F 3/3, aged 56.0 ± 9.8 yrs, body mass index 26.5 ± 6.9 kg/m², MSA-C/MSA-P 6/0, disease duration 4.9 ± 2.5 yrs, apnea-hypopnea index (AHI) 58.3 ± 16.9 /h; mean ± S.D.) entered the study. Laryngoscopies were done during sleep induced by propofol (PL) in order to visualize obstructive/stenotic portions of the upper airway and determine the optimal CPAP pressure to keep the vocal cords open. Nocturnal polysomnographies (PSG) were performed in all patients on a separate night. Three patients also underwent a second PSG to determine the effect of CPAP on SDB.

Results: Inspiratory pharyngeal obstruction and/or stenosis was observed in 5 patients and paradoxical vocal cord movement was observed in 4 patients during PL. In the latter patients, mean CPAP of 8.4 ± 1.8 (range 7 - 11) cmH₂O was needed to prevent paradoxical vocal cord movement during PL. Mean AHI decreased from 69.7 ± 7.9 /h(baseline) to 22.9 ± 17.7 /h(CPAP) in 3 patients on the PSG night. The 2 patients had residual AHI greater than 20/h and did not tolerate higher CPAP.

Conclusion: Even though sufficient CPAP will prevent paradoxical vocal cord movement, it is not necessarily effective in improving SDB in MSA patients. If vocal cord dysfunction is associated with sudden death in MSA, the high CPAP pressure required to normalize AHI might not be well tolerated and therefore lead to poor compliance.

0568

INTERMITTENT HYPOXIA VERSUS NORMOXIA IN OBSTRUCTIVE SLEEP APNEA AS A RISK FACTOR FOR STROKE

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Introduction: Obstructive sleep apnea syndrome (OSAS) characterised by the number of apnea/hypopnea events/h (AHI) is a heterogenous condition due to different oxygen levels. Three main subgroups are of interest. 1. cases with physiological normoxia - oxygen level higher than 90% 2. cases with sustained hypoxia (SH) - oxygen level lower than 90% during both apnea and interpena 3. cases with intermittent hypoxia and reoxygenation (IHR) - oxygen level lower than 90% during apnea but higher than 90% during interpnea In the present prospective longitudinal study we investigated the effect of normoxia or IHR on stroke occurrence.

Methods: Men /age 30-50 years/ without risk factors of cardio-embolism or evidence of large vessel disease and with positive history of hypertension - underwent polysomnography evaluation at our sleep clinic. Based on calculated apnea-hypopnea index, in severe cases (AHI higher than 30/h) CPAP treatment was offered. Patients not accepting CPAP therapy were followed up once pro year. Endpoints were either 3 year follow up ending with a control MRI, or recurrent symptomatic cerebrovascular events.

Category H—Sleep Disorders – Breathing

Results: 104 patients with normoxia and 188 with intermittent hypoxia/reoxygenation were included. Logistic regression analysis was carried out to confirm subgroup homogeneity regarding BMI, age, apnea severity, and risk factors (diabetes, elevated serum cholesterol and triglyceride level, drinking and smoking habit). Patients with IHR had a higher incidence of MRI progression (appearance of one or more new vascular lesions) or stroke recurrence (34/104 person) than did patients with normoxia (9/188). The Pearson's chi square test showed that intermittent hypoxemia significantly increased the risk of MRI progression (OR:2,55) compared with physiological normoxemia (OR:0,36).

Conclusion: OSAS characterized by intermittent hypoxia/reoxygenation is a more potent independent risk factor for cerebrovascular disease than OSAS cases with normoxia.

0569

SHORT-TERM COMPLIANCE WITH AUTO VS. BI-LEVEL BIPAP

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Introduction: Bi-level CPAP (Respironics™ BIPAP with bi-flex) is an efficient treatment modality for the management of obstructive sleep apnea/hypopnea syndrome. BIPAP is recommended whenever CPAP is not tolerated or unfeasible. Automated BIPAP devices afford treatment with the lowest possible airway pressure, in an optimized fashion. Bi-level and automated BIPAP were compared by monitoring patient compliance, therapeutic AHI, and airway pressures in patients with established, severe OSAHS, during a tryout treatment for 2 months.

Methods: BIPAP settings were adjusted manually (therapeutic presets: IPAP: 16±2, EPAP: 9,6±3,3, AHI: 4+-2,5, mean O2 saturation: 91+-2,1) in 50 patients with severe OSAHS (AHI: 57,3+-9,5, mean oxygen-saturation: 82,8+-9%, BMI: 48±11,5). Subjects were randomly assigned to treatment with the BIPAP M auto or the BIPAP bi-level device, manufactured by Respironics. After two months, mean duration of daily use (expressed in hours), therapeutic AHI, pressure correction rate (in patients using manual BIPAP), mean airway pressure (with auto BIPAP) and pressure values with device usage below 90 per cent were determined from Encore data.

Results: Mean duration of daily use was 5,8±1,8 hours with bi-level and 6,5±1,2 hours with auto BIPAP; whereas therapeutic AHI was 4,8±1,74 vs. 4,0±1,5 and mean O2 saturation was 90,1±2,1 vs. 90,9±2,2, respectively. Pressure correction (warranted by AHI >5) was necessary in 6 patients using manual BIPAP. The following (mean) values were recorded in subjects using auto BIPAP: IPAP: 13±2,6, EPAP: 7,5±2,2 and pressure values with device usage below 90 per cent: IPAP: 15,8±2, EPAP: 10,3±1,77

Conclusion: During the brief period of tryout treatment, mean therapeutic pressure was lower and the duration of daily use (in hours) was significantly longer with auto BIPAP. No substantial differences were ascertained between the two BIPAP modalities as regards residual AHI and mean O2 saturation.

0570

NEUROCOGNITIVE PERFORMANCE IN SERIOUS OSAS PATIENTS

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Introduction: Patients with obstructive sleep apnea syndrome (OSAS) show cognitive deficits, vigilance alteration and attentional decline. The aim of this study was to evaluate the neurocognitive performance in serious OSAS patients.

Methods: Our sample consisted of 115 healthy volunteers (83 males and 32 females; mean age 40,7 SD 10,1 years) and 31 serious OSAS patients (29 males and 2 females; mean age 51,7 SD 10,0 years). In patient AHI was 47,7±20,6/hour, min SaO2: 67±18%. We compared

patients with control subjects for performance on neuropsychological tasks with a load on executive-Wisconsin Card Sorting Test (WCST). The number of perseverative errors (WCST-P), non-perseverative errors (WCST-NP), completed corrected categories (WCST-CC), conceptual level responses (WCST-%CONC) and set to the first category (WCST-1st CAT) were measured.

Results: Serious OSAS patients achieved significantly fewer categories (3,06 SD 2,5 vs. 5,36 SD 1,5 p = 0.001), made a greater number of perseverative errors (25,22 SD 19,41 vs. 11,74 SD 11,67 p = 0.001), and had a greater number of perseverative responses (29,83 SD 25,11 vs. 13,07 SD 14,7 p = 0.001). They required more trials to complete the first category (57,84 SD 52,2 vs. 22,33 SD 23,66 p = 0.001) and gave fewer conceptual responses (46,06 SD 27,15 vs. 63,21 SD 13,25 p = 0.014) than controls.

Conclusion: These results suggest that patients with serious OSAS may have set-shifting deficits when compared to healthy subjects.

0571

SPIROMETRIC ABNORMALITIES IN SEVERE SLEEP APNEA

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Introduction: According to the recent study by Frank TL et al. (2007), the prevalence of COPD is 4.1% in the English population. This value is much higher, than the previously estimated 1 to 2% prevalence. Our study explored the frequency of spirometric abnormalities in patients with severe sleep apnea.

Methods: Measurements were performed on patients in the sitting position, using a Piston spirometer. Subjects were selected in view of the results of sleep diagnostics undertaken earlier by polygraphy or polysomnography. Respiratory function testing was performed on all patients (n=332) with a RDI higher than 30/hour; mean age of the subjects was 53.3 years (range 25 to 78 years), mean BMI was 33.1 (25.1-60.2). The proportion of patients who have never smoked was 37.5% (n=123); 35.54% of patients were ex-smokers (n=118), and 26.2% were active smokers (n=87). Four patients (1.2%) did not disclose data on smoking status.

Results: Pure obstruction (FER <70% and FVC >79%) was ascertained in 53/332 patients (15.96%). Mixed ventilatory impairment (FER <70% and FVC <80%) was found in 23 patients (6.93%), including a proportion of cases with moderate-to-severe airway obstruction. Restrictive ventilatory defect (FER >70% and FVC <80%, with FEV1 <80%) was diagnosed in 57 patients (17.17%). Spirometric abnormalities (obstructive + mixed + restrictive defects in combination) were detected in 133 patients (40.06%). The prevalence of airway obstruction was 18.7% among subjects who have never smoked, 23.73% among ex-smokers, and 28.74% among active smokers.

Conclusion: A substantial proportion (40.06%) of patients with severe sleep apnea are afflicted by abnormalities of respiratory function, manifested as an obstructive ventilatory defect in more than half of these cases (22.89%). Compared to the general population, the prevalence of the latter abnormality is much higher among patients with severe sleep apnea. Similarly, the proportion of patients with airway obstruction is significantly higher among smokers, than among individuals who have never smoked (28.7% vs. 18.7%).

0572

OBSTRUCTIVE SLEEP APNEA SYNDROME: COMORBIDITIES AND CHARACTERISTICS OF PATIENTS REFERRED FOR POLYSOMNOGRAMS BY A REGIONAL MEDICAL PRACTICE VERSUS A SLEEP DISORDERS CENTER

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Introduction: The primary study aim is to describe and better characterize clinical characteristics and comorbidities of patients who are referred for polysomnograms. Prior studies have shown that the primary care physicians referred mainly patients who are very obese and symptomatic.

Methods: A retrospective chart review was performed on all patients (n=80) who underwent polysomnograms in a sleep laboratory in September 2007 which were requested by either a Regional Medical Practice (RMP) or a Sleep Disorders Center (SDC). Demographic variables and polysomnographic data such as age, sex, BMI, Neck circumference, Epworth Sleepiness Scale and vascular risk factors (i.e., MI, stroke, hypertension, CHF, hyperlipidemia, DM, atrial fibrillation, smoking history, coronary artery disease) were collected. Subjects were stratified into two groups based upon the ordering physician, RMP (n=42) or SDC (n=38).

Results: The RMP diagnosed more primary snoring and severe OSAS than the SDC (31% versus 15.6% and 35.7% versus 15.8% respectively). The SDC diagnosed more mild and moderate OSAS than the RMP (28.9% versus 19% and 42.1% versus 14.2% respectively). The mean ESS score was higher with the SDC than the RMP in both the mild and moderate OSAS patients (11.8 versus 8.8 and 12.4 versus 7.2 respectively). The number of comorbidities was the same with both groups and all of the patients studied.

Conclusion: More education is needed in the community with an emphasis on screening patients for hypersomnolence with the ESS to enhance identification of patients with mild and moderate OSAS. Further investigation is needed to determine which other historical factors are useful in identifying patients with mild and moderate OSAS.

0573

DIAGNOSIS OF OBSTRUCTIVE SLEEP APNEA SYNDROME USING OVERNIGHT OXIMETRY MEASUREMENT

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Introduction: The gold standard for diagnosing obstructive sleep apnea syndrome(OSAS) is nocturnal polysomnography(NPSG). And it is rather expensive and somewhat inconvenient. Consequently, simpler and cheaper alternatives to NPSG have been proposed. Oximetry is appealing because of its widespread availability and ease of application. In this study, we have evaluated whether oximetry alone could diagnose or screen OSAS. The diagnostic performance of an analysis algorithm using arterial oxygen saturation(SaO₂) base on 'dip index', means of SaO₂, and CT90(the percent of time spent at SaO₂ <90%) was compared with that of NPSG.

Methods: Fifty-six patients were participated in this study. For each patient, NPSG with oximetry was done. We obtained three variables from the oximetry data such as the dip index most linearly correlated with respiratory disturbance index(RDI) from NPSG, mean SaO₂, and CT90 with diagnosis from NPSG. In each case, sensitivity, specificity and positive and negative predictive values of oximetry data were calculated

Results: Thirty-nine patients out of fifty-six patients were diagnosed as OSAS with NPSG. Mean RDI was 17.5. Mean SaO₂ was 94.9% and mean CT90 was 5.1%. The dip index [4%-4sec] was most linearly correlated with RDI(r=0.861). With dip index [4%-4sec]≥2 as diagnosis-

tic criteria, we obtained the sensitivity of 0.95, the specificity of 0.71, positive predictive value of 0.88, and negative predictive value of 0.86. Using mean SaO₂≤97%, the sensitivity of 0.95, the specificity of 0.41, positive predictive value of 0.79, and negative predictive value of 0.78 were obtained. Using CT90≥5%, we obtained the sensitivity of 0.28, the specificity of 1.00, positive predictive value of 1.00, and negative predictive value of 0.38.

Conclusion: The Dip index [4%-4sec] and mean SaO₂≤97% obtained from nocturnal oximetry data are helpful in diagnosis of OSAS. CT90≤5% can be also used in excluding OSAS.

0574

FACTORS THAT MAY AFFECT THE COMPLIANCE RATE IN CHILDREN USING NONINVASIVE CONTINUOUS POSITIVE AIRWAY PRESSURE

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Introduction: Obstructive Sleep Apnea (OSA) affects Children of different ages and had significant impact on their cognitive function, school performance and general health. Adenotonsillectomy (A&T) is usually the first line of therapy; however the Noninvasive Continuous Positive Airway Pressure (CPAP) constitutes the mainstay of treatment in a subpopulation of children, especially if A&T did not cure the disease completely. Factors that affect children's compliance rate with CPAP have not been yet thoroughly investigated. The goal of this study is to identify factors that may affect CPAP compliance rate in children with Sleep Apnea.

Methods: We studied CPAP compliance rates in 37 patients (24 M, 13 F) younger than 18 years of age (7-17 years) who have OSA (AHI 10.23 ± 8.84) by reviewing their CPAP device's smart card download data, which give an objective evidence of their usage patterns. Patients were considered to be compliant with CPAP therapy if he or she used the CPAP device for ≥4 hours per night on 70% of nights. Patients had Diagnostic nocturnal polysomnography and CPAP titration studies at accredited sleep laboratory, and were followed up regularly at sleep clinic affiliated with university hospital.

Results: Fifty nine percent of patients (total 22, 13 M, 9 F) were compliant with CPAP therapy compared to 13 patients (11 M, 4 F) who did not use CPAP on regular bases. There was no statistically significant difference between these two groups in their age, gender, BMI, AHI, CPAP pressure, history of A&T, Mallampati score, mouth breathing, psychiatric disorder, or family history of CPAP usage (P values > 0.05).

Conclusion: CPAP compliance rate in children does not seem to be affected by age, gender, weight, severity of sleep apnea, CPAP pressure, history of adenotonsillectomy, Mallampati score, mouth breathing, psychiatric disorder, or family history of CPAP usage. Further studies with larger numbers are warranted to evaluate these findings, and to explore other factors that may improve CPAP compliance rate in children.

0575

PARENT RATINGS OF EXECUTIVE FUNCTIONING AND SLEEP-DISORDERED BREATHING IN CHILDREN SCHEDULED FOR ADENOTONSILLECTOMY

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Introduction: Childhood sleep-disordered breathing (SDB) is thought to have significant impact on executive and behavioral functioning. The

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gold standard in diagnosis of SDB is polysomnography, although less complicated methods have been shown to be useful in practice and research. The parent-completed Pediatric Sleep Questionnaire (PSQ) includes a validated SDB scale with subscales for snoring (5 items) and daytime sleepiness (4 items) that both discriminate reasonably well between children with and without SDB. Snoring associated with enlarged tonsils is a primary reason for referral to pediatric otolaryngologists. Daytime sleepiness, commonly reported in adults with SDB, may not be as obvious in children with SDB and has not been consistently linked with behavioral concerns in children. The purpose of the present study was to examine the relationships between snoring or daytime sleepiness, as reflected on PSQ subscales, and parent ratings of executive functioning in children scheduled to undergo adenotonsillectomy (AT), as reflected by scores on the well-validated Behavioral Rating Inventory of Executive Functioning (BRIEF).

Methods: Participants included 64 children, including 37 boys and 27 girls ranging in age from 5 to 12 years, who were referred for clinically-indicated AT. Parents completed the PSQ and BRIEF prior to surgery.

Results: The PSQ Sleepiness subscale was found to correlate significantly with all BRIEF composite subscales (Regulation: $r=.26$, $p<.04$; Metacognitive: $r=.32$, $P<.01$; Global Executive: $r=.32$, $p<.01$). The PSQ Snoring subscale showed no significant correlations with the BRIEF composite subscales.

Conclusion: Parental responses to questions about sleepiness, but not snoring, predict SDB-sensitive problems with executive functioning. These findings suggest that sleepiness may mediate any effect of SDB on executive functioning. Subjective sleepiness may be an important symptom in identifying children with SDB-related behavioral disturbances.

0576

THE PREDICTIVE VALUE OF EPWORTH SLEEPINESS SCALE IN IDENTIFYING GENDER RELATED DIFFERENCES OF OBSTRUCTIVE SLEEP APNEA IN A UNITED STATES BASED SLEEP CENTER POPULATION

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Introduction: It was believed that Obstructive Sleep Apnea (OSA) was predominantly a disorder seen in men, until Young T. et al concluded in 1993 that the prevalence of OSA among women is much higher than expected. Although Valipour A. et al in March 2007 were successful in observing significant differences in symptoms of men and women with OSA, there have been no studies comparing Epworth Sleepiness Scale (ESS) in males and females with different severities of OSA. The aim of our study is to identify gender-related differences in the ESS scores in subjects with mild, moderate and severe OSA in a United States based sleep center population.

Methods: Retrospective evaluation of 1100 subjects with 55.6% males and 44.4% females. All the subjects were referred to an American Academy of Sleep Medicine accredited sleep center at Bridgeport Hospital between February 2005 and November 2007. The ESS was administered to all the subjects prior to a standard polysomnogram. The subjects were then categorized into four groups based on the Apnea-Hypopnea Index (AHI): No OSA (AHI <5); Mild OSA (AHI 5-15), Moderate OSA (AHI 15-30) and Severe OSA (AHI >30). The ESS scores were then compared in males and females in the different groups by Analysis of Variance (ANOVA) test and further confirmed by Mann-Whitney/Wilcoxon Test.

Results: Out of 1100 subjects, 31.2% had No OSA, 25.6% had Mild OSA, 17.9% had Moderate OSA and 25.3% had Severe OSA. Mean AHI in females was 14.7 which was significantly lower than an AHI of 26.1 observed in males ($p <.0001$). On Analyzing the ESS scores in various groups based on the severity of OSA, only the Mild OSA group

was noted to have a significant gender-related difference in the ESS scores with a mean score of 10.3 in females and 8.6 in males ($p <.05$).

Conclusion: The ESS score can be higher in females than in males with mild OSA, but does not have any significant gender-related difference when patients approach moderate to severe OSA category. This result indicates different subjective perception of excessive daytime sleepiness in males and females with mild OSA.

0577

THE IMPORTANCE OF SLEEP POSITION IN TREATMENT PLANNING OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: Planning the treatment of patients with obstructive sleep apnea syndrome (OSAS) based on only total Apnea Hypopnea Index (AHI) values without taken into account the AHI in sleeping positions would result in failure to recognize the patients with positional OSAS and evaluation errors as early as in diagnosis stage. The aim of this study was to evaluate the importance of sleep position in treatment planning of OSAS patients.

Methods: We performed a retrospective evaluation of 170 patients with positional OSAS studied in our sleep center. AHI values in non-supine and supine positions were evaluated, and patients in which OSAS severity increases with supine position (i.e. the mild ones that become moderate or severe, or the moderate ones that become severe) were included in the study.

Results: The patients were divided according to their AHI values as Group A (AHI=5-15, mild OSAS patients), and Group B (AHI>15, moderate and severe OSAS patients). 37 patients were classified as Group A and 133 patients as Group B. There were no significant differences between two groups compared with Epworth Sleepiness Score, average oxygen saturation and additional conditions (hypertension, congestive heart failure, coronary artery disease, cerebrovascular disease).

Conclusion: That there were no differences between two groups is an indication of the fact that damage starts at an early stage in patients with mild OSAS. False evaluations in diagnosis stage will result in wrong treatments. If palliative treatments are applied to patients with mild OSAS in which severity increases in supine position, OSAS related complications could emerge in much earlier stages. In conclusion, patients with positional OSAS should be evaluated as different clinical entity and treatment plan should be made accordingly. Thus, development of OSAS related complications could be prevented in earlier stages.

0578

IS THERE A DIFFERENTIAL RESPONSE TO ADAPTIVE SERVOVENTILATION IN PATIENTS WITH CENTRAL OR COMPLEX SLEEP APNEA RELATED TO OPIOID USE VERSUS CONGESTIVE HEART FAILURE?

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Introduction: Adaptive servoventilation (ASV) uses fuzzy logic to anticipate ventilatory support requirements and is approved for use in central sleep apnea (CSA) and complex sleep apnea syndrome (CompSAS). These conditions may occur in the setting of both congestive heart failure (CHF) and use of opioid medications. Compared to that associated with CHF, opioid-related CSA breathing demonstrates a less periodic pattern with a shorter cycle length. We hypothesized that ASV would be less successful in treatment of CSA and CompSAS secondary to opioid use than in the setting of CHF.

Methods: Retrospective study of patients with CSA/CompSAS and either chronic opioid use or CHF who had a diagnostic polysomnogram

and ASV titration at our Center between December 2006 and October 2007. We identified 16 patients with chronic opioid use and 26 patients with CHF. The primary outcome measure was ASV treatment success, defined by achievement of an apnea-hypopnea index (AHI) <10 with ASV treatment.

Results: Both opioid and CHF groups were predominantly male (69% vs 88%, $p>0.05$) and had significant baseline sleep disordered breathing at baseline as measured by AHI (median (IQR): 31(48.3) vs 40.5(47.3), $p=0.57$). The opioid group was younger (61.5(17.1) vs 73.5(20.7), $p=0.022$) and had fewer polysomnographic arousals at baseline (36.5934.2) vs 55.1(39.2), $p=0.02$). ASV was successful in 73.8% of cases (CHF 69.2% vs opioid 81.3%, $p=0.49$). There were no significant differences in ASV-treated AHI (CHF 3.0(11.5) vs opioid 1.5(3.5) $p=0.49$), arousal index (CHF 24.2(21.9) vs opioid 15.5(20.8), $p=0.09$), central apnea indices, or optimal level of end expiratory pressure (CHF 7(4) vs opioid 6.5(3.5), $p=0.39$) between the groups.

Conclusion: ASV appears to be equally efficacious in opioid- and CHF-related central sleep apnea syndromes. However, the relatively small sample size of this study may result in insufficient power to detect such a difference.

0579

RESPIRATION AND SLEEP IN OSA PATIENTS TREATED WITH CPAP VS. AUTO BILEVEL PRESSURE RELIEF- PAP

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Introduction: CPAP is the gold standard therapy for OSA, but some patients cannot adequately comply with this treatment due to difficulty exhaling against a fixed pressure. Accordingly, there is a need to develop more comfortable modes of ventilation. Auto Bilevel Pressure Relief-Positive Airway Pressure (ABPR-PAP) is an alternative to manually titrated CPAP therapy for OSA. The aim of this study was to evaluate sleep, efficacy and 3 month compliance of ABPR-PAP compared to CPAP in a prospective, double blind, randomized trial.

Methods: We included 35 patients (age 53,3±10,9 years; BMI 31,0±5,0kg/m²; ESS 10,0±4,2; 34 males) with a first time diagnosis of moderate to severe OSA, who underwent one night of successful CPAP titration. Patients were then randomized to the CPAP or the ABPR-PAP treatment group. The same device (BIPAP Auto, Respironics) was used to deliver both CPAP and ABPR-PAP. The RDI was determined using polysomnography before treatment (RDI 43,4±18,7/h) and under ventilation.

Results: 18 received CPAP, the others APBR-PAP. The groups were similar demographically and in the severity of OSA. There were no serious adverse events during the treatment. CPAP was fixed by a sleep expert according to the results of the titration night (range 7-13cmH₂O) and ABPR-PAP varied (range 5-15cmH₂O). RDI decreased in the CPAP group to 6,6±6,2/h and in the ABPR-PAP group to 5,2±4,0/h in the first night (N=35). After three month the RDI decreased further in the CPAP group to 4,9±6,5/h and in the ABPR-PAP group to 1,7±1,6 /h (N=20). Sleep improved under both modes of ventilation. Compliance was not statistically significant different between treatment groups.

Conclusion: ABPR-PAP effectively treats OSA and improves sleep quality. Further research is needed to identify which subgroups of patients may benefit from this new mode of PAP therapy.

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0580

EXPANDING INSTRUCTIONS FOR THE EPWORTH SLEEPINESS SCALE MAY INCREASE SENSITIVITY OF THE TEST FOR OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: The Epworth Sleepiness Scale (ESS) may correlate poorly with the severity of the Obstructive Sleep Apnea Syndrome (OSAS) as manifest by the Apnea Hypopnea Index (AHI). One reason is that while respondents have the propensity to doze in the ESS's eight situations, some avoid dozing by engaging in physical or mental activities, thereby underreporting EDS (Excessive Daytime Sleepiness). Normal scores may exclude patients with OSAS from further testing. To eliminate subjective bias, subjects with suspected OSAS who reported daytime sleepiness but had a normal ESS (ESS1), completed a second ESS (ESS2) which included an instruction not to consciously resist sleep in the eight situations. Correlations were independently made between ESS1 and ESS2 and the AHI.

Methods: 70 consecutive patients with EDS and suspected OSAS with a normal ESS (ESS1) completed an ESS2. For comparison, 36 subjects without any sleep complaints (controls) and 35 insomniacs completed an ESS1 and ESS2. Overnight polysomnograms were performed in the suspected OSAS patients. Logistic regressions with ESS1 and ESS2 as exploratory factors and the AHI as the responsive variable were separately performed. ESS1 and ESS2 results for controls and insomniacs remained within normal limits i.e.<10.

Results: Controls: ESS1 5.39 ±3.01; ESS2 7.56 ±3.66. Insomniacs: ESS1 and ESS2 were 2.33 ± 2.23 and 4.21 ± 2.95. OSAS: ESS1 and ESS2 were 6.34 ±1.58 and 12.29 ±3.6. The mean AHI was 37.8 ±28.8. The AHI and ESS1 logistic correlation model had no significant relationship $p=0.1052$. Correlation between ESS2 and AHI was significant $p<0.0001$.

Conclusion: Some patients with OSAS and EDS may underscore ESSs, precluding themselves from further diagnostic testing. Adding an instructional sentence to complete the ESS 'so as not to consciously resist sleep' would prevent underscoring and more accurately reflect the true clinical status regarding EDS. The additional instruction does not affect ESS scores of controls and insomniacs.

0581

SHORT-TERM WEIGHT GAIN FOLLOWING CPAP TREATMENT OF OBSTRUCTIVE SLEEP APNEA

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Introduction: Although we confirm previous finding that suggest long-term improvement in weight control with CPAP treatment of Obstructive Sleep Apnea (OSA), we have observed an initial increase in weight during the first 4 weeks of CPAP use. We analyzed this data to assess variables that might provide clues to the underlying physiological mechanisms.

Methods: Retrospective analysis of records from a community-based sleep center.

Results: The results from the initial 50 patients are presented here. The initial weight was 106.4 +/- 25 kg. The weight 4 weeks after CPAP titration was up at 107.4 +/- 25 kg ($P<0.02$). To distinguish this from continued weight gain, comparison was made to weight at 6 months in 21 of the patients with available follow up. For this subgroup the weight did not increase, and may demonstrate a downward trend (105.0 +/- 24 kg at 4 weeks vs 104.1 +/- 23 kg at 6 months. There was no effect of time of year, or gender. A tendency to inverse correlation with symptomatic sleepiness was noted.

Conclusion: We have found an increase in weight after 4 weeks of treatment of OSA with CPAP therapy. As there may be an association with improved alertness, we speculate that a central nervous system mecha-

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nism to increased appetite might have an initial effect. The effect on weight is not seen after 6 months of treatment.

0582

UTILIZATION OF BODY MASS INDEX IN PREDICTING THE SEVERITY OF APNEA-HYPOPNEA INDEX

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Introduction: An association has been reported between Apnea Hypopnea Index (AHI) and Body Mass Index (BMI) in patients with Obstructive Sleep Apnea (OSA). Obesity is the most important risk factor for OSA. It is estimated that 70% of OSA patients are obese. In the morbidly obese, the prevalence may reach 80% in men and 50% in women. However, linear correlation between AHI and BMI has not been tested. The purpose of this study is to identify if such correlation exists.

Methods: This is a single centered retrospective chart review study. We reviewed the records of 1097 patients who underwent evaluation and polysomnography at Bridgeport Hospital Sleep Center (AASM Accredited) between February 2005 and November 2007. The patients were categorized according to BMI using the latest WHO classification of obesity. The X-Y scatter of AHI and BMI was plotted on the graph and correlation was tested using linear regression.

Results: There were 44.4% females and 55.6% males in the study with mean AHI of 21.1. The mean AHI was found to be 10.2, 18.0, 19.6 and 29.7 for pre-obese (BMI 25-30), obese class I (BMI 30-35), class II (BMI 35-40) and class III (BMI >40) respectively ($p < 0.001$). The linear regression between AHI and BMI demonstrated no correlation (Correlation Coefficient (r) = 0.06, $p < 0.001$).

Conclusion: Our findings indicate that although the mean AHI increases with the severity of obesity, there is no linear correlation between absolute AHI and BMI values in individual patients. This supports the multifactorial pathogenesis of OSA syndrome and implies that severity of OSA varies when correlated with BMI in individual patients as compared to a group.

0583

CYCLIC ALTERNATING PATTERN IN WOMEN WITH SLEEP-DISORDERED BREATHING: A COMPARISON OF PRE- AND POST-MENOPAUSE

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Introduction: Apnea-hypopnea index (AHI) is more important in obstructive sleep apnea (OSA) postmenopausal than in premenopausal women despite similar complaints of sleepiness and fatigue. Cyclic alternating pattern (CAP) is a measure of NREM sleep instability. We investigate the differences of CAP in these 2 groups and compared to normal controls.

Methods: Polysomnography and blind-to-condition CAP analysis were performed in 18 OSA women (50% postmenopausal) and 18 normal controls (12 premenopausal). Statistical analysis: Mann-Whitney U tests for independent, nonparametric variables (mean \pm SD).

Results: Comparison of OSA pre- versus post-menopause groups were different for age (36.3 \pm 3.1 versus 51.1 \pm 0.8, $p = 0.001$), but similar for BMI (23.2 \pm 1.5 versus 26.5 \pm 1.7), AHI (15.3 \pm 4.1 versus 21.6 \pm 6.6), and oxygen saturation nadir (92.4 \pm 0.5 versus 90.4 \pm 1.2), and for sleep tabulation: total sleep time (413.8 \pm 24.1 versus 383.7 \pm 20.9 minutes), % sleep efficiency (81.5 \pm 4.2 versus 82.2 \pm 3.9), % stage 1 (7.9 \pm 1.6 versus 6.7 \pm 1.4), % stage 2 (55.5 \pm 3.0 versus 54.1 \pm 3.8), % stage 3 (12.2 \pm 1.9 versus 12.1 \pm 1.8), % stage 4 (8.8 \pm 1.5 versus 8.1 \pm 2.1) and % REM (15.6 \pm 1.8 versus 19.0 \pm 2.0). There was a similar CAP rate (67.1 \pm 5.6 versus 69.5 \pm 3.6), mean phase A (7.1 \pm 0.3 versus 7.1 \pm 0.4 second), mean phase B duration (19.5 \pm 1.1 versus 19.5 \pm 1.1 second), and CAP index (93.94 \pm 10.7 versus 99.2 \pm 5.4 per hour). Ratio of % subtype A1 (56.9 \pm 2.63 versus

50.9 \pm 4.5), A2 (27.6 \pm 2.1 versus 26.2 \pm 2.0), A3 (17.5 \pm 2.8 versus 22.9 \pm 3.1) were similar. The only difference was increase in A3 in stages 1 and 2 ($p = 0.019$ and 0.03) in postmenopausal women. OSA subjects were different from normal controls: premenopausal: age 25.7 \pm 5.6, CAP rate 33 \pm 8, A1: 68.0 \pm 14.0, A2: 19.5 \pm 12.2, A3: 11.9 \pm 17, postmenopausal were respectively: 27.0 \pm 4.0, 65.0 \pm 17.0, 19.9 \pm 9.0, 13.0 \pm 10.0.

Conclusion: Despite differences in AHI, CAP rate was importantly increased in pre and post menopausal women compared to normal with a more important sleep instability in stages 1 and 2 in postmenopausal women.

0584

ASSOCIATION BETWEEN WEIGHT AND CHANGE IN SLEEP-DISORDERED BREATHING IN THE BASELINE AND FOLLOW UP SURVEYS OF THE TUCSON CHILDREN'S ASSESSMENT OF SLEEP APNEA STUDY (TUCASA)

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Introduction: Obesity may predispose children to sleep-disordered breathing (SDB). However, the relationship between weight change and incidence, progression, or remission of SDB is not well defined.

Methods: A total of 319 children aged 6 to 12 years underwent unattended home polysomnogram (PSG) and anthropometric measurements as part of the baseline TuCASA study. Approximately 5 years later these children completed a follow up PSG and a second anthropometric evaluation. Body mass indexes (BMI) at baseline and follow up were used to predict baseline and follow up respiratory disturbance index (RDI) and RDI 3% as indicators of respiratory events. Baseline and follow up BMI were also used to predict change in RDI and RDI 3% determined by follow up minus baseline values.

Results: Children were 51% male and 64% Caucasian. Baseline values were mean 9 years of age, and median 16.8 BMI, 4.4 RDI, and 0.5 RDI 3%. Follow up values were mean 13.7 years of age, and median 20.5 BMI, 1.6 RDI, and 0.2 RDI 3%. BMI, RDI, and RDI 3% difference were 3.2, -2.68, and -0.23 respectively. Linear regression models adjusted for age showed significant association between baseline BMI and baseline RDI (coeff. = 0.148, $p = 0.026$) and RDI 3% (coeff. = 0.084, $p = 0.004$). Baseline BMI was associated with difference in RDI (coeff. = -0.146, $p = 0.045$) and RDI 3% (coeff. = -0.008, $p = 0.03$); follow up BMI was associated with difference in RDI (-0.186, $p = 0.002$), and RDI 3% (coeff. -0.07, $p = 0.025$).

Conclusion: Baseline and follow up BMIs were associated with modest changes in RDI and RDI 3%. These changes were not significantly different by gender.

0585

CLINICAL CHARACTERISTICS AND PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN NON-OBESE PATIENTS

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Introduction: Obstructive sleep apnea (OSA) is usually associated with obesity. 10% of patients with OSA are non-obese. We sought to determine the clinical characteristics and prevalence of OSA in patients with normal BMI.

Methods: Single institution retrospective chart review at an accredited sleep center. We reviewed all baseline polysomnograms (PSGs) conducted over an eleven-month period. We defined OSA as a minimum of Apnea-Hypopnea Index (AHI) > 5. Normal BMI was defined as between 18.5 to 27.

Results: 720 baseline PSGs were performed over eleven month period. 139 had normal BMI. Of these 39 patients met the criteria (28%) and

represented 5.5% of all baseline PSG's (19.3%). Twenty-seven patients were male (69 %). Average age was 57 years (range 14 -81). Average BMI was 23.9 (range 18.5-27). Snoring (24/39) and excessive daytime sleepiness (15/39) were the commonest presenting complaints. Mean AHI was 22.3 (range 5.5-90). 38 patients were treated with nasal continuous positive air way pressure (CPAP) and one with positional therapy.

Conclusion: In our centre, non-obese patients represented 19.3% of all patients evaluated for OSA. Of these 28% actually had OSA. The prevalence of OSA with normal BMI was 5.5 % of all baseline studies. OSA in non-obese patients was three times more common in males, especially middle aged and older adults. Unlike previous reported studies of high prevalence in elderly (> 75 years), a higher prevalence was noted among advanced middle-age (age 45-65 yrs) 17/39. 8/39 were early old age (65-75 years) and 8/39 were early middle aged (30-45 years). Commonest presenting symptoms were still snoring and excessive day time sleepiness as seen in obese patients. A high clinical suspicion is necessary for diagnosis of OSA in non-obese individuals, rather than considering obesity as a primary indicator. These patients are treated similar to obese OSA patients.

0586

CO-MORBIDITIES ASSOCIATED WITH OBSTRUCTIVE SLEEP APNEA IN NON-OBESE PATIENTS

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Introduction: To determine co-morbidities associated with Obstructive Sleep Apnea (OSA) in non-obese patients.

Methods: Single institution retrospective chart review at an accredited sleep center. We reviewed baseline sleep studies of 221 patients with normal BMI. We defined obstructive sleep apnea as a minimum of Apnea-Hypopnea Index (AHI) > 5. Normal Body Mass Index (BMI) was defined as between 18.5 to 27. Patients with BMI above 27 were excluded. Patients who met the criteria for OSA with normal BMI were identified. All the associated co-morbid medical conditions were reviewed.

Results: 221 baseline polysomnograms (PSGs) were reviewed. 62 patients met criteria for OSA. 48/ 62 patients were males (77%). Average age was 53 (range 14-81), average BMI was 22 (range 19-27) and mean AHI was 22 (range 5.1-90). Commonest presenting symptoms were snoring and excessive day time sleepiness. Commonest co-morbidities were: Hypertension 30/62 (48 %), Coronary artery disease 21/62 (34%), GERD 16/62 (26 %), Cardiac arrhythmias 15/62 (24%), Diabetes 11/ 62 (18%), Depression 11/62 (18 %) and Hyperlipidemia 11/ 62 (18 %). 56 patients were treated with nasal continuous positive air way pressure (CPAP) and 6 with positional therapy +/- with ENT evaluation.

Conclusion: Middle aged males with normal BMI seems to be at risk for OSA. Most common co-morbidities observed in non obese OSA patients were Hypertension, CAD, GERD, Cardiac arrhythmias, Diabetes, Depression and Hyperlipidemia, similar to OSA in obese patients. With the exclusion of obesity as a confounding factor, OSA seems to be a common factor associated with these co-morbidities both in obese and non-obese individuals. This study suggests relationship between sleep apnea and these co-morbidities. CPAP seems to be the best modality of treatment.

0587

CLINICAL CHARACTERISTIC FEATURES OF REM SLEEP RELATED BREATHING DISORDERS

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Introduction: We have previously reported prevalence, clinical features and effect of treatment in patients with REM sleep-related breathing dis-

orders (SRBD). This present study involves a larger patient sample. We also attempted to assess associated co-morbidities.

Methods: Single institution retrospective chart review at an accredited sleep center. We reviewed both baseline and CPAP titration studies. REM Obstructive Sleep Apnea (OSA) was defined as apnea-hypopnea index (AHI) two times the total sleep time (TST) AHI and three times the NREM AHI. REM AHI had to be a minimum of 5. Non-apneic hypoxemia occurring only in REM sleep was defined as REM Hypoxemia.

Results: 84 patients met criteria. 59/84 patients were female (70%) and 25/84 were males. Average age was 49 (range 25-76). Average BMI was 39.5 (range 23-56). Snoring (59/84), excessive day time sleepiness (37/84), fatigue (24/84) and apnea (20/ 84) were the most common presenting complaints. Mean AHI was 8.1 (range 1.8-27), REM AHI was 34.25 (range 3 -87) and NREM AHI was 3.57 (range 0.0-18). 8/84 had REM hypoxemia, 9/84 combination of REM hypoxemia and REM OSA. 67/84 had REM OSA. 4/8 patients with REM hypoxemia were treated with oxygen therapy and another 4/8 patients received oxygen and positional therapy. 9 patients were treated with combination of oxygen and CPAP therapy for REM OSA and hypoxemia. Of 67 patients with REM OSA, 61 received CPAP therapy and 6 treated with positional therapy.

Conclusion: REM SRBD was three times more common in females. Higher BMI (average 39.5) and middle aged patients (average 49 years) seems to be at risk for REM SRBD. Common co-morbidities were: hypertension, depression, diabetes mellitus, hyperlipidemia, and GERD. We emphasize that by incorporating the REM AHI and REM-related hypoxemia into the treatment decision horizon, patients with REM SRBD can be effectively treated. It is important to titrate CPAP settings in REM sleep for optimal therapeutic effect.

0588

THE EFFECT OF SLEEP POSITION ON OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH SEPTAL DEVIATION

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Introduction: The lateral recumbent position causes ipsilateral nasal congestion and contralateral decongestion, and thus it affects nasal obstruction. Nasal obstruction is considered as one of the important factors that influence the pathophysiology of obstructive breathing disorders during sleep. The aim of this study was to evaluate the association between septal deviation and the changes of parameters determined by polysomnography (PSG) according to the sleep positions.

Methods: This study included 29 patients suffering from obstructive sleep apnea (OSA) and septal deviation who underwent overnight PSG including positional AHI and acoustic rhinometry (AR). The minimal cross-sectional area (MCA) of the nasal cavity was measured by AR in order to determine the narrow side of the nasal cavity. The apnea-hypopnea index (AHI) according to the sleep positions was evaluated in relation to septal deviation.

Results: The 29 patients had the mean BMI of 25.83±3.92 kg/m², 12 of whom had BMI<25 kg/m² and 17 of whom had BMI≥25 kg/m². The mean AHI for all patients was 28.84±27.76/hr. The AHI with the wide side of the nasal cavity down in the lateral position was 16.27 ± 26.44, and it was significantly smaller than that obtained with the narrow side down (25.93 ± 31.92; P = 0.007, paired t test). In addition, the relative percentage of sleeping time with the wide side of the nasal cavity down in the lateral position was 77.01 ± 53.95 and this obtained with the narrow side down was 63.18 ± 35.63. This difference was not statistically significant (P = 0.316, paired t test).

Conclusion: There was a significant correlation between septal deviation and the AHI of different sleep position. The presence of septal deviation may modify the effect of sleep positions on respiratory disturbance.

0589

SNORING IS AN INDEPENDENT RISK FACTOR FOR ASTHMA IN HISPANICS

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Introduction: The increasing prevalence of asthma has been linked to obesity, air pollution and tobacco smoke. Recently it has been suggested that sleep disordered breathing plays a role in the nocturnal worsening of asthma and that snoring may be part of the allergic spectrum of disease. We investigated the association of snoring with the diagnosis of asthma.

Methods: We performed a population-based survey in San Diego County using the Waksberg random digit dialing procedure and the Kish intra household selection method to administer a telephone questionnaire dealing with sleep health. 1342 Hispanics of Mexican descent and Non-Hispanic Whites ≥ 18 yrs of age were interviewed. The prevalence of asthma was determined by the subject's report of prior diagnosis. Only subjects who gave information on snoring were included in the asthma risk factors analysis (age, gender, BMI, smoking, snoring, n = 873).

Results: Non-Hispanic Whites had a significantly higher prevalence of asthma compared to Hispanics of Mexican descent (14.2% vs 9.7%, p = 0.012). Logistic regression analysis indicated that female gender and greater BMI were predictors of asthma in Non-Hispanic Whites (n = 453, p < 0.05). Similar analyses revealed that female gender, greater BMI and lifetime duration of snoring were predictors of asthma in Hispanics (n = 420, p < 0.026).

Conclusion: Snoring was found to be an independent risk factor for asthma in Hispanics of Mexican descent but not in Non-Hispanic Whites when controlled for age, BMI, gender and smoking. Smoking was not found to be a risk factor for asthma in either population. Our findings suggest that snoring is a comorbid condition of asthma in Hispanics of Mexican descent but not in Non-Hispanic Whites.

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0590

HYPOPNEA DEFINITIONS VIII.4.A AND VIII.4.B FAIL TO DETECT CLINICALLY SIGNIFICANT OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME IN LEAN PATIENTS

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Introduction: Since 1988, hypopnea definitions have utilized 2-5% oxygen desaturations, 30-50% air flow reductions and electroencephalogram (EEG) arousal in various combinations. The 1999 American Academy of Sleep Medicine (AASM) definition included airflow reduction terminated by arousal. The AASM recently published two definitions to improve inter-rater reliability by decreasing the emphasis on arousal and flow reduction. Lean patients with obstructive sleep apnea hypopnea syndrome (OSAHS) desaturate less than obese patients and are therefore differentially affected by these changes. Standardization is important, but a flawed standard could be detrimental to patient care.

Methods: 35 lean subjects (15 male, 20 women, 5 post-menopausal) with sleep-disordered-breathing related complaints had diagnostic polysomnograms (PSG) scored in randomized and blinded fashion utilizing arousal (OHAr) and desaturation (OHO2) dependant scoring methods. OHO2 included the most liberal elements of Rules VIII.4.A (30% flow reduction) and VIII.4.B (3% desaturation). Reflecting the 2007 rule,

OHO2 required 3% desaturations. Reflecting the 1999 rule OHAr required EEG arousal. Both required > 30% flow reduction for > 10 seconds. Subsequently, all patients had treatment (CPAP, oral appliance (OA), or surgery) and post-treatment PSG.

Results: Mean (sd) AHI-OHAr and AHI-OHO2 were 26.9 (7.3) and 6.4(3.1) respectively (p < 0.0001). All AHI-OHAr were > 15. All AHI-OHO2 were < 15. Fifteen (43%) had AHI-OHO2 < 5. Mean (sd) BMI was 24.4(1.0). Minimum oxygen saturation was 88%. Twelve (86%) with CPAP, five (83%) with oral appliance, and fifteen (100%) with surgical intervention reported satisfactory resolution of their presenting complaints. Post-treatment AHI-OHAr mean (sd) was 2.4 (1.6) (p < 0.0001).

Conclusion: Even the most liberal interpretation of rules VIII.4.A and VIII.4.B failed to identify OSAHS in lean patients that require and ultimately benefit from treatment. This inappropriate reduction of the AHI unacceptably reduces detection and treatment for patients. Increasing proficiency in flow reduction and EEG arousal recognition may provide a more appropriate method for improving inter-rater reliability.

0591

ATTENTION DEFICIT-HYPERACTIVITY DISORDER IN CHILDREN WITH SLEEP DISORDERED BREATHING

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Introduction: ADHD (attention deficit/hyperactivity disorder) is one of the most common psychiatric disorders of childhood and adolescence; it's estimated to affect 3 to 6% of school aged population in Italy. The core symptoms of ADHD (inattention, difficulty in regulating behaviour and hyperactivity) are strikingly similar to those caused by disrupted sleep and sleep deprivation, as many investigators and clinicians pointed out. Sleep disordered breathing in childhood includes a spectrum of disorders that vary in severity, ranging from OSAS (obstructive sleep apnoea syndrome) at one end, to primary snoring (snoring without ventilatory abnormalities); an important line of research has focused on the identification of neurobehavioural deficits in clinical populations of children with diagnosed sleep disorders. Purpose of our study was to examine the possibility of associating ADHD and different stages of sleep disordered breathing.

Methods: The sample consisted in 84 children (from 3 to 13 years of age) with sleep disordered breathing; all of them underwent an overnight polysomnographic assessment: 42 of them suffered from OSAS, and 42 from primary snoring. Parents completed a well-validated questionnaire (inattention/hyperactivity scale, IHS) to rate the extent to which the 18 DSM IV category A symptoms of ADHD apply to their children; we considered "high" scores those corresponding to 12 or more positive answers among 18 symptoms items.

Results: We found a significantly higher prevalence of hyperactive and inattentive behaviour in children with SDB, compared to general population (11,9% vs 3,9%;, p < 0,01; O.R. 3.3); besides, children suffering from OSAS showed a higher IHS score (p = 0,03) compared with children with primary snoring.

Conclusion: data coming from clinical observations and surveys suggest that an association between sleep disordered breathing and ADHD exists; given the complexity of these relationships and the impact of both ADHD and sleep disorders in pediatric population, further research is needed.

0592**THE EFFECT OF THERAPEUTIC PILLOW ON POSITIONAL OBSTRUCTIVE SLEEP APNEA**Han J¹, Hong J¹, Choi K¹, Ko C², Kim K¹¹Seoul Sleep Center, Seoul, South Korea, ²Evezary Research Institute on Sleep and Environment, Seoul, South Korea

Introduction: A typical positional patient may resolve his breathing abnormalities during sleep merely by avoiding the supine posture. The purpose of this pilot study was to examine the effect of positional therapy with a new therapeutic pillow (Sleep Thera®) designed to support positional patients of obstructive sleep apnea (OSA) to keep lateral posture comfortably without attaching forced devices such as tennis balls, posture alarm, or fasteners.

Methods: Subjects were patients who were diagnosed to have positional OSA as the respiratory disturbance index (RDI) was more than twice as high in the supine position than in the lateral position and the total RDI was ≥ 5 in the polysomnography (PSG). They underwent second PSG with the use of newly designed therapeutic pillow. The values of second PSG were compared with those of first PSG to evaluate the effect of the therapeutic pillow.

Results: Seven men and six women participated in this study. The mean of age was 45.2 (range, 17-71) years old, and the mean of BMI was 23.1 (range, 19.3-23.8). While they were utilizing the therapeutic pillow, the mean (\pm s.d.) of total RDI was decreased from 13.6 (\pm 9.6) to 5.0 (\pm 4.6). Each mean of RDI in REM and in NREM was decreased similarly with total RDI. Out of 10 mild OSA patients, 8 became normal. All of 2 moderate OSA patients became normal. The one severe patient was improved into moderate state (overall cure rate=76.9%). The mean of sleep efficiency and arterial oxygen saturation was increased from 78.7% to 86.8%, from 90.5% to 92.8%, respectively.

Conclusion: This study presented that positional OSA patients were treated or improved by positional therapy using the therapeutic pillow.

0593**SLEEP ALTERATION IN INTENSIVE CARE UNIT: A DESCRIPTIVE STUDY**Drouot X^{1,3}, Roche Campo F², Thile A², Galia F², Brochard L^{2,3}, d'Ortho M^{2,3}¹Service de Physiologie, Hopital Henri Mondor, Creteil, France, ²Service de Reanimation Medicale, Hopital Henri Mondor, Creteil, France, ³INSERM U841, Faculte de Medecine, IM3, Creteil, France

Introduction: Critically ill patients in Intensive Care Units suffer from severe sleep alterations. These disruptions include decreased total sleep time, pronounced reduction of non REM sleep and REM sleep, along with an intense sleep fragmentation. In addition, conventional scoring rules may not be adapted to study sleep in these patients, impeding an acute sleep analysis. The aim of this study was to describe sleep micro and macro-structure in critically ill patients.

Methods: We studied 27 consecutive ICU patients admitted for acute hypercapnic exacerbation requiring more than 24 hours of noninvasive ventilation treatment. A 17-hour polysomnographic study was performed between the second and third day. Exclusion criteria were clinical encephalopathy, previous neurological or psychiatric disease, neuroleptic or sedative drugs administration within the preceding 48 hours.

Results: In 8 of 27 patients, usual sleep EEG patterns were replaced by an "atypical sleep" with absence of sleep spindles and K complexes. In these patients, waking EEG was also altered: background EEG frequency was higher in patients with normal sleep EEG (8.3 ± 0.3 Hz vs 5.8 ± 0.4 Hz; $p < 0.005$). Age, arterial pH, pCO₂ and disease severity were similar in patients with atypical or normal EEG pattern. Prolonged noninvasive ventilation therapy and endotracheal intubation were more frequent in patients with altered sleep EEG pattern (7/8 vs 7/19; $p < 0.05$). In 5 of 19 patients with normal sleep EEG pattern, hypnograms showed a polyphasic organization of sleep: patients took brief episodes of sleep

(with short SWS and REM sleep latencies) separated by prolonged periods of wakefulness. While sleep efficiency was similar in patients with and without polyphasic sleep, mean fragmentation indices (arousal and awakenings/hour) were lower in the former (20 ± 3 vs 38 ± 5 ; $p < 0.05$).

Conclusion: Quantification of wake/sleep EEG patterns and analysis of sleep hypnograms could identify distinct sleep patterns, which could be associated with outcome.

0594**THE EFFECT OF ACETAZOLAMIDE, O₂, AND O₂/CO₂ MIX ON CARDIORESPIRATORY RESPONSE DURING SLEEP AT 5400 M**Rodway GW^{1,2}, Windsor JS²¹Nursing, University of Pennsylvania, Philadelphia, PA, USA,²Caudwell Xtreme Everest, University College London Centre for Altitude, Space and Extreme Environment Medicine, London, United Kingdom

Introduction: Various therapies have been utilized to prophylax or treat the periodic breathing frequently encountered during sleep at high altitude. However, studies of modalities used to treat this form of sleep disordered breathing have not typically compared several different therapeutic options in the same trial. This pilot study sought to compare the effect of 3 periodic breathing prophylaxes - acetazolamide, low flow O₂, and low flow O₂/CO₂ mix - on basic cardiorespiratory response during sleep at 5400 m altitude.

Methods: 15 healthy trekkers, with identical ascent profiles and no signs or symptoms of altitude illness, served as subjects. All study participants arrived at 5400 m after a gradual 14 day ascent from Kathmandu, Nepal. On their second night at 5400 m, subjects were randomly assigned to one of four different groups: control (n = 4); 1 L/min. O₂ via a demand system during sleep (n = 3); 1 L/min. O₂/CO₂ mix (1.5% CO₂) via a demand system during sleep (n = 4); or 125 mg acetazolamide 30 min. before bedtime (n = 4). Heart rate, respiration rate, blood oxygen saturation, tidal volume, and apnea hypopnea index were measured. Variables were measured continuously during sleep with a Vivometrics Lifeshirt.

Results: There were no statistically significant differences ($p < 0.05$) in the measured variables of the acetazolamide, O₂, or O₂/CO₂ arms of the study compared to the control group.

Conclusion: The small number of subjects, the large variation in subject response in each arm, the modest doses of gas and acetazolamide given, and a conservative ascent profile may explain the results to some extent. Future studies using similar methodology should endeavor to include larger numbers of subjects with an ascent profile that is faster and thus more representative of common sojourns to altitudes over 5000 m.

Support (optional): This study was supported by Caudwell Xtreme Everest, a research project coordinated by the UCL Centre for Altitude, Space and Extreme Environment Medicine, University College London, London, UK.

0595**POSTOPERATIVE MONITORING OF ESOPHAGEAL PRESSURE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA WHO HAD UNDERGONE TONSILLECTOMY WITH UVULOPALATOPHARYNGOPLASTY**

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Introduction: Postoperative management is very important for patients with obstructive sleep apnea hypopnea syndrome (OSAHS). To realize a better postoperative management, we elucidated the necessity of postoperative monitoring of esophageal pressure (Pes).

Methods: A prospective randomized controlled study design was employed. Adult OSAHS patients were divided into two groups: those administered autoadjusted continuous positive airway pressure (CPAP) before, on, and after the first postoperative night (CPAP group) and those

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not administered CPAP before and after surgery (non-CPAP group). Tonsillectomy with uvulopalatopharyngoplasty (UPPP) under general anesthesia was performed on all the patients. On the first postoperative night, continuous overnight monitoring of Pes and oxygen saturation was carried out simultaneously with oxygen supplementation in both groups in the patient's room of the general ward.

Results: There were significant differences in oxygen desaturation index (ODI) between preoperative and the first postoperative night in the CPAP and non-CPAP groups. There were also significant differences in mean inspiratory maximal end-apneic esophageal pressure swing (Pes nadir) between preoperative and the first postoperative night in the CPAP and non-CPAP groups. The CPAP group showed a significantly improved mean Pes nadir on the first postoperative night compared with the non-CPAP group, although there was no significant difference in ODI on the first postoperative night between the CPAP and non-CPAP groups.

Conclusion: Continuous Pes monitoring with oxygen supplementation and CPAP administration was beneficial in the detection and minimization of respiratory disturbances in postoperative patients with OSAHS who had undergone tonsillectomy with UPPP under general anesthesia.

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0596

SUBCLINICAL ISCHEMIC BRAIN LESIONS AND OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME

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Introduction: Obstructive sleep apnea-hypopnea syndrome (OSAHS) has been reported to play a part in the occurrence of ischemic stroke. The aim of this study is to investigate the prevalence and relationship of subclinical ischemic (SI) brain lesions in patients with OSAHS.

Methods: Fifty five patients have been enrolled, who were diagnosed as OSAHS using nocturnal polysomnography. The patients filled out the sleep questionnaire including the Epworth sleepiness scale (ESS), Stanford sleepiness Scale (SSS) and Beck depression index (BDI). All of them had brain MRI or CT, and laboratory tests including lipid and coagulation profile. We analyzed the difference of body mass index (BMI), neck circumference (NC), sleep parameters including apnea-hypopnea index (AHI), respiratory disturbance index (RDI) and sleep architectures between OSAHS patients with and without SI brain lesions. We compared risk of SI lesions between subgroups of patients with mild OSA ($5 \leq \text{AHI} < 15$) and with moderate to severe OSA ($\text{AHI} \geq 15$).

Results: Among 55 patients (aged 54.5 ± 9.8 years old, 37 males and 18 females), 26 had SI lesions (SI group) while the other 29 did not (non-SI group). There were no differences in BMI (26.2 ± 3.1 vs. 25.2 ± 2.1 kg/m², $p=0.285$) or NC (39.2 ± 4.1 vs. 38.1 ± 3.2 cm, $p=0.289$). Patients in SI group showed significant decrease in proportion of stage 2 sleep, increased stage 1 sleep and arousal index compared with non-SI group ($p < 0.05$). Lesion subtypes in SI group were small vessel occlusion (78.2%), large artery occlusion (12.7%), and unclassified or both (9.1%). Moderate to severe OSA group showed more frequent SI lesions than mild OSA group (58.5% vs. 14.3%, $p=0.004$) and lower values of the lowest O₂ desaturation ($82.4 \pm 8.0\%$ vs. $89.6 \pm 2.8\%$, $p < 0.001$).

Conclusion: Moderate to severe obstructive sleep apnea contributes to the occurrence of silent ischemic brain lesions, especially small vessel occlusions, associated with oxygen desaturation and nocturnal sleep disruption.

0597

SHORT TERM RESULT OF MANDIBULAR ADVANCEMENT DEVICE IN KOREAN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Retroglossal obstruction and redundancy of the pharyngeal airway are the main causes of surgical treatment failure. Several surgical techniques such as genioglossus advancement and maxillo-mandibular advancement have been introduced to overcome the treatment failure. However, these surgeries cannot be easily accepted in Asians whose jaws are relatively smaller than Caucasians. Mandibular advancement device (MAD) has been used to prevent retroglossal or retropalatal collapse in patients with obstructive sleep apnea (OSA). The aim of this study is to evaluate prospectively the efficacy of MAD in Korean patients with OSA.

Methods: Twenty eight patients (27 males and 1 females; mean age of 51.5 ± 9.8 years) with OSA were included in this study from March through August 2007. Questionnaires for sleep quality and sleepiness and polysomnographic data were assessed before and at least 3 month after intraoral MAD application.

Results: The mean apnea/hypopnea index (AHI) decreased significantly ($p < 0.00001$) from 37.2 to 14.0. The success rate defined by AHI < 10 and 50% reduction of AHI were 46% (14/24) and that defined by AHI < 20 and 50% decrease of AHI were 64% (18/24). Even most of the patients who were not categorized into success group had decreased AHI. Sleep architecture, duration of apnea, duration with O₂ saturation less than 90%, number of snoring and total arousal were improved significantly after treatment without major side effects. Epworth sleepiness scale, sleep position change and lowest oxygen saturation did not change significantly.

Conclusion: MAD improved the nocturnal respiratory function and sleep quality in patients with OSA significantly. MAD can be used as an good alternative because it is noninvasive, easy to manufacture, and has good results in OSA patients.

0598

PREVALENCE AND CLINICAL CHARACTERISTICS OF HYPERTENSIVE PATIENTS WITH HIGH VS LOW RISK OF OSAS

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Introduction: Obstructive sleep apnea syndrome (OSAS) is a risk factor of hypertension as well as other cardiovascular diseases. Earlier studies indicate that CPAP treatment might decrease cardiovascular morbidity and mortality in OSAS patients. It is thus important to identify individuals at risk of OSAS more efficiently than today. The aim of the study was to examine the prevalence of high risk of OSAS in a primary care population with hypertension, as well as to describe clinical characteristics of hypertensives with high vs. low risk of OSAS.

Methods: 46 consecutive patients (40% males) with hypertension ($>140/90$ mmHg) were enrolled from a primary care setting. They completed the Berlin Sleep Apnea Questionnaire (BSAQ), Epworth Sleepiness Scale, Minimal Insomnia Symptoms Scale. Blood pressure, BMI, neck circumference, waist-to-hip ratio and blood samples (lipids, creatinine, blood glucose) were also registered.

Results: 72% of the patients met the BSAQ criteria for high risk of OSAS. They reported a higher prevalence of loud ($p<0.01$) and frequent ($p<0.0001$) snoring, complaints from others regarding snoring ($p<0.0001$), more witnessed apneas ($p<0.05$) and non-restorative sleep ($p<0.0001$). No significant differences were found regarding blood pressure, EDS, blood glucose, lipids, creatinine or antropometric data between the groups.

Conclusion: This study indicates that more than 70% of all patients with hypertension at a primary care clinic might have a high risk of OSAS. The lack of significant differences in other clinical data needs to be interpreted with care, due to the low power of this pilot study.

0599

CLINICAL AND POLYSOMNOGRAPHIC FEATURES IN COMPLEX SLEEP APNEA SYNDROME

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Introduction: Some patients with obstructive sleep apnea syndrome (OSAS) develop problematic central apneas with acute application of continuous positive airway pressure (CPAP), herein called complex sleep apnea syndrome (CompSAS). We sought to compare clinical and polysomnographic (PSG) features between patients with CompSAS and OSAS.

Methods: We performed a retrospective review of patients studied in our sleep disorders center. A total of 270 patients were included in the study. CPAP titration was prescribed in patients with Apnea Hypopnea Index (AHI) ≥ 15 . Patients who developed a central AHI ≥ 5 following titration PSG are diagnosed as CompSAS.

Results: There were 258 patients with OSAS and 12 with CompSAS. Diagnostic apnea-hypopnea index (AHI) was higher in patients with CompSAS. CPAP suppressed obstructive events, but residual AHI, mostly from central apneas, remained high in patients with CompSAS. Average and minimum oxygen saturation was lower in patients with CompSAS. In both diagnostic and titration PSG, the duration of central apneas was longer in patients with CompSAS. Similarly, the number of central apneas was more much in patients with CompSAS in diagnostic PSG. CompSAS patients were less sleepy than OSAS. CPAP titration was prescribed in 83 cases; there were no differences required CPAP pressures between CompSAS and OSAS. When CompSAS patients were compared with OSAS patients for additional conditions, congestive heart failure incidence was higher in CompSAS.

Conclusion: The underlying factors responsible for the development of central events on CPAP in patients with CompSAS are not well understood, but it seems likely that CompSAS patients have more instability in respiratory and/or cardiovascular control at baseline than patients with OSAS. Further research is needed to appreciate more about its pathophysiology, which may help in discovering management strategies.

0600

WORLD TRADE CENTER (WTC) EXPOSURE AND SLEEP DISORDERED BREATHING: IS THERE AN ASSOCIATION?

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Introduction: Pulmonary disease associated with exposure to the World Trade Center (WTC) disaster has been described over the past six years. The FDNY WTC Medical Screening Survey Questionnaire demonstrated a significant increase in a multitude of respiratory symptoms, including a sizeable proportion that resulted from minor upper airway anatomical abnormalities. In addition, twenty-four percent of the firemen answering the survey reported new-onset sleep disturbance. Although

the cause for their sleep-related complaints is likely multifactorial, the high prevalence of upper airway abnormalities in these individuals may place this population at an increased risk for sleep disordered breathing and contribute to their sleep complaints. The objective of this study is to assess if individuals who had exposure to the WTC site have an additional risk of sleep disordered breathing compared with non-exposed sleep clinic patients.

Methods: We reviewed the charts of adult patients who had undergone NPSG at our institution between 2001 and 2007. One hundred and forty-three subjects had WTC exposure and had undergone NPSG. Forty-nine clinical controls without WTC exposure were identified and group matched for age, gender, and BMI. The AHI was the primary outcome measure.

Results: Seventy-six percent of the WTC-exposed group were men, and 59.2% of the clinical controls were men. The groups were similar in BMI and age (WTC mean BMI = 29.9 vs clinic control mean BMI = 31.7 and WTC mean age = 46.6 vs clinic control mean age = 48.0). There was no significant statistical difference in the median AHI for each quartile of BMI - WTC AHI vs CONTROL AHI for each quartile: 1st qrtile: 5.39 vs 5.32, 2nd qrtile: 8.88 vs 9.65, 3rd: 9.3 vs 14.9, 4th: 25.2 vs 20.8. Again, the data was not statistically significant for exposed vs non-exposed within each age group - WTC AHI vs CONTROL AHI for age <40: 13.0 vs 13.8, age 40-49: 14.9 vs 15.8, age >49: 19.0 vs 22.3.

Conclusion: Exposure to the WTC disaster does not appear to be associated with an increased risk for an elevated AHI despite this population having an increased incidence of upper airway abnormalities. Further studies may be warranted to assess for the presence of flow limitation, the risk of more rapid progression to OSAS over time, and if there is an increased association of sleep disordered breathing in WTC exposed individuals compared with healthy controls.

0601

PREVALENT HYPERTENSION AND SLEEP DISRUPTION IN A COHORT OF MIDDLE AGED AND OLDER ADULTS

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Introduction: It is hypothesized that the effects of sleep-disordered breathing (SDB) on health outcomes are mediated through intermittent hypoxemia and/or sleep fragmentation. To parse the relative contribution of these two factors, we compared the frequency of transitions between sleep stages NREM, REM, and Wake as measure of sleep fragmentation among those participants with and without hypertension.

Methods: Sleep was divided into NREM, REM, and Wake and the total number of each possible transition type were calculated for 5,599 participants in the Sleep Heart Health Study. Generalized estimating equations for the relative frequency of each sleep stage transition type comparing hypertensive to normotensive participants were constructed. Hypertension was defined as SBP>140mmHg, DBP>90mmHg, or use of anti-hypertensive medications.

Results: Hypertension was reported in 51.8% of the sample. Higher numbers of Wake-to-NREM and NREM-to-Wake transitions (WN: 26.1±14.5 vs. 24.4±11.3, $p<0.001$, NW: 23.9±14.2 vs. 21.9±1.9, $p<0.001$) and lower numbers of NREM to REM and REM to NREM transitions (NR: 6.3±3.5 vs. 6.7±3.5, $p<0.001$, RN: 3.5±2.9 vs. 3.6±2.7, $p=0.283$) were observed in hypertensives compared to normotensives. In models that adjusted for age, sex, body weight, and AHI, a higher frequency of transitions between NREM and Wake were observed among hypertensive compared to normotensives subjects (WN: relative risk [RR] 1.12, 95% confidence interval [95% CI] 1.12-1.13 and NW: RR 1.11, 95%CI 1.11-1.12). Transitions between NREM and REM were less common in those subject with hypertension (NR: RR 0.81, 95%

Category H—Sleep Disorders – Breathing

CI 0.80-0.82, and RN: RR 0.70, 95% CI 0.69-0.71) compared to those without.

Conclusion: A greater degree of sleep disruption was associated with prevalent hypertension, even after adjustment for several confounders. These findings suggest that sleep fragmentation may contribute to SDB-related cardiovascular outcomes. Further research is needed to determine whether sleep disruption as a predictor of incident disease.

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0602

GENDER DIFFERENCES IN PRESCRIBED MEDICATIONS IN SLEEP DISORDERS PATIENTS

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Introduction: Medications significantly affect sleep and may exacerbate, cause or ameliorate a sleep disorder. There have been few epidemiological studies on gender differences for prescribed medications for sleep disorders patients.

Methods: A retrospective analysis was conducted for gender differences in prescribed medications for sleep disorders patients. The data was analyzed for two ICSD-2 codes, Obstructive Sleep Apnea (OSA) and Periodic Limb Movement Disorder (PLM).

Results: The percentage differences in prescribed medications for 1651 consecutive patients (641 females, 1010 males) were analyzed for drug class, OSA and PLM. For OSA patients 29.3% were female and 70.7% were male. Hypnotic medications were prescribed for 3.9% of females and for 4.6% of males. Antidepressant medications were prescribed for 40.9% of females and for 16.6%. 16.5% of females were on respiratory medications as compared to 9.5% of males. Analgesics were prescribed for 29.1% of females and for 17.6% of males. 63.0% of females were on cardiac medications compared to 61.9% of males. Gastrointestinal medications were prescribed for 34.7% of females and for 27.8% of males. 18.9% of females were on diabetic medication as compared to 17.6% of males. For PLM patients 9.4% of females were on hypnotics compared to 5.6% of males. Antidepressants were prescribed for 45.1% of females and for 24.0% of males. 12.5% of females were on respiratory medications as compared to 10.0% for males. Analgesics were prescribed for 33.6% of females and for 14.1% of males. Cardiac medications were prescribed for 61.1% of females and for 66.3% of males. Gastrointestinal medications were prescribed for 40.6% of females and for 27.2% of males. 61.1% of females were taking diabetic medications as compared to 66.3% for males.

Conclusion: Further research is indicated to determine the effects of medications on gender differences in sleep disorders patients. The significant gender differences in antidepressant use for OSA patients is of importance in designing treatment protocols.

0603

SNORING, INSOMNIA AND SUBCLINICAL ATHEROSCLEROSIS IN THE NORTHERN MANHATTAN STUDY (NOMAS)

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Introduction: Sleep disordered breathing is associated with stroke, but its association with subclinical atherosclerosis is controversial. Increased carotid artery Intima-Media Thickness (IMT) is a marker for subclinical atherosclerosis and an independent risk factor for vascular disease. Habitual snoring is a symptom of sleep disordered breathing and, along with insomnia, is a common sleep-related complaint. The aim of our study was to determine the relation between snoring, insomnia and carotid IMT.

Methods: As part of NOMAS, an ongoing prospective population-based study to determine incidence, risk factors and outcomes of stroke, 750 stroke-free participants (mean age 65 +/- 8 years; 38% men; 60% Hispanic, 25% black, 32% white) with carotid IMT measurements who provided responses to a sleep questionnaire were analyzed. Habitual snoring was defined as self-reported snoring > 4 times per week. The presence of insomnia was based on the sum of responses to three items on the Hamilton rating scale for depression. Carotid IMT was assessed by high-resolution B mode ultrasound and calculated as a composite measure of the common and internal carotid arteries and carotid bifurcation. Multivariate linear regression models were used to identify relations between snoring, insomnia and carotid IMT.

Results: Habitual snoring was present in 29.3%, and insomnia in 24.5% subjects. The mean total carotid IMT in the group was 0.97 +/- 0.12 mm; 0.96 +/- 0.12 mm among those with habitual snoring and 0.97 +/- 0.13 mm among those with insomnia. After controlling for age, gender, race, ethnicity, BMI, hypertension, diabetes, smoking, LDL, HDL and presence of cardiac disease, snoring (parameter estimate = -0.003, p=0.76) and insomnia (parameter estimate = 0.019, p=0.08) were not independently associated with increased carotid IMT.

Conclusion: Self-reported snoring and insomnia were not associated with subclinical atherosclerosis in our study. This observation is in accordance with the recently reported results from the Sleep Heart Health Study.

0604

EFFICACY OF VARIABLE POSITIVE AIRWAY PRESSURE (VPAP) TREATMENT ON SYMPTOMATIC PATIENTS WITH COMPLEX SLEEP APNEA WHO FAIL CPAP AND BIPAP

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Introduction: Complex sleep apnea is a less common subtype of sleep apnea that so far has been relatively difficult to treat with conventional CPAP and BIPAP therapy. Significant cardiac disease or chronic opiate therapy have been reported to be strong associations in most but not all patients. Variable positive airway pressure therapy (VPAP; RESMED) is a relatively new treatment modality recently available for treatment of these patients.

Methods: Charts of 11 patients diagnosed (Medicare criteria) over the last year with complex sleep apnea were reviewed. All of these patients had symptoms of witnessed apnea, chronic sleepiness and fatigue. On polysomnography or low pressure positive pressure titration, they all had frequent arousals and significant desaturations due to central apneas not correctable by CPAP and BIPAP therapy. The lowest pretreatment Central apnea Index for the group was 47/hr and 10/11 patients had desaturations below 82%. The End expiratory pressure (EEP) that improved the apnea index by more than 80% was selected for home therapy.

Results: In eight patients (72.7%) with excellent compliance, significant improvement was noted in fatigue, daytime sleepiness and Epworth scores following home VPAP therapy at 2 or more months. One patient discontinued use due to claustrophobia. No change was noted by one patient who continued to use the device and one patient had poor compliance due to multiple unrelated hospital admissions. The mean EEP for the group was 6 and all had minimum and maximum pressure support of 3 and 10 cm water respectively. Cardiac disease appeared to be the underlying cause in most (63%).

Conclusion: Symptomatic complex apnea is more common in patients with cardiac disease and appears to be eminently treatable with VPAP. Daytime sleepiness, fatigue and Epworth scores all appear to improve significantly. Whether this clinical improvement translates to improved cardiac survival remains to be seen.

0605

NOCTURNAL BRUXISM AS A PROTECTIVE MECHANISM AGAINST OBSTRUCTIVE BREATHING DURING SLEEP

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Introduction: Nocturnal Bruxism, defined as TMJ discomfort on awakening or witness grinding or clenching during sleep, is recognized to occur in many patient with OSA. In some, this is to the degree that results in chronic pain. Clinical experience has demonstrated improvement in Bruxism following treatment with CPAP. We sought to identify the frequency of the relationship between Bruxism and Sleep Related Breathing disorders and the response in Bruxism by treating with CPAP.

Methods: We retrospectively reviewed 571 consecutive charts of patients diagnosed with OSA and prescribed CPAP therapy at the Sadler Clinic Sleep Disorders Center at least six months prior to our assessment. All patients filled out a sleep questionnaire that assessed for nocturnal Bruxism, plus the information from the history was utilized for inclusion in the study. NPSG testing with performed on all patients to establish the diagnosis of OSA. We included patients tested with the addition of the Pes and found to have the UARS in our OSA group. A follow up questionnaire was utilized to assess outcome for this study.

Results: Of the 571 OSA patient charts reviewed: 139 had Bruxism (24% of the OSA population). 95 patients were successfully contacted for follow up questioning by phone. 69 stated using CPAP to some degree of which 56 reported nightly use (100% compliant). 26 patients were not using CPAP. Of all those using CPAP, 35 stated Bruxism improved (50.1%) Of those 100% compliant with CPAP 32 stated Bruxism improved (57%) Of those not using CPAP only 5 stated Bruxism improved (19.2 %).

Conclusion: We postulate that nocturnal Buxism is a compensatory mechanism of the upper airway to help overcome upper airway obstruction by activation of the clenching muscles which results in bringing the mandible, and therefore the tongue, forward. We recognize that this process may reduce the obstruction and therefore increasing the need for adding Pes (Pressure in the esophagus) monitoring to NPSG testing. This is why we included patients with the UARS in our OSA group. After treating the airway with CPAP this protective mechanism is no longer needed and over time the Bruxism resolves. This study suggests such a compensatory mechanism is the etiological force behind nocturnal Bruxism in many patients. Additional assessment of this relationship is in progress and may result in earlier identification of those patients with sleep related obstructive breathing.

0606

ORAL APPLIANCES TITRATION FOR OSAS: IS THERE ANY PREDICTABLE VARIABLE?

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Introduction: The efficacy of oral appliance for mild and moderate Obstructive Sleep Apnea Syndrome (OSAS) has been proved by many Level I and II evidence studies, but most predictor factors of success are still unknown. We analyzed if OSAS severity, patients age and/or Body Mass Index (BMI) could be predictor factors of the necessary amount of mandibular advancement for the success of the treatment (AHI<5/h) with the oral appliance ARMIO-BR.

Methods: Seventy-six consecutive patients with polysomnographic diagnosis of OSAS were referred for ARMIO-BR protocol. Forty-five achieved success with the treatment (6F/39M), baseline AHI

22.7(±11.7)/h and AHI 1.8(±1.4) after ARMIO-BR titrated, mean age 49.5(±11.9) years, BMI 27.5(±3.9)kg/m², 14 patients with mild, 20 with moderate and 11 patients with severe OSAS, considering the AASM criteria. We compared the amount of mandibular advancement with ARMIO-BR titrated between mild and moderate OSAS patients, mild and severe OSAS patients and between moderate and severe OSAS patients. We also compared patients with BMI ≤ 25kg/m² to obese patients (BMI>30kg/m²) and the adults (20-59 years) and aged patients (≥ 60years old). Statistical analysis was scored by T-test.

Results: There was no significant statistical difference in the final mandibular advancement between mild and moderate OSAS patients (p=0.12) neither between mild and severe OSAS patients (p=0.34), and between moderate and severe OSAS patients (p=0.75). Comparing the amount of mandibular advancement between patients with BMI ≤ 25kg/m² to obese patients (BMI>30kg/m²) and between adults (20-59 years) and aged patients (≥ 60years old), statistical difference was not found either.

Conclusion: These results do not indicate that OSAS severity, BMI and patients age could be predictive factors of the necessary amount of mandibular advancement to achieve treatment success with ARMIO-BR and the dentist should still consider the titration protocol to achieve the maximum mandibular advancement with comfort for each patient.

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0607

PERSISTENCE OF CYCLIC VARIATION IN HEART RATE (CVHR) IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA TREATED WITH OPTIMAL CPAP

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Introduction: Cyclic variations of heart rate (CVHR) are fluctuations of the heart rate (HR) occurring with obstructive apneas and hypopneas. We tested whether CVHR persists in treated OSAHS patients despite optimal CPAP therapy.

Methods: To determine whether CVHR persists after successful CPAP titration, we extracted ECG tracings from forty split night studies and scanned them on a Holter analyzer (MARS 8000, GE Medical Systems, Milwaukee, WI). CVHR was measured from a plot of normal-to-normal interbeat intervals during the 2 hr diagnostic period and again during ~2 hrs of optimal CPAP titration using a program written in MatLab (Mathworks, Natick, MA). CVHR specifically associated with clinically scored PSG events (respiratory events and periodic leg movements) was also determined. CVHR was defined as ≥6 bpm change in HR lasting for ≥10 sec, but ≤1 minute.

Results: Mean apnea-hypopnea index (AHI) was 32.6 during the diagnostic portion of the study and 1.1 during optimal CPAP. There were almost four times as many CVHR-based events compared to PSG-based events. Optimal CPAP was associated with a reduction of CVHR events from baseline (217±86/hr vs. 93±61/hr). However, optimal CPAP did not abolish CVHR in the majority of patients. During optimal CPAP titration: 5 patients had ≤ 5 events/hr, 3 had 6-15 /hr, 4 had 15-25 /hour, 10 had 25-50 /hr and 18 had > 50 CVHR/hr during optimal CPAP. When CVHR during optimal titration was limited to episodes associated with PSG scored events there were many fewer events: 27 patients had ≤ 5 CVHR events/hr, 8 had 6-15/hr and 5 had ≥15/hr (range 26-87).

Conclusion: Patients have persistent CVHR despite optimal CPAP. CVHR likely reflects continued sub-clinical respiratory events associated with autonomic arousals that do not meet current PSG scoring criteria for clinical events. Titrating CPAP to eliminate the sub-clinical respiratory events associated with CVHR could potentially improve clinical symptoms and compliance.

0608

RAPID EYE MOVEMENT (REM) SLEEP RELATED OBSTRUCTIVE SLEEP APNEA- DO WE NEED TO TREAT IT?

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Introduction: Patients with rapid-eye-movement sleep-related obstructive sleep apnea (REM-OSA) are often not treated due to a relatively low total apnea-hypopnea index (AHI) and due to perceived lack of benefit on symptoms. We tested the hypothesis that REM-OSA results in similar clinical symptoms as OSA in general and that treatment of this condition with continuous positive airway pressure (CPAP) would improve these symptoms.

Methods: Patients who fulfilled criteria for REM-OSA (total AHI \leq 15.0 events/hour, REM-AHI \geq 10.0/hr, non-rapid eye movement (NREM) AHI \leq 10.0/hr, ratio of REM-AHI to non-REM AHI of \geq 2.0 and REM sleep duration $>$ 15% of total sleep time) were identified from overnight polysomnography (PSG) records at our center between September, 2003 and December, 2005. Obstructive apneas were scored if there was $>$ 90% decrement in airflow for $>$ 10 seconds and hypopneas were scored if there is 50-90% decrement in the nasal pressure transducer channel for $>$ 10 seconds with concurrent oxygen desaturation $>$ 3% or EEG arousal.

Results: Of 1268 patients undergoing PSGs, 182 had REM-OSA. Forty met criteria for mild REM-OSA (REM AHI of 10-15/hour), 101 for moderate REM-OSA (15.1-30/hour) and 41 for severe REM-OSA ($>$ 30/hour). Patients with more severe REM-OSA had a higher BMI ($p < 0.0001$). The groups did not differ in medical co-morbidities (hypertension, coronary artery disease and diabetes) or Epworth Sleepiness Scale score (mean $>$ 10 in all groups). Patients with mild REM-OSA were least likely to receive CPAP treatment, with only 50% receiving CPAP, compared to 81% of more severely affected patients ($p < 0.0006$). Of the patients who received CPAP machines, 40.0% of mild REM-OSA, 41.4% of moderate REM-OSA, and 37.5% of severe REM-OSA patients reported treatment benefit with no significant difference in the three groups.

Conclusion: Regardless of their total AHI, patients with REM-OSA experience daytime sleepiness and benefit from treatment with CPAP, although many are not treated.

0609

THE EFFECT OF BODY MASS INDEX ON OBSTRUCTIVE SLEEP APNEA SEVERITY AND CONTINUOUS POSITIVE AIRWAY PRESSURE COMPLIANCE IN WEST VIRGINIA

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Introduction: Obstructive sleep apnea (OSA) is a common condition in morbidly obese patients. Obesity is a common problem in West Virginia and the Appalachian area. The goals of the current study are to explore the relationship between BMI and both OSA severity, and Continuous Positive Airway Pressure (CPAP) compliance in our patients' population.

Methods: Medical records were surveyed for all subjects who had a diagnosis of OSA treated with CPAP and followed with available compliance card. The database was reviewed for subject's demographic data, weight, height, PSG finding, and compliance card report. BMI was quantified in five categories (underweight, normal BMI, overweight, obese, and morbidly obese). The relationship between BMI and OSA severity and CPAP compliance was studied using Person correlations coefficient with BMI dummy coded (0-5).

Results: Out of 469 charts reviewed, 182 patients were included in the study. Subjects' mean age was 49.76 kg/m² (SD=12.26). Mean BMI was 38.39 (SD= 9.31, range= 18.5- 65.7). The mean BMI was significantly lower for males 36.80 (SD= 8.86), than females 40.46 (SD=9.52) ($p=0.08$). Only 7 subjects (3.8%) had normal BMI, one (0.5%) was underweight, 26 (14.3%) were overweight, 73 (40.1%) were obese, and 75 (41.2%) were morbidly obese. BMI correlated significantly with age ($r = -0.27$, $p=0.001$), AHI ($r = 0.25$, $p=0.001$), SaO₂ during sleep ($r = -0.15$, $p=0.04$), and CPAP pressure needed to treat the OSA ($r = 0.28$, $p=0.002$). The correlations between BMI and subjective rating of sleepiness ($r = 0.12$, $p=0.38$), the average hours of device used ($r = -0.03$, $p=0.60$) and the percent of days the device was used $>$ 4 hrs/day ($r = -0.047$, $p=0.53$) were not significant.

Conclusion: In our patient population with OSA, most of the patients were overweight or obese. Higher BMI was related with increased severity of OSA, but did not affect CPAP compliance. Larger studies should be conducted to confirm these findings.

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0610

INCREASED MALLAMPATI GRADE IS ASSOCIATED WITH PREGNANCY-INDUCED HYPERTENSION

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Introduction: Increased Mallampati grade is associated with sleep-disordered breathing (SDB). SDB has been shown to be an independent predictor of hypertension in several epidemiological studies. None of these studies included pregnant women. We therefore sought to determine whether Mallampati grade – as a proxy of SDB – is associated with pregnancy-induced hypertension (PIH).

Methods: A retrospective review of both the University of Michigan Obstetrics and Obstetric Anesthesiology clinical databases was performed for all women presenting to the Labor and Delivery unit for an 18-month period prior to November 2007. Mallampati grades I/II were considered low risk for SDB and grades III/IV were considered high risk for SDB. PIH was considered present if systolic or diastolic blood pressures were above 140 and/or 90mmHg respectively after 20 weeks of gestation.

Results: A total of 5389 obstetric charts were reviewed. Seven percent of women had a Mallampati grade III/IV. Such women were more likely to be older (30.2 \pm 6.0 years vs. 29.2 \pm 5.9 years, $p \leq 0.001$), have a higher pre-pregnancy body mass index (BMI; 25.1 \pm 11.1 vs. 22.8 \pm 8.9, $p \leq 0.001$), but no difference in third-trimester BMI. Twelve percent of women had PIH. Mallampati grade III/IV independently predicted PIH, with an adjusted odds ratio of 1.7 (95% Confidence Interval 1.2-2.2, $p \leq 0.001$).

Conclusion: A Mallampati grade of III/IV, as a proxy measure of SDB risk, independently predicts adverse maternal outcome as defined as pregnancy-induced hypertension. Use of a routine physical examination technique to identify pregnant women at risk for SDB may have great cost-effective, clinical utility.

0611

COMPREHENSIVE SLEEP APNEA DISEASE-SEVERITY INDICES PREDICT CPAP USE BETTER THAN BASELINE APNEA-HYPOPNEA INDEX OR DAYTIME SLEEPINESSBalakrishnan K^{1,2}, James KT^{2,1}, Weaver EM^{1,2}¹Otolaryngology - Head & Neck Surgery, University of Washington & Harborview Medical Center, Seattle, WA, USA, ²Sleep Apnea Research Group, University of Washington & Harborview Medical Center, Seattle, WA, USA

Introduction: The benefits of continuous positive airways pressure (CPAP) depend on adequate use. While various disease burden measures (apnea-hypopnea index (AHI) and subjective measures) predict use, none is superior statistically or clinically. This cohort study evaluates the validated, comprehensive Sleep Apnea Severity Index (Index) as a predictor of CPAP use. The Index combines physiologic (AHI, lowest oxyhemoglobin saturation), subjective (daytime sleepiness), anatomic (pharyngeal morphology), and anthropometric (obesity) measures of disease burden into a single three-stage index score. We also tested a modified Index, replacing pharyngeal morphology with a validated tonsil-size measure.

Methods: We hypothesized that the baseline Index and modified Index predict average nightly objective CPAP use better than baseline AHI or Epworth Sleepiness Scale at 6 months \pm 2 weeks after diagnosis. We collected baseline data (Index, confounding variables) at the time of diagnostic polysomnography, and 6-month data (objective CPAP use, questionnaire) by mail. Spearman correlations with bootstrapped 95% confidence intervals (CI) evaluated univariate associations; multivariate regression adjusted for predetermined confounders.

Results: We studied 237 adult newly diagnosed sleep apnea patients from the Seattle Sleep Cohort with mean age 47 ± 12 years, 55% male, mean AHI 54 ± 30 events/hour, and mean 6-month CPAP use 74 ± 138 minutes/night. Fifty-five patients (23%) did not use CPAP at all at six months. Six-month CPAP use correlated with baseline Index ($r=0.15$, 95% CI [0.005, 0.29]) and modified Index ($r=0.14$, 95% CI [-0.002, 0.29]) significantly better than with AHI ($r=0.04$, 95% CI [-0.10, 0.17]) ($p<0.05$) or Epworth Sleepiness Scale ($r=0.04$, 95% CI [-0.09, 0.18]) ($p<0.05$). Multivariate regression confirmed these findings.

Conclusion: We previously showed that the Sleep Apnea Severity Index and the modified Index reflect baseline disease better than AHI. These results suggest they also anticipate CPAP use 6 months post-diagnosis better than AHI or Epworth Sleepiness Scale, providing prognostic value beyond initial evaluation.

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0612

WEIGHT LOSS AFTER BARIATRIC SURGERY IMPROVES, BUT DOES NOT RESOLVE OBSTRUCTIVE SLEEP APNEALettieri CJ^{1,2}, Eliasson AH^{1,2}, Greenburg DL²¹Pulmonary, Critical Care and Sleep Medicine, Walter Reed Army Medical Center, Washington DC, DC, USA, ²Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD, USA

Introduction: Weight loss can reduce the severity of obstructive sleep apnea but may not resolve this disorder. We sought to determine the effects of surgical weight loss on the presence and severity of obstructive sleep apnea in obese individuals.

Methods: Prospective cohort study of consecutive patients referred for sleep evaluations prior to bariatric surgery after screening positive for excessive daytime sleepiness (Epworth Sleepiness Scale >10) and clinically suspected sleep apnea. Polysomnography was obtained prior to and one year following surgery. We compared the effects of surgical weight loss on body-mass index, respiratory disturbance index and continuous positive airway pressure requirements. We also assessed compliance with postoperative CPAP use.

Results: Twenty-four individuals were enrolled. Mean age was 47.9 ± 9.3 years and 75% were women. Obstructive sleep apnea was identified pre-operatively in all subjects, 16 (67.7%) of which had severe disease. Surgical weight loss significantly reduced weight and apnea severity. Body-mass index decreased from 51.0 ± 10.4 to 32.1 ± 5.5 Kg/m² ($p<0.001$) and respiratory disturbance index decreased from $47.9 \pm 33.8.0$ to 24.5 ± 18.1 events/hour ($p<0.001$). We also observed improvements in CPAP requirements (11.5 ± 3.7 to 8.4 ± 2.1 cmH₂O; $p=0.001$), Epworth Sleepiness Scale (15.0 ± 5.0 to 10.6 ± 4.0 ; $p<0.001$) and nocturnal oxygen saturation nadirs (76.5 ± 12.1 to 84.5 ± 5.8 ; $p=0.004$). However, 23 of 24 96% of subjects still met criteria for obstructive sleep apnea syndrome. Most patients continued to have either moderate ($n=11$; 41.7%) or severe ($n=7$; 29.2%) disease. In addition, 20 (83.3%) had persistent nocturnal hypoxia (oxygen saturation $<90\%$). Compliance with CPAP postoperatively was poor and was used by only 5 patients with persistent sleep apnea.

Conclusion: Surgical weight loss significantly reduces a patient's respiratory disturbance index. However, most patients continue to have moderate or severe obstructive sleep apnea. As such, bariatric surgery should not be considered a curative procedure and continued use of CPAP post-operatively should be encouraged.

Support (optional): None

0613

ESZOPICLONE IMPROVES THE QUALITY OF POLYSOMNOGRAPHY: A PROSPECTIVE, RANDOMIZED, PLACEBO-CONTROLLED TRIALLettieri CJ^{1,2}, Quast TN¹, Eliasson AH^{1,2}¹Pulmonary, Critical Care and Sleep Medicine, Walter Reed Army Medical Center, Washington, DC, USA, ²Medicine, Uniformed Services University of the Health Sciences, Bethesda, MD, USA

Introduction: Poor sleep during polysomnography can result in unsatisfactory studies. Incomplete CPAP titration causes difficulties in prescribing therapeutic pressures. Non-benzodiazepine hypnotics improve sleep efficiency without disrupting sleep architecture or exacerbating sleep-disordered breathing. We hypothesized that premedication with eszopiclone would improve sleep duration and continuity, thereby improving polysomnographic quality.

Methods: We conducted a prospective, double-blinded, randomized, placebo-controlled trial assessing the quality of polysomnography with eszopiclone premedication. We compared sleep latency, efficiency, total sleep time and apnea-hypopnea index between eszopiclone 3mg or matching placebo. We also compared rates of inadequate studies between groups, defined as insufficient sleep time (<120 minutes or sleep efficiencies $<70\%$) or incomplete CPAP titrations (>5 events/hour on the highest CPAP or complete intolerance).

Results: We enrolled 226 subjects, 113 received eszopiclone and 113 placebo. Eszopiclone premedication significantly improved all measured variables. The eszopiclone group experienced reduced sleep latency (21.7 ± 27.1 vs. 32.6 ± 38.2 minutes, $p=0.014$), improved sleep efficiency ($87.6 \pm 10.8\%$ vs. $78.1 \pm 15.6\%$, $p<0.001$), less wake after sleep onset (39.2 ± 31.9 vs. 64.5 ± 45.4 minutes, $p<0.001$) and prolonged sleep time (346.5 ± 53.1 vs. 312.2 ± 64.2 minutes, $p<0.001$). Sleep efficiencies $\leq 70\%$ were significantly more common with placebo (21.2% vs. 7.1%, $p=0.004$). Eszopiclone facilitated greater ablation of events during CPAP titration. Residual events were lower (5.7 ± 10.3 vs. 11.9 ± 19.6 , $p=0.02$) and incomplete CPAP titrations were less frequent (31.1% vs. 48.0%, $p=0.04$) with eszopiclone. Both non-usable (7.1% vs. 2.7%, $p=0.22$) and poor quality studies (46.0% vs. 26.5%, $p=0.004$) were more common with placebo. Eszopiclone was associated with a number needed to treat of only 5 to prevent one poor quality sleep study and 23 to prevent one non-usable study. Side effects were uncommon and did not differ between groups.

Conclusion: Pretreatment with eszopiclone significantly improved polysomnographic quality and CPAP titrations. Eszopiclone may im-

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prove patients overall experience in the sleep lab and decrease the need to repeat polysomnograms.

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0614

ANTIHYPERTENSIVE MEDICATION BURDEN AS A RISK MARKER OF OBSTRUCTIVE SLEEP APNEA

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Introduction: Despite being considered an independent risk factor for cardiovascular disease, obstructive sleep apnea (OSA) is significantly under-recognized in the general clinical setting. Established clinical markers are necessary to help improve the identification of individuals at high-risk for OSA.

Methods: We sought to investigate the association between antihypertensive medication burden and sleep apnea presence and severity in a cohort of 496 subjects (mean age=59 years, 65% female, 38% African American) at risk for CVD (Heart SCORE). At-home overnight portable monitoring (ApneaLink™) for determination of apnea hypopnea index (AHI) was performed [0 to 5 = normal (n=157), 6 to 15 = mild OSA (n=217), > 15 = moderate to severe OSA (n=122)]. The number and type of antihypertensive medications (BP meds) taken was documented.

Results: Subjects taking ≥ 2 BP meds (n=52) had a higher frequency of AHI ≥ 6 (83%) compared to 1 BP med (n=125, 74%) and no BP meds (n=319, 64%), $p<0.0001$; odds ratio of 1.96 and 3.73 for 1 and ≥ 2 BP meds, respectively. In analysis of covariance controlling for age, gender, race, BMI, diabetes, LDL, history of hypertension, and normal or abnormal BP subjects taking ≥ 2 BP meds had more severe OSA (adjusted mean AHI=14.6) compared to those taking 1 BP med (adjusted mean AHI = 12.9) or no BP meds (adjusted mean AHI = 10.2), $p=0.02$. Beta-blockers were the most commonly reported BP meds in OSA subjects and were used in 30% of individuals with moderate to severe OSA, followed by ACE inhibitors (18%), calcium channel blockers (14%), and other BP meds (18%).

Conclusion: In this study we identified the number of BP meds as a potential independent marker of OSA presence and severity. Screening for OSA should be strongly considered in patients on any BP medication and particularly in patients on ≥ 2 BP meds.

0615

SHORT TERM USE OF CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) REDUCES PAIN, PARTICULARLY IN WOMEN AND PATIENTS TAKING PAIN MEDICATION

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Introduction: Chronic pain affects one in five patients. Sleep disturbances including reduced sleep efficiency, increased stage 1 and non-REM sleep are common in patients with pain disorders. Poor sleep might contribute to lowering pain thresholds and to hyperalgesia (Roehrs et al 2006). In this study, we examined the 1) prevalence and severity of pain in patients with and without sleep apnea, and 2) short term effects of CPAP use on pain.

Methods: Following IRB approval, we retrospectively examined 250 polysomnographically diagnosed patients with sleep apnea (AHI >20) and compared them with 250 patients without sleep apnea (AHI <5). Patients rated pain on a 0-10 scale before and after diagnostic polysomnography. Sleep apnea patients began CPAP during their baseline PSG, (split-night) or during a second night of CPAP titration (46%).

Results: Forty-seven percent of sleep apnea patients (mean AHI = 68) reported baseline pain of 1 or more versus 58% without sleep apnea (mean pain score = 1.7 and 2.0 respectively, $p=ns$). Compared to baseline, split-night ($p<0.001$) and second night CPAP titrations ($p=0.016$) decreased pain ratings in apnea patients. Significant predictors of pre-sleep pain in sleep apnea patients included higher BMI, arthritis, depression, fibromyalgia, and lower education. In split-night studies, women (decrease = 1.2, $p=0.01$) and those taking pain medications at baseline (decrease = 2.1, $p=0.002$) had the greatest reduction in pain after CPAP treatment. Over both types of titration, CPAP decreased women's pain by 0.9, $p=0.01$ and of those taking pain medications by 1.7, $p=0.002$.

Conclusion: More sleep disorders center patients (apnea and non apnea) report pain than the general population and use of CPAP reduces pain. Potentially, CPAP mediated sleep improvements e.g. REM rebound, sleep consolidation, reduce pain. Study limitations include no CPAP-placebo control and only one post CPAP pain rating in the morning after titration.

Support (optional): Internal

0616

EARLY PREDICTORS OF COMPLIANCE IN SLEEP APNEA PATIENTS TREATED WITH CONTINUOUS POSITIVE AIRWAY PRESSURE

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Introduction: Effectiveness of Continuous Positive Airway Pressure (CPAP) as a treatment for Obstructive Sleep Apnea (OSA) can be limited by poor compliance. Our goal is to explore retrospectively the effect of 41 pre-CPAP predictors, individually and in combinations, on short-term compliance. We plan to specify a combination of factors that may predict with high sensitivity and specificity high-risk population for non-compliance and to target this group with an early intervention.

Methods: All adult OSA patients with available compliance cards following with our sleep center were included. The database was reviewed for suggested pre-CPAP predictors including demographic data, medical, mental and substance abuse history, physical exam, and other possible predictors of PSG findings. The relationship between the predictors and three compliance measures (average hours of device use, percent of days more than 4 hours use and percent of days the device was used) were investigated using Pearson correlation coefficient, independent sample-t test and one-way ANOVA.

Results: 190 subjects were included in the final analysis, 80 females (42.1%). Age range was between 20 and 89, Mean age= 49.89 (12.21). Being a male and living with a spouse correlated significantly with a higher number of hours of CPAP use ($p=0.02$ and 0.03) but not with the other two measures of compliance. Previous palatal surgery correlated significantly with percent of days the device was used ≥ 4 hrs ($p=0.037$). Apnea Hypopnea Index (AHI) correlated positively and significantly with the three measures of compliance ($p=0.04$, $p=0.006$ and $p=0.019$). Lowest SaO₂ correlated negatively and significantly with compliance. Other predictors are discussed individually and in combination.

Conclusion: Male gender, living with a spouse, previous palatal surgery, higher AHI, and lower lowest SaO₂ during PSG predicted early CPAP compliance. We suggest a pre-CPAP evaluation form to predict compliance with accepted sensitivity and specificity and are in the process of collecting more data.

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0617

PREDICTORS OF AN UNSUCCESSFUL TITRATION IN SPLIT-NIGHT POLYSOMNOGRAMSCohen D¹, Hershner SD¹, Consens FB¹, O'Brien LM²¹Departments of Neurology, Michael S. Aldrich Sleep Laboratory, University of Michigan, Ann Arbor, MI, USA, ²Department of Oral & Maxillofacial Surgery, University of Michigan, Ann Arbor, MI, USA

Introduction: Split-night polysomnograms (PSG) are used to expedite the diagnosis and treatment of obstructive sleep apnea. A major limitation is that they are not always successful and a retitration may be required. We sought to determine if specific variables may predict which patients are more likely to have an unsuccessful split-night PSGs.

Methods: 18 months of split night polysomnogram data was reviewed. Studies were excluded if they were not initial studies, the patient refused Continuous Positive Airways Pressure (CPAP), did not meet split-night criteria, or had incomplete data. Subsequent titration PSGs were also reviewed for those whose split-night PSG was not successful, in order to obtain final CPAP pressures for all subjects.

Results: A total of 402 studies were initially identified and 209 subjects (71% male) fitted the above criteria. Thirty-seven subjects (21%) had unsuccessful split-night PSGs. Similar proportions of men and women required a further titration study (16.9% vs. 19.7% respectively). Subjects whose split-night PSGs were unsuccessful had a higher body mass index (BMI; 41.6±10.3 vs. 36.4±9.4), age (53 +/- 11.4 v 50 +/- 12.7 years old), and a higher apnea/hypopnea index (AHI; 33.5±22.5 vs. 22.6±14.8, p=0.027). BMI and age significantly predicted an unsuccessful split-night PSG (R²=0.107, p=0.001). Neither AHI or gender were in the model. A BMI≥30 was associated with a split-night failure (p=0.004). In a linear regression to determine variables associated with the final CPAP pressure required, regardless of whether this pressure was reached during the split-night or retitration PSG, AHI and BMI were significant predictors (R²=0.23, p<0.001).

Conclusion: Disease severity was not found to play a significant role in determining which subjects had unsuccessful split-night studies. Rather, increasing BMI and advancing age were predictive of an unsuccessful split-night study. Although the overall majority of split-night studies were successful, physicians may want to reconsider ordering split-night studies on older patients with BMI >30.

0618

THE EFFICACY AND COST OF PRE-OPERATIVE SCREENING FOR OSAHSFriedman M^{1,2}, Soans R², Osei M², Soans R²¹Department of Otolaryngology, Rush, Chicago, IL, USA, ²Department of Otolaryngology, Advocate Illinois Masonic Medical Center, Chicago, IL, USA

Introduction: The increased risk of perioperative complications in patients with OSAHS is well known. The ASA has established practice guidelines with clear recommendations for patients identified as having OSAHS. Most institutions, however, have not established any formal screening programs to identify patients. The purpose of the study is to propose and test a formal screening program and to estimate the cost and efficacy of the program.

Methods: A prospective non-randomized controlled study. An IRB approved screening program was instituted at a tertiary care teaching hospital. 350 consecutive pre-operative patients were "re-screened," after informal screening by the anesthesia resident. The formal re-screening was comprised of two components: (1) the Berlin questionnaire administered by one of the authors, and (2) physical findings, identifying the Friedman Tongue Position (formerly the Modified Mallampati Position), tonsil size and neck circumference. The number of patients identified as high risk was compared for three screening techniques: (1) informal resident history, (2) Berlin Questionnaire, (3) The Berlin Questionnaire combined with physical findings.

Results: The informal screening based on resident history identified 30 of 350 patients as being high risk for sleep apnea (8.5%). The use of the Berlin questionnaire increased the number of patients identified to 95 of 350 (27.2%). By using both the Berlin Questionnaire and physical findings of Friedman Tongue Position, BMI and tonsil size, the number of patients increased to 104 of 305 (29.7%). The mean time required (and therefore the cost) of having a medical professional to administer the Berlin questionnaire and examine for physical findings was 4 minutes per patient.

Conclusion: Formal pre-operative screening with a validated technique such as the Berlin questionnaire combined with Friedman Tongue Position results in a highly effective screening process that identifies patients at high risk for OSAHS. However this formal screening process is associated with extra time and extra cost.

0619

RELATIONSHIP BETWEEN WEIGHT AND NECK CIRCUMFERENCE AND SLEEPINESS IN DIVISION I-A COLLEGE FOOTBALL PLAYERS

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Introduction: Studies have shown that individuals who are overweight may be at a higher risk for developing obstructive sleep apnea syndrome (OSAS) than those at a normal weight. The Epworth Sleepiness Scale (ESS) is an accepted indicator of individual sleepiness. In this study, we studied a population of college football players to determine whether degree of sleepiness increased with increasing weight and/or neck circumference.

Methods: All 12 Atlantic Coast Conference college football programs were invited to participate. All players surveyed were active team members during the 2006-2007 football season. The players were asked to complete a survey which included an Epworth Sleepiness Scale, and questions about weight and neck size.

Results: 560 players consented to the study of which we received 547 completed surveys. The surveys demonstrated a player weight range of 150-365 lbs. (X= 234.5 ± 48.9 lbs.), neck size of 35.6-66.0 cm (X=44.8 ± 3.8 cm), and an ESS score range of 0-21 (X=9 ± 3.9). The correlation coefficient when comparing weight and ESS score was -0.1480. The correlation coefficient when comparing neck size and Epworth score was -0.0036. We concluded that there was no statistically significant relationship between increasing weight or neck circumference and increased ESS score.

Conclusion: In this study, almost half of the players surveyed (47.5%) had an ESS score of 10 or greater. The fact that this population exhibits such a high degree of excessive daytime sleepiness and are typically larger than a normal aged-matched population may artificially reduce the magnitude of the correlation. Age, circadian factors, and rigorous academic/athletic schedules reducing total sleep time may also be contributors to excessive daytime sleepiness that would be independent of weight and potential sleep-disordered breathing.

0620

CHANGES IN FUNCTIONAL ACTIVATION AFTER PAP TREATMENT IN OBSTRUCTIVE SLEEP APNEA (OSA) PATIENTS

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Introduction: Obstructive-Sleep-Apnea-syndrome (OSAs) is associated with both cognitive and functional deficits. Most of them improve after Positive Airway Pressure (PAP) treatment, which corrects patients' respiratory pattern. We used neuropsychological tests and functional-magnetic-resonance-imaging (fMRI) to investigate whether such an improvement in cognitive functioning and quality-of-life reflects a change in cerebral activity underlying these functions.

Methods: 11 males OSA patients served as subjects. OSA diagnosis was made with polysomnography (AHI>30h). Patients were evaluated at baseline (before treatment) and at follow-up (after 3 months treatment with PAP). Cognitive challenges were evaluated using neurocognitive tests, along with subjective scales as ESS, BDI, and quality-of-life questionnaires. During fMRI-scanning participants performed a 2-back working-memory task.

Results: The longitudinal neurocognitive evaluation showed a significant improvement after the treatment in tests of short and long-term memory, attention and executive-functioning, and in ESS and quality-of-life scales, which at baseline were significantly impaired compared with controls. Behavioral results during fMRI-scanning showed an improvement in 2-back performance after treatment which approached statistical significance (p = 0.068). Paired t-tests on fMRI data showed increased cerebral activations after treatment in occipital and parietal regions (calcarine gyrus, ventral medial precuneus and middle occipital gyrus), right temporal pole and middle cingulate cortex. Decreased activations after treatment were observed in the left inferior frontal gyrus (pars triangularis and opercularis), anterior cingulate cortex, right thalamus and hippocampus bilaterally.

Conclusion: Longitudinal neurocognitive tests confirmed the partial reversibility of cognitive dysfunction in OSA patients after PAP. The stronger occipital and parietal activity might reflect an enhancement of visual attention following treatment. The decrease in frontal and hippocampal activity likely reflects the reduced need for additional resources which characterize pre-treatment OSAs. These changes reverse some of the compensatory activation seen at baseline compared to normal controls.

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0621

DIFFUSION TENSOR IMAGING (DTI) IN OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: DTI is used to assess the integrity and organization of white matter; in particular, diffusion anisotropy maps give information about the impact of degenerative or vascular changes on white matter.

OSA causes hypoxemia and fragmented sleep, which lead to neurocognitive deficits. Neurocognitive problems in OSA are thought to result from either sleep fragmentation or intermittent hypoxemia or their interaction. The aim of the study is to assess with DTI whether OSA may be associated with significant modifications in brain diffusion maps, possibly reflecting the effects of hypoxemia.

Methods: 15 untreated male patients (mean age 43.7 ± 7.5) with severe OSA (AHI ≥30) and 15 normal controls matched for age, verbal IQ, education, gender, and hypertension were studied. All subjects underwent brain imaging with a high-resolution magnetic resonance scanner. Measures of fractional anisotropy (FA) were assessed in patients and normal controls. For this preliminary report 9 patients with OSA and 13 normal controls have been analysed. DTI data have been collected using a 3 Tesla scanner (Philips Achieva), with the following acquisition parameters: TR/TE=1100/57msec, 35 directions of the diffusion gradients, b-value= 1000s/mm², voxel size= 1.95x1.95x2.3mm. FA maps were calculated using Brainvisa software. To compare subjects, DT images were spatially normalized to a standard brain template (MNI). Voxel-by-voxel statistical analysis was performed using SPM5 software with a threshold of significance of p<0.001 and a minimum extension of 10 voxels for the significant clusters. Functional abilities were assessed with neuropsychological tests as well as with functional brain imaging techniques and are described elsewhere.

Results: The comparison between patients and normal controls showed decreases in FA in the long fronto-parietal fiber tracks belonging to the superior longitudinal fasciculus, bilaterally. The reverse comparison (controls vs. patients) did not reveal significant regional differences, supporting the correctness of normalization preprocessing. Decrease of FA might be attributed to hypoxic damage.

Conclusion: Long fronto-parietal white matter tracks appear to be affected in OSA. These preliminary results need to be confirmed in the whole sample of patients and normal controls. The results about the effects of PAP treatment will clarify whether the white matter changes may be related to inflammation and ischemia.

Support (optional): Research supported by Respironics Foundation

0622

BRAIN MORPHOLOGY IN OBSTRUCTIVE SLEEP APNEA (OSA) PATIENTS AND NORMAL CONTROLS

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Introduction: OSA leads to sleep fragmentation and intermittent hypoxemia. Neurocognitive problems in OSA are thought to result from either directly sleep fragmentation or intermittent hypoxemia or their interaction causing a possible damage or alteration of neural structures. Aim of the study was to assess structural brain changes in severe untreated OSA (AHI≥30) patients.

Methods: Voxel-based morphometry (VBM) was used to assess patterns of grey matter atrophy in a group of 17 patients with OSA (mean age 42.7 ± 7.8) compared to a group of 15 healthy controls. The two groups were age- and gender-matched. VBM data were collected using a 3 Tesla scanner (Philips Achieva). Statistical analysis was performed using SPM5 software. In order to collect valid results, an analysis with a correction based on cluster extension was used. Furthermore, age and total intracranial value (TIV) were introduced as covariates.

Results: We found two clusters of grey matter loss in OSA patients compared to normal controls respectively in the right superior frontal gyrus

and in the left superior parietal lobule. The reverse comparison (controls vs. patients) did not reveal significant regional differences.

Conclusion: The few VBM studies of OSA patients gave inconsistent results; in particular, some investigations found no evidence of grey matter changes in OSA patients; other studies showed a regional grey matter loss in the frontal cortex, parietal cortex, temporal lobe, anterior cingulate, hippocampus, and cerebellum. Different data analysis methods may explain some of these inconsistencies. The present findings confirm the existence of a grey matter loss in OSA patient with a conservative statistical analysis. The evaluation of treatment effects will clarify the actual impact of gray matter changes in relation to cognitive dysfunction.

Support (optional): Research supported by Respiroics Foundation

0623

NEUROCOGNITIVE FUNCTION AND QUALITY OF LIFE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA (OSA) BEFORE AND AFTER PAP TREATMENT

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Introduction: Sleep fragmentation and intermittent ipoxemia from OSA have been shown to have a negative impact of neurocognitive function. Literature data on improvement after treatment are mixed. Aim: to evaluate neurocognitive function and quality of life (QoL) in OSA patients at baseline (BL) compared to age-matched normal controls and to assess changes after 3 months of PAP treatment.

Methods: 15 male untreated patients with severe OSA (AHI ≥ 30) and 15 normal controls matched on age, education, gender, and hypertension status. All patients and controls have been evaluated at BL and after 3-months treatment (fixed PAP with C-flex) (T1). Neurocognitive functioning (attention, vigilance, memory, executive function, visuo-constructional abilities), sleepiness (ESS), mood (BDI), QoL (SF-36 and FOSQ) and quality of sleep (PSQI) were assessed at BL and at T1. Non parametric Mann-Whitney U Test was used to evaluate differences between patients and normal subjects (BL) and non parametric Wilcoxon Test was used to assess treatments effects (BL versus T1).

Results: 15 patients (mean age 43.7 \pm 7.5, education 12.3 \pm 2.8) and 15 matched healthy subjects were evaluated. Patient showed significantly lower score than healthy subjects in: short term memory (MBT) (Digit Forward: p=0.000; Corsi's Test: p=0.001); long term memory (MLT) (Rey List Learning: p=0.013; Rey List Recall: p=0.008) and executive function (Digit Backward: p=0.001; PASAT error: p=0.000; Stroop: p=0.026; Error Stroop: p=0.000; Copy's Rey Picture: p=0.015; TrialA: p=0.033; TrialB: p=0.006). Moreover patients also had significantly lower score at ESS, PSQI and QoL (p<.05). Up to today eleven patients completed the follow-up study. Preliminary results on this sample show an overall significant improvement on cognition over time (p<.010). Moreover patients showed improvement of neurocognitive test that reach normal subjects scores except for one executive function test (Trial B). Also ESS, PSQI and QoL showed a significant improvement over time (p<.005).

Conclusion: Our data showed that cognitive functions impaired when compared to normal controls at BL significantly improved after PAP treatment over time reaching the scores of healthy subjects.

0624

A RANDOMIZED, IN LAB COMPARISON OF AUTO TITRATING POSITIVE AIRWAY PRESSURE VS. CONVENTIONALLY TITRATED CONTINUOUS POSITIVE AIRWAY PRESSURE FOR TREATING OBSTRUCTIVE SLEEP APNEA

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Introduction: Initiation of CPAP in patients with OSA usually requires in-lab, CPAP titration, but there is growing interest in the use of auto-titrating positive airway pressure (APAP) to treat OSA. This study is a comparison of the initial, in-lab efficacy of APAP compared to conventional CPAP in treating OSA.

Methods: Twenty CPAP naïve patients with confirmed moderate to severe OSA on diagnostic polysomnography were randomized to treatment with APAP or to titrated CPAP by certified scoring sleep technologist. The primary outcome was control of OSA, as defined by improvement in AHI to <5. Patients on APAP not adequately controlled after 1 hour were switched to conventional CPAP titration.

Results: Baseline characteristics were similar when comparing between groups in regards to age (50 \pm 8.5 vs. 48 \pm 13.8), BMI (35.0 \pm 9.6 vs. 35.0 \pm 7.0), gender distribution (64% vs. 56% male), neck circumference (16.9 \pm 2.3 vs. 16.6 \pm 2.1) and baseline AHI (28.4 \pm 13.8 vs. 31.6 \pm 28.5). Of 11 subjects randomized to an initial CPAP titration, OSA was controlled in 7. Out of 9 subjects randomized to APAP, 3 (33%) were not adequately controlled and were switched to CPAP. Of these 3 patients, subsequent CPAP titration resulted in OSA control in 1 patient but lack of control in the other 2. Overall, among patients receiving CPAP (initial or after failed APAP), OSA was controlled in 8/14 (57%) compared to 6/9 (66%) among patients receiving APAP.

Conclusion: APAP using the ResMed S8 Autoset Vantage™ is comparable to titrated CPAP in the initial control of OSA as defined by improvement in AHI to <5 during in-lab treatment. It is important to note that both CPAP and APAP were often inadequate in controlling OSA in this tertiary referral center patient group. Factors predicting adequate response to APAP, as well as longer-term efficacy of APAP are being investigated.

0625

FEASIBILITY OF SCREENING ADULT SURGICAL PATIENTS FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive Sleep Apnea (OSA) is associated with a number of adverse health consequences including increased risk during surgery and complications during surgical recovery. Due to the majority of individuals with OSA being undiagnosed, an OSA risk assessment should be performed on all surgical patients pre-operatively.

Methods: During this prospective study, 2,614 adult surgical patients at the pre-operative assessment clinic were assessed in an academic hospital. The Berlin Questionnaire was completed during preoperative medical assessment to determine risk for OSA.

Results: During intake, it was found that 159 (6%) of the 2,614 patients had a previous diagnosis of OSA. Patients with a previous diagnosis were excluded from further analysis. Out of the remaining 2,316 patients, 671 (29%) screened high risk. Patients who scored high risk were given a color-coded wrist band, OSA risk signs were placed above re-

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covery beds to alert staff, and patients were positioned laterally when possible during recovery. The subset of patients screened as high risk were also educated about OSA and encouraged to undergo polysomnogram (PSG) evaluation.

Conclusion: Implementing a screening questionnaire during pre-operative assessment can quickly and efficiently identify potential patients with OSA. This study demonstrates the feasibility of screening all pre-operative patients for OSA and implementing extra safety measures for high risk patients in a large, academic hospital.

Support (optional): This work was supported by the Barnes Jewish Foundation.

0626

CHARACTERISTICS OF ADULT SURGICAL PATIENTS SCREENED AT HIGH RISK FOR OSA

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Introduction: Due to the associated morbidity and mortality, obstructive sleep apnea (OSA) is a major health risk of adult surgical patients. This observation study evaluates high risk OSA patients, as determined by a validated questionnaire, and the prevalence of co-morbidities associated with OSA.

Methods: All patients undergoing surgery at an urban academic hospital underwent an OSA risk assessment as part of the pre-operative evaluation. Data was collected from 617 patients (282 males) undiagnosed with OSA that screened high risk on the Berlin Questionnaire.

Results: Patients testing high risk were age 55.4±14.5 and had a BMI of 32.3±7.8. Out of 42 admitting services, high risk patients were found to be most prevalent in the following services: general surgery 27%, orthopedics 19%, urology 10%, ophthalmology 9%, and gynecology 8%. The prevalence of co-morbidities was as follows: 418 (62%) hypertension, 117 (17%) diabetes, 85 (13%) coronary artery disease, and 41 (6%) chronic obstructive pulmonary disease.

Conclusion: This study affirms that certain co-morbidities known to place outpatients at high risk for OSA remain an important risk factor for surgical patients in the hospital. This analysis identified the surgical admitting services of general surgery, orthopedics, urology, ophthalmology, and gynecology to have the largest prevalence of patients screened at high risk for OSA.

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0627

THE RELATIONSHIP BETWEEN DIABETES MELLITUS AND OBSTRUCTIVE SLEEP APNEA AND THE EFFECT OF CONTINUOUS POSITIVE AIRWAY PRESSURE ON HGA1C

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Introduction: Obstructive sleep apnea (OSA) is part of a metabolic syndrome, characterized by obesity, hypertension and diabetes mellitus (DM). Our goals are to explore the prevalence of DM among patients diagnosed with OSA, to explore the effect of DM diagnosis on the severity of sleep apnea compared to non-diabetic counterparts, the effect of CPAP use on HgA1c levels, and the effect of DM diagnosis on CPAP compliance.

Methods: Medical records were surveyed for all subjects who had a diagnosis of OSA, had been treated with CPAP and followed up with our sleep center. The database was reviewed for subject's demographic and

medical history data. Records of HgA1c levels before and after CPAP initiation were compared.

Results: Out of 50 patients included in the study 11 (22%) were diagnosed with DM. Diabetic subjects had a mean HgA1c of 7.83 mg/dl (±1.75) before CPAP initiation and 8.06 mg/dl (±1.40) after CPAP treatment (non-significant difference). The AHI score was not significantly different between DM and Non-DM counterparts (28.36 vs 31.81). DM patients had a lower compliance compared to non-DM counterparts on the three compliance measures: 1) percent of days the device was used (83.04, ±20.15 vs 86.02, ±20.6), 2) average hours of use (3.81, ±2.59 vs 4.88, ±2.26) and 3) percent of days more than 4 hours use (52.43, ±33.82 vs 63.17, ±32.02).

Conclusion: A large percent of OSA patients have DM. DM status is not related to OSA severity but may affect compliance to CPAP treatment. Larger studies should be conducted to confirm these preliminary findings.

0628

DOES SNORING OBJECTIVELY AFFECTS THE BED PARTNER'S QUALITY OF SLEEP?

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Introduction: Snoring is present in nearly 35 % of the middle aged population. The bed partner alleges that his sleep could be disturbed by the snoring to the point of having to sleep apart. Objective : to objectively measure the effect of snoring and OSA on the sleep of the snorer's bed partner.

Methods: We prospectively studied couples in which the wife complained of her husband's snoring because it disturbed her sleep quality. Exclusion criteria regarding the wife were the following : snoring or deafness. The patient and his spouse underwent one recording together and the wife underwent a standard polysomnography without her husband. Snoring, ventilatory and sleep parameters were analysed. The wife's sleep parameters were compared in the presence and absence of her husband.

Results: 21 couples were included and performed the two studies. Seven couples were excluded because of the presence on the wife's recording of snoring more than 10% of the sleep time (6 cases) and presence of OSA (1 case). Five patients spent less than 10% of their sleep time snoring. Among these 5 couples, 3 wives spent more time snoring than their husbands. Mean snoring energy, % of time snoring and snoring index were respectively 89±/- 4 dB, 23.1±/- 21,5%, 185 ±/- 170/h. Sleep time, sleep efficiency, sleep latency time of arousal during sleep, microarousal index of the spouse with and without her husband were comparable. The only parameter which was significant was a higher % NREM 2 of the spouse with the bed partner (p=0.009).

Conclusion: Snoring does not alter most current parameters of evaluation of quality of sleep besides NREM2 duration. In some cases, wives had unknown snoring with, in 14% of the couples, the wife having longer periods of snoring than her snoring husband.

0629

POSTOPERATIVE HYPOXEMIA IN SLEEP APNEA PATIENTS ON POSITIVE AIRWAY PRESSURE: POSSIBLE CAUSES AND ASSOCIATIONS

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Introduction: OSA is a risk factor for perioperative cardiopulmonary complications. Positive Airway Pressure (PAP = CPAP or Bilevel pres-

sure support) may reduce complication rates. Previously we reported significant postoperative hypoxemic events, as documented by a standardized nursing protocol, despite use of optimal PAP. We hypothesized that postoperative hypoxia in OSA patients on PAP was due to uncontrolled OSA.

Methods: A prospective observational study at an urban academic center was performed. Patients with PAP-controlled OSA (no SpO₂ < 89% on their optimal PAP setting) who underwent non-upper-airway and non-thoracic surgery were included. They were monitored in dedicated “OSA beds” and used their prescribed PAP postoperatively. Nocturnal oximetry recordings were done on the first postoperative night. Primary outcome was Time with SpO₂ < 89%. Patients were divided into nocturnal postoperative desaturators (PD, Time with SpO₂ < 89% more than 5% of Total Recorded Time or ½ hour) and postoperative nondesaturators (ND). Oximetry readings were read independently by two blinded Sleep Physicians.

Results: 14 patients were enrolled. 7 (50%) had nocturnal oximetry c/w uncontrolled sleep apnea (3 of 3 in the PD group, and 4 of 11 in the ND group). In the PD group, the mean time with SpO₂ < 89% was 2.5 hours. The PD group had lower postoperative average SpO₂ (91% vs. 96%, P = 0.03), lower postoperative nadir SpO₂ (75% vs. 88%, P = 0.01), a higher baseline AHI (46.8 vs. 19, P = 0.02) and a higher baseline supine AHI (50 vs. 18, P = 0.02). There were no significant differences in gender, comorbidities, PAP settings, postoperative narcotic use, or type of anesthesia or surgery. There were no postoperative complications in either group.

Conclusion: Prescribed PAP settings may not be adequate in the postoperative setting, with a significant proportion of OSA patients developing hypoxemia from what appears to be uncontrolled OSA. Patients with severe OSA may be at higher risk of becoming hypoxemic.

0630

EFFICACY OF ORAL APPLIANCE IN THE TREATMENT OF MILD TO MODERATE OBSTRUCTIVE SLEEP APNEA

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Introduction: Dental clinicians soon realized that odontology could play an important role in the treatment of obstructive sleep apnea syndrome (OSAS). Of the many kinds of OA (oral appliance), the adjustable mandibular repositioner appliances (MRAs) have been the most researched and have presented significant results due to allow gradual mandibular protrusion. Various clinic research papers support the effectiveness of OA in the treatment of snoring and mild OSAS. The literature also hints that they can be effective in mild to moderate OSA in specific cases. The aim of this prospective study was evaluating the efficacy of in the treatment of mild to moderate OSAS Brazilian patients.

Methods: A prospective study was conducted at the Sleep Disorders Laboratory in Brazil. Patients were eligible for inclusion criteria if they were more than 18 yr of age, presented at least a 7mm maximum protrusion, 40mm of mandibular opening, 08/10 teeth in each arch and if their overnight diagnostic sleep study showed an AHI of between 6 and 30/h. Patients with temporomandibular dysfunction and clinically significant coexisting disease (e.g., diabetes) were excluded. Twenty-two of 29 patients matched the inclusion criteria.

Results: A over night diagnostic sleep study showed a mean apnea/hipopnea index (AHI) of 18.7 ± 6.4 in a range of 6.0 to 25.0. The OA chosen was the adjustable PMPositioner. The total titration reached 08 weeks and was approximately 9mm. Patients used the appliance during 6 month and then underwent another PSG with appliance in situ. AHI was reduced from 18,7±6,4 to 5,6±4 (p<0,05), the mean SaO₂nadir increased from 81± 7,8 to 87±5,5(p<0,05) and REM% increased from

18,6±4,2 to 21,4±4,3 (p<0,05), the sleep stage 1,2,3,4 (S1,S2,S3,S4) and sleep efficiency (SE) showed no statistical significance (p>0,05).

Conclusion: We can conclude that OA was effective to treat mild to moderate OSAS patients.

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0631

PREDICTORS OF CONTINUOUS POSITIVE AIRWAY PRESSURE USE DURING THE FIRST WEEK OF TREATMENT

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Introduction: Nonadherence to continuous positive airway pressure (CPAP) remains the major impediment to effective treatment for obstructive sleep apnea (OSA). About half of OSA patients use their CPAP nightly and the pattern of adherence is established during the first week. The purpose of this study was to identify predictors of CPAP use during the first week of treatment from four categories of factors: pre-treatment clinical and demographic factors, pre-treatment perceptions of self-efficacy, immediate treatment-delivery efficacy, and immediate disease-reduction efficacy.

Methods: Patients with AHI ≥ 15 and prescribed CPAP were recruited. Adherence was measured using a microprocessor monitor within the machine. The ResMed Autoset-Clinical System set to manual CPAP pressure was used to measure residual events, mask leak, and airflow limitation. Self-Efficacy was measured with the Perceived Self-efficacy Scale for Sleep Apnea.

Results: Mean CPAP use during the first week from 90 patients (54% male) was 3.45 ± 2.67 h/night. Among the 19 side effects of CPAP use, only being less intimate was significantly correlated with CPAP adherence (r=-0.30, p=0.02). A series of multiple regression models were used to examine the contribution of the four categories of factors to the CPAP adherence. The final model included three covariates including data from 56 patients and accounted for 25.3% (p = 0.002) of the variance in the mean CPAP use. Reduced CPAP use was simultaneously associated with less intimacy (p = .048), being African-American (p = .011), and higher residual AHI (p = .044).

Conclusion: Assessing the presence of residual AHI and troubleshooting the impact of CPAP treatment on intimacy may be important in promoting CPAP adherence. Why race affects CPAP use needs further exploration. Further studies on development of a practical instrument for detection of patients who are likely to become nonadherent to CPAP and development of maximally effective interventions to enhance CPAP use are necessary.

0632

POLYSOMNOGRAPHIC DETECTION OF LEAK DURING PAP TITRATION

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Introduction: A variety of techniques help determine mouth and or mask leaks during in-laboratory PAP titration. These techniques include digital readout of the PAP controller, unstable leak signal with pressure alterations, truncated airflow signals during expiration with or without expiratory snoring, a precipitous rise of airflow signals at the beginning and/or end of each breath, lack of airflow rise with pressure increases, disproportional; change in the relationship between PAP-generated airflow signals and thermodynamic airflow monitors and relative humidity reduction of a nasal mask during mouth breathing. The lack of leak recognition during titration may lead to unnecessarily high PAP pressures and increased arousals. The purpose of this study was to determine a simple method of determining leak during PAP titration.

Category H—Sleep Disorders – Breathing

Methods: This study was a retrospective review of 120 patients on CPAP. Subjects were divided into mild, moderate or severe apnea categories. Subjects ranged in age from 15-72 years and body habitus measured by BMI ranged from normal to morbidly obese. Standard polysomnography (PSG) was performed measuring CPAP generated flow from the ResMed controller (V) and pressure and flow (PV) from a port in the CPAP circuit located at the connection between the tubing and CPAP unit interfaced with a pressure transducer. Both measures were recorded on the PSG.

Results: In all patients, increasing CPAP pressures were associated with a shift of both V and PV signals. With a leak, only PV showed obvious changes in the signal where V signals remained stable.

Conclusion: High leak associated with mask or mouth during PAP titration elicits a concurrent shift of PV signals with little or no change of V signals. Given that different CPAP machines use different amounts of pressure for leak compensation, technologists observing indicators of leak can avoid increasing CPAP pressures until the leak is rectified ultimately minimizing exogenous arousals.

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0633

OPIOID-ASSOCIATED SLEEP APNEA: A COMPARISON OF POSITIVE AIRWAY PRESSURE RESPONDERS TO NON-RESPONDERS

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Introduction: Chronic opioid use is prevalent. In opioid users with sleep apnea syndrome, central apneas may develop with CPAP use. For these patients, other modalities of sleep apnea treatment (Bilevel Pressure Support = BPS, Adaptive Servo Ventilation = ASV) have been proposed. We describe and compare two groups of patients according to their response to Positive Airway Pressure (PAP) treatment.

Methods: All sleep apnea patients diagnosed at our sleep center in the year 2007 that were using opioids at the time of their sleep study were identified. Patients were categorized by whether or not they responded to any PAP (non-responders failed to respond to all PAP modalities). We compared responders (RE) with non-responders (NR) using standard statistical methods.

Results: Eleven patients were analyzed, 7 RE and 4 NR. Demographics for the entire group: average age 59 years (+/-15.2), 55% were women, and the average BMI was 37.3 kg/m² (+/- 9.0). The average baseline AHI was 58 (+/-30.4). RE and NR did not differ in terms of age, gender, BMI, the morphine equivalent narcotic dose (172.3 +/- 192.9 mg vs. 190.0 +/-126.2 mg, p=0.98), weight adjusted morphine equivalent dose, concurrent use of hypnotic medications, or the initial central apnea index. However, there was a significant difference in the initial AHI (76.8 +/-18.4 for RE and 25.9 +/-14.4 for NR, p=0.001) and a trend towards a difference in the % of sleep apnea that was central in nature (27.1% +/-17.0 in RE vs. 41.9% +/- 8.6 in NR, p =0.09) at the time of the initial study.

Conclusion: In this small pilot study, 36% of opioid users who developed complex apnea on CPAP could not be controlled with BPS or ASV. Those failing all modes of PAP had more significant central sleep apnea on their initial CPAP titration, possibly suggesting enhanced respiratory instability.

0634

A NOVEL EXPIRATORY PRESSURE DEVICE TO TREAT MILD-MODERATE OSA

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Introduction: The purpose of this study was to evaluate the efficacy of a disposable expiratory pressure device (Provent; Ventus Medical, Inc.) in patients with mild-moderate OSA (≥ 5 AHI ≤ 30).

Methods: The study design involved overnight polysomnographies (PSGs; 1-control and 3 different expiratory resistances [50, 80, and 110 cmH₂Osec laboratory PSG with the device/liter]) to identify the therapeutic device resistance to be used at home for one month with repeat PSG. The device consists of a small valve attached to adhesive tape placed over each nostril. Once sealed, the valves increase pressure during expiration. There were 19 males/five females (age 47.5±9.8, BMI 29.2±4.6). Latin-square analysis assessed for potential order effects on the first four nights. Subjects were assigned a device based on an algorithm designed to identify the lowest therapeutic resistance. ANOVAs were used to assess the effect of treatment on AHI and subjective sleepiness (Epworth Sleepiness Scale; ESS).

Results: The GLM analysis showed significant treatment effects (p<.05), but not order (AHI 15±6.9, 6.8±4.6, 7.1±5.5, and 9.1±7.4 on control and resistance nights, respectively). Post-hoc testing demonstrated significantly higher control night AHI than on treatment nights, which were comparable. A repeated measures analysis for AHI of control night, assigned resistance setting, and follow-up night had a main effect. Control night AHI was significantly higher (15±6.9) than assigned device (4.6±3.6) or follow-up night (10.1±7.6); device night had a significantly lower AHI than follow-up night (all p<.05). ESS scores decreased significantly (p<.001) from control night (8.5±4.2) to final night (6.1±4.2). The percent of nighttime snoring decreased significantly (p<.05) with both assigned device (12.8±19.8) and follow-up nights (16.2±23) compared with control night (31.2±24.1).

Conclusion: The results confirm the efficacy of the device in the treatment of OSA. It significantly reduced respiratory events and sleepiness over a one month therapeutic trial. From the patient perspective, it significantly decreased snoring, thus likely increasing acceptance of the product.

0635

ETHNIC VARIANCE IN SLEEP-DISORDERED BREATHING AMONG HISPANIC AND CAUCASIANS

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Introduction: Ethnic factors can influence the sleep apnea phenotype through a multitude of mechanisms. These differences could in turn influence the presenting symptom profile. Such variance has been less well-documented amongst Hispanics with respect to Caucasians.

Methods: A retrospective review of a large database of patients (n=780) with obstructive sleep apnea (OSA), defined by a AHI of >5, was carried out. Epworth sleepiness scores, presence of key symptoms of OSA, measurements of neck circumference, as well as BMI, and various sleep study parameters were systematically reviewed and tabulated.

Results: The data included 229 Hispanic males, 262 Caucasian males, 143 Hispanic females, 146 Caucasian females. Severity of OSA was highest in Hispanic males (p < 0.0005). As compared to Caucasian males, Hispanic males tended to be younger (mean age 50 +/- 14 yrs vs. 56 +/- 14.7 yrs; p < 0.001) and more obese (mean BMI 37 +/- 8 vs. 35 +/- 7; p < 0.001), and have larger necks (18 +/- 2, vs. 17 +/- 1.5; p

< 0.05) No such differences were seen in females. Overall Caucasian females tended to have the least degree of sleepiness, both as measured by average ESS (mean 9.5 +/- 4.8) as well as a percentage of patients with abnormal ESS (39.7% vs. 49%; $p < 0.001$), even with the same severity of OSA.

Conclusion: There are marked ethnic differences in key phenotypic features that are involved in recognition profiles related to OSA.

0636

GENDER DIFFERENCE IN UPPER AIRWAY DIMENSIONS IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Gender plays an important role in modifying the phenotypic profile of obstructive sleep apnea. Previous studies assessing upper airway morphology in sleep apnea have yielded conflicting results. It is generally seen that there is a strong predisposition to OSA in men despite men in general having larger pharyngeal airspace. The objective of this study was to compare upper airway size as assessed by both neck circumference and the Modified Friedman score in patients with OSA.

Methods: Consecutive patients seen in the sleep lab with a diagnosis of OSA (AHI > 5). Patients had an assessment of upper airway anatomy as well as measurements of BMI and neck circumference. In addition data from routine questionnaires as well as indices of OSA were tabulated and analyzed.

Results: Data was analyzed from 227 males and 118 females. Mean age was comparable between the genders. Severity of OSA as measured by AHI was also similar. BMI was significantly higher in females as expected (37 +/- 8.4 vs. 35 +/- 7.2; $p < 0.0005$). Neck circumference was larger in males (18 +/- 2 in. vs. 16 +/- 1.6in; $p < 0.0005$) and a significantly higher percentage of males had abnormally large necks (> 17" in males and > 16" in females)- 55.9% vs. 29.4%; $p = 0.015$. Significantly more males had high scores on the Modified Friedman upper airway classification (> 3 or 4) - 58.6% vs. 48.3%; $p = 0.015$. Supine AHI was seen to be far greater in males (41 +/- 27 vs. 29 +/- 27; 0.024).

Conclusion: Males with OSA seem to have significantly more abnormal upper airway anatomic features than females. These may influence gender differences in both severity of OSA and its postural (gravitational) dependence.

0637

ETHNIC DIFFERENCES IN THE POLYSOMNOGRAPHIC FEATURES OF OBSTRUCTIVE SLEEP APNEA

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Introduction: REM sleep is often identified as the stage of sleep in which people are most vulnerable for having sleep-disordered breathing (SDB). Gender has been shown to influence this behavior, but how ethnic factors influence this has not yet been well-described to our knowledge. We wished to test the null hypothesis that ethnic factors would have no influence on severity of SDB in REM sleep.

Methods: A retrospective study of consecutive adult patients seen at our sleep center with OSA, as defined as a AHI of >5, was carried out. Split night studies, titration studies and studies where patients had less than 10min of REM sleep were excluded. Details of their polysomnography were tabulated and analyzed. Groups were matched for age, BMI, gender distribution as well as overall AHI.

Results: 177 Hispanics and 154 Caucasians were included in the study. Mean age (53 +/-12 yrs vs. 55 +/-13; $p = 0.064$;) and BMI (36 +/- 7 vs. 35 +/- 8; $p = 0.145$) were comparable between the two groups. Pro-

portion of males-females was also similar - 114M;63F in Hispanics vs. 102M;52F in Caucasians; $p = 0.087$. Overall AHI was similar (- 36 +/- 26 in Hispanics vs. 33 +/- 27; $p = 0.218$) as was the O2 nadir (76 +/- 11% vs. 76 +/- 12%; $p = 0.78$) Amount of REM sleep was identical between the two groups - 18 +/- 7% in both. REM AHI was significantly higher in Hispanics (REM AHI 40 +/- 25 vs. 33 +/- 23; $p = 0.019$).

Conclusion: Ethnic factors do influence REM sleep -dependent vulnerability to SDB. This suggests that an interaction may exist among genetic factors influencing airway size and function, and vulnerability for REM SDB.

0638

EFFECT OF NASAL CPAP UPON REGIONAL CEREBRAL BLOOD FLOW IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: To investigate the effects of nasal continuous positive airway pressure (CPAP) therapy on rCBF of OSA patients during wakefulness.

Methods: Interictal 99mTc-ethylcysteinate dimer (ECD) single photon emission computed tomography (SPECT) was performed before nasal CPAP application in OSA patients and normal subjects and then repeated after nasal CPAP therapy for more than 6 months. For SPM analysis, all SPECT images were spatially normalized to the standard SPECT template and then smoothed using a 12-mm full width at half-maximum Gaussian kernel.

Results: Twenty-seven male OSA patients (mean age, 46.5 ± 7.7 years) were enrolled in this study (apnea-hypopnea index, AHI>30/hour). Seventeen male patients (45.4±7.0 years, mean AHI = 64.2±20.9 /hr) had undertaken nasal CPAP therapy. The mean duration of nasal CPAP therapy was 185±3.5 days and the mean CPAP usage time per day was 5.4±1.1 hours. The mean AHI and mean ESS were significantly decreased to 3.8±1.1/hour and 3.5 ± 0.7, respectively after nasal CPAP treatment. SPM analysis showed that rCBF in OSAHS patients (N=27) was significantly reduced in bilateral parahippocampal gyri and right lingual gyrus compared with normal subjects (false discovery rate corrected $p < 0.05$). Moreover, AHI of patients were negatively correlated with rCBF in right pericentral gyrus and right cuneus (uncorrected $P < 0.001$). After nasal CPAP treatment, rCBF significantly increased in bilateral orbital gyri, right superior frontal gyrus, bilateral precentral and anterior cingulate gyri, left anterior insular and superior temporal gyri, and right hippocampal tail (uncorrected $p < 0.005$).

Conclusion: Our study demonstrates that rCBF during daytime awake state was deranged in severe OSA patients. Furthermore, a long-term treatment of nasal CPAP significantly improved rCBF on several cerebral cortices.

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0639

ADULT PERCEPTIONS OF THE DIAGNOSIS AND TREATMENT OF OBSTRUCTIVE SLEEP APNEA: A MIXED METHODS STUDY EXAMINING THE INFLUENCE OF PATIENT EXPERIENCES AND BELIEFS ON CONTINUOUS POSITIVE AIRWAY PRESSURE ADHERENCE OUTCOMES

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Introduction: Health beliefs, perceptions of diagnosis and treatment, and self-efficacy may contribute to differences in continuous positive airway pressure (CPAP) adherence among adult obstructive sleep apnea (OSA) patients. The purpose of the research is to describe adult OSA patients' beliefs and perceptions about the OSA diagnosis and treatment with CPAP and self-efficacy relative to CPAP adherence outcomes.

Methods: A mixed methods concurrent nested design, predominantly qualitative (semi-structured, individual interviews) with an embedded quantitative data collection procedure (mask-on time at effective pressure CPAP adherence at one week) was used. Interviews were conducted post-diagnosis and post-one week CPAP treatment.

Results: Across-case analysis (n=15) identified distinctly different beliefs and experiences between CPAP adherers and nonadherers. Adherers had defined beliefs of risk associated with OSA, had positive beliefs in their ability to use CPAP, identified outcome expectations prior to treatment exposure that were consistent with early experiences on CPAP, had more facilitators than barriers from the outset, and facilitators became less important later in treatment as adherers developed personal goals and reasons for using CPAP. Nonadherers described an absence of perceived symptoms and risks associated with OSA, described few expectations about being diagnosed and treated for OSA, did not identify positive responses to CPAP after initial exposure, had difficulties with early use of CPAP which influenced decisions to reject or stop treatment, described low belief in their ability to use CPAP, which was reinforced with negative experiences in early treatment phase, and described few treatment facilitators and more treatment barriers.

Conclusion: Adults have unique beliefs and experiences during diagnosis and treatment of OSA, yet similar beliefs emerge within adherent and nonadherent groups. Understanding that nonadherent and adherent CPAP users have different beliefs/perceptions is a critical step in early identification of those at high risk for nonadherence and development of targeted intervention strategies.

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0640

CARDIOVASCULAR EFFECTS OF INTERTRIGEMINAL REGION STIMULATION

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Introduction: It has been shown, that intertrigeminal region (ITR) plays a substantial role in regulation of both sleep-related apnea and vagal mediated reflex apnea. However, efferents of ITR and its physiological functions are not well defined. In this work we investigated cardiovascular effects of glutamate injections in ITR along with alteration of autonomic regulation, induced by bilateral vagotomy.

Methods: Experiments were conducted on 9 ketamine/xylazine anesthetized rats. Glutamate (10 mM, 30 mL) was injected to ITR before

and after bilateral vagotomy. Blood pressure in femoral artery, ECG and respiration were registered continuously and digitized with sampling rate 200 Hz. Cardio-respiratory indices were analyzed 60s prior and 90s following the ITR injections in 30s segments. Estimated variables included: systolic (SP) and diastolic (DP) blood pressure, pulse pressure (PP), heart rate (HR), breath duration (TT) and their coefficients of variation. Effects of injections and vagotomy were assessed by t-test.

Results: Injections of glutamate to ITR evoked immediate apnea. The significant reaction of blood pressure was observed in the first 30s after injection. Both systolic and diastolic blood pressure variability increased significantly (p=0.04 and p=0.035 respectively). This effect was not altered after vagotomy. Analysis of mean values of HR and PP did not reveal significant changes followed by glutamate injection.

Conclusion: The results suggest the involvement of the ITR in systemic response, which appeared during apnea and included respiratory and cardio-vascular components.

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IMPROVEMENT IN MICROVASCULAR REACTIVITY WITH POSITIVE AIRWAY PRESSURE THERAPY FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: Obstructive sleep apnea (OSA) has been associated with impaired macrovascular function, which has been found to improve after treatment with continuous positive airway pressure (CPAP) and weight loss surgery. However, changes in microvascular function associated with OSA have not been studied. We hypothesize that (1) CPAP and (2) weight loss due to bariatric surgery will both improve macrocirculatory and microcirculatory vasoreactivity in obese patients with OSA without cardiovascular co-morbidities.

Methods: Obese subjects without cardiovascular co-morbidities, with and without OSA were studied before and after CPAP and bariatric surgery. Microvascular function was measured with LASER Doppler flowmetry before and after iontophoresis of acetylcholine and sodium nitroprusside (SNP). Macrovascular function was assessed by brachial artery ultrasound before and after flow mediated dilation and SNP administration.

Results: To date, four subjects have been studied before and after 4-6 months CPAP therapy. In these subjects, AHI decreased from a mean of 39±20 to 5±2 events/hr without any change in weight. To date, three subjects have been studied both before bariatric surgery and 6-7 months after bariatric surgery. Mean body weights decreased from 128±9 to 98±12 kg post surgery, with a concomitant decrease in AHI from 17±1 to 9±1 events/hr. Endothelial dependent microvascular reactivity improved after treatment with CPAP from 50±7% to 72±12%, but did not improve after bariatric surgery. No major change in endothelial independent microvascular reactivity or macrovascular reactivity was apparent following CPAP or bariatric surgery, although the study is ongoing.

Conclusion: Although preliminary, our results suggest that otherwise healthy population of obese OSA patients have improvements in microvascular reactivity with therapy.

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0642

CORRELATION BETWEEN SLEEP APNEA AND SELF-REPORTED DAYTIME SLEEPINESS AND PITTSBURGH SLEEP QUALITY INDEX

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Introduction: Obstructive sleep apnea syndrome (OSAS), which results from upper airway obstruction during sleep, is a well known cause of daytime sleepiness. Epworth Sleepiness Scale (ESS) is a convenient tool for measuring subjective daytime sleepiness and has been widely used in clinical settings. The Pittsburgh Sleep Quality Index (PSQI) is another self-rated questionnaire assessing sleep quality, and is one of the commonly used assessments in sleep centers. However, there are only few reports focusing on the relationship between sleep apnea, subjective daytime sleepiness and PSQI. In our study, we aimed to determine whether a simple self-report of overall sleep quality by PSQI and daytime sleepiness are associated with the severity of OSAS in patients with sleep apnea.

Methods: Seventy patients presenting with a chief complaint of snoring or sleep-disordered breathing completed the PSQI and the ESS, and underwent an overnight polysomnography (PSG). PSG data were reviewed with the following variables: age, body mass index (BMI), snoring index and apnea-hypopnea index (AHI).

Results: Their mean age was 51±12 years (80% men), mean BMI was 25±3kg/m², mean AHI was 18±21 events/h, mean ESS score was 10±5, and mean PSQI score was 8±3. According to AHI, patients with apnea were significantly more likely to have higher BMI ($P < 0.01$) and snoring index ($P < 0.003$) than patients without apnea. Increasing AHI was significantly associated with worsening ESS scores ($P=0.017$, $r=0.286$), as well as snoring index ($p=0.003$, $r=0.348$). However, linear-regression results showed that the PSQI global sleep-quality score was neither related to AHI, nor to the ESS, nor to the other remaining parameters such as age, BMI, snoring index.

Conclusion: Our results suggest that the severity of obstructive sleep apnea is likely to be associated with subjective daytime sleepiness, but correlate poorly with the self-reported global PSQI.

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TIME COURSE OF BLOOD PRESSURE, HEART RATE AND LOCOMOTOR ACTIVITY IN MICE WITH CHRONIC INTERMITTENT HYPOXIA

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Introduction: Chronic intermittent hypoxia (IH), as seen in obstructive sleep apnea, elevates blood pressure in rodents. We studied cardiovascular adaptation during IH in regards to locomotor activity. We hypothesized that changes in activity over time contributes to the adaptation.

Methods: Six adult male C57BL mice were instrumented for telemetric measures of mean arterial pressure (MAP), heart rate (HR) and locomotor activity (LA). Following recovery and acclimatization, animals were individually housed in chambers under 12-12 light-dark cycles. Recordings of IH, MAP, HR, and LA were started 24 hours prior to IH. IH was defined as 1-min hypoxia (nadir O₂ 5-7%) followed by 1-min normoxia, and repeated for 8 daytime hours for 10 days. Over exposure days 1, 3, and 10, data are presented from daylight during IH (DAIH: 5 cycles during inactivity that was determined by behavior observation), daylight at the following morning prior to instituting IH (DA: 2 hours), and nighttime following the exposure (NOC: 8 hours).

Results: During DAIH at 1, 3, and 10 days, MAP significantly increased compared with baseline (baseline 107±5, day 1: 135±7, day 3: 114±5, day 10: 117±1 mmHg, all $p < 0.05$), and significantly lower at days 3 and 10 than day 1 ($P < 0.05$ respectively). For DA, compared with

baseline, MAP increased over time (baseline: 115±/-3; day1: 128±/-4; day 3: 121±/-5; day 10: 125±/-3 mmHg; all $p < 0.05$). For NOC, baseline MAP was 121±/-2 mmHg, and did not change with IH over time. During DAIH, HR increased significantly at day 1 compared with baseline (531±/119 vs. 661±/-78 bpm, $p < 0.05$), but not at any other time period. There were no significant changes in LA over time compared with baseline at DAIH, DA, or NOC.

Conclusion: There is an adaptation in the cardiovascular response to IH over time. The cardiovascular adaptation is independent of changes in LA.

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ACCEPTANCE AND ADHERENCE OF A NOVEL DEVICE IN THE TREATMENT OF MILD TO MODERATE OBSTRUCTIVE SLEEP APNEA

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Introduction: Acceptance and adherence are paramount to treatment success. Prescribed therapies for OSA may be accepted by patients and tried initially, but many patients who initially accept therapy may fail to adhere to it. Novel mask designs and pressure delivery systems have enhanced some patients' acceptance of and adherence with CPAP therapy. For other patients, particularly those with mild to moderate disease, simpler therapeutic options may be a better alternative.

Methods: The Provent™ device (Ventus Medical, Inc.) is a small nasal insert which provides expiratory positive airway pressure (EPAP). The device consists of a valve which is placed into the nares, anchored externally by an adhesive tape. In this prospective study, subjects with mild to moderate OSA ($5 \leq \text{AHI} < 30$) were studied with three types of EPAP resistances. Subjects were given the most effective resistance to use at home for 30 days, and were instructed to maintain daily logs of device use. Acceptance was defined as the subject's agreement to begin home use of the device. Adherence was defined as a subject's report of a device placed at bedtime that was still attached to the nares at final out-of-bed time. The number of adherent nights was divided by the total number of nights of potential use. Nightly sleep hours were calculated by diary report.

Results: Twenty-seven subjects were enrolled in the study. One subject withdrew and two subjects were lost to follow-up before the initial polysomnograms were completed. All 24 remaining subjects accepted the device for home use. Across all 24 subjects, the device was worn for 725 of 768 potential nights for an adherence rate of 94%. Mean reported sleep time for nights used was 7.4 hours.

Conclusion: High levels of acceptance (100%) and adherence (94%) were observed with this new therapeutic option for the treatment of mild to moderate OSA.

0645

OREXIN (HYPOCRETIN) GENE TRANSFER IMPROVES NARCOLEPTIC SYMPTOMS IN OREXIN NULL MICE

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Introduction: Narcolepsy is a neurodegenerative disorder linked to the loss of orexin neurons. A behavioral phenotype that resembles narcolepsy occurs in mice when the orexin gene is deleted. Gene transfer has proven to be an effective neurobiological tool in a number of neurodegenerative diseases but it is not yet known if it can also correct a sleep disorder. Here we constructed a replication-defective herpes simplex virus-1 (HSV-1) amplicon-based vector to test if orexin gene transfer could reverse the symptoms of narcolepsy in orexin knockout mice with narcolepsy phenotype.

Methods: First, the mouse prepro-orexin gene was inserted into the HSV-1-PrpUC vector and then the expression of transferred orexin gene was confirmed by reverse-transcription PCR and immunohistochemistry in cultured cells. Then the same vector was delivered into the lateral hypothalamus (LH) of orexin knockout mice, and mice were then sacrificed at various intervals after delivery to determine the lifespan of the expression of the gene product. Lastly we injected the vector into the LH of another batch of orexin knock out mice (n=13) and we examined its effects on sleep-wake paying special attention to changes in cataplexy attacks and the REM sleep. Sleep was measured during the 2nd and 4th days post-injection. Control mice (n=9) were injected with vector carrying solely the reporter gene (GFP). Sleep was also recorded from wildtype (WT) mice (n=9) of the same background strain (C57BL/6J) and age (3-7 months old; 20-35 g) as the orexin knockouts.

Results: Numerous orexin-A immunoreactive neurons in the LH of orexin knockout mice were evident 1-3 days after gene transfer followed by a decline after the 4th day. Orexin gene transfer into the LH decreased the incidence of cataplexy by 60% (versus control vector), and the levels of REM sleep during the second half of night were same as WT.

Conclusion: HSV-1 vector-based orexin gene transfer reorganized and improved REM in knockout mice. This methodology provides an efficient tool to determine how sleep becomes reorganized in an animal model where the underlying network exists but the sleep abnormality results from a missing gene.

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0646

HCRT-2 SAPORIN LESIONS OF THE VENTROLATERAL PERIAQUEDUCTAL GRAY (VLPAG) IN MICE AFFECT THE CIRCADIAN DISTRIBUTION OF SLEEP AND WAKE

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Introduction: In both the rat and mouse models of narcolepsy there is a pronounced increase in REM sleep at night compared to wild-type rodents. Using the neurotoxin hypocretin-2-saporin (HCRT2-SAP), we have lesioned key arousal neurons in an effort to determine the pathway responsible for regulating REM sleep. Lesion of the dorsolateral pons, which has been implicated in REM sleep regulation, does increase REM sleep at night. Here we investigate the ventrolateral periaqueductal gray (vIPAG) which we have hypothesized is a gate between hypothalamic and a pontine REM sleep center based on initial data from Sastre et al., (Neuroscience, 74:415, 1996).

Methods: Mice homozygous for the TgN(GadGFP)45704SwN transgene were used. These mice express enhanced green fluorescent protein (eGFP) under the control of the mouse Gad1 gene promoter, thereby revealing the GABA neurons. These mice (n=8) were implanted with sleep recording electrodes (isoflourane) and HCRT2-SAP (8.7ng/23nl) was injected (glass pipette) in the vIPAG. In some TgN(GadGFP) mice (n=5) sleep was recorded without conducting any lesions. Sleep was recorded in 12:12 light dark (LD) and constant dark (DD) conditions.

Results: Two weeks after lesion of the vIPAG the most striking effect was an inversion of the diurnal rhythm of REM sleep, with NREM and wake being equally distributed during the day and night. Cataplexy was not evident.

Conclusion: Over the last few years we have lesioned a number of HCRT targets using HCRT2-SAP and the changes in the diurnal distribution of sleep after vIPAG lesions are the most pronounced. Either loss of HCRT input or of the vIPAG neurons increases REM sleep at night and decreases it during the day. This suggests that the vIPAG may be a vital link in the maintenance of the circadian distribution of sleep and wake pattern.

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MANIPULATION OF SKIN TEMPERATURE IMPROVES NOCTURNAL SLEEP IN NARCOLEPSY

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Introduction: Besides excessive daytime sleepiness, disturbed nocturnal sleep is a major complaint of patients with narcolepsy. Previously, we showed alterations in skin temperature regulation in narcoleptic patients that were related to increased sleepiness (Fronczek et al., Sleep 2006). Furthermore, temperature manipulations improved daytime vigilance and maintenance of wakefulness (Fronczek et al., Sleep 2008 in press). In healthy subjects, we showed that sleep depth was sensitive to subtle skin temperature manipulations (Raymann et al., Brain 2008 in press). We here tested the hypothesis that direct control of nocturnal skin temperature might be applied to improve the disturbed sleep of narcoleptic patients.

Methods: Participants were eight patients (5 males) diagnosed with narcolepsy with cataplexy according to the ICSD-2 criteria, age 28.6 ± 6.4 years (mean ± standard deviation), range 18-35 years. During two nights sleep was recorded polysomnographically while proximal and distal skin temperature were manipulated using a comfortable thermosuit that induced skin temperature to slowly cycle with an amplitude of only 0.4 degrees Celcius within the comfortable range normally observed during sleep. Logistic regression was used to evaluate the effect of skin temperature manipulation on the probability of occurrence of different sleep stages and nocturnal wakefulness.

Results: Proximal skin warming significantly suppressed wakefulness and enhanced slow wave sleep (SWS). In contrast, distal skin warming enhanced wakefulness and stage 1 sleep at the cost of SWS and REM sleep. The optimal combination of proximal skin warming and distal skin cooling led to a 160% increase in SWS, a 50% increase in REM-sleep and a 68% decrease in wakefulness, compared to the least beneficial combination of proximal skin cooling and distal skin warming.

Conclusion: Subtle skin temperature manipulations under controlled conditions significantly improved the typical nocturnal sleep problems in narcolepsy. These results indicate that skin temperature control could have therapeutic relevance.

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FAMILIAL NARCOLEPSY, OBESITY AND TYPE 2 DIABETES WITH HYPOCRETIN DEFICIENCY

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Introduction: Narcolepsy is mainly a sporadic disease and believed to be autoimmune-mediated. This is underlined by the fact that 75% of reported monozygotic twins are discordant for narcolepsy-cataplexy suggesting, as in autoimmune disorders, a multi-factorial and therefore complex rather than a simple genetic condition. Nevertheless, up to 10% of cases may be found in a familial context with an autosomal dominant mode of inheritance. We describe the first dizygotic twin pair concordant for narcolepsy in a family in which narcolepsy cosegregates with obesity and type 2 diabetes with an autosomal dominant mode of transmission.

Methods: A Spanish family was clinically investigated and underwent whole night polysomnography and multiple sleep latency test based on the standard methods. Laboratory investigations included high resolution HLA DQB1 genotyping, mutation analysis of Prepro-hypocretin (HCRT), Hypocretin-Receptor-1 and -2 (HCRTR1, HCRTR2) genes as well as CSF hypocretin-1 measurements.

Results: The pedigree consists of four generations including a dizygotic male twin pair in the third generation concordant for narcolepsy with cataplexy and obesity. Four additional family members were also diagnosed with narcolepsy and cataplexy while at least 7 other family members were known to have suffered for excessive daytime sleepiness (EDS). Furthermore, the family consists of several members affected by type 2 diabetes and/or obesity, which partially cosegregates with narcolepsy or EDS. HLA genotyping in twins showed no association with DQB1*0602 while CSF measurements revealed hypocretin deficiency. Mutation analysis ruled out any pathogenic mutation in the coding regions and exon-intron boundaries of the hypocretin ligand and receptor genes.

Conclusion: This unique familial case clearly represents a genetic form of narcolepsy with an autosomal-dominant mode of inheritance, not necessarily associated with HLA-DQB1*0602 but with hypocretin deficiency without any pathogenic mutation in hypocretin ligand or receptors. Our findings raise the possibility of a common genetic contribution to narcolepsy, obesity, and type 2 diabetes as already suggested in sporadic narcolepsy.

0649

NARCOLEPSY-CATAPLEXY: ACTION OF TWO GABA-2 AGONISTS, BACLOFEN AND SODIUM OXYBATE ON CLINICAL SYMPTOMS

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Introduction: Comparison of 2 gaba-2 medications: sodium oxybate and baclofen on nocturnal sleep, daytime sleepiness and cataplexy was performed on narcoleptic subjects. The aims were to evaluate the similarity of action on the narcolepsy symptoms, to better understand how sodium oxybate act on narcoleptic symptoms and to evaluate the possibility to add baclofen as a treatment of narcolepsy in men.

Methods: 28 narcoleptics, 26 of them teen-agers with relatively recent onset of narcolepsy-cataplexy and HLA DQB1 0602, participated to the study. Each baclofen subject was matched for age and gender to a sodium oxybate subject. Clinical scales Epworth Sleepiness Scale (ESS),

Pediatric Sleepiness Scale (PDSS), Visual analog scale (VAS) for sleepiness, daily logs for cataplectic attacks were collected. Polysomnogram (PSG) and multiple sleep latency test (MSLT) were monitored. If sleepiness was a risk for subject, the known stimulant without effect on EDS and cataplexy, modafinil could be prescribed by the treating physician. Prescription should last 3 months and if modafinil had been prescribed tests at 3 months were re-done without the stimulant medication.

Results: Both drugs impacted on nocturnal sleep with increase in delta EEG but baclofen had no effect on EDS and cataplexy at 3 months intake.

Conclusion: Mechanisms by which sodium oxybate improved cataplexy and EDS is not directly due to its gaba-2 properties. Baclofen act on nocturnal sleep of narcoleptic but low dosage at bedtime is necessary as morning somnolence may be an important problem in these patients.

0650

EVOLUTION OF NARCOLEPSY SYMPTOMS IN FAMILIES

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Introduction: Family history of narcolepsy has been reported in 6% to 40% of narcoleptic individuals. The risk for narcolepsy-cataplexy is estimated to be 10-40 times higher among the first-degree relatives of narcoleptic individuals than in the general population. The risk for a first-degree relative of developing excessive daytime sleepiness or other symptoms of REM anomalies is uncertain and evolution of symptoms is unknown.

Methods: We collected information on 1,383 individuals; 186 of them had narcolepsy and 1,197 were family members. A 3-year follow-up interview was completed for 379 subjects. In both cases, interviews were conducted by telephone with the Sleep-EVAL system.

Results: At follow-up, daytime sleepiness was increased in 34.2% of the family members. Frequency of cataplexy increased from 1% to 3% in the follow-up period. Hynagogic hallucinations remained unchanged. Development of new narcolepsy symptoms was mostly seen in family members younger than 26 years. A total of 3 family members developed narcolepsy in the follow-up period, 2 of them were DQB1*0602 positive.

Conclusion: Risks for narcolepsy and narcolepsy symptoms are high in family members of narcoleptic individuals and show a genetic vulnerability to REM anomalies. Excessive daytime sleepiness was the symptom that increased the most over a 3-year period.

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0651

CHARACTERISTICS OF CATAPLEXY AND CATAPLEXY-LIKE SYMPTOM IN PATIENTS WITH EXCESSIVE DAYTIME SLEEPINESS

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Introduction: Cataplexy, the most unique symptom of narcolepsy, is regarded as a pathognomonic symptom in patients with narcolepsy. Typical cataplexy is defined by an abrupt decrease in muscle tone associated with intense emotions. However, cataplexy-like symptoms have reported in certain group of narcolepsy, other sleep disorders with excessive daytime sleepiness, and even healthy controls. Therefore, it is necessary to differentiate typical cataplexy from cataplexy-like symptoms to make a correct diagnosis of narcolepsy.

Methods: From 2000 to 2006, 204 patients who visited the Sleep Clinic of St. Vincent's Hospital, Catholic University, with excessive daytime sleepiness as their major symptoms were evaluated. Clinical interview, SSI, Multiple Sleep Latency Test (MSLT), Human Leukocyte Antigen

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(HLA) typing, hypocretin-1 measurement were performed. The patients were divided into two groups; narcolepsy with typical cataplexy and other sleep disorders. In this study, 51 questionnaire items of the SSI were applied to differentiate triggering factors, types, duration and frequency of cataplexy in two groups.

Results: Typical cataplexy is triggered by pleasant emotions, like laughing, joking, and quick verbal response in a funny context. On the other hand, cataplexy-like symptoms are triggered by physical fatigue, tension, stress, angry, excitement, and athletic activities which have negative emotions. The duration of typical cataplexy was shorter than that of cataplexy-like symptoms. And the frequency of sudden muscle weakness was higher in the patients with typical cataplexy. Both HLA-DQB1*0602 allele and low CSF-hypocretin concentration (<110pg/mL) also were frequently observed in the typical cases.

Conclusion: Our study is the unique report that defines comprehensive characteristics of cataplexy and cataplexy-like symptoms in excessive daytime sleepiness patients. By the result of our study, narcolepsy with typical cataplexy could be diagnosed more correctly and further study is needed to elucidate the pathophysiology of cataplexy.

0652

GENDER AND DIAGNOSIS DEPENDENT DIFFERENCES IN OBJECTIVE AND SUBJECTIVE MEASURES OF TREATMENT RESPONSE IN NARCOLEPSY AND OBSTRUCTIVE SLEEP APNEA

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Introduction: Multiple sleep latency testing (MSLT), the gold-standard objective measure of sleepiness, does not consistently predict subjective treatment responses in primary sleep disorders. We compared treatment responses in OSA (O) and Narcolepsy (N) subjects using objective and subjective measures of sleepiness and mood: MSLT (mean SL), pupillometry (Pupillary Unrest Index; PUI), Epworth Sleepiness Scale (ESS), visual analog sleepiness scale (VAS), Profile Of Mood States (POMS) and Beck Depression Inventory (BDI).

Methods: Following overnight polysomnography, 12 (11M, 1F) O subjects and 20 (6M, 14F) N subjects completed a 4 nap MSLT, pupillometry and VAS (4 trials each), POMS, ESS and BDI. The full-protocol was then repeated 1 month following institution of CPAP for O subjects, and 3 months following re-institution of stimulants for N subjects.

Results: The N subjects showed a significant correlation between improvements in SL and POMS ($r = 0.52$, $p = 0.02$). Unexpectedly, SL and VAS changes in this group were negatively correlated ($r = -0.77$, $p = <0.0001$). In O subjects, improvement in PUI exhibited significant correlations with improvements in POMS, BDI and VAS ($r=0.74$, $p=0.02$; $r = 0.74$, $p=0.02$; $r=-0.77$, $p=0.01$). SL change showed no correlations. Amongst male subjects, change in POMS significantly correlated with PUI, VAS and BDI changes ($r=0.51$, $p=0.04$; $r=-0.71$, $p=0.002$; $r=0.82$, $p<0.0001$). SL demonstrated no correlations. Female subjects again demonstrated only the unanticipated negative relationship between SL and VAS ($r=-0.68$, $p=0.009$).

Conclusion: We conclude that changes in objective SL and subjective VAS, in response to treatment in women with narcolepsy are negatively correlated: despite objective improvement in sleepiness, these subjects displayed an increase in subjective sleepiness. Treatment response in men with either OSA or narcolepsy includes improved mood. In men, changes of PUI rather than SL, appears to perform better as a physiological correlate of subjective treatment response.

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0653

PREVALENCE AND IMPACT OF SEVERE FATIGUE -SEPARATE FROM SLEEPINESS- IN PATIENTS WITH NARCOLEPSY

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Introduction: Excessive daytime sleepiness and cataplexy are the core symptoms of narcolepsy. Many patients also complain about fatigue, a subjective experience of mental or physical exhaustion that does not disappear after a period of sleep. Patients as well as doctors often have trouble distinguishing between daytime sleepiness and the physical feeling of tiredness. As the presence of fatigue is associated with a lowered general health status in various neurological disorders, we investigated the prevalence of severe fatigue in patients with narcolepsy.

Methods: A total of 127 narcoleptic patients were approached by mail to participate, 81 patients (65%) returned a completed questionnaire. All patients fulfilled the ICSD-2 diagnostic criteria of narcolepsy with cataplexy. Experienced fatigue was assessed using the Checklist Individual Strength (CIS), a 20-item questionnaire measuring fatigue during the past two weeks. In addition the quality of fatigue, self efficacy, general psychopathology, functional impairment and quality of life was assessed using validated scales. Comparisons were made between patients with (CIS-fatigue score >35) and without severe experienced fatigue.

Results: Fifty patients (62.5%) reported severe fatigue. There were no sex or age differences between patients with and without severe fatigue. Interestingly, fatigued patients more often used stimulant medication (64% vs. 40%, $p=0.02$). Both groups had the same amount of daytime sleepiness however (Epworth Sleepiness Score 14.3 ± 0.6 vs. 13.1 ± 0.8 , $p=0.22$), confirming the separation between sleepiness and fatigue. Fatigued patients reported significantly more catastrophizing thoughts and less general control over symptoms. Severe fatigue resulted in a significantly increased functional impairment (using the Sickness Impact Profile), and a lowered general quality of life (SF-36).

Conclusion: A majority of patients with narcolepsy suffer from severe fatigue, which can be distinguished from daytime sleepiness. Severe fatigue was associated with functional impairment and a lowered quality of life.

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0654

THE UTILITY OF MSLT AND MWT IN DIFFERENTIALLY DIAGNOSING PATIENTS WITH DISORDERS CAUSING EXCESSIVE DAYTIME SLEEPINESS

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Introduction: There are various disorders that cause patients to experience excessive daytime sleepiness (EDS). This study investigated the usefulness of MSLT and MWT, which can be performed on the same day, in differentially diagnosing patients with EDS, narcolepsy or idiopathic hypersomnia (IH).

Methods: We analyzed a total of 105 patients (58 male and 47 female, mean age 26 ± 2 , and BMI 21.6 ± 0.3) with EDS and an AHI of 5 or less. The examination of protocol in each subject included 4 to 5 MSLT trials and 4 30-minute MWT trials. The Narcolepsy group was diagnosed as having a mean sleep latency (MSL) on MSLT less than or equal to 8 min and two or more SOREMPs. IH was diagnosed as a MSL of 8 min

or less and fewer than two SOREMPs on MSLT. The control group was classified as MSL more than 8 min and fewer than two SOREMPs on MSLT and subjective feeling of EDS.

Results: There was no significant difference in subjective sleepiness (ESS) among the narcolepsy, IH and control groups. Mean MSLT sleep latencies among the narcolepsy, IH and control groups were 3.6 ± 2.2 , 5.8 ± 2.0 , and 12.9 ± 2.7 , respectively. On MWT, there was no significant difference in MSL between control individuals and those with IH (27.1 ± 3.5 vs. 21.9 ± 5.8), but there was a significant difference of that between IH and narcolepsy (21.9 ± 5.8 vs. 14.3 ± 8.4).

Conclusion: There was no significant difference in subjective sleepiness among control individuals with EDS, patients with IH, and patients with narcolepsy. It was suggested that MSLT and MWT performed on the same day were useful for differentially diagnosing the patients with narcolepsy and IH.

0655

IDIOPATHIC HYPERSOMNIA: A RETROSPECTIVE STUDY OF 85 CASES

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Introduction: Recently published practice parameters identified a need for studies on treatment of hypersomnias such as idiopathic hypersomnia (IH). We describe the clinical characteristics of ICSD-2 defined IH patients, emphasizing response to pharmacotherapy.

Methods: A retrospective review of our database identified 997 patients, utilizing “idiopathic hypersomnia” as keywords. We subsequently excluded patients who did not meet ICSD-2 criteria, those receiving sedatives, with sleep apnea (AHI ≥ 5 per hour), periodic limb movements of sleep (PLMI ≥ 15 per hour), circadian rhythm sleep disorders, dementia, traumatic brain injury, stroke, multiple sclerosis, chronic pain, and hepatic or renal failure.

Results: Of 85 IH patients identified, 16 were subcategorized with long sleep time, and 69 without long sleep time. MSLT results revealed mean sleep latencies (minutes) of 4.57 ± 1.92 and 4.77 ± 1.66 for those with and without long sleep time, respectively ($p=0.63$). Median (IQR) duration of follow up was 2.4 (4.7) years. Methylphenidate was most commonly used as a first-line agent prior to December, 1998, but afterwards modafinil became the most common first drug. At the last recorded follow-up visit, 92% of patients were on monotherapy (methylphenidate > modafinil), and 8% were on combination therapy. 65% reported complete symptomatic relief, 26% reported partial relief, and 9% reported no relief. Median (IQR) change in ESS scores were as follows: complete responders -9(4), partial -6(9) and non-responders +2(9). 49 patients tried one medication and 36 tried two or more medications. The most common adverse effects associated with methylphenidate were insomnia, gastrointestinal distress, and anorexia, and those most commonly associated with modafinil were expense, headache and nausea.

Conclusion: The majority of patients with IH respond well to pharmacotherapy. Methylphenidate may be more effective than modafinil, despite the fact that it is less commonly used initially. Taking into account cost and other variables, further comparisons are warranted.

0656

CSF HISTAMINE LEVELS IN NARCOLEPSY, IDIOPATHIC HYPERSOMNIA AND OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction: In order to recognize the functional significances of CSF histamine levels in patients with hypersomnia, we tried to evaluate if histamine contents are altered in several types of hypersomnia with and without hypocretin deficiency.

Methods: Sixty-seven narcolepsy subjects, 26 idiopathic hypersomnia (IHS), 16 obstructive sleep apnea syndrome (OSAS), and 73 neurological controls were included. All patients were Japanese. The diagnosis was made according to ICSD2.

Results: We found significant reductions in CSF histamine levels in hypocretin deficient narcolepsy with cataplexy (mean \pm SEM; 176 ± 25 pg/ml), hypocretin non-deficient narcolepsy with cataplexy (97 ± 38 pg/ml), hypocretin non-deficient narcolepsy without cataplexy (113 ± 16 pg/ml), and idiopathic hypersomnia (161.0 ± 29.3 pg/ml), while the levels in OSAS (259 ± 46 pg/ml) did not statistically differ from those in the controls (333 ± 22 pg/ml). Low CSF histamine levels were mostly observed in non-medicated patients, and significant reductions in histamine levels were evident in non-medicated patients with hypocretin deficient narcolepsy with cataplexy (112 ± 16 pg/ml) and idiopathic hypersomnia (143 ± 28 pg/ml), while the levels in the medicated patients were in the normal range.

Conclusion: The study confirmed reduced CSF histamine levels in hypocretin-deficient narcolepsy with cataplexy. Similar degrees of reduction were also observed in hypocretin non-deficient narcolepsy and in idiopathic hypersomnia, while the CSF histamine levels in OSAS (non central nervous system hypersomnia) were not altered. The decrease in histamine was more specifically observed in the non-medicated subjects, suggesting that CSF histamine is a biomarker reflecting the degree of EDS of hypersomnia of central origin.

0657

AVERAGE HYPOCRETIN AND ELEVATED AGRP IN THE CSF OF PATIENTS WITH ANOREXIA NERVOSA

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Introduction: Anorexia nervosa (AN) is a complex disease characterized by abnormal feeding behaviour, food aversion and acute disturbances in the body shape. The human feeding physiology is precisely regulated by the autonomic nuclei of the hypothalamus. The neurons of arcuate nucleus, lateral hypothalamic nuclei and other areas produce and release both the orexigenic (orexin, AGRP) and anorexigenic (alpha-MSH) signaling substances. There have been several studies in which these substances were measured in the plasma, but there are no studies in which they were measured in the cerebrospinal fluid (CSF).

Methods: In the present study we assessed CSF orexin, AGRP and alpha-MSH levels in two AN patients and compared them with 10 control subjects. The patients and control subjects gave informed consent and this study was approved by the local ethical committee. Case1 was a 34y female with a BMI of 10.9 and Case2 was a 21y female with a BMI of 13.7. Both cases were diagnosed as AN by DSM-IV.

Category I—Sleep Disorders – Narcolepsy/Hypersomnia

Results: In AN patients, CSF orexin levels were in the normal range (Case1: 250pg/ml, Case2: 330pg/ml, controls: 290+/-50pg/ml) and AGRP levels were 2 to 3 times elevated (Case1: 520pg/ml, Case2: 350pg/ml, controls: 180+/-30pg/ml). Alpha-MSH was not detected in the CSF of the AN patients and controls.

Conclusion: This is the first report of normal orexin and elevated AGRP levels in the CSF of patients with AN, while in the plasma, Yoshiuchi (2006) reported increased levels of AGRP in AN patients. Further research is needed to know (i) whether the elevated AGRP levels are primary or secondary due to the fasting, and (ii) the discrepancy between normal orexin and elevated AGRP levels.

0658

ANTI-AQUAPORIN 4 ANTIBODY ASSOCIATED SYMPTOMATIC NARCOLEPSY DUE TO HYPOTHALAMIC LESIONS WITH MULTIPLE SCLEROSIS

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Introduction: We have reported that several symptomatic narcolepsy cases are due to hypothalamic lesions with multiple sclerosis (MS) and low hypocretin levels. The brain MRI lesions of these cases were not typical of classical MS. These cases showed very rare locations and shapes of lesions, such as extremely localized hypothalamic and periaqueductal lesions. The reason for these shapes has been totally unknown. Neuro-myelitis optica (NMO) is one type of MS typically manifesting transverse myelitis and bilateral optic neuritis. NMO-IgG, a disease-specific autoantibody, was discovered in several patients, and the target antigen of NMO-IgG was recently identified as the aquaporin-4 (AQP4) water channel protein (Pitcock2006). Brain lesions of NMO are identified and have been reported that they are often seen in the hypothalamic region. Since no cases have been reported about the relationship between the symptomatic narcolepsy and anti-AQP4 antibodies, we measured the anti-AQP4 antibodies in six cases with symptomatic narcolepsy due to hypothalamic lesions of MS.

Methods: Serums obtained from cases with symptomatic narcolepsy due to hypothalamic lesions were tested for anti-AQP4 antibodies by a sensitive detection method. CSF hypocretins were also measured by RIA.

Results: Three out of six patients had serum anti-AQP4 antibodies. All six cases presented hypersomnia, symmetrical hypothalamic lesions on MRI, and decreased CSF hypocretin levels, all of which improved simultaneously after steroid treatment.

Conclusion: It has been demonstrated that in some MS patients who are seropositive for anti-AQP4 antibodies, hypothalamic and periaqueductal lesions correspond to brain regions where high AQP4 expression is observed. We considered that the hypothalamic lesions of our 3 cases with symptomatic narcolepsy could be caused by the immune reactivity of anti-AQP4 antibodies. This may be the reason for the rareness of the locations and shapes of the lesions. We propose to measure anti-AQP4 antibodies in patients in which symmetrical hypothalamic lesions and hypersomnia were observed.

0659

SYMPTOMATIC CATAPLEXY AND SUSPECTED NIEMANN-PICK DISEASE TYPE C

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Introduction: Narcolepsy, cataplexy and CSF orexin are closely related. However, there are few diseases other than narcolepsy that are accompanied by cataplexy. In this report, we report a study on cataplexy and CSF orexin in diseases other than narcolepsy.

Methods: The subjects are two patients who visited the Akita University Hospital. Cataplexy was seen and Niemann-Pick disease Type C (NPC) was suspected in both cases. Physical examinations and tests for NPC were performed. Measurements of orexin concentration were also performed to evaluate cataplexy.

Results: The first patient was diagnosed with hepatic function disorder and hepatomegaly a month after birth, but grew up well until 4 years old. At the age of 5, the patient began to show gait disorder. At 8 years old the patient was referred to our hospital for detailed investigation. At the initial visit, there was a mild hepatomegaly and the margin of the spleen was palpable. Brain MRI and CT findings showed atrophy of both cerebral hemispheres. The patient began to show frequent daytime cataplexy from around the age of 9, and by the age of 10 was showing symptoms of vertical oculomotor disturbance. CSF orexin concentration was 174pg/ml, intermediate level. NPC was suspected as a result of elevation of Filipin stains for fibroblast. NPC1 gene analysis was performed, and the diagnosis of NPC was confirmed. The second patient was diagnosed with panic disorder and went under medical treatment at 24 years old. Cataplexy attacks frequently occurred around age 26. The patient also experienced hypnagogic hallucinations and nightmares and visited our clinic for detailed investigation. The patient's orexin concentration was 173pg/ml. Adult type NPC was suspected, but (1) Bone marrow puncture does not reveal Niemann-Pick cells, (2) Filipin stains for fibroblast are negative for cholesterol, and (3) no abnormalities are seen as a result of NPC1 gene analysis. The cataplexy attacks improved with treatment of clomipramine 150mg/day.

Conclusion: The patient's CSF orexin concentrations were intermediate level in both cases. In the first patient, diagnosis of NPC was confirmed by gene analysis. The diagnosis of second is still unknown and only symptomatic treatment is being provided.

0660

AUTONOMIC CORRELATES OF DAYTIME SLEEPINESS

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Introduction: Emerging technical and analytical strategies have facilitated performing polysomnography outside of the sleep laboratory. Among these is the novel technique to derive measures of sleep/wake architecture, cardiorespiratory activity and autonomic modulation from the ECG signal. Yet it is unclear whether ECG derived measures of autonomic tone reflect levels of daytime sleepiness or arousal. We aimed to determine if ECG derived measures of autonomic activity correlate with MSLT derived measures of daytime sleepiness.

Methods: Subjects were selected from a population based study on CFS conducted by the Centers for Disease Control (CDC). A total of 368 PSGs (preceded or followed) by MSLT's were included. Patients with extreme sleepiness (MSLT<5) were excluded. The remaining subjects

were categorized as follows: G1 (MSLT's ≥ 5 but ≤ 9.99 ; $n=138$), G2 (MSLT ≥ 10 ; $n=128$). Respiratory Disturbance Index (RDI) and cortical arousals were calculated from the PSG. The ECG obtained during the PSG was analyzed to yield values of mean RR intervals (RRI), number of autonomic arousals, and spectral parameters of the RRI, namely: VLF (0.008-0.04Hz), LF (0.04-0.15Hz), HF (0.15-0.5Hz), and balance (LF/HF) during the entire night. Two tailed t-test was used to determine for significant differences between groups.

Results: Significantly increased HF power was observed in G1 during sleep, but not during wake periods ($p < 0.05$). LF was also higher in G1 during Non REM sleep only ($p < 0.05$). Mean RRI was significantly higher (lower HR) in G1 during the night (0.92 ± 0.10 vs. 0.87 ± 0.09 , $p < 0.001$). Mean RDI was similar in G1 and G2 (4.4 ± 7.0 , 5.8 ± 8.3 respectively, $p = 0.16$). The number of autonomic arousals was also similar (170 ± 98 in G1 and 167 ± 113 in G2; $p = 0.80$).

Conclusion: Subjects with mild to moderate daytime sleepiness, exhibit lower HR and higher HF power, a manifestation of increased parasympathetic activity. These differences do not result from either sleep related breathing disturbance or sleep disruption. We speculate that the increased parasympathetic tone does not allow sleepy subjects to achieve the same degree of cortical arousal as healthy ones, and makes them prone to fall asleep. These findings suggest that autonomic tone has a role in maintaining wakefulness.

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0661

CHARACTERISTICS OF DAYTIME SLEEPINESS (DS), EVALUATED BY EPWORTH SLEEPINESS SCALE (ESS) IN PATIENTS WITH NARCOLEPSY, COMPARED WITH OTHERS SLEEP DISORDERS (SD)

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Introduction: The term Narcolepsy has been used almost synonymously of EDS; however, it refers to a specific REM and NREM sleep disorder. It is a sleep disorder characterized by difficulty in staying alert with uncontrollable daytime sleep attacks. Sleep mechanisms control is supposed to be broken, leading to frequent nighttime awakenings and daytime sleep episodes. Narcolepsy has the following clinic findings: excessive daytime sleepiness (EDS), cataplexy (sudden onset of muscle weakness, usually provoked by emotions; sleep paralysis (general muscle weakness followed by awakenings); hypnagogic hallucinations (visual or auditory phenomena preceding the beginning sleep and sleep fragmentation (ICSD - 2, 2005). Objective: To evaluate sleepiness in patients with narcolepsy and compare it to sleepiness in other diseases. We analyzed 92 men and 61 women aged 18 to 72 years who presented DS above 9 points in ESS (Johns, 1991), who were not using hypnotics medications.

Methods: 153 individuals with DS were selected patients, through clinical examination, anamnesis, polysomnography and ESS (Johns, 1991, 14:540-545).

Results: from 153 analyzed patients, the narcolepsy DS average was 19 ± 1.79 points and DS in other diseases was 16 ± 0.65 . Other presented DS were: sleepwalking/depression with 13; Sleep Related Breathing Disorders (SRBD) with 15; OSA/PLMS with 16; PLMS with 16; OSA with 16; OSA/Restless Legs Syndrome (RLS) with 16; Primary and Idiopathic Hypersomnia with 18.

Conclusion: Narcolepsy is a sleep disorder with the highest sleepiness. Idiopathic Hypersomnia showed the second higher sleepiness, very close to Narcolepsy. We suggest considering Narcolepsy and Idiopathic Hypersomnia in patients with severe sleepiness.

0662

NARCOLEPSY AND NICOTINE: A PRELIMINARY EXAMINATION

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Introduction: Nicotine is a stimulant, available in multiple formulations, that could theoretically increase alertness. However, the typical health risks are magnified in narcolepsy since falling asleep while smoking creates a risk of burns and fires. No study has examined the extent or consequences of nicotine usage by narcolepsy patients.

Methods: As a first phase unpublished data was obtained from the community-based study of narcolepsy (Silber et al, 2002). The second phase consisted of a 25 item questionnaire distributed at the 2007 Narcolepsy Network national meeting to obtain more information.

Results: In the Olmsted County database 62.5% of narcolepsy patients were past or present smokers. Seventeen questionnaires were completed. 47% of respondents were past or present nicotine users (all smokers at one point). All respondents identified nicotine as an effective in decreasing sleepiness. 37% fell asleep while smoking. 25% smoked in bed. Burns were reported by 75% involving clothing, furniture or carpet. One respondent started a fire. One respondent substituted nicotine patches for cigarettes years ago to continue a "powerful" means to decrease cataplexy. All tried to quit smoking but described difficulty because sleepiness worsened without nicotine.

Conclusion: This is the first description of nicotine use by narcolepsy patients. Burns are a potentially serious complication for patients smoking nicotine. Although burns appear to be common in our preliminary survey, the lack of a denominator precludes conclusions about their frequency. Narcolepsy patients who smoke may have more trouble quitting because of increased sleepiness. The role of nicotine, particularly in transdermal forms, to self-medicate sleepiness and cataplexy merits more study.

Support (optional): Piscopo Narcolepsy fund of the Mayo Foundation

0663

NARCOLEPSY SYMPTOM SEVERITY IN RELATION TO HLA-DQB1*0602 ALLELE FREQUENCY

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Introduction: The allele HLA-DQB1*0602 is considered a marker of narcolepsy and may modulate sleep in healthy individuals. We examined the association between HLA-DQB1*0602 allele frequency and measures of narcolepsy symptom severity in a population-based sample of patients with narcolepsy.

Methods: We ascertained cases of physician-diagnosed narcolepsy in King County Washington via multiple overlapping methods from July 1, 2001 to June 30, 2005. We recruited 237 cases (mean age 48 years, 64% female) who underwent an in-person interview for the following narcolepsy symptom severity instruments: the Epworth Sleepiness Scale, the Ullanlinna Narcolepsy Scale, and the SF-36. During the interview, DNA was obtained from buccal swabs and genotyping of the HLA-DQB1*0602 allele was performed using quantitative DNA amplification and fluorescence detection with sequence-specific probes yielding: 117 with zero copies; 99 with one; and 18 with two. We used a planned contrast in ANOVA to test for trends in scores across the three allele frequency groups.

Results: We found a dose response relationship between HLA-DQB1*0602 allele frequency and sleepiness as defined by the Epworth Sleepiness Scale (mean [sd]: zero copies=14.8 [5.4]; one=16.1 [5.0]; and two=18.4 [3.5]; $p < 0.01$ for trend) and narcolepsy severity as defined by the Ullanlinna Narcolepsy Scale (zero copies=11.5 [7.2]; one=16.0 [7.6];

Category I—Sleep Disorders – Narcolepsy/Hypersomnia

and two=17.3 [8.7]; $p < 0.01$ for trend). No similar relation was observed for the SF-36, either for the individual measures or the summary measures for physical health (zero copies=42.8 [11.6]; one=42.8 [11.9]; and two=39.9 [13.9]; $p=0.34$ for trend) or mental health (zero copies=43.9 [11.8]; one=46.1 [11.7]; and two=44.7 [11.5]; $p=0.79$ for trend).

Conclusion: In this population-based sample, narcolepsy symptom severity varied in a dose response manner according to HLA-DQB1*0602 allele frequency. This finding supports the notion that genetic variability in HLA-DQ modulates the narcolepsy phenotype.

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0664

NARCOLEPSY AND THE SICKNESS IMPACT PROFILE, A GENERAL HEALTH STATUS MEASURE

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Introduction: The Sickness Impact Profile (SIP) was designed to assess functional status of patients with chronic diseases. It contains 136 items grouped in 12 categories and two dimensions. We used the SIP to characterize the functional impact of narcolepsy on patients.

Methods: We ascertained patients with physician-diagnosed narcolepsy in King County, Washington using multiple overlapping methods from 2001 July 1 to 2005 June 30. We recruited 226 patients (mean age 48 years, 65% female) who underwent in-person interviews and completed the Epworth Sleepiness Scale, the Ullanlina Narcolepsy Scale, and the SIP. Strengths of associations were assessed with Pearson's correlation coefficients.

Results: Percent of overall dysfunction on the SIP (mean 10.3) was significantly correlated with the Epworth Sleepiness Scale (0.33, $p < 0.001$) and Ullanlina Narcolepsy Scale (0.41, $p < 0.001$). Mean percent of total dysfunction was higher for the psychosocial (13.2) than physical dimension (5.0). Mean percent of total dysfunction in descending order for categories was: Sleep and Rest (23.6), Alertness Behavior (22.6), Recreations and Pastimes (20.6), and Work (15.3). Ten items were endorsed by at least a third of patients: 3 items concerned sleep; 3, doing less work around the house and on hobbies; and 2, social isolation. The sixth most commonly endorsed item was, "My sexual activity is decreased," and the seventh, "I forget a lot, for example, things that happened recently, where I put things, appointments."

Conclusion: In this population-based sample, mean percent of total dysfunction on the SIP in patients with narcolepsy (13.2) was higher than what has been found in prior studies in the general population (3.6) and similar to what has been found for other chronic disabling conditions. Although the SIP was strongly correlated with the disease-specific measures of narcolepsy severity, it also captured a wealth of information not available in other tools.

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0665

CSF HYPOCRETIN-1 (OREXIN-A) MEASUREMENT IN PEDIATRIC AND TEENAGE PATIENTS WITH SLEEP DISORDERS

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Introduction: The diagnosis of narcolepsy in children is challenging, because the expression of the symptoms may be different though those in children are similar to those in adults, and polysomnography as a diagnostic test are often difficult to undergo or interpret in children. We previously described that low hypocretin-1 levels are specific for

narcolepsy-cataplexy in children and teenagers as the same as in adults (Arii2004, Kaneko2005). This study addresses the more evidence by analysis of 84 subjects from pediatric and teenage patients with sleep disorders.

Methods: CSF samples were collected from patients under 19 years of age with narcolepsy with cataplexy (N/C; n=37), narcolepsy without cataplexy (Nw/oC; n=13) and idiopathic hypersomnia (IHS; n=34). CSF hypocretin-1 was measured in crude CSF using radioimmunoassay kits (Phoenix Pharmaceuticals). We used the cut-off of 110pg/ml, values above 200pg/ml were considered normal as described by Mignot(2002). Sleep disorders were diagnosed clinically and using sleep studies (nocturnal PSG and multiple sleep latency test; MSLT). Patients were classified based on their primary diagnosis using the ICSD2, blind of HLA and hypocretin-1 results.

Results: CSF hypocretin-1 levels were low in 31, intermediate in 2 and normal in 4 out of 37 subjects from N/C patients. The levels were low in 2 and normal in 11 out of 13 subjects from Nw/oC. The levels were intermediate in 4 and normal in 30 out of 34 patients with IHS. Sleep studies and HLA showed diagnostically negative findings or one positive finding in 18 out of 37 N/C patients, in 4 out of 13 Nw/oC patients, and in 30 out of 34 IHS patients. The number of patients under the age of 8 was 10 out of 37 N/C, none of 13 Nw/oC, 4 out of 34 IHS.

Conclusion: N/C was clinically diagnosed by based on symptoms, but the patients were young and provided insufficient diagnostic findings by sleep studies. Measuring hypocretin-1 was useful for early diagnosis of closer to onset and definitive evidence of abnormal hypocretin neurotransmission.

0666

VIGILANCE CHANGE BY ACUTE HISTAMINE DEPLETION WITH α -FMH IN OREXIN/ATAXIN-3 NARCOLEPTIC AND WILD TYPE MICE

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Introduction: Histamine-system is important for wake-promotion, and altered histamine neurotransmission is suggested in narcolepsy. A recent study in rats however, reported that lesions of histaminergic neurons do not affect sleep/wake patterns. We also reported that acute deprivation of histamine release by α -FMH (a histamine decarboxylase inhibitor) injection did not alter sleep in rats. These reports made the roles of histamine more puzzling. In the current study, we evaluated the effects of α -FMH on sleep in wild type (WT) mice and in orexin/atxin-3 transgenic (TG) narcoleptic mice to examine whether these mice exhibit altered responses to histamine depletion.

Methods: TG narcoleptic mice (C57BL/6, congenic-line) and WT littermates (n=7 for each group) were used. The mice were surgically prepared for sleep-polygraph recordings. Three doses (50, 100 and 200 mg/kg i.p.) of α -FMH and a vehicle administration during dark periods (ZT12) were performed. Data were analyzed for the six hours following drug administration (from ZT13), and each 10-second epoch was scored.

Results: In contrast to the results observed in rats, α -FMH doses up to 100 mg/kg decreased wake about 20% (6 hour total-amount after injection) and enhanced NREM (400-700 %) and REM sleep (40-300%) in a dose dependent manner. α -FMH effects at 200 mg/kg were similar but smaller than that at 100 mg/kg, suggesting that this dose of α -FMH may have non-specific effects. Both TG and WT mice responded to α -FMH in a similar fashion.

Conclusion: These results are compatible with the current concept that histaminergic neurotransmission is involved in maintaining wakefulness. The results are however, in contrast to those obtained in rats, and a significant species difference likely exists in roles of histamine in sleep/wake control. Our results also suggest that the histaminergic system is functioning without the hypocretin system in the mice. Further studies

in the roles of histamine in sleep/wake regulations and in sleep disorders are warranted.

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0667

HPLC ANALYSIS OF IMMUNORECTIVE-HYPOCRETIN-1 SIGNALS IN THE CSF FROM PATIENTS WITH NARCOLEPSY-CATAPLEXY WITH- AND WITHOUT-HYPOCRETIN DEFICIENCY AND HEALTHY CONTROLS

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Introduction: The major pathophysiology of human narcolepsy has been revealed to be hypocretin ligand deficiency, and this is tightly associated with occurrence of cataplexy and HLA positivity (HLA DQB1*0602). The hypocretin deficiency is clinically detected by undetectably low immunoreactive-hypocretin-1 [IR-hcrt 1] signals (by radioimmunoassay [RIA]) in the CSF. However, it is also known that up to 10 % of narcolepsy-cataplexy subjects (including HLA DQB1*0602 positive subjects) exhibit normal CSF hypocretin-1 levels, and an involvement of hypocretin neurotransmission in these subjects is obscure. In the current study, we have examined the patterns of HPLC separation of hypocretin signals in these subjects to see if secreted hypocretin peptide are different (abnormal peptide cleavages) from those of healthy controls and of narcolepsy without cataplexy (with normal hypocretin-1 levels).

Methods: One ml of CSF from 6 narcolepsy-cataplexy with normal IR-hcrt 1, 3 narcolepsy-cataplexy with undetectable IR-hcrt 1, and 5 healthy control subjected were applied to HPLC separation (µBondpak C18, a linear gradient of acetonitrile containing 0.1% TFA from 10% to 60% at a flow rate of 1ml/min). One-minute fractions were collected for 40 minutes. Each HPLC fraction was dried up and applied to the RIA for hypocretin-1 measures. The separation patterns of IR-hcrt 1 of each subject were then compared.

Results: We found two major IR-hcrt peaks (12 to 14 min and 19 to 23 min) in all 5 controls, and the latter peak corresponds to the retention time of the authentic hypocretin-1 peptide. Both peaks do not exist in all 3 patients with narcolepsy-cataplexy with undetectable IR-hcrt 1, suggesting that the first peak is also likely a hypocretin peptide signal (i.e. peptide fragment with IR-hcrt 1). We found that separation patterns of IR-hcrt 1 of 6 narcolepsy-cataplexy with normal IR-hcrt 1 were identical with those of healthy controls.

Conclusion: We could not find any evidence suggesting that abnormal processing/degradation of the hypocretin peptide is involved in narcolepsy-cataplexy with normal IR-hcrt 1. If altered hypocretin signaling is involved in these subjects, the receptor and its downstream function from the hypocretin signaling are likely involved in these subjects.

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IMAGING CRANIAL ANGIOSOMES IN HYPERSOMNIA

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Introduction: Thermography can monitor skin temperature regulation in the cranial angiosomes. Normal Forehead Nose Temperature Ratio (FNTR), nose is colder by 6-8 degrees C compared to the forehead. Stabilization of FNTR following treatment in hypersomnia, relating to changes in the arteriovenous shunting between the internal and external carotid angiosomes, under trigeminal vasomotor control and hypothalamic regulation was imaged.

Methods: Infrared imaging (with FLIR A 40 Camera) of facial temperature was done in a temperature and humidity controlled draft free laboratory using committee for the protection of human subjects approved protocol (induced hyperoxia five minutes 100% oxygen inhalation) and drug challenge with Modafinil (Provigil™) in four, Dextro-Amphetamine/Amphetamine (Adderell™) in two and Methylphenidate (Ritalin™) in one. Thermograms done at baseline, for 20 minutes after hyperoxia and 1-2 hours after the drug. Normal response to hyperoxia is vasoconstriction. Altered response can be decreased/ absence of response or paradoxical vasodilatation. Seven Caucasians, six females, one male, 51-67 yrs, with hypersomnia evaluated by sleep medicine/clinical neurological exam, lab testing and PSG/MSLT. Their Epworth Sleepiness Scale 11 to 20. HLA DQ tested in 7, positive in 4. MSLT sleep onset latency mean 6.9 minutes. One patient had two SOREMS. AHI normal in six. Seventh patient AHI 6.9. She lost 35 pounds before thermography testing.

Results: 0.5 degree C change is significant. Vasomotor response to hyperoxia at baseline was not normal for the group. Skin temperature regulation was calculated as FNTR. Baseline FNTR, group mean 1.88 degree C, after treatment 5.97 degree C. Closing of arteriovenous shunts in external carotid angiosomes made nose colder. FNTR improved in six patients. Seventh patient, FNTR no improvement.

Conclusion: Altered response to hyperoxia indicates possible role of oxygen radicals in hypersomnia. Drug effect correlated with improvement in FNTR. Cranial- facial skin temperature regulation imaging in hypersomnia can be correlated with sleep propensity.

0669

CORRELATION BETWEEN HLA PROFILE AND SLEEP PARAMETERS IN NARCOLEPTIC PATIENTS

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Introduction: Strong correlation has been detected between narcolepsy and special HLA haplotypes (DRB1*1501, and DQB1*0602). However narcolepsy can be observed also without the presence of these alleles.

Methods: Among 58 patients that were diagnosed with narcolepsy (including 11 cases with the narcolepsy-cataplexy syndrome), HLA testing was done in 41 patients (11 male and 30 female with a mean age of 40 years [range: 20 to 75 years]). Laboratory testing was done on blood samples obtained in 10-ml heparinized tubes. Following the separation of lymphocytes, a proportion of the lymphocyte pool was used for identifying A-B-C antigens on microtitre plates, with appropriate antisera. DNA-level analysis with the PCR SSP/SSO method was performed on the other proportion of lymphocyte samples.

Results: HLA testing of 41 patients showed narcolepsy-cataplexy genes (DRB1*1501 and DQB1*0602) in 21 cases. Seven of these subjects had the narcolepsy-cataplexy syndrome, whereas in the other 14 patients, excessive daytime sleepiness was not accompanied by cataplexy. HLA testing was negative in 20 narcoleptic patients (without history of cataplexy). We found differences between the HLA positive and negative groups in the polysomnographic (PSG) and MSLT results. The average PSG sleep latency was 18.34 min (SD: 17.09) in the HLA negative and 12.14 min (SD: 9.21) in the HLA positive group. The average MSLT sleep latency was 11.70 min (SD: 4.30) in the HLA negative and 7.40 min (SD: 5.47) in the HLA positive group. Sleep onset REM was observed in two cases in the HLA negative and in eight cases in the HLA positive group.

Conclusion: According to our results HLA positive narcoleptic patients have shorter sleep latencies, have more frequent sleep onset REM and have a more complete clinical picture.

0670

IS NARCOLEPSY A NEURODEGENERATIVE DISEASE?

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Introduction: A dysfunction in hypocretinergic neurotransmission causes narcolepsy. It remains to be clarified why hypocretin cells are selectively lost in narcolepsy. A neurodegenerative process with protein aggregation may be involved. To test this hypothesis, ubiquitin staining targeting remaining hypocretin cells was performed. We also studied additional markers of inflammation.

Methods: To screen for ubiquitinated protein aggregation in hypocretin cells and related inflammation findings, we studied the distribution of ubiquitin, microglial activation marker AIF1, reactive astrocytic marker GFAP and hypocretin immunoreactivity in the perifornical hypothalamic area of narcoleptic and control brains. We used sections from 4 narcolepsy (3 with comorbid dementia), 5 non-neurological controls and 5 dementia subjects.

Results: Hypocretin cell number was markedly decreased in all 4 narcolepsy subjects, but no ubiquitinated inclusion bodies were observed in remaining hypocretin cells. AIF1 and GFAP immunoreactivity in the adjacent perifornical area did not show abnormal increase. Colocalization of ubiquitin cytoplasmic staining in some hypocretin cells was observed in the 3 narcolepsy subjects with dementia but not in the narcolepsy case without dementia. Control subjects with or without dementia also had a few ubiquitin colocalization in hypocretin cells. The percentage of ubiquitin/hypocretin double positive cells was higher in narcolepsy subjects comorbid with dementia.

Conclusion: Abnormal ubiquitinated protein aggregates was not observed in hypocretin cells of narcolepsy subjects without dementia. The hypothesis that narcolepsy is a neurodegenerative disease is unlikely, although a neurodegenerative process without inclusion body formation might trigger the hypocretin cell apoptosis. Further studies evaluating the hypocretin cell changes at disease onset may help clarify how selective hypocretin loss occurs. The observation of ubiquitin colocalization in hypocretin cell of dementia patients suggests that hypocretin cell function could be impaired in dementia.

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0671

EVALUATIONS OF FRAGMENTED REST/ACTIVITY PATTERNS AS A PREDICTION OF SLEEP FRAGMENTATION IN MICE WITH DISEASE MODELS

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Introduction: Sleep/wake fragmentation is one of the major sleep abnormalities of narcolepsy in human and animal models. As sleep analysis with head stage implantation is required for the evaluation of sleep/wake fragmentation in animal models, it can be done only in a specialized sleep laboratory. We had proposed that sleep/wake fragmentation could be detected with high resolution locomotor analysis. In the current study, we attempt to develop a standardized method for the detection by locomotor monitoring using an orexin/ataxin-3 transgenic (TG) narcoleptic and histamine H3 receptor knockout (H3 KO) mice.

Methods: TG, H3 KO, and wild type (WT) mice for each group with standard sleep-implants and the telemetry-transmitters for activity-monitoring (Mini-Mitter, OR) were used. Activity data were collected with

a 10 sec time-bin during 24-hr light-dark cycle (LD12:12) with sleep-recording. As a separate experiment, locomotor-activity was measured with infrared beam-detection system (AccuScan Instruments Inc, OH). The original data from both methods were then summed to calculate the activity for longer time-bins (30sec-120min). Each time-bin was defined as 'active-phase' or 'inactive-phase' in light, dark, and 24 hour periods by applying the thresholds (the mean activity-count of each period). The mean duration of the active-phase and inactive-phase as well as state change frequency were computed for genotype comparison.

Results: We found that TG narcoleptic but not H3 KO mice frequently change their activity states over 24 hours, and the mean duration of active period of TG mice during dark and that of inactive period during both light and dark periods are significantly shorter than those of WT mice. These results are consistent with the sleep fragmentation determined by sleep recordings in TG and H3 KO mice. The difference in narcoleptic mice was however best detected between 30 sec to 5 minute time-bins (lowest p values), and there was no significant difference with longer time bins.

Conclusion: Our results suggest that sleep fragmentation can be assessed by locomotor monitoring with high time-resolution (20 sec to 5 minutes time-bin), that corresponds to the mean wake and sleep bout of mice. This method does not require headstage implant surgeries and sleep recording systems. The evaluation method is fast, fully objective, and normalized for each animal. Our standardized method in mice can be used for the rapid screening of one of the principal sleep abnormalities.

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0672

EVALUATIONS OF WAKE PROMOTING EFFECTS OF HISTAMINE H3 ANTAGONIST IN H3 RECEPTOR KNOCKOUT MICE

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Introduction: Recent experiments demonstrated that the histaminergic system is one of the important wake-promoting systems. An altered histaminergic neurotransmission is also suggested in human narcolepsy and other hypersomnias. We have reported that imidazole (thioperamide) and non-imidazole (JNJ-10181457) H3 receptor antagonists promote wakefulness in the mouse narcoleptic model. In order to further characterize and contrast the effects of these two H3 antagonists, we have evaluated the wake promoting effects of thioperamide and JNJ-10181457 in mice lacking H3 receptors (H3-KO mice).

Methods: H3-KO (n=8, congenic, C57BL/6J back-ground) and sex/age/background matched wild-type (WT) mice (n=8) were surgically prepared for EEG/EMG recordings. The mice were subjected to administration of two doses of thioperamide (1 and 4 mg/kg i.p.), JNJ-10181457 (3 and 10mg/kg, p.o.), and one respective vehicle administration during the light period at ZT2. In addition, effects of modafinil (200 and 400mg/kg, p.o.) were also evaluated in these mice. Six-hour post drug data were analyzed, and each 10-second epoch was scored visually as wake, REM, or NREM sleep.

Results: Thioperamide, JNJ-10181457, and modafinil increased wake and reduced NREM and REM sleep in WT mice in a dose-dependent manner compared to their respective vehicle sessions for each compound. We found that the wake-promoting effects of JNJ-10181457 were completely abolished in H3-KO mice (no significant effect from the vehicle session). Interestingly, we observed that thioperamide at 4mg/kg significantly reduced wake and increased NREM in H3-KO mice. Both WT and H3-KO mice responded to modafinil and wake was enhanced equally in WT and H3-KO mice.

Conclusion: The results that wake-promoting effects of non-imidazole H3 antagonist, JNJ-10181457, was completely abolished in H3-KO

mice suggest that the wake-promoting effects of JNJ-10181457 are truly mediated by antagonism of H3 receptors. The fact that an imidazole H3 antagonist, thioperamide, significantly reduces wakefulness in H3-KO mice suggests that the imidazole binding property may interfere with the wake-promoting effect of H3 antagonism by thioperamide. Differences in other pharmacological properties between thioperamide and JNJ-10181457 may also be involved in the distinct effects observed in H3-KO mice. These results are informative if we develop H3 antagonists as wake-promoting agents for the treatments of narcolepsy and other hypersomnia, and further studies are warranted.

Support (optional): This study was supported by National Institutes of Health Grants 1R03MH079258 and 5R01MH072525.

0673

TREATMENT FOR HYPERSOMNIA AND TREATMENT PROBLEMS IN JAPAN

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Introduction: In October 2007, the problem of excessive prescription of methylphenidates for depression in Japan was addressed, and the Ministry of Health and Welfare imposed new prescription regulations, under which, as of 2008, methylphenidate can only be prescribed for narcolepsy by only specially qualified doctors. Modafinil has been prescribed since April 2007 and have gradually taken the place of methylphenidate. However, because they cost more, some patients prefer methylphenidate. In the following, we present the content and dosage of central nerve stimulants(CNS) for hypersomnia.

Methods: Hypersomnia outpatients (narcolepsy, idiopathic hypersomnia, behaviorally induced sleep insufficient syndrome) were retrospectively investigated by means of clinical records for sex, age, duration of treatment, onset age, content of CNSs and dosage of CNSs.

Results: There were altogether 49 cases (male; 35, female;14 with cases increasing on the presentation day). The diagnosis was 35 narcolepsy (the average age ;21.7±11.3 years old and three were late onset narcolepsy including narcolepsy after the head injury by the traffic accident), seven idiopathic hypersomnia, and four sleep apnea with behaviorally induced sleep insufficient syndrome. Fifteen were narcolepsy patients treated by modafinil only (without other drugs such as hypnotics). The other narcolepsy patients were treated using more than two CNSs or with methylphenidate (and/or pemoline).

Conclusion: CNSs, especially methylphenidate, sometimes provoke psychiatric symptoms (irritability, excitability, delusion). We experienced three patients with narcolepsy who exacerbated psychiatric symptoms. Patients switching from methylphenidate to modafinil are gradually increasing despite some problems such as expensive price (\$5 for one tablet) of modafinil, restrictions on prescription (14 days) and restriction on dosage (highest dose; 300mg). Because of these reasons, methylphenidate or pemoline must be added to modafinil.

0674

RELATIONSHIPS BETWEEN SLEEPINESS, FATIGUE, AFFECTIVE SYMPTOMS AND NON-RESTORATIVE SLEEP COMPLAINTS

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Introduction: The lack of distinction in the clinical use of terms like fatigue and sleepiness is still an important issue. Associated environmental and socio-demographic factors to daytime fatigue associated conditions are poorly described in general population samples. The main purpose of the present study was to contribute to the distinction between fatigue and

sleepiness and to their links to non-restorative sleep (NRS) complaints, to social habits and to the intensity of related affective symptoms in non-clinical population sample.

Methods: We randomly selected 130 subjects (mean age 39.3, 18-65) from a general population sample in the Belgian French speaking community. A structured and validated computer assisted web-interview was administered. Demographic data, sleep habits, subjective fatigue with the fatigue severity and the Pichot fatigue scales, sleepiness with the Epworth and the Stanford Sleepiness Scales and affective symptoms with the Hospital Anxiety and Depression Scale were measured.

Results: 35% of women and 32% of men reported a NRS complaint. Furthermore 55% of all subjects were globally not satisfied with their sleep quality. Both fatigue and sleepiness were correlated to affective symptoms. Furthermore sleepiness and the intensity of daytime fatigue were positively correlated. NRS, global sleep satisfaction and having consulted a doctor for sleep disorders were linked to higher scores on all psychometric scales (all $p < 0.001$) but not irregular working hours, shift working and present hypnotic consumption. Mean values on all scales showed no sex related differences.

Conclusion: NRS can simultaneously present complaints of daytime fatigue and sleepiness. Correlation of subjective fatigue and sleepiness is not often mentioned. These results therefore show the difficulty and the partial lack of distinction in the concepts of fatigue and sleepiness. As fatigue and sleepiness can hide somehow very different pathogenic processes, the use of well-structured psychometric tools in clinical practice is necessary.

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0675

COMORBIDITY IN A PATIENT COHORT WITH NARCOLEPSY

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Introduction: Narcolepsy frequently goes along with other significant sleep disorder comorbidities, e.g. REM sleep behavior disorder (RBD), restless legs syndrome (RLS), periodic limb movements in sleep (PLMS), and obstructive sleep apnea syndrome. Furthermore, an association of narcolepsy with an increased body mass index (BMI) has been reported.

Methods: In this retrospective study, 64 patients with PSG confirmed narcolepsy according to ICSD 2 criteria were included. Information regarding sleep disorder comorbidities was gathered from patient histories, medical and polysomnography reports. Frequencies of the sleep disorders are presented in comparison to published data from the general population.

Results: Sixty-four patients (37 men, 27 women) with a mean age of 42.0 ± 15.4 years were analyzed. Fifty-six patients (87.5%) had narcolepsy with cataplexy. The following additional sleep disorders were frequent among patients with narcolepsy according to published data: RLS 23.4% (general population: 5-10%), PLMS 54.8% (general population: 5-44%), RBD 6.6% (general population: 0.5), REM sleep without atonia 70.5%, sleep talking 16.4% (general population: 5%), bruxism 13.1% (general population: 6-12%), confusional arousals 16.7% (general population: 3.6-4.8%), obstructive sleep apnea syndrome 29.5% (general population: 2-4%). Eighteen patients (28.1%; 10 men, 8 women) had a BMI above the 90th percentile (general population: 10 %).

Category I—Sleep Disorders – Narcolepsy/Hypersomnia

Conclusion: This study confirms that narcolepsy is associated with multiple other sleep disorders, and replicated that the BMI percentiles of patients with narcolepsy are more often above 90. In patients with narcolepsy all these comorbid sleep disorders should be carefully assessed and treated if indicated.

0676

DISRUPTION OF CIRCADIAN MELATONIN SECRETION IN PEDIATRIC CRANIOPHARYNGIOMA SURVIVORS WITH HYPERSOMNOLENCE

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Introduction: Sleep complaints, daytime hypersomnolence, and obesity are common sequelae of craniopharyngioma treatment. We investigated rest/activity cycles, polysomnography, and plasma melatonin oscillations in four patients in order to gain insight into the mechanisms underlying their daytime sleepiness.

Methods: Four patients (ages 15-22 years) with self-reported sleep difficulties or daytime hypersomnolence were enrolled. Three completed the study. All patients had hypopituitarism and obesity, one had hemianopia. Wrist actigraphy was performed for four weeks prior to admission to the hospital. During weeks 1-2, no specific instructions regarding sleep/wake habits were administered. During weeks 3-4, patients were instructed to maintain strict and consistent sleep and waking times. Stimulant medications were discontinued in the 4th week. Subjects were then admitted to the hospital for 72 hours. Two-day polysomnography (PSG) was performed and plasma melatonin was measured approximately every 20 minutes for 3 days.

Results: Wrist actigraphy demonstrated normal rest/activity cycles in all three patients; however, time-to-bed was irregular despite the study protocol instructions. Mean plasma melatonin levels were markedly diminished (2.7 ± 0.07 , 0.82 ± 0.12 , and 0.61 ± 0.02 pg/mL, respectively). Peak melatonin levels were also abnormal and without a consistent acrophase (1.9 pg/mL (at 6 AM), 4.5 pg/mL (at 8 PM), 7.1 pg/mL (at 2 AM), respectively, compared to historical controls (50-60 pg/mL at early morning acrophase). Polysomnography showed normal efficiency with no other architectural or pathological abnormality.

Conclusion: Our data demonstrate suppressed and arrhythmic secretion of plasma melatonin in craniopharyngioma survivors yet preservation of normal rest/activity cycles. Polysomnography did not divulge a unifying explanation for the patients' perceived sleep/arousal difficulties. We surmise that the restorative quality of sleep may be adversely affected by disruption of circadian melatonin secretion in obese craniopharyngioma survivors. These findings require further investigation.

0677

CORRELATIONS BETWEEN SLEEP ARCHITECTURE AND DAYTIME SLEEPINESS IN NARCOLEPTIC PATIENTS

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Introduction: Daytime sleepiness (DS) is the main symptom in narcolepsy. However, the relationship of DS with sleep architecture is scarcely known.

Methods: Objective: To study the correlation between DS, assessed by the Epworth Sleepiness Scale (ESS) and Multiple Sleep Latency Test (MSLT), and sleep architecture. A group of 28 untreated narcoleptic patients was studied and compared to a control group. The diagnosis of

narcolepsy was made using a structured interview, a polysomnographic record and the MSLT.

Results: Compared to control subjects, narcoleptic patients showed a significant increase in the percentage of wakefulness, light sleep, number of arousals and awakenings; and a decrease in Total Sleep Time (TST), Sleep Efficiency (SE), Slow Wave Sleep (SWS), Sleep Latency and REM Sleep Latency. No significant differences were found in the percentage of REM sleep when control and narcoleptic subjects were compared. A Pearson correlation analysis between ESS and polysomnographic data revealed a positive relation between DS and nocturnal wakefulness, sleep stage 1 and number of awakenings. A negative correlation was found between the ESS and TST, sleep efficiency, sleep stages 2 and 4 and REM sleep latency. In determining the relationship between the MSLT and sleep architecture we found a positive correlation between the MSLT and TST, sleep stage 2 and REM sleep latency; and a negative correlation between the MSLT and nocturnal wakefulness. We found a negative relationship between the MSLT and the percentage of diurnal REM sleep in the MSLT.

Conclusion: Our data support the hypothesis that nocturnal sleep characteristics will determine the level of DS in patients with narcolepsy.

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0678

HYPOCRETIN DEFICIENCY IN NARCOLEPSY WITH ATYPICAL OR WITHOUT CATAPLEXY

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Introduction: Whereas almost all cases with narcolepsy-cataplexy are HLA-DQB1*0602 positive and hypocretin deficient, almost nothing is known on the frequency of hypocretin deficiency in cases with atypical or no cataplexy (narcolepsy without cataplexy per ICSD2).

Methods: One hundred and thirty two patients with a diagnostic code of narcolepsy without cataplexy (86) or with atypical cataplexy (46) and available CSF hypocretin value were included, together with 190 controls. Subjects with a possible diagnosis of secondary narcolepsy were excluded. Subjects were mostly recruited at Stanford, or studied in collaborating centers. Many isolated samples also came from various centers in the United States.

Results: A similar percentage of cases without (16.3%) or with atypical (21.7%) cataplexy had low CSF hypocretin-1 (≤ 110 pg/ml), all but 3 being HLA-DQB1*0602 positive. This finding strongly suggests that atypical cataplexy (not triggered by usual emotions or very infrequent) does not have any diagnostic value in predicting hypocretin deficiency. Interestingly, we noted that a significant number of samples in this group had intermediary levels (110-200 pg/ml), suggesting partial deficiency in some cases without cataplexy. Preliminary ROC analysis versus control samples suggested that a cut off of 200 pg/ml may be more predictive than a cut-off of 110 pg/ml in this group. Finally, patients with hypocretin deficiency but no/atypical cataplexy were younger, closer to onset, and more severely affected than those without hypocretin deficiency. Approximately half are younger children likely to develop cataplexy within the next 10 years.

Conclusion: These studies demonstrate that a minority of cases without cataplexy, especially severe and close to onset, are hypocretin deficient. As these subjects are HLA positive, HLA typing prior to a lumbar puncture may be advisable. Pharmacological response studies in subjects with versus without hypocretin deficiency would be desirable to determine clinical significance of hypocretin deficiency in cases without cataplexy.

0679

MODAFINIL'S EFFECT ON CORTICAL EXCITABILITY IN NARCOLEPSY PATIENTS

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Introduction: A previous study showed human narcolepsy has an impaired balance between excitatory and inhibitory intracortical circuits that leads to cortical hypoexcitability. Modafinil, a vigilance-promoting agent, did not significantly enhance the motor excitability in healthy subjects. To evaluate whether modafinil changes the cortical excitability in human narcolepsy.

Methods: We consecutively recruited 31 drug naïve narcoleptics (18 male, mean age 26.7 yrs) and 38 age- and gender- matched normal subjects. We measured TMS parameters [resting motor threshold (rMT), motor evoked potential (MEP) amplitudes, cortical silent period (CSP), intracortical inhibition (ICI) and facilitation (ICF)]. The TMS parameters were measured in dominant hemisphere before and 3 hours after single dose 400mg of modafinil or placebo administration and compared within and between patients and controls.

Results: Compared to normal subjects, drug-naïve narcolepsy patients showed the increased rMT ($42.0 \pm 8.7\%$ in patients vs. $38.4 \pm 5.1\%$ in normal subjects, $p=0.033$, independent t-test), prolonged CSP duration, and increased SICI (interstimulus interval 2, 3ms) ($p < 0.05$). MEP amplitudes (at 120 - 150% rMT stimulation) and ICF (interstimulus interval 10, 15 ms) were not different between patients and normal subjects. Modafinil/placebo crossover study was performed in 18 narcolepsy patients and 21 normal subjects. After modafinil administration, MEP amplitudes were increased (at 120 - 150% rMT stimulation), CSP durations were shortened (at 140, 150% rMT stimulation), ICI was reduced, and ICF was significantly increased in narcoleptics ($p < 0.05$), but no change was observed in normal subjects. On the other hand, placebo administration produced no changes in the TMS parameters in both patients and normal subjects.

Conclusion: These findings suggest cortical hypoexcitability in human narcolepsy and single dose modafinil significantly changed the cortical excitability in narcoleptics, but not in normal subjects.

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0680

REPORTED SLEEPINESS WHILE DRIVING AMONG COLLEGE STUDENTS

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Introduction: This study determined the prevalence of reported sleepiness while driving in a cohort of college students and related this behavior to subjective sleepiness levels.

Methods: A total of 263 students completed the survey, which included demographics and sleepiness measures. Average age was 20.9 ± 3.2 , with 67 males and 196 females. Subjective sleepiness was determined with the Epworth Sleepiness Scale (ESS) and the Sleep-Wake Activity Inventory (SWAI). Cutoff scores to define sleepiness were ≥ 10 on the ESS and ≤ 40 on the SWAI. Most were not sleepy ($n=146$; 55.5%), 103 were sleepy only on the ESS, and 14 were sleepy on the SWAI (12 of whom were concurrently sleepy on the ESS). Students were asked to respond yes or no to the items "Have you ever fallen asleep at the wheel?" and "Have you ever gotten into a wreck because you were sleepy?"

Results: Groups did not differ by age, but the non-sleepy group had more males (31% males, 69% females) and the ESS-sleepy group had more females (16% males, 84% females) than expected; the SWAI sleepy group had 29% males and 71% females. Seventeen percent of

students admitted to falling asleep at the wheel, and six admitted to having an accident due to sleepiness. A chi-square of groups by fallen asleep while driving response was significant ($p=.04$), with 36% of those sleepy on the SWAI responding yes, 21% of those sleepy on the ESS responding yes, and 12% of those non-sleepy responding yes.

Conclusion: A high prevalence of sleepy driving is reported among college students. Falling asleep while driving is more prevalent among sleepy individuals. Sleepiness as defined by the SWAI seems to be a better instrument to identify risk for this dangerous behavior.

0681

THE TREATMENT OF ELDERLY PATIENTS WITH PRIMARY INSOMNIA AND DAYTIME SLEEPINESS WITH EVT 201 IMPROVES SLEEP INITIATION, SLEEP MAINTENANCE, AND DAYTIME ALERTNESS

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Introduction: EVT 201 is a partial positive allosteric modulator of the GABA_A system. A Phase II study of EVT 201 was conducted in elderly primary insomnia patients with daytime sleepiness.

Methods: A randomized, multicentre, double-blind, placebo-controlled, parallel-group design was used to assess the hypnotic efficacy of EVT 201 1.5 mg and 2.5 mg during seven consecutive nights. Polysomnography (PSG) was performed on two consecutive nights for screening and on nights 1, 6 and 7 of treatment. At Screening, patients were required to have a mean Total Sleep Time (TST) of 240 - 410 minutes and a mean Multiple Sleep Latency Test (MSLT) latency of ≥ 4 minutes and ≤ 16 minutes. Daytime assessments on Day 8 included the MSLT, Rey Auditory Verbal Learning Test (RAVLT), Psychomotor Vigilance Task (PVT) and the Karolinska Sleepiness Scale (KSS). PSG Total Sleep Time (TST) was the primary endpoint.

Results: Participants were 149 elderly patients with DSM-IV primary insomnia (53 males, 96 females; mean age 71.3 yrs, range 65-86 yrs). Compared to placebo, EVT 201 1.5 mg and 2.5 mg increased TST (30.9, 56.4 min respectively, $p=0.0001$, $p<0.0001$); reduced WASO (-15.2, -36.1 min respectively; $p=0.01$, $p<0.0001$); reduced LPS (-15.9, -19.9 min respectively; $p=0.009$, $p=0.001$) and reduced WASO in hours 5-8 (-4.1, -16.3 min respectively; $p=0.4$, $p=0.001$). Both doses also improved subjective sleep quality and usual subjective efficacy measures. A significantly longer mean MSLT latency was observed on Day 8 with both doses, compared to placebo (2 min increase; $p=0.03$, both doses). No serious or unexpected treatment emergent adverse events were noted.

Conclusion: EVT 201 improved PSG measures of sleep onset and sleep maintenance, showing evidence of efficacy throughout the night in elderly patients at the same doses as in adult patients. The improvement of sleep was accompanied by significantly improved physiological alertness during the day.

Support (optional): The study was sponsored by Evotec.

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INSOMNIA IN A SHIFT WORKING POPULATION AND ITS CORRELATIONS WITH FATIGUE AND SLEEPINESS

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Introduction: Although insomnia is an omnipresent phenomenon in shift workers, knowledge about the relationships among insomnia, working schedule, fatigue and sleepiness in this population is limited. The objective of this survey was to address the above-mentioned issue.

Methods: Four hundred and forty workers from a major employer in Canada completed the Athens Insomnia Scale (AIS), Fatigue Severity Scale (FSS) and Epworth Sleepiness Scale (ESS). Participants were divided into 4 study groups according to the frequency of their night-shift work schedule: never (Group 1); < 4 days per month (Group 2); 1-2 days per week (Group 3); ≥ 3 days per week (Group 4). Mean scores of the AIS were compared across the groups. Correlations analysis between the scores of the AIS and those of the FSS, as well as those of the ESS, were performed separately in night-shift workers (including Groups 2-4; $n=274$) and non-shift workers (Group 1; $n=166$).

Results: There is a significant linear tendency between shift frequency and the mean scores of the AIS ($F_{3,436}=6.66$; $P<0.001$). The mean AIS score of Group 4 (9.68 ± 4.62) is significantly higher than those of

Group 1 (7.20 ± 4.48 ; $P<0.001$), Group 2 (7.44 ± 4.04 ; $P=0.015$) and Group 3 (7.83 ± 4.54 ; $P=0.019$). Among night-shift workers, there is a strong, positive correlation ($r=0.606$; $P<0.001$) between the scores of the AIS and those of the FSS, but the correlation between the scores of the AIS and those of the ESS is only borderline ($r=0.323$), while in non-shift workers the corresponding r values are 0.553 and 0.248, respectively.

Conclusion: In working population, an increasing frequency of night-shift work is associated with a greater severity of insomnia. Fatigue, but not sleepiness, was found to be associated with insomnia. This relationship is stronger and more significant in night-shift workers compared to non-shift workers.

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APD125, A SELECTIVE SEROTONIN 5-HT_{2A} RECEPTOR INVERSE AGONIST, SIGNIFICANTLY IMPROVES THE KEY PARAMETERS OF SLEEP MAINTENANCE IN PATIENTS WITH PRIMARY INSOMNIA

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Introduction: Chronic insomnia is a condition affecting 10-15% of the adult population, and for most, particularly the elderly, sleep maintenance is the major issue. APD125 is a highly selective inverse agonist of the 5-HT_{2A} receptor. In phase 1 studies, APD125 improved sleep maintenance and was well tolerated.

Methods: Adult patients ($n=173$) with DSM-IV defined primary insomnia characterized by difficulty maintaining sleep were randomized into a multicenter, double-blind, placebo-controlled, 3-way crossover study to compare 2 doses of APD125 (10 mg and 40 mg) with placebo. Each treatment period was 7 days with a 7-9 day washout period between treatments. Paired polysomnographic readings (PSGs) were performed at screening and at nights (N) 1/2 and N 6/7 for each treatment period.

Results: APD125 was associated with significant improvements in key PSG sleep maintenance parameters. Wake time after sleep onset (WASO) decreased by 52.5 min (10mg) and 53.5 min (40mg) from baseline to N 1/2, ($p<0.0001$ for both vs placebo), by 51.7 min ($p=0.0131$) and 48.0 min ($p=0.1994$) at N 6/7, respectively, and by 37.8 min at N 1/2 and 44.0 min at N 6/7 for placebo. Robust APD125 effects were also seen with wake time during sleep (WTDS) ($p<0.0001$ N 1/2, $p<0.001$ N 6/7). Importantly, the number of arousals and number of awakenings improved significantly with APD125 treatment as compared to placebo, as did slow wave sleep ($p<0.0001$ for both doses at both timepoints). As expected, based on the patient population and the mechanism of action of APD125, there were no improvements in latency to persistent sleep. No SAEs were reported and no meaningful differences in AE profiles were observed between either dose of APD125 and placebo. APD125 did not result in next day cognitive impairment as measured by Digit Span, Digit Symbol Copy and Digit Symbol Coding Tests.

Conclusion: APD125 produced clinically and statistically significant improvements in parameters of sleep maintenance and sleep consolidation and was well tolerated in adults with primary chronic insomnia characterized by difficulty maintaining sleep.

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SOCIAL SUPPORT AND SLEEP IN ELDERLY INSOMNIA PATIENTS AND GOOD SLEEPER CONTROLS

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Introduction: Higher levels of social support are associated with better mental and physical health. Scant research has investigated links between social support and sleep. Given that social factors play a prominent role in the aging process, understanding the influence of social support on sleep may be particularly important in elderly populations. We examined the association between specific types of social support and subjective and objective measures of sleep in a sample of elderly, good sleeper controls (GSC: n=30; F=18; M=70.86 years) and elderly, insomnia patients (n=61; F=40; M=72.02 years).

Methods: Sleep was measured objectively using actigraphy in the home environment (M=13 days). Actigraphy outcomes included: sleep latency (SL), wakefulness after sleep onset (WASO), sleep fragmentation, and total sleep time. Sleep quality and daytime sleepiness were measured using the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale (ESS), respectively. Three types of perceived social support were measured: belonging (availability of people one can do things with), appraisal (availability of a confidante), and tangible (availability of material aid) support. All analyses adjusted for age, sex, depressive symptoms, patient status, and perceived general health. Separate linear regression models examined the influence of each of the social support subtypes on the self-report and actigraphy outcomes after adjusting for covariates and the interaction between support type and patient status.

Results: Greater belonging support was associated with less daytime sleepiness, WASO and sleep fragmentation, but these effects were only significant among GSC. Similarly, greater appraisal support was associated with less WASO and fragmentation, but only in GSC. Tangible support was not associated with any of the sleep outcomes.

Conclusion: Having a sense of belonging to a social group or having someone to confide in is associated with better sleep among elderly GSC. However, elderly individuals with insomnia may fail to benefit from the positive influences of social support.

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0685

CHRONIC INSOMNIA WITH OBJECTIVE LOW SLEEP EFFICIENCY IS ASSOCIATED WITH A HIGH RISK FOR HYPERTENSION

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Introduction: It has been suggested that insomnia, with an objective, low sleep efficiency, is associated with hyperarousal including hypersecretion of cortisol that may lead to significant medical problems, e.g., hypertension. The goal of this study was to assess the risk of hypertension in chronic insomnia associated with low sleep efficiency.

Methods: We examined this question cross-sectionally in a general random sample of 1,741 men and women from Central Pennsylvania who were recorded in the sleep laboratory for one night. "Insomnia" was defined by a complaint of insomnia with a duration of ≥ 1 year. "Difficulty sleeping" was defined as a complaint of difficulty falling asleep, staying asleep, or early final awakening. As a cutoff point of low sleep efficiency, we used the median value of percent sleep time for each group. We employed a logistic regression model to assess the association between insomnia, sleep difficulty, and low sleep efficiency with hypertension controlling for age, sex, BMI, diabetes, and sampling weight.

Results: Insomnia or sleep difficulty without low sleep efficiency was not associated with a significant risk for hypertension. However, the risk

for hypertension was synergistically and significantly increased in insomnia with low sleep efficiency [adjusted OR (95% CI) 3.69 (2.13, 638) $p < 0.01$]. Also, the risk for hypertension was significantly increased but less so for persons with sleep difficulty and low sleep efficiency [adjusted OR (95% CI) 1.63 (1.11, 2.39) $p < 0.05$].

Conclusion: These results suggest that insomnia with low sleep efficiency is associated with increased risk for hypertension in a degree comparable to the other common sleep disorders, i.e., sleep disordered breathing. Objective measures of sleep duration of insomnia may serve as useful predictors of the biological severity of chronic insomnia. Finally, insomnia with low sleep efficiency may represent a phenotype within chronic insomnia that may respond differentially to treatment.

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THE IMPACT OF PRESCRIBING HYPNOTIC MEDICATION ON COMPLIANCE WITH BEHAVIORAL TREATMENT FOR INSOMNIA

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Introduction: The efficacy of cognitive-behavior therapy (CBT) for insomnia is well established, but improvement is highly dependent on compliance with therapeutic recommendations. Adding hypnotic medication may potentially influence compliance with CBT, either decreasing compliance due to lower motivation to comply with more demanding behavioral procedures, or enhancing compliance because of the rapid sleep relief provided by medication. This study aimed at investigating the impact of medication on compliance with behavioral treatment procedures for insomnia.

Methods: Participants were 160 adults (aged 30-72 years old, mean = 50.3; 60.6% women) meeting criteria for chronic insomnia. They were randomized to six weekly group CBT sessions either alone (n = 80) or combined with medication (10 mg zolpidem taken nightly) (n = 80). Compliance was assessed weekly by the therapists with ratings of the restriction of time spent in bed (number of nights per week adhering to the prescribed sleep window) and stimulus control procedures (10-point Likert scale). Compliance ratings were compared between the two conditions and correlated with several baseline measures (i.e., socio-demographics, sleep diary variables, measures of insomnia severity, beliefs and attitudes, depression and anxiety symptoms, health-related quality of life, fatigue, and treatment evaluation).

Results: No significant group differences were found for weekly compliance ratings or for the overall six-week averages, except for compliance with restriction of time in bed on week 5, which was higher in the CBT condition. The proportions of participants with high, intermediate, or low compliance were similar in both conditions. Significant correlates of higher compliance were (a) for the combined condition: lower baseline scores of depressive symptoms, fatigue, dysfunctional beliefs and attitudes about sleep, health-related impairment, and insomnia consequences, and (b) for the CBT condition: lower baseline scores on measures of insomnia severity and consequences, shorter insomnia duration, and higher treatment acceptability.

Conclusion: These results suggest that adding medication to CBT does not impede nor enhance compliance with behavioral treatment procedures for insomnia. Nonetheless, compliance appears to be associated with different variables depending on whether CBT is delivered alone or in combination with medication. Further studies should investigate more thoroughly potential mediators of compliance for different treatment regimens.

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INSOMNIA AND NEUROPSYCHOLOGICAL PERFORMANCE: A META-ANALYSIS

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Introduction: Individuals with insomnia consistently report difficulties pertaining to their cognitive functioning (e.g., memory, concentration). However, studies comparing their performance to that of normal sleepers on neuropsychological tests have generated contradictory or inconclusive findings. This meta-analysis was conducted to quantitatively summarize available data about the magnitude of differences between individuals with primary insomnia and normal sleepers on neuropsychological test performance.

Methods: Reference databases (PubMed, PsychInfo, Dissertation Abstracts International) were searched for studies comparing adults with primary insomnia to normal sleepers on neuropsychological measures. Neuropsychological variables for which effect sizes could be computed were extracted from each study. Variables were classified independently by two judges (licensed neuropsychologists) according to the main cognitive function expected to be measured. Individual effect sizes (Cohen's *d*) were weighted by their variability and combined using a fixed effects model. Average effect sizes and their 95% confidence intervals were computed for each cognitive function.

Results: Seventeen studies met inclusion criteria, totalising 324 individuals with insomnia and 301 normal sleepers. Significant impairments ($p < .05$) of small to moderate magnitude were found in individuals with insomnia for tasks tapping episodic memory ($ES = -0.38$), manipulation in working memory ($ES = -0.36$), verbal fluency ($ES = -0.32$), problem solving ($ES = -0.30$), sustained attention/vigilance ($ES = -0.29$) and retention in working memory ($ES = -0.19$). Individuals with insomnia also tended to perform worse, although not significantly so, on tasks measuring divided attention ($ES = -0.33$), selective attention ($ES = -0.29$) and cognitive flexibility ($ES = -0.26$). Performance was not significantly impaired for tasks assessing psychomotor functions ($ES = 0.14$), alertness ($ES = -0.07$), visual scanning ($ES = -0.11$), procedural learning ($ES = -0.01$), and reading speed ($ES = -0.16$).

Conclusion: Individuals with insomnia exhibit neuropsychological impairments for several cognitive functions, including complex attention, working memory, episodic memory and executive functions. While the data suggests that these impairments are of small magnitude, further comparisons with normative data are warranted to establish their clinical significance. Future studies should include larger and more controlled samples and use more sensitive instruments before reaching a definitive conclusion.

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EXAMINING A COMPREHENSIVE COGNITIVE-BEHAVIORAL MODEL OF INSOMNIA FOR BREAST CANCER PATIENTS: A DAILY PROCESS ANALYSIS

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Introduction: Using a daily process approach, the current study examined a comprehensive cognitive-behavioral model of insomnia in early-stage breast cancer patients.

Methods: For 28 consecutive days, 41 women completed morning diaries assessing sleep, nighttime pain and hot flashes, and dysfunctional sleep-related thoughts and behaviors during the day and night, and evening diaries assessing daytime pain, fatigue, hot flashes, and mood. All

diaries were collected using an automated telephone-based system. Using random effects multilevel modeling, within-person relations among these variables were examined.

Results: Results revealed that less efficient sleep and poorer sleep quality were significantly related to higher levels of nighttime pain ($p < .01$) and hot flashes ($p < .05$). Of note, time-lagged effects were also found. In terms of antecedents of insomnia, results revealed that higher levels of dysfunctional sleep-related thoughts and sleep inhibitory behaviors during the previous day and night significantly predicted less efficient sleep and poorer sleep quality that night (all $p < .01$). In terms of consequences of insomnia, analyses revealed that less efficient sleep and poorer sleep quality the previous night significantly predicted higher levels of fatigue and hot flashes the next day (all $p < .05$). These analyses also revealed that less efficient sleep the previous night significantly predicted lower levels of positive mood the next day ($p < .01$). Finally, these analyses revealed that poorer sleep quality the previous night significantly predicted higher levels of pain and lower levels of dysfunctional sleep-related thoughts the next day (all $p < .05$).

Conclusion: Findings suggest that future clinical practice and research should use a more comprehensive conceptualization of insomnia, including not only dysfunctional sleep-related thoughts and behaviors, but also fatigue, pain, hot flashes, and mood, to better understand and treat insomnia in this population.

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VARIABILITY AND PREDICTABILITY IN SLEEP PATTERNS OF INSOMNIA: A REPLICATION STUDY

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Introduction: Specific sleep patterns had been previously identified among patients suffering from chronic insomnia. This study replicates Vallieres et al.'s (2005) study examining in a larger sample if the night-to-night variability observed in insomnia follows specific, predictable, patterns. Furthermore, this study aims at characterising sleep patterns using objective sleep variables and clinical factors.

Methods: The sample included 146 participants (60% women, mean age 51) meeting diagnostic criteria for primary insomnia. Participants underwent three nights of polysomnographic recordings, completed self-reported questionnaires, and kept daily sleep diaries for an average of 48 days ($SD = 18.6$). Variables derived from the sleep diaries were: Sleep efficiency (SE), sleep onset latency (SOL), wake after sleep onset (WASO), and Total Sleep Time (TST). The following criteria were used to define an insomnia night: a SOL and/or WASO ≥ 60 minutes, with a $SE \leq 80\%$.

Results: Among the 146 participants, 29 were part of the previous study. Therefore, time-series diary data of 117 participants were used to compute conditional probabilities to have an insomnia night after 1, 2, or 3 consecutive insomnia night. Conditional probabilities were submitted to a k-means cluster analysis. A three-cluster solution was retained ($R^2 = 75.7\%$). The first cluster included 38 participants (32.5% of the sample) exhibiting an unpredictable insomnia pattern, with probabilities to have an insomnia night after 1, 2, or 3 insomnia nights of 0.55 to 0.62, respectively. The second cluster included 30 participants (25.6% of the sample) with a low and decreasing probability to have an insomnia night following insomnia nights (0.34 to 0.12). The third cluster included 49 participants (41.9% of the sample) exhibiting a high probability to have an insomnia night (0.82 to 0.87). One way ANOVAs revealed significant differences among clusters on SOL, WASO, TST, and SE from sleep diaries. In addition, results showed that age, insomnia severity index scores, and mental fatigue significantly differed among clusters. No significant difference among clusters was found on PSG sleep variables.

Conclusion: These findings replicate the three same predictable sleep patterns and provide additional evidence that unpredictability is a less prevalent feature of insomnia than previously suggested. These results

show that sleep perception and insomnia severity are important to differentiate the three sleep patterns observed.

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POLYSOMNOGRAPHIC SLEEP PARAMETERS IN INSOMNIA SUFFERERS VERSUS NORMAL SLEEPERS: ROC CURVE ANALYSES

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Introduction: While quantitative criteria derived from sleep-log data have proven useful for classification of primary insomnia, efforts to develop quantitative insomnia criteria from polysomnographic (PSG) data have found no combination of objective severity and frequency criteria cutoffs that reliably discriminate insomnia sufferers from normal sleepers. In these analyses, we examined objective sleep parameters in adults with primary insomnia versus normal sleepers.

Methods: Participants were 78 well-characterized primary insomnia sufferers and 79 age-matched normal sleepers who completed 3 consecutive in-lab PSGs and 3 consecutive in-home PSGs. A randomly determined 50% of each sample underwent lab PSG first, whereas the remainder completed in-home PSG first. Mean values of time in bed (TIB), total sleep time (TST), sleep onset latency (SOL), middle of the night WASO (MWASO), terminal wake time (TWSO), and sleep efficiency (SE%) were calculated separately for the home and lab sleep settings. Receiver operating characteristic (ROC) curves were used to plot the sensitivity and specificity of each sleep parameter in each setting over all possible values, with areas under the curve (AUC) calculated and tested for significance.

Results: All ROC curve analyses were in the low range for test accuracy (AUC < 0.70). ROC analyses of the sleep measures derived from lab PSG showed group discrimination was worst for SE% (AUC = .366) and best for MWASO (AUC = .623). SE% (AUC = .396) also was the worst group discriminator in the home setting, whereas SOL (AUC = .623) appeared to be the best. These findings indicate poor discrimination of insomnia sufferers from normal sleepers on the basis of PSG measures considered.

Conclusion: Objective sleep parameters derived from multiple nights of home- and lab-based PSG did not reliably discriminate adults with primary insomnia from normal sleepers. These results support the current practice recommendation that PSG is not indicated for the routine evaluation of insomnia. Because insomnia is diagnosed on the basis of a subjective sleep complaint, sleep logs are more appropriate and have more utility than PSG in classifying primary insomnia.

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IMPAIRED MEMORY CONSOLIDATION DURING SLEEP IN PRIMARY INSOMNIA

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Introduction: Compelling evidence from animal and human studies indicates that healthy sleep facilitates neural plasticity and memory consolidation. The authors sought to determine whether memory consolidation during sleep and wakefulness is impaired in patients with primary insomnia compared to good sleeper controls.

Methods: Memory performance (procedural mirror-tracing task, declarative visual and verbal learning task) and general neurocognitive

performance were measured before and after a 12-hr period containing either wakefulness (morning-evening) or polysomnographically monitored sleep (evening-morning) in 30 patients with primary insomnia according to DSM-IV criteria (19 females, aged 46±4.3 years) and 48 sex, age and IQ matched good sleeper controls.

Results: Good sleeper controls in the sleep condition showed a significantly enhanced procedural and declarative memory consolidation compared to good sleeper controls in the waking condition (MANOVA, $p < 0.05$). Good sleeper controls in the sleep condition showed a significantly enhanced procedural memory consolidation compared to insomnia patients in the sleep condition (MANOVA, $p < 0.05$, large effect sizes for procedural memory consolidation, low to medium effect size for declarative memory consolidation). Memory consolidation did not differ significantly between good sleeper controls in the waking condition, insomnia patients in the waking condition, and insomnia patients in the sleep condition (MANOVA, $p > 0.1$).

Conclusion: Primary insomnia is associated with a significant sleep-associated impairment of procedural memory consolidation and a less pronounced impairment of declarative memory consolidation. Future work is needed to determine the impact of interventions on improving sleep and memory in patients with primary insomnia.

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SLEEP VARIABILITY AND ITS RESPONSE TO BRIEF BEHAVIORAL TREATMENT IN LATE LIFE INSOMNIA

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Introduction: Individuals with chronic insomnia (CI) are assumed to have poor sleep habits including variable sleep times, but few studies have systematically examined within-subject variability. We examined variability of sleep diary measures in older adults with and without CI. Among individuals with CI, we also examined variability before and during Brief Behavioral Treatment for Insomnia (BBTI) or an Information Control condition (Info).

Methods: Participants were community-dwelling adults with chronic comorbid or primary insomnia (CI; $n=61$, 41F, $M=71.4$ years) or no insomnia (NI; $n=31$, 20F, $M=70.7$ years). After diagnostic evaluation and screening PSG, participants completed a two-week sleep diary. CI were then treated with either BBTI ($n=28$) or Info ($n=33$), and completed sleep diaries for four weeks during intervention. Each subject's mean and standard deviation (SD) were calculated for sleep diary variables. Group means for within-subject mean and SD were then compared with t -tests.

Results: Baseline: CI and NI did not differ in mean within-subject bedtime or rise time, but CI had significantly worse sleep latency, wake after sleep onset, total sleep time, sleep efficiency, and sleep quality (p values $< .0001$). Within-subject SD was greater for CI than NI for all sleep diary measures except bedtime (p values $< .0001$). Treatment: Baseline-intervention changes in mean bedtime did not differ between BBTI and Info, but BBTI had a larger change in mean rise time and all other sleep diary measures (p values $< .04$). BBTI also showed larger baseline-intervention reductions in within-subject SD for bedtime, rise time, sleep latency, and total sleep time vs. Info (p values $< .04$).

Conclusion: Older adults with CI reported worse and more variable sleep than NI. BBTI was associated with earlier rise time, reduced variability of bedtime and rise time, and reduced severity and variability of sleep disturbances. Sleep variability may be an important treatment target in chronic insomnia.

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0693

SLEEP-DISORDERED BREATHING IN TREATMENT-SEEKING CHRONIC INSOMNIA PATIENTS DEPENDENT ON SEDATIVE/HYPNOTICS

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Introduction: Scant objective data are available on sleep-disordered breathing (SDB) among treatment-seeking chronic insomnia patients using sedating prescription medications. Based on AASM nosology/current practices (RDI \geq 15/AHI \geq 5), we hypothesized that greater than 50% of this cohort would meet SDB diagnostic criteria.

Methods: Chronic insomnia patients reporting sedative/hypnotic use at least a few times a week or more completed diagnostic PSG at Maimonides Sleep Arts & Sciences from April 2005 thru October 2007. Extracted data included demographics, insomnia severity, prescription medication type, and polysomnographic respiratory indices.

Results: Two hundred fifty-one chronic insomnia patients [59% females; mean (SD)Insomnia Severity Index (ISI) = 19.0 (5.72)] reported frequent use of sedating prescription medications (92% nightly use). Medication type and mean (SD) ISI for five groups were: benzodiazepines (BZ) 14%/18.6 (5.6), non-benzodiazepines (NBZ) 22%/18.8 (6.2), antidepressants (ANTI) 19%/17.6 (6.6), mood stabilizers (MOOD) 5%/17.7 (5.2), and multiple drug types (MULTI) 41%/20.1 (5.0). Mean (SD) RDI by groups were: BZ 44.2 (29.7), NBZ 51.4 (22.5), ANTI 43.4 (20.3), MOOD 53.0 (34.0) and MULTI 46.8 (26.5). Diagnosis of SDB by percent of drug type group based on RDI: BZ 91%, NBZ 96%, ANTI 91%, MOOD 100%, and MULTI 95%. Mean (SD) AHI by groups were: BZ 13.8 (19.8), NBZ 21.2 (22.4), ANTI 18.8 (20.6), MOOD 26.4 (37.0), and MULTI 22.0 (27.2). Diagnosis of SDB by percent of drug type group based on AHI: BZ 66%, NBZ 72%, ANTI 81%, MOOD 75%, and MULTI 72%. Comparison of group means for RDI or AHI were not statistically significant [(F(4,246)=.975, p=.42, F(4,246)=.86, p=.49)].

Conclusion: An extremely large proportion of treatment-seeking chronic insomniacs who regularly used or were dependent on sedating prescription medications were diagnosed with SDB. The findings support our previous hypothesis that the regular use of prescription sleep aides is a marker for undiagnosed sleep-disordered breathing.

Support (optional): Maimonides Sleep Arts & Sciences, and the Sleep And Human Health Institute

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THE RELATION OF SLEEP COMPLAINTS AND DAYTIME FUNCTIONING

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Introduction: Insomnia is associated with three broad areas of impairment: persistent difficulty initiating and maintaining sleep, distress and complaints about sleep difficulties, and impaired daytime functioning. It is unclear, however, how these areas of impairment are interrelated. The relation between sleep complaints and daytime functioning was investigated after controlling for demographic variables, health variables, and quantitative sleep characteristics.

Methods: The analyses were conducted using data from an epidemiological survey of sleep and daytime functioning collected in Shelby County in the Memphis, Tennessee area. A hierarchical regression model with four sets was used to test the effect of sleep complaints on daytime functioning. Set 1 included age, race, and gender. Set 2 was composed of nine dichotomous health variables. Set 3 included the following sleep diary variables: sleep onset latency, wake time after sleep onset, total sleep

time, terminal wake time, and sleep efficiency. Set 4 included a single dichotomous variable representing the presence or absence of an insomnia complaint. The daytime functioning variables included as dependent measures were: Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS), and Insomnia Impact Scale (IIS).

Results: All five dependent measures yielded significant findings in our models after a Bonferoni correction. After controlling for the demographic, health, and sleep parameter sets, the presence or absence of a sleep complaint, tested on step 4 of the model, produced a significant change in the amount of explained variance in BDI ($\Delta R^2 = .04$, F(1, 716) = 37.52, p < .001), STAI ($\Delta R^2 = .05$, F(1, 716) = 43.79, p < .001), ESS ($\Delta R^2 = .01$, F(1, 716) = 8.12, p = .005), FSS ($\Delta R^2 = .02$, F(1, 716) = 19.23, p < .001), and IIS ($\Delta R^2 = .02$, F(1, 716) = 20.76, p < .001). The three sets included as controls were also significant predictors of daytime functioning for all measures except ESS, where set 4 was the only significant predictor.

Conclusion: These findings suggest that individuals' perceptions of their sleep quality contribute to differences in their reported daytime performance, which are not accounted for by quantitative sleep assessments, health surveys, or demographic factors. Complaints of poor sleep may be tied to a mind-set among some individuals that causes them to be distressed with their sleep and increases their dissatisfaction with their daytime functioning.

Support (optional): Research supported by National Institute on Aging grants AG12136 and AG14738

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COGNITIVE AND ATTENTIONAL CHANGES FOLLOWING COGNITIVE BEHAVIOUR THERAPY (CBT) FOR PERSISTENT INSOMNIA ASSOCIATED WITH CANCER: A RANDOMIZED CONTROLLED TRIAL (RCT)

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Introduction: Sleep disturbance can be caused, or exacerbated, by the stress of having cancer. Indeed, up to 40% of patients have significant and persistent sleep problems. Whereas CBT is effective for primary insomnia, the treatment literature on insomnia related to cancer is sparse. Moreover, little is known about psychological changes following CBT for insomnia in this population.

Methods: Pragmatic, two-centre RCT of CBT versus treatment as usual (TAU). Patients meeting diagnostic criteria for persistent insomnia were recruited after completion of active anti-cancer therapy for breast, prostate, colorectal or gynaecological cancer. Major assessments were at baseline, post-treatment and 6-month follow-up. CBT comprised 5, weekly, 1-hour, small group sessions led by a cancer nurse following a validated CBT manual. TAU comprised usual care. Outcomes were measured using standard questionnaires/rating scales and computerized-testing of the emotional Stroop task.

Results: Data from 150 participants (103F; mean age 61yr.) analysed on intention-to-treat basis. Significant reductions in sub-scales of the Dysfunctional Beliefs and Attitudes about Sleep scale, and the Sleep Disturbance Questionnaire were observed in CBT, relative to TAU (all ES > 1.19). These self-report changes were mirrored by reductions in sleep-related attentional bias on the Stroop task [F(2,126)=8.50, p < .001]. This is a cognitive probe paradigm where delayed reaction time to the task of colour naming may be attributed to the salience of the word stimuli per se (sleep, cancer, neutral). Both subjective and objective findings were maintained at 6-months.

Conclusion: This pattern of mental/cognitive shift associated with successful CBT treatment for insomnia in cancer patients appears similar to that observed in primary insomnia. Furthermore, this is the first study,

in any insomnia group, to show cognitive attentional changes with CBT. The study supports the notion that insomnia associated with cancer may be treated similarly to the primary insomnia syndrome.

Support (optional): This research was supported by Cancer Research UK and the Dr. Mortimer & Theresa Sackler Foundation.

0696

EFFICACY OF COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA (CBTI) IN GROUP FORMAT

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Introduction: Although CBTI has been established as one of the standard treatments for chronic insomnia, at present, it is not widely available because limited number of clinicians are trained to deliver this type of therapy. We report clinical significance of a 7-session, 9-week CBTI delivered in group format by a behavioral sleep medicine clinician, in Milan, Italy.

Methods: Data were from 83 consecutive series of sleep clinic patients (41 women, 41 men; age 19-72 yrs, M=41.9±12.7 yrs) with chief complaint of insomnia. Each CBTI group consisted of 10-14 patient. The 7 treatment sessions occurred at Week 1 (assessment and goal setting), 2 (sleep education), 3 (anxiety and stress management), 4 (stimulus control and sleep restriction), 6, 7 (cognitive restructuring, and SC & SR continued) and 9 (review and relapse prevention).

Results: Compared to baseline sleep diary data, CBTI resulted in significant improvement, including sleep latency (38±40min vs. 20±14min), WASO (57±49min vs. 23±20min), TST (5.9±1.3h vs. 6.2±1.0h), sleep efficiency (78±14% vs. 88±8%), and sleep quality (5.0±2.1 vs. 6.0±2.1 on 1=very poor...10=excellent Likert scale). Among patients (77%) who took sleep medications at baseline, ¼ of them completely got off sleep medication and an additional 31% decreased medication by ≥50% by Week9. Patients rated 68±24% accomplishment of their personal treatment goals. Drop out rate was 6%, and 89% of patients rated moderate or higher level of treatment satisfaction. Based on Insomnia Severity Index score classification, 85% of patients no longer have clinical insomnia (ISI score ≤14; ISI score 17.0±5.0 at baseline vs. 9.6±5.0 at Week9).

Conclusion: CBTI in group format result in clinically meaningful improvement in sleep and facilitated substantial reduction in sleep medication use. CBTI is well received by patients. In light of high prevalence of chronic insomnia, group CBTI represents a cost-effective and a mechanism of dissemination for making this therapy more available.

0697

SLEEP QUALITY AND DISTURBANCES IN RETURNING VETERANS: PRELIMINARY COMPARISONS WITH PRIMARY INSOMNIA AND GOOD SLEEPERS

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Introduction: Combat-exposed veterans returning from ongoing conflicts often report distressing sleep disturbances, including insomnia. However, the severity of sleep disturbances in the new cohort of veterans has not been compared to other groups of good sleepers of insomnia patients. The goal of this study was to compare sleep quality and disturbance among Operation Iraqi Freedom (OIF) veterans and age and sex equated participants with primary insomnia (PI) and good sleepers (GS).

Methods: Data from a sample of 14 OIF veterans (M age= 30.5 ± 7.4) with post-deployment adjustment disorders were compared to data from 14 patients with PI (M age= 30.5 ± 8.9) and 14 GS (M age= 30.0 ± 7.5). PI and GS subjects were free of medical and psychiatric disorders. Sleep

quality and disturbances were assessed using the Pittsburgh Sleep Quality Index (PSQI) and electronic sleep diaries collected over an average of 7.5 ± 1 days. Disruptive nocturnal behaviors (DNB) were assessed using the PSQI-Addendum for PTSD (PSQIA). Group differences on sleep quality, sleep diary measures, and DNB were assessed using one-way ANOVAs.

Results: OIF veterans reported significant worse sleep quality and sleep efficiency, increased sleep latency and wake time after sleep onset, and a greater number of nocturnal awakenings than GS (all p <.001). However, OIF veterans did not differ from PI subjects on any of the sleep measures, except for the PSQIA. OIF veterans endorsed significantly more severe DNB than both PI and GS (p <.001). Mean nightmare frequency as assessed by prospective diaries in OIF veterans was 1.1 ± 1.5 nightmares/week.

Conclusion: Insomnia comorbid with post-deployment adjustment disorders was as severe as insomnia in PI and was accompanied by nightmares and other DNB. These findings highlight the need for sleep-focused assessments and treatments in this new cohort of combat-exposed military veterans.

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0698

INSOMNIA, DEPRESSION AND FATIGUE IN 823 CANCER PATIENTS UNDERGOING CHEMOTHERAPY: A URCC CCOP STUDY

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Introduction: Insomnia and fatigue are distressing symptoms for cancer patients. While much is known about fatigue, relatively little is known about the prevalence of insomnia in cancer patients during treatment.

Methods: As part of a larger study (A URCC CCOP Study), 823 patients with a variety of cancer diagnoses were evaluated for the prevalence of insomnia complaints using items from the Hamilton Depression Rating Scale. Insomnia was assessed following the first two cycles of chemotherapy.

Results: Median age of the sample was 58 and 73% (N=597) were female. During cycle 1 of chemotherapy, 80% reported insomnia problems and nearly half met diagnostic criteria for insomnia. Women tended to be more likely to report insomnia ($\chi^2 = 5.63, p = .08$) as were younger patients ($\chi^2 = 12.25, p = .002$). Significant differences were found in prevalence of insomnia by diagnosis, with colon cancer patients reporting the lowest number of insomnia complaints. There was a significant positive association between insomnia complaints at cycle 1 and cycle 2 of chemotherapy ($r = .55, p < .000$) with an average 60% of patients reporting that their sleep complaints remained unchanged from cycle 1 to cycle 2. Patients meeting criteria for insomnia had significantly more mood disturbance (POMS), depression (CES-D), and fatigue (FSCL, MAF) than those who did not meet criteria for insomnia (all, $p < .001$).

Conclusion: Patients receiving chemotherapy exhibit a prevalence of insomnia that is nearly three times higher than that of the general population. While this may, initially, be ascribable the level of life stress that accompanies being diagnosed with cancer, the persistence of insomnia across treatment and into remission remains inordinately high. Our data suggests 3x higher during treatment and data from Savard and colleagues suggests 2x higher during remission. Taken together, these prevalence rates suggest that behavioral factors may be interacting with disease factors to produce greater insomnia morbidity.

Support (optional): Supported in part by (U10-CA37420 and R25-CA102618)

0699

A NON-INTERVENTIONAL STUDY TO OBJECTIVELY VALIDATE NON-RESTORATIVE SLEEP AS A COMPONENT OF INSOMNIA DISTINCT FROM DIFFICULTY INITIATING OR MAINTAINING SLEEP

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Introduction: Insomnia is characterized by difficulty initiating or maintaining sleep (DIS or DMS) and/or non-restorative sleep (NRS). NRS has been described based on patient reports, which reveal significant functional impairment. This is the first study to validate NRS using objective measures.

Methods: Subjects complaining of waking unrestored or unrefreshed (NRS) ≥ 3 times/week over the previous 3 months were assigned to cohorts - DIS, DMS, DIS+DMS, or NRS only - based on self-reports then verified objectively by polysomnography (PSG) on two consecutive nights. Healthy volunteers (HV) were also assessed. Objective measures of latency to persistent sleep (LPS) and wake after sleep onset (WASO) were obtained via PSG. Subjective endpoints including the Epworth Sleepiness Scale (ESS), Multidimensional Assessment of Fatigue (MAF) and Pittsburgh Insomnia Rating Scale (PIRS) assessed daytime function. All assessments were performed at screening and repeated after one month.

Results: Self-characterization on enrolment produced the following cohorts: DIS (n=138), DMS (n=44), DIS+DMS (n=125), NRS only (n=192), HV (n=80). PSG confirmed 56 (40.6%), 18 (40.9%), 37 (29.6%), 115 (59.9%) and 52 (65.0%) cases, respectively. Initial PSG measures were similar in NRS only and HV cohorts: LPS 13 and 10 min, respectively, versus >60 min in DIS and DIS+DMS cohorts; WASO 32 and 30 min, respectively, versus >90 min in DMS and DIS+DMS cohorts. Repeat PSG one month later gave consistent results. Subjective assessments revealed a different pattern: initial ESS scores were 8.6 in NRS only subjects, compared with 5.9-7.5 in other insomnia cohorts and 2.4 in HV. Equivalent MAF scores were 24.0, 23.0-26.9 and 3.0, and PIRS scores were 44.6, 61.5-76.4 and 4.7. Similar patterns were observed one month later.

Conclusion: This study highlights a cohort of subjects with NRS in whom PSG demonstrates an absence of DIS or DMS. Daytime functional impairment in these subjects was similar to those with DIS and DMS.

Support (optional): This research was sponsored by Pfizer Inc.

0700

SWA DYNAMICAL EVIDENCE OF LESSENERD HOMEOSTATIC PRESSURE IN PRIMARY INSOMNIA

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Introduction: The pathophysiology of chronic insomnia is poorly understood. We lack a physiologic marker for this condition. In prior work, conventional polysomnographic indices and non-REM spectral measures have failed to consistently differentiate chronic insomnia patients and controls. Based on evidence for a decrease in homeostatic sleep drive in chronic insomnia(1), we compared a measure of homeostasis, slow-wave activity (SWA) dynamics over the night, in chronic primary insomnia and control populations.

Methods: Subjects (primary insomnia = 51; controls = 56) were screened via DSM-IV structured interview plus polysomnography, and had up to 6 nights of PSG. SWA dynamics was estimated via best-fit exponential and linear functions of 30-second epoch artifact-free sleep EEG spectral

delta power. A slope and intercept was computed for each night and averaged within subject and then compared across groups.

Results: A significantly slower decline of SWA was found in the insomnia patients vs controls (-2.8 ± 1.8 vs. -2 ± 1.4 ; $F_{4,102} = 4.89$, $p = 0.029$). Interestingly, this was only significant with the linear fit.

Conclusion: These findings are consistent with lessened homeostatic sleep pressure in primary insomnia patients vs. controls. This may explain the effectiveness of sleep restriction therapy (2). A linear model differentiated insomnia and controls groups better than an exponential function. Further work is needed to define the function that will best identify the SWA homeostasis alteration in insomnia.

0701

EFFICACY AND SAFETY OF DOXEPIN 1 AND 3 MG IN A 3-MONTH TRIAL OF ELDERLY ADULTS WITH CHRONIC PRIMARY INSOMNIA

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Introduction: Efficacy and safety of doxepin (DXP) was evaluated in elderly insomniacs. This trial represents the longest randomized clinical trial of nightly dosing with polysomnography (PSG) assessment in the elderly.

Methods: Elderly adults meeting DSM-IV-TR criteria for primary insomnia were randomized to 12 weeks of DXP 1mg (N=77), 3mg (N=82), or placebo (PBO; N=81). Efficacy was assessed in the sleep lab with PSG and at home with sleep diaries (IVRS). Selected endpoints are reported corresponding to first and last assessment points.

Results: DXP 3mg demonstrated significant improvement on night (N) 1 in wake-time-after-sleep-onset (WASO; primary endpoint; $p < 0.0001$), total sleep time (TST; $p < 0.0001$), overall sleep efficiency (SE; $p < 0.0001$), SE in each third-of-night ($p < 0.005$) and SE in hours 7 ($p < 0.005$) and 8 ($p < 0.0001$), all versus PBO. Improvements were sustained at N85 for all variables, with significance maintained for WASO, TST, overall SE, SE in the 2nd and final third-of-night, and SE hour 7. DXP 3mg significantly improved the IVRS variables latency to sleep onset (wks 1 and 12, $p < 0.05$), TST (wks 1 and 12, $p < 0.01$), and sleep quality (wks 1 and 12, $p \leq 0.01$). Several outcome-related parameters were also significantly improved, including CGI severity and improvement. Significant improvements were observed for DXP 1mg for several measures and at several timepoints, including WASO, TST, overall SE and LSO. There was no significant next-day residual sedation and no reports of anticholinergic effects or memory impairment. Incidence of adverse events and discontinuation rates were low and comparable between groups.

Conclusion: In elderly adults with insomnia, DXP 1 and 3mg produced significant and clinically meaningful improvements in sleep onset, sleep maintenance and early morning awakenings that were maintained for most parameters. Both doses were well-tolerated, with no next-day residual effects. These data suggest that DXP 1 and 3mg are effective and well-tolerated in this trial, the longest PSG evaluation of elderly adults with insomnia.

Support (optional): This study was fully funded and supported by Somaxon Pharmaceuticals, Inc., San Diego, CA.

0702

CAREGIVER-RELATED INSOMNIA IS ASSOCIATED WITH IMPAIRMENTS IN HEALTH AND FUNCTIONING: THE PITTSBURGH AGEWISE CAREGIVER STUDY

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Introduction: Caregiving can be rewarding, stressful, and bad for one's health. Although recent studies have documented significant sleep disturbances in dementia caregivers, little is known about their consequences to health and functioning. The present study evaluated psychosocial and physical correlates of sleep in dementia caregivers prior to and following a randomized clinical trial (RCT) for the treatment of caregiver stress and insomnia.

Methods: Participants were 59 dementia caregivers (67% female, mean age 74 years) who were living at home with and providing care for their spouse. In-home sleep studies were conducted at baseline and following an 8-week intervention (stress management + healthy sleep practices OR attention-only control). Participants also underwent psychiatric and medical evaluations. Caregiver-related insomnia was defined as meeting at least 1 of the following criteria: PSQI > 10, PSG-assessed sleep latency > 30 minutes or sleep efficiency < 80%. We hypothesized that dementia caregivers with insomnia would report greater symptoms of burden, fewer interpersonal resources and show evidence of poorer overall health.

Results: On average, participants slept a total of 6 hours, took 25 minutes to fall asleep, and spent over an hour awake during the night. Fifty-nine percent of the sample exhibited caregiver-related insomnia. Compared to caregivers who were good sleepers, caregivers with insomnia reported decreased emotional intimacy with their spouse ($p < .05$), felt less able to leave their spouse home alone ($p < .05$), and endorsed significantly lower levels of social support ($p < .01$). General health ratings were lower and IL-6 levels were higher in caregivers with insomnia ($p < .05$).

Conclusion: Health and functioning was compromised in dementia caregivers with insomnia. The breadth and impact of these cross-sectional relationships suggests that sleep in elderly caregivers merits greater attention from researchers and clinicians alike.

Support (optional): AG-020677, HL-76852, RR-00052, RR-024153

0703

SLEEP REACTIVITY TO STRESS AND INSOMNIA: GENETIC AND ENVIRONMENTAL CONTRIBUTIONSFriedman NP¹, Roth T², Wright KP³, Drake CL²

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Introduction: Sleep reactivity to stress may predispose individuals to insomnia. The aim of this study was to determine the genetic and environmental etiology of sleep reactivity to stress, as measured by the Ford Insomnia Response to Stress Test (FIRST), and its relation to insomnia symptoms (difficulty falling asleep, difficulty staying asleep, and non-refreshing sleep).

Methods: Participants were 873 individual twins (590 female, 283 male), aged 18-28 ($M=22.5$, $SD=2.6$) from the Colorado Longitudinal Twin and Community Twin Studies who completed an online sleep survey. Genetic analyses included 305 complete twin pairs (169 MZ, 136 DZ). The survey included the 9-item FIRST and questions about the severity and frequency of insomnia symptoms and daytime impairment.

Results: Preliminary findings from this ongoing study suggest significant ($p < .05$) genetic (~30%), no shared environmental, and moderate to large nonshared environmental (~70%) influences on FIRST scores.

Aggregated insomnia symptoms show similar estimates of genetic and environmental influences. Heritability estimates for individual insomnia symptoms are low to moderate (~.15 to .35), with non-refreshing sleep showing the highest estimate. Significant genetic (~.60) and non-shared environmental (~.45) correlations between FIRST scores and aggregated insomnia symptoms indicate that FIRST scores correlate with insomnia symptoms because they share both genetic and environmental influences. However, each measure also had significant unique genetic and environmental influences, indicating that they are not identical constructs.

Conclusion: Sleep reactivity to stress has a genetic component. The finding that FIRST scores and insomnia symptoms share genetic influences is consistent with the hypothesis that sleep reactivity may be a genetic vulnerability for developing insomnia. However, similar to insomnia, environmental influences unique to individuals also appear to contribute to sleep reactivity to stress. These findings emphasize the importance of assessing environmental exposures as well as underlying diathesis in future studies aimed at determining the genetic components contributing to insomnia.

Support (optional): Henry Ford Hospital Sleep Center, and NIH grant MH075814

0704

POLYSOMNOGRAPHIC INDICES OF POOR SLEEP ARE ASSOCIATED WITH DAYTIME ARTERIAL BLOOD PRESSURE IN SUBJECTS SUFFERING FROM INSOMNIALanfranchi PA², Morin CM¹

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Introduction: Epidemiological studies reported a link between self reported poor sleep and hypertension. In this study we examined the relationship between subjective and polysomnographic (PSG) sleep measures and daytime values of blood pressure (BP) in subjects with chronic insomnia.

Methods: One hundred eight subjects (66 women, age 50±10 years) complaining of moderate to severe chronic insomnia (Insomnia Severity Index ≥15), in the absence of any significant medical or psychiatric co-morbidity and other sleep disorders, were studied. Subjects underwent: baseline assessment including measurements of arterial BP and body mass index (BMI); sleep diaries for 2 weeks; and 3 consecutive nights of PSG recordings. Subjective sleep variables were: total sleep time (TST), sleep efficiency (SE), wake time after sleep onset (WASO). PSG variables were: TST, SE, WASO, number of awakenings lasting ≥1 minute (AWA1), microarousal index (MA), periodic leg movement index (PLMi), respiratory disorder index (RDI). Pearson correlation coefficients were calculated between systolic and diastolic BP (SBP and DBP) and age, BMI, subjective and objective sleep variables. Variables which correlated significantly ($p < 0.05$) with SBP and DBP were included in a multivariate model.

Results: Both SBP and DBP were associated with age ($p < 0.0001$) and BMI ($p < 0.0001$). Neither SBP nor DBP correlated with subjective sleep variables. SBP correlated with PSG WASO ($p < 0.0001$), AWA1 ($p < 0.0001$), SE ($p < 0.0001$), PLMi ($p < 0.0001$). At the multivariate analysis the adjusted predictors of SBP were BMI ($p < 0.0001$), WASO ($p < 0.01$) and PLMi ($p < 0.05$). In a subgroup of 45 subjects with BMI ≥25 kg/m² AWA1 and PLMi were independent predictors of SBP ($p < 0.05$), with BMI showing a borderline association ($p = 0.06$).

Conclusion: In subjects with chronic insomnia objective measures of sleep loss and sleep fragmentation are independently associated with daytime values of SBP supporting the hypothesis that sleep loss and fragmentation might be implicated in the development of hypertension in this condition.

0705

FACTORS ASSOCIATED WITH LONG-TERM INSOMNIA COURSE

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Introduction: Despite increasing evidence that insomnia is a prevalent condition and is associated with significant medical and psychiatric morbidity, the long-term course of insomnia remains poorly understood. The objective of the present study was to examine correlates of insomnia persistence, remission and relapse over a two-year period.

Methods: 388 adults (mean age = 44.8 years old; 69% women) were selected from a larger population-based sample on the basis of presenting insomnia at baseline. Participants completed questionnaires assessing sleep, psychological and health-related variables at several time-points. Data were examined at baseline, 1-year and 2-year follow-ups (FU) only. Sleep status was based on algorithms using standard diagnostic criteria for insomnia. Three courses were compared: persistence (insomnia at all three time points), remission (individuals classified as good sleepers at both FUs after baseline) and relapse (good sleepers at 1-year FU and insomnia at 2-year FU). Mixed-model repeated measure analyses of variance were conducted to assess differences in evolution of the different variables in time among the three insomnia courses.

Results: The following variables were significantly different across the three insomnia courses: anxiety and depression levels, perception of stress, worry severity, energy level, and perception of mental health (all $p < 0.05$). All of these variables fluctuated in the direction expected with the insomnia course. For example, while the depression and anxiety levels remained stable in time in individuals who had persistent insomnia, mean scores on these variables decreased significantly in those whose insomnia had remitted while in the relapse group, scores concomitantly decreased with the improvement of sleep quality and increased with the deterioration of the sleep status. The evolution of the physical health variables (ex. pain, BMI, general health perception) was not related to either insomnia course.

Conclusion: These results show a close temporal relationship between the course of insomnia and psychological distress variables. Temporal course modifiers remain to be examined.

Support (optional): Research supported by the Canadian Institutes of Health Research (MT42504).

0706

ESZOPICLONE REVERSES BRAIN HYPERAROUSAL IN INSOMNIA: EVIDENCE FROM [18F]-FDG PET

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Introduction: Insomnia patients have shown persistent metabolic activity in arousal neural networks during sleep relative to wakefulness. The current study aimed to determine if eszopiclone, a non-benzodiazepine cyclopyrrolone, reverses this hyperarousal in insomnia patients via [18F]-FDG PET studies of waking and NREM sleep.

Methods: 106 subjects were screened, 23 received in person assessments and 12 met DSM-IV criteria for Primary Insomnia. Of these, 7 subjects (4 women / 3 men, mean age + s.d. = 32.6 + 12.2 years) completed 2 weeks eszopiclone 3 mg qhs open label treatment. Pre- and post-treatment assessments included sleep diary, 3 nights of polysomnography, and waking and NREM sleep [18F]-FDG PET scans. Paired t-tests and voxel-based repeated measures ANCOVA (group = pre- vs. post, repeated measure = metabolism in waking and sleep, covarying for global metabolism) were performed.

Results: Pre- to post-treatment, insomnia subjects showed improvements in all subjective measures of sleep (e.g., PSQI Total = 12.3 + 2.4 pre- vs. 7.6 + 2.5 post-treatment, paired $t(6) = 3.78$, $p = 0.009$). Brain imaging analyses showed that the reduction in relative metabolism in an

arousal network from waking to NREM sleep was greater following eszopiclone treatment than before. This included the pontine reticular formation and ascended into the midbrain, subthalamic nucleus, culmen of the cerebellum, and thalamus. Related neocortical areas showing this interaction included the orbitofrontal cortex, superior temporal lobe, right paracentral lobule of the posterior medial frontal lobe, right precuneus, dorsal cingulate gyrus and portions of the frontal lobe. Comparisons involving only sleep, but not wake, revealed similar regions of post-treatment reductions in relative metabolism.

Conclusion: Eszopiclone reverses a pattern of CNS hyperarousal in insomnia patients during NREM sleep. The inhibitory actions of eszopiclone are largely on a CNS arousal neural network within sleep that includes the pontine and midbrain reticular activating system.

Support (optional): Sepracor; MH66227; MH061566; AG20677; MH24652; RR000056

0707

WHERE DO SIGNIFICANT IMPROVEMENTS OCCUR DURING CBTi?

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Introduction: This study determined the rate of improvement in subjective sleep parameters during cognitive-behavioral therapy for insomnia (CBTi).

Methods: Insomnia patients were seen by a third-year psychology doctoral student in a practicum placement supervised by a licensed psychologist and board-certified sleep medicine physician. Eight males and 13 females completed the eight session protocol described by Perlis et al (age 42.1±15.4). Because the 7th session covered individually determined topics, this session was not included in the analyses. Sleep diary data was entered weekly; if two weeks elapsed between visits, overall average was used. Subjective questionnaires (Insomnia Severity Index, ISI; Dysfunctional Beliefs and Attitudes about Sleep, DBAS; and Sleep-Wake Activity Inventory, SWAI) were completed at baseline, between sessions four and five, and after treatment completion.

Results: Repeated measures analysis showed a main effect of time on sleep efficiency ($p < .01$). Post-hocs demonstrated the only significant session-by-session change occurred between baseline and initiation of sleep restriction/stimulus control after session two (77.2% to 87.3%). ISI scores decreased significantly ($p < .001$), specifically from baseline to midway ($p < .001$, 20.5±4.2 to 11.8±5) to termination ($p < .0001$, to 5.9±3.6). DBAS scores decreased significantly ($p < .001$), specifically from baseline to midway ($p < .01$, 101.7±24 to 82.6±18.9) to termination ($p < .001$, to 52.5±24.7); there was a main effect of gender where females had higher average DBAS scores (85.4±15.6) than males (68.3±12.1). There was a time effect on SWAI-Nocturnal Sleep scores ($p = .01$), where scores improved from baseline to midway ($p < .01$, 20.3±5.6 to 17.5±5.3) but did not significantly change from midway to termination (21.8±15.5).

Conclusion: The rate of improvement of sleep efficiency during CBTi seems to be most significant after the introduction of sleep restriction/stimulus control, and the benefits persist across the remainder of treatment. Improved ratings on subjective questionnaires suggest additional benefits from other aspects of CBTi.

0708

SEROTONIN TRANSPORTER (5HTT) GENE POLYMORPHISMS AND RISK OF PRIMARY INSOMNIA

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Introduction: We have previously reported that a functional polymorphism of the serotonin transporter (5HTT) promoter (5HTTpr) was associated with significant variation in basal slow-wave sleep (SWS) expression in humans. The presence of the short form of the promoter (“S”) was linked to significantly greater SWS, but it did not significantly alter the likelihood of insomnia. However, other functional polymorphisms of the 5HTT gene have been characterized, and it remains unclear whether they may additively contribute to variations in sleep and insomnia risk.

Methods: As part of an ongoing study of physiologic correlates of insomnia, 62 subjects meeting diagnostic criteria for primary insomnia lasting at least one year (31f; age 18-54, mean 31.5y) and 68 normal sleepers (35f; age 20-50, mean 32.4y), screened for psychiatric and medical disease, underwent genotyping for two functional polymorphisms of the 5HTT gene: the long and short alleles of the 5HTT promoter (5HTTpr L/S) and the Intron2 VNTR (9/10/12 repeats). PSG data were collected on a standard schedule on two successive nights and scored by a single scorer blind to genotype.

Results: ANCOVA analysis controlling for age and gender showed that the two polymorphisms are additively associated with variation in basal SWS. Both the 5HTTpr “S” allele and the Intron2-VNTR 9/10-repeat alleles are associated with equivalent increments in SWS at baseline. Subjects with both alleles have SWS amounts significantly greater than subjects with only one. Significant effects on other PSG sleep variables were not seen. The distribution of alleles among subjects with and without a complaint of insomnia was not random: those with PI were significantly more likely to have neither of the high-SWS alleles (ChiSq = 3.98, p<.05). Using a more stringent criterion for insomnia diagnosis (ISI > 10), segregation of alleles was more pronounced. Subjects with neither high-SWS allele were 30 times more likely to meet the insomnia threshold than those with neither SWS allele (ChiSq = 6.98, p<.05.)

Conclusion: These data provide further evidence that functional polymorphisms in the 5HTT gene are associated with significant variation in PSG sleep. In addition, this genetic variation is cumulatively linked to alterations in the risk of PI. Polymorphisms associated with decreased basal SWS are linked to increased risk of insomnia. While these effects may be causally linked, the absence of other PSG correlates of 5HTT genetic variation suggests they may be independent findings.

Support (optional): Supported by MH63968 (GSR).

0709

INSOMNIA SIGNIFICANTLY AFFECTS THE SCHOOL PERFORMANCE OF COLLEGE STUDENTS

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Introduction: Recent studies by these authors in junior/high school students demonstrate that student reports of restless aching legs at sleep onset occurring at least once a week or every night, and difficulty concentrating significantly affect grade point average (GPA). An every day complaint of sleepiness and difficulty waking in the morning resulted in significantly lower self reported GPA's. This study extends that work into a college population.

Methods: The questionnaire utilized in this study was an 18 question frequency scaled (1=never - 5=every night) sleep disturbance question-

naire based on validated and indexed questions. Socioeconomic data was obtained but proved difficult to evaluate for this population. This questionnaire was distributed to students to psychology, nursing and medical classes as part of a presentation on “Sleep in Young Adults.” School performance is based on self reported GPA with 32 nursing and medical residents excluded from analysis because educational performance was not GPA based. GPA data was analyzed for 64 students; mean age 27.4 (range 17-59).

Results: GPA (Range 2.0-4.0) was split at the median (3.4) to form two groups: Low GPA and High GPA. There were no significant associations between GPA and age, gender or ethnicity. In chi-square analyses comparing each of the sleep variables (grouped according to whether or not the student exhibited the behavior ‘at least once a week’ or more) with GPA (low and high), students with lower GPAs were significantly more likely to have difficulty falling asleep than students with higher GPA's (69.7% vs. 40.0%; p=.018); they were also more likely to experience leg kicks or twitches at night (53.1% vs. 30.0%; p=.065). Students with lower GPA's were more likely to report waking at night and having trouble falling back to sleep (65.6% vs. 37.9%; p=.031) and difficulty concentrating during the day (72.7% vs. 43.3%; p=.018).

Conclusion: In this adult college population the complaint of difficulty concentrating during the day continues to significantly impact school performance. Insomnia complaints in this population (difficulty getting to sleep and/or maintaining sleep) are significantly associated with a decline in school performance based on self reported GPA. The primary sleep complaints significantly affecting school performance in college students (insomnia) differ from the daytime sleepiness variables that were found in the author's previous studies to significantly affect GPA in junior/high school populations.

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0710

THE EFFECTS OF TEMPERATURE BIOFEEDBACK ON SLEEP LATENCY

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Introduction: Insomnia affects approximately 10% of the population. Wirz-Justice et. al. group has shown that sleep onset is best predicted by an increase in the amount of hand and foot warming relative to more proximal areas. In this pilot study we trained sleep-onset insomniacs to increase their hand temperature during the day by means of temperature biofeedback. We hypothesized that sleep latency at night would thereby be decreased.

Methods: Four female and one male subject complaining of sleep-onset insomnia were randomly assigned to either a treatment (N=3) or control group (N=2). All subjects were then given a sleep log to complete upon awakening in the morning for one week. Biofeedback training was then initiated. This included 4-5, 30-minute training sessions over several weeks. Subjects were taught to either increase (treatment) or decrease (control) hand temperature. After completion of the biofeedback training subjects were asked to use the biofeedback technique they had learned at bedtime. They were given another sleep log to complete for one-week. The pre and post biofeedback sleep logs were then compared.

Results: Subjects in the treatment group had a decrease in sleep latency after biofeedback training (mean 15.9min, SD 50.1 min) while controls had an increase in sleep latency (mean 7.5min, SD =26.9min). Mean change in hand temperature at the end of each biofeedback session was -2.83 C (SD=1.59) in the control group, and +0.91 C (SD=0.76) in the treatment group. A Pearson's r correlation was used to analyze the relationship between mean change in sleep latency (pre-post) and mean hand temperature change at the end of each biofeedback session. This

Category J—Sleep Disorders – Insomnia

test was chosen because subjects' ability to learn temperature biofeedback varied greatly. All values were transformed to z-scores for analysis. The Pearson correlation yielded an $r = -.374$ ($P = 0.573$). these data included an outlier in the treatment group, who chose to go to bed an hour earlier each night during the post-treatment monitoring period. Consequently sleep latency for this subject increased by a mean of 33 minutes after treatment. If the outlier was not included, $r = -.626$ ($p=.374$).

Conclusion: These preliminary data suggest that ability to increase hand temperature may be correlated with decreased subjective sleep latency. Temperature biofeedback of the hand may be an effective treatment for sleep onset insomnia. We are continuing to collect data for this study.

Support (optional): This research was supported by a Weill Medical College, General Clinical Research Center MO1 RR00047 grant.

0711

PREVALENCE OF SLEEP DISTURBANCES IN LONG-TERM BREAST CANCER SURVIVORS

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Introduction: Breast cancer survivors (BCS) represent 22% or 2.2 million of the estimated 9.8 million cancer survivors in the United States. This number is projected to increase each year. Current evidence suggests that 48-90% of BCS suffer from poor sleep. However, it is unclear what factors contribute to the occurrence of poor sleep in long-term survivors. Therefore, this analysis examined psychobiological factors that contributed to the prevalence of poor sleep in BCS.

Methods: Analysis of cross-sectional data included descriptive and frequency statistics to describe sample characteristics and prevalence of high global sleep scores on the Pittsburgh Sleep Quality Index (PSQI) questionnaire. Logistic regression was used to determine factors contributing to poor sleep based on PSQI cut-off scores >5 .

Results: The sample consisted of 246 BCS who were a mean age of 48 years old ($SD=8.50$), Caucasian (76%), employed (73%), married or partnered (73%), postmenopausal (70%), with a college education (58%), and with at least one concurrent medical problem (43%). Women were not taking endocrine therapy (67%) and were a mean of 5.62 years ($SD=2.03$) post-treatment. Results showed that 65% of BCS scored at or above the cut-off for poor sleep. Minority BCS (OR=3.14), with hot flashes (OR=2.68), low levels of physical functioning (OR=2.57), and high depressive symptoms (OR=4.62) were more likely to have global scores > 5 on the PSQI ($p < 0.05$). Disease and treatment variables did not predict poor sleep.

Conclusion: Poor sleep is a problem in long-term BCS. Knowledge of contributing factors provides useful information during clinical evaluations and treatment of BCS reporting poor sleep. Additional research is needed to determine the impact of poor sleep on quality of life and develop/test effective interventions for long-term BCS.

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0712

BIOFEEDBACK FOR PSYCHOPHYSIOLOGICAL INSOMNIA: ANALYSIS OF PATIENT AND TREATMENT CHARACTERISTICS IN 30 PATIENTS

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Introduction: Psychophysiological insomnia is the most common type of primary insomnia and accounts for about 15% of chronic insomnia patients seen at sleep disorders center. Characterized by conditioned arousal and inability to relax, it is one of the difficult forms of insomnia

to treat. Biofeedback has been used for the treatment of insomnia, but research on its efficacy is limited. Despite being used for more than three decades, there are no guidelines on the patient characteristics, number or type of sessions, etc and it is still categorized under "guidelines" in the most recent AASM practice parameters on insomnia.

Methods: Retrospective chart review of 30 patients with a primary diagnosis of Psychophysiological Insomnia referred for Biofeedback treatment. Data on patient's demographic and functional variables, severity of insomnia, treatments used for insomnia, stress coping mechanisms, motivation to try Biofeedback therapy, different types of therapy used, response (change in CGI) rates were collected.

Results: 70% of the subjects were females in the age range 21-80 years with a mean age of 42 years. More than 90% of the patients had tried at least 2 different hypnotics/sedatives with unsatisfactory results. Although majority of the subjects wanted non-pharmacological solution for insomnia, about one-third of the patients had a negative view of Biofeedback prior to treatment. However, most of these individuals had a more optimistic view by the end of the first session. All patients felt that immediate and objective feedback on the monitor screen helped them to relax better. The respiratory Biofeedback and EMG biofeedback were found to be most effective and also easy to administer and practice. 70% patients were rated as "very much improved" or "improved" on CGI after 2-3 sessions. Patients with problems of somatized tension responded best.

Conclusion: Patients with Psychophysiological insomnia had a positive outcome and preferred biofeedback treatment to pharmacological treatments. Majority of the patients wished they had better access and insurance coverage to Biofeedback. They were willing to recommend Biofeedback therapy for other patients with insomnia.

0713

PHARMACOKINETICS OF A LOW DOSE, SUBLINGUAL FORMULATION OF ZOLPIDEM TARTRATE IN ELDERLY SUBJECTS

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Introduction: To maintain a favorable risk/benefit profile with hypnotic drugs in elderly subjects (>65 years), the doses employed have been half those used in non-elderly adults to account for the expected increase in exposure arising from reduced clearance. This study evaluated the pharmacokinetics and safety of a novel low dose, sublingual zolpidem tartrate (SZT, Intermezzo®) formulation in elderly subjects.

Methods: Healthy elderly ($N=24$) and non-elderly adults ($N=24$) participated in this randomized, open-label, crossover study to compare the pharmacokinetics of two doses (1.75, 3.5 mg) of sublingual zolpidem tartrate (SZT) lozenges in the elderly with a 3.5 mg dose of SZT in non-elderly adults. PK assessments began prior to dosing and continued for 12 hours post-dose.

Results: A zolpidem plasma concentration that would be expected to produce sedation was reached at approximately 15 minutes with SZT 1.75 and 3.5 mg in the elderly and 3.5 mg in adults. C_{max} was slightly lower in the elderly dosed with SZT 1.75 mg (40.66 ng/ml) versus that in adults dosed with SZT 3.5 mg (61.87 ng/ml). Similarly, the total exposure over 4 hours (AUC_{0-4hr}) was lower in the elderly 1.75 mg group (100.45 ng*hr/ml) than the adult 3.5 mg group (149.99 ng*hr/ml). The elimination half-life was essentially unchanged, being 2.75 hrs in the elderly 1.75 mg group, and 2.62 hrs in the non-elderly 3.5 mg group.

Conclusion: Sublingual zolpidem tartrate produces dose-proportional plasma concentration curves in the elderly. When given to elderly individuals, the SZT 1.75 mg lozenge produces C_{max} and AUC levels lower than those seen in non-elderly adults dosed with SZT 3.5 mg. Both 1.75 and 3.5 mg SZT lozenges were safe and well tolerated in both populations.

Support (optional): This study was fully funded and supported by Transcept Pharmaceuticals, Inc., Richmond CA.

0714

PHARMACOKINETICS OF THE SUBLINGUAL ZOLPIDEM TARTRATE 3.5MG LOZENGE COMPARED TO THE ORAL ZOLPIDEM TARTRATE 10 MG TABLET

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Introduction: The ideal *prn* therapeutic agent for insomnia patients who awaken in the Middle-of-the-Night (MOTN) and have difficulty returning to sleep would allow the patient to return to sleep rapidly and awaken the next morning with no residual effects. This study compared the pharmacokinetic profile of a 3.5mg dose of a sublingual zolpidem tartrate (SZT) lozenge intended for *prn* MOTN use, with that of the commercially available 10mg bedtime dose of oral zolpidem tartrate (OZT).

Methods: Randomized, open-label crossover study involving daytime dosing with SZT 3.5mg lozenges (Intermezzo®) and OZT 10mg tablets (Ambien®) in 36 healthy subjects aged 19-64 (mean=34 years) following an overnight fast. PK assessments began prior to dosing and continued for 8 hours post-dose.

Results: Despite an SZT lozenge sublingual dose that was approximately two thirds lower than the OZT dose, the 15 minute zolpidem plasma concentrations ($C_{15\text{ min}}$) were significantly higher for SZT lozenges (19.85 ng/ml) than for OZT (12.49 ng/ml), $p < 0.05$. Also $AUC_{0-15\text{ min}}$ was nearly three times higher for SZT, but total exposure (AUC_{0-t}) over 8 hours was significantly lower for SZT 3.5mg lozenges (201.40 ng*hr/ml) as compared to OZT 10mg tablets (525.29 ng*hr/ml).

Conclusion: This study provides pharmacokinetic evidence of the potential of low dose SZT lozenges to provide faster onset of sedation while reducing overall zolpidem exposure. The initially faster SZT rate of absorption versus the higher dose of OZT provides evidence that a portion of the SZT dose underwent buccal absorption. Furthermore, the low 3.5mg dose of SZT limits zolpidem exposure which should minimize the risk for next day sedation and impairment when administered during an MOTN insomnia episode.

Support (optional): This study was fully funded and supported by Transcept Pharmaceuticals, Inc., Richmond CA.

0715

FREQUENCY AND TIMING OF MIDDLE-OF-THE-NIGHT (MOTN) AWAKENINGS AS DESCRIBED USING AN INTERACTIVE VOICE RESPONSE SYSTEM

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Introduction: Frequent middle-of-the-night (MOTN) awakenings are a common insomnia complaint. A recent epidemiological survey found that many individuals with frequent nocturnal awakenings also present with other insomnia symptoms. During a study evaluating the efficacy of sublingual zolpidem tartrate (SZT) 3.5mg lozenges, the frequency and timing of subjects' nocturnal awakenings during a two week screening period were evaluated.

Methods: Adults (N=638) with a diagnosis of DSM-IV-TR primary insomnia and a history of prolonged MOTN awakenings participated in a two week, single blind, placebo controlled screening period for a 28 day out-patient study. Subjects called into an Interactive Voice Response System (IVRS) after each MOTN awakening that persisted for at least 10 minutes. Subjects also called the IVRS every morning to confirm they had 4 hours remaining in bed at the time of their MOTN awaken-

ing. At the end of the 14 day single blind screening period, 299 subjects with significant MOTN insomnia were randomized to 4 weeks of double-blind treatment based on an IVRS screening record of at least 2 MOTN awakenings ≥ 30 minutes and 1 MOTN awakening ≥ 60 minutes per week.

Results: On average, all screened subjects experienced awakenings on 5.2 nights per week; and the mean number of awakenings with 4 hours sleep remaining was 4.4 per week. The 299 randomized subjects had a mean of 5.2 awakenings with 4 hours sleep remaining per week; and the 339 non-randomized subjects had 3.5 per week.

Conclusion: In adults with insomnia characterized by sleep maintenance difficulties, MOTN awakenings occur on average about 5 nights per week. About 85% of these awakenings occur with 4 hours of sleep remaining and thus are early enough in the night to allow *prn* MOTN dosing with the SZT 3.5mg lozenge.

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0716

AN INTERNET INTERVENTION FOR ADULT INSOMNIA

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Introduction: Although approximately one third of the U.S. adult population reports symptoms of insomnia, fewer than 15% of individuals with insomnia actually receive treatment. Although CBT for insomnia (CBT-I) is considered the treatment of choice, availability is limited by many factors, including lack of trained clinicians, poor geographical distribution of knowledgeable professionals, expense, and inaccessibility to treatment and clinicians due to work schedules and competing commitments. Given the significant need for insomnia treatment and the difficulties in obtaining CBT-I, the Internet may prove an effective tool for large-scale dissemination of this proven treatment.

Methods: This presentation will examine the efficacy of a cognitive-behavioral intervention for insomnia delivered via the Internet (SHUTi: Sleep Healthy Using The Internet). SHUTi is a 6 week structured, interactive, self-guided, and tailored intervention. Traditional face-to-face CBT-I, including the behavioral, cognitive, and educational components, has been operationalized and transformed for Web delivery. To evaluate the intervention, 44 participants were randomized to either the SHUTi intervention or a wait-list control. Measures of sleep, mood, cost, and cognitive functioning were collected at pre- and post-treatment. Additional measures of sleep were collected throughout treatment.

Results: Participants tended to be female (77%) with a mean age of 45. On average, participants reported having 5 nights/week of sleep difficulties for approximately 10 years, and all met DSM-IV criteria for primary insomnia. Preliminary data examining pre-post change scores on the Insomnia Severity Index show that sleep improved significantly for SHUTi users over the 6-week intervention ($M=15.75 \pm 4.93$ to $M=6.00 \pm 4.46$), whereas control participants showed no change during the treatment period ($M=16.11 \pm 2.49$ to $M=15.53 \pm 3.70$), $F(1,37)=31.31$, $p < .001$. Sleep efficiency also significantly improved for the experimental group from pre to post assessment (66% to 88%), with no change for the controls (69% to 67%), $F(1,34) = 25.78$, $p < .001$. The experimental group increased TST by 80 minutes and the control group increased by 9 minutes.

Conclusion: Findings suggest that an Internet delivered self-help program can significantly improve insomnia in adults. Given the ability to disseminate this type of treatment broadly at relatively low cost, this intervention has the potential to make a significant impact.

0717

SLEEP CONSEQUENCES OF WORKING FOR UNIVERSITY STUDENTS

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Introduction: Proportion of working college students has reached nearly 60% at the beginning of the new millennium. Working and studying have been documented to impact on academic performance. However, little is known about how it impacts on sleep quality.

Methods: 1,529 students (59.9% males and 40.1% females) living in the Stanford campus dormitories were interviewed at the end of the 2007 winter semester. Students were aged between 15 and 45 years. The sample was composed of 42.8% of undergraduate students. The telephone interviews included extracurricular activities, social network, health, sleeping habits, sleep and mental disorders.

Results: A total of 62.4% of the students were engaged in extracurricular activities (Working: 35.6%; Voluntary work: 22.9%; inter-collegial sport team: 6.7%; other extra-curricular activity: 32.5%) at the time of the interview. Students were engaged on average 16 hours per week in these activities. Insomnia and excessive daytime sleepiness were frequent complaints among students: 6.3% of them complained of a non-restorative sleep (NRS), 9.7% of a difficulty maintaining sleep (DMS) and 5.6% of difficulty initiating sleep (DIS) at least 3 nights per week. Moderate or severe daytime sleepiness (EDS) was reported by 27.2% of them. A sleep duration <6 hours was reported by 17.9% of the students. In multivariate models after adjusting for age, gender, health and mental disorders, being a student engaged in extracurricular activities more than 10 hours per week was a significant predictor for NRS (OR:3.0); sleep duration < 6 hours per night (OR: 2.9) and excessive daytime sleepiness (OR:2.1).

Conclusion: A sizable number of working students are sleep deprived with a sleep duration about one hour shorter than the norms for this age group. As a result, they are twice more likely to be sleepy during the daytime. Furthermore the double occupation negatively affects their academic performance.

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0718

AN EXERCISE INTERVENTION FOR SLEEP DISTURBANCE IN OLDER ADULTS: EFFECTS AT 3 AND 6 MONTHS POST-INTERVENTION

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Introduction: Insomnia is prevalent in older adults and previous studies have shown that exercise can improve sleep, mood, and quality of life. This study aimed to evaluate the long-term impact of an exercise program on subjective sleep disturbance, daytime sleepiness, depression, and quality of life in older adults with primary insomnia 3 and 6 months post intervention.

Methods: Ten healthy, sedentary older adults were randomized to a 16 week exercise intervention. Eligibility for the study included a diagnosis of primary insomnia by clinical interview and a Pittsburgh Sleep Quality Index (PSQI) score > 5. Post intervention data at 3 and 6 months were available for 5 subjects (age M= 60.7 SD=3.83). A physical activity questionnaire, Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), the Center for Epidemiologic Studies Depression Scale (CES-D), and the SF-36 quality of life measure were administered at baseline, post-intervention, 3 month and 6 month follow-up.

Results: PSQI declined significantly post-intervention (M=10.6 at baseline versus M= 4.8 post-intervention, p<.05) and remained below

baseline at 3 and 6 month follow-up (M= 5.4, p<.05 and M= 6.2, p > .10, respectively). A similar pattern was found for daytime sleepiness. A non-significant decrease in depression was observed at post-intervention, 3 and 6 month follow-up. Post treatment improvements in vigor were reported at post treatment (p < .05), and 6 month follow-up (p <.05) but not at 3 month follow-up. At 3 and 6 month follow-up, all four participants with available follow-up exercise data reported continuing with moderate intensity exercise at least 3 times per week.

Conclusion: Improvements in sleep quality and psychosocial functioning were maintained below baseline levels, post-intervention. Results suggest a moderate intensity exercise program for older adults has durable positive effects on sleep disturbance, depression, daytime sleepiness, and quality of life.

0719

INSOMNIA WITH LOW SLEEP EFFICIENCY IS ASSOCIATED WITH HIGH SALIVARY CORTISOL LEVELS IN CHILDREN

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Introduction: Insomnia in adults, particularly in those with low objective sleep efficiency, is associated with activation of the HPA axis. In this study we examined whether children with insomnia and low sleep efficiency also have elevated cortisol levels.

Methods: 393 subjects from a subset of a community sample assessing the prevalence of SDB in children were evaluated in our GCRC for one night in sound-attenuated and temperature-controlled rooms. Every child had a thorough clinical history and physical examination, subjective questionnaires completed by the parents and a 9h complete polysomnographic study. In addition, an evening saliva sample (6:00-7:00pm) before dinner and a morning saliva sample (6:00-7:00AM) before breakfast were obtained for the assessment of cortisol concentrations. Insomnia was defined by the following two questions: Does your child have trouble falling asleep or staying asleep? and is your child restless during sleep?. As a cut off point for low sleep efficiency, we used the median value of percent sleep time.

Results: A univariate analysis demonstrated significantly higher morning levels of cortisol in the insomnia group with low sleep efficiency than both the control and insomnia without low sleep efficiency groups (p=0.002, p=0.001, respectively). Evening cortisol levels were also significantly higher in the insomnia group with low sleep efficiency than the insomnia without low sleep efficiency group. Both analyses controlled for BMI percentile, age and gender.

Conclusion: Insomnia combined with objective low sleep efficiency is associated with high cortisol levels, which is consistent with the findings in adults, suggesting physiologic hyperarousal. Furthermore, these data suggest that objective measures of sleep duration in children may predict the biological severity of the disorder. Finally, insomnia with low sleep efficiency may represent a specific phenotype within this disorder which may respond differentially to therapeutic strategies.

0720

DISCREPANCIES BETWEEN SUBJECTIVELY REPORTED AND OBJECTIVELY MEASURED SLEEP PARAMETERS DECREASED FOLLOWING A BEHAVIOURAL, SINGLE COMPONENT, THERAPY FOR INSOMNIA

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Introduction: Self-reported and polysomnography (PSG) sleep are very often mismatched in both adults and the elderly presenting with primary insomnia (PI). Furthermore, several studies highlighted that,

despite positive treatment effects being evidenced by sleep diary data, there were only very small treatment effects, if any, when PSG data were considered. Interestingly, the difference between subjectively reported and objectively measured sleep continuity (sub-ob discrepancy) has been found to be greater for people with insomnia as compared to normal sleepers. This study examined the impact of a single component therapy for insomnia on both self-reported and PSG sleep and sub-ob discrepancy.

Methods: A complete data set (two weeks pre- and three weeks post-treatment sleep diary data and two days pre- and two days post- home PSG) was available for thirty-five GP and self-referred volunteers aged 20-70 years, with PI. Participants formed 3 groups: ‘QHR in bed’, ‘QHR out of bed’ and control. The QHR asked ‘read if not asleep within a quarter of an hour’.

Results: Following the QHR treatment, statistically significant increases in self-reported i) total sleep time (TST), and ii) sleep efficiency (SE) were found for both the QHRin and QHRout groups (all $p < .05$) but not for the control group. In contrast, there were no differences for PSG data (all $p > .05$). When the sub-ob discrepancies were analysed, they were found to be statistically significantly smaller, for both the QHRin and the QHRout, at the end of the intervention than at baseline for i) TST (both $p < 0.02$) and ii) SE (both $p < 0.01$). In contrast the control group sub-ob discrepancy did not change.

Conclusion: The QHR improved reported but not PSG sleep. Interestingly, the sub-ob discrepancies decreased at post-treatment. By considering previous research, this latter finding could be, very tentatively, interpreted as a shift towards normalcy and an indication of decreased fast electroencephalogram activity following the QHR.

Support (optional): Research supported by Greater Glasgow Primary Care NHS Trust

0721

CBT-I FOR INSOMNIA AND QUALITY OF LIFE IN CANCER CAREGIVERS

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Introduction: Caregivers of cancer patients report insomnia and decreased Quality of Life (QOL). CBT-I is effective in reducing insomnia symptoms. This study explored the effects of a home based CBT-I on insomnia and QOL outcomes in caregivers of cancer patients.

Methods: Caregivers of cancer patients who reported symptoms of insomnia (ICSD-2 criteria), were ≥ 21 years of age, had no previous diagnosis of depression or other sleep disorders, were invited to participate and randomized to intervention or control conditions. Sixty-four individuals have completed the study protocol. The PSQI and Actigraph were used to assess insomnia and the Caregiver Quality of Life Index (CQOLI) was used to assess quality of life at 6 points over 4 months. The intervention included stimulus reduction, sleep hygiene, relaxation, & education elements. Goal attainment scaling (GAS) was used to individualize the intervention. A nurse delivered content in two 2-hour sessions at study weeks 2 and 4.

Results: Participants were female (65%), spouses (65%) and adult children (20%) with a mean age of 52 (SD=15years). Baseline PSQI averaged 9.1. Actigraph averages were: latency 24 minutes; duration 5.9 hours; efficiency 78%. Post intervention PSQI averaged 7.1, latency improved 7 minutes, duration increased 60 minutes and efficiency increased to 85.8%. QOL scores averaged 59 at baseline and 51 post intervention (lower scores = increased QOL). PSQI and QOL scores were strongly correlated ($r=0.45$, $p=0.00$). Significant post intervention between group differences were seen in PSQI ($t=2.17$, $p=0.03$) and QOL ($t=1.94$, $p=0.05$) scores.

Conclusion: Family caregivers of persons with cancer exhibit moderate to severe levels of insomnia and report decreased QOL. Insomnia and QOL were strongly correlated in this group. One-on-one home based CBT-I combined with GAS provided caregivers with skills and knowl-

edge to improve their insomnia. Improvements in insomnia were associated with improvements in QOL.

Support (optional): NIMH R21MH067600

0722

ETHNIC DIFFERENCES IN SLEEP ARCHITECTURE AND CONTINUITY IN HEALTHY SELF-REPORTED GOOD SLEEPERS

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Introduction: Normative data has largely ignored possible ethnic differences in sleep. Recent work demonstrates significant ethnic disparities in sleep disorders, but few studies have explored ethnic differences in healthy, “good” sleepers. This study examined: 1) ethnic differences across subjective and objective measures of sleep and 2) whether differences were related to perceived stress and diurnal cortisol profiles.

Methods: 59 good sleepers (Mean Age=26.25 \pm 6.11, African-American $n=15$, Asian-American $n=14$, Caucasian $n=30$), completed a medical exam, blood testing, psychodiagnostic interviews, two-weeks of sleep diaries and actigraphy, followed by two laboratory polysomnographic (PSG) studies. Salivary cortisol samples were obtained at seven time points throughout the days following PSG.

Results: Groups were matched on sex, education, marital status, BMI, blood pressure, and employment. African-Americans were slightly older than Asian-Americans and Caucasians (Mean Age= 30.73 \pm 6.42). All analyses included age as a statistical covariate. Sleep diaries revealed no ethnic differences ($p > .05$) on sleep quality or continuity. Actigraphy, however, demonstrated that African-Americans differed ($p < .005$) from Asian-Americans, and Caucasians on mean Sleep Efficiency% (75.33 \pm 7.21; 86.27 \pm 4.53; 84.53 \pm 5.59) and mean Sleep Latency (30.80 \pm 20.03; 15.80 \pm 12.34; 14.04 \pm 10.53), respectively. PSG revealed no differences on sleep continuity for either night. On both nights, minorities exhibited decreased Slow Wave Sleep (SWS)%: African-Americans (8.48 \pm 6.72) < Asian-Americans (13.53 \pm 5.28) < Caucasians (18.16 \pm 5.46) ($p=.003$). No sleep disorders were identified, nor did groups differ on apnea-hypopnea or periodic limb movement indices. No differences were found on perceived stress or diurnal cortisol profiles ($p > .05$).

Conclusion: In the natural environment, individuals report similar sleep quality; however, minorities demonstrate impaired actigraphic sleep continuity. Under laboratory conditions, minorities demonstrate decreased SWS, but comparable sleep continuity. Reductions in SWS appear to be unrelated to differential perceived stress, psychological symptoms or hypothalamic pituitary-adrenal axis function. Examination of whether decreased SWS in healthy minorities reflects benign variability or an early biomarker of future health disparities demands further investigation.

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0723

RANDOMIZED CONTROLLED TRIAL OF COGNITIVE-BEHAVIORAL THERAPY FOR INSOMNIA ASSOCIATED WITH ALCOHOL DEPENDENCE: PRELIMINARY FINDINGS

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Introduction: Insomnia during recovery from alcohol dependence is common and contributes to relapse, yet evidence-based treatment options are limited. In a randomized controlled trial, we compared cognitive-behavioral therapy for insomnia - alcohol (CBTI-A) to a behavioral placebo treatment (BPT, desensitization) for improving sleep and daytime functioning in recovering alcoholics.

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Methods: Fourteen participants with DSM-IV alcohol dependence and insomnia but no other medical, psychiatric, or sleep disorders were randomized to 8 sessions of individual CBTI-A or BPT. Eight participants completed treatment (CBTI-A: n=4, 47.5 ± 3.1 years of age, 156.2 ± 185.1 days abstinent, baseline Insomnia Severity Index [ISI] score 16.8 ± 4.3; BPT: n=4, 40.8 ± 15.5 years of age, 161.2 ± 138.8 days abstinent, baseline ISI score 16.8 ± 3.7). Daily sleep diaries were completed throughout treatment. The ISI, Multidimensional Fatigue Inventory [MFI-20], Beck Depression Inventory (BDI-II), State-Trait Anxiety Inventory -Trait [STAI-T], Quality of Life [SF-36], and Therapy Evaluation Questionnaire [TEQ] were completed pre- and post-treatment.

Results: Most outcomes showed no pre-treatment group differences, but CBTI-A was rated as more logical (p=0.02). CBTI-A improved nighttime awakenings (CBTI-A: 2.8 ± 0.5 to 1.5 ± 1.0, BPT: 2.2 ± 1.3 to 1.8 ± 1.3, p=0.02) and SF-36 Physical Functioning (CBTI-A: 48.1 ± 6.7 to 52.8 ± 5.7, BPT: 50.2 ± 8.3 to 51.2 ± 8.8, p=0.02) more than BPT, with a trend for wake after sleep onset (p=0.06). Sleep latency, sleep efficiency, and daytime functioning measures ISI, BDI, STAI-T, MFI-20 General Fatigue and Reduced Activity subscales, and five SF-36 subscales improved in both groups (all ps<.05). Post-treatment TEQ ratings showed that CBTI-A participants were more willing to recommend treatment to others with insomnia.

Conclusion: CBTI-A improved sleep and daytime measures more than BPT. CBTI-A patients were more willing to recommend treatment to others. Retention rates were low. The relationship between sleep and relapse remains to be explored.

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0724

THE PREVALENCE OF INSOMNIA SYMPTOMS AND COMORBIDITIES ACROSS INSOMNIA SEVERITY INDEX CATEGORIES IN A COMMUNITY-BASED SAMPLE

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Introduction: The Insomnia Severity Index (ISI) is a validated measure of insomnia severity. We explored how ISI categories relate to insomnia symptoms and comorbidities.

Methods: A total of 2,292 health plan enrollees, over-sampling for those with insomnia based on health claims, completed a telephone survey between April and June of 2006. Participants were categorized in four ISI categories and compared on reported nighttime and daytime insomnia symptoms and on comorbidities.

Results: In this sample, 39.3% had no insomnia, 33.6% had subthreshold, 21.2% had moderate and 5.9% had severe insomnia based upon the ISI. The percentage of each ISI group with difficulty initiating sleep (DIS), difficulty maintaining sleep (DMS) and early morning awakenings (EMA) > 3/week increased linearly with ISI severity. The percentage of DIS was 5.1%, 37.2%, 70.1% and 93.4% in the no insomnia, subthreshold, moderate and severe groups, respectively (Chi-Square <0.0001). Similar trends were observed for DMS and EMA with 18.3%, 59.8%, 87.4% and 97.1% reporting DMS (Chi-Square < 0.0001) and 8.7%, 36.4%, 67.4% and 89.8% reporting EMA across the 4 ISI groups (Chi-Square < 0.0001), respectively. Overall, 2.1%, 17.1%, 49.3%, and 82.5% of the respective 4 groups reported having all three symptoms > 3 nights per week (Chi-Square < 0.0001). ISI severity also differentiated among the reported frequency of impaired cognitive function (3.2%, 30.2%, 65.2%, and 93.4%, Chi-Square < 0.0001), impaired physical function (11.0%, 53.7%, 88.5% and 96.4%, Chi-Square < 0.0001), and impaired emotional function (4.8%, 33.7%, 64.7%, and 91.2%, Chi-Square < 0.0001). Comorbid pain (22.8%, 46.0%, 58.8% and 70.1%, Chi-Square < 0.0001) and depression (15.9%, 40.6%, 59.4% and 78.8%, Chi-Square < 0.0001) also increased linearly with ISI severity.

Conclusion: The concordance of ISI severity categories with the frequency measures of insomnia symptoms and comorbidities further validates the ISI as a research and clinical assessment tool.

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0725

FREQUENCY AND DURATION OF USE OF PRESCRIPTION AND OVER THE COUNTER SLEEP PROMOTING MEDICATIONS

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Introduction: The frequency or duration of sleep promoting medications use in recent years is little known. This analysis examines use patterns in a non-random sample selected from a health plan claims database.

Methods: 1181 individuals with an insomnia related claim and 1111 randomly selected individuals were surveyed by telephone between April and June in 2006 (61.5% female; mean age: 51.7 yrs; range 18-81).

Results: We identified 519 (22.6%) subjects who reported use of a prescription sleep-promoting medication (PSM; 70.5 % female; mean age 54.1 + 13.3 yrs.), 267 (11.7%) who reported use of an over-the-counter (OTC; 70.0 % female; mean age 52.8 + 14.2 yrs.) sleep-promoting medication, and 155 (6.8%) who reported using both (66.5 % female; mean age 52.3 + 12.9 yrs.). There was no statistically significant age or sex differences in those who used a prescription, OTC or both (P = 0.383 & 0.743 respectively). For those reporting PSM use, the duration was 1-5, 5-10, and >10yrs for 51.9 %, 5.5%, and 10.3 %, respectively. The duration did not systematically differ between those who used PSM only or PSM and OTC only (Chi Square = 0.101). For those reporting OTC use the duration of use was 1-5, 5-10, and > 10yrs for 50.8%, 3.8%, and 6.8 %, respectively. For those reporting PSM use past month frequency was every night, 5-6 nights/wk, 1-4 nights/wk and <1/wk for 49.4%, 8.0%, 33.5%, and 9.0% respectively. Frequency of OTC use was every night for 24.4% of users, 5-6 nights/wk for 10.2% of users, 1-4 nights per/wk, for 50.2%, and < 1/wk for 15.2%.

Conclusion: Nearly 68% of PSM users and 61% of OTC users reported use durations >1yr and 57.4% of PSM users take medication >5 nights/week. These data suggest that insomnia is a chronic problem for the majority of these individuals.

Support (optional): Funded by Eli Lilly & Company

0726

CO-MORBIDITY OF INSOMNIA AND MEDICAL DISORDERS IN YOUNG ADULTS

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Introduction: Insomnia is prevalent in the general population—9-12% of adults have chronic insomnia—and has been shown to be co-morbid with many medical disorders. Younger adults are generally healthier than older adults, but there is little data on the co-morbidity of chronic insomnia and medical disorders in this population. The current study examined the prevalence of current medical disorders between young adults with (PWI) and without insomnia (PWOI).

Methods: An undergraduate college student sample completed a health survey and a one-week sleep diary. Participants were asked questions to determine the presence, frequency, duration, and disturbance of current sleep problems. Participants with non-insomnia sleep problems (e.g., apnea, narcolepsy) were excluded from the analysis. Students also completed a checklist of medical disorders.

Results: Over the course of two semesters 1,068 students (age M=20.43, SD=4.81) completed the study—a return rate of 79.5%. Analyses found

10% of participants met our criteria for insomnia, similar to rates of chronic insomnia in the general population. Previous studies have found a prevalence of medical disorders, which range from 1.2% - 18.7% in PWOI and 7.3% - 50.4% in PWI. In our sample the overall prevalence rates for specific medical disorders were 0.3% - 10.6% in PWOI and 0.0% - 10.6% in PWI. Prevalence rates for any current medical disorder were 29.3% for PWOI and 30.8% for PWI. In our sample, odds ratios for specific medical disorders between PWI and PWOI ranged from 0.61 - 3.11. No specific intergroup differences were statistically significant.

Conclusion: Compared to previous studies in this area, our participants appear to have lower prevalence rates of medical disorders than the general population. While our young adults with insomnia reported higher rates of medical disorders than those without insomnia, the odds ratios between groups again appeared to be smaller than those found in the general population. The primary import of this study is that it demonstrates that young adults with insomnia have relatively less co-morbid medical disorders than those in the general population. This suggests that this sample might be ideal to study longitudinally, to help better elucidate the relationship between insomnia and medical disorders (i.e., reciprocal or cause-and-effect).

0727

THE AFFECTS OF ANXIETY ON SLEEP QUALITY

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Introduction: Anxiety and insomnia can cause negative consequences including reduced performance and health problems (Jansson, & Linton, 2006). Few studies have examined the affect of anxiety on sleep quality in college students. The present study examined the relationship between anxiety and sleep quality.

Methods: Undergraduate students (N=824) enrolled in psychology classes finished a health survey including questions about their anxiety levels and sleep habits.

Results: A series of polynomial regression analyses were performed with anxiety levels, measured by the State-Trait Anxiety Inventory (STAI) as the independent variable and various outcome measures (e.g. ISI, DBAS, ESS, MEQ, and MFI) as the dependent variables. To control for experiment wise error, we set our significance level at ($p < .01$). There was a significant quadratic trend in ISI total score ($p < .01$), DBAS total score ($p < .001$, general fatigue ($p < .001$), physical fatigue ($p < .001$), reduced activity ($p < .001$), reduced motivation ($p < .001$), and mental fatigue ($p < .001$).

Conclusion: Data shows a significant relationship between anxiety and insomnia (ISI), dysfunctional beliefs about sleep (DBAS), and different types of fatigue and motivation (MFI). Examinations of these relationships showed an inverted U in which too little or too much anxiety was associated with worse functioning on these measures.

0728

MORNINGNESS AND EVENINGNESS RELATIONSHIP TO COLLEGE GPA

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Introduction: The Morningness/Eveningness Questionnaire (MEQ) is intended to classify people as morning or evening types. The present study examines the relationship between morningness/eveningness preferences and cumulative GPA.

Methods: Undergraduate students (N=824) who were enrolled in psychology classes completed a health survey which included questions regarding sleep habits and aspects of daytime functioning.

Results: A multiple linear regression analysis was run with cumulative GPA as the dependent variable, and SAT Verbal and Math scores, self-rated academic and social ability, importance to graduate from college, alcohol use disorders identification test, perceived stress scale, COPE,

total sleep time, sleep efficiency, bedtime, and MEQ entered as independent variables using a stepwise procedure. The final linear model included academic ability, social ability, SAT verbal scores, and MEQ scores, and predicted 21% of the variability in cumulative GPA, $F(4, 324) = 21.36, p < .001$. Standardized beta weights were: academic ability ($\beta = .31$), social ability ($\beta = .16$), SAT verbal scores ($\beta = .16$), and MEQ scores ($\beta = .15$). When all other scores were held constant, for every one standard deviation (SD) increase in MEQ (i.e., increased morningness), there was a .15 SD increase in cumulative GPA.

Conclusion: Even after controlling for other traditionally significant predictors of college GPA, morningness was a predictor of better grades in college. This could open the possibility of the ability to treat college students to become more morning types as a way to improve their academic performance. It is interesting to note that the more socially adept a student was, the lower their GPA tends to be.

0729

PREDICTORS OF INSOMNIA REMISSION FOLLOWING GROUP CBTI

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Introduction: Generalization from research on predictors of outcome in primary insomnia to clinic patients remains unclear. This study sought to identify patient characteristics that predicted insomnia remission in a clinical sample of patients using the receiver operating characteristic (ROC) analysis.

Methods: ROC analysis was conducted on 325 patients who reported sleep onset latency > 30 minutes or wake after sleep onset > 30 minutes on > 3 nights during a one-week baseline sleep diary. Participants attended a 7-session group cognitive behavior therapy for insomnia (CBT-I) and provided sleep diaries past the third session. Predictor variables: age, gender, last sessions attended, and baseline values for depression (BDI), Morningness/Eveningness questionnaire, Beliefs and Attitudes about Sleep, sleep quality, sleep onset latency, time awake after sleep onset (WASO), total sleep time (TST), nights of sleep medication use, days with napping, and SD of lights out and out of bed times. Remission was defined as not meeting criteria for sleep onset or sleep maintenance insomnia at the last available diary week.

Results: The best predictor of remission was baseline WASO < 49 minutes ($\chi^2 = 14.3, p < .001$), with 51% remitting. For those with WASO > 49 minutes, the best predictor was SD (out_of_bed) > 67 minutes, with 36% remitting ($\chi^2 = 6.8, p < .001$). Among those with WASO > 49 and SD (out_of_bed) < 67 minutes, the best predictor was TST < 4 hours, 47% remitting ($\chi^2 = 8.3, p < .001$). As there were only 17 patients with high WASO, regular out of bed time, and low TST, the latter pattern is likely less meaningful than the other two.

Conclusion: Patients with less severe sleep maintenance insomnia were the most likely to remit. Among patients with more severe sleep maintenance insomnia, those with less regular out of bed times were more likely to remit than those with a more regular out of bed time.

0730

INSOMNIA AND PHYSICAL COMPLAINTS IN ADOLESCENTS

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Introduction: Approximately 9.4% of adolescents experience insomnia (Johnson et al., 2007). A little research exists that evaluates the relationship between insomnia in adolescents and physical complaints. The current study examined the comorbidity of adolescent insomnia and physical complaints.

Methods: The current study utilized data from a national longitudinal study (Urdu, 2003), which evaluated health and health behaviors in 6504

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adolescents. Analysis included 4684 adolescents (mean age 15.96 years (SD = 1.56), 52% females) who completed an in-home interview. Insomnia was operationally defined as a report of insomnia “Almost everyday” or “Everyday” during the past year. Participants were excluded if no ethnicity, gender, or insomnia data were given.

Results: Of the participants, 9.6% of the adolescents reported insomnia. In general, adolescents with insomnia more frequently reported good, fair, or poor health (43.8% vs. 29.3%) versus adolescents without insomnia who more frequently reported excellent or very good health (56.2% vs. 70.7%), insomnia versus no insomnia, respectively. Adolescents with insomnia reported higher prevalence rates of headaches (16.5% vs. 5.8%), feeling hot (7.6% vs. 1.6%), stomachaches (10.9% vs. 3.0%), cold sweats (2% vs. .6%), physical weakness or illness (8.5% vs. 1.5%), sore throat or cough (5.1% vs. 2.1%), feeling tired for no reason (20.5% vs. 5.7%), painful or frequent urination (3.1% vs. .9%), feeling very sick (3.3% vs. .6%), waking up feeling tired (47.9% vs. 19.4%), skin problems or acne (25.3% vs. 13.6%), dizziness (6.5% vs. 1.7%), chest pains (3.3% vs. .8%), muscle or joint aches (19.8% vs. 6.6%), menstrual cramps (15.8% vs. 7.8%), and poor appetite (13.1% vs. 2.9%) versus adolescents without insomnia, respectively.

Conclusion: A significant relationship exists between adolescent insomnia and physical complaints. The exact nature of the relationship is not clear as cross-sectional data cannot determine causation. However, the current study identifies insomnia as a potential factor in physical complaints in adolescents. Additional research should explore possible causal direction as well as the implications on treatment for both the insomnia and physical complaints.

0731

THE AFTERMATH OF RASH ACTION: REGRETS, COUNTERFACTUAL THINKING, AND INSOMNIA

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Introduction: A recent investigation suggests that one facet of impulsivity, namely, urgency, is associated with disturbing hypnagogic and dreamlike mentation, thereby fueling sleep disturbances (Schmidt, Gay, & Van der Linden, in press). The present study sought to explore the content of sleep-impeding mentation in individuals high in urgency. It was hypothesized that when retiring for the night, such individuals are prone to counterfactual thinking and associated affective experiences such as regrets, shame and guilt.

Methods: A sample of undergraduate students (N=101) completed three questionnaires: the UPPS Impulsive Behavior Scale (Whiteside & Lynam, 2001), the Insomnia Severity Index (Morin, 1993), and an 8-item questionnaire on counterfactual thinking and associated feelings during the pre-sleep period.

Results: The main findings were as follows: (a) Urgency predicted insomnia severity (B=.241, SE=.085, t=2.824, p<.01); (b) urgency predicted counterfactual thinking (B=.496, SE=.077, t=6.411, p<.001); (c) counterfactual thinking predicted insomnia severity (B=.375, SE=.089, t=4.219, p<.001); and (d) the effect of urgency on insomnia severity was fully mediated by counterfactual thinking (Sobel test: Z=3.53, p<.001).

Conclusion: To our knowledge, the present study is the first to provide clear evidence for a link between urgency, counterfactual thinking, and insomnia. Moreover, our findings concerning sleep-impeding feelings of regret, shame and guilt suggest that the implication of affective experiences in insomnia deserves more attention in future research.

0732

WHAT DOES SLEEP EFFICIENCY MEAN AT WEEKENDS?

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Introduction: Sleep efficiency ((TST/TIB)x100) is widely regarded as a useful index of sleep quality. In studies comparing people with insomnia (PWI) and control ‘good sleepers’, average differences in sleep efficiency (SE) of 10%-15% are typical, with efficiencies below 80% considered ‘poor’. However, the assumption, implicit in SE, that time awake in bed is indicative of degraded sleep, may not hold for those periods of volitional restfulness spent awake in bed at weekends. Using data from a prospective comparison of PWI and controls, these analyses were designed to assess and compare the weekday v weekend SEs of PWI and controls.

Methods: Daily sleep diaries were maintained by 86 participants aged 25 - 50 years (43 PWI meeting DSM IV criteria for primary insomnia and 43 controls) for 9 months. Subjective SE, sleep quality and time in bed (TIB) were averaged for each day within each group. Weekend sleep was operationalized as sleep occurring on a Friday (F), Saturday (Sat) or Sunday (Sun) night. Wednesday (W) was selected as the reference weekday. Data were analyzed using repeated measures group (PWI/controls) by time (W, F,Sat,Sun) multivariate ANOVAs and paired t-tests.

Results: SE was consistently and significantly lower among PWI with mean differences of 11.0%, 10.0%, 9.4% and 10.1% for F, Sat, Sun and W (group main effect: F = 35.39; p < 0.001). Across days (W thru Sun) SE changed uniformly for both groups, with a noticeable decrease in SE reported on Saturday (time main effect F = 4.3; p < 0.01). There was no significant group x time interaction effect. Post hoc t-tests for time showed significant differences only between the W reference (mean = 84.6% +/- 10.3) and Sat (mean = 82.1 +/- 9.5; t = 3.63; p < 0.001) and Sun (mean = 83.2 +/- 8.8; t = 2.31, p < 0.01). TIB also showed a significant effect of time independent of group, with highest values (relative to W) reported for Sat and Sun. For both groups, variations in SE were unrelated to variations in subjective sleep quality.

Conclusion: SE shows a marked ‘weekend effect’ characterized by longer TIB, which is not related to subjective sleep quality and does not discriminate between PWI and good sleepers. The results support the view that the construct validity of SE varies between weekends and weekdays.

0733

EXPLORING THE IMPACT OF INSOMNIA ON CANCER SURVIVORS: A QUALITATIVE CONTENT ANALYSIS

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Introduction: Disturbed sleep is a frequent symptom of concern for cancer patients with approximately one-third reporting insomnia that negatively affects quality of life. The consequences of poor sleep are potentially far-reaching and include impaired daytime functioning and psychosocial adjustment. There is evidence that intervening at a psychosocial level using cognitive behaviour therapy (CBT) is an effective treatment for insomnia associated with cancer. However, non-pharmacologic treatments are rarely offered to this population. The purpose of this study was to explore the ways in which poor sleep impacts upon quality of life and to consider how we best facilitate the routine assessment of sleep disruption/disorder in cancer populations.

Methods: A qualitative research study was undertaken with a reference group of 12 cancer patients (8F, mean age=57yrs) with insomnia. 3 focus groups were conducted to explore: (i) when did your sleep first become disturbed? (ii) what caused this disruption? (iii) what was the impact of poor sleep? (iv) what information/advice did you receive from your

health care provider regarding your sleep? (v) what would be the best way to provide insomnia information/advice? The transcripts were independently examined by two readers who identified the participants' responses and the themes that subsequently emerged. Results were also fed-back to the participants in order to provide further validation.

Results: The focus groups yielded valuable information on the impact of sleep disturbance. Key emerging themes from the content analysis were: sleep disturbance was caused by cancer diagnosis/treatment; insomnia negatively affects daytime functioning and quality of life (i.e. low mood, high anxiety, feelings of guilt, irritability, lack of concentration, impaired interpersonal relationships); patients did not report sleeping difficulties to oncologists, and oncologists did not provide any sleep-related information/advice to patients; providing sleep-related information to patients during their cancer treatment would be welcomed and may prevent the development of a chronic sleep problem.

Conclusion: Insomnia is a common, intrusive and persistent disorder that impacts upon post-treatment adjustment and quality of life in cancer survivors. Patients report that sleep disturbance receives little attention by oncology professionals and by integrating a routine assessment of sleep into the cancer care framework, those in need of insomnia intervention would be identified.

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0734

EFFICACY OF INTERNET BASED INDIVIDUALIZED CBT FOR INSOMNIA

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Introduction: The multi-component behavior therapy is standardized and modeled in a computer to support consultants. This method provides a systematic and consistent approach to the therapy and increases the efficiency of the consultant. The patients collect and submit the required data via internet in order to facilitate timely data collection and the ease of use for the patients. The treatment consists of 8 sessions offering sleep hygiene, sleep restriction, stimulus control and cognitive therapy. Patients enroll for the treatment after completing a symptom check list, a detailed sleep interview and an attitude and beliefs questionnaire. Before treatment is started, patients log their desired improvement by the end of the therapy. This paper reports the efficacy of the treatment in realizing the desired goal.

Methods: 56 Patients kept a weekly sleep diary. Each week the diary and additional information from the patient were submitted to the consultant. This information was analyzed and a personalized treatment was offered every week. This communication took place over the internet. Sleep efficiency, sleep onset, total sleep time (TST), wake after sleep onset (WASO) and the subjective sleep quality on a five point rating scale were computed from the sleep diary. The final values after 7 consults were compared to the baseline values of the first week, using the non-parametric Wilcoxon signed rank test. In the first consult the patients were asked to specify their desired sleep pattern by the end of the therapy. This desired sleep pattern of the patient was compared with the obtained sleep pattern after 7 consults.

Results: Sleep efficiency and TST were significantly increased ($p < 0.01$) and sleep onset and WASO were significantly decreased by the end of the treatment. ($p < 0.05$). Sleep quality was higher after the treatment, but failed to reach significance. After 7 consults the patients were able to achieve their desired TST by 86%. This computerized method of CBT for insomnia reduced the time needed by the consultant per consult by 75 - 80%.

Conclusion: It can be concluded that the effect of CBT offered over the internet is comparable to face-to-face treatment of insomnia, as published in the literature. The computerized method is a convenient tool.

It saves the CBT consultant valuable time, without sacrificing too much in individual contact.

0735

FOUR SESSIONS OF CBT FOR SELF-REFERRED PERSONS WITH INSOMNIA

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Introduction: The emphasis that RCTs place on controlling variables other than the one of interest is often accomplished at the expense of generalizability to the typical treatment seeker. A second issue to consider when determining the clinical usefulness of an intervention is cost/time effectiveness. The present study takes both of these issues into consideration and assesses a relatively short (4 session) cognitive-behavioral intervention in a minimally screened sample of self-referred persons with insomnia (PWI).

Methods: The participants are a subset from a concurrent study validating actigraphy for the measurement of sleep in PWI. Eligible participants met diagnostic criteria for insomnia as described in the International Classification of Sleep Disorders. The only exclusionary criterion was the presence of another sleep disorder. In the present study, the sample was limited to participants who chose to take part in individual therapy as compensation for their time and effort in the actigraphy study. Therapy consisted of relaxation training, sleep hygiene, and stimulus control. Sleep diaries were used to collect data and compute the following sleep continuity variables: sleep onset latency (SOL), number of awakenings (NWAK), wake time after sleep onset (WASO), total sleep time (TST), sleep efficiency percent (SE) and sleep quality rating (SQR).

Results: There were significant improvements in 5 of 6 sleep measures at post-treatment. For SOL, $t(23) = 3.14$, $p < .01$; For WASO $t(23) = 3.61$, $p < .01$; For TST, $t(23) = -3.04$, $p < .01$; For SE, $t(23) = -5.14$, $p < .01$; For SQR, $t(23) = -3.95$, $p < .01$. Of those participants who completed at least two sessions of treatment, 72% reported at least a 50% reduction in SOL or WASO, or at least a 10% improvement in SE.

Conclusion: Clinicians may want to consider a relatively short cognitive-behavioral intervention for complex, self-referring persons complaining of chronic insomnia.

Support (optional): This research was supported by grants from the Mini Mitter Company, Inc. and the Methodist Healthcare Foundation.

0736

INSOMNIA TREATMENT PREFERENCES OF OPERATION ENDURING FREEDOM /OPERATION IRAQI FREEDOM VETERANS: PRELIMINARY FINDINGS

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Introduction: Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) veterans have substantial complaints of sleep disturbance. There is a paucity of research with the OIF/OEF veteran population, including sleep-related issues. The purpose of this ongoing study is to determine insomnia treatment preferences of OIF/OEF veterans and their willingness to use and ability to complete sleep measures commonly employed in insomnia treatment research.

Methods: OIF/OEF combat veterans who experienced a blast exposure or other injury during deployment and complained of sleep onset or maintenance insomnia of at least one month duration with daytime impairment participated. The veterans completed sleep, mood, PTSD, and treatment preference questionnaires during a 60 minute interview, and

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were asked to take home and use 2 weeks of daily sleep diaries (DSDs) and a wrist actigraph.

Results: Preliminary findings include five completed (of 18 planned) interviews of male veterans ranging in age from 25 to 37 years with an insomnia duration of one to five years. All veterans served in Iraq from 15 to 23 months involving one to three deployments. The Insomnia Severity Index revealed a moderate to severe problem (18 to 26), the Beck Depression Inventory-II was in the moderate to severe range (22 to 45), and all veterans scored positively on the PTSD Checklist-M (61 to 75). The veterans found non-pharmacological and pharmacological treatment acceptable. They preferred relaxation therapy (n=4) and pharmacological treatment (n=4) followed by stimulus control instructions (n=3), sleep restriction therapy (n=2), mindfulness-based intervention (n=1), and sleep education and hygiene (n=1). Three veterans preferred individual treatment but none wanted a group format. Electronic approaches such as MP3 files and the internet were the preferred non-pharmacological treatment delivery methods using 4 weeks of 30 to 60 minute treatment in the evening or with 24 hour access. Three veterans took DSDs home and two completed them using a daily voice mail service. Four veterans took an actigraph watch home but only one wore it and completed 14 days.

Conclusion: The preliminary findings suggest that a combination of pharmacological and non-pharmacological insomnia treatment may be preferred. Alternative treatment delivery methods may need to be offered. Sleep measures other than the DSD and actigraph may need to be evaluated for use in insomnia studies of this population.

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0737

PHYSICAL EXERCISE CAN IMPROVE SLEEP QUALITY OF INSOMNIAC PATIENTS?

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Introduction: Some evidences suggest that physical exercise can improve sleep quality of insomniac patients. The aim of this study was to evaluate and compare the acute effect of three modalities of physical exercise in anxiety state and in the sleep quality in insomnia patients.

Methods: Thirty-six patients (8 men and 28 women) with primary chronic insomnia (mean age 44.4 ± 8) were selected to participate of the study. Two methods were used to evaluate sleep quality; sleep log and polysomnography, after a night of laboratory adaptation. IDATE-State questionnaire was used to evaluate anxiety state. The protocol included three experimental groups (moderate aerobic exercise - MAE, n = 9, heavy aerobic exercise - HAE, n = 9, moderate strength exercise - MSE, n = 9) and a control group (CTL, n=9).

Results: The polysomnographic results showed reduction in the sleep onset latency - SOL (54%) and in the wake time - WT (36%), increase in total sleep time - TST (21%) and in the sleep efficiency - SE (18%) in the MAE group, after exercise session. Significant increase in the TST (37%) and reduction in the SOL (40%) were observed In the sleep log of volunteers of the group MAE. Finally, a significant reduction (7%) In the anxiety state was also observed after moderate aerobic exercise session.

Conclusion: The results suggest that an acute session of moderate aerobic exercise, but not heavy aerobic or moderate strength exercises, can reduce the anxiety state and improve the sleep quality of insomnia patients.

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0738

ANTIDEPRESSANTS AS FIRST LINE TREATMENT OF INSOMNIA IN NON-DEPRESSED PATIENTS

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Introduction: Current pharmacologic treatment of insomnia includes the use of antidepressants in patients who do not meet DSM-IV R criteria for Anxiety or Mood disorders. Review of the literature reveals that tricyclic antidepressants, SSRIs, and trazodone are the most frequently prescribed. Little evidence exists from polysomnographic based, double blind, and placebo-controlled studies that these medications are effective in the first line treatment of insomnia.

Methods: An on line search of the literature from 1965 to the present was made. Studies on non-depressed patients with insomnia were selected. Studies that did not include PSG based Level I data were rejected. The REM latency, REM density, sleep onset latency and wake after sleep onset were compared.

Results: Tricyclic antidepressants with mild sedative properties showed some improvement in sleep latency measurements over placebo, REM suppression, and REM onset delay but showed no statistical significance in improving sleep continuity. SSRIs demonstrated tolerability, REM suppression, REM onset delay but no improvement over placebo in their effect on sleep onset latency. In several instances, this class demonstrated worsening of sleep fragmentation although this effect tended to diminish over time. Trazodone showed some acute improvement of sleep onset latency over placebo but not chronic improvement at dosages of 50 - 100 mg.

Conclusion: There is little evidence to support the use of antidepressants as first line treatment of insomnia in non-depressed patients. Drug-drug interaction, side effects or sudden discontinuation effects may be under reported. Studies that demonstrate changes in PSG criteria alone are not sufficient. Of note, patients often reported subjective improvement in quality of sleep and daytime symptoms when study data demonstrated no change or some deterioration of measured parameters.

0739

USE OF THE CANNABINOID NABILONE FOR ANALGESIA AND PROMOTION OF SLEEP IN CHRONIC, NON-MALIGNANT PAIN PATIENTS: A PLACEBO-CONTROLLED, RANDOMIZED, CROSSOVER INSOMNIA PILOT STUDY

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Introduction: Evidence suggests that cannabinoids can alleviate pain and improve sleep but there are no randomized, placebo controlled studies evaluating the effect of synthetic cannabinoids such as nabilone (Cesamet). The objectives of this study are, in 11 patients with insomnia and chronic, non-malignant pain, (1) to evaluate the effect of nabilone (1mg) on patient-reported pain measures and sleep; and (2) to determine if nabilone causes daytime sleepiness.

Methods: This was an 8-week double-blinded, placebo-controlled, randomized, crossover clinical pilot study. Following baseline assessment, subjects were randomly assigned to one of two study groups: Group 1 received nabilone for the first four weeks followed by four weeks of placebo administration, and the order was reversed in Group 2. Overnight sleep assessment and tests of daytime sleepiness and alertness were conducted at the start of the study and at the end of the first and second four-week periods.

Results: All study patients had a significant reduction in pain symptoms (assessed by the McGill Pain Questionnaire) with nabilone treatment. The improvements in sleep efficiency and total sleep time did not reach significance but in 5 of the 11 patients there were consistent and signifi-

cant improvements in sleep with nabilone treatment. Further, nabilone treatment did not result in daytime sleepiness or diminished alertness in the study patients. There were no differences between placebo and baseline values for any of the above measures.

Conclusion: Nabilone (1mg) decreased pain symptoms in all study patients. Despite its clear analgesic effect, nabilone did not cause daytime sleepiness or impaired alertness. About half the study patients responded very favourably to nabilone treatment and had substantial improvements in their sleep.

Support (optional): Funding for this study was provided by Valeant Canada.

0740

DEFINING NOCTURIA WITH SLEEP DIARIES:

PREVALENCE AND CORRELATES IN ELDERLY PERSONS

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Introduction: Considerable controversy surrounds the role of nocturia in the poor sleep of elderly populations. In a sample of elderly persons, we examined the prevalence and correlates of nocturia in nightly diaries used in screening for trials of behavioral interventions for insomnia.

Methods: Subjects were 119 elderly (mean age = 63.0; 44 men, 75 women) self-identified poor sleepers. Nocturia was not mentioned in recruitment advertising. Following a telephone screening, subjects called every AM to voice mail for 2 weeks, reporting sleep data. Prompts inquired about awakenings associated with bathroom trips. Subjects were not asked whether awakenings occurred because of perceived need to void. The proportion of awakenings associated with bathroom trips was calculated for every night and averaged within subjects.

Results: Nocturia was defined if bathroom trips constituted at least 50% of nightly awakenings. Using this definition, 55.5 % (66/119) of subjects incurred nocturia. Overall number of nocturnal awakenings did not differentiate those with nocturia ($p = .373$). Based on initial interview, nocturia was unrelated to gender, reported history of prostate disease (men), deviated septum, hypertension, cardiac disease, cancer, sleep onset difficulty, difficulty returning to sleep, and usual total sleep time (all NS). Nocturia was related to poorer overall health ($p = .0003$), longer sleep latency ($p = .009$), older age ($p = .001$), lower Epworth Scores ($p = .045$), and history of arthritis ($p = .027$).

Conclusion: Among an elderly sample not specifically recruited for frequent nocturnal bathroom trips, voiding at night was exceedingly common. Because total number of awakenings was no higher in individuals with nocturia and nocturia was also associated with arthritic pain and poorer health, data could be interpreted to suggest that perceived need to void and consequent bathroom trips occurred secondary to awakenings from other causes. However, causality remains equivocal in these descriptive data.

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0741

NORMAL SLEEP AND INSOMNIA IN AFRICAN AMERICANS AND CAUCASIAN AMERICANS: A META-ANALYTIC SUMMARY

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Introduction: There has been equivocal evidence on the comparisons in sleep between African Americans (AA) and Caucasian Americans (CA). Contradictory results have been found in regards to sleep continuity, architecture, quality, and perceived distress. The goal of the current study

was to identify the presence and magnitude of ethnic differences in normal sleep and insomnia among adult-aged individuals.

Methods: The research articles included in this meta-analytic summary met the following criteria: (a) samples of AA and CA, (b) adult populations, (c) numerical data to compute effect size calculations, (d) measures of either subjective and/or objective sleep and (e) were published articles.

Results: A total of 26 studies presented data on a variety of sleep variables; however, the number of articles per each sleep variable ranged from 4 to 8. Using Cohen's d , effect sizes in the medium to large range were found for objective TST, SE, and SOL indicating that the sleep continuity of normal AA sleepers was poorer than CA. A medium effect size was determined for percentage of slow wave sleep (SWS) indicating that CA tend to produce a greater percentage. There were no differences for REM and stage 1 percentage, and sleep quality; however, there was a small to medium effect size for stage 2 percentage signifying the lack of SWS in AA may be distributed into stage 2 sleep. Lastly, there were no differences in insomnia symptomatology such as sleep complaints, difficulty initiating, and maintaining sleep. The exception was a small to medium effect size for early morning awakenings which CA report more than AA.

Conclusion: Overall, normal AA sleepers appear to sleep worse than CA objectively, and AA and CA are just as likely to report most insomnia types.

0742

A QUALITATIVE ANALYSIS OF DAYTIME FUNCTIONING AND QUALITY OF LIFE IN PERSISTENT INSOMNIA USING FOCUS GROUPS AND AUDIO-DIARIES

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Introduction: Both the ICSD-2 and DSM-IV-TR acknowledge that insomnia is a 24-hour disorder, citing daytime impairment (e.g. social, occupational, or other important areas of functioning) as a key diagnostic cornerstone. However, there is little published literature on how insomnia actually impacts upon these important areas, or indeed how insomnia affects individual quality of life (QoL), as opposed to generic health-related quality of life. This study sought to characterise, using qualitative methodologies, the daytime experience of insomnia, and the extent to which it poses limitations on important areas of functioning.

Methods: 11 participants (9f; age range 20-64, $M=38$) with persistent primary insomnia, according to DSM-IV criteria, were recruited to take part in one of three focus group discussions. Areas explored included: the typical daytime consequences of poor sleep; impact on important life domains e.g. social, relationship, and occupational functioning; compensatory/coping strategies employed to deal with sleep disturbance; and the predicted influence on individual QoL, if chronic sleep disturbance were to cease. To further gain an 'insider's perspective', a sub-sample ($n=8$) of the 11 participants, were asked to keep an audio-diary for seven consecutive days, in which entries were made twice a day: (1) to appraise sleep quality on awakening, and (2) to reflect on events of the day and their relationship with the previous night's sleep. Focus groups and audio-diary entries were taped, transcribed verbatim, and submitted to a thorough qualitative analysis, using Interpretative Phenomenological Analysis (IPA). A sleep Psychologist, with special expertise in daytime aspects of insomnia, checked themes and supporting quotes for transparency; any discrepancies were then discussed.

Results: Key emergent themes included the limiting, and in some cases, debilitating nature of insomnia; impact on psychological, cognitive, and physical factors; feelings of isolation, and lack of understanding from others; guilt and self-blame for not sleeping well; and coping strategies to deal with impairments in work performance and socialising.

Category J—Sleep Disorders – Insomnia

Conclusion: Important novel data were generated on the daytime experience of insomnia, and its impact upon functioning and overall quality of life. Audio-diaries offer a useful qualitative resource to further explore, and characterise, insomnia disorder.

0743

NEUROCOGNITIVE FUNCTIONING IN POOR SLEEPERS: RESULTS FROM THE BRAIN RESOURCE INTERNATIONAL DATABASE

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Introduction: Despite subjectively reporting deficits in several cognitive abilities, primary insomniacs fail to show conclusive objective evidence of daytime impairment. Methodological limitations proposed to account for this apparent incongruence, include small and heterogeneous sample sizes, and a limited range of tests to probe cognitive functioning. This study attempted to overcome these difficulties by comparing normal (NS) and poor sleepers (PS) on a comprehensive neuropsychological test battery, and the auditory ‘oddball task’ (Event-related potentials:ERPs).

Methods: PS (n=59,42f; M age=38) and NS (n=59,42f; M age=38) were selected from the Brain Resource International Database, a normative database of >2000 healthy controls who have undergone a standardized protocol, probing multiple aspects of brain function. The database excludes those with a history of neurological, psychiatric or other serious medical conditions. Inclusion criteria for PS included the presence of an insomnia complaint for at least 3–4 times per week in the last month. Subjects were excluded if they showed any indication of another sleep disorder. The neuropsychological battery assessed a wide range of cognitive domains. Given the association between the oddball paradigm and the late P300 component, we focused on this particular latency window, investigating possible group differences across three electrode sites (Fz,Cz,Pz) for latency (ms) and amplitude (μV).

Results: A MANCOVA on the neuropsychological dependent variables (covariates: age, education), failed to reveal a main effect of group, though there was a trend towards significance ($p=0.054$). Inspection of one-way ANCOVAs revealed that this trend was mediated by enhanced performance of PS relative to NS on a simple task of attention. Given the limited literature on ERPs and daytime functioning in PS, we carried out unadjusted univariate ANCOVAs (covariate: age) on the three electrode sites. PS showed significantly reduced latencies to target tones at sites Cz ($F=7.25, p=0.008$; 335ms v 348ms) and Pz ($F=5.62, p=0.02$; 347ms v 357ms), with no significant group differences for amplitude.

Conclusion: Results indicate that PS perform as well as NS at the ‘output’ level. The increased detection of rare tones, evidenced by speeded latencies of the P300 component, may be indicative of daytime hyperarousal, possibly accounting for maintenance of performance on cognitive tests. An international standardized database for investigating aspects of insomnia merits consideration.

Support (optional): We acknowledge the support of the Brain Resource International Database (under the auspices of The Brain Resource Company) for use of the normative data set.

0744

COVERT ATTENTION TO SLEEP IN THOSE WITH PRIMARY INSOMNIA: NO EVIDENCE FOR AN ATTENTIONAL BIAS

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Introduction: Espie et al (2006) propose a route into primary psychophysiological insomnia (PI) along the attention-intention-effort pathway which focuses on the inhibition of sleep-wake automaticity. A con-

tributing factor to this is selective attention to sleep (alongside explicit attention to sleep and effort in the sleep engagement process). Previous work carried out establishing selective attention to sleep in PI has used presentation times of 500ms, a time period associated with overt attention. With present work in the anxiety field finding strong evidence for selective attention to threatening stimuli at shorter, covert presentation times, the aim of this study was to further understand the role of anxiety as a contributing factor to this phenomenon.

Methods: A Posner paradigm was employed to obtain a measure of attentional disengagement to positive sleep, negative sleep and neutral words. A 2x2x3 between participants design was used to analyse responses obtained from 25 PI and 25 normal sleepers (NS). The reaction time of interest was the time taken by the participant to respond to the target which was invalidly cued by a word presented for 100ms.

Results: Comparisons were made between means for selected factors. Analyses found no significant effects of sleep group ($F(1,26)=1.81, p .19$), or word valence ($F(2,52)=.264, p .769$) and no significant interaction for either the engagement or disengagement components. However, a comparison of mean state anxiety scores for these two groups using a t-test found a significant difference with individuals meeting diagnostic criteria for insomnia producing a mean score which indicated higher anxiety levels ($F(1,26)=7.77, p .01$).

Conclusion: Previous research has shown those meeting criteria for insomnia selectively attend to sleep related stimuli. However, in the present study, we found no attentional bias in PI at a shorter, covert presentation time. This raises questions on the underlying mechanism of selective attention in PI and supports the need for further investigation into the role of emotion, arousal and expectancy theory.

Support (optional): This work was supported by the ESRC.

0745

CHANGE IN SLEEP CORRELATES WITH CHANGE IN POST-DEXAMETHASONE CORTISOL IN PATIENTS WITH REFRACTORY DEPRESSION TREATED WITH ECT

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Introduction: There is a large body of evidence linking dexamethasone suppression test (DST) non-suppression and depression; interestingly, this hypothalamic-pituitary adrenal (HPA) hyperactivity seems to be more likely to occur in depressed patients who also report poor sleep or have polysomnographic evidence of disturbed sleep. In order to further examine this relationship, we carried out this pilot study in severely depressed patients to determine if the change in DST cortisol occurring with electroconvulsive therapy (ECT) treatment is related to changes in sleep.

Methods: The study population consisted of 44 subjects with severe refractory major depression without medical or neurologic co-morbidities or medications that would be expected to affect HPA axis function. Only subjects who were DST non-suppressors prior to ECT treatment were included. Multiple regression analyses were performed in which the change in cortisol level was the dependent variable and the change in total MADRS score and the change in the sleep item of the Montgomery-Asberg Depression Rating Scale were predictor variables.

Results: Improvement in the sleep item of the MADRS was significantly correlated with a decrease in cortisol levels ($R^2=0.27$; $P<0.02$). However, we did not find a significant relationship between change in total MADRS score and the change in cortisol level.

Conclusion: While preliminary, these findings suggest that HPA axis hyperactivity occurring in patients with MDD may be more closely associated with disturbances in sleep than other aspects of MDD. Key words: insomnia, depression, cortisol.

0746

PSYCHOLOGICAL DISTRESS IN PREGNANT WOMEN WITH INSOMNIA

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Introduction: The aim of this study was to investigate whether psychological distress differed among women with perceived insomnia or no insomnia in their last trimester of pregnancy.

Methods: The data for this study were drawn from an ongoing cohort prospective study on Insomnia and Postpartum Depression. The study was approved by the relevant ethical committees. Written informed consent was obtained from all participants. Psychological Distress was assessed using the Portuguese version (Azevedo et al., 1991) of the Profile of Mood States (POMS; McNair et al., 1971), a 65 adjective Likert scale. The present work focuses on 4 of its six mood dimensions: Tension-Anxiety, Depression-Dejection; Anger-Hostility, Fatigue-Inertia. To evaluate sleep five items were used: 3 items to assess insomnia symptoms and 2 items to measure daytime impairment. Insomnia and Mood States were self-reported considering the previous month. Based on sleep items three distinct groups were formed: a group with insomnia (women who referred symptoms of insomnia and sleep related daytime impairment; n=44, 14.3%); a group with insomnia symptoms alone (n=188, 61.0%) and a control group without insomnia complaints (n=73, 23.7%). One Way Anova Tests and Post-Hoc Tests were applied to compare differences between groups in POMS sub-scales scores. The sample comprises 308 women, in their last trimester of pregnancy, mean age 29.81 years (SD=4.60; Range=19-44), 64.9% nulliparous.

Results: The Insomnia group reported on average significantly higher values on Tension-Anxiety, Fatigue-Inertia and Anger-hostility subscales compared with the insomnia symptoms (p=.002, p<.001, p=.003, respectively) and the control group (p<.001, p<.001, p<.001, correspondingly). Significant differences were also found between the Insomnia symptoms group and the control group with respect to Tension-Anxiety (p=.001), Fatigue-Inertia (p=.011) and Depression-Dejection (p=.031).

Conclusion: Findings of this study revealed that women with perceived insomnia experience significant Psychological Distress in late pregnancy.

Support (optional): Funded by Fundação para a Ciência e Tecnologia de Portugal (FCT-57068/SAU-ESP/2004)

0747

PRELIMINARY ANALYSES FROM THE CLEAR YOUR HEAD BEFORE BED STUDY OF COLLEGE STUDENT INSOMNIACS

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Introduction: Worry, rumination and maladaptive thinking are significant contributors to the onset and course of chronic insomnia. Written emotional expression exercises may benefit individuals with poor sleep by facilitating the restructuring of maladaptive cognitions associated with pre-sleep arousal, thereby decreasing the latency to sleep onset (Harvey & Farrell, 2003). The aim of this study is to explore the effects of a self-regulation written emotional expression exercise on pre-sleep cognitive arousal among college students who endorse symptoms of chronic insomnia.

Methods: To date, 51 college students with chronic insomnia have been enrolled and randomly assigned to either: (a) a sleep hygiene plus a 4-day (Sunday through Thursday) self-regulation writing task; or (b) a sleep hygiene only condition. All participants provided ratings of pre-sleep cognitive arousal (PSAS), sleep quality (PSQI-G), beliefs about sleep, daytime symptoms (fatigue and pain), and sleep-related safety be-

haviors at baseline and after the completion of the writing exercise (one week follow-up after baseline). Both groups completed daily sleep logs during the week of the writing exercises.

Results: Data provided by 17 men and 31 women were usable, yielding an average PSQI-G score of 11.08 and sleep onset latency (SOL) of 40 minutes. Preliminary analyses were undertaken using the primary measures of interest, SOL and PSAS. Both SOL and PSAS scores significantly decreased from baseline to follow-up [F (1, 44) = 4.16, p = .02; and F (1, 43) = 5.02, p = .03, respectively], but neither varied by condition.

Conclusion: Interestingly sleep hygiene alone, or participation in the study itself, resulted in significantly reduced pre-sleep arousal and sleep onset. Preliminary analyses suggest that while written expression exercises tend to be robust, continued collection of additional participants may be necessary to obtain ample power in order to demonstrate an effect on insomnia symptoms.

0748

RAPID SLEEP ONSET IN PATIENTS WITH CHRONIC INSOMNIA WITH NO TOLERANCE OR REBOUND INSOMNIA AFTER 14 DAYS OF TREATMENT WITH ADIPIPLON

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Introduction: Adipiplon, a GABAA partial agonist with preference for $\alpha 3$ subunit receptors, promoted a rapid onset of sleep as assessed by Latency to Persistent Sleep (LPS) in a model of transient insomnia. This study was intended to confirm these findings in patients with chronic insomnia treated for 14 days.

Methods: This randomized, double-blind, placebo-controlled, parallel-group, two week study enrolled 258 patients with chronic insomnia who were less than 65 years old. The study compared five formulations of adipiplon to placebo in reducing LPS. Sleep maintenance and quality of sleep were evaluated as secondary endpoints. After qualifying baseline PSGs, patients returned to the sleep lab for the first two nights of treatment followed by nightly dosing at home before returning to the sleep lab for the last four treatment nights, including a two night placebo run out.

Results: Adipiplon demonstrated statistically significant improvement over placebo for reducing LPS at all doses and formulations tested (decrease from baseline of 23.2 minutes for placebo and 47.1 - 56.4 minutes for the 5 adipiplon-treated cohorts). The LPS reduction persisted over the 2 weeks. On abrupt drug withdrawal, the LPS was no worse than baseline, indicating no rebound insomnia. Although this study was not powered to show sleep maintenance, all drug treated groups showed a numerical improvement over baseline. Adipiplon was generally well tolerated with adverse events primarily reflecting the drug's pharmacological effects, including sedation, somnolence and dizziness. There was one drug-related serious AE due to a protocol violation by the subject.

Conclusion: Adipiplon is a potent, well-tolerated, sedative hypnotic, effective in promoting rapid onset of sleep in patients with chronic insomnia. There was no evidence of tolerance over the 2-week treatment period, and no evidence of withdrawal upon abrupt discontinuation. This study provided information to support the selection of a formulation and doses for investigation in Phase 3.

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0749

EFFECTS OF ETHANOL ON SLEEP IN INSOMNIACS: AN ANALYSIS BY HALVES OF THE NIGHT

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Introduction: Insomniacs self administer low ethanol doses for sleep and as tolerance develops with nightly use the dose is increased. At high doses in healthy individuals ethanol on the first night disrupts sleep in the second half of the night. We sought to determine whether a similar initial second-half sleep disruption occurs at low doses in insomniacs.

Methods: An analysis of ethanol effects by halves of the night was carried out in 40, 21 - 55 years old, primary insomniacs with no history of alcoholism. All met DSM IV criteria for insomnia and had a PSG sleep efficiency of < 85% on a screening 8 hour NPSG and no signs of another primary sleep disorder. They were randomized to receive 0.0, 0.3, 0.45, 0.6g/kg ethanol before sleep for 6 consecutive nights. Standard 8 hour NPSGs were done and nights 2 and 6 were compared by halves of the night among the 4 doses using mixed design MANOVAs.

Results: Across all doses, more stage 3-4 was found in half 1 (F = 15.57, p < 0.001) of nights 2 and 6 and more REM in half 2 (F = 15.88, p < 0.001). Stage 1 was reduced in half 2 of nights 2 and 6 (F = 5.11, p < 0.03) with increasing doses and REM sleep was increased (F = 5.06, p < 0.03). Sleep efficiency was increased relative to placebo on half 2 of night 2 with increasing doses, which was lost on night 6 (F = 6.30, p < 0.02).

Conclusion: Ethanol showed dose related improvements in sleep efficiency and reductions in stage 1 sleep in insomniacs in half 2 of initial nights. While this effect is lost by night 6, the absence of an initial second-half sleep disruption may explain why insomniacs use ethanol frequently as a sleep aid.

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0750

COST-EFFECTIVENESS OF ESZOPICLONE FOR THE TREATMENT OF ADULTS WITH PRIMARY INSOMNIA

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Introduction: The clinical benefits of pharmacotherapy for the treatment of insomnia have been studied extensively. In this analysis, the cost effectiveness (CE) of eszopiclone for the treatment of primary insomnia (PI) was assessed.

Methods: Data from a 6-month clinical trial were combined with data from a claims database and published literature to assess the quality-adjusted life years (QALY) gained and costs associated with eszopiclone or placebo in adults with PI (n=824). Quality-of-life data were collected using the SF-36 and preference-based utility scores were derived using a published algorithm. To model medical and absenteeism costs, patients were classified at each timepoint as having remitted (≤7 on the Insomnia Severity Index [ISI]) or not remitted (>7 on the ISI). Patients not in remission were assumed to experience higher direct medical and absenteeism costs, as evidenced in a retrospective analysis of a claims and absenteeism database of self-insured employers. Presenteeism costs (lost productivity while at work) were based on responses to the Work Limitation Questionnaire. Differences in QALYs and costs from baseline for both treatments were calculated and CE ratios were derived. Uncertainty surrounding the CE ratio was addressed via univariate sensitivity analyses, bootstrapping, and multivariate probabilistic sensitivity analyses.

Results: Eszopiclone use resulted in a net gain of 0.0137 QALYs at a net cost of \$67 for the 6-month utilization period. The incremental increase in cost associated with eszopiclone was therefore slightly less than \$5,000 per QALY gained. Excluding absenteeism and presenteeism costs, the CE ratio increased to ~\$33,000 per QALY gained, which is below the generally accepted CE threshold of \$50,000. Extensive sensitivity analyses indicate that the results are robust.

Conclusion: Based on the model used in this study, eszopiclone appears to be cost effective, especially when lost productivity costs were included, for the treatment of chronic PI in these adults.

Support (optional): Support for this study provided by Sepracor Inc.

0751

SELF-GUIDED IMAGERY FOR THE TREATMENT OF INSOMNIA IN THE SLEEP LAB

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Introduction: Insomniacs may have difficulty falling asleep or returning to sleep in a sleep lab during diagnostic PSG testing. Therapist guided imagery has been used to treat insomnia. In our clinic, we observe that insomnia patients can be taught and receive benefit from the use of self-guided imagery. We hypothesized self-guided imagery instructions can be provided to, applied by, and help insomnia patients manage sleeplessness during a diagnostic sleep study.

Methods: On the night of their diagnostic PSG at Maimonides Sleep Arts & Sciences, insomnia patients were given a handout explaining mental imagery concepts. A questionnaire asked all patients to rank their ability to picture images in their mind's eye. Patients were instructed to use imagery at bedtime or during the night to re-initiate sleep. Following their study, the patient reported whether or not they used imagery, and if it was helpful, had no impact, or hindered sleep.

Results: A total of 96 chronic insomnia patients (mean Insomnia Severity Index 18.8, SD=5.1; mean age 50.7, SD=15.7; mean BMI 30.9, SD=8.6; 62.2% female) were tested for possible sleep-disordered breathing. In the morning, 90 patients reported use of imagery to assist in falling or returning to sleep, and 6 patients did not. Among imagery users, 48 of 90 (53.3%) found imagery helpful; 39 of 90 (43.3%) felt imagery had no impact; 3 of 90 (3.33%) felt imagery hindered sleep.

Conclusion: Greater than 90% of insomnia patients were instructed on and applied self-guided imagery in the sleep lab, and more than half of users reported that this clinical tool was helpful in managing insomnia during the sleep test. Self-guided imagery appears to be a helpful tool inside the sleep lab environment. Research should evaluate the utility of self-guided imagery for insomnia outside the sleep lab.

Support (optional): Maimonides Sleep Arts & Sciences, and the Sleep and Human Health Institute

0752

NOCTURIA AS A PREDICTIVE TOOL FOR SLEEP-DISORDERED BREATHING IN CHRONIC INSOMNIACS

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Introduction: Diagnostic PSG is not routinely ordered for insomnia patients because these patients may not complain about sleep breathing problems. In contrast, insomniacs may report the end organ symptom nocturia, a complaint pathophysiologically linked to SDB via increased production of atrial natriuretic peptide (ANP). We hypothesize SDB (AASM: RDI ≥ 15) prevalence will be equivalent in chronic insomniacs with nocturia irrespective of the presence of self-identified sleep breathing problems.

Methods: Patients with a primary complaint of chronic insomnia, who seek treatment at Maimonides Sleep Arts & Sciences, routinely undergo

diagnostic PSG whether or not they complain of sleep breathing problems. Instead, we screen insomnia patients for end-organ symptoms such as nocturia. Chronic insomnia patient charts were reviewed for secondary self-identified sleep breathing problems and nocturia. Data presented are demographics, reports of nocturia and self-identified sleep breathing problems, Insomnia Severity Index (ISI), and objective RDI.

Results: Two groups emerged from 224 chronic insomnia patients [mean(SD): ISI 20.0 (4.9); age 50 years (15.4); BMI 28.6 (7.6); 57.6% female] who underwent diagnostic PSG: 124 insomniacs with no self-identified sleep breathing problems (No-SBP) (65.3% female), 100 insomniacs with self-identified sleep breathing problems (SBP) (48% female), with no significant demographic differences between groups except sex ($P=.01$). SDB diagnoses were confirmed in 95.2% of the No-SBP group compared to 98% in the SBP group [mean(SD)RDI=43.6 (20.6) versus RDI=56.4 (26.4), $F(1,229)=17.2$, $P<0.001$]. Nocturia sensitivity was similar in No-SBP 86.4% versus SBP 87.7%, as was nocturia positive predictive value (PPV): No-SBP 94.4% versus SBP 97.7%.

Conclusion: SDB was extremely prevalent in both groups, irrespective of breathing complaints, albeit the self-identified sleep breathing problem group showed a significantly higher RDI. In this treatment seeking sample of chronic insomniacs, nocturia proved a useful screening symptom and corroborated the routine use of diagnostic PSG for SDB assessment.

Support (optional): Maimonides Sleep Arts & Sciences, and the Sleep and Human Health Institute

0753

INSOMNIA AND SLEEP LOSS: REPORTED EFFECTS ON PERFORMANCE, SAFETY, AND PRODUCTIVITY

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Introduction: A work-based survey explored how sleep disruption and insomnia affected reported performance, safety, and productivity in work populations, and related treatment use.

Methods: Individuals in four U.S.-based companies completed an anonymous, 55-item, online survey. Respondents were classified according to DSM-IV-TR minimum criteria for 'primary' and 'secondary' insomnia (IN) and ICSD minimum criteria for insufficient sleep syndrome (ISS). The remaining respondents were classified as 'at-risk' (a medical, psychological or sleep condition that precluded IN or ISS) or 'good sleep' (did not meet criteria for any other group). The survey questions related to sleep, performance and safety. Health-related limitations in ability to work and associated productivity losses were measured using the Work Limitations Questionnaire (WLQ). Differences in outcome measures and treatment use between groups were examined with chi-square tests.

Results: 4,188 respondents completed the survey (40.00±11.21 years, 53.4% male), with 9.6% (n=403) meeting the diagnostic criteria for IN and 5.9% (n=247) meeting the criteria for ISS. The remaining respondents included 39.6% (n=1660) 'at-risk' and 44.8% (n=1878) 'good sleepers.' The IN group reported the greatest memory impairment ($p<.01$) and social functioning ($p<.001$). Nodding off while driving was reported most by the ISS group ($p<.05$). IN (6.1%) and ISS (5.5%) groups reported the greatest ($p<.05$) productivity loss compared to the at-risk (4.6%) and good sleep (2.5%) groups. IN (27.8%), ISS (21.1%) and at-risk groups (25.6%) all reported over-the-counter medication use greater than the good sleep group (11.8%, $p<.001$). Insomnia-specific prescription medication use was greater ($p<.05$) in the IN group (30.3%) vs. the ISS (8.9%), at-risk (14.0%) and good sleep (4.4%) groups.

Conclusion: Reports of insomnia and sleep disruption among work-based respondents are prevalent, with self-reported effects on performance, safety, and productivity. The insomnia group reported the great-

est productivity loss, memory impairment and worst social functioning compared to the other sleep groups.

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0754

REM AND NREM POWER SPECTRAL ANALYSIS ON TWO CONSECUTIVE NIGHTS IN RELATION TO SLEEP QUALITY IN PSYCHOPHYSIOLOGICAL AND PARADOXICAL INSOMNIA SUFFERERS

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Introduction: Power spectral analysis (PSA) studies have shown differences between chronic insomnia sufferers (INS) and good sleepers (GS). However, they are often based on only one night of PSG recordings and sleep quality in chronic insomnia sufferers may vary across nights. Considering this fluctuation, the objective of this study is to examine differences in PSA of GS, psychophysiological (Psy-I) and paradoxical (Para-I) insomnia sufferers on two consecutive nights, controlling for sleep quality differences between groups.

Methods: Sixty-eight drug-free participants (23 GS, 25 Psy-I and 20 Para-I) completed three nights of PSG recordings. The first five sleep cycles of Nights 2 and 3 were retained for PSA. The frequency activity (ranging from 0.00 to 35.00Hz) was computed at C3 site. Absolute power spectral values of REM and NREM sleep were log transformed. For each frequency band, means of the sleep cycles of each night were computed. Afterwards, mean values of both nights were averaged. Sleep quality was defined as mean objective and subjective sleep efficiency (OSE; SSE) of both nights.

Results: Repeated measures ANCOVAs, including one within-subject factor (frequency), one between-subject independent factor (group) and as covariates age, gender and sleep quality, were performed on PSA values, in REM and NREM sleep and for OSE and SSE separately. All ANCOVAs showed no clear differences ($p > .05$) between groups and no significant effect of OSE or SSE. Only a trend for a significant difference was observed in NREM sleep suggesting greater spectral activity in all frequency bands in Par-I compared with GS and Psy-I.

Conclusion: The absence of significant difference across GS, Psy-I and Para-I contrasts with previous studies. Averaging PSA and sleep quality of two nights might cover subtle differences between groups attributable to sleep difficulties variations. Also, controlling for sleep quality might partially explain the similarities between INS and GS.

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0755

RELATIONS BETWEEN OBJECTIVE SLEEP MEASURES AND COGNITIVE EVOKED POTENTIALS AMONG INSOMNIA SUFFERERS

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Introduction: Relative to good sleepers (GS), psychophysiological insomnia sufferers (Psy-I) objectively show longer SOL, increased WASO, shorter TST and lower SE. Hyperarousal has been suggested as a core component of chronic insomnia. Event-related potentials (ERPs) are informative tools for assessing arousal levels. If these levels vary according to sleep quality remains poorly understood. The goal of this study is to document relationships between objective sleep measures and different ERPs.

Methods: 15 Psy-I and 16 GS underwent four consecutive nights of PSG recordings. ERPs were recorded in the evening and upon awakening (third and fourth night; N1, P2) as well as at sleep-onset (fourth night; N350). Auditory stimuli consisted of 'standard' (70 dB, 2000 Hz,

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.85 probability) and ‘deviant’ stimuli (90 dB, 1500 Hz, .15 probability). Pearson’s correlations were computed between objective sleep variables (WASO, TST, TWT and SOL) and the amplitude of ERP components.

Results: In Psy-I, analyses revealed that N1 amplitude, on the third evening, for both stimuli, was negatively correlated with WASO of the previous night (standard, $r = -.58$; deviant, $r = -.75$). Furthermore, N1 amplitude, at sleep-onset for the deviant stimulus was negatively correlated with WASO of the third night ($r = -.68$). As such, N1 amplitude decreased as WASO increased. P2 amplitude for the standard stimulus on the third evening correlated with TST of the same night ($r = .51$). Thus, P2 amplitude increased as TST increased. For GS, no significant relations were observed. Furthermore, in both groups, none of the mornings’ ERPs correlated with any sleep measures.

Conclusion: These results suggest that arousal levels (N1-P2 amplitudes) in Psy-I vary according to objective sleep measures, especially WASO and TST. Surprisingly, no relationships were observed in GS. It might be possible that it is only once a certain arousal threshold is reached that it is noticeable.

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0756

THE ASSOCIATION OF CANCER WORRY AND SLEEP COMPLAINTS AMONG WOMEN

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Introduction: Literature on associations between sleep and cancer indicates that 30-50% of individuals with a cancer diagnosis report sleep complaints. We examined whether cancer worry is associated with sleep complaints among women with no specific diagnosis of breast cancer.

Methods: Women were 1274 community-based Brooklyn residents (age range: 50-70 years) participating in a cross-sectional ‘Women’s Health Project’; 28% were White and 72%, Black. Analysis focused only on women without a history of a physician-diagnosed cancer (n=1038). Participants were recruited using a stratified, cluster sampling technique. Interviewers of the same ethnicity as the participants gathered data regarding sociodemographic factors, physical health characteristics, sleep complaints, and cancer worry. Sleep complaint was defined as a report of either difficulty initiating sleep, difficulty maintaining sleep, or early morning awakening. Cancer worry was assessed with the Cancer Attitude Inventory.

Results: Of the sample, 65% of the women reporting that they worried about developing breast cancer; 49% reported a sleep complaint. Twenty-seven percent indicated that cancer worry affected their mood; 25% indicated that it affected their daily activity. Fisher’s Exact test showed the rate of sleep complaints was significantly greater among women with cancer worry [$\chi^2=25.17$, $p<0.001$]; the estimated odds ratio was: 1.92 [95% CI:1.48—2.47, $p<0.001$]. Logistic regression analysis, adjusting for effects of ethnicity, stress, and perceived risk of developing cancer, yielded odds ratio for sleep complaints of 1.45 [95% CI:1.09—1.92, $p<0.001$]. Thus, even after adjusting for effects of covariates, the odds of reporting sleep complaints for women who worry about cancer were nearly 50% greater than odds for women who reported no cancer worry.

Conclusion: A significant number of women worrying about cancer may be experiencing sleep disturbances, even in the absence of a breast cancer diagnosis. These women could benefit from cognitive-behavior therapy, which improves sleep as well as daytime functioning.

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0757

COMBINING MINDFULNESS MEDITATION WITH CBT FOR INSOMNIA: LONG-TERM EFFECTS

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Introduction: Recently, a unique intervention combining mindfulness meditation with CBT-I was shown to have benefits at post treatment. The aims of this study were to examine the long-term effects of this intervention from end-of-treatment (EOT) to 12 months post-treatment and to explore the relationship between insomnia symptoms, mindfulness skills, and meditation practice during the follow-up period.

Methods: Non-parametric analyses were conducted on 21 participants who provided follow-up data at 6 and 12 months post treatment. At each time point, participants completed one week of sleep and meditation diaries, the Pre-Sleep Arousal Scale (PSAS), Insomnia Severity Index (ISI), Kentucky Inventory of Mindfulness Skills and a number of measures on insomnia symptoms including the Glasgow Sleep Effort Scale (GSES).

Results: Analyses examining the pattern of change across time (EOT, 6-month, 12-month) revealed significantly lower scores on the ISI ($p < .05$) at 12 months compared to the previous two time points. Participants who reported at least one insomnia episode (> one month) during the follow-up period (n = 7) had higher scores on the PSAS ($p < .05$) and GSES ($p < .05$) at EOT compared to those with no insomnia episodes (n = 11). Correlations among mindfulness skills, meditation practice, and insomnia symptoms revealed significant negative correlations ($p < .05$) between mindfulness skills and daytime sleepiness at each of the 3 time points.

Conclusion: These results suggest that the benefits of CBT-I combined with mindfulness were generally maintained during the 12-month follow-up period with indications that higher pre-sleep arousal and sleep effort at EOT are associated with relapse of insomnia. In addition, having more mindfulness skills is associated with less perceived daytime sleepiness although the length and frequency of meditation practice does not appear to have a clear relationship with insomnia symptoms.

0758

THE FICKLE NATURE OF ACTIGRAPHY: NOT ALL MOVEMENT IS THE SAME

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Introduction: Actigraphy (ACT) has been increasingly popular for the study of sleep patterns in normal sleepers and insomnia sufferers. Implicit in such research is the assumption that ACT provides an accurate estimate of the sleep/wake measures of interest and does so consistently across individuals. The current exploratory study was conducted to test this assumption.

Methods: Twenty-six (Mage = 28.0±4.7yrs.) normal sleepers and 29 (28.2±6.0 yrs.) primary insomnia (PI) sufferers completed 6 nights (3 in-home & 3 in-lab) of ACT and polysomnography (PSG) monitoring. R&K criteria were used to derive PSG sleep/wake measures, whereas ACT sleep/wake measures were obtained using ACT scoring software. The mean ACT/PSG differences for measures of onset latency (SOL), total sleep time (TST), wake after onset (WASO), and sleep efficiency (SE) were calculated for each subject in each setting and the resultant difference scores were subjected to a hierarchical cluster analysis. Within and between group analyses were then conducted to help characterize the resulting subgroups.

Results: Results showed the sample could be optimally divided into 3 groups. In Group 1 (n = 37), ACT/PSG correlations ranged from .47 (WASO) to .92 (TST), whereas within-group t-tests showed ACT significantly underestimated PSG SOL. In Group 2 (n = 11), ACT/PSG correlations ranged from .83 (WASO) to .95 (TST), but ACT underestimated PSG TST and SE and overestimated WASO. In Group 3 (n = 7), ACT/PSG correlations ranged from .54 (SOL) to .85 (WASO); ACT overestimated TST and SE while underestimating WASO. Group 2 had significantly more minutes of slow wave sleep per night than did the other groups. Group 3 had a significantly lower SE and higher WASO on PSG than did the other groups. Groups did not differ significantly in their mean ages, gender compositions or proportions of PI sufferers they included.

Conclusion: Since the results show that the accuracy of ACT sleep/wake time measures differs across subgroups, the meaning of these measures may vary substantially across individuals. The findings also suggest that the nature of an individual's objective sleep may influence the accuracy of the ACT measures obtained.

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0759

USE OF ACTIGRAPHY FOR PREDICTING INSOMNIA THERAPY RESPONSE: AN UPDATE

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Introduction: Researchers are increasingly using actigraphy in insomnia studies to track treatment outcomes. However, it is yet to be determined whether actigraphy can predict insomnia treatment response. This report describes ongoing work to identify pre-treatment actigraphic indices that discriminate insomnia treatment responders from non-responders.

Methods: This study enrolled well-screened VA outpatients who met Research Diagnostic Criteria for insomnia disorder and had an average diary total wake time (TWT) > 60 minutes/night. Enrollees completed actigraphy (1 week) and the Pittsburgh Sleep Quality Index (PSQI) before treatment. They then were randomized to 4 biweekly sessions of CBT (20 primary-PI & 21 comorbid-CMI insomnia) or a sleep hygiene (SH) therapy (20 PI, 20 CMI). The PSQI and other measures were repeated immediately following therapy and again six months later. Patients who showed a > 50% reduction in their PSQI scores from pre-therapy to their study endpoint were labeled responders; the remainder were labeled non-responders. Regression analyses were used to identify pre-therapy actigraphy measures that predicted treatment response. Composite scores were calculated for each subject using weights derived from the regression analysis, and these scores were then tested via Receiver-Operator Characteristic Curve (ROC) analysis to determine how well they predicted treatment response.

Results: Due to missing data, 67 (23 responders; 44 non-responders) were classified using PSQI criteria. Regression analyses showed pre-therapy actigraphic mean total sleep time and WASO along with within-subject standard deviations of the number of nocturnal awakenings and sleep efficiency resulted in significant ($R^2 = .21/p = .007$) prediction of responders. ROC analyses of regression-derived composite scores showed good ($AUC = .813/p = .001$) separation of responders from non-responders. Subgroup analyses showed much better prediction for PI responders ($AUC = .90/p = .001$) than for CMI ($AUC = .70/p = .09$) responders.

Conclusion: Results suggest actigraphy is useful for predicting PI patients' insomnia therapy response.

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0760

HOW VALID ARE THE DSM-IV-TR AND ICSD-2 INSOMNIA NOSOLOGIES?: PRELIMINARY RESULTS FROM A MULTI-TRAIT/MULTI-METHOD DIAGNOSTIC TRIAL

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Introduction: DSM-IV-TR and ICSD-2 provide distinctive classification schemes for insomnia disorders. DSM-IV-TR "lumps" insomnia disorders into a few globally defined categories, whereas ICSD-2 "splits" them into numerous specific subgroups. This ongoing dual-site project was initiated to test the validity of DSM-IV-TR and ICSD-2 insomnia diagnoses.

Methods: Patient volunteers who meet research diagnostic criteria for insomnia undergo evaluations with each of 6 sleep specialists. Two specialists use solely a structured sleep interview. Another pair uses a standard clinical interview and reviews patients' history questionnaires and sleep logs. The third pair formulates impressions from interview, questionnaire, sleep log and polysomnography (PSG). Clinicians then rate how well (0 = "doesn't fit at all"; 100 = "fits extremely well") each of 10 DSM-IV-TR and 37 ICSD-2 insomnia diagnoses "fit" the patient. Using data from 155 (67.1% women; MAge = 51.8±13.7 yrs.) enrollees, we computed mean diagnostic ratings within each clinician dyad for each patient and then computed inter-dyad Spearman correlations of these mean ratings across patients. Resultant correlations were then placed into multi-trait/multi-method matrices to examine the convergent validity (i.e., "heteromethod-monotrait" correlation) of the DSM-IV-TR and ICSD-2 insomnia categories.

Results: Results showed moderately good convergent validity (r 's = .53 to .69) across assessment methods for DSM-IV-TR alcohol-induced insomnia and the insomnias related to mental and medical disorders. ICSD-2 diagnoses most strongly supported (r 's = .56 to .77) were idiopathic insomnia, restless legs syndrome, and the insomnias due to mental and medical disorders. Least supported were the ICSD-2 inadequate sleep hygiene and paradoxical insomnia diagnoses. Clinicians with and without PSG information disagreed most often when rating DSM-IV-TR primary insomnia and breathing-related sleep disorder diagnoses and the ICSD-2 obstructive sleep apnea diagnosis.

Conclusion: Results supported the validity of some but not all DSM-IV-TR and ICSD-2 insomnia diagnoses and suggest PSG may deserve an increased role in insomnia assessment.

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0761

HEALTHCARE UTILIZATION PATTERNS PREDICT INSOMNIA TREATMENT RESPONSE

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Introduction: Previous studies suggest insomnia patients are more prone to utilize the healthcare system than are matched patients without insomnia. This analysis was conducted to determine if the pre-therapy utilization rates of insomnia patients predict their responses to behavioral insomnia therapies.

Methods: This study enrolled well-screened VA outpatients who met Research Diagnostic Criteria for insomnia disorder and had an average diary total wake time > 60 minutes/night. Enrollees completed study measures including the Pittsburgh Sleep Quality Index (PSQI) before treatment. They then were randomized to 4 biweekly sessions of CBT (20 primary-PI & 21 comorbid-CMI insomnia) or a sleep hygiene (SH)

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therapy (20 PI, 20 CMI). The PSQI and other measures were repeated immediately following therapy and again six months later. Patients who achieved a PSQI score < 6 by the end of treatment were labeled remitters; the remainder were labeled non-remitters. A logistic regression model adjusting for treatment group assignment was used to determine if healthcare utilization rates (# clinic visits) in the 6-month pre-therapy period predicted post-therapy insomnia remission. Two patients in remission at baseline were not included in this analysis.

Results: Those who failed to achieve PSQI-defined remission status had about twice as many clinic visits in the 6-months before therapy as did those who achieved remission (mean = 12.3 vs. 7.1). Results of the logistic regression analysis showed a significant ($p = .0303$) relationship between pre-therapy healthcare utilization rates and post-treatment insomnia remission status. CBT group assignment also significantly ($p = .0416$) enhanced likelihood of post-therapy remission.

Conclusion: Insomnia patients who show relatively low pre-treatment healthcare utilization rates are most prone to show clinically significant improvement with behavioral insomnia therapies. Further study is needed to determine if augmented behavioral therapies or pharmacotherapy best meets the treatment needs of insomnia patients who frequent healthcare providers.

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0762

HOME IS WHERE THE SLEEP IS: EFFECTS OF IN-LAB AND IN-HOME SLEEP MONITORING ON THOSE WITH AND WITHOUT INSOMNIA

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Introduction: For insomnia sufferers, laboratory polysomnography (LPSG) may obviate typical sleep-disruptive practices and conditioned environment cues that perpetuate sleep disturbance in the home sleeping environment. As such, LPSG may temporarily improve sleep of insomnia sufferers thus reducing the observed sleep differences between them and normal controls. This study examined whether home-based monitoring (HPSG) shows greater differences between insomnia sufferers and controls than does LPSG.

Methods: Seventy-four (37 women; MAge=51.9 yrs.) well-screened primary insomnia sufferers and 77 (37 women; 51.1 yrs.) age- and gender-matched normal sleepers underwent 3 consecutive LPSGs and 3 consecutive HPSGs. A randomly determined 50% of each sample underwent LPSG first, whereas the remainder completed HPSG first. R&K scoring procedures were used to derive common measures of sleep consolidation and architecture for each night's sleep. A series of ANOVA's were then conducted to evaluate the main and interaction effects of subject type, sleep setting, and order of studies on the sleep parameters derived.

Results: Analyses showed significant group x place x order effects for measures of sleep onset latency ($p = .009$), wake time after onset ($p = .002$), stage 2% ($p = .04$) and SWS% ($p = .004$). Among the subgroups completing LPSG first, those with insomnia showed significantly longer onset latencies at home, but higher values of WASO in the lab than did matched controls. The insomnia group who slept in the lab first also showed a significantly greater % of the night in stage 2 sleep in the lab and in SWS at home whereas the insomnia sufferers completing HPSG first showed the reverse trend.

Conclusion: Results provide some support for our prediction that HPSG would reveal greater differences between insomnia sufferers and controls than would LPSG. Findings also demonstrate the monitoring process itself and the novel LPSG setting may separately influence the objective sleep observed.

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0763

INTER-RATER RELIABILITY FOR INSOMNIA DIAGNOSES DERIVED FROM THE DUKE STRUCTURED INTERVIEW FOR SLEEP DISORDERS

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Introduction: Insomnia research has long been hampered by the lack of a widely available SCID-like structured interview for establishing DSM-IV-TR and ICSD-2 insomnia diagnoses. This report presents inter-rater reliability for insomnia diagnoses using the newly developed Duke Structured Interview for Sleep Disorders (DSISD).

Methods: Two sleep specialists separately interviewed a series of 155 patients ($N = 155$; 67.1% women; MAge= 51.8±13.7 yrs.) who met research diagnostic criteria for insomnia using the DSISD. The clinicians then independently rated how well (0 = "not at all"; 100 = "very") each of 10 DSM-IV-TR and 37 ICSD-2 insomnia diagnoses "fit" each patient. Inter-rater agreement for DSM-IV-TR and ICSD-2 insomnia diagnoses was assessed via use of Spearman correlational analyses.

Results: Correlations suggested moderate to good inter-rater agreement for the DSM-IV-TR categories of primary insomnia ($r=.46$), breathing-related sleep disorder ($r=.75$), circadian rhythm disorder ($r=.44$), dys-somnia NOS ($r=.42$) and the insomnias related to mental ($r=.57$) and medical ($r=.44$) disorders. Moderate to good inter-rater agreement was also noted for ICSD-2 psychophysiological insomnia ($r=.50$), idiopathic insomnia ($r=.67$), obstructive sleep apnea ($r=.74$), restless leg syndrome ($r=.71$), periodic limb movement disorder ($r=.52$), delayed sleep phase syndrome ($r=.71$), and insomnias related to mental ($r=.57$) and medical ($r=.47$) conditions. Inter-rater agreement was poor (r values < .20) for ICSD-2 paradoxical insomnia and inadequate sleep hygiene.

Conclusion: These initial results suggest that sleep specialists show moderate to good inter-rater agreement for insomnia diagnoses established solely from the DSISD. Additional research is needed to determine if inter-rater agreement rates can be improved by special training techniques or access to additional diagnostic information (e.g., SCID results, sleep log data).

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0764

THE PREVALENCE OF DISTURBED SLEEP AND FATIGUE IN SHIFT WORK - A NATIONAL, REPRESENTATIVE SAMPLE

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Introduction: Very little information is available on the prevalence of sleep disturbances in relation to shift work, particularly pertaining to the diagnostic category "shift work sleep disorder". The present study was an attempt to arrive at a population estimate of disturbed sleep in shift work.

Methods: This study used the biannual work force surveys with questions on shift work added. 8000 subjects were interviewed (response rate 65%) of which 450 had shift work that includes night work. Questions asked about the proportion of night shifts that were associated with disturbed sleep or fatigue, respectively, and how many days off or day shifts that were associated with disturbed sleep or fatigue. In addition we asked to what extent disturbed sleep or fatigue, respectively, constituted

a problem in life. A subject was classified as suffering from disturbed sleep in connection with night work if $\geq 50\%$ of the night shifts were disturbed. The same criterion was used for fatigue and for day work and days off.

Results: 7.7% saw disturbed sleep as a great or rather great problem in their lives. The figure for fatigue was 10.0%. 21% suffered from disturbed sleep, 45% from fatigue and 30% from at least one of the two. When those with problems on $\geq 50\%$ of day shifts or days off were removed the results became 7.4% 9.8% and 13.1%, respectively. When only those with great or rather great problems were included the prevalence in the working population became 0.06%, 0.07% and 0.10%, respectively.

Conclusion: The prevalence of sleep/fatigue problems unique to shift work is small, but is dependent on the criteria used.

0765

STRESS-COPING, SLEEP HYGIENE PRACTICES ARE CORRELATED WITH PRIMARY INSOMNIACS IN A JAPANESE GENERAL POPULATION

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Introduction: Stress copings (SC) and sleep hygiene practices (SHP) are commonly thought to be associated with the vulnerability to primary insomniacs (PI). The purpose of this study is 1) to estimate the prevalence of PI in a Japanese general population, and 2) to determine the correlation between the incidence of PI and either SC or SHP.

Methods: A nationwide general population survey was conducted in June 2000, using a self-administered questionnaire. A population was selected randomly from among 300 communities throughout Japan. We analyzed data from 24,551 individuals aged 20 years or older. The subjects who met the following criteria were defined as PI according to DSM-4 criteria; presence of sleep disturbances, showing more than 3 out of 10 somatic and psychological complaints, and suffering moderate to severe daytime consequences. The subjects are asked to choose stress-copings (12 items) and sleep hygiene practices (5 items).

Results: The prevalence rate of PI in Japanese was 10.6% (male 8.9%, female 12.2%), and PI was most prevalent in their thirties. The multiple logistic regression analyses showed that 6 items of SC and SHP ($P < 0.05$) were positively associated with the incidence of PI and only one item was negatively associated with PI. "Bearing without action" showed the most significant positive association (OR=2.00, {95%CI; 1.75-2.28}) among the six. Other 5 positively associated items are "Smoking" "Venting his/her emotion by talking to others" "Making an effort to solve the problems actively" "Eating something" "Drinking alcoholic beverages". "Try to have regular daily habits" was the negatively associated with the incidence of PI (OR=0.70, {95%CI; 0.63-0.78}).

Conclusion: The present data suggest that some SC and SHP are significantly correlated with the incidence of PI, and provide important information about sleep hygiene attitudes for the Japanese general population.

0766

EFFECTS OF ADIPIPLON ON LATENCY TO PERSISTENT SLEEP (LPS) IN A TRANSIENT INSOMNIA STUDY PREDICTS EFFECTS IN A CHRONIC INSOMNIA PATIENT POPULATION

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Introduction: Adipiplon, an $\alpha 3$ preferring GABAA partial agonist, has been shown to induce rapid onset of sleep and sleep maintenance without unwanted next day effects. Models of insomnia are sometimes used as proof of concept, but the predictability of results from insomnia models for studies with insomniac patients has not been well defined. This analysis compares the results for LPS in a transient insomnia (TI) model and in a study of chronic insomnia (CI) patients.

Methods: A Phase 2a, double-blind, parallel-group trial in 369 healthy volunteers compared 4 doses of adipiplon versus placebo in a TI model using both first night effect and a 2-hour phase advance. A subsequent Phase 2b double-blind, parallel-group study included 2 doses of the same formulation of adipiplon and placebo in 258 CI patients. Mean LPS from the single PSG night in the TI study was compared to mean LPS from the first 2 treatment nights in the CI study.

Results: In the TI model, 1, 3, 10 and 20mg of adipiplon produced an LPS of 17.8 - 6.6 minutes, significantly shorter ($p < 0.0001$ overall) than placebo (30.8 minutes) with relative reductions in LPS compared to placebo of 42% to 79%. In the CI study, a significant reduction in LPS to 16.2 and 13.0 minutes with 3 and 7mg adipiplon ($p < 0.01$ for both) was seen compared to placebo (46.0 minutes); a decrease relative to placebo of 65% and 72%. The dose response in the TI study, in terms of percent decrease from placebo, accurately predicted the LPS reduction from placebo for the 2 doses in the CI study. Adipiplon was generally well tolerated in both studies with headache, dizziness, somnolence/sedation and nausea reported most commonly.

Conclusion: LPS reduction with multiple doses of adipiplon, versus placebo, in a TI study predicted well the relative LPS reduction achieved in CI patients.

Support (optional): Neurogen Corp.

0767

NEW APPROACHES TO INSOMNIA EXPERIENCE MEASUREMENT: STRUCTURED SELF-REPORT ON INSOMNIA

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Introduction: What are the most characteristic types of experience during insomnia nights? Is it cognitive arousal, physiological arousal, worry, negative affect, dream-related awakenings, or other types of experience? We are seeking ways to monitor and record the experiential details of insomnia. We have developed three measurement tools.

Methods: First is Insomnia Experience Monitoring (IEM). IEM collects during-the-night, audio recording samples of the insomnia experience. The self-report samples are recorded with a non-invasive device. Second is the Insomnia Experience Log (IE Log), designed for completion in the morning (along with a sleep diary to collect sleep pattern information). The IE Log can be used to teach people with insomnia about putting into words the types of insomnia experience that they have. The third is the Insomnia Experience Questionnaire (IEQ), a retrospective self-review questionnaire. The IEQ asks the person to identify the types of experience that best characterize his/her history of insomnia nights, from a checklist of 44 types of experience.

Results: A representative sample of 18 long awakenings monitored with the *free-response* IEM procedure showed frequent negative experi-

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ences. In rank order, 97% of oral reports noted “thinking too much,” 71% noted “worrying,” 60% noted “body too aroused,” and 37% noted “negative emotions.” Pilot data for the *forced-choice* IE Log (52 maintenance insomnia nights) showed four experience types as dominant. Dream-related awakenings (32% of the logs rated as the most characteristic experience), physiological arousal (30%), worry (18%), and excessive cognitive activity (16%) were dominant. A 2-group study with the *forced-choice* IEQ showed one significant difference between the 2 groups. Onset insomnia was more often characterized as being related to physiological arousal, and maintenance insomnia was more often characterized as related to worry.

Conclusion: At least 5 experience types appear to characterize insomnia nights: excessive cognitive activity, excessive physiological arousal, worry, negative affect, and dream-related awakenings.

Support (optional): National Institute on Drug Abuse grant DA13574 and National Institute on Aging grant AG14738

0768

IDENTIFYING POTENTIAL COMPLICATING FACTORS IN TREATING INSOMNIA IN VETERANS

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Introduction: Veterans referred for mental health sleep intervention have demonstrated mixed results: Many never show for initial appointment or fail to follow through beyond first session, while those who persist often make marked improvements. The purpose of this study was to identify factors that may potentially interfere with participation and ultimate sleep improvement.

Methods: Participants consisted of 46 veterans (58.7 ± 9.6 years old, range 36-82) from the Southern Arizona VA Health Care System who were referred for behavioral sleep intervention and participated in a group screening appointment. In addition to general background questionnaire, veterans completed the Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI) during the introductory meeting.

Results: Sleep Pattern: Most veterans (n = 39) reported clinical insomnia in the moderate to severe range (46% moderate, 18% severe), and only 4% reported no clinically significant insomnia (n = 2). Average hours slept per night was 4.5 (± 1.3) and sleep efficiency was 57% (± 18%). Co morbidity: Most (85%) veterans were being treated for at least one major mental disorder. 65% suffered from a mood disorder, 54% had PTSD, 24% anxiety disorder, 9% schizophrenia and 4% personality disorder (55% had two or more diagnoses). Virtually all (93%) veterans were being treated for at least one serious health problem. 76% suffered from a cardiac problem, 41% had respiratory complications and 17% had diabetes. In addition, 74% suffered from chronic pain. All but two of the veterans were on some type of medication (average 9.4 ± 4.7) and 57% were currently taking sleep medications.

Conclusion: Results indicate that veterans typically present with a myriad of mental and physical problems for which they are taking multiple medications. This finding suggests that behavioral sleep medicine interventions employed in the VA must be tailored to address both mental and physical disorders.

0769

USE OF NATURAL PRODUCTS AS A SLEEP/HEALTH PROMOTING PRACTICE

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Introduction: Despite a paucity of data on efficacy and safety of natural (herbal and dietary) products, their use appears to be widespread. Insomnia is among the most common conditions treated with such products

marketed as sleep aids. The present study aimed at examining the prevalence of natural products use for sleep and its correlates in a population-based sample.

Methods: A randomly selected sample of adults (n = 997; 59.9% women) from the province of Quebec completed a postal survey on sleep, use of sleep-promoting products (natural products, prescribed medication, over-the-counter medication and alcohol), physical and mental health, lifestyle habits and demographics. Respondents were grouped based on whether they used natural products for sleep either exclusively, used them in combination with other types of sleep aids, or did not use any sleep promoting products.

Results: A total of 18.5% of respondents reported having used natural products as sleep aids in the past 12 months. Of those, 10.3% relied on them exclusively, while 8.2% used them in combination with other types of sleep aids. Natural products users were predominately females (74.5% and 65.4% vs. 57.5%), p<0.001) and had higher education levels (p<0.05). Those who reported exclusive use were younger than the others (mean 38.9 (SD 13.5) vs. 44.2 (SD 14.0) and 43.5 (SD 14.1) years; p<0.05). After controlling for sleep difficulties severity, both groups of natural products users were more involved in health-promoting behaviors (e.g., exercised three or more times/week, non-smoking, lower alcohol intake, BMI < 25) than the non-users group (p<0.05). Furthermore, exclusive use of natural products was associated with a nearly 5-fold increase of self-reporting a good health status (OR=4.9; 95% CI:1.13-21.3).

Conclusion: These results suggest that the use of natural products as a sleep aid is a common practice in the general population. Often associated with a general health-promoting lifestyle, this practice may reflect the common perception that natural products are necessarily beneficial for sleep and without risks due to adverse effects and interactions with other medications and diseases.

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0770

REM SLEEP IN INSOMNIACS WITH SLEEP STATE MISPERCEPTION

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Introduction: Subjects who have Sleep State Misperception (SSM) report being awake if woken during REM cycles that occur during the latter part of the night. Furthermore, REM sleep is experienced differently throughout the night in those with SSM. The current study looks at the possibility that people with SSM may have more REM occurring during the second half of sleep duration than those without SSM (non-SSM). The second objective was to investigate reasons why REM occurring later in the sleep cycle is perceived differently by comparing REM related apnea/hypopnea indices (REM-AHI) between sample groups during the second half of the total sleep time.

Methods: Subjects with self reported insomnia (N=13) spent one night in the lab for a nocturnal polysomnographic study. Each patient was asked to estimate the percentage of the night they felt that they had slept. Subjects were subdivided into SSM (n=9) and non-SSM (n=4) based on the discrepancy between reported amount of sleep and actual sleep time. Groups were compared on the amount of REM, and REM-related AHI occurring during the second half of the polysomnogram.

Results: The percentage of REM sleep occurring during the second half of the night was not significantly different between groups. Similarly, there was not enough evidence to conclude that the REM-AHI during the second half of sleep duration is higher in subjects with SSM compared to non-SSM subjects.

Conclusion: Self-reported insomniacs with SSM do not have a greater percentage of REM sleep during the latter half of their sleep cycle compared to insomniacs without SSM. Furthermore, REM sleep during the

latter part of the night in the SSM individuals is not perceived differently than those in the non-SSM group due to a higher REM-AHI.

0771

CBT FOR INSOMNIA IS ASSOCIATED WITH DECREASED FATIGUE AND DIMINISHED IL-6 LEVELS IN CHRONIC PAIN PATIENTS

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Introduction: Insomnia is a highly prevalent co-morbid disorder in chronic pain (CP) patients, with fatigue a common symptom in both insomnia and CP patients. Circulating levels of the proinflammatory cytokine interleukin-6 (IL-6) have been shown to be elevated in a variety of populations, including insomnia and CP subjects. The current study assesses to what extent fatigue and IL-6 are related in a sample of CP patients with insomnia and whether cognitive behavioral therapy for insomnia (CBT-I) reduces fatigue and/or IL-6 levels.

Methods: Twenty subjects with insomnia and chronic, non-malignant pain originating in the spine were randomized to either CBT-I or control conditions (wait-list control or a CBT for pain control). Groups did not differ with respect to any baseline variables. To date, 16 have completed the study; IL-6 samples have been analyzed for 13 subjects. Among the battery of instruments, subjects completed the Multidimensional Fatigue Inventory (MFI) at pre and post treatment. Blood was drawn between 8-10 am at both time points, frozen at -80 degrees Celcius and enzyme-linked immunoassay subsequently performed in batches to determine circulating IL-6 levels. ANOVAs were performed to assess time by group interactions.

Results: When times and groups were collapsed (n=26), fatigue and IL-6 were found to be positively correlated (Pearson's $r=.41$; $p=.03$). From the pre to post assessments, subjects in the CBT-I group (n=7), compared to controls (n=6), had diminished fatigue ($F=7.3$; $p=.02$) and trended towards decreased levels of IL-6 ($F=3.4$; $p=.09$).

Conclusion: These preliminary results suggest that 1) fatigue is positively associated with IL-6, 2) CBT-I improves the complaint of fatigue, and 3) CBT-I may reverse a marker of diminished immune function. Further work is required to test and establish what, if any, causal chain exists between improved sleep and improved immune function.

Support (optional): F32NS049789; K23NR01048; Rochester Center for Mind-Body Research (1R21AG023956); American Sleep Medicine Foundation

0772

THE EFFECTS OF A TART CHERRY JUICE BEVERAGE ON SLEEP IN OLDER ADULTS WITH INSOMNIA

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Introduction: Anecdotal evidence suggests that a new proprietary tart cherry juice blend made by CherryPharm, Inc. (Geneva, NY) improves sleep in some athletes. Tart cherries contain melatonin as well as polyphenolic compounds shown to act as anti-inflammatories. The current study was designed to assess subjective sleep continuity effects of the proprietary juice in healthy, older adults with insomnia.

Methods: Nineteen subjects with insomnia (Insomnia Severity Index [ISI] >10 and mean 2 wk sleep diary values of sleep latency [SL] and/or wake after sleep onset [WASO] > 30 minutes) who were otherwise medically and psychiatrically healthy were enrolled in a placebo-controlled, double-blind, cross-over trial. Three subjects withdrew and 1

was dropped from analysis due to elevated thyroid function. The final sample had a mean age of 71.6(5.4), a BMI of 25.8(4.6) and 7 of 15 were women. Following intake and 2 wks of sleep diaries, subjects were randomized to receive either (A) 2 wks treatment juice (the proprietary, whole tart cherry juice blend from CherryPharm, Inc.), 2 wks wash-out, and 2 wks placebo (black cherry Kool-Aid mixed with water, clouding and coloring agents, and sucrose) or (B) the reverse order of treatment and placebo juices (each delivered in identical 8 oz. bottles and consumed 2x/day (morning and evening)). Subjects maintained sleep diaries throughout the study and completed self-report instruments following juice and placebo wks. Percent change on the ISI and the diary variables were tested by paired-sample t-tests; changes on validated depression and fatigue scales were similarly assessed.

Results: No order effects were observed. Subjects experienced significant pre-post improvements in SL, WASO, sleep efficiency (SE), total sleep time (TST) and the ISI (all $p<.05$). Compared to placebo, the treatment juice was associated with greater improvements in SL ($p=.047$), WASO ($p=.011$) and the ISI ($p=.062$). SE and TST were not significantly different between juices, though there were modest trends in favor of the treatment juice; depression and fatigue scores were unchanged. Pre-post effect sizes (Cohen's d) for the treatment juice were approximately 0.50.

Conclusion: The results suggest that CherryPharm's tart cherry juice blend has some beneficial effects on sleep in older adults with insomnia. Given that these findings were achieved following a brief treatment period (2 weeks), further study is warranted.

Support (optional): This study was funded by CherryPharm, Inc; WRP receives support from F32NS049789, K23NR01048, Rochester Center for Mind-Body Research (1R21AG023956), American Sleep Medicine Foundation.

0773

THE CLINICAL APPLICATION OF ACTIGRAPHY IN THE SLEEP DISORDERS CLINIC

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Introduction: Actigraphy is a promising alternative to polysomnography to measure sleep parameters over multiple days. Recently published practice parameters for the use of actigraphy in sleep assessment state that actigraphy is useful to evaluate sleep duration and sleep patterns. However, currently actigraphy remains underutilized in the clinical treatment of sleep disorders in adults and children.

Methods: Actigraphy data consisting of at least 7 nights of recording time was analyzed for 15 consecutive patients in our Sleep Disorders Clinic. The results and clinical implications of 3 characteristic cases are described further.

Results: Case 1: A 37 year old woman with obstructive sleep apnea and restless legs syndrome endorsed persistent hypersomnolence despite treatment of both conditions. The patient provided a history of obtaining 8.5-9 hours of sleep per night. Actigraphy data indicated the patient averaged 7.38 hours of sleep at home. Case 2: An 11 year old boy with autism exhibited frequent nighttime awakenings. Actigraphy showed prolonged wake periods during the latter part of the night when the patient's bedtime was earlier than 9 pm. Case 3: A 4 year old girl with parental report of difficulty falling asleep at night. Actigraphy demonstrated average sleep onset latency of approximately 1 hour.

Conclusion: The 3 cases demonstrate common clinical scenarios in which actigraphy aids in treatment. In the first case the patient demonstrated misperception of her total sleep time. Actigraphy demonstrated greater than 1 hour of subjective overestimation of average sleep time per night. The second case indicated the patient had difficulty maintaining sleep throughout the night when he had an earlier bedtime and by delaying his bedtime the patient had marked improvement in his sleep. The third case showed persistent prolonged sleep onset latency despite

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a regular bedtime. Actigraphy helped confirm the parental report of insomnia. Further study with a larger dataset is underway.

0774

POOLED ANALYSIS EXAMINING THE EFFECTS OF RAMELTEON 8 MG ON OBJECTIVE SLEEP LATENCY IN ADULTS WITH CHRONIC INSOMNIA AT NIGHTS 1 AND 2

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Introduction: Ramelteon is an MT1/MT2 melatonin receptor agonist indicated for the treatment of insomnia characterized by difficulty with sleep onset. In several previous clinical studies, ramelteon decreased latency to persistent sleep (LPS) in subjects with chronic insomnia. The current study is a pooled analysis of 4 clinical trials examining the ability of ramelteon 8 mg to reduce objectively measured LPS at Nights 1 and 2.

Methods: The current pooled analysis examined 4 randomized, double-blind, placebo-controlled clinical trials of ramelteon in subjects with chronic insomnia. The analysis included adults (age 18-83 years) with chronic insomnia who took ramelteon 8 mg or placebo. The primary endpoint of each trial was mean LPS, measured by polysomnography (PSG) on Nights 1 and 2.

Results: Subjects who took ramelteon 8 mg (n=566, mean age 46.7 years) or placebo (n=556, mean age 47.8 years) were included in the analysis. Mean LPS at baseline was similar between the 2 groups (66.6 min placebo, 66.9 min ramelteon). Mean LPS at Nights 1 and 2 for the ramelteon 8 mg group (30.2 min) was significantly less than the mean LPS for the placebo group (43.3 min); the difference between the 2 groups was 13.1 minutes (P<0.001).

Conclusion: This pooled analysis demonstrated that ramelteon 8 mg, on average, reduced LPS by approximately 13 minutes compared to placebo on Nights 1 and 2 of treatment in adults with chronic insomnia. The results from this analysis are similar to those that have been reported in analyses of other classes of insomnia medications compared with placebo.

Support (optional): This study was supported by Takeda Pharmaceuticals.

0775

A 6-MONTH POLYSOMNOGRAPHY STUDY OF RAMELTEON 8 MG IN SUBJECTS WITH CHRONIC INSOMNIA: POST-HOC ANALYSIS OF SUBJECTS WITH AT LEAST 50% REDUCTION IN LATENCY TO PERSISTENT SLEEP

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Introduction: Chronic insomnia is a prevalent condition that may require long-term treatment in some patients. Ramelteon is a selective MT1/MT2 melatonin receptor agonist indicated for insomnia treatment characterized by difficulty with sleep onset. This study evaluated long-term efficacy of ramelteon in adults.

Methods: In a 6-month polysomnography study, adults (18-79 years) with chronic insomnia received ramelteon 8mg (n=225) or placebo (n=222) 30 minutes before bedtime every night for 6 months in a randomized, double-blind study. Objective sleep latency was evaluated by polysomnography on the first 2 consecutive nights of Week 1, the last 2 nights of Months 1, 3, 5, and 6, and Week 1 of the 2-week, single-blind, placebo run-out. The impact of study drug on next-day memory and balance, quality of life, adverse effects, and vital signs was also recorded at each office visit. Rebound insomnia and withdrawal effects were evaluated during the placebo run-out. In this analysis, the primary endpoint was the percentage of patients who achieved at least 50% reduction in latency to persistent sleep (LPS) from baseline with ramelteon versus placebo.

Results: A greater percentage of subjects in the ramelteon group than in the placebo group achieved at least 50% reduction in LPS at Week 1 (60.7% vs 39.6%; P<0.001), Month 1 (64.0% vs 51.4%; P=0.005), Month 3 (61.8% vs 51.4%; P=0.009), Month 5 (60.9% vs 51.4%; P=0.017), and Month 6 (61.8% vs 53.2%; P=0.047). No statistically significant next-day residual effects were detected during ramelteon treatment. No withdrawal symptoms or rebound insomnia were detected after discontinuation of ramelteon. Most adverse events were mild or moderate in severity.

Conclusion: In adults with chronic insomnia, the majority experienced ≥50% reduction in LPS throughout long-term (6 months) ramelteon treatment. There were no significant next-day residual effects, and no rebound insomnia or withdrawal symptoms upon discontinuation of ramelteon.

Support (optional): This study was supported by Takeda Pharmaceuticals.

0776

INSOMNIA MEDICATION USE AND THE PROBABILITY OF AN ACCIDENTAL EVENT IN A COMMERCIAL POPULATION

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Introduction: Many of the pharmacological treatments for insomnia have been associated with next-day somnolence, which may lead to an increased risk of accidental events. The purpose of the current study was to examine the risk of accidental events in patients prescribed a sedating antidepressant (SAD), or a benzodiazepine receptor agonist (long-acting benzodiazepine [LAB], short-acting benzodiazepine [SAB], nonbenzodiazepine [nBz]), relative to a selective melatonin receptor agonist (MR).

Methods: Patients with newly initiated pharmacological treatment for insomnia were identified from the Thomson MarketScan® Commercial Claims and Encounter database (January 1, 2000, through June 30, 2006). Accidental events were identified from medical claims using International Classification of Disease 9th revision codes. Probit models were used to evaluate the probability of an accidental event and proportional hazard models were used to evaluate the time to an accidental event.

Results: Patients from a commercial population were included in the analysis (4,132 MR, 175,564 SAD, 344,557 LAB, 127,252 SAB, and 563,298 nBz). After controlling for baseline demographic and clinical characteristics (age, gender, comorbidities, and concomitant medications), the risk of an accidental event during the 60-day period following treatment initiation was greater for patients taking a SAD (OR=1.54), LAB (OR=1.50), SAB (OR=1.53), or nBz (OR=1.51), relative to patients taking a MR (p≤0.05 for all). Adjusted hazard ratios (h) during the 60-day follow-up period indicated there was also less time to an accidental event in these patients compared to those prescribed a MR (SAD [h=4.18; p=0.044], LAB [h=3.53; p=0.075], SAB [h=4.10; p=0.047], nBz [h=3.83; p=0.058]).

Conclusion: In the current analysis, different classes of insomnia medications were associated with varying levels of risk for accidental events. Despite the apparent lower risk of accidental events in the selective melatonin receptor agonist group, no definitive conclusions can be drawn because of the disproportionately smaller number of subjects in this group.

Support (optional): This study was supported by Takeda Pharmaceuticals.

0777

THE COGNITIVE BEHAVIORAL TREATMENT OF INSOMNIA: A CLINICAL CASE SERIES STUDY

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Introduction: There is substantial clinical trial evidence that Cognitive Behavioral Therapy for insomnia (CBT-I) is efficacious. The present analysis provides treatment outcome data for CBT-I as applied in a “real world” setting.

Methods: A chart review of our Insomnia and Behavioral Sleep Medicine Clinic was conducted for patients seen within the last 14 months (1 clinician 20% time). Patients with chronic insomnia were seen weekly or biweekly for 2-8 sessions of CBT-I. Sleep was monitored prospectively using sleep diaries.

Results: 54 patients were evaluated. 4% were not referred for CBT-I, 15% elected not to pursue treatment, 5% were unable to complete sleep diaries, 33% failed to complete > 4 sessions, 4% had concomitant conditions which either interfered with, or required treatment before, CBT-I. 91% of the sample was Euro-American, 42% were female. The average age of “completers” was 50 (+/- 10). The average age of onset was 40 and the average duration of the insomnia was 10 years. 47% of the treatment sample had comorbid mental health diagnoses and 91% had one or more coexisting medical conditions. Baseline data were compared to end of treatment data using paired t-tests. Outcome measures were arrayed in terms of change scores and percent change for SL, WASO, NOA, TST and SE%. All pre-post comparisons for the clinical case series were significant at $p < .05$ except TST. On average, subjects completing therapy were about 60% improved for SL and WASO, corresponding to an average 55% reduction in SL (effect size = 0.92), 64% in reduction in WASO (effect size 1.06), 30% decrease in NOA (effect size 0.42), and 6% increase in TST (effect size = 0.34).

Conclusion: Despite the level of medical and psychiatric morbidity in our clinic sample, the clinical outcomes observed appear comparable in magnitude to the clinical trial’s meta-analytic norms.

0778

THE EFFECTS OF MODAFINIL ON SLEEP CONTINUITY IN SUBJECTS WITH PRIMARY INSOMNIA: A SECOND STUDY

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Introduction: Recently, it was found that 100 mg doses of modafinil, when administered qam, tended to reduce sleep latency in patients with Primary Insomnia (PI). This finding prompted a second study to evaluate whether an alternative regimen with modafinil (bid vs qam dosing) might produce significant independent effects and potentially additive effects for the combination of modafinil and CBT.

Methods: Physically and mentally healthy subjects with PI were randomized to one of four treatment conditions: 1) 100 mg Modafinil + a monitor only condition (M); 2) Placebo + 8 weeks of CBT-I (CBT); 3) 100 mg Modafinil + CBT (M+CBT); 4) Placebo + a monitor only condition (NoTX). Subjects were instructed to take medication twice daily (qam and 2pm). Sleep diary data were acquired daily for the duration of the study.

Results: 18 subjects (13/18 female; mean age 54.4+11.0 yrs) with PI participated in this study. Significant effects were resolved for pre-to-post change within and across all the active treatment groups. Each of the treatments produced significant change from pre-to-post treatment for WASO. Increased SE% was observed for CBT and trends ($p < 0.11$) were evident for the two modafinil groups. Only CBT produced significant changes for NOA. The treatment groups significantly differed for WASO, NOA and SE%. The distribution of the mean data for WASO

and SE% were stepwise where the smallest effects were for NoTX and the largest effects were for combined treatment (CBT+M).

Conclusion: Modafinil, when administered bid at a 100 mg doses, may produce independent effects on sleep continuity and that these effects may augment those obtained with CBT. Given these results, and those of the one prior published study, optimal therapy with modafinil is likely to require tailoring the dose, and time of dose, to the individual.

Support (optional): This work was supported by a grant from Cephalon Inc.

0779

CHRONIC INSOMNIA: COMORBIDITY WITH DEPRESSION

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Introduction: Chronic insomnia typically occurs in association with other clinical conditions. Impairments in health, function, and quality of life are central features of insomnia, and the risk for psychiatric disorders, especially depression, is well known. The main goal of this study is to determine if there are clinical and polysomnographic differences in insomniac patients with and without depression.

Methods: 44 adults aging 21-65 ys, both genders, with chronic insomnia complaints underwent Beck Depression Inventory (BDI) and Polysomnography (PSG) to assess the presence or absence of depression. The patients answered a questionnaire. According to the International Classification of Sleep Disorder (ICSD-2) normal or abnormal PSG the variables were considered: difficulties initiating or maintaining sleep, snoring, obstructive sleep apnea, periodic limb movement disorder, sleep efficiency, sleep latency, REM latency, delta and REM amounts.

Results: Depression was present in 73% of the patients with insomnia. They showed: middle age 42.yrs, female gender 56%, incomplete high school 38%. familial gain until US\$ 250 at month, married 44%, white race 72%, alcohol 28%, drugs 6% and nicotine 19% use, medication 71%, sleep paralysis 28%, sleepwalking 28%, Rem Sleep Behavior Disorder (RBD) 3%, sleep inertia until 15 minutes 41% and nightmares disorders 50%. 93% of chronic insomnia patients with depression had abnormal PSG compared to 92% in the other group. Insomnia without depression showed: middle age 4yrs, male gender 67%, incomplete high school 50%. familial gain above US\$ 500 at month, married 50%, white race 76%, alcohol 18%, drugs and nicotine use 0%, medicine use 75%, sleep paralysis 17%, sleepwalking 8%, RBD 0%, sleep inertia until 15 minutes 58% , nightmares 17%.

Conclusion: Poor social level, alcohol, drugs and nicotine use, impairment in familial context and parasomnias predominate in the depression group. PSG abnormalities suggest the importance of this exam in patients with chronic insomnia complaints.

0780

INITIAL INSOMNIA AS A POTENTIAL PREDICTOR OF DEPRESSION SEVERITY AND SUICIDALITY IN DEPRESSED ADOLESCENT INPATIENTS

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Introduction: In adults, Major Depressive Disorder has been classically associated with terminal insomnia. In pediatric patients, insomnia associated with depression has not been as widely investigated. We report a pilot study investigating the relationship between the timing of insomnia, severity of depression, and suicidality.

Methods: 32 inpatients aged 13-18 who met DSM-IV criteria for Major Depressive Disorder were included in the study. Some exclusion criteria included diagnoses of mental retardation, pervasive developmental disorder, seizure disorder, psychotic disorder, and patients with medical causes of depression. After appropriate consent was obtained, patients

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were evaluated with a structured interview (K-SADS-PL), and completed two inventories: the Beck Depression Inventory and the Suicide Probability Score. Data obtained from the K-SADS-PL were used to classify symptoms of insomnia based on duration of sleep latencies and wakefulness after sleep onset. Records were reviewed and data were abstracted and analyzed using multiple regression, t-test, and Chi Square test. Importantly, K-SADS-PL defined initial insomnia as sleep latency greater than 2 hours.

Results: 40% of 32 inpatients described initial insomnia by K-SADS-PL criteria. After statistical analysis, a significant relationship between initial (but not middle or terminal) insomnia was found to correlate in a univariate fashion with depression severity ($p = 0.005$) and suicide probability ($p = 0.034$). Unexpectedly, a significant correlation between middle insomnia and use of serotonin reuptake inhibitors was found.

Conclusion: This pilot study suggests a pattern of insomnia associated with depression distinct from that described in adult patients, and suggests initial insomnia as a potential predictor of severity of adolescent depression and suicidality. This study is cross-sectional, which limits its ability to predict causality. The sample size is small and therefore, selectivity of the sample may restrict the variance of the measures. Regardless of its findings, further investigation is warranted to elucidate this study's significance.

0781

SLEEP MISPERCEPTIONS AND SLEEP COMPLAINT IN AN ELDERLY POPULATION

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Introduction: Sleep misperceptions (SMs) commonly co-occur with sleep complaints. However, debate continues whether SMs follow a daily or occasional pattern, and whether SMs represent a general pessimistic bias of sleep or relate only to specific sleep variables. The current study investigated misperceptions of sleep onset latency (SOL) and wake after sleep onset (WASO) in complaining and noncomplaining sleepers. We hypothesized: 1.sleep complaint would relate to an occasional pattern of extreme SMs and 2.complaint would not be related to a general pessimistic view of sleep, specifically SOL over-estimates would not necessitate WASO over-estimates and vice versa.

Methods: 103 community-dwelling older adults (Mage=72.81, SD=7.12) wore an Actiwatch-L® (24hrs/day) and concurrently completed sleep diaries for two weeks. Participants were grouped as either complainers or non-complainers based on a yes/no response to, "Are you currently having difficulty with your sleep at night?" Daily values for actigraphically-measured SOL and WASO were subtracted from respective sleep diary estimates to calculate two SOL and two WASO misperception variables: number of days over-estimated and average amount over-estimated.

Results: A 2X4 MANOVA revealed a significant group effect ($F_{4,89}=7.65$, $p<0.001$). Follow-up testing revealed complainers over-estimated WASO more frequently than noncomplainers ($M_{complainers}=3.67\pm 0.74$ days versus $M_{non-complainers}=1.27\pm 0.22$ days; $F_{1,92}=14.85$, $p<0.001$). Frequency of SOL over-estimation did not differ by group (~ 7 days; $F_{1,92}=0.01$, $p=0.94$). Interestingly, on nights that over-estimation occurred, the average amount over-estimated was greater for complainers than noncomplainers for both SOL ($M_{complainers}=22.54\pm 2.74$; $M_{non-complainers}=14.21\pm 1.17$; $F_{1,92}=9.63$, $p<0.01$) and WASO ($M_{complainers}=44.62\pm 10.01$; $M_{non-complainers}=14.48\pm 3.54$; $F_{1,89}=13.13$, $p<0.001$). For both groups, SOL over-estimates did not correlate with WASO over-estimates.

Conclusion: As predicted, over-estimating did not occur daily among complainers; however, on days over-estimating occurred, their estimates were more extreme on average than noncomplainers. The finding that SOL and WASO over-estimates did not correlate supports previous find-

ings suggesting SMs are not a general pessimistic bias but instead relate to specific aspects of sleep.

0782

EFFICACY AND SAFETY OF DOXEPIN 6 MG IN A 4-WEEK OUTPATIENT TRIAL OF ELDERLY ADULTS WITH PRIMARY INSOMNIA

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Introduction: Efficacy and safety of doxepin (DXP), a selective H1 antagonist at the dose studied, was evaluated in elderly adults with sleep maintenance insomnia.

Methods: This was a double-blind, placebo-controlled outpatient trial. Elderly adults meeting DSM-IV-TR criteria for primary insomnia were randomized to 4 weeks of nightly treatment with either DXP 6mg (N=130) or placebo (PBO; N=124). Efficacy was assessed with patient-reports and clinician ratings. Patient-reported endpoints included total sleep time (TST), wake after sleep onset (WASO), latency to sleep onset (LSO), and Patient Global Impression scale (PGI). Primary analysis was Week 1 TST.

Results: DXP 6mg demonstrated significant improvement in TST and WASO at Week 1 (both p-values <0.0001) compared with PBO. These significant improvements were maintained at Weeks 2, 3 and 4 (all p-values <0.05). Though there were no statistically significant changes in LSO, a significantly higher proportion of patients in the DXP 6mg group reported faster sleep onset (based on PGI) at Weeks 2, 3 and 4 (all p-values <0.05; Week 1 $p=0.0564$) compared with PBO. DXP 6mg significantly improved sleep quality (wks 1, 3 and 4, $p<0.05$) and several outcome-related parameters, including the severity and improvement items of the Clinician Global Impression scale (Weeks 1 and 2) and the Insomnia Severity Index (Weeks 1-4), all versus PBO. There was no significant next-day residual sedation and no reports of anticholinergic effects (eg, dry mouth) or memory impairment. Safety profiles were comparable between groups.

Conclusion: In elderly adults with insomnia, DXP 6mg produced significant improvements in sleep maintenance and duration that were sustained through the trial. Though LSO was not significantly improved versus PBO, significantly more patients taking DXP 6mg reported faster sleep onset on the PGI. These data indicate that DXP 6mg is effective and well-tolerated in elderly adults with chronic primary insomnia.

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0783

DOXEPIN 3 AND 6 MG IN A 35-DAY TRIAL OF ADULTS WITH PRIMARY INSOMNIA: EFFECTS FOLLOWING DISCONTINUATION

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Introduction: One of the concerns with hypnotic medication usage is rebound insomnia. This study evaluated the effects of discontinuing doxepin (DXP), a selective H1 antagonist at the doses studied, after 5 weeks of treatment.

Methods: Adults meeting DSM-IV-TR criteria for primary insomnia were randomly assigned to nightly doses of DXP 3mg (N=75), 6mg (N=73) or placebo (PBO; N=73) for 35 days, followed by 2 nights of single-blind placebo (PBO) to evaluate discontinuation (DC) effects. A total of 203 patients (67 PBO, 67 DXP 3mg, 68 DXP 6mg) had discontinuation data. Rebound insomnia was defined as ≥ 35 minute increase in wake after sleep onset (WASO) compared to baseline. Withdrawal symptoms were assessed using the benzodiazepine withdrawal symptom questionnaire (BWSQ) and with spontaneously reported adverse events.

Results: Mean WASO remained improved relative to baseline for DXP 3 and 6 mg on the 1st DC night (PBO=21 minutes; DXP 3mg=18 minutes; DXP 6mg=24 minutes), with sustained improvement on the 2nd DC night. Additionally, the incidence of rebound insomnia was similar across groups. Across the two nights, rebound insomnia was experienced by 1% of the PBO group, 1% of the DXP 3mg group, and 4% of the DXP 6mg group. The mean change in the BWSQ was similar across groups. Approximately 8% of patients in each treatment group experienced an adverse event during the 2 night DC period. There was no evidence of physical dependence, withdrawal syndrome, or worsening insomnia.

Conclusion: As reported previously, administration of DXP 3 and 6mg in adults with chronic primary insomnia resulted in significant and clinically meaningful effects on sleep onset, sleep maintenance, and prevention of early morning awakenings that were sustained across the trial. These sleep improvements were not followed by rebound insomnia or withdrawal effects upon discontinuation of DXP treatment.

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0784

EFFICACY OF DOXEPIN 3 AND 6 MG ON EARLY MORNING AWAKENINGS IN ADULTS WITH PRIMARY INSOMNIA

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Introduction: Chronic insomnia is often accompanied by waking too early and being unable to fall back to sleep. Though it is a core symptom of DSM-IV insomnia, it is seldom addressed in sleep trials. The present analysis examined the impact of doxepin (DXP), a selective H1 antagonist at the doses studied, on parameters associated with this symptom in adults.

Methods: Patients in this randomized, double-blind, placebo-controlled study reported ≥ 3 months of DSM-IV-TR insomnia. Patients were randomly assigned to nightly doses of DXP 3mg (N=75), 6mg (N=73) or placebo (PBO; N=73) for 35 days. Efficacy was evaluated with polysomnography (PSG) over an 8-hr period. Selected endpoints from the first and last timepoints, nights 1 (N1) and 29 (N29), are reported to evaluate early morning awakenings (EMA). PSG endpoints of EMA included wake-time-after-sleep (WTAS), sleep efficiency (SE) in the last quarter-of-the-night (SE-LQN), SE in the last third-of-the-night (SE-LTN), and SE at hour 8. Next-day residual effects were assessed using the Digit Symbol Substitution Test (DSST), the Symbol Copying Test (SCT), and a Visual Analog Scale (VAS) for sleepiness.

Results: On N1, DXP 3 and 6mg significantly improved SE-LQN ($p \leq 0.0008$), SE-LTN ($p \leq 0.0002$), WTAS ($p \leq 0.0030$), and SE at hour 8 ($p < 0.0001$), all compared with PBO. These improvements were sustained at N29, with significance versus PBO maintained for 6mg on SE-LQN, SE-LTN and SE at hour 8. In terms of next-day residual effects, there were no significant group differences in the DSST, SCT, or VAS at any timepoint during the trial.

Conclusion: In adults with chronic insomnia, DXP 3 and 6mg significantly improved PSG parameters associated with early morning awakenings, a prevalent symptom. These improvements were sustained through the final hour of the night with no next-day residual effects. These data suggest that DXP 3 and 6mg are effective at preventing early morning awakenings without causing next-day residual effects.

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0785

CONSISTENCY OF SYMPTOM IMPROVEMENT IN ELDERLY ADULTS WITH CHRONIC INSOMNIA TREATED WITH DOXEPIN 1, 3 AND 6 MG

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Introduction: This report reviews global symptom and severity assessment from trials evaluating doxepin (DXP), a selective H1 antagonist at the doses studied, in elderly adults with insomnia.

Methods: Two randomized, double-blind, placebo-controlled trials of doxepin 1, 3 and 6mg in elderly adults with a DSM-IV-TR definition of primary insomnia were conducted. Study A was a 3-month trial [N=240; DXP 1 and 3mg versus placebo (PBO)]; Study B was a 4-week trial (n=255; DXP 6mg versus PBO). Symptom improvement was assessed with several measures, including the 2-item Clinical Global Impression scale (CGI) and the Insomnia Severity Index (ISI). Selected endpoints are reported corresponding to first (Study A: Day 14; Study B: Day 7) and last assessment points.

Results: DXP 3 (Study A; $p < 0.01$) and 6mg (Study B; $p < 0.05$) significantly improved CGI-Severity and CGI-Improvement versus PBO at the first assessment point. At the end of 3 months in Study A, DXP 1 and 3 mg significantly improved (all p-values ≤ 0.01) both CGI items versus PBO, with insomnia symptoms rated one category less severe by clinicians in both DXP groups compared with PBO. DXP 3 (Study A) and 6mg (Study B) significantly improved ISI scores at the first and last assessment points versus PBO.

Conclusion: In these two trials of elderly adults, DXP 1, 3 and 6mg each produced significant and clinically meaningful improvements in clinician-rated assessments of illness severity and therapeutic effect and in patient-rated assessments of therapeutic effect, beginning as early as one week and lasting as long as 3 months. Both patients and clinicians perceived consistent symptom improvement beyond the traditional analyses of quantitative nighttime sleep patterns. These data suggest that elderly adults taking DXP at doses of 1, 3 and 6mg experienced improvements in both sleep and global treatment outcome that improved across time.

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0786

PSYCHOLOGICAL INFLUENCES ASSOCIATED WITH POOR SLEEP

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Introduction: Although many assume that sleep deprivation drives insomnia complaints, available data indicate those who complain of insomnia are not necessarily poorer sleepers. A dichotomy therefore appears to exist between daytime functioning and the perceived experience of sleep, with those exhibiting more daytime impairment being

Category J—Sleep Disorders – Insomnia

more likely to complain of poor sleep. This suggests four groups warranting assessment: complaining good (CGS) and poor sleepers (CPS), and non-complaining good (NGS) and poor sleepers (NPS). The present study compared sleep and daytime functioning between these groups in a normative sample.

Methods: Random-digit-dialing was used to survey sleep and daytime function for 2-weeks. Sleep was subjectively assessed with diaries. Daytime function measures included: Epworth-Sleepiness-Scale (ESS), Insomnia-Impact-Scale (IIS), Fatigue-Severity-Scale (FSS), Beck-Depression-Inventory (BDI); State-Trait-Anxiety-Inventory (STAI). Subjects (N=734) were classified based on presence/absence of a sleep complaint and on quantitative sleep (poor/good). Poor sleep was defined as sleep latency and/or WASO>30 minutes, occurring >2 nights/week, for at least 6-months.

Results: Prevalence of the two sleep complaint groups increased across age, with >40% of elderly complaining of poor sleep. Multivariate analyses indicated that within their respective sleeping group (CGS versus NGS; CPS versus NPS), people with an insomnia complaint reported significantly worse sleep on virtually all measures ($p<0.05$). Additionally, the two complaint groups had significantly ($p<0.05$) worse daytime impairment in measures of immediate insomnia impact (ESS, IIS, FSS) and mood (BDI, STAI) than those who did not irrespective of how well they slept. These differences were large, with clinically significant daytime function impairments in the two complaint groups.

Conclusion: Overall the data from this random sample indicate that the presence of an insomnia complaint is strongly associated with marked daytime impairment in measures of immediate insomnia impact and mood. These results suggest that the perception of sleeping poorly is more closely associated with daytime impairment than quantitative sleep patterns.

0787

SLEEP LATENCY DATA USING THE NOCTURNAL SLEEP LATENCY PROFILE (NSLP): PROOF OF CONCEPT

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Introduction: The consistency of prolonged sleep latency (SL) in insomnia, within or across nights, and before and after treatment, is incompletely understood. The NSLP was developed to characterize this consistency. It contains 3 nighttime trials of going to sleep, including initial SL, and SL after forced awakenings in sleep cycles 2 and 3. We characterized the NSLP in insomnia and control subjects, before and after treatment.

Methods: Subjects were free of medical, sleep, or psychiatric disorders other than primary insomnia. Four controls (38±12 years, all females) and 11 primary insomnia patients (46±12 years, 9 females) underwent the NSLP on 2 baseline nights to test reliability. Patients underwent repeat NSLP after 3 weeks of open treatment with eszopiclone 3 mg nightly and behavioral therapies for insomnia. Baseline and post-treatment SLs were determined by two methods: first 20-second epoch of stage 1 (ST1) and by stable sleep in stage 2 (SST2). Baseline SLs were correlated across parallel trials within the NSLP in baseline nights. A mixed model tested fixed effects of treatment, trial within the NSLP, and SL scoring method, with each patient being a random effect.

Results: Including all subjects, SLs from the second trial within the NSLP were highly correlated ($r=0.85$, both SL methods) across baseline nights. NSLP trials 1 and 3 were not correlated. High correlations for the second trial persisted with the controls removed ($r=0.96$, ST1 method; $r=0.89$, SST2 method). Mixed effects modeling showed significant effects of trial within the NSLP ($p=0.001$), baseline vs. post-treatment ($p=0.0077$), and SL method ($p=0.0011$).

Conclusion: SL reliability at baseline was strongest not for initial SL, but for SL after a forced awakening. Treatment reduced SL, but had no

differential effect on trials within the NSLP or on different SL definitions. The NSLP may be a new outcome measure for insomnia research.

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0788

INDIVIDUALS WITH PRIMARY INSOMNIA DO NOT DISSIPATE THEIR SLEEP NEED DURING THE NIGHT

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Introduction: Primary insomnia (PI) is the difficulty initiating and/or maintaining sleep, or experiencing non-restorative sleep in the absence of another disorder. Despite the distress over their sleep quality, individuals with PI do not demonstrate significant abnormalities in their overall sleep architecture. However recent studies suggest important differences between individuals with PI and normal sleepers. For example, PI participants had increased beta band frequency, especially at the beginning of the night (1). According to the two-process model, the beginning of the sleep period is associated with high levels of delta activity during non rapid eye movement sleep (NREMS), believed to represent sleep need. Delta power (DP) declines as the night progresses indicating the ‘dissipation’ of sleep need. Differences in the delta and alpha bands have been reported between ‘short-’ and ‘long-sleepers, wherein sustained elevated DP and elevated alpha were found in ‘short-sleepers’ (2). Here we tested whether participants with PI do not dissipate their sleep need during the night, which could explain the experience of non-restorative sleep, and assessed whether they expressed spectral markers similar to ‘short sleepers’.

Methods: 22 participants meeting diagnostic criteria for insomnia and 22 controls slept in the lab for two nights for polysomnography (PSG) testing. PSG data were staged and spectral analysis was performed on NREMS from the first and last hour of the sleep period.

Results: No differences in delta power at the beginning of the night were apparent between control and PI participants, however at the end of the night the PI group did not show a decline in delta power. In addition, PI had higher levels of alpha activity in NREMS at both beginning and end of the night.

Conclusion: Combined these observations suggest that individuals with PI fail to dissipate their sleep need during sleep. Additionally, the high alpha activity may indicate that individuals with PI are ‘short-sleepers’.

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0789

EFFECTIVENESS OF ACUPUNCTURE TREATMENT IN PATIENTS WITH ANXIETY-RELATED INSOMNIA

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Introduction: Acupuncture is an ancient medical procedure used worldwide for the treatment of a number of diseases. Recently, some scientific reports indicate that anxiety symptoms ameliorate after acupuncture treatment. Additionally, anxiety-related insomnia is a frequent sleep disorder. In the present study, we analyzed the effectiveness of acupuncture on anxiety related insomnia.

Methods: Adults complaining of insomnia were recruited at the sleep clinic. Those who fit the criteria for anxiety-related insomnia and have no other illness were selected. Patients (N = 9) were polysomnographically recorded for one night before beginning acupuncture treatment. In addition, a Hamilton scale for anxiety assessment was applied. Needles

were placed in the same location in all the patients; these locations are traditionally related to insomnia and anxiety. Two weekly sessions of 30 minutes were given to all the patients for 5 weeks. After the treatments ended, patients were again polysomnographically recorded and the Hamilton scale was applied once again.

Results: Results showed a significant reduction in anxiety scores ($p < 0.0001$). Concerning sleep parameters, the significant changes observed were: a significant reduction of total time in wakefulness ($p < 0.0012$), an increase in total sleep time ($p < 0.0004$), an increase of sleep efficiency ($p < 0.0011$) and a reduction of sleep onset latency ($p < 0.02$). Additionally, in all cases the patients' subjective perception was a considerable improvement.

Conclusion: The present results are consistent with previous reports about the relaxing effects of acupuncture and suggest that anxiety-related insomnia can be diminished with this treatment.

0790

A MULTIDIMENSIONAL APPROACH TO MEASURING AFFECT AND AROUSAL IN GOOD AND POOR SLEEPERS

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Introduction: Psychological and physiological hyperarousal have been consistently linked to the pathophysiology of insomnia. However, the exact nature of psychological hyperarousal remains unclear. Theories of emotion suggest that affect can be measured along two dimensions: valence and arousal. The aim of this study was to use this multidimensional approach to investigate valence and arousal of emotion in good and poor sleepers.

Methods: 175 undergraduate students (65% female, ages 18-24) completed the Pittsburgh Sleep Quality Index (PSQI) and the Self-Assessment Manikin (SAM), a 9-point Likert scale using cartoon-like manikins as anchors. Participants were asked to complete SAM ratings separately for valence and arousal based on their current (daytime) feelings and their feelings at bedtime the previous night. Good and poor sleepers were classified according to PSQI total score > 5 . One-way ANOVAs were conducted on daytime and bedtime SAM ratings and correlations were conducted between SAM ratings and the PSQI components for good and poor sleepers separately.

Results: Poor sleepers reported significantly greater negative valence and arousal at bedtime ($p < .05$) and greater negative valence during the day ($p = .08$) compared to good sleepers. Among poor sleepers, daytime valence was correlated with the sleep quality component of the PSQI ($r = .35, p < .01$) and bedtime arousal was correlated with the sleep disturbances component of the PSQI ($r = .38, p < .01$). Among good sleepers, bedtime arousal was negatively correlated with the daytime dysfunction component of the PSQI ($r = -.24, p < .05$).

Conclusion: Both valence and arousal appear relevant in distinguishing good and poor sleepers. Among each group, a distinct pattern was found between SAM dimensions and sleep-related symptoms. These findings suggest that a multidimensional approach to measuring affect might provide further insights into the role of hyperarousal in insomnia.

0791

SLEEP DISTURBANCE AND SYMPTOMS DURING AND AFTER CANCER TREATMENT IN WOMEN WITH BREAST CANCER

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Introduction: Sleep disturbance is common among breast cancer patients during and after cancer treatment. It has been found to be associated with depression and fatigue. Also, these combinations of symptoms have been a negative impact on the quality of life. However, few studies

have explored the differences in symptoms (i.e., depression and fatigue) reported by women with breast cancer whether they had sleep disturbance or not at the end of the first cycle of chemotherapy (T1), after the completion of their cancer treatment (T2), and at the 4-6 month follow up study visit after the completion of their cancer treatment (T3).

Methods: Secondary data analysis from a randomized clinical trial. Seventy-four women diagnosed with breast cancer, mean age 49 (SD=9.3), completed Demographic Questionnaire, Symptom Checklist, General Sleep Disturbance Scale(GSDS), Piper Fatigue Scale, CES-Depression Scale, and Quality of Life-CA.

Results: Mean functional status was 87% (0-100, Karnofsky Performance Score) at baseline. 81% earned over \$40,000 /year income, mean education level 16.2 yrs, 65% married, 46% employed, and 76% white. At baseline, 51% (n=38) of women had sleep disturbance (GSDS score > 45). Women who had "sleep disturbance" at baseline had higher mean scores in depression and fatigue than the "no sleep disturbance" group. While the average number of symptoms was higher in women who had "sleep disturbance" at baseline (T1, T2, and T3, only T1 was statistically significantly different ($p < .01$). At each time point, QOL was predominantly explained by depression and fatigue (57%, 76%, and 71% respectively). Sleep group membership did not influence outcome of QOL at each time point.

Conclusion: This study provides support for the presence of sleep problems in breast cancer women at the beginning of cancer treatment. "sleep disturbance" women experienced more depression, fatigue and lower QOL, but these relationships were temporal at each time point.

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0792

DETERMINANTS OF DYSFUNCTIONAL BELIEFS IN INSOMNIA PATIENTS

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Introduction: Previous studies have demonstrated that dysfunctional belief about sleep is a crucial perpetuating factor in patients with chronic insomnia. However, the factors which may relate to insomnia patients' dysfunctional beliefs still lack a comprehensive investigation. The aim of this study is trying to find the determinants of dysfunctional beliefs in insomnia patients and further understand the role of dysfunctional beliefs in the developmental etiology of insomnia.

Methods: 85 insomnia patients receive the diagnostic interview and were inquired their insomnia history. The Insomnia Severity Index (ISI), Dysfunctional Beliefs and Attitudes about Sleep Questionnaire (DBAS), Center for Epidemiological Studies Depression Scale (C.E.S.D), and Beck Anxiety Inventory (BAI) were applied to measure patients' insomnia related phenomena.

Results: Multiple regression analysis show only insomnia severity and are the most robust predictors of sleep related dysfunctional beliefs. The R square is 0.19 ($p = .001$). The coefficient correlation about insomnia severity is 0.93 ($p = 0.01$), and depression is 0.43 ($p = 0.04$). The demographic data, insomnia persist time, and anxiety aren't fit the regression model to predict the degree of dysfunctional beliefs.

Conclusion: Only insomnia severity and depression can predict the sleep related dysfunctional beliefs. It may illustrate the dysfunctional beliefs are developing with insomnia progress and highly related with depress mood. To deal with insomnia patients' dysfunctional beliefs, clinicians should consider patients' insomnia severity and depress mood.

Support (optional): Department of Health, Executive Yuan, ROC

0793

QUANTIFYING EMG ACTIVITY IN REM SLEEP BEHAVIOR DISORDER (RBD): A POLY-EMG STUDY

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Introduction: According to the recently revised ICSD-2 criteria, the diagnosis of RBD requires demonstration of REM sleep without atonia by polysomnography. However, it is unclear which muscle or combination of muscles is most sensitive to detect the excessive REM sleep EMG activity seen in RBD. We aimed to investigate which muscles are most sensitive to detect excessive EMG activity in RBD.

Methods: Seventeen RBD patients (8 idiopathic, 9 symptomatic due to Parkinson disease) were included in this study. They underwent polysomnography including EMG registration of 13 different muscles. Phasic EMG activity in REM sleep was quantified for each muscle separately.

Results: A mean of 1459.6 ± 613.8 3-second REM sleep mini-epochs were scored per patient. Mean percentages of phasic EMG activity were in descending order: mentalis (42 ± 19), flexor digitorum superficialis (29 ± 13), extensor digitorum brevis (23 ± 13), abductor pollicis brevis (22 ± 12), sternocleidomastoid (22 ± 12), deltoid (19 ± 11), biceps brachii (19 ± 12), gastrocnemius (18 ± 9), tibialis anterior (right, 18 ± 13 ; left, 16 ± 10), rectus femoris (left, 11 ± 7 ; right, 9 ± 7), and thoraco-lumbar paraspinal muscles (6 ± 5). Simultaneous recording of the mentalis, flexor digitorum superficialis and extensor digitorum brevis muscles detected 82% of all mini-epochs containing phasic EMG activity. This combination was more sensitive than any other three-muscle combination.

Conclusion: In cases of suspected RBD, polysomnographic studies should include simultaneous phasic EMG evaluation of the mentalis, flexor digitorum superficialis and extensor digitorum brevis muscles.

0794

SLEEP RELATED EATING DISORDER (SRED) IN PSYCHIATRIC GENERAL OUT-PATIENT CLINIC

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Introduction: SRED is a novel disorder characterized by compulsive eating during sleep with an altered level of consciousness. The aim of the study was to estimate the prevalence and associated factors of SRED among psychiatric population.

Methods: A cross-sectional survey was conducted in an University affiliated adult general psychiatric clinic over a 4-week period with a structured sleep questionnaire on including SRED features. Those questionnaire-positive responders and 15% of the negative responders were invited for second phase clinical interviews for confirmation of sleep diagnosis. The detailed demographic characteristics, psychiatric illness, psychotropic medications and medical illness were further obtained via computerised record system for those subjects with recent 1 year attacks.

Results: The 1-year weighted prevalence of SRED was 2.4% in our clinic. They were predominantly female (81.8%), with mean age 41.5 ± 2.3 years, BMI 25.0 ± 4.7 and a mean duration of SRED features 2.4 ± 2.1 year. Majority of the subjects consumed high calories food or carbohydrates and 9% consumed frozen food. Over 80% had a co-morbid diagnosis of NREM sleepwalking. Comparing with the non-SRED group, SRED subjects had more depressive illness (59.1% vs 33.6%, $p < 0.05$) and various sleep disturbances including insomnia, snoring, recurrent nightmares and sleep related hallucination. They were more likely taking polypharmacy (95.5% vs 71.1%, $p < 0.05$), particularly zolpidem in the combination with antidepressants (selective serotonin reuptake in-

hibitors (SSRI) or sedative antidepressants). Among all factors, zolpidem had the strongest odds ratio (OR 20.2, 95% CI 7.8- 52.1, $p < 0.001$). About 15% of those taking regular therapeutic dose of zolpidem developed SRED condition.

Conclusion: SRED in psychiatric population is not uncommon. Its aetiology is complex with interacting effect from sleep disruptions, mental stress and psychotropic medications. Subjects suffering from chronic insomnia and depression, taking chronic, regular therapeutic dosage of zolpidem with combination of antidepressants, particularly sedative antidepressants and SSRI have heightened risk of SRED.

0795

SLEEP-ISOLATED TRICHOTILLOMANIA: CLINICAL CHARACTERISTICS

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Introduction: Trichotillomania is an impulse control disorder that creates an irresistible urge to pull out one's own body hair. It is one cause of unexplained hair loss and affects approximately 1 to 2% of Americans; most are undiagnosed. We previously reported the first sleep-isolated trichotillomania (SITTM) and suggest it may be a new NREM sleep parasomnia. This study aimed to further characterize SITTM and determine its level of recognition by dermatologists.

Methods: 5000 dermatologists practicing in the United States were sent an 11-question survey regarding clinical characteristics of patients they have recognized with SITTM. Responses were anonymous.

Results: Of 285 (5.7%) respondents, 5 (1.8%) described a total of 7 patients (5 female) with SITTM. Average age was 15.2 ± 14 years (5 were \leq age 10). Diagnosis was made clinically (not further described) in 4 (57.1%), by direct observation (son of respondent) in 1 (14.3%), and biopsy in 2 (28.6%). Three treatments were reported: 4 (57.1%) psychiatric referrals, 1 (14.3%) olanzapine 5mg, and 1 (14.3%) head shaving. Only olanzapine and head shaving were followed by known improvement. One patient had obsessive compulsive disorder (OCD) and anxiety, one had OCD, anxiety, and depression, and 1 had depression and had a sibling born in the year prior to symptom onset. Family history of parasomnias was negative in 1 patient, and unknown in 6.

Conclusion: These limited findings suggest SITTM is infrequently diagnosed by dermatologists and probably heterogeneous. Most in this small sample are children and most are female. Three of 7 had psychiatric diagnoses. Dermatologists may consider SITTM more in patients with psychopathology; conversely, psychopathology may increase susceptibility to SITTM. Improvement only in the patients treated with olanzapine and head shaving is too limited to generalize as effective but may be helpful to some clinicians. Further study is needed.

0796

REM SLEEP BEHAVIOR DISORDER IN PARKINSON'S DISEASE: A POLYSOMNOGRAPHIC STUDY OF 77 PATIENTS

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Introduction: It has been suggested that REM sleep behavior disorder (RBD) is frequent in Parkinson's disease (PD), affecting between 15 to 50% of patients. However, this estimate is based on studies with relatively small sample of PD patients or which have used clinical criteria only for the diagnosis of RBD. The aim of the present study was to

evaluate the frequency of RBD using polysomnography (PSG) in a large sample of PD patients.

Methods: Seventy-seven consecutive nondemented PD patients (50 men; mean age, 65.19 ± 9.85 ; mean disease duration, 5.67 ± 3.82 ; mean Hoehn and Yahr stage, 1.98 ± 0.77) were studied in a sleep laboratory for one night. PSG recording included EEG, EOG, chin EMG and infrared video monitoring. We used the International Classification of Sleep Disorders-II criteria for the diagnosis of RBD. The cutoff for excessive tonic or phasic EMG activity during REM sleep was defined as two standard deviations above the mean of 50 healthy age-matched controls (i.e. 29% for tonic EMG activity and 17% for phasic EMG activity).

Results: Forty-two percent of PD patients (32/77; 26 men) showed RBD based on PSG criteria. An additional 16% of PD patients (12/77; 6 men) had excessive tonic or phasic EMG activity during REM sleep without any history of behavioral manifestations during sleep or video-confirmed movements during REM sleep in the laboratory. The proportion of men with PD having RBD (52%) was higher than that of women (22%) [χ^2 test = 5.23; df = 1; $P = 0.02$]. No significant difference was observed on age, disease duration, or disease severity between PD patients with RBD and those without RBD.

Conclusion: This study shows that a large number of PD patients have RBD based on PSG criteria. However, an important subgroup of PD patients did not have RBD and show normal REM sleep muscular atonia. Future studies are warranted to determine if the pattern of neurodegeneration in PD is different depending on the presence or absence of RBD.

Support (optional): Fonds de la Recherche en Santé du Québec and Canadian Institutes of Health Research.

0797

MILD COGNITIVE IMPAIRMENT IN PARKINSON'S DISEASE WITH REM SLEEP BEHAVIOR DISORDER

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Introduction: Parkinson's disease (PD) is often associated with dementia or mild cognitive impairment (MCI). It has been reported that PD patients with REM sleep behavior disorder (RBD) show poorer performance on neuropsychological tests measuring executive functions, memory and visuospatial abilities. The aim of the present study was to investigate whether MCI is associated with RBD in PD.

Methods: Thirty-nine PD patients without dementia or depression (23 with polysomnography-confirmed RBD and 16 without RBD) and 25 healthy controls underwent a comprehensive neuropsychological assessment. Cognitive tests measuring executive functions and attention (letter and semantic fluency tests, Trail Making test part B, Stroop color word test, Digit span), memory (Rey auditory verbal learning test, immediate and delayed recall of the Rey complex figure), and visuospatial abilities (copy of the Rey complex figure, Block design subtest from the WAIS-III, Bells test) were administered. We compared the performance of all participants with valid normative data and we used the criteria and subtype classifications (i.e. amnesic, single nonmemory domain, or multiple domains slightly impaired) for MCI in PD described elsewhere (Janvin *et al.* Movement Disorders 2006).

Results: No between-group difference was observed for age or educational level. The two PD subgroups did not differ on PD clinical variables. Of the 23 PD patients with RBD, eight were cognitively intact, whereas 15 (65%) were diagnosed with MCI [amnesic, n = 2; single nonmemory domain, n = 7; multiple domains slightly impaired, n = 6].

All PD patients without RBD were cognitively intact while one of the control subjects had amnesic MCI. The proportion of PD patients with RBD having MCI was higher than that of PD patients without RBD (χ^2 test = 14.31; df = 1; $P = 0.0002$) and that of control subjects (χ^2 test = 17.54; df = 1; $P = 0.0001$).

Conclusion: This study shows that MCI in PD is strongly associated with the presence of RBD. Since studies have shown that MCI is associated with the development of subsequent dementia in PD, this may suggest that PD patients with RBD are at elevated risk of developing dementia. Long-term follow-up of PD patients with and without RBD is needed to verify whether RBD is a risk factor for the development of dementia in PD.

Support (optional): Fonds de la Recherche en Santé du Québec and Canadian Institutes of Health Research.

0798

REM SLEEP BEHAVIOR DISORDER IN PATIENTS WITH NARCOLEPSY

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Introduction: REM sleep behavior disorder (RBD) has been described in narcolepsy but there is insufficient information regarding the frequency and characteristics of this association. The aim of our study was to describe the frequency and characteristics of RBD in narcolepsy.

Methods: One hundred and eight consecutive patients with narcolepsy (73 male, 35 female; 74% with cataplexy) diagnosed in our center and studied with nocturnal polysomnography (PSG) were included. Patients treated with antidepressants and those without bed partner were excluded. Patients and their partners were systematically asked about the presence of vivid/aggressive dreams, vigorous movements or vocalizations during sleep. The presence of at least two of these symptoms was considered suggestive of RBD. We classified EMG activity during REM sleep -in chin and left and right tibialis anterior muscles- as normal or excessive. Clinical characteristics of narcolepsy were correlated with symptoms of RBD.

Results: Symptoms suggestive of RBD were reported by 61/108 (56.4%) of the patients, most of them (57/61) with cataplexy. EMG activity during REM sleep was considered excessive in 47/108 (43.5%) patients, in most (41/47) with reported RBD symptoms. Twenty out of 61 (33%) patients with symptoms suggestive of RBD had normal EMG activity in REM sleep in the PSG, whereas 6/47 (13%) with no RBD symptoms had abnormal EMG activity. Patients with excessive EMG activity during REM sleep had more often cataplexy than those without (92% vs. 60.6% respectively; $p = 0.0002$). Males and females had similar frequency of RBD. RBD intensity was mild in 71% of the patients although in most cases (52%) appeared several times per week.

Conclusion: RBD is common in narcolepsy, particularly in patients with cataplexy, and has no male predominance. A significant number (33%) of narcoleptic patients with symptoms suggestive of RBD have normal EMG activity during REM sleep.

0799

FLOURINE-18 FLUORODEOXYGLUCOSE (18F-FDG) POSITRON EMISSION TOMOGRAPHY (PET) IN A PATIENT WITH ZOLPIDEM TARTRATE INDUCED SOMNAMBULISM, SLEEP-EATING, AND SLEEP-DRIVING: ON AND OFF MEDICATION

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Introduction: We are aware of no previous 18F-FDG-PET studies of zolpidem induced parasomnias. Zolpidem is a hypnotic which acts at the GABA(A) receptor and is indicated for short-term insomnia. Sleep re-

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lated disorders including somnambulism, sleep-eating and sleep-driving have been reported with zolpidem. A 51 year old insomniac who used zolpidem 10 mg nightly since 2003 is described. A few weeks after starting zolpidem she began walking, eating, and had one episode of driving while asleep.

Methods: An 18F-FDG-PET was obtained a month after discontinuation of zolpidem. The following day FDG was administered one hour after the oral administration of zolpidem and then a second PET was performed.

Results: Episodes of sleep-eating, sleepwalking and sleep-talking occurred 3 nights/week, 1 to 2 hours after sleep onset. Sleep-talking: the patient would speak unintelligibly with her eyes closed and would then open her eyes when questioned by her husband. Sleep-eating: the patient would leave her bedroom to go to her kitchen where she would eat a loaf of bread, cold cereal, or left-overs. The following morning she would have abdominal fullness, find her kitchen messy and have complete amnesia. The patient would also leave her home. (As a preventive measure she installed alarms on her front doors to wake her from sleep if she opened it overnight.) Sleep-driving: the patient drove approximately 10 miles from her home and was found on the road-side behind the wheel asleep. After her evaluation the patient was titrated off of zolpidem, and all sleep related activities immediately ceased.

Conclusion: Pre- and post-zolpidem 18F-FDG-PET images will be presented with accompanying statistical parametric analysis of cortical and subcortical areas.

0800

CASE SERIES OF REM SLEEP BEHAVIORAL DISORDER (RSBD)-LIKE DISORDER IN PSYCHIATRIC OUT-PATIENT CLINIC

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Introduction: RSBD-like features have been associated with psychotropic usage and our clinical epidemiological study reported a 1-year prevalence of RSBD-like disorder of 3.8% in psychiatric out-patient setting (Lam et al submitted). The present study further characterised the clinical and polysomnographic (PSG) features of these subjects having RSBD-like disorder.

Methods: Thirty subjects with RSBD-like disorder were diagnosed. The demographic data, clinical features, psychotropic usage and PSG features were analyzed.

Results: This series consisted of slightly more female, 56.7% (17/30); mean age 40.2 ± 9.7 years; mean duration of illnesses 3.6 ± 6.4 years (range, 0.25- 30 years). About 46% (N=14) sustained moderate to severe degree of sleep related injury. None of them suffered from any neurodegenerative disorders. Nearly two third of the subjects had depressive spectrum disorder (63.3%), followed by anxiety spectrum disorder (20%). Sleep disturbances were common: frequent insomnia (60%), recurrent nightmares (60%) and sleep paralysis (36.7%). All subjects were taking psychotropic medication and majority (86.7%) was given antidepressants particularly selective serotonin reuptake inhibitor (70%). PSG were completed in 13 subjects (43.3%) and 84.6% (11/13) had PSG features suggestive of RSBD. Four out of 11 subjects also suffered from obstructive sleep apnea (OSAS) but their RSBD features persisted after usage of CPAP. One subject reported cataplexy-like symptom and her MSLT revealed shortened MSL and 3 SOREMPs. Regarding the remaining two subjects with no PSG evidences of RSBD, one had substance abuse of zopiclone with clinical features suggestive of both NREM and REM parasomnia, and his PSG revealed moderate OSAS and mild PLMS.

Conclusion: RSBD-like disorder in psychiatric population did exist and was co-morbid with other sleep disturbances. Depression and use of antidepressants particularly SSRI appeared to be risk factors. Further study will be needed to determine whether this RSBD-like disorder will

share similar pathophysiology and neuropsychiatric outcome with typical RSBD.

0801

RAPID EYE MOVEMENT SLEEP WITHOUT ATONIA (RWA) IN PATIENTS ON SEROTONERGIC ANTIDEPRESSANTS (SA)

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Introduction: REM sleep Without Atonia (RWA) defined as the loss of muscle atonia during REM sleep, may precede the onset of REM sleep behavior disorder (RBD). Serotonergic antidepressants (SA) use has been shown to be associated with RWA. It is not known if the degree of RWA is a predictor of RBD, and if it is related to the length of SA exposure. We hypothesize that SA exposure length is an important predictor of the degree of RWA.

Methods: Retrospective chart review of veteran male subjects aged 40-60 who had polysomnography between 2001 and 2006 for evaluation of sleep-related breathing disorder was performed. Exclusion criteria included less than twenty minutes of REM, severe medical or neurological disease, alcohol, clonazepam, neuroleptic, or anticonvulsant use. Subjects were divided into those taking SA (exposure range=1-123 months) and those without exposure. Fluoxetine equivalents were calculated for all SA doses. Polysomnography was scored for the presence of RWA (tonic and phasic) using previously published criteria. Scorers were blinded to subject group and inter-rater reliability was performed ($r > 0.9$).

Results: Twelve subjects taking SA and twelve age and comorbidities-matched individuals (except for mood disorders) were identified. Tonic, but not phasic, submental EMG activity during REM sleep was significantly more common in the SA group than in the control group ($11.79\% \pm 12.04$ vs. $0.63\% \pm 0.76$, $p = 0.004$). The correlation between the degree of tonic submental EMG activity and the length of exposure to SA was not significant ($r = 0.35$, $p = 0.27$). There was no significant correlation between the SA dose and the degree of RWA ($r = 0.22$, $p = 0.49$).

Conclusion: Previous findings of a relationship between SA use and RWA were replicated. Although no significant correlation was found between SA exposure length and degree of RWA, review of the scatter plot suggests that a significant correlation may be observed with a larger sample size. No correlation was found between the SA dose and the degree of RWA. Future studies should control for the presence of depression.

0802

TREATMENT OF CATATHRENIA WITH CONTINUOUS POSITIVE AIRWAY PRESSURE

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Introduction: Cases of catathrenia characterized by monotonous irregular groans during sleep have been reported several times since De Roeck and Van Hoof reported it first in 1983. However, treatments of catathrenia were reported very recently and limited for only women who made groaning sounds at all stages of sleep during the entire night. We present three cases of catathrenia patients treated with continuous positive airway pressure (CPAP). They include two men and are all producing expiratory groaning mainly during rapid eye movement (REM) sleep. Catathrenia was defined as a parasomnia in the International Classification of Sleep Disorders Diagnostic and Coding Manual (ICSD-2).

Methods: From November 2005 to October 2007, 8 patients with nocturnal groaning visited or were referred to our sleep clinic for the evaluation of the disorder. Patients underwent physical examination, neurologic and otorhinolaryngologic exams, questionnaires, and a full-night 18-channel digital video-polysomnographic evaluation. Among 8

catathrenia patients, three patients underwent a second video-PSG where CPAP was manually titrated to the minimum pressure required to eliminate groaning, sleep apneic events, and oxyhemoglobin desaturations.

Results: The patients were 22 or 23 years old and with body mass index (BMI) of less than 21. They produced expiratory groans mainly during REM sleep in the second part of the night. They also had other sleep symptoms such as mild snoring, mouth breathing, or bruxism. All had a normal RDI, but one woman had an oxygen desaturation nadir of 86%. The titrated CPAP for one man and one woman was 6 cm H₂O, and for the other man was 7 cm H₂O. With the use of CPAP, the groaning and other sleep symptoms were disappeared and oxygen saturation was improved.

Conclusion: Our report presented that catathrenia was treated with CPAP in men as in women. It supports the previous opinions that catathrenia should be included in the sleep-related breathing disorders rather than parasomnias.

0803

ELECTROENCEPHALOGRAPHIC ABNORMALITIES IN PATIENTS WITH PARASOMNIA

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Introduction: The diagnosis of parasomnia is made clinically. There is no definite test for positive confirmation, though PSG can be helpful to rule out causes of arousal, and added video-EEG monitoring can rule out seizures as a cause. We report EEG abnormalities noted in patients with NREM parasomnia.

Methods: We analyzed polysomnograms from patients referred for full montage video EEG + PSG for evaluation of abnormal nocturnal behaviors, recorded between 10/1/2005 and 3/1/2007, evaluating demographics, indications, and results, including any unusual EEG features. Data were recorded on a Nihon-Kohden system. Automatic spike-seizure detection utilized the Persyst software, in addition to visual inspection.

Results: Of 102 patients tested, 28 had known epilepsy, and 74 had either unusual nocturnal behaviors (n=30), or unusual daytime symptoms (with a sleep disorder versus sub-clinical seizures considered in the differential diagnosis). Among the patients with unusual nocturnal behaviors, three patients had abnormally shaped k-complexes, with a spike on top of the rising line of the complex. The sharply contoured wave was asymmetric or unilateral, with maximal negativity in the left or right temporal or frontocentral region. There were no associated nocturnal clinical changes seen on the video recording, and none of the patients had a confirmed diagnosis of epilepsy. In these four patients, clinical history was strongly suggestive of parasomnia. In one, the sleepwalking was time-linked to treatment with Zolpidem, and promptly resolved after the medication was stopped.

Conclusion: Abnormally shaped k-complexes have been originally described in patients with generalized epilepsy, and later, in focal epilepsies. These abnormal complexes were believed to reflect arousal abnormalities. It is possible that an abnormal arousal patterns may have lead to abnormal k-complexes among patients with NREM parasomnia as well.

0804

CATATHRENIA: A NORTH AMERICAN EXPERIENCE

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Introduction: Descriptions of catathrenia (sleep-related expiratory groaning) are few and mostly originate from European sources. Only some report a good response to CPAP therapy. We undertook a study at our center to evaluate the characteristic features of catathrenia and response to CPAP treatment.

Methods: Retrospective study of patients with a final diagnosis of catathrenia who had an overnight polysomnogram with synchronized audio at our center between January 2000 and October 2007.

Results: The age of patients at time of diagnosis in our 11 patients (6 M: 5 F) was 47.9 ± 15.1 years (mean±SD). Median BMI was 30.7 kg/m². 36% of patients presented with the chief complaint of expiratory noises during sleep while the remaining presented with fatigue, snoring, stridor and possible sleep disordered breathing. ESS was 7.6 ± 4.5 (mean±SD). Number of catathrenia events among patients during polysomnography varied from 2 to 175 episodes with event duration ranging from 0.5 to 27.3 seconds. Only 43% of the catathrenia episodes were two seconds or longer. 48% of the episodes occurred in stage N2, 26% in R, 23 in N1, and 3% in N3. Eight of the 11 patients (72.7%) had associated OSA (defined by an AHI > 5), and were treated with CPAP during polysomnography. Five had no catathrenia episodes on CPAP and 3 had a significant decrease in the number of episodes (78.5±39.5% decrease, p<0.001).

Conclusion: Unlike previous case reports and series, the diagnosis of catathrenia was made in middle aged adults rather than younger patients, and occurred in all stages of sleep, though most commonly in stage N2 than stage R. Although most patients had episodes lasting more than 2 seconds in accordance with the ICSD-2 description, more than half the catathrenia episodes were less than 2 seconds. CPAP was effective in reducing the episodes in almost all patients with OSA.

0805

ATYPICAL DREAM-ENACTING BEHAVIORS IN REM SLEEP BEHAVIOR DISORDER (RBD), INVOLVING ABUSE-RETALIATION DREAMS, CULTURE-SPECIFIC DREAMS, AND RELIGION-SPECIFIC DREAMS

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Introduction: RBD usually features enactment of altered dreams of fighting with unfamiliar people/animals, or of culture-specific sports dreams.

Methods: Records at 3 sleep centers from 3 different countries were reviewed for examples of atypical dream-enacting behaviors in PSG-documented RBD.

Results: 5 examples from 3 categories: A) Abuse/retaliation dreams (related to prior verbal-physical abuse-USA); B) Culture-specific dream (Japan); C) Religion-specific dream (Taiwan). A) i) A 43 y.o. female with narcolepsy-cataplexy (& bipolar disorder), on 110/day methylphenidate, developed RBD when imipramine was increased to 225 mg/day; her husband often observed defensive posturing, arm flailing, and punching that corresponded to dreams of her mother/sister berating her & hitting her during childhood. ii) A 43 y.o. man with monosymptomatic narcolepsy (& alcohol abuse in remission; major depression controlled with 300 mg hs clomipramine) developed RBD with "fighting dreams"(observed by his wife) involving hitting back at his previously verbally/physically abusive alcoholic father. iii) A 58 y.o. married man (without psychopathology) developed idiopathic RBD & dream-enactments involving "punching out" a hypercritical father during his childhood; prior to RBD he had no retaliation dreams. B) A 51 y.o. Japanese man (without neurologic/ psychiatric d/o), in a home sleep video recording had an episode from 2:43:58-2:45:59 a.m. in which he enacted a Samurai warrior dream that culminated with grabbing an imaginary sword & stabbing 12 times in rapid succession. Prior to the culmination, moments of hypotonia

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(slumping forward) occurred during the sequence. C) A 26 y.o. Taiwanese man with a 10 yr history of narcolepsy/cataplexy (& no psychopathology) had 5 PSG-MSLTs over 10 years, with the latest PSG (age 26 yrs) first-documenting RBD (while taking modafinil, methylphenidate, imipramine, trazodone). The pt. & mother reported that he was a devote Taoist; 3 times daily he enacted at home the “eight-general (wikipedia)” special Taoist religion temple worship ceremony lasting 4 min, 40 sec; during his latest PSG, in REM sleep he faithfully enacted this temple worship in bed, with sitting up, kneeling & fully bowing down, immobile, with sustained muscle tone.

Conclusion: Narcolepsy/cataplexy(& Rx) and/or past abuse/psychopathology may be predisposing factors for atypical dream-enactment in RBD, along with intense religious devotion. Further search for atypical dream-enactment in RBD, including across cultures, is encouraged.

0806

STRUCTURAL LESIONS ASSOCIATED WITH REM SLEEP BEHAVIOR DISORDER

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Introduction: Rapid eye movement (REM) sleep behavior disorder (RBD) is frequently associated with the synucleinopathies Parkinson’s disease, multiple system atrophy, and dementia with Lewy bodies. Patients with “idiopathic” RBD often develop dementia or parkinsonism in the future. Infrequently acute onset RBD occurs with drug intoxication or withdrawal, or anatomic lesions involving the brainstem. The site of the structural lesion in RBD is not well known and very few cases have been reported where a causal relationship between anatomical lesion and onset of RBD is suggested.

Methods: IRB approved retrospective review of medical records and brain imaging studies of patients diagnosed with RBD at the Mayo Clinic Center for Sleep Medicine since 1986.

Results: Five patients (2 women/ 3 men; mean age at RBD diagnosis 64.4 years, mean age at RBD onset 63 years) had RBD and intra- or parapontine lesions resulting in compression and/ or distortion of dorsolateral pontine structures: one dorsal pontine tegmentum demyelinating lesion during an acute multiple sclerosis exacerbation, two cerebello-pontine angle meningiomas, one petrous ridge meningioma, one large fusiform basilar artery aneurysm. Four patients had no symptoms or signs of dementia or parkinsonism. Cognitive dysfunction and bradykinesia in one patient improved after petrous ridge meningioma resection and shunting of obstructive hydrocephalus caused by the tumor. Resolution of the demyelinating plaque and resection of the meningioma led to resolution of RBD in two patients; all other patients were treated with bedroom safety measures, clonazepam, melatonin, and/or pramipexole with variable symptomatic improvement.

Conclusion: The findings suggest that structural lesions involving the dorsolateral pons can result in RBD. We suggest that patients, especially women, with acute onset RBD or chronic RBD unassociated with dementia or parkinsonism be carefully assessed for other neurologic symptoms and signs and an MRI of the brain performed if there is suspicion of a structural lesion.

0807

POLYSOMNOGRAPHIC CORRELATES OF RESTLESS LEGS SYNDROME IN THE SLEEP HEART HEALTH STUDY

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Introduction: Sleep disturbance is the primary clinical morbidity of RLS, and is also thought to mediate other important secondary features of the disorder. Nevertheless, there are no reports of the polysomnographic correlates of RLS from population-based samples.

Methods: This is a cross-sectional observational study of 1271 men and 1550 women (mean age of 67.4 years) enrolled in the Sleep Heart Health Study, a community-based study of the cardiovascular consequences of sleep-disordered breathing. RLS was defined by positive responses on a self-administered questionnaire to the four IRLSSG diagnostic criteria, with symptoms occurring at least five times per month and associated with at least moderate distress. Unattended, in-home polysomnography for sleep stage (by EEG, EOG and EMG), and sleep-disordered breathing (by impedance plethysmography, pulse oximetry, airflow and oral-nasal thermistor), but not leg movements, was performed on the night of a home visit. Data were assessed using general linear models with adjustment for age, sex, race, BMI, presence of cardiovascular disease (CVD), administration of medications for diabetes mellitus (DM), and respiratory disturbance index (RDI).

Results: Subjects with RLS had longer sleep latency (40.7 vs 26.8 min, $p < .0001$), lower sleep efficiency (74.1 vs 76.8, $p = .01$), and higher arousal index (19.8 vs 17.6, $p = .008$) than those without RLS (adjusted means from regression models). Sleep latency and arousal index were progressively abnormal as the frequency of RLS symptoms increased from 5-15 times per month to 6-7 times per week. No differences in sleep stage percentages were observed between those with and without RLS. There was a trend for those with RLS to have a lower probability of having an RDI >15 than those without RLS.

Conclusion: This first polysomnographic data from a non-clinical, community-based sample of individuals with RLS documents sleep disturbance in the home even in individuals with intermittent symptoms.

Support (optional): Study supported by National Heart Lung and Blood Institute.

0808

INITIAL MANAGEMENT OF RLS AUGMENTATION WITH ROTIGOTINE PATCH

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Introduction: The rotigotine patch (rotigP) provides 24-hour dopaminergic therapy for RLS, perhaps offering advantage for management of RLS augmentation. 12 patients with severe RLS augmentation on shorter-acting dopaminergic (sDA) therapy were switched to rotigP and followed for efficacy, safety, and adverse events.

Methods: 2006 European standards of the IRLSSG defined RLS augmentation. All patients had 4-hour shift in initial presentation; 8 had upper body symptoms. RotigP was initiated at 2 mg/24 hours and increased q5-7d to effect or arbitrary maximum of 6 mg/24. sDA, principally pramipexole, was concurrently tapered q5-7d. 6 patients also taking opioids tapered q5-7d after sDA discontinuation. IRLS was compared pre-rotigP administration and at study end. Descriptive statistics are offered on patient experience.

Results: 12 patients (7F:5M, mean age: 59.1 yrs [ranges in brackets: 45-73]) had RLS for 24 years [6-55]. sDA (10 on pramipexole@1.375 mg/d [0.375-3.5] and 2 on ropinirole@2.75 mg/d [2.5-3]) administered for 60.9 months [16-115]. Augmentation on sDA was severe based

on dosing frequency of 3.3qd [1-6] and patient-estimated first symptom at 11:30 a.m. [06:00-15:00]. Six patients also received supplemental opioids for a mean of 58.3 months [8-132]. 9/12 continued on rotigP, 3/12 discontinued (reasons: 1/12 for efficacy, 2/12 for efficacy/AEs; 2/6 on opioids). IRLS for all patients dropped from 20.1 [12-32] to 10.9 [0-28] on rotigP utilized for 2.72 months [0.6-5] at 4.33 mg/24 [3@2mg, 4@4mg, 5@6mg]. AEs included site reaction (3), patch slippage (2), achiness (2), anxiety (2), nausea (1), EDS (1).

Conclusion: Rotigotine patch, at least over 3 months, improved RLS augmentation in 75% of 12 patients. Preliminarily, ratio of milligram dosing appears to be 4:1 for rotigP:pramipexole. Dosing >6mg/24 may be needed. Augmenting patients on supplemental opioids may respond less to rotigP. Efficacy assessment at 1+ year is needed.

0809

EFFECT OF ACUTE AND CHRONIC PHYSICAL EXERCISE ON PATIENTS WITH PERIODIC LEG MOVEMENTS

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Introduction: Non-pharmacological interventions may be suitable for improving sleep quality. The objective of our study was to evaluate the effects of two types of physical exercise (acute intensive and chronic) on sleep pattern in periodic leg movements (PLM) patients.

Methods: The study involved two types of physical exercise. The acute intensive exercise group consisted of 22 volunteers who underwent a Maximum Effort Test and a PSG on the following night. The chronic exercise group included 11 patients who performed 72 physical training sessions undergoing 3 PSG studies on the night of sessions 1, 36 and 72. Blood samples were collected from both acute and chronic groups for β -endorphin dosage.

Results: Our results showed that both forms of physical exercise lowered the levels of PLM, as for the results related to sleep pattern the acute physical exercise increased Sleep Efficiency, REM sleep and reduced Wake after Sleep Onset, already the chronic physical exercise increased Sleep Efficiency, REM sleep and reduced Sleep Latency. We also found a significant negative correlation between β -endorphin release after acute intensive exercise and PLM levels ($r = -0.63$).

Conclusion: The physical exercise may improve sleep pattern and reduce PLM levels, possibly associated to the way in which physical exercise acts on the opioidergic system. We suggest that the physical exercise may be useful non-pharmacological treatment for PLM.

Support (optional): Psychopharmacological Research Support Foundation (AFIP) and the FAPESP (03/06297-3, and CEPID 98/143033).

0810

REGULATION OF NEURONAL DOPAMINE RECEPTOR SIGNALING BY IRON CHELATION

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Introduction: Restless Leg Syndrome (RLS) is associated with diminished brain iron concentrations and with altered dopaminergic function, though the connection between the two is unclear. The current study was designed to examine the effects of cellular iron insufficiency on D2 receptor expression and signaling.

Methods: A human neuroblastoma cell line (SH-SY5Y) carrying the long form of the human dopamine D2 receptor (D2L) was used to study the effect of cellular iron concentration on dopaminergic signaling in vitro. The iron chelator deferoxamine (DFO) was used to decrease iron availability. Adenosine deaminase (ADA) was used to minimize inter-

Category L—Sleep Disorders – Movement Disorders

ference by the endogenous adenosine system. Prior to stimulation, the cells were serum-starved and treated with ADA in the presence or absence of DFO. Unstimulated cells were used to determine D2L receptor expression. Cells treated with the D2-selective agonist quinpirole were used to assess extracellular signal-regulated kinase (ERK) activity. Cells pre-treated with various doses of quinpirole were then treated with forskolin to measure the inhibition of cyclic adenosine monophosphate (cAMP) accumulation. D2L receptor and ERK were evaluated with immunoblots, while cAMP was evaluated with enzyme-linked immunosorbent assays.

Results: Acute DFO treatment resulted in decreases in D2L receptor expression and a concomitant attenuation of quinpirole-induced ERK activation as well as attenuated inhibition of intracellular cAMP accumulation.

Conclusion: It seems that maintenance of iron is responsible for sustaining neuronal sensitivity to dopaminergic stimuli. Iron insufficiency decreases D2L receptor expression, which, in turn, leads to attenuated dopaminergic signaling.

Support (optional): Work supported by NIH grant PO1-AG21190 and IRP NIDA funds.

0811

IRON DEFICIENCY IN RATS RESULTS IN FUNCTIONAL UP-REGULATION OF ADENOSINE A2A RECEPTORS AND FUNCTIONAL DOWN-REGULATION OF ADENOSINE A1 RECEPTORS

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Introduction: Restless Leg Syndrome (RLS) is associated with diminished brain iron concentrations and with altered dopaminergic function, though the connection between the two is unclear. One possible mechanism is the involvement of adenosine, in view of the well-established adenosine-dopamine receptor-receptor interactions in the brain. In fact, a recent study found an increased expression of striatal A2A receptor (A2AR) in iron-deficient mice. In the present work we analyzed the changes in central adenosine A1 receptor (A1R) and A2AR expression and function in rats with iron deficiency.

Methods: The expression of transferrin receptor, A2AR and A1R in different brain areas was analyzed by Western blotting in Sprague-Dawley rats treated with iron deficient diet and in controls. The same two groups of animals were studied for their ability to show locomotor activation with the administration of a selective A2AR antagonist (MSX-3), and A1R antagonist (CPT) and the non-selective adenosine receptor antagonist caffeine.

Results: Iron deprivation resulted in an increased expression of A2AR in the striatum and cortex, but not the mesencephalon. On the other hand a significant decrease in the expression of A1R was demonstrated in the cortex of iron-deprived rats compared to controls. The striatal and mesencephalic expression of A1R remains to be analyzed. Moreover, a functional up-regulation of A2AR and a functional down-regulation of A1R were indicated by MSX-3 and CPT being more and less efficient, respectively, at inducing locomotor activation in iron-deprived rats. No similar significant differences in locomotion were obtained with caffeine.

Conclusion: Brain iron deprivation in rats causes a functional up-regulation of A2AR and down-regulation of the A1R. This suggests an abnormal adenosinergic system in individuals with RLS and its associated brain iron insufficiency.

Support (optional): Work supported by NIH grant PO1-AG211 and IRP/NIDA funds.

0812

ENDOGENOUS OPIOID LEVELS ARE DECREASED IN THALAMUS OF RESTLESS LEGS SYNDROME PATIENTS COMPARED TO CONTROLS: A POST-MORTEM STUDY

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Introduction: Opioids are an effective treatment for the signs and symptoms of RLS. When the opioid receptor blocker naloxone is given to opioid treated RLS patients in a blinded fashion, there is a qualitative and quantitative return of the sensory and motor signs and symptoms of RLS. Opioid receptor PET scans show binding of ligand that is inversely proportional to the severity of RLS symptoms in areas serving the medial pain system including thalamus. These data suggest altered central processing of sensory information in RLS patients and implicate the endogenous opioid system with its enkephalins and endorphins in the sensory and motor aspects of RLS. We therefore compared Beta endorphin, Met-enkephalin and Leu-enkephalin levels in thalamus and Substantia Nigra of RLS patients compared to controls.

Methods: 5 adult patients who met ICSD criteria for RLS and 5 controls without neurological disease and with the same age distribution were studied. The brains were harvested at autopsy. One half of each brain was fixed in paraformaldehyde (PFA) in phosphate buffered saline (PBS) for pathologic evaluation. Paraffin sections were stained with antibodies for Beta-endorphin (1:500, Chemicon, Temecula, CA, rabbit, polyclonal), Met-enkephalin (5ug/ml, Dako, Chemicon, Temecula, CA, rabbit, polyclonal), and Leu-enkephalin (1:500, Chemicon, Temecula, CA, rabbit, polyclonal).

Results: In thalamus, there were reductions of Beta-endorphin and Met-enkephalin positive cells by 37.5% (p = .006) and 26.4% (p = .028), respectively, in RLS patients compared to controls. There was no difference in Leu-enkephalin in thalamus. In Substantia Nigra, there were no differences in Beta endorphin, Met-enkephalin, and Leu-enkephalin.

Conclusion: These results suggest that there may be impaired central processing of pain in Restless Legs Syndrome and these data further implicate the endogenous opioid system with its enkephalins and endorphins in the pathogenesis of RLS.

0813

TRANSDERMAL LISURIDE IN PATIENTS WITH SEVERE RESTLESS LEGS SYNDROME: RESULTS FROM A PLACEBO- AND ROPINIROLE-CONTROLLED, DOUBLE-BLIND, RANDOMIZED, MULTICENTER, 12-WEEK EFFICACY AND TOLERABILITY STUDY

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Introduction: The 8 α -Ergoline Lisuride is a potent dopamine agonist approved for oral treatment of Parkinson's disease (PD). Due to its high receptor affinity and short plasma half-life it can also be used parenterally, e.g. as a transdermal patch (Transdermal Therapeutic System, TTS), and thus might be ideal when it comes to compare short- and long-acting dopaminergic effects on RLS symptoms. We describe the first head-to-head comparison of the transdermal patch Lisuride (LIS) compared to oral Ropinirole (ROP) and placebo (PLA) in the treatment of severely and chronically disabled RLS patients.

Methods: This was a multicenter, randomized, double-blind, placebo-controlled flexible-dose study with 12-week treatment in three treatment arms (LIS TTS patches: 10, 20, 30 cm² every other morning, ROP 0.25 to 3 mg / day, matching placebos).

Results: 309 patients (73% females, age 58 years) were randomized (LIS: 152, ROP:78, PLA: 79). The average dosages were 2.3 mg/day

for ropinirole and 0.25 mg/24h for lisuride. Lisuride was superior to placebo with regard to change from baseline to last assessment in the IRLS total score (baseline adjusted LS-means difference: $d=-7.5$, $p<0.0001$). There was a strong tendency towards superior efficacy of lisuride over ropinirole ($d=2.6$, $p=0.076$, 95% CI: -5.9 ; $+0.7$). Ropinirole was superior to placebo ($d=-4.9$, $p=0.003$). Responder rates (50% improvement between baseline and endpoint) were higher under LIS (56.1%) than under PLA (26.0%, $p<0.001$) and ROP (41.3%, $p=0.047$), but statistically not different between ROP and PLA ($p=0.195$). The three treatments differed in frequency of drug-related adverse events (AEs): local skin reactions (LIS, ROP, PLA: 24.3%, 5.1%, 2.5%), gastrointestinal symptoms (27.0%, 46.1%, 19.0%), fatigue (11.2%, 17.9%, 8.9%), and headache (6.6%, 14.1%, 12.7%).

Conclusion: In this first active- and placebo-controlled trial in RLS research, transdermal lisuride was very efficacious in a flexible dosage regimen compared to placebo in the treatment of moderate to severe RLS. More patients had a clinically relevant benefit from lisuride therapy than from ropinirole which was highly effective in this trial. Local skin reactions at the application site are associated with the patch treatment but systemic side effects known from oral dopaminergic treatment are less frequent. It is concluded that continuous dopaminergic stimulation is an efficacious and well tolerated treatment option for moderate to severely disabled RLS patients.

Support (optional): The clinical trial was sponsored by Axxonis Pharma, Berlin, Germany

0814

ADULT RLS PATIENTS SHOW LOWER SERUM FERRITIN OCCURS WITH EARLIER AGE-OF-ONSET OF RLS SYMPTOMS INDICATING RLS MAY IMPAIR THE NORMAL AGE-RELATED INCREASE IN BRAIN IRON

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Introduction: Recent genetic studies showed a strong relation between serum ferritin and one of the introns associated with RLS. Serum ferritin also shows a weak but significant relation to CSF ferritin and CSF ferritin of adults correlates with age-of-onset of RLS with lower ferritin for earlier onset. It was therefore hypothesized that serum ferritin in RLS patients should similarly relate to age-of-onset of RLS.

Methods: In our large family history study we obtained serum ferritin and history of RLS on family members of RLS patients and matched control probands. Diagnosis and history was obtained from the validated Hopkins Telephone Diagnostic Interview. Serum ferritin relates to gender and age. The analyses, therefore, used a step-wise multiple regression with independent factors or age, gender, and age-of-onset.

Results: Data were available from 64 family members all but 6 were from families with RLS. Serum ferritin related most significantly to age-of-onset (F to remove 17.0) and then gender (F to remove 10.3) but not to age (F to enter 3.7). Multiple correlation was 0.552 (F =13.4, $df=2,63$). Serum ferritin correlated significantly with age-of-onset without considering other factors ($r=0.43$, $p=0.0004$). Removing ferritin > 200 mcg/l as probably phase then the relationship with age-of-onset improves somewhat ($r=0.44$). The correlation is also significant for only females ($r=0.47$, $p=0.004$) and only males ($r=0.48$, $p=0.02$). Removing the 6 subjects who came from families of control probands did not alter these results. Duration of RLS disease did not account for age-of-onset effect.

Conclusion: Lower serum ferritin in adult RLS patients indicates an RLS disease process that expresses itself earlier in life. Similar results were observed for CSF ferritin in other RLS patients. RLS may impair the normal brain iron increase with age reaching a critical level at earlier ages and lower adult levels with more severe impairment.

Support (optional): This project was supported in part by NIH grants PO1-AG21190 and R01-NS38704.

0815

A DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE ESCALATION STUDY OF THE PHARMACOKINETICS OF ORAL XP13512 IN HEALTHY ADULTS

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Introduction: XP13512 is a novel prodrug of gabapentin that provides improved absorption and dose-proportional exposure via high-capacity nutrient transporters in the intestinal tract. This study assessed the single-dose pharmacokinetics of oral XP13512 compared with placebo in healthy adults.

Methods: XP069 was a double-blind, placebo-controlled, escalating-dose, crossover study of XP13512 in healthy adults. Thirty-two individuals were randomly assigned to receive XP13512 followed by placebo, or placebo followed by XP13512, with a one-week washout period between treatments (XP13512 doses: 2400 mg, 3600 mg, 4800 mg, and 6000 mg taken after a meal, $n=8$ per dosing cohort). Adverse events (AEs), electrocardiograms, and laboratory parameters were evaluated. Blood samples were obtained predose through 36 hours post-dose and were analyzed by LC-MS/MS. Concentration data for XP13512 and gabapentin were analyzed by noncompartmental methods.

Results: XP13512 was well-absorbed and converted rapidly to gabapentin. Gabapentin exposure was proportional to each XP13512 dose: C_{max} = 11.4, 16.2, 22.7, and 28.9 $\mu\text{g/mL}$; $AUC_{(0-inf)}$ = 118, 175, 254, and 322 $\mu\text{g}\cdot\text{hr/mL}$; T_{max} = 6.9, 7.5, 6.6, and 8.6 hr, at 2400, 3600, 4800, and 6000 mg XP13512, respectively. Levels of the intact XP13512 were low and transient. Dizziness (50.0%), nausea (25.0%) and somnolence (15.6%) were the most frequently reported AEs during treatment with XP13512 (>15% of subjects for all doses); somnolence was evident at the 4800 and 6000 mg doses. There were no electrocardiogram abnormalities or serious AEs; no individuals withdrew due to an AE.

Conclusion: XP13512 provided dose-proportional exposure to gabapentin in healthy adults up to the 6000 mg dose. Levels of the intact prodrug were low and transient at all doses.

Support (optional): XenoPort, Inc., Santa Clara, CA, USA

0816

EFFECT OF FOOD ON THE CLINICAL PHARMACOKINETICS OF XP13512 IN HEALTHY VOLUNTEERS

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Introduction: XP13512 is a pharmacologically advanced, non-dopaminergic treatment under investigation for treatment of Restless Legs Syndrome (RLS). XP13512 is absorbed throughout the intestinal tract by high-capacity nutrient transporters and provides dose-proportional gabapentin exposure. We examined the effect of food on the pharmacokinetics of XP13512 in healthy adults.

Methods: Twelve subjects received single 1200 mg (2 x 600 mg tablets) doses of XP13512 in an open-label, randomized, crossover study (XP087) design with four meal types: fasted, low fat (~6% fat calories, 200-300 kcal), moderate fat (~30% fat calories, 500-600 kcal), and high fat (~50% fat calories, 1000 kcal), with at least 5 days of washout between treatments. Plasma and urine samples were obtained pre-dose and over 36 hours post-dose and analyzed using LC-MS/MS. Concentration data for gabapentin were analyzed by noncompartmental methods. The area under the plasma concentration-time curve ($AUC_{(0-t)}$) and the peak plasma concentration of gabapentin was used to assess bioavailability. Adverse events (AEs), electrocardiograms, and laboratory parameters were evaluated.

Category L—Sleep Disorders – Movement Disorders

Results: Mean bioavailability of gabapentin, the cleaved product of XP13512, was 42% (fasted), 64% (low fat), 65% (moderate fat), and 76% (high fat). The time to maximum gabapentin concentrations in plasma was approximately 5 hours for fasted and low-fat meals and 7 hours for moderate- and high-fat meals. XP13512 was well-tolerated. AEs were mild in intensity; dizziness, balance disorder and somnolence were the most common AEs (>20% of subjects). No serious AEs or AEs leading to discontinuation were reported.

Conclusion: XP13512 administration with food enhances gabapentin exposure compared with fasted conditions; a low fat meal of 200-300 calories, containing 6% fat, increases bioavailability by 22% compared with fasted conditions.

Support (optional): XenoPort, Inc., Santa Clara, CA

0817

XP13512 REDUCES RESTLESS LEGS SYNDROME SYMPTOMS AND ASSOCIATED SLEEP IMPAIRMENT: RESULTS OF A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY

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Introduction: XP13512 is a pharmacologically advanced, non-dopaminergic treatment under investigation for treatment of Restless Legs Syndrome (RLS). We evaluated RLS symptoms and sleep impairment in adults with primary RLS treated with XP13512 compared with placebo.

Methods: XP052 was a 12-week, multicenter, double-blind, placebo-controlled trial. Patients were randomized 1:1 to receive XP13512 (n=112) 1200 mg or placebo (n=108), taken at 17:00 with food. RLS symptoms were assessed using International Restless Legs Scale (IRLS) total score and proportion of responders on the Clinical Global Impression - Improvement (CGI-I) Scale (co-primary endpoints). Sleep impairment was assessed using Medical Outcomes Study (MOS) Sleep Scale Sleep Disturbance, Adequacy and Quantity domains, and daytime somnolence by MOS Daytime Somnolence domain and Epworth Sleepiness Scale (ESS) (secondary endpoints).

Results: At Week 12 LOCF, the mean [SD] change from baseline in IRLS total score was significantly greater for XP13512 (-13.2[9.21]) compared with placebo (-8.8[8.63]) (mean treatment difference [MTD] -4.5, 95% CI: -6.9, -2.1). An ANCOVA, adjusted for baseline and pooled site, demonstrated an MTD of -4.0 (95% CI: -6.2, -1.9; p=0.0003). Significantly more patients treated with XP13512 (76.1%) were classified as “much improved” or “very much improved” (CGI-I), compared with placebo (38.9%) (adjusted odds ratio: 5.1, 95% CI: 2.8, 9.2; p<0.0001). XP13512 significantly improved measures of sleep impairment severity (Disturbance, Adequacy and Quantity; p<0.01) at Week 12 LOCF and decreased daytime somnolence compared with placebo (Week 12 LOCF MOS Daytime Somnolence [p=0.0018]; Week 12 ESS mean [SD], XP13512 vs. placebo: 6.1[4.7] vs. 7.0[4.6]). The most commonly reported adverse events (>10% of patients reporting; XP13512 vs. placebo) were somnolence (any): 27% vs. 7%, and dizziness: 20% vs. 5%. All events were transient and graded mild or moderate in intensity.

Conclusion: XP13512 significantly reduced RLS symptoms compared with placebo and is associated with significant improvements in sleep measures and decreased daytime somnolence.

Support (optional): XenoPort Inc, Santa Clara, California, USA.

0818

CLINICAL PHARMACOKINETICS OF XP13512: A SUMMARY OF FOUR HEALTHY VOLUNTEER STUDIES

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Introduction: XP13512 is a novel prodrug of gabapentin, which exhibits improved absorption and dose-proportional gabapentin exposure via high-capacity nutrient transporters in the intestinal tract. These studies compared the pharmacokinetics of XP13512 with gabapentin (Neurontin[®], hereafter comparator) and placebo, in healthy adults.

Methods: Four studies of immediate release (IR) or sustained release (SR) XP13512 were conducted. XP006: single doses of IR_XP13512 (350, 700, 1400, 2100 and 2800 mg) or approximately equimolar comparator (200, 400, 800, 1200 and 2100 mg) versus placebo. XP018: multiple doses of IR_XP13512 (350, 400, 800, 1200 and 1400 mg b.i.d) versus placebo. XP022: a randomized, open-label, crossover study of 1200 mg SR_XP13512 (fed/fasted) versus 600 mg comparator (fasted). XP044: a crossover study of SR_XP13512 (300, 600 and 1200 mg) in fasted and fed states. Blood and urine samples were collected at baseline and throughout 36 hours post-dose. Drug concentrations were analyzed by LC-MS/MS. Adverse events (AEs), electrocardiograms, and laboratory parameters were evaluated.

Results: Gabapentin exposure from IR_XP13512 was dose-proportional; bioavailability was >68% for all doses (182-1458 mg-equivalents gabapentin) compared with 65% (200 mg) to 27% (1400 mg) for comparator. SR_XP13512 provided 37% (fasted) and 52% (fed) greater gabapentin exposure than comparator (mean AUC_(0-inf) = 54.5 and 83.0 vs. 39.7 µg*hr/mL; mean C_{max} = 4.2 and 6.4 vs. 3.7 µg/mL, SR_XP13512 fasted and fed vs. comparator respectively). Bioavailability of gabapentin from SR_XP13512 was 27% (fasted) and >60% (fed) greater than comparator. Sustained delivery of gabapentin was observed (mean T_{max} = 4.9, 5.0 and 4.7 hr [fasted] and 9.83, 7.27 and 7.92 hr [fed] at 300, 600 and 1200 mg, respectively) with SR_XP13512 administration. The most common AEs (reported by >15% of patients) were nausea, dizziness, somnolence, and headache. No drug-related serious AEs were reported.

Conclusion: XP13512 provides predictable and sustained, dose-proportional gabapentin exposure with increased absorption.

Support (optional): XenoPort, Inc., Santa Clara, CA, USA.

0819

THE IMPACT OF SLEEP LOSS IN U.S. INDIVIDUALS WITH RESTLESS LEGS SYNDROME

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Introduction: Significant sleep disturbance is the primary complaint in about 2/3 of people with Restless Legs Syndrome (RLS); severe symptoms produce one of the most profound chronic sleep losses observed among chronic medical conditions. This study assessed the relationship between RLS symptoms and self-reported sleep disturbance and their impact on health and work among subjects with RLS in the U.S.

Methods: An online survey was completed by 205 subjects with RLS, as identified by scores on the validated 9-item RLS Short Form Diagnostic Questionnaire (RLS-SFDQ9). Subjects completed seven questions on outcomes resulting from RLS symptoms related to poor sleep: increased colds/sickness, mood, personal injury, and driving accidents. Item psychometric properties were evaluated using exploratory factor analysis and Cronbach's alpha, and responses were compared across individuals with mild, moderate, severe or very severe RLS symptoms (International Restless Legs Scale (IRLS) total score: 0-10 [11.7% subjects], 11-20 [41.5%], 21-30 [38.5%] and >31 [8.3%], respectively).

Results: Overall, 31% of subjects indicated severe/very severe sleep disturbance and 35.1% indicated moderate sleep disturbance due to RLS,

measured using the IRLS. Of all subjects, 31.2% reported over-reacting emotionally to routine work activities, 26.2% reported making simple mistakes at work, and 15.6% reported poor decision-making. Comparing themselves to others, 7.8% of subjects reported frequent onset of colds/other illnesses, 18.1% reported injuring themselves often, 52% reported occasionally driving when sleepy, 9% reported frequently driving when sleepy, and 15.3% reported a driving accident. Psychometric evaluations identified the negative-work-consequences (NWC) domain, comprising three items assessing agitation, simple mistakes, and poor decision-making at work. RLS severity was positively associated with NWC ($r=0.52$; $p<0.001$; $n=122$), overall productivity loss ($r=0.54$; $p<0.001$; $n=98$) and sleep disturbance severity ($r=0.81$; $p<0.001$, $n=205$).

Conclusion: Many subjects with RLS report not only sleep disturbance, but negative health and work consequences that are positively correlated with RLS symptom severity.

Support (optional): GlaxoSmithKline Pharmaceuticals Inc., Research Triangle Park, USA.

0820

THE IMPACT OF RESTLESS LEGS SYNDROME IN THE WORKPLACE

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Introduction: Restless Legs Syndrome (RLS) may impact an individual's work productivity either through the associated chronic sleep loss or through limits on the individual's ability to remain still and attentive during sedentary aspects of work.

Methods: An online consumer panel survey was completed by 205 subjects with RLS, as identified by scores on the validated 9-item RLS Short Form Diagnostic Questionnaire (RLS-SFDQ9). Subjects completed the International Restless Legs Scale (IRLS), including a sleep disturbance question, and Work Productivity and Activity Impairment Questionnaire modified for Restless Leg Syndrome (WPAI:RLS), whose domains include time lost from work (absenteeism), reduced on-the-job effectiveness, overall work productivity loss and social activity impairment. WPAI:RLS domain scores were compared across individuals with mild, moderate, severe or very severe RLS symptoms (IRLS total score: 0-10 [11.7% subjects], 11-20 [41.5%], 21-30 [38.5%] and >31 [8.3%], respectively).

Results: Subjects with RLS were 49.1 (11.4) (mean [SD]) years old; 87.8% were female and 99% Caucasian; 50.2% of individuals were employed and 14.6% worked as volunteers. Among the employed, mean (SD) work time missed directly attributed to RLS was 0.6 (2.3) hours over two weeks (1.1% absenteeism), on-the-job effectiveness was reduced by 13.5% and work productivity loss was 14.1% (equivalent to 5.64 hours lost per 40-hour work week). Productivity losses were significantly associated with disease severity ($r=0.54$; $p<0.0001$): no loss was reported among individuals with mild symptoms (0%), while individuals with moderate (7.4%), severe (20.1%), or very severe symptoms (57.8%) reported increasing levels of lost productivity. The negative impact on overall work productivity was positively associated with severity of sleep disturbance ($r=0.38$; $p<0.0001$). RLS had a significant negative impact on voluntary work productivity. For all subjects, impairment in ability to perform daily activities was 24.7%.

Conclusion: RLS has a significant negative impact on sleep and work productivity. Productivity loss increases with disease severity.

Support (optional): GlaxoSmithKline Pharmaceuticals Inc., Research Triangle Park, NC, USA.

0821

MORPHOLOGICAL DIFFERENCES BETWEEN PLM, APNEA, AND BASIC AUTONOMIC ACTIVATION EVENTS IN THE CHANNELS RECORDED BY THE WATCH-PAT DEVICE

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Introduction: The Watch PAT (WP100) is an ambulatory device validated for the diagnosis of obstructive sleep apnea (OSA), monitoring changes in autonomic activation. One of the potential criticisms of using it instead of polysomnography may be the lack of tibialis-anterior recording to quantify periodic leg movements (PLM). As PLM was shown to affect autonomic activation during sleep, we hypothesized that it performs differently than apneas and spontaneous changes in autonomic tone in the signals recorded by the WP100 (actigraphy, PAT, pulse rate). **Methods:** 22 OSA suspected patients (21 M), aged 51+/- 11 with BMI 31+/- 6 underwent full night standard PSG recording in the sleep lab with simultaneous WP100 recording. Mean PSG scoring of AHI was 15±14 and PLM index 17.8 ±22. The related changes in signals recorded by the WP100 were quantified. The data was then compared between apneas, PLMs and spontaneous autonomic events which are defined by PAT amplitude decrease coupled with increased pulse rate. Those changes in PLM and apnea events were normalized by the mean value of the changes in spontaneous events for each patient.

Results: PAT Amplitude Reduction :1.21 SE 0.048 1.44 SE 0.067* 1 SE 0.027* Increase in heart rate:1.47 SE0.053 1.604 SE0.073* 1 SE 0.029*, Time Difference Between Peak pulse Rate and Peak PAT Amplitude:2.4 SE 0.17 Sec -0.15 SE 0.22 Sec * -1.23 SE 0.06 * Sec. Actigraph Normalized Energy (a measure of the amount of movement):2.035 SE 0.39 1.764 SE0.54 1 SE0.22*, Time Between Max PAT Amplitude And Movement: 4± SE 0.30 Sec 6 SE 0.39 Sec* 4 SE 0.102 Sec, All values are for PLM apnea and spontaneous respectively. (* stands for significance $P<0.05$ compared to PLM). SE is the mean Standard Error provided by Matlab Multcompare (ANOVA).

Conclusion: Utilizing indirect physiological signals such as general movement (actigraphy), pulse rate and neuro-vascular signal (PAT), we found that apnea and spontaneous autonomic activation are morphologically different from PLM. The autonomic system reacts in a hierarchic way to apnea, PLM events and spontaneous modulation.

Support (optional): Itamar Medical Ltd. Cesarea, Israel; 2Sleep Lab, Rambam Medical Center, Technion, Haifa, Israel.

0822

ABNORMAL SUBCLINICAL EMG ACTIVATION OF THE GASTROCNEMII MUSCLES DURING GAIT IN RESTLESS LEGS SYNDROME

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Introduction: The objective of this study was to detect the eventual presence of a minor voluntary motor involvement in Restless Legs Syndrome (RLS), not detectable clinically, which might be observed by means of a sophisticated instrumental analysis of movement, such as gait analysis.

Methods: Gait analysis was performed and surface EMG activity was recorded from 8 muscles: tibialis anterior, gastrocnemius lateralis, gastrocnemius medialis, and soleus of both legs of 13 RLS patients and 8 normal controls.

Results: Ten out of the 13 RLS patients and none of the normal control group showed a mild abnormality of the EMG activation of the gastrocnemius muscles during gait which, however, had no detectable effects on its kinematics.

Category L—Sleep Disorders – Movement Disorders

Conclusion: These results might be interpreted as the effect of an impaired supraspinal dopaminergic control with possible action on spinal structures involved in the control of gait. This mild EMG abnormality might constitute an additional supportive feature for the diagnosis of RLS in difficult cases.

0823

PREVALENCE, COMORBIDITY AND RELATIONSHIP TO MENOPAUSE: RESTLESS LEGS SYNDROME AMONG WOMEN IN THE GENERAL POPULATION

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Introduction: RLS has a female preponderance and the prevalence increases with age. During the menopausal transition, several biological functions, including sleep, are affected. Declining estrogen secretion may lead to changes in brain neurotransmitters and instability in hypothalamic centers. Prior studies have discussed the possibility that female hormones can play a role in the clinical manifestation of RLS. Given the female preponderance for the syndrome and the sleep disturbances experienced by women during the menopausal transition, more information on RLS and its association to ovarian steroids and menopause are mandated. The aim of the present study was to estimate the prevalence of RLS in Swedish women, associated symptoms and comorbidities, in particular vasomotor symptoms, menopause and use of hormone replacement therapy (HRT) among those women who suffer from RLS.

Methods: A random sample of 5000 women between the ages of 18-64 years was selected from the general Swedish population. They were sent diagnostic questions on RLS, general health, sleep problems, reproductive health and menopausal state.

Results: Response rate was 70.3%. 15.7% were diagnosed as having RLS. The prevalence increased with age. RLS-subjects were more affected by symptoms of affected sleep and depressed mood. Comorbidity with heart disease was more common, whereas hypertension and diabetes mellitus were not more frequently encountered. There was a strong significant relationship between vasomotor symptom and RLS (OR 2.0) but no elevated odds for RLS among hormone therapy users were seen.

Conclusion: There is a strong association between vasomotor symptoms and RLS. However, when hormonal substitution was present, there was no elevated odds for RLS. This emphasizes the need to evaluate hormone therapy as a possible treatment for RLS in postmenopausal women suffering from vasomotor symptoms.

0824

EFFECTS OF PRAMIPEXOLE ON SLEEP AS MEASURED BY THE MEDICAL OUTCOMES STUDY (MOS) SLEEP SCALE DIMENSIONS OTHER THAN SLEEP DISTURBANCE IN PATIENTS WITH RESTLESS LEGS SYNDROME

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Introduction: Symptoms of restless legs syndrome (RLS) are worst at night and interfere with sleep in most patients with moderate or severe disease. Pramipexole is a D3/D2 dopamine agonist with proven efficacy for the primary symptoms of RLS. Our objective was to test the ability of pramipexole to improve various aspects of sleep, in addition to sleep disturbance (reported elsewhere), in RLS patients using a multidimensional sleep scale.

Methods: In this 12-week, double-blind study, adults with moderate to severe RLS were randomized to receive pramipexole once a day (flexibly titrated from 0.125-0.75 mg) or placebo. Changes in dimensions of sleep were measured using the Medical Outcomes Study (MOS) Sleep Scale at baseline and after 4 and 12 weeks of treatment.

Results: At baseline, median MOS scores in the placebo (n=178) versus pramipexole (n=177) group were 35.0 versus 30.0 for sleep adequacy, 6.0 versus 6.0 (hours) for sleep quantity, and 26.7 versus 26.7 for somnolence, respectively. After 12 weeks, median change from baseline was greater for pramipexole (20.0, 0.3, and -13.3) than for placebo (10.0, 0.0, -6.7) for adequacy, quantity, and somnolence scores, respectively. Significance over placebo was achieved for adequacy (P=.0008), with a trend towards significance demonstrated for quantity (P=.0795) after 12 weeks. Significant improvements over placebo were also noted at week 4 for sleep adequacy (P=.0002) and sleep quantity (P=.0099). Reduction in somnolence did not reach significance (P=.1101).

Conclusion: A truly effective RLS treatment must be able to improve sleep, in addition to the core symptoms of RLS. In this study, pramipexole was significantly superior to placebo in the sleep adequacy dimension of the MOS Sleep Scale after 4 and 12 weeks of treatment. In addition, pramipexole showed a trend toward improvement in MOS sleep quantity and was numerically superior to placebo in somnolence.

Support (optional): Supported by Boehringer Ingelheim GmbH

0825

ONCE-DAILY PRAMIPEXOLE RAPIDLY IMPROVES DAYTIME SLEEPINESS RELATED TO RESTLESS LEGS SYNDROME

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Introduction: Restless legs syndrome (RLS) is a sensorimotor disorder with a circadian variation in symptomatology. Symptoms are worst at night, resulting in sleep disturbances. Sometimes, daytime sleepiness occurs as an indirect effect and can impair daytime function, reduce quality of life, and increase risk for mood disorders.

Methods: Adults with moderate/severe RLS participated in a 12-week, randomized, double-blind study comparing pramipexole (0.125-0.75 mg once daily [flexibly dosed]) with placebo. Question 6 of the RLS-6 asked if patients were "tired or sleepy during the day" in the past week (0=none/not at all, 10=very severe), and item 5 of the International RLS Study Group Rating Scale (IRLS) measured "tiredness or sleepiness" in the past week (0=none, 4=very severe). Measures were taken at day 9, and weeks 2, 4, and 12.

Results: The intent-to-treat population included 178 pramipexole and 179 placebo patients. Tiredness/sleepiness was significantly reduced from baseline in the pramipexole group (vs placebo) on both measures at all time points. The median change for RLS-6 question 6 was -1.0 vs -0.5 at day 9, and -2.0 vs -1.0 at weeks 2, 4, and 12 (P≤.007 for all, Wilcoxon rank test), while the percentage of patients who improved in IRLS item 5 was 64.2% vs 53.5% at day 9, 74.6% vs 56.0% at week 2, 79.7% vs 57.7% at week 4, and 78.7% vs 61.5% at week 12, with pramipexole vs placebo, respectively (P<.05 for all, Chi²-test). Changes in tiredness from baseline were highly correlated at all time points (Spearman's r>0.39, P<.0001).

Conclusion: Pramipexole effectively reduced daytime tiredness/sleepiness in RLS patients throughout this 12-week trial. Significant improvements in tiredness/sleepiness were evident within 9 days of initiating pramipexole, and consistent over time and across measures.

Support (optional): Supported by Boehringer Ingelheim GmbH

0826**GLOBAL IMPROVEMENT IN PATIENTS WITH RESTLESS LEGS SYNDROME FROM A DOUBLE-BLIND, PLACEBO-CONTROLLED PRAMIPEXOLE TRIAL**Partinen M¹, Chaudhuri K², Sohr M³, Lainey E⁴, Albrecht S³¹Neurology, University of Helsinki, Helsinki, Finland, ²Movement Disorders Unit, King's College Hospital, London, United Kingdom, ³Boehringer Ingelheim GmbH, Ingelheim, Germany, ⁴Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA

Introduction: Restless legs syndrome (RLS) is a distressing and disabling disorder for approximately 3% of the general population who experience moderate or severe symptoms. These symptoms are worst at night, often causing sleep disturbance. Daytime function is also impaired, as both a direct and indirect effect of RLS symptoms. Pramipexole has been shown to improve a broad range of symptoms associated with RLS. Patient-centered outcomes, rated by patients and their physicians, are best evaluated with global assessments.

Methods: Patients with moderate to severe RLS were treated for 12 weeks with pramipexole (flexibly titrated from 0.125-0.75 mg daily) or placebo. Improvement in condition during the past week (compared with baseline) was assessed on a scale of 1 (“very much better/improved”) to 7 (“very much worse”) by clinicians (Clinical Global Impression-Global Improvement [CGI-I] scale) at day 9, and weeks 2, 4, and 12 and by patients (Patient Global Impression [PGI] scale) at the same times plus days 1 and 5.

Results: Responder rates (percent improved to at least “much better/improved”) were higher in the pramipexole group (n=178) than the placebo group (n=179) for both PGI and CGI-I at all time points (for CGI-I: 52.5% vs 23.0% at day 9, 64.0% vs 39.1% at week 2, 69.7% vs 41.9% at week 4, 66.3% vs 40.2% at week 12; for PGI: 16.4% vs 8.0% at day 1, 36.2% vs 15.2% at day 5, 44.1% vs 19.6% at day 9, 53.1% vs 34.1% at week 2, 65.7% vs 39.7% at week 4, 62.9% vs 38.0% at week 12; P<.05 for PGI at day 1, P<.001 for all other comparisons).

Conclusion: Global improvement as assessed by both patients and clinicians was significantly higher in the pramipexole group compared to the placebo group, starting with initiation of therapy and sustained consistently throughout the 12-week study.

Support (optional): Supported by Boehringer Ingelheim GmbH

0827**PRAMIPEXOLE RAPIDLY IMPROVES RLS-ASSOCIATED LIMB PAIN**Aarskog D¹, Partinen M², Sohr M³, Lainey E⁴, Albrecht S³¹Colosseumklinikken, Oslo, Norway, ²Skogby Sleep Clinic, Espoo, Finland, ³Boehringer Ingelheim GmbH, Ingelheim, Germany, ⁴Boehringer Pharmaceuticals, Inc., Ridgefield, CT, USA

Introduction: Patients with restless legs syndrome (RLS) typically describe unpleasant sensations in their limbs that provoke an urge to move. These sensations are often perceived as painful and pain relief is an important goal of RLS treatment. Pramipexole is a D_{3/D2} dopamine agonist indicated for treatment of moderate/severe RLS. Previous studies have not evaluated its effect on limb pain.

Methods: In a large, multinational, randomized, double-blind trial, adults with moderate to severe RLS received pramipexole (0.125-0.75 mg, flexibly titrated) or placebo for 12 weeks. Limb pain was measured at baseline and after 1 day, 5 days, 9 days, 2 weeks, 4 weeks, and 12 weeks of treatment using a 100-mm visual analog scale (VAS) where 0=no pain and 100=unbearable pain.

Results: In the intent-to-treat population at baseline, median VAS pain score was 55.0 in the pramipexole group (n=178) and 50.0 in the placebo group (n=179). Median reductions from baseline were greater in the pramipexole group than in the placebo group after 1 day (-7.0 vs -5.0; P=.3606); 5 days (-15.5 vs -5.0; P=.0001); 9 days (-20.0 vs -8.0;

P=.0003); 2 weeks (-27.5 vs -15.0; P<.0001); 4 weeks (-32.0 vs -13.0; P<.0001) and 12 weeks (-33.5 vs -11.0; P<.0001).

Conclusion: RLS-related limb pain was rapidly and consistently relieved by pramipexole. As compared with placebo, pramipexole significantly reduced pain as early as 5 days after start of treatment. A placebo response was observed in the first weeks, but it declined thereafter. With pramipexole, pain relief continued to improve further over the course of the study and was maintained for the full 12 weeks.

Support (optional): Supported by Boehringer Ingelheim GmbH

0828**EFFECTS OF PRAMIPEXOLE ON QUALITY OF LIFE IN PATIENTS WITH RESTLESS LEGS SYNDROME**Partinen M¹, Ferini-Strambi L², Sohr M³, Lainey E⁴, Albrecht S³¹Skogby Sleep Clinic, Espoo, Finland, ²Centro di Medicina del Sonno, San Raffaele, Milan, Italy, ³Boehringer Ingelheim GmbH, Ingelheim, Germany, ⁴Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, CT, USA

Introduction: Restless legs syndrome (RLS) is a sensorimotor disorder whose symptoms increase at night and with inactivity, and often result in sleep disturbance, impairment in daytime function, and mood disturbance. Quality of life (QOL) can be substantially reduced in patients with pronounced RLS symptoms.

Methods: 356 patients (aged 18-80 years) with RLS and a score >15 on the International RLS Study Group Scale (IRLS) were enrolled into a 12-week, randomized, double-blind, placebo-controlled study. Pramipexole (a non-ergot D3/D2 dopamine agonist) was started at 0.125 mg, flexibly uptitrated to a maximum of 0.75 mg per day. QOL was measured at baseline, 4 weeks, and 12 weeks with the Johns-Hopkins RLS-QOL, an 18-item self-assessment of RLS' impact on daily activities, concentration, sexual activity, and work over the previous 4 weeks. Higher scores, providing a total score based on 13 items, indicate better QOL.

Results: The majority of the study population was female (68.0%) and white (99.5%). Mean age was 56.6 years. At baseline, median RLS-QOL score was 70.0 in the pramipexole group (n=178) and 67.5 in the placebo group (n=178). Median RLS-QOL score change from baseline was significantly greater in the pramipexole group than the placebo group at both time points measured: 15.0 vs 10.0 (P<.0001) at 4 weeks and 17.5 vs 12.5 (P=.0100) at 12 weeks.

Conclusion: Patients with RLS frequently experience reduced QOL. Once-daily treatment with pramipexole significantly improved QOL within 4 weeks of initiation, and improvement was maintained for the whole 12-week trial.

Support (optional): Supported by Boehringer Ingelheim GmbH

0829**LACK OF RECOGNITION OF EXCESSIVE FRAGMENTARY MYOCLONUS AMONG COMMUNITY SLEEP PROFESSIONALS**

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Introduction: Excessive Fragmentary Myoclonus (EFM) was first described over two decades ago, but is rarely described in clinical practice. Whether this is due to a low incidence of this finding or to a lack of awareness is unknown. In an attempt to determine the sleep community's recognition of EFM, a survey was conducted among technicians and sleep physicians at an AASM seminar.

Methods: Survey participants were recruited from a classroom of 300 sleep professionals, using an electronic voting device to select answers to multiple-choice questions with responses electronically tallied.

Results: 180 attendees chose to participate. Respondents were primarily sleep physicians (39%) and sleep technicians (50%). Most (85%) were unfamiliar with recently published criteria for scoring EFM, and did not document EFM in their reports (89%). Most participants (70%)

Category L—Sleep Disorders – Movement Disorders

indicated that they had not encountered any EFM cases in their practice. Nearly all (94%) indicated EFM was rare, with ≤ 5 EFM cases identified in the preceding six months. 94% of respondents indicated that they did not have specific amplitude criteria for EFM scoring. The remaining participants were divided between using 25 μ V, 40 μ V, 50 μ V, and 75 μ V as the minimum amplitude required. Most participants (61%) were undecided if documenting EFM was important, and 71% were undecided as to its clinical relevance. 5% indicated they had a specific therapy for EFM, while 43% said they did not. 51% indicated they were undecided as to whether they would start a specific therapy.

Conclusion: Survey participants are predominantly unfamiliar with EFM and are undecided as to its clinical importance. Among those who reported some experience with EFM, scoring criteria were erratically applied, and amplitude criteria appeared to be particularly problematic. A companion abstract will provide information on options for identifying amplitude criteria and additional guidance for other scoring criteria.

0830

RESTLESS LEGS SYNDROME: A COMMUNITY-BASED STUDY OF PREVALENCE IN BRAZIL

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Introduction: After the publication of the minimal criteria for the diagnosis of restless legs syndrome (RLS) by the International Restless Legs Syndrome Study Group (IRLSSG) in 1995, epidemiological studies of this disorder, in Europe and United States, was done in general populations worldwide, commonly yielding prevalence values in the range of 5-10%. Furthermore, there are only few studies from other geographic regions that indicate much lower frequencies of RLS. Our purpose was to determine the prevalence of RLS in a small community of São Paulo State, Brazil.

Methods: The study was conducted in Cássia dos Coqueiros (CQ), a small city in São Paulo State, Brazil. The adult and urban population of CQ was 1217 according to the 2007 National Census. A population-based, cross-sectional study was performed. The epidemiologic survey consisted of face-to-face, door-to-door interviews and was conducted by a neurologist with expertise in sleep medicine. Adult residents in the urban region of CQ, aged 18 years or more, were eligible for inclusion in the study. RLS was diagnosed if the respondents answered affirmatively to all questions of the four essential National Institutes of Health/IRLSSG criteria for diagnosis of RLS.

Results: We interviewed 1155 subjects, the rate of participation being 94.9%. The prevalence of RLS in the life was 7.7% (10.2% in women, 5% in men). Women were more affected than men (OR=2.26; [CI=1.39-3.66]), after the logistic regression analysis. Moreover subjects from families with monthly incomes higher than US\$1.575 showed higher prevalence of RLS (OR=2.60; [CI=1.30-5.20]) when compared to subjects from lower income families.

Conclusion: This is the first Brazilian population study on RLS which reveals prevalence of the disorder in an urban population at 7.7%. Larger studies are warranted to better characterize RLS in Brazil.

Support (optional): CNPq-CAPES

0831

ROPINIROLE CR EXTENDED-RELEASE EFFECTS ON SYMPTOMS OF RESTLESS LEGS SYNDROME (RLS) AND ASSOCIATED SLEEP DISTURBANCE AS MEASURED BY POLYSOMNOGRAPHY (PSG)

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Introduction: Sleep disturbance (delayed onset, reduced efficiency, multiple awakenings) is the primary morbidity of RLS attributable to the sensory symptoms of RLS and periodic limb movements (PLMs).

Methods: Study RRL103660 was a 12-week, randomized, double-blind PSG study. Subjects with moderate-to-severe primary RLS and associated objective and subjective sleep disturbance completed an adaptation night PSG to rule out other sleep disorders, followed by a 2-night PSG to confirm eligibility and serve as baseline. Eligible, subjects were randomized to ropinirole CR (n=20) or placebo (n=19), 0.5-6mg/day flexibly titrated, taken 1-2 hours before usual symptom onset (≥ 4 pm). Primary endpoint was mean change from baseline to Week 12 LOCF in PLM index (PLMs per hour). Secondary endpoints included indexes of PLMs associated with arousal (PLMAI), objective and subjective parameters of sleep, International Restless Legs Rating Scale (IRLS), and Clinical Global Impression (CGI) scale. Tolerability was assessed by adverse event reporting, labs, and cognitive function tests.

Results: Improvements from baseline in PLMI were greater with ropinirole CR relative to placebo (-23.23 vs. -16.61, respectively) at Week 12 (LOCF), although not statistically significant (p=0.26). Improvements in PLMAI were statistically significant (adjusted treatment difference -5.69; p=0.02). Ropinirole CR showed greater improvements (though non-significant) in both sleep latency and total sleep time assessed by PSG and post-sleep questionnaire. RLS symptoms improved with ropinirole CR as evidenced on the IRLS and greater proportion of CGI responders. Next day cognitive function was similar in both groups. The most common AE was nausea (20% ropinirole CR; 16% placebo).

Conclusion: Ropinirole CR did not result in a significant reduction in PLMI compared to placebo, though did significantly reduce PLMAI which may be a more clinically meaningful subset of PLMs. Ropinirole CR also produced improvement (although not statistically significant) in RLS symptoms, sleep parameters (objective and subjective), and was generally well tolerated.

Support (optional): Study sponsored by GlaxoSmithKline.

0832

VALERIAN (VALERIANA OFFICINALIS) IMPROVES SLEEPINESS AND SYMPTOMS OF RESTLESS LEGS SYNDROME (RLS)

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Introduction: The most common complaint in people with RLS is the inability to fall asleep due to uncontrollable feelings in the legs at rest or bedtime only relieved with movement. The use of valerian, which acts like a benzodiazepine, may enhance sleep and improve symptoms of RLS. Valerian may be an option for persons with RLS who choose not to use dopaminergics because of negative side effects, when medications stop working, or during a "drug holiday". The purpose of this study was to compare differences in RLS Symptom Severity (RLS Symptom Severity Scale) between two groups who were sleepy and not sleepy (Epworth Sleepiness Scale) after 8 weeks of 800 mg of valerian treatment.

Methods: Secondary analysis of a prospective, randomized, double-blind, placebo-controlled pilot (n=37)

Results: Data was collected at baseline and 8 weeks comparing use of valerian and placebo on sleep disturbances (PSQI and EES), severity of symptoms (IRLSS), fatigue (FSS), depression (CES-D), and qual-

ity of life (RLS-QLI) from 37 participants ages 36-65. The treatment group (n=17) received 800 mg of valerian for 8 weeks. Of the 17 valerian recipients, significant differences were found in subjective sleepiness scores ($p=.01$) before and after treatment. In those participants receiving valerian that scored a 10 or higher on the ESS, significant differences were also reported in the “sleepy” subjects ($p=.02$). A strong positive association between changes in sleepiness and RLS symptom severity was found in the valerian group ($p=0.006$).

Conclusion: The results of this pilot suggest that the use of 800 mg of valerian for 8 weeks improves symptoms of RLS and decreases daytime sleepiness. Valerian may be an alternative treatment for the symptom management of RLS with positive health outcomes and improvement of quality of life. Larger, phase III clinical trials are needed to explore the use of valerian in persons with RLS.

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0833

RESTLESS LEGS SYNDROME (RLS) GENDER EFFECT AND COMORBIDITY IN A SICILIAN COHORT

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Introduction: According to most literature reports, RLS prevalence is higher in women, especially during typical periods of life, such as pregnancy or menopause. The aim of our study was to evaluate the impact of RLS in female patients referred to our sleep centre.

Methods: We retrospectively analyzed all clinical features of the patients diagnosed for RLS over the last year.

Results: 19 out of 41 patients were women. No statistical differences were found as far as mean age of onset (M 45.2 and F 51.2 yrs) and IRLS-RS score (M 25.6 and F 27) between males and females. 10/41 (9 F) patients had a positive familial history for RLS with an earlier age of onset. 7 women and 17 men were diagnosed as idiopathic RLS. In women mean parity was 2.3: in 5/19 first symptoms coincided with 1^o pregnancy, worsening thereafter and in 3/19 occurred upon menopause. Mean ferritin levels were lower in women (45,4 µg/dl F and 64,3 µg/dl M, $p<0.05$); mood disorders more frequent in women, OSAS in men. 13 patients suffered from hypertension and 7 from thyroid disorders, 9 were on statins for hypercholesterolemia. 2 women had a co-occurring nocturnal eating disorders (NES). Different Dopa-agonists (pramipexole, ropinirole, cabergoline) were prescribed to all patients and after one month of therapy IRLS-RS score decreased with statistical significance (7.1, $p<0.01$).

Conclusion: No gender differences were found in our sample as far as RLS prevalence. In women however a positive familial history, lower iron levels, mood and eating disorders occurred more frequently than in men. A + familial history correlates with earlier symptoms onset and iron and thyroid alterations Pregnancy and menopause induced symptoms in 20% of our sample. Dopa-agonists improved RLS in all patients as well as blood pressure values and mood disorders in 1/5 of the sample leading to total or partial discontinuation of specific therapy.

0834

PERIODIC LIMB MOVEMENT DISORDER AND LUMBAR VERTEBRAL DISEASE

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Introduction: Periodic Limb Movement Disorder (PLMD) is a movement disorder of sleep that causes disruption, decreased quality of sleep, and decreased quality of life. Studies have implicated primary and sec-

ondary forms, but few have investigated lumbar vertebral pathology as a cause. PLMD was investigated in an observational, retrospective, cross-sectional study which analyzed polysomnographic evidence of leg movements in association with physical and mental health that could explain the disorder.

Methods: Patients were referred by their family practitioner for poor sleep quality. 77 participants were chosen based on polysomnographic results of a periodic limb movement index (PLMI) of greater than five per hour. Data was collected from the polysomnographic study, a questionnaire, and results of lumbar vertebral imaging.

Results: There was a positive correlation ($r=0.40$, $p<0.01$) and clinical significance [$F(1,76)=16.2$, $P<0.0001$] between age (above and below 55) and PLMI. 58.4% of patients had lumbar vertebral disease on lumbar imaging. 5.2% had no lumbar pathology on lumbar x-ray but had clinical symptoms. 36.4% did not have imaging available, but 53.6% of these had lower back ache. Patients with Obstructive Sleep Apnea and PLMD had no resolution of PLMD on CPAP therapy. Other disorders known to cause PLMD were not seen in a majority of the patients.

Conclusion: Lumbar vertebral pathology is a very common cause of PLMD, and patients should have lumbar imaging to rule this out. Patients currently being treated for PLMD without ruling out lumbar pathology may be receiving treatment for an undetermined cause. Patients should be offered physiotherapy to strengthen lumbar musculature, and counseling regarding posture, back care, and precautionary measures. The need for anti-inflammatory medication must be determined for disease processes such as osteoarthritis. Use of medications only to suppress leg movements or arousals may not be adequate therapy.

0835

LATER TREATMENT TIMES FAVOR THE EXPRESSION OF RESTLESS LEGS SYNDROME INDEPENDENT OF PERIODIC LIMB MOVEMENTS IN CHRONIC HEMODIALYSIS

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Introduction: When administered early in the day, hemodialysis (HD) has been associated with better nocturnal sleep. We sought to determine if this observation might reflect treatment time expression of Restless Legs Syndrome (RLS) and periodic leg movements of sleep (PLMs), recognized correlates of morbidity in patients on HD.

Methods: Fifty-eight (58) chronic, stable African American HD patients maintained a specific treatment time for a three month period and underwent two nights of attended polysomnography (PSG) one week apart. Subjects also completed an RLS questionnaire. Demographic and clinical data were obtained via chart review. There were no significant differences between the two nights of PSG, thus data were averaged. Descriptive and nonparametric statistics were used for data analyses.

Results: The mean age of the subjects was 51.4 (11.8); 33 (56.9%) were male. Ten (17.2%) subjects endorsed consensus criteria for RLS; 7 were female and 3 were male, a difference approaching significance ($\chi^2 = 3.7$, $p = .06$). There were no differences between those suffering versus those not afflicted with RLS with regard to demographic variables, cause of renal failure, body mass index, dialysis vintage (months receiving treatment), laboratory measures (including iron indices), or periodic limb movement index ($X = 18.1$, $SD = 27.1$ for the entire group). Subjects experiencing RLS started dialysis significantly later in the day ($X = 10:55$; $SD = 2:24$ vs. $8:42$, $SD = 2:42$, $Z = -1.8$, $p = .015$) and tended to end treatment later (14:16, $SD = 2:46$ vs. 12:28 = 2:41, $Z = -1.8$, $p = .07$).

Conclusion: Chronic renal failure and HD appear to represent a state that favors dissociation of sensory from motor components of the RLS/PLMs phenotypic spectrum. Later dialysis treatment times may alter circadian systems and cause physiological changes which enhance the expression of RLS and known sleep disruption independent of PLMs. Elucidating the factors underlying this apparent treatment time depen-

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dent dissociation of sensory from motor components of RLS may shed novel insight into the pathophysiology of RLS.

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0836

AMPLITUDE AND SLEEP STAGE DISTRIBUTION OF EXCESSIVE FRAGMENTARY MYOCLONUS IN POLYSOMNOGRAPHY: A CORRELATIVE ANALYSIS

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Introduction: Excessive fragmentary myoclonus (EFM) consists of brief, asynchronous, twitch-like movements appearing asymmetrically in sleep. The new AASM Manual for the Scoring of Sleep and Associated Events does not provide amplitude criteria for scoring EFM, although older observational series suggest 50µVs. We report data from various amplitude criteria using blinded comparisons.

Methods: In an ongoing project, sequential EFM patients from 2 sleep centers are being analyzed. Present data is based on 6 men and 1 woman (mean age 57) using a standardized protocol for sensitivity, tonus threshold, impedance, amplitude measurements and sleep stage using a blinded scoring comparison. The first twenty minutes of wake, Stage 1-2, SWS and REM are each analyzed. EFMs ≥ 25 , ≥ 40 , and ≥ 50 microvolts (μ Vs) in negative deflection above the baseline are counted in tibialis EMG channels bilaterally.

Results: The mean EFM Index per minute for wake, regardless of impedance, was: 6.69 \pm 6.19 for $\geq 25\mu$ V amplitude; 2.27 \pm 2.13 for $\geq 40\mu$ Vs; and 1.57 \pm 1.84 for $\geq 50\mu$ Vs. For sleep stages the EFM indexes are included by stage and amplitude used for measurements. Stage 1-2: 6.90 \pm 6.08 for $\geq 25\mu$ Vs; 3.02 \pm 3.58 for $\geq 40\mu$ Vs; and 2.12 \pm 2.79 for $\geq 50\mu$ Vs. SWS: 9.49 \pm 8.04 for $\geq 25\mu$ Vs; 2.45 \pm 3.13 for $\geq 40\mu$ Vs; and 1.32 \pm 1.92 for $\geq 50\mu$ Vs. REM: 15.82 \pm 12.4 for $\geq 25\mu$ Vs; 6.47 \pm 4.63 for $\geq 40\mu$ Vs; and 4.13 \pm 4.05 for $\geq 50\mu$ Vs. Phasic REM: 20.02 \pm 16.90 for $\geq 25\mu$ Vs; 9.08 \pm 7.62 for $\geq 40\mu$ Vs; and 5.87 \pm 6.98 for $\geq 50\mu$ Vs. Tonic REM: 13.93 \pm 11.31 for $\geq 25\mu$ Vs; 5.16 \pm 3.57 for $\geq 40\mu$ Vs; and 3.20 \pm 2.92 for $\geq 50\mu$ Vs. Additional patients are being analyzed.

Conclusion: Regardless of sleep stage, voltage criteria set at $\geq 25\mu$ Vs appeared to be a sensitive yet reliable indicator for EFM activity vs. using 50µVs. There appear to be differences between phasic and non-phasic REM. Our method of measuring EFM amplitude appears to be reproducible and useful during various sleep stages and may help clarify EFM criteria in the future.

0837

DOES PERIODIC LIMB MOVEMENTS DURING SLEEP OCCUR IN THE UPPER LIMBS?

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Introduction: Periodic limb movements during sleep (PLMS) is characterized by the involuntary movements which mainly make dorsal flexion movements of leg ankle joints repetitively. There are a few reports that PLMS rarely appears in the upper limbs, but the incidence is not clarified because polysomnography (PSG) recording of just lower limbs was usual in almost all the sleep institutions. Then, we examined the incidence of periodic upper limb movements during sleep.

Methods: From June 2004 to March 2005, 415 patients (348 men and 67 women, average age 45.8 \pm 15.2 years old) was conducted PSG in our institution (140 persons for diagnostic PSG and 275 persons for CPAP titration). Electrodes were added to both arms in addition to the usual recording of the movements of the upper limbs. We selected the extensor carpi ulnaris muscle for the sensors since it was comparatively easy to touch the muscles and has a wrist extension functionality. Following the

ASDA criteria (1993) for diagnosing PLMS, we did not count arousal, respiratory events, the lower limb events, and other body movements during the sleep session.

Results: Only one among 415 patients (0.2%) had periodic upper limb movements, with the index (per total sleep time) of 30.6. In this case for CPAP titration, the appearance time of the periodic arm movements is not defined because upper limbs were not recorded at the first diagnostic PSG. The periodic arm movements were recorded in 13 patients, but lower limb movements went ahead and judged it as body movement with the leg motion.

Conclusion: The PLMS often accompanied with electroencephalographically arousals causes excessive daytime sleepiness and insomnia. Incidence of periodic upper limbs movements during sleep was very low (0.2%) in 415 persons; but if PLMS is suspected by interview through a patient or a bed partner, it is necessary to measure PLMS of the upper limbs if needed. Moreover, in addition to wearing electrodes on the side extensor carpi ulnaris, it is necessary to examine whether it appears also in other muscles of the upper limbs, such as biceps brachii and triceps brachii.

0838

DIFFERENCES BETWEEN PERIODIC LEG MOVEMENTS IN RESTLESS LEGS SYNDROME AND REM BEHAVIOR DISORDER

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Introduction: About 70% of idiopathic REM sleep behavior disorder (RBD) patients present a periodic leg movements (PLM) index greater than 10. The aim of the study was to compare the time structure of leg movements (LM) during sleep of patients with RBD with that of patients with restless legs syndrome (RLS) or controls.

Methods: The polysomnographically recorded tibialis anterior (TA) activity during sleep was analyzed by means of a new approach able to consider duration, intermovements interval, sleep stage and time of night distribution, and periodicity. Twenty patients with idiopathic RBD, 37 with idiopathic RLS and 14 age-matched controls, were consecutively recruited.

Results: Most of RBD patients (85%) presented periodic leg movements during sleep (PLMS). PLMS occurred more frequently during NREM sleep in RLS and during REM sleep in RBD. PLMS resulted shorter in duration, less often bilateral, and with a higher inter-movement interval in RBD compared to RLS. Number of PLMS decreased across the night in both RBD and RLS, but not in controls. In all subjects LM periodicity clearly depended on sleep state, with higher values during NREM than during REM sleep. RBD showed a lower LM periodicity compared to RLS in each of the sleep states.

Conclusion: Significant differences together with some similarities in LM time structure were observed between RBD and RLS; for this reason, our approach seems to indicate that their phenotype might be dependent on two factors: disease and sleep stage.

0839

USE OF A SEQUENTIAL COMPRESSION DEVICE TO TREAT RESTLESS LEGS SYNDROME

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Introduction: Various agents (e.g., dopamine agonists, opioids) have proven efficacious for management of restless legs syndrome (RLS). However, some RLS patients either show no response to these agents or

they prefer non-pharmacological interventions. This report describes an investigation to test a sequential compression device (SCD) for treating RLS.

Methods: A series of 20 adult patients who met criteria for RLS were enrolled in this trial that used a multiple-baseline, open label research design. Patients first completed a questionnaire that assessed RLS severity and sleep logs for 1-2 weeks prior to initiating treatment. They then utilized a Kendall model 7325 SCD in their homes nightly for 1 week during which they again completed the RLS severity questionnaire and nightly sleep logs. With-in subject changes were tested statistically, and a case-by-case review was conducted to identify responders and non-responders.

Results: Within group t-tests showed the sample of patients reported significantly lower RLS severity during the week of SCD therapy than they did during the baseline phase ($p = .002$). Analyses of sleep log data showed the group as a whole reported significantly less wake time after sleep onset ($p = .05$) per night and they felt significantly better upon awakening ($p = .05$) during the SCD week than during the period without the SCD. A case-by-case review of the data showed that 14 of the 20 patients reported marked benefits from the treatment, whereas the remaining 6 showed no response to treatment. Treatment responders showed significant improvements on the restless legs symptom questionnaire ($p = .001$) and sleep diary measures of WASO ($p = .001$), sleep efficiency ($p = .01$) and how well rested they felt ($p = .03$) during the treatment week as compared to the baseline period. The 6 non-responders did not show and significant changes between the baseline period and treatment week on any study measures.

Conclusion: The SCD showed promising results for RLS management with over twice as many patients reporting benefits as those who displayed no response. Additional randomized controlled trials with this therapy seem warranted.

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0840

IRON DEFICIENCY RESULTS IN INCREASED ADENOSINE A2A RECEPTOR SIGNALING IN HUMAN NEUROBLASTOMA CELLS

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Introduction: Restless Leg Syndrome (RLS) is associated with diminished brain iron concentrations. Recent studies to examine the effects of low brain iron, found an up-regulation of striatal A2A receptors in diet-induced, iron-deficient mice. The current study was designed to further explore the effects of diminished iron on A2A receptor signal transduction.

Methods: Increasing doses (0.1 - 100 nM) of the selective A2A receptor ligand, CGS-21680, was used to stimulate cyclic AMP levels in cultured SH-SY5Y neuroblastoma cells in the absence or presence of the iron chelator desferrioxamine (DFO). Cells under serum-starved conditions were treated with DFO (50 μ M) for 24 hours. Intracellular cyclic AMP levels were measured with enzyme immunoassay (EIA). Adenosine A2A receptor and transferrin receptor expression was assessed by western blot.

Results: DFO treatment resulted in a five-fold increase in A2A receptor expression. The DFO treatment caused cellular iron insufficiency as indicated by an increase in the level of cellular transferrin receptors. CGS-21680 application produced a dose dependent increase in [cAMP] i accumulation with EC50 of 3.7 nM. DFO treatment produced a “left

shift” in the dose-response curve of [cAMP]i accumulation with with an EC50 of 0.4 nM.

Conclusion: Iron deprivation of neuronal cells causes an increased sensitivity to adenosine receptor (A2A) ligands. This increased sensitivity may be suggestive of altered downstream signal transduction pathways. This alteration may also change dopamine receptor functioning because adenosine receptors form telomers with dopamine receptors. This may be a mechanism by which iron insufficiency produces the dopaminergic features of RLS.

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0841

HEART RATE CHANGES DURING PERIODIC LEG MOVEMENTS IN PATIENTS WITH RESTLESS LEGS SYNDROME

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Introduction: Cardiovascular changes related to periodic leg movements during sleep might affect the cardiovascular system of otherwise healthy patients. Restless legs syndrome has been associated in population-based studies with increased risk for coronary artery disease and hypertension. Many studies published in the last few months found that during periodic limb movements at night blood pressure and heart rate rise appreciably. In our study we evaluated the changes in heart rate during periodic limb movements in patients with restless legs syndrome.

Methods: 9 patient with RLS (7 women, mean age 52.3 ± 12.2 years, 2 men, mean age 56.2 ± 10.1 years) underwent one night polysomnography with continuous heart rate monitoring. We recruited patients diagnosed with RLS based on the clinical criteria by International Restless Legs Syndrome Study Group (IRLSSG). We excluded patients taking beta-blockers. The patient were asked to perform voluntary movements mimicking PLMS (Fake PLMS) as a control for PLMS during polysomnography. We analyzed 277 movements: 32 Fake PLMS, 135 periodic limb movements is sleep with cortical arousals (PLMSA), 110 periodic limb movements in sleep without cortical arousals (PLMSNA).

Results: There was a rise in heart rate after PLMSA (HR: 5.7 ± 4.3) and PLMSNA (HR: 4.5 ± 3.7) as compared to Fake PLMS (HR: 2.2 ± 2.5). The increase in the heart rate didn't reach statistically significance.

Conclusion: In our study we found, that there was a rise in heart rate with periodic limb movements in sleep with cortical arousals and without cortical arousals compared to Fake PLMS. Although the rise of the heart rate that didn't reach statistically significance, it could contribute to the risk of cardiovascular diseases in these patients.

0842

RESTLESS LEGS SYNDROME IN WOMEN WITH HEAVY MENSTRUAL BLEEDING

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Introduction: Restless legs syndrome (RLS) has been described as an idiopathic disorder or a symptomatic syndrome often associated with iron deficiency. Menstrual disorders are common gynecologic conditions and heavy menstrual bleeding (HMB) increases the risk of iron deficiency in premenopausal women. In order to assess the frequency of RLS among patients with HMB as compared to controls, we performed a cross-sectional study.

Methods: Sixty-one women were studied, including 21 consecutive patients attending Urogynecology clinics at a referral hospital for HMB and 40 female hospital staff with no past or present of HMB or others gynecological disorders. HMB was defined as menstrual periods with 10 or more bleeding days and more than 30 sanitary pads needed. Patients

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and controls had no history of regular or recent blood donation, iron supplementation, other possible causes of blood loss or co-morbidities, nor were they taking drugs associated with RLS. All subjects were submitted to a face-to-face interview by a sleep specialist. Diagnosis of RLS was based on IRLSSG criteria.

Results: RLS was present in seven patients with HMB (33.3%) and in three controls (7.5%). When women with RLS were compared to women without RLS, no significant difference was observed related to age (41.5 ± 6.9 versus 41.5 ± 5.7) ($p=0.9$) or ethnic distribution ($p=0.6$). Women with RLS presented higher mean number of bleeding days (12.3 ± 6.7 versus 8.5 ± 8.1) ($p=0.03$) and mean number of sanitary pads needed (104.2 ± 72.6 versus 61.7 ± 113) ($p=0.01$). Among women with HMB, those with RLS presented a longer duration of menstrual disorder (2.4 ± 1.5 months) as compared to women without RLS (5.6 ± 1.9 months) ($p=0.05$).

Conclusion: RLS is more frequent among patients with HMB than healthy controls and seems related to duration of menstrual disorder. Further studies should better investigate the role of menstrual disorders in RLS prevalence.

0843

STROKE PATIENTS WITH AND WITHOUT RESTLESS LEGS SYNDROME

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Introduction: Restless Legs Syndrome (RLS) is a common disorder, affecting 5-10% of the general population. Recent investigations show RLS and related periodic limb movements of sleep to be associated with blood pressure elevations (Siddiqui F 2007, Pennestri MH 2007). It is well known that hypertension is a significant risk factor for stroke. The role RLS in vascular disease needs further exploration. Therefore, we aim to investigate the 1) prevalence of RLS in patients with recent strokes and 2) whether RLS in the stroke population is associated with other sleep disturbances.

Methods: We screened 68 patients who were admitted to the University of North Carolina's stroke center with documented ischemic or hemorrhagic strokes. Patients were divided into two groups (with/without RLS symptoms). Information such as, gender, BMI, Epworth Sleepiness Scale (ESS), Sleep-Disordered Questionnaire (SDQ) and Insomnia Severity Index (ISI) were obtained. Person correlation coefficient were used with $p < 0.05$.

Results: 45% (31 out of 68) of patients endorsed RLS symptoms. Average age for the RLS group was 65 yo; without RLS group was 61 yo. Patients with RLS were more likely to experience excessive daytime sleepiness and insomnia and endorse symptoms of sleep apnea: ESS ($p < 0.0007$), ISI ($p < 0.002$), SDQ ($p < 0.008$). There was a trend to hemorrhagic strokes in patients without RLS ($p < 0.08$). Age, race and BMI showed no difference between the two groups.

Conclusion: These findings indicate that 1) the prevalence of RLS is high in patients with stroke; 2) Stroke patients who endorsed RLS have an added risks of having other sleep disorders that include insomnia, daytime hypersomnolence and sleep apnea. The impact of RLS on the risk of developing cerebrovascular disease needs further exploration.

0844

OBSTRUCTIVE SLEEP APNEA IN RESTLESS LEGS SYNDROME PATIENTS

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Introduction: Even though obstructive sleep apnea (OSA) and restless legs syndrome (RLS) are common sleep disorders, only few studies on the relationship between OSA and RLS have been reported. The purpose of this study was to investigate the prevalence and related factors of OSA in RLS patients.

Methods: Subjects were 100 consecutive patients (35 men and 65 women) who visited our sleep clinic with chief complaints suggestive of RLS and were confirmed with RLS by physician sleep specialist. They all underwent polysomnography. Data of their physical examination and clinical tests were analyzed.

Results: The mean (s.d.) of age was 50.3(14.0) years old (range, 15-79); BMI was 23.3(3.3) (range, 14.7-36.4); and minimum oxygen saturation was 86.6 (4.3) (range, 77-98). Sixty-two percent of them had OSA; 34% were in mild ($5 \leq \text{AHI} < 15$); 20% were moderate ($15 \leq \text{AHI} < 30$); and 8% were severe ($\text{AHI} \geq 30$). Ninety-one percent of them were in abnormal RDI ($\text{RDI} \geq 5$). The prevalence of OSA in men was higher than women (68.6%, 58.5%, respectively), but it was not significant. Compared to non-OSA group, OSA group was older ($p=0.0031$), and had higher BMI ($p=0.0023$). When age and sex were adjusted, the odds of OSA were 1.22 times greater (95% confidence interval [CI], 1.05-1.43) for RLS patients as BMI increased one unit. Age had also an independent effect on OSA (adjusted odds ratio, 1.05 for one year older; 95% CI, 1.01-1.09).

Conclusion: High prevalence of OSA in RLS patients suggests that RLS is related to OSA. Physicians should consider examining OSA if he/she meets RLS patients who are especially older and/or in high BMI.

0845

DEVELOPMENT OF RESTLESS LEGS SYNDROME DURING PREGNANCY. RELATIONSHIP TO SNORING AND EDEMAS

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Introduction: We aimed to study how restless legs syndrome (RLS) develops during pregnancy, and whether this is related to occurrence of snoring and/or edemas.

Methods: 151 women who visited one antenatal care clinic during the first, second and third trimester of pregnancy at all occasions answered a questionnaire concerning snoring (rarely-seldom, sometimes, often, always), subjective fatigue and sleepiness, and edemas. RLS was diagnosed from 4 questions (unpleasant feelings from the legs at rest causing urge to move, relief from symptoms when moving, worsening of symptoms in the evenings, symptoms more than once per month).

Results: 4% of the women snored before, and 23/151 (15%) of the women developed snoring during pregnancy. In the first trimester, 15% of the non-snorers and 25% of those who snored habitually reported RLS. In the second trimester, 17% of the non-snorers and 34% of the snorers reported RLS. In the third trimester, 27% of the non-snorers and 42% of the snorers suffered from RLS. The difference was significant ($p < 0.05$) in the second and third trimesters. 69% of the women developed edemas (67% non-snorers and 78% snorers), and 32% of them also had RLS in the 3rd trimester. However, in the non-edema group 25% also got RLS (n.s.).

Conclusion: RLS-symptoms are very common during pregnancy and show a marked progression. Women who snore have an increased prevalence of RLS compared to non-snorers. Edemas do not seem to explain the increased occurrence.

0846

A RETROSPECTIVE REVIEW OF THE INCIDENCE OF PLM IN PATIENTS TREATED WITH CPAP

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Introduction: Sleep complaints are commonly reported by patients with obstructive sleep apnea (OSA) or periodic limb movements (PLM). However, few studies have examined the characteristics of patients with PLM in conjunction with OSA or determined whether OSA masks the

diagnosis and treatment of PLM. This descriptive study evaluates the incidence of PLM in OSA patients.

Methods: A retrospective chart review of polysomnograms (PSG) over five years was conducted at Washington University Sleep Medicine Center. Out of the 10,689 PSG performed, there were 6,377 split night studies and 1,545 were started on continuous positive airway pressure (CPAP). Of those patients started on CPAP, 361 returned for a CPAP titration. Patients started on supplemental oxygen, bi-level positive airway pressure (BIPAP), or not fixed were excluded from the study. PLM recorded during PSG were analyzed in the 103 remaining patients. PLM were scored according to AASM practice parameter criteria.

Results: 103 patients were divided into two groups according to periodic leg movement index (PLMI). Group 1 was comprised of patients with a PLMI > 5 (n=44) on at least one PSG and Group 2 included patients with a PLMI < 5 (n=58) for both PSGs. 43% of the patients exhibited a PLMI > 5. Demographics were similar between Group 1 and Group 2 (mean age 53.2±10.3 vs. 49.6±13.9, baseline AHI 47.7±31.5 vs. 60.1±44.6, optimal pressure 10.6±2.5 vs. 10.8±3.4, optimal pressure during titration study 11.7±2.9 vs. 12.0±3.6, and residual AHI at optimal pressure 2.4±2.9 vs. 2.5±2.6). In Group 1, 9 patients experienced PLM only during the split night study, 14 patients presented PLM during both studies, and 21 patients exhibited PLM only during the subsequent titration study.

Conclusion: While OSA may have accounted for some of the PLMI and complaint of sleep disturbances, this study demonstrates the need for further studies to assess the correlation between OSA and PLM and the possibility of OSA masking PLM.

0847

RESTLESS LEGS SYNDROME IN CHILDREN

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Introduction: Restless Legs Syndrome (RLS) diagnosis is based on the International Restless Legs Syndrome Study Group (IRLS). These criteria apply both to adults and children but children are required to describe the sensations in the legs in their own words in order to fit the definitive criteria for RLS, what creates difficulties to study epidemiology and to treat this disease in that population. Objectives: To describe clinical features of children diagnosed with RLS in a Brazilian Sleep Center.

Methods: We analyzed the files of 40 patients (18 girls) aged 4 to 13 years, referred to the Neuro-Sono outpatient clinic at Federal University of Sao Paulo, Brazil, during 2007, with complaints of legs sensations. We applied the specific criteria of the IRLS to decide if the patient had or not RLS and assessed associated clinical features such psychological and cognitive acquisition in those diagnosed RLS patients.

Results: Out of 40 patients, 11 (27.5%; 6 girls) presented RLS as a definitive diagnosis. Out of the 11 RLS patients, 8 presented one or more psychological features: 2 had anxiety, 4 lack of limits, 4 attention deficits, 4 hyperactivity, 1 delay in cognitive acquisition, and one cognitive problems. Three children presented RLS as a unique complaint. Seven presented ferritin lower than 50 ng/ml. All patients in treatment reported decrease in legs sensations and subsequent improvement in sleep quality.

Conclusion: The majority of patients referred to a sleep center with legs sensation does not fill out the strict criteria for RLS, and a pure RLS in children is also not common, being frequent its association to hyperactivity, anxiety, lack of limits, and cognition problems in our population.

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0848

RLS: INTERDISCIPLINARY APPROACH

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Introduction: Restless Legs Syndrome (RLS) is a sleep disorder, characterized by an irresistible urge to move the legs, unpleasant sensations, mostly at night, improving with movement. These symptoms induce insomnia, cognitive deficit, depression, anxiety, interfering in daily activities. Objective: To verify if education, regular physical activity, and CBT are an adequate RLS intervention.

Methods: Among 2,200 medical files of Neuro-Sono outpatients clinic, UNIFESP, we identified 100 patients (65 females), aged 20-86 years, with confirmed RLS diagnosis by a physician, according to International RLS Study Group. 20 patients (17 females) were assessed and treated by an Interdisciplinary Group for 3 months. Physician evaluated patients who were treated with non ergolinic dopaminergic agonists. Psychologist assessed history of life, International RLS Severity Scale, BDI, BAI, RLS Quality of Life Instrument, ESS. Occupational Therapist provides information about lifestyle and environment factors. Monthly, physical therapists and educators promoted physical activities in group. At the end of each session, RLS Quality of Life Instrument was applied.

Results: This pilot study showed that one week after treatment RLS severity reduced from severe to mild in 80% of patients, but many patients were still complaining of insomnia and anxiety index were also high, besides lower than before drug therapy. Interdisciplinary approach started at the second visit, including CBT and the above cited interventions. Anxiety level, depression, and insomnia reduced drastically and a significant bond to the health care team developed, helping to improve self confidence and quality of life. The overall impression was that a more broad approach accelerated the improvement and disclose a state of happiness hidden for many years in our sample of RLS patients.

Conclusion: Interdisciplinary approach provided a better understanding of patient and illness, showing to therapists and patients how to deal with complex features of many RLS, connecting effective treatment with better lifestyle.

Support (optional): * Supported by FAPESP # 00/07513-3, # 99/08189-6, and Uniter-Sono.

0849

ROTIGOTINE TRANSDERMAL PATCH IS EFFECTIVE IN THE TREATMENT OF IDIOPATHIC RLS: RESULTS OF A 6-MONTH, MULTICENTER, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL IN THE US

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Introduction: Rotigotine is a non-ergolinic D₃/D₂/D₁ dopamine agonist with 5HT_{1A} agonistic and α₂-adrenergic antagonistic properties. The aim of this multicenter, 6-month, double-blind, placebo-controlled trial was to evaluate the efficacy and safety of rotigotine transdermal patch against placebo in patients with moderate to severe idiopathic RLS.

Methods: Multicenter, randomized, double-blind, placebo-controlled, 5-arm parallel-group trial with 4 fixed doses of rotigotine 0.5-3mg/24h (2.5-15cm²). The co-primary efficacy parameters were the IRLS sum score and the CGI item I.

Results: A total of 505 patients (52 ± 13 years, 61% female) were randomized at 58 sites in the US. The mean baselines scores were: IRLS 23.3±5.0 and CGI 4.7±0.7. The improvement net effects versus placebo at 6 months were -2.2±1.2, 2.3±1.2, -4.5±1.2 (p<0.001), and -5.2±1.2 (p<0.001) in the IRLS and -0.35±0.19, -0.32±0.19,

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-0.65±0.19(p<0.001) and -0.90±0.19(p<0.001) in CGI item I for rotigotine 0.5, 1, 2, and 3mg/24h, respectively.

Conclusion: Therapy with rotigotine transdermal patch in doses of 2 and 3mg/24h over a period of 6 months resulted in a statistically significant and clinically relevant reduction in the IRLS score and CGI item I compared to placebo and was well tolerated.

0850

INCIDENCE OF RESTLESS LEGS SYNDROME IN PATIENTS EVALUATED FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: Restless Legs Syndrome (RLS) and Obstructive Sleep Apnea (OSA) are common disorders. Epidemiologic studies estimate that 10% of adults have RLS, 3.4% have symptomatic RLS and 5% have OSA. RLS and OSA have overlapping symptoms including hypersomnolence, frequent leg movements and frequent nocturnal awakenings. RLS and OSA may both be present in the same patient. We hypothesize that patients undergoing a polysomnography (PSG) will have a higher incidence of RLS than in the general population.

Methods: Prospective study at two community based American Academy of Sleep Medicine accredited sleep centers in Kentucky, USA. Participants were patients over age 18 undergoing a PSG for OSA (n=357; mean±SD, 48±13 years, 104±25 kg). Following informed consent the Cambridge-Hopkins RLS questionnaire, Epworth Sleepiness Scale and an in-house questionnaire regarding initial insomnia were administered. Patients subsequently deemed to have RLS completed the International RLS scale. Standard data were collected from the PSG.

Results: OSA was diagnosed in 319 patients, of which 32.3% had definite or probable RLS. In the 38 patients whom did not have OSA, 23.7% had definite or probable RLS. In all patients, RLS was severe in 9.2% (IRLS-scale>20) and moderate in 12.6% (IRLS-scale 11-20). The incidence of RLS (31.4%) in patients undergoing a PSG was statistically significantly higher than the 10% estimated for the general population (Chi-squared; p<0.001).

Conclusion: The incidence of RLS in patients undergoing a PSG was statistically significantly higher than in the general population. All patients undergoing a PSG should be specifically asked about RLS symptoms. Evaluating OSA provides an opportunity to identify other significant sleep disorder not otherwise detected through PSG.

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0851

THE PREVALENCE OF RESTLESS LEG SYNDROME IN TAIWANESE ADULTS

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Introduction: Restless leg syndrome (RLS) is a common sensorimotor disorder which affect 5-10% of general population. The prevalence of RLS is widely studied in western country after revision of the criteria. The reports of the prevalence of RLS in Asian population are rare and with methodology confounded. Since the genetic difference of RLS between races had been raised in recent studies, it is necessary to have a

prevalence data from Asian population according to the standard criteria and methodology.

Methods: Computer-assisted telephone interviewing (CATI) was used in this survey. Taiwanese residents aged over 15 were the investigation subjects. Questions in the telephone interview obtained data for RLS, chronic insomnia symptoms, major medical conditions and demographic information. Pre-test of the questions, training course for the interviewer, and pre-interviewing meeting were done before the survey. From Oct. 25, 2006, to Nov. 6, 2006, 4011 persons successfully completed the interview during the investigation period. This number reached the requirement of a 95% confidence interval (CI) and bias of 3%.

Results: The prevalence of RLS among adults who fit for all 4 criteria in Taiwan was 1.57%. The BMI is higher in RLS group. RLS population has higher percentage to complain chronic insomnia. RLS population also has a higher incidence to comorbid with hypertension, cardiovascular disease, respiratory disease arthritis, backache and mental illness. Female with RLS also have a higher incidence to have post-menopausal syndrome. Incidence of anemia and hemodialysis(H/D) was not high in RLS population which may due to subjects themselves was not aware of anemia or the prevalence of H/D is too low.

Conclusion: The prevalence of RLS in Asian population is as low as 1.57%. Association of RLS with chronic diseases needs further longitudinal observation and study.

0852

VALIDATION OF AN ABBREVIATED PRE-POLYSOMNOGRAPHY QUESTIONNAIRE FOR SCREENING RESTLESS LEGS SYNDROME

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Introduction: The prevalence of restless legs syndrome in a sleep laboratory referral population may be as high as 40%. Questionnaires often administered prior to polysomnography (PSG) could potentially uncover patients with previously undiagnosed RLS. We evaluated whether an abbreviated questionnaire could be used to screen patients for RLS and validated it against the International Restless Legs Syndrome Study Group Severity (IRLS) Score.

Methods: Seventy three consecutive patients (37 women and 36 men) with mean age and BMI of 48 years and 35.2 kg/m² respectively, were referred for PSG to evaluate for a sleep disorder, completed the questionnaire that included a question with a modifier about RLS - "Have you experienced before sleep or on awakening from sleep any restlessness of legs - nervous legs, creeping, crawling sensation or twitching?/ Does anything relieve the sensation? (e.g.) getting out of bed/ massage/ medications etc.". We defined restless legs syndrome (RLS) as an IRLS score ≥ 4 and moderate to severe restless legs if a patient had an IRLS score of ≥11 (RLSsev). The kappa statistic (k) was used to measure agreement, beyond chance, between the single question in the pre-PSG questionnaire and (1) IRLS or (2) RLSsev.

Results: Thirty-six patients (49.3%) had RLS, and 29 (39.7%) had RLSsev. The abbreviated questionnaire correctly predicted whether or not the patient had RLS 92% of the time. Sensitivity and specificity were 97% and 86% respectively. Agreement was highly significant (k=84%, 95% CI = 71% - 96%). The question also predicted RLSsev with a sensitivity and specificity of 97% and 73% respectively (k =65%, 95% CI = 48% - 82%).

Conclusion: This study confirms the previously reported high incidence of undiagnosed RLS in a PSG referral population. An abbreviated pre-PSG questionnaire can be used to reliably screen patients for RLS. Further studies in a non-selected population are needed.

0853

REGIONAL CEREBRAL BLOOD FLOW CHANGES IN PATIENTS WITH RESTLESS LEGS SYNDROMECho J^{1,2}, Lee J³, Joo E¹, Tae W¹, Hong S¹

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Introduction: To investigate the regional cerebral blood flow (rCBF) changes in the patients with restless legs syndrome (RLS), we performed 99mTc-ethylcysteinate dimer (ECD) single photon emission computed tomography (SPECT) in RLS patients and normal controls.

Methods: Interictal 99mTc-ECD brain SPECT was performed in 36 drug naïve RLS patients (M/F=11/15) and sex/age matched normal controls. Patients met the International Restless Legs Syndrome Study Group criteria for RLS. During screenings, patients underwent neurological examinations, screening laboratories. They scored the International Restless Legs Scale (IRLS), the Epworth Sleepiness Scale (ESS), and the Stanford Sleepiness Scale (SSS). For SPM analysis, all SPECT images were spatially normalized to the standard SPECT template and then smoothed using a 12-mm full width at half-maximum Gaussian kernel. The ANCOVA test was used to compare rCBF of RLS patients and normal controls.

Results: Mean age of patients was 48.3 ± 10.0 years old. Mean score of IRLS was 26.6 ± 6.0 (ranged 11 - 38), which suggested that patients had moderate to severe RLS symptoms. Mean ESS was 7.5 ± 2.7 and mean SSS was 2.5 ± 1.1 . Mean ferritin level was 50.0 ± 31.7 ng/ml (ranged 3.4 - 259). Sixteen patients performed overnight polysomnography and all of them accompanied periodic limb movements during sleep [total PLMS index; 50.0 ± 31.7 , movement arousal index; 6.0 ± 3.4 /hour]. SPM analysis of brain SPECT images between 36 RLS patients and 30 sex/age-matched normal subjects showed increased rCBF in right putamen and insula in RLS patients at uncorrected $p < 0.005$.

Conclusion: Our study demonstrates rCBF increase in right putamen and insula areas in RLS patients.

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0854

PHASIC MUSCLE ACTIVITY DURING SLEEP IN BILATERAL VERSUS UNILATERAL PARKINSON'S DISEASE (PD)

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Introduction: PD is associated with excessive phasic EMG (PEM) activity during sleep. We compared PEM in patients with predominantly unilateral (UNI) vs bilateral (BI) disease.

Methods: 55 PD pts (X age = 63.4; SD = 10.7; 44 M; 11 W) with PD (15 BI, 40 UNI) underwent PSG. PEM was quantified as previously described (Bliwise et al, J Clin Neurophysiol 2006; 23: 59-67). We examined: mentalis, left and right brachioradialis (LA, left arm; RA, right arm) and anterior tibialis (LL, left leg; RL, right leg), from both REM/NREM sleep. Data were analyzed blind to the patient's clinical condition and are presented as the % of 2.5 sec intervals with muscle activity.

Results: BI and UNI did not differ in disease duration (9.3 vs 9.8 yrs) or L-dopa daily dose (680 vs 720 mg). Differences in mentalis were NS (REM, $p = .761$; NREM, $p = .279$). BI had significantly higher PEM rates from nearly all limb muscles in both REM and NREM (LA REM, $p = .012$; LA NREM, $p = .0006$; RA REM, $p = .039$; RA NREM, $p = .008$; LL REM, $p = .004$; LL NREM, $p = .024$; RL REM, $p = .042$; RL NREM, $p = .115$). PEM in BI was typically twice that of UNI, e.g., for BI LA REM = 0.26 whereas for UNI LA REM = 0.15; for NREM, corresponding LA values were .19 vs .10).

Conclusion: Elevated PD PEM is compatible with extranigral pathology in mesopontine tegmental nuclei governing phasic and tonic REM-sleep early in PD, or loss of pallidal inhibitory influences upon these nuclei. The ability for PEM to differentiate BI from UNI that are otherwise matched for traditional clinical measures of disease severity argues for further investigation of sleep specific pathological motor activity in pre-clinical and clinical characterization of PD.

Support (optional): NS-050595

0855

SIXTY FOUR PERCENT OF PATIENTS WITH IDIOPATHIC REM SLEEP BEHAVIOR DISORDER DEVELOPED A NEUROLOGICAL DISORDER AFTER A MEAN CLINICAL FOLLOW-UP OF 7 YEARS

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Introduction: We previously showed that in our sleep center 45% patients with idiopathic REM sleep behavior disorder (IRBD) developed a neurological disorder after a mean follow-up of 5 years (Lancet Neurol 2006;5:572). The aim of our study was to determine the frequency and nature of the neurological diseases that developed after two additional years of follow-up.

Methods: Clinical history, neurological examination and neuropsychological tests were performed in November 2007 to those patients that were diagnosed with IRBD between 1991 and 2003 at our sleep center. Diagnosis of Parkinson's disease (PD), dementia with Lewy bodies (DLB), multiple system atrophy (MSA) and mild cognitive impairment (MCI) were done according to published criteria.

Results: In November 2007, 44 patients (39 men, 5 women) were evaluated. Their reported RBD onset was 62.6 ± 7.3 years and current age was 75.7 ± 6.4 years. After a follow-up of 6.8 ± 2.6 years in our sleep center, 28 (63.6%) patients developed a neurological disease: PD in 10 (4 with associated dementia), DLB in 8, MSA with pure cerebellar syndrome in 1, and MCI in 9 in whom visuospatial dysfunction and memory impairment were prominent. During the additional two years of follow-up 2 patients with mild cognitive impairment converted into DLB, 7 subjects with IRBD developed MCI and 1 with IRBD developed PD.

Conclusion: At our sleep center, 64% of IRBD patients developed a neurological disorder after a mean follow-up of 7 years. Patients with IRBD are at high risk of developing PD, DLB, MCI and MSA.

0856

SLEEP DISORDERS IN OCULOPHARYNGEAL MUSCULAR DYSTROPHY: A CLINICAL AND POLYSOMNOGRAPHIC STUDY

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Introduction: Oculopharyngeal muscular dystrophy (OPMD) involves oropharyngeal and extraocular muscles. We speculate that OPMD might be associated with sleep disorders such as obstructive sleep apnea, similar to other neuromuscular conditions including myotonic dystrophy, Duchenne muscular dystrophy, amyotrophic lateral sclerosis, and myasthenia gravis. To date, only one adult patient with OPMD with obstructive sleep apnea has been reported.

Methods: We identified four patients with OPMD by clinical examination and genetic testing. We analyzed extensive clinical data including Epworth sleepiness scales (ESS), data from overnight polysomnography, and witnessed accounts from patients' bed partners and family members regarding their sleep patterns.

Results: The four patients with genetically confirmed OPMD were male and ranged in age from 53 to 69 years old. Three were of Hispanic and one of German descent. All patients had witnessed accounts from their bed partners of snoring and excessive daytime sleepiness (ESS 9-10). Polysomnography revealed a reduced sleep efficiency ranging from 69% to 85%. Three patients had obstructive sleep apnea and three patients had an increased periodic limb movement index (PLM index range 26/h-31/h).

Conclusion: To our knowledge, this cohort of patients represents the largest group of patients with OPMD evaluated for a sleep disorder. OPMD patients in this cohort were found to have obstructive sleep apnea and periodic limb movements. OPMD may contribute to pharyngeal dilator muscle dysfunction and impair the maintenance of upper airway patency by affecting the compliance and collapsibility of the upper airway. Both obstructive sleep apnea and periodic limb movements likely contributed to the excessive daytime sleepiness in this patient population.

0857

THE PREVALENCE OF SLEEP DISORDERED BREATHING IN STROKE AND TIA PATIENTS: A META-ANALYSIS

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Introduction: Obstructive sleep apnea is common in stroke and transient ischemic attack (TIA) patients, but the prevalence of OSA in this population is unknown.

Methods: The prevalence of SDB in stroke and TIA patients was determined by meta-analysis using a random-effects model with weighted averages. A systematic literature search of MEDLINE through October 2007 was conducted to find articles that evaluated acute stroke and TIA patients with polysomnography for SDB. Stroke and TIA patients were combined because studies have found equivalent rates of SDB in both groups and most studies did not differentiate between stroke and TIA. Studies were excluded if a future article by the same author included patients from the same date range ($n=7$).

Results: Thirty-six articles reported prevalence of SDB in stroke or TIA patients. Twenty-two articles including 1712 patients were included. The SDB was primarily obstructive in most patients. The prevalence of sleep disordered breathing in stroke and TIA patients with apnea-hypopnea index (AHI) of >5 , >10 , >20 , >30 , >40 were 76% (95%CI 67-82%),

62% (95%CI 57-66%), 39% (95%CI 33-45%), 28% (95%CI 20-39%), and 13% (95%CI 10-18%) respectively. The prevalence of AHI>10 was not significantly different in patients evaluated in the within 72 hours of stroke or TIA onset (58% (95%CI 53-64%) compared to after 72 hours (64% (95%CI 55-73%). In a subanalysis of the studies in which ischemic stroke and TIA data could be isolated from hemorrhagic stroke data, the prevalence of AHI >5 in hemorrhagic stroke patients was 67% which was not significantly different from the combined prevalence of 76%.

Conclusion: SDB is very common in stroke and TIA patients and is primarily obstructive in nature. Evaluation for sleep disordered breathing in this population should be done to decrease risk of future cardiovascular events, and decrease stroke morbidity and mortality.

0858

CAP ANALYSIS IN TEMPORAL LOBE EPILEPSY

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Introduction: Increase in Cyclic alternating pattern (CAP) rate has been described in patients with epilepsy. However, data in patients with Temporal Lobe Epilepsy (TLE) is still scant. The aim of this study was to analyze CAP expression during NREM sleep in patients with TLE comparing to control group.

Methods: We performed a study comparing sleep parameters measured in 13 TLE patients (33.8 ± 8.5 years old) to those of 13 age and gender matched controls (26.1 ± 9.2 years old). All patients underwent MRI, and were diagnosed as having temporal lobe epilepsy, treated with anti-epileptic drugs, without seizures for at least 4 weeks prior to the study. Sleep and CAP parameters were analyzed according to international criteria. The comparison of the two groups was performed with the Mann-Whitney U test.

Results: All subjects in this protocol showed normal sleep efficiency. TLE patients showed: lower sleep latency (5.8 ± 2.4 vs 14.2 ± 7.6; p=0.002); lower duration of the stage IV (30.8±14.8 vs 51.4±12.5 minutes, p=0.001); and higher arousal index during sleep (10.2 ± 2.9 vs 6.3 ± 1.7; p=0.001); and higher arousal index during NREM sleep (10.3 ± 3.4 vs 6 ± 2; p=0.001), compared to normal controls. Arousal index during REM sleep was similar in both groups (9.7 ± 3.8 versus 7.4 ± 2.4; p=0.075). Patients with TLE showed an increase in CAP rate (44 ± 5.2% versus 31.8 ± 3%; p<0.001) and longer CAP time (133.8 ± 15.6 min. versus 99.4 ± 9.6 min; p<0.001) when compared to control group. No difference was found for CAP phase A duration (9.3 ± 1.2 sec. vs 8.7 ± 0.6 s; p<0.131). While phase B was longer for patients with LTE (22.9 ± 1.7 vs 21.5 ± 1.8 s; p<0.05). Subgroup analysis considering both genders did show significant differences.

Conclusion: Patients with treated TLE showed an increased CAP rate and arousal index in relation to normal control subjects, suggesting an increased instability of NREM sleep, and a more fragmented sleep. The authors hypothesize that sleep instability and fragmentation in patients with TLE are due to epilepsy itself, suggesting an effect on systems responsible for the maintenance and stability of sleep. Sleep instability and fragmentation may influence seizure control.

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0859

SLEEP EDUCATION CLASSES FOR PARENTS OF CHILDREN WITH AUTISM SPECTRUM DISORDERS

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Introduction: This research program was designed to improve sleep in children with autism spectrum disorders (ASD) using non-pharmacological methods. Children with ASD have a high prevalence of insomnia. Our hypothesis is that parents of children with autism and insomnia can teach their children to become better sleepers and that enhanced sleep in children with ASD will result in improved daytime behavior. Additionally, parents may also benefit from better sleep and become empowered by their successes in this program, allowing them to more effectively meet the special needs of their children.

Methods: We provided a structured setting in which small groups of parents (approximately three to five families at a time) learned about establishing effective sleep habits for their children with ASD. All children had a clinical diagnosis of ASD, confirmed by the Autism Diagnostic Observation Schedule, and did not have a history of epilepsy. A series of three two-hour workshops were conducted on-site at The Vanderbilt Children's Hospital. Workshops were led by two physicians with presentations as well as breakout sessions, homework, and question-and-answer periods. Sleep and behavior questionnaires, in addition to one-week of actigraphy, were collected prior to the workshop and one month after the workshop. Data were analyzed using paired t-tests to detect change.

Results: To date, we have analyzed data obtained from 12 children, ages 3-10 years, whose parents have completed the workshop. Improvements were seen in the total scale as well as several insomnia-related subscales of the Child Sleep Habits Questionnaire (CSHQ), including bedtime resistance, sleep onset delay, sleep duration, and sleep anxiety (p ≤ 0.03), but not subscales related to sleep-disordered breathing and parasomnias (p > 0.1). Significant improvements were also noted in the affective (p = 0.007) and attention-deficit hyperactivity (p = 0.027) domains of the Child Behavior Checklist (CBCL) but not in other domains. Review of individual actigraphy records showed improvements in sleep latency and night wakings.

Conclusion: Sleep education classes improve sleep parameters and aspects of daytime behavior in children with ASD. We are continuing to carry out these classes, aiming for a sample size of 25-30 children. Future directions include expanding our classes to incorporate adolescents, bringing our program into community settings, and developing a teaching role for non-physician educators.

Support (optional): Organization for Autism Research and the Vanderbilt General Clinical Research Center

0860

THE INFLUENCE OF OBSTRUCTIVE SLEEP APNEA ON ALZHEIMER'S DISEASE: A PROSPECTIVE STUDY

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Introduction: There is an association between Alzheimer's disease and sleep disordered breathing. This study evaluates the interaction between polysomnographic and blood parameters of OSA (obstructive sleep apnea) and non-OSA AD (Alzheimer's disease) patients and normal aged controls.

Methods: Thirty-seven, patients, 49-91 yrs, 12 males, 25 females, with mild to moderate Alzheimer's disease, (22 OSA, 15 non-OSA) and 22 normal aged controls, 63-85 yrs, 10 males, 11 females (14 OSA, 7 non-

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OSA) were included. Polysomnography, EEG spectral analysis, laboratory tests and cognitive evaluation using ADAS-cog subscale were performed. Cognitive and sleep data were analyzed using factorial ANOVA. Main effects were presence of OSA and AD.

Results: AD patients with OSA showed reduced microarousal index compared with non-OSA while increased microarousal index was found in non-AD with OSA (interaction $p<0.05$). There was a reduction in REM sleep percentage in AD patients independently of OSA condition ($p<0.05$). Overall, frontal, parietal, temporal and occipital slowing ratio was increased in AD patients without OSA effect ($p<0.05$). Folic acid levels were significantly reduced in OSA and AD patients (interaction $p<0.05$). Platelet count was increased in OSA patients with no AD effect ($p<0.05$). LDL and Na levels were increased in AD patients ($p<0.05$). Calcium, amylase, and TGP levels were reduced in AD patients ($p<0.05$). ADAS-cog scores were significantly different between AD and non-AD patients, as expected. OSA did not influence ADAS-cog score.

Conclusion: Microarousal index was paradoxically reduced in OSA-AD patients. OSA did not affect cognitive scores in AD patients. The combination of OSA and AD was associated with reduced folic acid levels.

Support (optional): FAPESP AFIP

0861

PERIODIC LIMB MOVEMENT AND RESTLESS LEG SYNDROME IN SPINAL CORD INJURY — IMPLICATION OF SPINAL CORD GENERATOR

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Introduction: The periodic limb movement (PLM) has been found in much different type of conditions including normal and pathologic status. However, its pathophysiological nature is still uncertain. It has closely linked with arousal in many studies, and indicated arousal heralding the onset of PLMS. Nevertheless, PLMS had been reported in cases of spinal cord injury (SCI), which is devoid the influence of brain and brainstem.

Methods: Seven cases of SCI with cervical transected quadriplegia and twelve cases of non-SCI were recruited. The cerebral activities prior to the onset of limb movement (LM) were spectrally analyzed separately in quiescent period prior to the PLM cluster and 3 inter-movement interval periods within PLM cluster including short (5-20 sec), intermediate (20-40 sec) and long (40-90 sec) periods. The PLM in wake (PLMW) and heart rate variability were analyzed in each case.

Results: The cerebral activity prior to the onset of LM had no statistical difference in quiescent and inter-movement periods between cases with and without SCI. The frequency of short inter-movement period was 46% vs. 88% in non-SCI vs. SCI cases respectively. The PLMW was predominantly in every case with SCI, but not existing in any cases without SCI. Autonomic activities were very fluctuated in various sleep stages, not in wake stage, in cases of SCI.

Conclusion: Since the cerebral activities had no statistical difference between the cases with and without SCI, the cerebral activities should have no causal relation to the onset of PLM. Predominant PLMW, frequent short inter-movement period and fluctuated autonomic activities in sleep in cases of SCI could be related to the dis-inhibition from brain and brainstem. Thus, persistent PLM and PLMW in cases of SCI may indicate the PLM to be generated from spinal cord, not in brain or brainstem, particularly the RLS.

0862

REST-ACTIVITY RHYTHM IN PATIENTS WITH PROGRESSIVE SUPRANUCLEAR PALSY

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Introduction: Progressive supranuclear palsy (PSP) is a neurodegenerative disease resulting from the aggregation of tau proteins. Symptoms include axial dystonia, bradykinesia, falls, dysphagia, and vertical gaze palsy. Patients may also experience behavioral and personality changes, cognitive decline, and sleep disturbances. Although a high degree of nighttime sleep fragmentation, reduction in sleep time, disorganization of sleep stages, and decreased REM episodes have been documented to occur in PSP, no studies have been done to examine rest-activity rhythm disruption and circadian abnormalities in this population. The purpose of this ongoing descriptive study is to explore the characteristics of sleep, wake and circadian rhythms in patients with PSP.

Methods: To date, five community dwelling subjects diagnosed with PSP have participated in actigraphic data monitoring continuously over a two-week period (AW64 Actiwatches, Minimitter). Mini-Mental State Exam (MMSE) and Clinical Dementia Rating (CDR) scores were collected. Rest-activity rhythm variables were calculated using both parametric and nonparametric methods. Primary family caregivers completed the Epworth Sleepiness Scale.

Results: Subjects were, on average, 67 years old (SD=8) and 60% female. Mean MMSE score was 26.60 (SD=3.36) and mean CDR total score was 1.10 (SD= 0.55). All participants experienced nighttime sleep difficulties. The average Epworth Sleepiness Scale score was 8.00 (SD=4.85). Circadian measures exhibited weak interdaily stability and large intradaily variability. The strength (mean relative amplitude) of the rhythm was low as was the goodness of fit to cosinor analyses (r^2 mean=0.056, SD=0.047). Mean nighttime sleep was 73% (SD=13%), daytime sleep was 47% (SD=22%), and daytime immobility was 38% (SD=19%). The ratio of daytime average activity counts per epoch to nighttime activity counts per epoch was 3.46 (SD= 2.30).

Conclusion: These results indicate that PSP is associated with disruption in circadian rhythm and sleep measures. Further, these disruptions appear to occur early in the disease.

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0863

AGRYPNIA EXCITATA

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Introduction: Agrypnia Excitata (AE) is a generalized overactivity syndrome characterized by loss of slow-wave sleep, mental oneirism and marked motor and autonomic sympathetic activation. AE was described in fatal familial insomnia (FFI), Morvan's fibrillary chorea (MC) and delirium tremens (DT). We describe the recurrence of AE in three cases.

Methods: All patients performed video-polysomnography. The first case was a sporadic Creutzfeldt-Jakob (sCJD) case. This 77-year-old male patient was relevant for seven months history of gait ataxia, daytime hypersomnolence and complex 'oneiric' behaviours at wake-sleep transition. 1H-MRS and neuropathologic examination showed thalamic involvement. Molecular studies revealed a VV2 sCJD subtype. The second case was a 71-year old male patient with a MC. He presented with severe

weight loss, depression, burning legs pain, insomnia, excessive sweating and gait disturbance. Electromyography documented neuromyotonia and the absence of sympathetic skin responses (SSR). The third case was a 69-year-old male patient with daytime hypersomnolence, complex motor behaviour in sleep and mild dementia. 1H-MRS failed to show spongiform degeneration. Furthermore EMG was negative for neuro-myotonia and SSR was normal.

Results: Video-PSG documented in the first patient polygraphic data consistent with those of FI with alternating epochs of Wake/Wake-REM and N1/N1-REM and subcontinuous motor activity (parcellar and segmental myoclonic jerks or more complex purposeful repetitive behaviours). In the second patient PSG documented the presence of wake for most (81.3%) of the time, intermixed with brief period of theta activity and rapid eye movements. Continuous motor activity was also documented. The patient was treated with plasmapheresis and immunoglobulin iv leading to significant improvement of insomnia, neuromyotonia and sleep pattern (documented polygraphically). In the third case the PSG showed the presence, for most of the recording (64.1% of total recording time), of sleep pattern consistent with that of FI. However, a two-hours period (35.9%) was characterized by physiologic sleep (presence of sleep spindles, K-complexes and SWS). PSG also documented subcontinuous motor activity (myoclonic parcellar and segmental jerks) in all stages.

Conclusion: Agrypnia excitata may characterize different neurological diseases and offers some interesting issues for discussion on involvement of thalamic-limbic circuits in the neurophysiology of sleep

0864

SLEEP AND AUTONOMIC DYSFUNCTION

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Introduction: We have observed dysautonomia in conjunction with hypersomnia in a clinical subset of patients that fail to demonstrate other clinical sleep disorders. We speculate that autonomic dysfunction (AD) may be independently associated with hypersomnia. In order to assess such an association, a cohort of patients with autonomic dysfunction undergoing both comprehensive autonomic reflex testing and polysomnography were evaluated.

Methods: Autonomic testing and polysomnography (PSG) from 2005 through 2007 were retrospectively reviewed. Sleep history was retrieved from a comprehensive sleep questionnaire done at the time of PSG. Hypersomnia and insomnia were rated on a scale of 1(best) to 5(worst). Groups were compared using descriptive statistics and Fisher Exact Test.

Results: Forty four of 51 patients had abnormal AD testing and complete records were reviewed (31 females, mean age 45.4 +/- 13.1 years). Sleep complaints included hypersomnia (n=20; 45%), insomnia (n=15; 34%), and sleep disordered breathing (n=9; 20%). In this group, 34 (77%) demonstrated isolated sympathetic dysfunction (SYMD), 4 (9%) isolated parasympathetic dysfunction (PARD), and 6 (14%) patients with both systems involvement. Isolated PARD was associated insomnia in 4 (100%) while only 9 (26%) patients with SYMD had insomnia (p < 0.001). When OSA (AHI >5 events/hr.) was excluded (n=14), the remaining 30 patients demonstrated severe hypersomnia scores (4.2 +/-0.2) with 24 out of 30 patients (80%) having scores > 4. Of these patients, 27 patients (90%) had SYMD.

Conclusion: Hypersomnia is common in patients with autonomic dysfunction referred for polysomnography independent of sleep apnea and other common sleep disorders. This group demonstrates predominantly sympathetic dysfunction. A second group demonstrating predominantly parasympathetic dysfunction presents with primarily insomnia. We suggest that autonomic dysfunction may be an independent contributor to hypersomnia and that further study is warranted.

0865

MULTICENTRE CASE-CONTROL STUDY ON RESTLESS LEGS SYNDROME IN MULTIPLE SCLEROSIS: THE REMS STUDY

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Introduction: The existence of a symptomatic form of restless legs syndrome (RLS) secondary to multiple sclerosis (MS) is still controversial. The aim of the study was to assess the prevalence and the possible associated risk factors of the RLS in MS by a prospective, controlled, face to face, multicentre epidemiological survey.

Methods: Twenty Sleep Centers, certified by the Italian Association of Sleep Medicine, participated to the investigation. Eight hundred and sixty one patients affected by MS and on 649 control subjects were included. Data regarding demographic, clinical, presence of the international criteria for RLS and the severity of RLS, hematological tests and visual analysis of cerebro-spinal MRI were collected.

Results: The prevalence of RLS was 19% in MS and 4.2% in control subjects, with a risk to be affected by RLS of 5.4 (CI ± 95%: 3.56-8.26) times greater for MS patients than for controls. In MS patients the following risk factors for RLS were found to be significant: older age, longer MS duration, the primary progressive MS form, higher global, pyramidal and sensory disability, and the presence of leg jerks before sleep onset. MS patients with RLS more often referred sleep complaints and a higher intake of hypnotic medications than MS patients without RLS. Iron storage indicators, creatinine and folate plasmatic levels did not differ between MS patients with or without RLS. RLS associated to MS was more severe than that of control subjects.

Conclusion: RLS is significantly associated to MS, especially in patients with severe pyramidal and sensory disabilities. These results strengthen the idea that the inflammatory damage correlated to MS, probably involving long cerebro-spinal nervous pathways, may induce a secondary form of RLS. As well as in idiopathic cases, RLS has a significant impact on sleep quality in MS patients, therefore it should be searched especially in the case of insomnia unresponsive to the common hypnotic drugs.

0866

INTERMITTENT HYPOXIA DURING SLEEP IS ASSOCIATED WITH DEFECTS IN THE MYELIN SHEATH

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Introduction: Intermittent hypoxia (IH) is recognized as one of the hallmarks of obstructive sleep apnea syndrome (OSAS), the most severe form of sleep disordered breathing (SDB). Exposure to IH leads to oxidative neuronal and cognitive impairment in rodents. However, little is known on how glial cells respond to sleep-associated IH. In this study, we determined the effects of acute IH exposure on oligodendrocytes in developing and adult mice.

Methods: Postnatal day 2 (P2) pups and young adult mice (P50) were exposed to either 4 days of IH (8% O₂/21% O₂/90s switch/12hrs during the light cycle), or normoxia (RA, 21% O₂). The brain and spinal tissues were dissected for myelin staining and immunohistochemistry at different post-exposure days. Before the young adult mice were sacrificed, the conductive properties of neural pathways were evaluated by motor evoked potential measurements elicited by magnetic stimulation (M-MEP). This technique is capable of monitoring the integrity of descending tracts of nervous system.

Results: Compared to age-matched normoxic controls, fewer anti-MAG labeled fibers were found in corpus callosum and spinal cord after early postnatal IH exposures, indicating that myelination developed in a de-

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laid fashion in these mice. Furthermore, myelin sheaths in adult mice undergoing the IH exposures displayed losses in their lipid components and myelin-related proteins, which may underlie the electrophysiological deficits.

Conclusion: These findings suggest that myelin-forming cells are susceptible to alterations in the oxygenation patterns, and that acute IH can induce both neuronal and oligodendroglial injury.

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0867

RISK OF SLEEP-DISORDERED BREATHING IN PARKINSON'S DISEASE AND NON-BLOOD RELATIVES

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Introduction: Case series suggest that sleep disordered breathing (SDB) may be common in Parkinson's disease (PD) patients, but comparisons to appropriate controls from similar environments have rarely been made. We used the Berlin Questionnaire (BQ) and Obstructive Sleep Apnea Questionnaire (OSAQ), both previously validated as screens for SDB, to assess SDB risk in PD and to test potential associations between SDB in these patients and quality of life, as measured by the SF-36.

Methods: Patients and non-blood relatives (often spouses) without PD were recruited from a University-based Parkinson's disease clinic. All subjects, required to have a Mini Mental State Examination score > 16, completed the BQ, OSAQ, SF-36, and Epworth Sleepiness Scale (ESS). Movement disorder specialists completed the Unified Parkinson's Disease Rating Scale (UPDRS).

Results: 63 of 96 PD patients (65.6%) were male, vs. 17 of 58 controls (29.3%, $p < .01$). The proportions of PD patients, in comparison to controls, with positive BQ or positive OSAQ were not significantly different ($p=0.29$ and $p=0.11$ respectively, adjusted for age). Patients with PD, in comparison to control subjects, had similar rates of positive BQ scores ($p=0.13$). However, those patients with moderate to severe PD (stages 3, 4, and 5; $n=28$), in comparison to controls, did more often show positive BQ scores ($p < 0.01$). PD patients with positive BQ scores, in comparison to those with negative BQ scores, showed lower quality of life scores (SF-36, $p=0.003$). Sleepiness (ESS>10) was more common among PD subjects than controls, but this relationship was not appreciably diminished after controlling for snoring or witnessed apneas.

Conclusion: PD may increase risk for SDB primarily when PD has reached moderate to severe stages. However, our data do not suggest that SDB will explain the excessive subjective sleepiness commonly reported by PD patients.

0868

SLEEP DISTURBANCES IN CAREGIVERS OF CHILDREN WITH EPILEPSY

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Introduction: Sleep patterns of parents of healthy children has been documented. Some studies have addressed the effect of chronic illness in caregivers sleep. Children with epilepsy, especially in they have nocturnal seizures may disrupt caregivers sleep. There have been no studies documenting the effect of children with epilepsy in caregivers sleep patterns.

Methods: We conducted a survey about children with epilepsy and their caregivers sleep disturbances and described preliminary findings. The inclusion criteria included children with epilepsy from 1 month to 18

year-old who presented to NYU Comprehensive Epilepsy Center outpatient clinic.

Results: There were 22 patients with epilepsy screened. The mean age was 6.5 years and 12 were boys. There were 10 patients who had nocturnal seizures. Eleven patients had a learning disability. Sixteen children slept on her own bed and 5 children slept with their parents most of the time. Eight children reported troubles to fall asleep and 7 children reported to have problems to sleep through the night. The caretakers had an average of 7.15 hours of sleep at night, but 12 of them reported no adequate sleep. Seven caregivers reported troubles to fall asleep and mentioned worries about intensity of child seizures and general well being of the child as the main reasons. Six caregivers reported their sleep to be worse now than before their children epilepsy diagnosis. Seventeen caregivers reported fatigue and 12 reported not feeling refreshed in the mornings. There were no enough patients to establish a relationship of children seizure frequency with their caregivers sleep disturbances.

Conclusion: The caregivers of children with epilepsy reported fatigue and non restorative sleep. The caregivers also reported problems to fall asleep mostly related to worries about seizure intensity and child's well being.

0869

DIAGNOSTIC UTILITY OF SLEEP LABORATORY TESTING IN PATIENTS WITH MEMORY PROBLEMS IN THE PRESENCE OF SNORING, FATIGUE AND SLEEPINESS

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Introduction: The prevalence of sleep disorders on objective laboratory testing in patients with memory problems is unclear. As sleep disorders are often easily treatable, accurate diagnosis of sleep problems in these patients is important not only to decrease morbidity but also to mitigate drug related costs. As the population ages, the burden of both of memory problems and sleep disorders is expected to increase exponentially.

Methods: Charts of 48 eight patients with chronic memory problems and negative imaging studies from a clinical neurology practice who underwent sleep studies as a part of the workup over the last 6 months were reviewed. Patients who had symptoms of snoring underwent polysomnography and patients who had unexplained fatigue/sleepiness underwent polysomnography followed by MSLT testing. All patients were followed up and memory problems reassessed periodically. 23 (50%) had neuropsychology evaluations as well and all underwent electroencephalography studies. Patients who met clinical criteria for Alzheimers/Lewy body disease were also treated with appropriate medications. Seventeen patients (35.4%) were under 60 years of age and twenty two (45.8%) were women.

Results: 36/48 (75%) were diagnosed with obstructive sleep apnea (Medicare criteria) and 10/26 (38.4%) patients who underwent MSLT testing for unexplained fatigue/sleepiness had a mean sleep onset latency below 8 minutes. No patient had a periodic limb movement disorder arousal index over 20/hr. Two patients had REM behavior disorder and Parkinsonism. In 8/36 (22.2%) patients on CPAP therapy for obstructive sleep apnea, the memory problems significantly improved in 2-3 months.

Conclusion: Patients with snoring, fatigue, daytime sleepiness, and memory problems have a relatively high diagnostic yield when evaluated in the sleep laboratory. Evaluation for correctable sleep disorders should be added to the workup for dementia especially when symptoms of sleep disorders are present.

0870

PREDICTORS OF SLEEP APNEA IN EPILEPSY: DOES SEIZURE CONTROL MATTER?

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Introduction: Recent reports suggest an increased prevalence of OSA in patients with medically refractory epilepsy (Malow et al., 2000) and older adults with late-onset or worsening seizures (Chihorek et al., 2007). No study has investigated OSA prevalence to assess the impact of seizure control.

Methods: This is a cross-sectional study involving adults with epilepsy. Subjects completed a series of questionnaires and underwent PSG followed by MSLT. Sleep apnea was defined by an AHI > 5. Independent variables included mean monthly seizure frequency, number of anti-epileptic drugs (AEDs), measures of daytime sleepiness (self-reported EDS, Epworth Sleepiness Scale, mean sleep latency), age, gender and BMI). Univariate analyses were performed using univariate logistic regression models, crude odds ratios (OR) and the likelihood ratio test (LRT) for significance. Multiple logistic regression models were fit to describe the relationship between AHI and the covariates.

Results: 61 subjects; 28 with OSA and 33 without OSA were included. Subjects with OSA were older (46.25 + 14.23 vs. 37.88 + 11.73; p=0.01), slightly more likely to be male (64.71 vs. 35.29%; p=0.07) and had a higher BMI (31.57 + 6.61 vs. 26.66 + 5.29). There was no significant difference in seizure frequency between OSA (5.55 + 9.07) and nonOSA (3.93 + 8.15) groups (adjusted OR: 1.0; p=0.46). There was no strong association between AHI and the other variables.

Conclusion: In this sample, the odds of OSA did not vary by mean monthly seizure frequency or number of AEDs. Therefore, concern for OSA should not be restricted to the medically refractory population. Predictors of OSA appear to be similar to that observed in the general population (male gender, higher BMI, older age). Given the potential impact of OSA on seizure control, all people with epilepsy and traditional OSA risk factors should be screened accordingly.

0871

OBSTRUCTIVE SLEEP APNEA IN INTRACTABLE HEADACHE

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Introduction: Studies investigating headache and obstructive sleep apnea (OSA) have revealed conflicting data in regards to an association between headaches and OSA. Pavia T et al. (Archives of Internal Medicine, 1997) and Alberti A et al. (Acta Neurologica Scandinavica, 2005) have documented nocturnal and morning headaches as being associated with OSA, and Poceta JS and Dalessio DJ (Headache 1995) and Loh NK et al. (Archives of Internal Medicine, 1999) have demonstrated that treatment of obstructive sleep apnea can reduce or eliminate morning headache. However, there is lacking evidence in regards to an association between chronic daily headache and OSA.

Methods: We performed a retrospective review of all patients referred from the UNC Headache Clinic to the UNC Sleep Disorders Lab between 2003 and 2006. All patients underwent standard polysomnography (PSG) with additional nasal pressure and continuous end tidal CO₂ monitoring. Studies were scored using classical R&K criteria and respiratory events were scored using the AASM criteria. From the medical record, the patients' headache type, frequency, severity, and outcome were gleaned with follow-up data obtained for after 3 months of therapy. Clinical and PSG parameters were tabulated and subgroups with and without sleep apnea were compared using student's t test (p<0.05).

Results: 95 patients were identified with intractable headache, the majority (86%) having chronic daily headache and 81% having migraine

features. 52 patients had obstructive sleep apnea as determined by an AHI \geq 5.0, and 43 did not have obstructive sleep apnea. The obstructive sleep apnea group had more males (32.7% versus 9.3%, p=0.021), was older (45.8 years versus 39.8 years, p=0.013), and had a higher body mass index (BMI) (32.0 kg/m² versus 28.4 kg/m², p=0.0084) than the group without obstructive sleep apnea. Headache severity and number of headaches per month (27.2 versus 27.9) did not differ between the two groups prior to PSG evaluation. With treatment of OSA and continued medical management of headaches, the change in headache frequency (days per month) did not significantly change between the two groups (-7.0 versus -5.7, p=0.27).

Conclusion: We found that males with intractable headache are more likely to have OSA than females. However, in our cohort, we found that treatment of OSA with medical therapy for headache, did not provide a significant reduction in headache frequency over medical management of those without OSA.

0872

SLEEP PATTERNS IN COMBAT SERVICE VETERANS WITH MINOR TRAUMATIC BRAIN INJURY

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Introduction: Sleep complaints among minor traumatic brain injury (mTBI) patients are high. Some studies suggest a correlation with REM sleep dysregulation in moderate to severe TBI. We evaluated the sleep characteristics of recent combat veterans with mTBI in order to evaluate REM sleep characteristics.

Methods: We reviewed the polysomnographic and multiple sleep latency data from 22 marines who incurred minor traumatic head injury and compared overnight polysomnograms from four age and sex matched controls. A multi-channel polysomnogram was recorded on each patient and standard sleep parameters were evaluated. Additional nasal pressure and continuous end tidal CO₂ were monitored. Studies were scored using AASM sleep scoring criteria. Statistical analyses were done using an unequal student T-test.

Results: Thirty-six percent of our cohort had REM sleep latencies less than 60 minutes and 14 percent had REM sleep latencies less than 30 minutes. Eighteen percent of our cohort had greater than 30 percent REM sleep. No statistically significant differences were noted between the two groups with regards to sleep onset latency, REM onset latency, total sleep time, or sleep percentages. Multiple sleep latency testing reveals a mean sleep latency of 6.9 minutes with 7 (32%) of mTBI subjects demonstrating 2 or more sleep onset REM periods.

Conclusion: Although no statistically significant differences were noted for overnight polysomnogram data, observational findings suggest that mTBI patients may have greater disturbances of REM sleep compared to age matched controls.

0873

CENTRAL SLEEP APNEA IN EPILEPSY

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Introduction: Obstructive sleep apnea (OSA) and epilepsy are common treatable disorders in the general population. Obstructive sleep apnea is present in up to 24% of men and 9% of women, and several reports now suggest that patients with epilepsy are at particular risk. In medically refractory epilepsy, the prevalence of OSA has been reported to be as high as 50% in men and 19% of women. In contrast, no reports have examined the frequency of central sleep apnea (CSA) in patients with epilepsy. Though less common than OSA, CSA could potentially pose a significant problem in the presence of pathology or medications that

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affect the central nervous system. Our objective, therefore, was to assess whether CSA may be more common in epileptics than in “controls” matched for age, sex and apnea-hypopnea index (AHI).

Methods: Twenty five sleep laboratory referred patients with epilepsy and 25 referred controls were identified from a database. Each had undergone diagnostic polysomnography (PSG) that generated a CSA index (number of central apneas/hour), total duration of the central apneas (Td-CSA), and minimum SaO₂% during sleep as well as sleep efficiency.

Results: Subjects with epilepsy had a CSA index (1.39±3.14) that was no different from that of controls (1.33±2.50, T test p=0.921). The Td-CSA during sleep in subjects with epilepsy was marginally lower (49±103.78 seconds) than that for controls (131±249.10 seconds, p=0.079). Minimum SaO₂% and sleep efficiency did not differ between groups (p=0.61 and p=0.94, respectively).

Conclusion: Epilepsy patients referred for evaluation of OSA are not an increased risk of central sleep apnea, and their minimum oxygen saturation during sleep and sleep efficiency were similar to those of matched controls.

0874

COPD: SLEEP AND SHORT-TERM MEMORY

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Introduction: Patients with COPD often complain of confusion, inability to concentrate, and other symptoms related to memory. Length of sleep may affect the patient's ability to remember basic symbols and words. The aim of this analysis, which is part of a larger study, is to examine memory with regard to sleep length.

Methods: 8 COPD patients age 62±5.73 (range 51-69 yrs.), with an FEV₁= 41.17±11.60% predicted for age, sex and height, wore an actigraph overnight. The subjects then completed a visual and verbal memory test within a battery of computerized neuro-behavioral tests.

Results: Measurements of sleep included estimated total sleep time (TST)= 257.74±130.5 min., and estimated maximum length of sleep episode (EMLS)= 54.5±28.15 min. A significant correlation was found with estimated TST and both immediate (r=0.84 and p=0.009) and delayed visual memory (r=0.83 and p=0.02, respectively). Immediate and delayed verbal memory, however, were not found to have a strong correlation with estimated TST (r=0.11 and r=0.21 respectively). There was also a significant correlation between estimated TST and overall memory score (r=0.85 p=0.007) and overall memory percentile normed for age (r=0.91 and p=0.002). EMLS did not correlate with any of the memory related variables.

Conclusion: Results from this analysis show a strong correlation between the amount of time spent sleeping and visual memory. Most COPD patients, however, have an abbreviated length of sleep time in comparison to normal healthy patients. Most patients' tests of memory show low to below average scores. It may be that visual memory is more likely to be affected in declining sleep quality than verbal memory. However, unmeasured variables such as medication or PCO₂ may moderate or attenuate this relationship. The small sample size may preclude finding significance. Data collection is still being carried out.

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0875

PREVALENCE OF SLEEP DISORDERS IN PARA-ATHLETES WITH MEDULLARY INJURY

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Introduction: Studies have investigated the prevalence of sleep disorders (SD) in people with medullary injury (MI) and indicate worsening of sleep quality, especially difficulty in initiating sleep, frequent nocturnal awakenings, snoring, and apneas. Myoclonias, obesity, pain, neurogenic bladder, and sedentarism are frequently associated to SD in individuals with MI. Studies have included patients with chronic MI and sedentary patients. It is well known that the practice of physical exercise is important, leading to healthier behaviors and improving the quality and efficiency of sleep. Objectives: Investigate SD in Wheelchair Basketball (WCB) para-athletes with MI.

Methods: Transversal study carried out during two stages of the Brazilian WCB Championship in the 1st and 3rd division, in 2006 and 2007. Forty-two male para-athletes of teams from different regions in Brazil, mean age 30.8 years (17-51) and mean body mass index (BMI) of 23.9 (17-39). We evaluated the characteristics of the MI, WCB functional classification, and the SD by questionnaire.

Results: As to the characteristics of the MI, 64% were complete, 47% were caused by fire weapons and 90% led to paraplegia. As to the socio-demographic data, 41% have completed elementary and middle school education, 26% have completed high school, 33% have upper education and 55% are married. The para-athletes in this study slept in average 7 and a ½ hours per day, and 70% reported SD. The major SD found were snoring (30%), nocturnal awakening due to myoclonias (13%), excessive daytime somnolence (10%), insomnia (8%), delayed phase (5%), report of witnessed sleep apnea (5%). Of the para-athletes complaining of snoring, 58% had BMI > 25. The most frequent functional class was 1.0 (43%).

Conclusion: Besides the high level of physical activity, the prevalence of SD may be considered high in this population and also the loud snoring, deserving medical attention.

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0876

SLEEP DISORDERED-BREATHING IN PATIENTS WITH HEREDITARY MOTOR AND SENSORY DEMYELINATING POLYNEUROPATHY

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Introduction: Previous study has showed a greater frequency of sleep apnea in one family with hereditary motor and sensory demyelinating polyneuropathy (Charcot-Marie-Tooth disease type 1a).

Methods: In the present study, fifteen patients from eight families were recruited regardless the presence of sleep related symptoms and underwent full night assisted polysomnography, after answering the study questionnaire. The control group consisted in fourteen people, with no differences regarding age, sex, body mass index (BMI) or neck circumference measure (NCM).

Results: Patients showed greater frequency of sleep apnea, defined by apnea/hypopnea index (AHI) greater than five per hour (odds ratio = 11,7), greater AHI, apneas/hypopneas with greater maximum duration, more desaturation and more time with paradoxical breathing pattern. Patients also referred to snore louder and more frequently. Only one patient had central sleep apnea, with great predominance of obstructive events. None of them showed respiratory pattern suggestive of alveolar hypoventilation, although capnography was not utilized. There was no statistical significant difference regarding sleep architecture. There were

no cases of periodic limbs movements. The predictive characteristics were older age, greater BMI and NCM, frequent and loud snore.

Conclusion: The pharyngeal nerves involvement worsening the contractile function of the dilating pharyngeal muscles may represent the pathophysiological mechanism that explains the greater frequency of sleep apnea in the CMT 1a group. Patients with hereditary motor and sensory demyelinating polyneuropathy should be carefully evaluated for sleep symptoms, especially those who are older, obese, with a large neck, and who referred to snore loud and in a frequent basis. In these cases, the polysomnography may reveal sleep disordered breathing, even in the absence of excessive daytime sleepiness. The early diagnosis and treatment are particularly important in this population, because the intermittent hypoxia associated with sleep apnea may cause axonal injury to the peripheral nerves and worse the preexisting polyneuropathy.

0877

POLYSOMNOGRAPHY FINDINGS IN MULTIPLE SCLEROSIS PATIENTS IN SOUTHERN BRAZIL

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Introduction: There is growing awareness that sleepiness and fatigue may be related to sleep disruption in multiple sclerosis (MS). This study reports on retrospective polysomnography (PSG) findings pertaining to nine female MS patients attending a hospital-based care unit in Southern Brazil.

Methods: Subjects (aged 25-58, m.41y) had undergone standard AASM PSG studies between June 2006 and September 2007. Main sleep complaints were non-restorative sleep and nocturnal headache. Expanded Disability Status Scale (EDSS) scores ranged between 1 and 6,5 (m.2,9). Epworth Sleepiness scores were 4-12 (m.8,2). Body mass index was 18,4-31,7 (m.25,2).

Results: During sleep studies, snoring was detected in seven of 9 patients. Total sleep time was 274-453min (m.373,7min), with 56,2-92,5% sleep efficiency (m.77%). Arousal index was 3,3-27,5/h (m.15/h). A PLM index was computed for six patients, ranging from zero to 27/h (m.10,2/h). Global Apnea/Hipopnea Index (AHI) ranged from zero to 6,6/h (m.1,4/h); however, REM Sleep AHI ranged from zero to 90/h, averaging 18,6/h. Sleep efficiency below 85% was seen in patients with one or more of the following: snoring, higher scores on arousals or PLM, REM sleep apnea. A weak positive (0,43) correlation was seen between Epworth scores and sleep efficiency, but not between Epworth scores and EDSS. Sleep microstructure changes were seen in eight of 9 patients, including ambiguous NREM/REM sleep (1), NREM spindle asynchrony (5), paucity of sleep transients (2), prominent alpha sleep (3), and prominent high-amplitude REM theta activity (1).

Conclusion: In conclusion, markers of mild sleep disruption - snoring, higher scores on arousals and/or PLM, and isolated REM sleep apnea - were found for the majority of MS patients in this sample, and appear to be associated with lowered sleep efficiency and complaints of disrupted sleep and sleepiness. Prospective studies are needed addressing sleep problems, MS patient care and quality of life.

0878

THE RELATIONSHIP BETWEEN ANTHROPOMETRY AND OBSTRUCTIVE SLEEP APNEA (OSA) IN HIV-SEROPOSITIVE AND -SERONEGATIVE MEN

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Introduction: In the general population, anthropometric measurements, such as neck circumference (NC), waist circumference (WC) and body mass index (BMI), are useful screening tools for OSA. Whether anthropometry has similar utility among HIV-seropositive people is not known.

Methods: Three groups of participants were recruited from the Baltimore site of the Multicenter AIDS Cohort Study: HIV-seronegative men (HIV-; n=55), HIV-seropositive men receiving highly active antiretroviral therapy (HIV+/HAART+; n=49), and HIV-seropositive men not receiving HAART (HIV+/HAART-; n=29). Participants underwent a nocturnal sleep study with assessment of NC, WC, and BMI using NHANES III methodology. Moderate-severe OSA was defined as an apnea-hypopnea index ≥ 15 events/hour. Receiver Operator Characteristic (ROC) curves were used to compare the ability of different anthropometric measurements to discriminate those with moderate-severe OSA within each group and across groups.

Results: BMI (mean \pm SD) was greater in HIV- men (28.9 ± 6.2 kg/m²) than in the HIV+ groups (HAART+ = 25.5 ± 4.4 kg/m², p=0.002; HAART- = 24.6 ± 3.1 kg/m², p=0.001). Moderate-Severe OSA was found in 45% of the participants (HIV-:56%; HIV+/HAART+: 38%; HIV+/HAART-: 37%). After adjustment for BMI, the risk of OSA was similar between groups. In HIV- men, NC, WC, and BMI all had very good discriminatory performance to predict OSA (ROC areas-under-the-curve (AUC): 0.88, 0.87, 0.82, respectively). In contrast, the performance of these measurements was only fair among the HIV+/HAART+ group (AUCs: 0.71, 0.70, 0.64, respectively) and no different from chance in the HIV+/HAART- group (AUCs: 0.51, 0.38, 0.45, respectively). For example, the optimal cutpoint of 39.9 cm for NC predicted OSA with 87% sensitivity and 79% specificity among HIV- men, whereas among HIV+/HAART+ men the optimal NC cutoff of 39.2 cm had a sensitivity of only 67% and specificity of 70%.

Conclusion: Neck circumference, waist circumference, and BMI were better able to discriminate moderate-severe OSA in HIV-seronegative compared to HIV-seropositive men. This suggests that among HIV-infected men: 1) anthropometry may not be useful tool for OSA screening and 2) factors other than conventional anthropometry are likely contributing to the risk of OSA.

0879

SLEEP QUALITY IN LOWER INCOME ADULTS WITH HIV

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Introduction: The number of aging adults with HIV is increasing due to early detection and advances in life-extending medications. The synergistic effects of aging and HIV may have an effect on sleep quality that can also affect mood and everyday functioning.

Methods: A sample of community-dwelling, lower income adults (n=201) was surveyed regarding HIV status, mood using the Profile of Mood States (POMS) and sleep quality using the Pittsburgh Sleep Quality Index (PSQI).

Results: Half of the sample were HIV positive (n=98, Mean age=45 years, Range 24-67) and they were predominantly male (71%), homosexual or bisexual (57%), and African-American (69%). The com-

parison group (n=103, Mean age=38 years, Range 20-64 years) had fewer men (26%) but were predominantly African-American (69%) and heterosexual (94%). The mean annual household income for the HIV group was \$15,700 while the comparison group was \$36,000. Age and Global PSQI Score showed a weak but significant association ($r=0.19$, $p<0.01$), although no association was found when comparing by HIV status. While controlling for income, the HIV positive group reported significantly (ANCOVA $p<0.05$) more trouble falling asleep within 30 minutes, needing to use the bathroom, uncomfortable breathing, coughing or snoring, feeling too cold, bad dreams and pain. Household income in the HIV group was inversely related to the Global PSQI Score ($r=-0.26$, $p<0.01$), but not for the comparison group. When controlling for household income, the HIV positive group had significant associations between sleep efficiency and tension, depression, anger, fatigue, confusion, and the POMS total score.

Conclusion: These findings suggest that persons with HIV report more sleep problems and more negative affect associated with sleep than a comparable group without HIV. However, the effects of lower household income combined with HIV may play an important part in problems with both sleep and mood.

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0880

OXYGENATION, SLEEP, AND NEUROBEHAVIOR IN COPD

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Introduction: COPD patients are known to have poor neurobehavioral function. They also have difficulty with sleep, complaining of insomnia, frequent awakenings, and feeling unrefreshed. This study examined sleep and oxygenation during sleep in comparison with neurobehavioral function.

Methods: COPD patients wore an actigraph and ambulatory pulse oximeter for one night. The next morning they completed a computer-based battery of neurobehavioral tests.

Results: We report on the initial 21 subjects, who were 64 ± 8.2 years old, and had BMI = 24.7 ± 4.3 , FEV1 = 40.9 ± 10.1 % predicted, and FEV1/FVC = 46.9 ± 6.2 . Actigraphy measurements included estimated total sleep time (TST) = 252 ± 116 min, estimated awakenings during the night 26.3 ± 17.1 for estimated wakefulness after sleep onset (WASO) 203 ± 122.9 minutes. Although participants had a mean oxygen saturation (SO₂) during estimated sleep was 93.6%, they desaturated at least 6% for more than 8 seconds 1.8 ± 1.7 times a night, spending 35.3 ± 69.6 min with SO₂ $\leq 88\%$. All subjects performed below normal for their age on at least one neuropsychological test; many were below normal on all tests. The number of errors of commission on the continuous performance test correlated significantly with the estimated TST per night ($r=.84$, $p=.004$), estimated WASO ($r=.83$, $p=.005$), and estimated longest sleep episode ($r=-.74$, $p=.02$). Estimated TST correlated significantly with the number correct on the symbol digit coding test ($r=.71$, $p=.03$). Estimated sleep time spent with SO₂ $< 88\%$ correlated significantly with immediate verbal memory ($r=.63$, $p=.07$), with both the number correct and percent correct on the symbol-digit coding test ($r=-.64$, $p=.06$, and $r=-.91$, $p=.001$, respectively), and reaction time on the continuous performance test ($r=-.76$, $p=.02$). The number of desaturation events correlated negatively with both number correct and percent correct on the digit symbol substitution test ($r=-.72$, $p=.02$ and $r=-.57$, $p=.09$).

Conclusion: In COPD, sleep quality and nocturnal oxygenation are significantly related to neuropsychological function. Although causal associations can not be confirmed here, the correlations suggest that different aspects of sleep, including sleep disruptions and oxygen desaturation, affect different neuropsychological tests. Interventions to improve sleep or oxygenation during sleep may improve neurobehavioral function. Data collection continues.

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0881

SLEEP STATE TRANSITIONS ON SLEEP SPECTROGRAM - CORRELATION WITH HYPERTENSION AT A POPULATION LEVEL

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Introduction: To assess, at a population level, the correlation of sleep state transitions and the prevalence of Hypertension in the Sleep Heart Health Study, using a novel electrocardiogram (ECG) based method of estimating sleep physiology and pathology, the cardiopulmonary coupling-derived sleep spectrogram. We hypothesized that decreased sleep state transitions adjusted for age, sex, body mass index and respiratory disturbance index with 4% desaturation would confer a cardioprotective affect (reduced prevalence of hypertension).

Methods: Retrospective analysis of the Sleep Heart Health Study dataset using an estimate of cardiopulmonary coupling (RR variability and ECG-derived respiration). States detected are low (unstable sleep state), high (stable sleep state), and very low (wake or REM) frequency coupling. Transitions between states (per hour of sleep) were tabulated. Logistic regression was used to estimate odds ratios of prevalent hypertension risk.

Results: Various estimates of cardiopulmonary coupling were generated from 5247 (of the original 6441 datasets) subjects. Total of 6.3 +/- 1.7 transitions per hour were noted. Increased transitions from high (stable) to very low (wake) frequency coupling were associated with an increased risk of hypertension (OR=1.27, p=0.002). But, high (stable) to low (unstable) and vice versa transitions were associated with reduced risk of hypertension (OR=0.76, p=0.0001 and OR=0.82, p=0.002 respectively). Increased age was also associated with reduced transitions per hour of sleep.

Conclusion: Spectrographically determined sleep state transitions offer a potentially unique view of sleep physiology. Sleep is exceptionally dynamic, and "simplification" of these dynamic interactions may offer a unique view into understanding the pathophysiology of cardiovascular events. Stable to wake transitions which reflect increased arousal index, intuitively suggest increased risk of Hypertension. But, ultradian transitions between stable and unstable states appeared to be cardioprotective for unclear reasons. Determining cause and effect relationship requires further studies.

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0882

STUDY COMPARING PSG DATA IN INSOMNIA PATIENTS WITH HIV VERSUS MATCHED CONTROLS WITH INSOMNIA

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Introduction: Insomnia is estimated to affect up to 70% of those infected with HIV. However, limited data are available on the nature of the sleep difficulties in this population. Alterations in the distribution of REM and slow-wave sleep over the night have been reported and hypothesized to be due to co-morbid mood disturbances in this population, however, this has yet to be established. The purpose of this study was to test the hypothesis that there would be differences in self-reported and polysomnographic (PSG) sleep in HIV infected individuals with in-

somnia and matched insomnia controls not accounted for by medical or psychiatric disorders.

Methods: We selected 14 HIV+ subjects and matched them to controls based on age, sex, psychiatric disorders, substance abuse, medical disorders and ethnicity. Diagnosis of insomnia was based on the consensus of 6 clinician interviews. SCID was used to determine psychiatric diagnoses. Sleep data derived from an average of 2 nights of PSG data and an average of up to 2 weeks of daily sleep diaries.

Results: Multivariate analysis revealed an overall significant difference between HIV and control subjects as well as a significant group by gender interaction among the PSG sleep variables (p < 0.05). Post-hoc analyses identified that the HIV group had longer self-reported (p < 0.01) and PSG (p < 0.10) sleep onset latency, and lower self-reported sleep efficiency (p < 0.05), while HIV+ women had a greater percentage of Stage 1 sleep (p < 0.02).

Conclusion: This study provides preliminary evidence that HIV+ individuals with insomnia have significantly worse sleep than matched insomnia controls which is not due to greater medical or psychiatric disorder burden. The cause of this difference in sleep disturbance is unclear. Possibilities include the effects of HIV-related medications, psychosocial effects of being diagnosed with HIV, and neuropsychiatric effects of the virus.

Support (optional): National Institute of Mental Health Grant# R01MH067057

0883

SLEEP-DISORDERED BREATHING AND URINARY ALBUMIN EXCRETION IN COMMUNITY-DWELLING ELDERLY MEN

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Introduction: Sleep-disordered breathing (SDB) promotes an environment potentially deleterious to the cardiovascular system and other organs, including the kidney. However, the association between SDB and albuminuria, an early indicator of renal dysfunction, is uncertain.

Methods: 507 community-dwelling men age >=65 years (mean 76.0±5.3) enrolled in the MrOS Sleep study had spot urinary albumin excretion (UAE) measured and overnight polysomnography. SDB severity was categorized using the respiratory disturbance index (RDI) and percent total sleep time <90% SaO₂ (TST<90%). UAE was measured using the urinary albumin to creatinine ratio (ACR); geometric means are presented. Renal dysfunction was defined as MDRD estimated glomerular filtration rate <60ml/min/1.73m².

Results: Median ACR was 5.9 mg/gCr (range 1.6-523). Median RDI was 12 events/hour (range 0-78); 23% had mild SDB (RDI 5-14), 25% moderate (RDI 15-29), 13% severe (RDI ≥30). Men with higher RDI had higher ACR (9.36 mg/gCr among men with RDI ≥30 vs 6.71 mg/gCr among those with RDI <5, p=0.006); further adjustment for BMI somewhat attenuated this association (p=0.05). After excluding men with renal dysfunction (n=123), no association between SDB and mean ACR remained. However, even after adjustment for age, race, BMI, hypertension and diabetes, men who spent ≥10% TST<90% had higher ACR (10.4 g/gCr compared with 7.4 g/gCr among men who spent <1% TST<90%, p=0.038); results were somewhat attenuated after exclusion of men with renal dysfunction (p=0.066).

Conclusion: SDB, measured by elevated RDI or nocturnal hypoxemia, was associated with higher ACR. The relationship between ACR and RDI was slightly attenuated after BMI adjustment, with further attenuation after excluding men with renal dysfunction. However, a high level of nocturnal desaturation was associated with higher ACR, even after adjustment for demographics, BMI and co-morbidities, and attenuated further after excluding those with renal dysfunction. This suggests that

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the hypoxia component of SDB may mediate the effect of SDB on the kidney.

0884

INSOMNIA DISORDER IN PATIENTS WITH COPD

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Introduction: The prevalence and unique risk factors of insomnia disorder in COPD have not been clearly elucidated.

Methods: We surveyed 100 COPD patients regarding their sleep, medications, respiratory symptoms, daytime sleepiness (Epworth Sleepiness Scale, ESS), quality of life (SF-36) and physical activity (International Physical Activity Questionnaire).

Results: The mean age of the patients was 70 ± 9 years, FEV1 was $39 \pm 18\%$. Insomnia disorder (chronic sleep disturbance associated with impaired daytime functioning) was present in 24% of patients. Eight patients (16%) reported that shortness of breath interfered with sleep and had a trend towards having lower FEV1 (% predicted) than those without adverse effects of dyspnea on sleep (29% vs. 40%, $P=0.1$). Fifty two percent of patients were using oxygen and had lower insomnia prevalence (12% vs. 37%, $P=0.03$). Current smokers ($n=33$) had a significantly higher prevalence of insomnia than past smokers (42% vs. 15% $P=0.01$). Sixty percent of the patients believed that the inhalers helped their sleep, while the rest either believed they had no effect (30%) or were not sure (10%). The inhalers that most patients reported as being most helpful to sleep included albuterol (28% of patients) and formoterol (26%). Accordingly, there was a trend towards lower prevalence of insomnia in the 80 patients using beta-agonist inhalers (21% vs. 35%, $P=.09$). In contrast, the prevalence of insomnia tended to be higher in the 78 patients using anticholinergic inhalers (27% vs. 12%, $P=.1$). Insomniacs showed a trend towards increased use of prescription sedatives/anxiolytics (36% vs. 12%, $P=0.07$) and had more daytime sleepiness (ESS 9.2 vs. 4.3, $P=0.04$) than non-insomniacs. A higher percentage of insomniacs compared to non-insomniacs (45% vs. 27%, $P=0.02$) reported feeling sad or anxious sometimes or usually. The quality of life assessed by SF-36 scores was worse in COPD patients with insomnia than COPD patients without insomnia in several domains. There were no significant differences in physical activity between patients with or without insomnia.

Conclusion: COPD is frequently comorbid with insomnia disorder. The use of beta agonist inhalers and/or oxygen is associated with a lower prevalence of insomnia, while very severe COPD, worse dyspnea and smoking are associated with a higher prevalence of insomnia. Presence of insomnia in COPD portends worse quality of life, increased sedative use, more daytime sleepiness and worse depression and anxiety.

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0885

SLEEP DISORDERED BREATHING AND INCIDENT CARDIOVASCULAR EVENTS IN OLDER MEN: THE MROS SLEEP STUDY

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Introduction: Sleep disordered breathing (SDB) is associated with risk factors for cardiovascular disease, but the association between SDB and incident cardiovascular events remains uncertain, particularly in older adults.

Methods: To test the hypothesis that SDB is associated with increased risk of cardiovascular events in older men, we recorded in-home polysomnography (PSG) in a cohort of 2,905 men (mean age 76.4 years). Incident cardiovascular events were centrally adjudicated during 2.5 +/- 0.4 years of follow-up. The primary exposure, the apnea-hypopnea index (AHI), was defined as the number of apneas and hypopneas with $\geq 4\%$ oxygen desaturation per hour of sleep. The primary outcome (CVD) was a composite event, which included coronary heart disease (CHD), cerebrovascular, congestive heart failure, peripheral vascular disease (PVD) events, and other 'definite' unstable coronary artery syndromes. Secondary outcomes included incident CHD, PVD, stroke, and heart failure (HF). Cox proportional hazards models were used to examine the association between AHI and incident CVD outcomes, adjusting for age, race, BMI, comorbidities, physical activity levels, health and functional status. Results are presented as hazard ratios (HR) with 95% confidence intervals (CI).

Results: The median AHI was 11.7 (interquartile range 2.7 to 15.7). There were 337 CVD, 237 CHD, 56 PVD, 49 stroke, and 39 HF events confirmed. There was no relationship between AHI and incident CVD overall. However, older men with $AHI \geq 15$ were at 2.8-fold increased risk of HF compared to those with $AHI < 15$ (HR=2.8; 95% CI 1.4 - 5.4). Central apnea index ≥ 5 and obstructive apnea index ≥ 5 were both associated with increased HF risk (HR=3.5; 1.7 - 7.2 and HR=2.5; 1.2 - 5.1, respectively).

Conclusion: SDB as measured by AHI is strongly related to risk of HF in older men. Preliminary results suggest that both central and obstructive apneas predict risk for future HF events.

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0886

SLEEP DYNAMICS, AIRWAY INFLAMMATION AND OBSTRUCTION IN ASTHMA PATIENTS WITH SYMPTOMS OF SLEEP-DISORDERED BREATHING (SDB)

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Introduction: Previous data suggested that sleep fragmentation is a correlate of airway obstruction in patients with asthma and symptoms of SDB. However, the association of sleep dynamics with airway obstruction and inflammatory markers in these patients has not been described. We hypothesized that increased sleep instability will predict worse lower airway inflammation and obstruction.

Methods: Nineteen patients with persistent asthma (NAEPP steps 2-4 while on optimal therapy) and OSA symptoms underwent standard polysomnography, exhaled breath condensate collection for cysteinyl leukotrienes (cysLTs) assays (ELISA, n=12 samples) and spirometry. Measures of sleep stage dynamics (efficiency, number of stage changes, mean continuous sleep period duration, and transition probabilities) were computed. Linear regression was used for statistical modeling.

Results: Thirteen subjects (68%) were women and mean age was 50±10 (s.d.) years. Total sleep time was 364±67 minutes, sleep efficiency 77±10%, mean continuous sleep period duration 9.5±3.6 minutes (REM sleep 5.7±3.4), and probability of transition from any sleep stage to wakefulness was 26±5%. Mean evening (PM) cysLTs level was 172.5±92.7 and morning (AM) level 215.3±46.9 pg/ml. On spirometry, FEV₁% was 86±19. Lower total sleep time and sleep efficiency were associated with higher PM cysLTs (R²=0.43, p=0.02 and R²=0.41, p=0.02, respectively) and lower FEV₁% (R²=0.43, p=0.02 and R²=0.41, p=0.02). With shorter continuous sleep periods (of any stage), a significantly lower FEV₁% (R²=0.48, p=0.001) along with a non-significant suggestion of higher AM and PM cysLTs levels appeared (R²=0.23, p=0.12 for each). The first was particularly observed for REM sleep (R²=0.44, p=0.002). Higher probability of transition from any sleep stage to wake was associated with higher AM (R²=0.66, p=0.001) and PM (R²=0.48, p=0.01) cysLTs levels, and with lower FEV₁% (R²=0.37, p=0.006).

Conclusion: Sleep instability, particularly during REM sleep is associated with worse lower airway inflammation and obstruction in asthma patients with pre-existent SDB. Clarification of underlying causal pathways could lead to improved therapeutic strategies for these patients.

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0887

DEPRESSION, SLEEP, AND SLEEP-DISORDERED BREATHING IN CONGESTIVE HEART FAILURE (CHF)

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Introduction: There is an elevated incidence of depression and sleep disturbances in patients with HF. This study examined the potential relationship of depressed mood to disturbed sleep in HF.

Methods: Forty-two stable NYHA class II-IV HF patients (LVEF < 40%; mean 57.7 years of age) were recruited from the UCSD Heart Failure Program and the VA Medical Center Coronary Care Program. Thirty-nine healthy age-matched volunteers (mean 54.1 years of age) served as controls. Depressed mood was characterized by the Beck Depression Inventory (BDI). Sleep was recorded using standard polysomnography at the UCSD General Clinic Research Center Gillin Sleep Laboratory. Number of apneas and hypopneas/hour of sleep were used to determine the apnea hypopnea index (AHI). The presence of sleep apnea was defined as an AHI ≥ 10.

Results: BDI scores were higher in HF (11.4 versus 6.8; p=0.003), with more HF patients scoring above the BDI clinical cutpoint of 10 (53.3% vs. 21.0%; p<.001). A MANOVA testing all sleep variables and controlling for age and gender was significant for HF vs. non-HF classification (p=.001), with HF patients having more central apneas/hour (37.2 vs. 7.5; p=.008) but not obstructive apneas/hour (41.7 vs. 26.0; p=.156). More HF patients were apneic (70.5% vs. 27.7%; p<.001). HF patients spent more time in stage 1 sleep (60.3 min vs. 34.1 min; p=.001), marginally less time in slow wave sleep (38.2 min. vs. 52.3 min; p=.06), had lower mean O2 saturations (92.9% vs. 94.5%; p=.013) and spent more time at SpO₂ <90% (p=.006). In a hierarchical multiple linear regression analysis predicting BDI, older age (p=.026) and lower mean O2 saturation (p=.001), but not HF diagnosis, independently predicted higher BDI scores.

Conclusion: The higher incidence of depressed mood in HF is related to disrupted sleep, specifically the severity of hypoxia.

0888

EFFECT OF SEVERITY OF AIRFLOW OBSTRUCTION ON RAPID EYE MOVEMENT ASSOCIATED SLEEP APNEA IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Introduction: REM sleep is associated with physiologic changes including oxyhemoglobin desaturation which can be profound in severe COPD. The rate of desaturation in nocturnal airway obstruction is inversely proportional to the baseline SpO₂ level. Recommendations for scoring hypopneas in polysomnograms include a ≥4% desaturation from pre-event baseline. In COPD patients, a short duration flow limiting event occurring in non-REM sleep with <4% desaturation could have a ≥4% desaturation if it occurred in REM sleep. Equivalent episodes of flow limitations could result in hypopneas in REM but not in non-REM sleep. We hypothesized that ratio of REM AHI to NREM AHI increases with decreasing FEV₁/FVC.

Methods: We performed a retrospective chart review of our adult COPD patients, who had both PFTs and a sleep study during the last five years. Demographics, PFTs, and polysomnogram data were recorded. The FEV₁/FVC and REM AHI/NREM AHI were analyzed using Pearson correlation.

Results: Twenty of 178 COPD patients (34-83 years; 70% male; BMI 32.1±6.4) had both FEV₁/FVC <0.70 and REM sleep on polysomnogram. Awake mean saturation ranged from 89% to 98%. The correlation coefficient for FEV₁/FVC and REM AHI/NREM AHI was -0.508 (-0.78 to -0.08, 95 % CI; p=0.02). FEV₁ (-0.230; p=0.329) and FVC (0.161; p=0.524) did not correlate with REM AHI/NREM AHI. Correlation coefficients of REM/NREM AI and REM/NREM HI to FEV₁/FVC were -0.485 (p=0.03) and -0.650 (p=0.006), respectively.

Conclusion: The severity of airflow obstruction measured by FEV₁/FVC appears to significantly influence REM AHI/NREM AHI in COPD patients. The ratio of hypopnea index better correlates with FEV₁/FVC than does the ratio of apnea index, supporting the hypothesis that hypopneas are overestimated in REM sleep in COPD patients. Some cases of apparent REM dominant sleep apnea are likely consequent to marked hypoxemia of REM-associated hypoventilation from COPD, rather than from REM versus NREM upper airway changes.

0889

SLEEP QUALITY AND SLEEP-DISORDERED BREATHING IN ADULT CYSTIC FIBROSIS PATIENTS

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Introduction: Cystic Fibrosis (CF) patients may be predisposed to poor sleep quality and sleep-disordered breathing due to upper and lower airway abnormalities and impaired gas exchange. However, data about this issue are scarce. The objective of this study was to evaluate sleep architecture and nocturnal desaturation in adult CF patients, correlating with clinical status, pulmonary function testing and Doppler echocardiography findings.

Methods: In a prospective cross-sectional study, clinically stable adult CF patients and age-matched control subjects were submitted to an overnight polysomnography and to Epworth sleepiness scale and the Pittsburgh sleep quality index (PSQI) evaluation. Also, each CF patient had their nutritional status, pulmonary function, six-minute walking test (6MWT) and Doppler echocardiography assessed and correlated with oxygen desaturation during sleep.

Results: Eleven CF patients, mean age 24.4 ± 4.95 , and 11 matched-control subjects were enrolled in the study. The mean FEV1 for CF patients was $45.8 \pm 26.5\%$ of predicted. CF patients and control subjects had similar sleep duration, sleep latency, sleep efficiency, percentage of sleep stages and ESS score. However, CF patients had higher PSQI scores (4.36 vs. 2.64; $p < 0.05$) and a higher arousal index (7.06 vs. 1.2; $p < 0.05$) than controls. There was a moderate correlation of arousal index with FEV1 ($r = -0.6; p < 0.05$) and PSQI score ($r = 0.53; p < 0.05$). The apnea-hypopnea index was similar for control and CF subjects (0.83 vs. 0.37; $p > 0.05$). None patient fulfill criteria to Obstructive Sleep Apnea. Significant sleep-related desaturation was much more common in CF patients (54.5% vs. 0%; $p < 0.001$). The mean nocturnal SpO₂ (96.1% vs. 90.5%) and the minimum nocturnal SpO₂ (93.4% vs. 84.3%) were both significantly smaller in the CF group ($p < 0.001$). FEV1, resting SpO₂, SpO₂ at the end of 6MWT and peak flow velocity of the tricuspid regurgitant jet correlated significantly ($p < 0.05$) with nocturnal SpO₂ levels. Forward stepwise regression analysis identified resting SpO₂ as the single parameter that could best discriminate CF patients likely to experience nocturnal desaturation.

Conclusion: CF patients have disrupted sleep despite normal sleep latency and efficiency. Sleep-related desaturation is very common in adult CF patients and is not associated with apnea/hypopnea. The resting SpO₂ was the best predictor for nocturnal desaturation in CF patients.

Support (optional): FIPE/HCPA, Globalmed.

0890

DAYTIME SLEEPINESS, ALTERATIONS IN SLEEP AND ITS ASSOCIATION WITH HLA-DR, HLA-DQ IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS

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Introduction: The aim of this study was to assesses the level of sleepiness, alterations in sleep and its association with HLA-DR, HLA-DQ in Systemic Lupus Erythematosus (SLE) patients.

Methods: Forty-nine SLE women attending the outpatient Lupus Clinic at the Immunology and Rheumatology Department from the INCMNSZ with a mean age of 38.8 ± 11.4 years were studied polysomnographically and compared to twenty five matched healthy controls. Validated instruments were used to measure disease activity, fatigue, and depression symptoms. SLE patients were classified as Sleepy if they have a mean Multiple Sleep Latency Test (MSLT) ≤ 8 min. HLA typing was performed in the SLE group. Allele and genotype frequencies were obtained by direct counting. Gene frequencies were compared to a control group of healthy Mexican subjects.

Results: Lupus patients slept less than healthy women, have less sleep efficiency, greater number of awakenings, and higher percent of awake stage than the healthy women. More than sixty percent of the Lupus patients were classified as sleepy (MSLT 4.7 ± 2.1 min). SLE sleepy and non-sleepy groups did not differ in total sleep time and indexes of sleep efficiency or sleep continuity. The genetic frequency of HLA-DR2 (1501) and HLADQ*0602 was not associated with the level of sleepiness in SLE.

Conclusion: Excessive daytime sleepiness is high prevalent in Lupus, there is not a direct association between sleepiness and the genetic frequency of the HLADR or HLA-DQ alleles. The presence of sleep apnea or movement sleep disorders, medication, depression level and disease activity do not explain the occurrence of excessive daytime sleepiness in SLE.

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0891

PERSISTENT FATIGUE AND UNREFRESHING SLEEP IN CHRONIC FATIGUE SYNDROME: A MANIFESTATION OF CORTICAL HYPOAROUSAL?

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Introduction: Unremitting fatigue and unrefreshing sleep, hallmark traits of Chronic Fatigue Syndrome(CFS), have been attributed to disordered sleep physiology, perturbed sleep homeostasis, or sleep disordered breathing. We hypothesize that in CFS, complaints of persistent fatigue and unrefreshing sleep are manifestations of a diminished drive for wakefulness (hypoarousal) rather than perturbed sleep architecture or sleep disorder.

Methods: We conducted overnight PSG's in 35 CFS and 40 matched control subjects. PSG's were manually staged and epochs containing

artifact extracted. Fast Fourier transformation deconstructed each subject's EEG into frequency domains of alpha, delta, theta, sigma, and beta. The spectral power of each frequency domain was determined for successive 30 second epochs, and classified by sleep state. Comparisons of the spectral power of each frequency domain, within each sleep state, were made between CFS subjects and controls.

Results: We found no difference between CFS and control subject values of sleep architecture, multiple sleep latency times, or Epworth sleepiness scores. CFS Alpha power (mean \pm 1 SEM) was reduced in stage 2 ($1.42E-09 \pm 6.59E-12$ vs $1.73E-09 \pm 1.01E-11$, $p < 0.001$), Slow Wave Sleep (SWS) ($1.52E-09 \pm 1.44E-11$ vs $2.07E-09 \pm 2.43E-11$, $p < 0.001$), and REM ($6.48E-10 \pm 5.95E-12$ vs $8.76E-10 \pm 9.50E-12$, $p < 0.001$). CFS Delta power was increased in stage 1 ($4.87E-09 \pm 7.16E-11$ vs $4.22E-09 \pm 5.86E-11$, $p < 0.001$), reduced in SWS ($3.48E-08 \pm 2.29E-10$ vs $3.83E-08 \pm 2.36E-10$, $p < 0.001$), and increased in REM ($3.76E-09 \pm 2.73E-11$ vs $3.54E-09 \pm 5.35E-11$, $p < 0.001$). CFS Theta, Sigma, and Beta spectral power was significantly lower than in control subjects during stage 2, SWS, and REM.

Conclusion: CFS subjects exhibit reduced Alpha power in stage 2, SWS and REM, and reduced Delta power in SWS. These findings, together with those of increased Delta power in Stage 1 and REM sleep (both of which are characterized by predominantly low voltage fast frequencies) are consistent with our hypothesis of cortical "hypoarousal" in CFS. Future studies will better define the presence of putative hypoarousal in CFS as well as its association with symptoms of fatigue and unrefreshing sleep. In addition, we propose FFT analyses of electroencephalography as a unique biomarker in the assessment of CFS.

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0892

INFLUENCE OF GENDER ON FATIGUE AND SLEEP QUALITY OF PERSONS WITH OSTOMIES

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Introduction: Few studies have examined health-related quality of life (HR-QOL) relevant to disturbed sleep of colorectal cancer (CRC) survivors with ostomies; moreover, no studies have examined gender differences of ostomates on quality of sleep and fatigue.

Methods: HR-QOL was examined in this cross-sectional study of long-term (>5 years) CRC survivors with ostomies, who receive care at Kaiser Permanente health systems in California, Oregon, and Hawaii. Participants completed the City of Hope QOL Ostomy questionnaire, which includes demographic and scaled items, and narrative comments for 'greatest challenges' associated with having an ostomy. Two items, "fatigue" and "sleep disruption" (scale from 0 to 10), served as dependent variables. Age, ethnicity, education, partnered status, body mass index (BMI), and time since surgery were included in models. Data were analyzed using t-tests and ordinal logistic regression modeling with significance set at $p < 0.05$.

Results: Women ($n=118$) compared to men ($n=168$) were less likely to be partnered (25% vs. 55%, $p < 0.0001$). There were no differences for age, ethnicity, education, BMI, or time since surgery. Regression modeling for fatigue showed women to have lower HR-QOL compared to men (0.65 decrease, $p < 0.01$), adjusted for time since surgery (modest positive association, $p < 0.05$). Regression modeling for sleep disruption also showed women to have poorer HR-QOL (0.57 decrease, $p < 0.01$), adjusted for age (modest positive association, $p < 0.001$). CRC surgical controls without ostomy showed no significant gender difference for ei-

ther HRQOL item. Qualitative narrative comments suggest sleep disruption is associated with fear of or actual leakage during hours of sleep.

Conclusion: Women CRC survivors with ostomies report more fatigue and sleep disruption that may contribute to poorer HR-QOL compared to their male counterparts. Higher rates of fatigue for women are consistent with gender differences in other health conditions. These findings can provide a foundation for gender-specific ostomy interventions to improve sleep quality.

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0893

SLEEP DISTURBANCES IN END STAGE LUNG DISEASE

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Introduction: Patients with severe lung disease have poor health related quality of life (HRQL). Sleep disorders can contribute to decreased HRQL. However, there is little data quantifying the prevalence and severity of sleep disruption in these patients.

Methods: Retrospective survey of 20 patients with end stage lung disease referred for lung transplantation. Pulmonary function testing (PFT) and polysomnography (PSG) were performed to grade severity of lung disease and to evaluate for various sleep disturbances.

Results: Mean age was 64.6 ± 12.2 , 50% were male, BMI was 30.1 ± 5.5 . Ten (50%) had obstructive while 10(50%) had restrictive ventilatory defects. PFTs revealed Median FEV1 36%, FVC 51%, FEV1/FVC 60% and DLCO 36%. Thirty nine percent (7/18 available) showed Epworth score ≥ 10 . The median AHI was 9.3, 55% had AHI > 5 , and 30% had AHI > 15 . Forty percent had periodic limb movement index (PLMI) > 10 . Mean total sleep time was 273 ± 88.4 min, sleep efficiency was $67.8 \pm 20.4\%$, 65% had a sleep efficiency of $< 80\%$, and mean arousal index was 28.4 ± 19.2 . Mean light sleep (stage 1+2) was 77.2 ± 18.1 min, slow wave sleep (stage 3+4) was 11.9 ± 14.1 min and REM sleep was 10.5 ± 9.2 min. Median time less than 90% saturation was 13 min, however 11 patients used oxygen during the sleep study. There was no correlation between any polysomnographic parameters, sleepiness, or PFTs. There were no differences in sleepiness or indices of sleep fragmentation between patients with obstructive or restrictive lung disease.

Conclusion: In patients with end stage lung disease, whether restrictive or obstructive, there is a high prevalence of sleep fragmentation and organic sleep disorders, such as sleep apnea and periodic leg movement disorder. We suggest that part of the evaluation of end-stage lung disease patients include a thorough evaluation for sleep disorders.

0894

SYMPTOMS OF FATIGUE, INSOMNIA, AND DEPRESSION PRE-TREATMENT ARE ASSOCIATED WITH POOR QUALITY OF LIFE IN BREAST CANCER PATIENTS

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Introduction: Sleep disturbance, fatigue, and depression are three common symptoms in cancer patients. We investigated the association between a pre-treatment symptom cluster of these symptoms and quality of life (QOL) before and during the chemotherapy in breast cancer patients.

Category N—Sleep in Medical Disorders

Methods: 76 women (mean age=51.1 years, SD=9.1, range=34-79) with newly diagnosed stage I-III breast cancer and scheduled to receive at least 4 cycles of chemotherapy participated. Data were collected before (baseline) and during cycle 1 and cycle 4 of chemotherapy. A symptom cluster index (SCI) was computed for each woman based on her baseline scores of sleep quality (Pittsburgh Sleep Quality Index), fatigue (Multidimensional Fatigue Symptom Inventory-Short Form) and depression (Center of Epidemiological Studies-Depression). Three groups were formed: SCI 0 group with women with no symptoms (n=15); SCI 1-2 group with 1 or 2 symptoms (n=43); SCI 3 group with all three symptoms (n=18). Differences in QOL (Functional Assessment of Cancer Therapy-Breast, FACT-B; Functional Outcomes of Sleep Questionnaire, FOSQ) among the three groups over time were assessed with mixed-effects models (SAS Institute Inc 2003).

Results: At baseline, SCI 1-2 and SCI 3 groups reported significantly lower FACT-B (SCI 1-2: Mean=108.5±11.2; SCI 0: Mean=90.8±13.8; both $p<0.0001$) and lower FOSQ (SCI 1-2: Mean=18.1±1.9; SCI 0: Mean=17.4±2.4; $p=0.02$, $p=0.05$) scores than the SCI 0 (FACT-B Mean=125.2±7.8, FOSQ Mean=19.7±0.3) group. There were significant group ($p<0.001$) and time ($p<0.0001$) effects in both FACT-B and FOSQ scores, but no significant group-time interactions ($p=0.15$, $p=0.09$), indicating QOL was worse during treatment for all three groups, with those starting out with symptoms reporting the worst QOL during treatment.

Conclusion: All patients reported worse QOL during treatment than before, but patients with more pre-treatment symptoms suffered from worse QOL both before and during chemotherapy. Studies are needed to examine whether treatment of sleep, fatigue and mood would improve QOL in women undergoing chemotherapy.

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0895

SLEEP DISORDERS IN BRAIN TUMOR PATIENTS

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Introduction: Patients with neoplasms have increased prevalence of sleep disorders. Both the type of neoplasm and sleep disorder vary greatly. Only one prior pediatric study addressed the issue of sleep disorders in patients with central nervous system tumors. No similar study exists for the adult population. The aim of our study is characterize sleep disorders in adult central nervous system (CNS) tumor patients. Our hypothesis is that adult patients with CNS tumors have a unique susceptibility to sleep disorders.

Methods: This is a retrospective study of adult patients who had both 1) a diagnosis of a primary or metastatic central nervous system tumor and 2) a diagnosis of a sleep disorder and/or a sleep study. Charts identified by a database search were reviewed for histologic tumor type, sleep study results, and sleep disorder diagnosis. The findings of our study will be demonstrated through a descriptive analysis defining the characteristics of sleep disorders in adult brain tumor patients.

Results: Eleven patients were identified. The mean age of the subjects was 40.2 ± 18.7 years (16 to 64 years). Brain tumor types included 2 meningiomas, 2 oligodendrogliomas, 2 astrocytomas (WHO grade I and III), 1 anaplastic mixed glioma (WHO grade III), 1 craniopharyngioma, 1 germinoma, 1 acoustic neuroma, and 1 metastatic testicular tumor. The mean Epworth Sleepiness Scale score was 15.4 ± 4.77 . Sleep disorders included obstructive sleep apnea syndrome (63.6%), insomnia (27.3%), primary snoring (18.2%), seizure disorder (18.2%), periodic limb movement disorder (9.1%), and organic hypersomnia NOS (9.1%). Three of the patients (27.3%) had multiple sleep disorders. Narcolepsy, restless leg syndrome, and REM behavior disorder were not represented.

Conclusion: Brain tumor patients represent a heterogeneous population of patients in terms of age, sex, histologic type, presentation, disease

course, and also sleep disturbances. Due to this variety, a correlation between brain tumor type and specific sleep disorder diagnoses could not be made. Study limitations include limited patient number and retrospective design. Prospective studies with large patient numbers may delineate more specific associations of sleep disorders in brain tumor patients.

0896

DAYTIME PAIN AND NIGHTTIME SLEEP IN PATIENTS WITH FIBROMYALGIA: PRELIMINARY ANALYSES

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Introduction: Fibromyalgia (FM) has been conceptualized as a disorder in which symptom presence/severity is modulated by the reciprocal interaction of nocturnal sleep disturbance and cardinal daytime symptoms. This analysis was conducted in subjects enrolled to date in an ongoing insomnia research study. We examined the relationship between objective and subjective sleep measures and daytime pain in these FM patients.

Methods: Participants were 31 FM patients meeting Research Diagnostic Criteria for insomnia who completed sleep logs and actigraphy throughout a two-week assessment, from which subjective and objective estimates of time in bed (TIB), total sleep time (TST), total wake time (TWT), and sleep efficiency (SE%) were derived. Pain was rated on a 0-10 scale in response to an alarm on the actigraph, with ratings collected at 10AM, 3PM, and 7PM averaged together. Linear mixed models with random intercepts were used to determine if pain ratings predict subsequent night's objective or subjective sleep and if objective or subjective sleep predict next day's pain.

Results: Results showed that objective estimates of TIB and TST were statistically significant predictors of next day's pain, with increased TIB/TST predicting increased pain ($p < .01$). Similarly, increased pain predicted increased objective TIB/TST on the subsequent night ($p < .01$). At this point, no significant relationships were detected between pain and objective TWT or SE% or any subjective sleep parameter.

Conclusion: In these analyses, objective actigraphic data indicate a positive relationship between daytime pain and nighttime sleep, with elevated pain predicting increased TIB and TST, and increased TIB and TST predicting elevated pain the subsequent day. These results suggest that FM patients respond to pain with excessive time in bed, which in turn may disrupt the homeostatic and circadian mechanisms that control the normal sleep/wake rhythm.

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0897

EFFECT OF PARATHYROIDECTOMY ON SLEEP

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Introduction: Patients with primary hyperparathyroidism (PHPT) have significant neurocognitive complaints which are similar to patients with sleep inefficiency. The potential contribution of elevated parathyroid hormone levels to these symptoms has not been explored. A prospective, randomized controlled trial to measure sleep-related outcomes following parathyroidectomy was designed. An adverse effect on total sleep time (TST), sleep efficiency (SE), and daytime sleepiness was hypothesized for patients with PHPT, with improvement after surgical intervention.

Methods: Twenty-one patients were enrolled. Three were excluded due to lack of interpretable data. The remaining 18 (ages 53-82, 15 female) were equally and randomly assigned to the parathyroidectomy (treatment group) or delayed-parathyroidectomy (control group) arms. Wrist actigraphy was used to estimate TST and SE. The Epworth Sleepiness Scale (ESS) quantified daytime hypersomnolence. Measurements were made at baseline, 6 weeks post-intervention, and 6 months post-intervention. Intervention in the delayed group was a phone call.

Results: There was a significant improvement in ESS in the treatment versus the control (-8 v. -2, $p=0.017$) at the six week time point. The difference persisted as a trend at 6 months, but did not achieve statistical significance. There was no significant difference in TST at 6 weeks (-13 minutes v. -0.88 minutes, $p=.452$) or at 6 months (-3.44 v. -3.93, $p=.81$), nor for SE at 6 weeks (-0.77% v. 1.29%, $p=.542$) or at 6 months (1.23% v. -.07, $p=.810$).

Conclusion: No significant change in sleep architecture by actigraphy was noted following parathyroidectomy, but an improvement in the perception of daytime sleepiness was observed. Further correlation with parathyroid hormone and serum calcium levels may elucidate the underlying pathophysiology.

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0898

TO DETERMINE THE PRESENCE OF DEPRESSION, SLEEP DISORDERS, FATIGUE AND SLEEPINESS IN PATIENTS WITHOUT A PRIOR SLEEP COMPLAINT WHO ARE UNDERGOING ANESTHESIA

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Introduction: Fatigue, depression and daytime sleepiness are commonly reported in the general population. The purpose of the study is to determine the frequency of depression in patients referred for investigation to sleep clinic, with no previous history of sleep disorders. Further we wanted to determine the presence of fatigue and sleepiness in these patients.

Methods: Approximately 1000 Patients were screened in a study done by the Anesthesia department of the hospital to assess sleep apnea in patients referred for surgery. Of these 150 patients had a single night sleep study at the Sleep Research Laboratory at the Toronto Western Hospital. Patients had a detailed assessment including (completing rating scales) and a standardized psychiatric assessment. Questionnaires included: Athens insomnia scale, Epworth sleepiness scale, CES-D depression scale, Fatigue severity scale (FSS).

Results: Approximately 31% of the patients scored more than 16 on the CES-D scale (suggestive of depression). Fort five percent of the patients scored > 10 on the Epworth scale. More than a third scored >10 on the Athens insomnia scale and two thirds scored > 3 on the FSS scale suggesting that majority of the patients were fatigued. Of the “depressed” patients 63% were sleepy, 95.2% were fatigued and 47.1% had insomnia. Of the “non depressed” patients more than one third were sleepy, 55% were fatigued and 36% had insomnia. The differential for sleepiness is significant ($p < 0.0461$), for fatigue highly significant ($p < 0.011$) but not for insomnia.

Conclusion: Our findings suggest that majority of these patients were fatigued. One third had features of depression, insomnia and were sleepy during the day. These results emphasize the issue of co morbidity of sleep problems and symptoms in a population not complaining of sleep difficulties and the role of depression potentially exacerbating these factors.

0899

COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA IN BREAST CANCER SURVIVORS: A RANDOMIZED CONTROLLED CROSSOVER STUDY

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Introduction: Estimates of insomnia in women with breast cancer range from approximately 20% to 70%, with reports of poor sleep lasting years after completing cancer treatment. We report results on sleep from a study aimed at understanding the relationship between insomnia, fatigue, depression, and anxiety in breast cancer by treating insomnia with individual cognitive behavioral therapy for insomnia (CBT-I) and looking at effects of this treatment on the symptom cluster.

Methods: Fourteen breast cancer survivors (age M= 61 years, SD=11.6, range = 45-85) were randomly assigned to 6 weeks of CBT-I followed by 6 weeks of follow up, or to 6 weeks of treatment as usual (TAU) followed by 6 weeks of CBT-I.

Results: Participants in the CBT-I group reported less self-rated insomnia compared to the TAU group (Insomnia Severity Index: CBT-I, M=12.20, SD=6.57, range=2-19; TAU M=20.71, SD=3.99, range=16-26, $p=0.03$). The pooled analyses of pre and post CBT-I treatment for all 14 participants revealed significant improvements in sleep quality (PSQI score: Pre-treatment M=12.14, SD=3.21, range=9-19, post-treatment M=7.57, SD=4.22, range=3-16 $p=0.002$), sleep diary variables (minutes wake time after sleep onset, WASO: pre-treatment M=53, SD=43, range=3-164, post-treatment M=25, SD=26, range=0-96, $p=0.002$; Sleep efficiency, pre-treatment M=73, SD=15, range=35-92, post-treatment M=83, SD=11, range=57-98, $p=0.01$; Number of wakes, pre-treatment M=3, SD=1, range=1-6, post-treatment M=2, SD=2, range=0-7, $p=0.02$), actigraphy variables (WASO in hours, pre-treatment M=1.6, SD=0.66, range=0.7-2.5, post-treatment M=1.04, SD=0.31, range=0.6-1.6, $p=0.009$; Number of wakes, pre-treatment M=26, SD=7.8, range=14-36, post-treatment M=23, SD=6.3, range=13-33, $p=0.046$; Sleep percent pre-treatment M=82, SD=6, range=74-92, post-treatment M=86, SD=3, range=79-92, $p=0.02$) and weekly sleep medication count (pre-treatment M=1, SD=1.5, range=0-5, post-treatment M=0.07, SD=0.3, range=0-1, $p=0.02$). Benefits were maintained at a 6 week follow-up.

Conclusion: The results are comparable to previous studies that looked at group CBT-I therapies in breast cancer survivors and show that CBT-I improves sleep in breast cancer survivors.

Support (optional): CBCRP 11GB-0049, CBCRP 11IB-0034, NCI CA112035 and the Research Service of the VASDHS.

0900

DESCRIPTION OF TOTAL SLEEP TIME AND WAKE AFTER SLEEP ONSET WITHIN THREE EQUAL SLEEP PERIODS IN CHILDREN RECEIVING INDUCTION CHEMOTHERAPY FOR LEUKEMIA (ALL)

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Introduction: Describe pattern of fragmented sleep in children receiving induction chemotherapy using wrist actigraphy. Each child's actigraphy data was divided into 3 equal sleep periods per night, with the understanding that during the first third of the night deep sleep stages predominant, and that in the last third of the night REM sleep is most predominant.

Category N—Sleep in Medical Disorders

Methods: This is a prospective, longitudinal study of children with leukemia describing sleep activity using wrist actigraphy. Data were collected from 19 children for 3 consecutive nights of 3 periods each. Measures include total sleep time (TST) and wake after sleep onset (WASO) per sleep period. Analyses use linear mixed models with constant correlations and standard deviations (SDs). P-values were adjusted for multiple sleep period comparisons.

Results: TST was greater during the 1st third of the night. Estimated mean TST was 164, 147, and 149 minutes for sleep periods 1-3 respectively. Mean TST for period 1 was significantly larger than for period 2 ($p=.01$) and for period 3 ($p=.02$). There was no effect of day. The estimated within-subject correlation was $.58$ ($p<.01$) and the estimated SD was 43 minutes. WASO was greater in the middle third of the night. Estimated mean WASO was 14, 21, and 14 respectively for sleep periods 1-3. Mean WASO for period 2 was significantly larger than for periods 1 and 3 ($p<.01$) for both cases. There was no effect of day. The estimated within-subject correlation was $.24$ ($p=.01$) and the estimated SD was 12.

Conclusion: Wrist actigraphy can be used with children receiving chemotherapy to describe fragmented sleep as well as which third of the night's sleep may be most affected. Understanding the pattern of WASO may be beneficial in directing new sleep therapies to assure less fragmented sleep.

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0901

EFFECT OF BRIGHT LIGHT THERAPY ON SLEEP QUALITY AMONG BREAST CANCER PATIENTS UNDERGOING CHEMOTHERAPY: PRELIMINARY RESULTS

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Introduction: Sleep disturbances and fatigue are common in women with breast cancer undergoing chemotherapy. There is much evidence showing that others that suffer from sleep disturbances benefit from light therapy. We present preliminary data from an on-going clinical trial that investigates whether light would improve sleep in women who suffer from breast cancer and are undergoing chemotherapy.

Methods: 20 women (mean age=50.3 yrs, SD=8.4, range=35-70 yrs) who were diagnosed with stage I-III breast cancer, and were scheduled to receive at least 4 cycles of adjuvant anthracycline-based chemotherapy participated. Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI) at baseline (pre-chemotherapy) and during the last week of cycle 4 (C4). The participants were randomized into two treatment groups: bright white light (BWL; $n=10$) and dim red light (DRL; $n=10$). Each woman was exposed to 30 minutes of light (Litebook, Inc) each morning during all four weeks of chemotherapy.

Results: PSQI Use of Sleep Medication subscale for DRL increased from 0.9 (SD=1.29, range=0-3) at baseline to 1.4 (SD=1.26, range=0-3) at C4, while for BWL it decreased from 2.4 (SD=1.13, range=0-3) at baseline to 2.33 (SD=1.12, range=0-3) at C4. PSQI Daytime Dysfunction subscale for DRL increased from 0.5 (SD=0.7, range=0-2) at baseline to 0.8 (SD=0.79, range=0-2) at C4 while for BWL there was a slight decrease from 0.9 (SD=0.9, range=0-3) at baseline to 0.89 (SD=0.6, range=0-2) at C4.

Conclusion: Preliminary results suggest that bright white light may improve some aspects of sleep quality, as women in the BWL group used less medication and rated their daytime dysfunction as less severe than women in the DRL group. Additional data would increase statistical power and could strengthen these findings.

Support (optional): Supported by CBCRP 11IB-0034, NCI CA112035, M01 RR00827, Litebook Inc, and the Research Service of the VAS-DHS.

0902

FEATURES OF POLYSOMNOGRAPHIES AND QUESTIONNAIRES FROM A LARGE POPULATION OF WOMEN IN DISTINCT GYNECOLOGICAL STATUS

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Introduction: Sleep disturbances such as insomnia are a frequent complaint in women as these report more sleep difficulties than men. Women have more awakening episodes than men do and at menopause the apneic events values reach those of men. This fact instigates the exploration of how these alterations relate to the sleep architecture as a means to trigger and/or contribute to hormonal changes in women who find themselves in distinct phases of reproductive life. The aim of this study was to investigate how the most common gynecological alterations (menstrual cycle, premenstrual syndrome or menopause) can influence either subjective or objective sleep data.

Methods: 1306 women (18 to 98 years old) who sought clinical practice because of a sleep complaint. All subjects filled out a sleep and gynecological questionnaire. The patients were subsequently led to the room where the polysomnography (PSG) recording was conducted.

Results: Questionnaires revealed that women referring abnormal menstrual cycle had more difficulty falling sleep and complained more of snoring. PSG data confirmed an elevated apnea-hypopnea index (AHI) in these women. In contrast, normal menstrual cycle women presented higher sleep efficiency and lower AHI. Premenstrual syndrome was associated with more complaints of PLM, higher sleep efficiency and lower AHI. Women who took hormonal contraceptive had less snoring, and PSG indicated higher sleep efficiency (increased stages 3-4) and REM) and lower AHI, less awakenings, and reduced time in saturation under 90% (TSaO₂). Menopausal women with or without hot flashes had lower Epworth scores and more snoring complaints, and these were accompanied by lower sleep efficiency. PSG revealed higher AHI (with higher TSaO₂), PLM, and more awakenings. Hormonal therapy reduced snoring complaints and lowered AHI at PSG. Women with an abnormal cycle had 1.7 more chances of developing sleep disturbances when adjusted for age, BMI, dysmenorrhea, and premenstrual syndrome than those with a normal cycle.

Conclusion: Gynecological status exerts a marked influence on both sleep quality and objective parameters.

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0903

EFFECT OF BRIGHT LIGHT THERAPY ON FATIGUE IN BREAST CANCER PATIENTS UNDERGOING CHEMOTHERAPY

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Introduction: Fatigue is an almost ubiquitous complaint among cancer patients, and is observed in more than 75% of patients undergoing che-

motherapy. Bright light has been shown to have an alerting effect. We examined whether bright light therapy would improve fatigue in women with breast cancer undergoing chemotherapy.

Methods: Twenty women (mean age=52.6 yrs, SD=8.7, range: 32-70) diagnosed with stage I-III breast cancer were randomized into two treatment groups: bright white light (BWL; n = 10) or dim red light (DRL; n = 10) and instructed to self-administer light therapy (Litebook, Inc.) for 30 minutes every morning, during their first 4 cycles of anthracycline-based chemotherapy. Fatigue was assessed using the Multidimensional Fatigue Symptom Inventory - Short Form (MFSI-SF) pre-chemotherapy (baseline, BL) and during cycle 4 (C4) week 1 (W1). Mixed models were developed with group, cycle of chemotherapy, and the group-phase interaction included as covariates.

Results: Mean MFSI total scores for BWL were 17.6 (SE=8.5) at BL and 15 (SE=7.1) at C4W1, while the DRL mean MFSI total scores were -1 (SE=4.3) at BL and 19.1 (SE=9.0) at C4W1. These findings suggest a small improvement over this time in the BWL group, but a significant worsening of symptoms in the DRL group (group*time p = 0.0052).

Conclusion: Preliminary results showed that women exposed to bright white light during chemotherapy showed little change in fatigue, while women exposed to dim red light experienced worse fatigue. These data suggest that bright white light may prevent an increase in fatigue in women undergoing chemotherapy. We continue to explore this question and examine the relationship between improved fatigue and improved sleep.

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0904

AUTONOMIC ACTIVATION DURING NREM SLEEP IN FIBROMYALGIA PATIENTS

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Introduction: Fibromyalgia (FM) is a chronic condition characterized by diffuse musculoskeletal pain and specific tender points. Although the mechanisms underlying the FM syndrome have not been fully elucidated, research suggests that various components of the central nervous system are involved, including the pain-processing pathways and the autonomic nervous system. The purpose of this study was to evaluate autonomic changes in patients with FM using time and frequency domains analysis of heart rate variability (HRV).

Methods: After washout of anti-depressant treatment, muscle relaxants and analgesics, tender points were counted to ensure FM diagnostics. Twelve healthy patients and twelve with FM were selected. All patients underwent an overnight polysomnography, in which HRV analysis were carried out. For all the patients, absence of respiratory disorders were observed. Time and frequency domain (FFT) analysis of 5-minute windows of R-R intervals were calculated for SWS sleep periods.

Results: Time domain analysis showed that mean heart rate variability was lower in FM patients compared with controls (U- test, p = 0.015); similarly, the percentage of differences between adjacent R-R intervals over 50 ms (pNN50) was decreased in FM patients (U-test; 0.015). In the frequency domain analysis, high frequency (HF), low frequency (LF) and total power (TP) HRV components were significantly lower in FM patients than in controls (U-test, p=0.015, p = 0.008 and p=0.003 respectively)].

Conclusion: The main finding of this preliminary study was the reduction of parasympathetic and sympathetic components of HRV for FM patients, as observed in high and low frequency band of FFT analysis and pNN50 index in time domain. These results indicate that patients with fibromyalgia present an impaired autonomic nervous system. Better understanding of the pathophysiology of this entity is important in

order to provide more effective treatment and develop preventive measures to avoid long-term consequences.

Support (optional): Support: AFIP, FAPESP (CEPID 98/14303-3)

0905

AUTONOMIC NERVOUS SYSTEM DYSFUNCTION IN CHRONIC FATIGUE SYNDROME: A POPULATION-BASED STUDY

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Introduction: Autonomic Nervous System (ANS) dysfunction, manifested as increased heart rate (HR) with reduced heart rate variability (HRV), has been demonstrated in the awake Chronic Fatigue Syndrome (CFS) patients. We have extended those findings by establishing that increased HR with reduced HRV also persist during sleep. We aimed to determine the impact of individual sleep states on ANS activity, while accounting for potential circadian influences.

Methods: Continuous electrocardiographic data were collected during nocturnal polysomnography followed by multiple sleep latency test (MSLT), from 30 CFS subjects and 36 non-fatigued (NF) matched controls. HR, HRV, autonomic arousals, sympathetic and parasympathetic control, and sympatho-vagal balance were determined by algorithms developed at the Medical Physics Department at Tel Aviv University, and coded according to the sleep/wake state at night and day times. Medications and physical activity were also controlled for.

Results: CFS subjects exhibited increased HR (p<.001) during nocturnal wakefulness (W), Stages I and II (LS), slow wave (DS), and rapid eye movement (REM) sleep. These differences remained significant during sleep/wake states measured during daytime MSLT (p<.001). Power content in the very low frequency (VLF), low frequency (LF) and high frequency (HF) ranges, as well as the LF/HF ratio indicated that HF was significantly lower (p<.005) in CFS subjects during all states. In addition, VLF and LF power was also significantly lower (p<.05) in CFS subjects during LS. Both groups displayed similar sleep architecture, RDIs < 10, and similar numbers of cortical arousals. The frequency of autonomic (sub cortical) arousals was also similar.

Conclusion: Employing a novel approach, we demonstrate for the first time that the increased HR in CFS is unaffected by behavioral state (wakefulness, sleep) and circadian time. In addition, we establish that no difference exists in the frequency of sub cortical arousals between CFS and NF subjects. Finally we reaffirm our previous findings of normative values of sleep-wake architecture as well as the absence of clinically relevant levels of sleep disordered breathing in CFS. Thus, we postulate that the unremitting fatigue, a hallmark trait of CFS, is not a manifestation of perturbed sleep, nor a primary sleep disorder. Rather, we suspect a more generalized disturbance in central autonomic function contributes to the characteristic symptoms of CFS.

Support (optional): Chronic Viral Diseases Branch, Coordinating Center for Infectious Diseases, Centers for Disease Control & Prevention, Atlanta, GA, USA

0906

SLEEP/WAKE FUNCTIONING DURING AND FOLLOWING CANCER

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Introduction: Clinical observations suggest that cancer and its treatments disturb sleep/wake functioning; however, little data exist describing the characteristics and consequences of sleep problems in this population. As part of a larger effort to improve measurement of sleep/wake functioning, we explored the scope of difficulties with sleep in a diverse group of patients diagnosed with cancer.

Methods: We conducted 10 focus groups with patients recruited from the Duke University tumor registry and oncology clinics. Separate groups were held with patients in or before treatment for breast, prostate, lung, colorectal, hematological, and other (mixed) cancer types. Three groups were held with patients who were post-treatment. All groups were audio-recorded and transcribed. A note taker observed all groups and produced summaries of the themes covered and non-verbal dynamics. An independent auditor verified summaries against the transcripts.

Results: The 67 participants represented the continuum of care and a broad age distribution. One-third of participants were African American. Most participants described sleep problems either caused by or exacerbated by cancer. Pain, night sweats, and frequent waking for urination or medications were common physical factors disturbing sleep. Difficulties with sleep positioning disturbed sleep for patients with medical devices or recent surgery. Difficulty breathing disturbed sleep for patients with lung cancer or metastases. Anxiety or fear about prognoses, treatment decisions, and follow-up appointments (especially for those post-treatment) were common psychological factors affecting sleep. Participants reported somnolence during chemotherapy or radiation treatments. Many felt that sleep problems reduced their productivity, concentration, social interactions, and overall quality of life. Many also shared beliefs about the increased importance of sleep when fighting cancer.

Conclusion: We identified multiple ways that cancer and its treatments affect sleep. These findings underscore the need for interventions that minimize the negative impact of cancer and its treatments on sleep. Efforts are underway by the Patient-Reported Outcomes Measurement Information System (PROMIS) Network to develop a measure that reflects the breadth of concepts considered important by patients with cancer under the category of sleep/wake functioning.

Support (optional): National Cancer Institute supplement to NIH grant U01 AR52186-01

0907

EXCESSIVE SLEEPINESS PREDICTED BY SPECIFIC MEDICAL DISORDERS AND DEPRESSION: A POPULATION-BASED STUDY

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Introduction: Sleep restriction and sleep-related disorders are common causes of excessive sleepiness (ES). However, medical disorders and depression (MD/D) can also cause ES. The objective of this report is to determine the extent to which ES is associated with MD/D.

Methods: 2612 individuals (age 18-65; mean 42.61±12.53) were assessed after excluding suspected sleep disordered breathing (n=218),

narcolepsy (n=3), and shift workers (n=536). Participants were asked about sleep habits, Epworth Sleepiness Scale (ESS) and the following MD/D: cardiac disease, hypertension, diabetes, emphysema, asthma, thyroid disease, cancer, ulcers, colitis, arthritis, migraine, stroke, epilepsy, depression, neurological and gynecological disorders.

Results: Demographics and prevalence of disorders were similar to US Census data. 67% of our sample suffered from one or more current MD/D. The overall mean ESS(SD) was 7.7(4.4) and overall prevalence of ES (ESS≥10) was 30.7%. The mean ESS(SD) and the prevalence of ES in subjects with MD/D versus no MD/D were significantly higher: 7.9(4.5) vs. 7.3(4.2), p<0.05 and 31.4% vs. 29.4%, p<0.05, respectively. Mean ESS increased as a significant linear function of number of MD/D. At the level of specific disorders, the prevalence of ES was significantly higher for participants with ulcers (50% vs. 30.1%, p<0.05), migraines (37.1% vs. 29.9%, p<0.05), and depression (37.4% vs. 29.5%, p<0.05). Ulcers (RR;1.55[1.23-1.96]), migraines (RR;1.29[1.11-1.50]), neurological disorders (RR;1.47[1.10-1.95]) and depression (RR;1.29[1.12-1.48]) were found to be independent predictors of ES, after controlling for age, gender, time in bed and behavioral factors(alcohol intake, caffeine, and smoking). Participants with ulcers had the highest level of sleepiness, possibly due to the elevated level of reported sleep initiation and maintenance disturbances.

Conclusion: These data support the notion of increased level of sleepiness in MD/D. The finding that ES increased with the number of MD/D, suggests that ES producing effects are additive. Further research is needed to determine the relative contribution of different disorders in producing increased sleep drive directly or via disturbed nocturnal sleep.

Support (optional): Cephalon Inc.

0908

SLEEP ASPECTS AND SLEEPINESS IN PATIENTS WITH HEPATIC CIRRHOSIS

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Introduction: Although the sleep alterations are common in patients with cirrhosis, studies using the polysomnogram (PSG) as an instrument of evaluation are still scanty and little is known about the severity of liver failure on sleep parameters. The aim of this study was to characterize sleep parameters and sleepiness in cirrhotic patients and to assess a possible influence of the severity level of this disease on these parameters.

Methods: Methods: 42 cirrhotic patients(50,36±8,5y) treated at the hepatology outpatient service of Hospital São Paulo (UNIFESP/EPM) and 24 healthy volunteers(49,66±9,8y) were submitted to an all night polysomnographic evaluation and the Epworth Sleepiness Scale (ESS). The severity of the illness was assessed by the prognostic model of Child-Turcotte-Pugh (CTP) and patients were classified in classes : A(5-6 points), B (7-9 points) and C (10 or more points), being C the most severe.

Results: The polysomnographic findings showed lower sleep efficiency (p< 0,01), as well as an increase in the REM sleep latency (p< 0,01), as well as a lower REM sleep percentage (p< 0.01) in the cirrhotic group when compared with the control group .The ESS score did not show any difference. According to the CTP, the patients were classified as Child A (16 individuals), B (17 individuals) and C (9 individuals). There was a significant difference among CTP groups in regard to REM sleep percentage, significantly lower in group C when compared to group B (p<0.02) and group A (p< 0.03). There was also a moderate negative correlation between the Child Pugh score and REM sleep percentage (r= -0.47).

Conclusion: The findings suggest that cirrhotic patients present lower sleep efficiency as well as an increase in the REM sleep latency and a lower REM sleep percentage than healthy controls, and that the subjects with more accentuated liver failure have lower REM sleep percentage.

Support (optional): Support: AFIP, FAPESP (CEPID 95/14303-3)

0909**IMPACT OF PAINFUL DIABETIC PERIPHERAL NEUROPATHY ON SLEEP ARCHITECTURE USING POLYSOMNOGRAPHY**Eriksson ME¹, Gribble LC¹, Gouni R², Kerr D², Coppini DV³, Boyle J¹¹Faculty of Health and Medical Sciences, University of Surrey, Guildford, United Kingdom, ²Bournemouth Diabetes and Endocrine Centre, Royal Bournemouth Hospital, Bournemouth, United Kingdom, ³Poole Diabetes Centre, Poole General Hospital, Poole, United Kingdom

Introduction: Up to approximately 60 % of all diabetes patients develop neuropathy during the course of their illness, and 30% of these will also experience varying degrees of neuropathic pain, or so called painful diabetic peripheral neuropathy (DPN). Diabetic neuropathic pain is typically more severe at night, and depending on its quality and severity, is likely to have some impact on patients' sleep, leading to both physical and psychological complications.

Methods: Sleep architecture and pain interference for 27 (M = 15, F = 12, mean age of 62.8, ± 8.9) diabetic patients with painful peripheral neuropathy was studied. Overnight sleep was measured between 23.00h to 07.00h using polysomnography (PSG) and subjective sleep was assessed using sleep diaries. Pain severity and interference was measured by using the short form brief pain inventory (BPI).

Results: The BPI showed that pain had most impact on sleep and there was a correlation between years since neuropathy diagnosis and pain interference on sleep ($p < 0.05$). 85% of patients reported that their pain interfered with their sleep, with 31% having substantial interference (defined as BPI score of ≥ 5). Increased pain interference correlated with increased duration of stage 1 ($r = 0.74$, $p < 0.0001$) and increased PSG number of awakenings (NAW) ($r = 0.48$, $p = 0.017$). In addition, pain interference on sleep correlated significantly with subjective quality of sleep (sQOS) ($r = 0.47$, $p < 0.05$). All results are based on partial correlations for both age and gender.

Conclusion: These preliminary data provide objective evidence that DPN interferes with PSG measures of sleep. Higher pain interference is associated with increased NAW and duration of stage 1 sleep, and reduced quality of sleep suggesting that DPN is associated with fragmented and lighter sleep.

Support (optional): This Investigator-initiated research project is funded through a grant from Pfizer Ltd.

0910**PAINFUL DIABETIC PERIPHERAL NEUROPATHY: ASSESSMENT OF QUALITY OF SLEEP AND SLEEP CONTINUITY**Boyle J¹, Mills SL¹, Gouni R², Coppini DV³, Kerr D², Eriksson ME¹¹Faculty of Health and Medical Sciences, University of Surrey, Guildford, United Kingdom, ²Bournemouth Diabetes and Endocrine Centre, Royal Bournemouth Hospital, Bournemouth, United Kingdom, ³Poole Diabetes Centre, Poole General Hospital, Poole, United Kingdom

Introduction: The worldwide diabetes population is raising epidemic proportions, and the projected global prevalence for 2010 is 221 million, making it one of the most common chronic medical conditions. Diabetes Mellitus (DM) is a complex disease with many possible complications, one of which is painful diabetic peripheral neuropathy (DPN). Sleep disturbance is common in patients with DM and patients with painful DPN often report that their pain has a severe impact on their sleep.

Methods: 27 patients (M = 15, F = 12) with DM and painful DPN were enrolled in an ongoing study assessing sleep architecture and pain interference on sleep. Overnight sleep was measured between 23.00h to 07.00h using polysomnography (PSG) and subjective sleep was assessed using sleep diaries.

Results: Participants had a mean age of 62.8, ± 8.9, (range 38-79 yrs). Mean sleep efficiency (SE) was 78.1% and wake after sleep onset (WASO) was 86.81 min. Partial correlation for age and gender showed that subjective quality of sleep (sQOS) correlated significantly with WASO ($p < 0.05$). In addition, subjective number of awakenings (sNAW) correlated with SE and TST ($r = -0.67$, $p < 0.001$ for both), NAW ($r = 0.52$, $p < 0.05$), and WASO ($r = 0.51$, $p < 0.01$).

Conclusion: Diabetic patients with painful peripheral neuropathy had a mean sleep efficiency of 78.1%, suggesting poor sleep quality. Subjective measures of sleep (QOS and sNAW) correlated significantly with SE, WASO, TST and NAW suggesting that disruption of sleep continuity may have a major impact on patients' perception of sleep.

Support (optional): This Investigator-initiated research project is funded through a grant from Pfizer Ltd.

0911**SLEEP IN PAINFUL DIABETIC PERIPHERAL NEUROPATHY: SUBJECTIVE MEASURES AND ACTIGRAPHY ANALYSIS**Gribble L¹, Korimbocus A¹, Middleton B¹, Gouni R², Kerr D², Coppini DV³, Boyle J¹¹Faculty of Health and Medical Sciences, University of Surrey, Guildford, United Kingdom, ²Bournemouth Diabetes and Endocrine Centre, Royal Bournemouth Hospital, Bournemouth, United Kingdom, ³Poole Diabetes Centre, Poole General Hospital, Poole, United Kingdom

Introduction: Patients with painful diabetic peripheral neuropathy (DPN) invariably report poor sleep due to nocturnal exacerbations of their symptoms. Studies have shown a relationship between pain and poor sleep exists, but no studies have compared subjective sleep with actigraphy in this patient population.

Methods: 27 patients (15 male and 12 female with a mean age of 62.9 SD ± 8.9) have completed the baseline period (D1 - 8 placebo run-in) of a study investigating sleep and pain in patients with DPN. Measures included wrist actigraphy, subjective assessment of quality of sleep (QOS), subjective number of awakenings (sNAW) and the subjective pain severity and pain interference scores taken from the brief pain inventory short-form (BPI). Patients wore actiwatches from medical screening to end of study and completed the sleep assessments and BPI daily from the start of the placebo period to the end of study.

Results: Pain severity was associated with an increased perception of interference on sleep $r = 0.54$ ($p \leq 0.01$) and a significant reduction in QOS $r = 0.40$ ($p \leq 0.05$). Subjective NAW was associated with QOS $r = 0.49$ ($p \leq 0.01$) suggesting painful neuropathy fragments sleep reducing sleep quality. Actigraphy scores showed good inter-correlation, although there was little correlation between actigraphy and subjective measures of sleep and pain. Only QOS correlated with mean wake bout time $r = 0.44$ ($p \leq 0.05$) suggesting that increased wake bout time worsens subjective QOS.

Conclusion: Subjective measures show a relationship between pain and sleep with QOS decreasing with higher levels of pain severity and pain interference. Actigraphy did not correlate with subjective measures of pain, but there was some correlation with QOS. Our preliminary data highlight the importance of subjective measurements as markers of disturbed sleep, and suggest that painful DPN both fragments and reduces the quality of sleep.

Support (optional): This investigator-initiated research project is funded through a grant from Pfizer Ltd.

0912

PAIN SENSITIVITY IN SLEEPY VERSUS ALERT HEALTHY NORMALS

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Introduction: Acute 4-hr sleep restriction produces hyperalgesia in alert healthy normals. It has been shown that approximately 20% of the population is sleepy, as defined by MSLT, mostly due to mild chronic sleep restriction. This study compared pain sensitivity in sleepy versus alert healthy normals.

Methods: Twenty-seven healthy adults with normal sleep, 18-35 yrs, participated. Each underwent a screening 8-hr NPSG and MSLT (1000, 1200, 1400, and 1800 hrs) the following day. All had sleep efficiencies >85% on their NPSG and 13 had MSLT > 8min and 14 had MSLT < 7 min. All had a baseline 8-hr time-in-bed condition with a standard MSLT and pain assessment conducted the following day. Pain threshold was assessed (AM 1030 and PM 1430 hrs) using a novel radiant heat stimulation method. Finger withdrawal latency (FWL) in sec was measured to 5 randomly presented radiant heat intensities directed to the index finger pad of each hand.

Results: MSLT sleep latency in the sleepy group was 4.72 + 1.83 min and 13.04 + 4.90 min in the alert group. Validating the pain methodology, FWL decreased as a function of increasing heat intensity on AM (F=34.2, p<.001) and PM (F=23.16, p<.001) tests. Importantly, FWL on the AM test was reduced in sleepy relative to alert subjects (F=6.98, p<.01) and similarly on the PM test (F=7.38, p<.01). Further, the lowest heat intensity inducing finger withdrawal (i.e. latency < 21 sec) was lower in sleepy vs alert subjects (t=5.76, p<.001). There were no significant group by intensity interactions on either AM or PM tests.

Conclusion: These are the first data to show that normal variations in sleep time such as mild chronic sleep restriction results in differences in pain sensitivity. It suggests that clinical differences in pain sensitivity and response to analgesics are in part explained by sleep.

Support (optional): The Fund for Henry Ford Hospital, B10914 awarded to Dr Roehrs

0913

NEGATIVE MOOD MEDIATES THE RELATIONSHIP BETWEEN POOR SLEEP AND INCREASED PAIN IN CHRONIC PAIN PATIENTS

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Introduction: Sleep disturbances are extremely common among patients experiencing chronically painful conditions, with 50-70% of chronic pain patients reporting significant sleep disturbance. The presence of concomitant sleep problems can significantly complicate both the course and the management of chronic pain patients. Additionally, higher levels of negative mood have been reported among both chronic pain patients, and among individuals experiencing sleep disturbance. However, studies examining the relationships among negative mood, sleep, and pain, have reported conflicting findings about the importance of negative mood in the sleep-pain relationship.

Methods: 337 patients between 18 and 65 years of age, with chronic back, facial, or fibromyalgia pain, completed validated self-report measures of pain, mood, and sleep. Structural Equation Modeling (SEM) ex-

amined the relationships among these latent variables, and in particular, the role of negative mood in the relationship between sleep and pain.

Results: SEM analyses produced a significant model ($\chi^2(32)=41.77$, $p=0.12$, RMSEA=0.03), which provided an excellent fit for the data. A direct relationship was found between poor sleep and increased pain. However, when negative mood was also included in the model, it was shown to mediate the relationship between poor sleep and increased pain.

Conclusion: This model suggests that there are multiple pathways between sleep disturbance and individuals' pain experience. Specifically, poor sleep directly predicted increased pain among this sample of chronic pain patients. Additionally, the mediation results suggest that higher levels of negative mood may lead to decreased sleep, which can also result in more pain. This study helps to clarify the relationship between sleep disturbances, negative mood, and chronic pain, in order to improve understanding of the influences of these conditions on one another, as well as to inform interventions.

0914

COGNITIVE BEHAVIORAL THERAPY FOR INSOMNIA IN CHRONIC PAIN PATIENTS

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Introduction: The purpose of this study was to evaluate whether CBT for insomnia (CBT-I) can be successfully applied to insomnia associated with chronic (>6 months) non-malignant pain originating from the spine. We also proposed to assess whether clinical gains within the sleep domain are related to greater pain tolerance.

Methods: Subjects with insomnia and chronic non-malignant pain were recruited to participate in a parallel-groups, randomized, single blind, placebo-controlled trial. Subjects were stratified according to gender, age and ethnicity, then assigned using double matching to one of two groups: one receiving treatment (8 week course of CBT-I), the other group receiving a non-active control for measurement and therapist contact time. The subjects underwent one night polysomnography (PSG) to rule out intrinsic sleep disorders (e.g., OSA). Daily sleep continuity, mood and pain measures were obtained during the screening period, throughout treatment, and for follow up periods at two weeks at three and six months post treatment.

Results: Twenty-eight subjects (22 females) were randomized (19 CBT-I, 9 Controls). Mean age was 49+10 and 89% were caucasian. Significant group differences on sleep outcomes were found post treatment for sleep latency (p=.008), WASO (p=.019), and SE (p=.002); at 3 month for total sleep time (p=.025) and sleep efficiency (p=.035), and at 6 month WASO (p=.027), total sleep time (p=.011), and sleep efficiency (p=.009). Although significant differences on pain outcomes were not found at any time point, clinically relevant effect sizes were found at 6 month follow up for tolerability of pain (0.71), average daily pain severity (0.6).

Conclusion: Insomnia secondary to chronic pain can be effectively treated with cognitive behavioral therapy for insomnia and the treatment gains continue through 6 months post therapy. Additionally, this proof-of-concept study showed that CBT-I can have positive effects on patients' tolerability and severity of their pain.

Support (optional): NIH Grant #NR009080

0915**CORRELATIONS OF THE PAIN AND SLEEP EFFECTS OF PREGABALIN IN FIBROMYALGIA PATIENTS***Pauer L¹, Whalen E², Barrett JA², Zeiher B¹*¹Pfizer Global R&D, Ann Arbor, MI, USA, ²Pfizer Global Pharmaceuticals, New York, NY, USA

Introduction: Sleep disturbance is a prominent symptom in patients with fibromyalgia (FM). The objective of this study was to examine the correlation between pain and sleep effects of pregabalin (Lyrica®) in FM patients.

Methods: Patients meeting ACR criteria for FM for ≥ 3 months and who had pain VAS score ≥ 40 mm were treated for 13-14 weeks in 2 randomized, double-blind, placebo-controlled trials (Studies 1056 and 1077). A total of 1493 patients received either 300, 450 or 600mg/d pregabalin or placebo after a 1-week baseline phase. The primary efficacy parameter in each study was change in endpoint Mean Pain Score (MPS) which was collected on a daily diary with a numeric rating scale (range 0 [no pain]-10[worst possible pain]). Sleep was assessed using the Medical Outcomes Study Sleep Scale (MOS-SS). Pearson correlations were used to explore relationships between change in MPS and MOS-SS Overall Sleep Problem Index and the MOS-SS subscales.

Results: Pregabalin significantly reduced pain; differences from placebo in change from baseline to endpoint MPS were: 300mg/d, -0.55 ($P=0.003$); 450mg/d, -0.71; 600mg/d, -0.82 (each $P<0.0001$). Pain relief was evident within one week of initiating pregabalin treatment. Correlations by treatment between pain relief and MOS-SS Sleep Problem Index were as follows: for Study 1056: 0.60 (placebo), 0.49 (300mg/d), 0.51 (450mg/d), and 0.42 (600mg/d); for Study 1077: 0.44 (placebo), 0.41 (300mg/d), 0.32 (450mg/d), and 0.35 (600mg/d). Correlations between MPS and MOS-SS Sleep Disturbance subscale were statistically significant ($p<0.0001$) across treatment groups in both studies. Adverse events were consistent with known side effects of pregabalin; dizziness and somnolence were the most frequently reported AEs for patients who received pregabalin.

Conclusion: Pregabalin significantly reduced pain from FM at doses of 300 to 600mg/d. Pain relief correlated with beneficial effects on sleep as assessed by the MOS-SS Overall Sleep problems index and sleep disturbance subscale.

Support (optional): Study funded by Pfizer, Inc

0916**PREGABALIN IMPROVES PAIN AND SLEEP QUALITY IN FIBROMYALGIA***Pauer L¹, Whalen E², Barrett JA², Zeiher BG¹*¹Pfizer Global R&D, Ann Arbor, MI, USA, ²Pfizer Global Pharmaceuticals, New York, NY, USA

Introduction: Chronic pain and sleep disturbance are prominent in patients with fibromyalgia (FM). The objective of this study was to examine the correlation between the treatment effect of pregabalin (Lyrica®) on pain and sleep quality in FM.

Methods: Patients meeting ACR criteria for FM for ≥ 3 months and who had pain VAS score ≥ 40 mm were treated for 8-14 weeks in 3 randomized, double-blind, placebo-controlled trials. A total of 2022 patients received either 150, 300, 450 or 600 mg/d pregabalin, or placebo after a 1-week baseline phase. The primary efficacy parameter in each study was Endpoint Mean Pain Score (MPS) compared to baseline. Sleep Quality was assessed on a daily diary using numeric rating scale (range 0 [best possible sleep]-10[worst possible sleep]). Pearson correlations were used to explore relationships between changes in pain and changes in sleep.

Results: Pregabalin treatment at 300, 450 and 600 mg/d showed significant improvement in Endpoint MPS. Likewise, significant improvement was demonstrated for endpoint mean sleep quality across all pregabalin treatment groups. Treatment effects on pain and sleep quality were seen

within 1 week of treatment. Correlations by treatment between changes in pain and sleep were as follows: 0.71 (placebo), 0.65 (150 mg/d), 0.73 (300 mg/d), 0.66 (450 mg/d) and 0.67 (600 mg/d). Adverse events were consistent with the known side effects of pregabalin; dizziness and somnolence were the most frequently reported AEs for patients who received pregabalin and tended to resolve with treatment.

Conclusion: Pregabalin treatment at doses of 300, 450 and 600 mg/d significantly reduced pain and improved sleep quality in FM patients. Significant effects were seen within one week and the changes in pain correlated with changes in sleep quality across all treatments (including placebo).

Support (optional): Study funded by Pfizer, Inc

0917**THE SLEEP QUALITY SCALE AND THE MEDICAL OUTCOMES STUDY SLEEP SCALE IN SUBJECTS WITH FIBROMYALGIA: PSYCHOMETRIC EVALUATION AND MEDIATION EFFECTS***Cappelleri JC¹, Bushmakina AG¹, Martin S², Petrie CD¹, Dukes E³, Zeiher BG¹*¹Pfizer Global Research and Development, Groton, CT, USA, ²Pfizer Global R&D, Ann Arbor, MI, USA, ³Pfizer Global Pharmaceuticals, New York, NY, USA

Introduction: This study investigated the application of the multi-domain Medical Outcomes Study (MOS) Sleep Scale and the one-item, 10-category Sleep Quality Scale in subjects with fibromyalgia (FM).

Methods: Data were obtained from two double-blind, controlled Phase 3 studies with pregabalin (300, 450, 600mg/d) in approximately 1500 subjects with FM. For the MOS Sleep Scale, confirmatory factor analyses, Cronbach alphas, and corrected item-to-total correlations were undertaken at baseline and follow-up. Clinically important differences were estimated using the Patient Global Impression of Change Scale. A mediation model was undertaken to identify and explicate the mechanism that underlies an observed relationship between treatment and sleep outcomes.

Results: In most instances, the Bentler's Comparative Fit Index (CFI) on the MOS Sleep Scale was ≥ 0.9 , indicating acceptable model fit. Cronbach's alphas increased over time for the multi-item domains on Sleep Disturbance (range: 0.78-0.87), Sleep Somnolence (0.71-0.78), and Adequacy (0.36-0.77). For Sleep Quality, estimated test-retest reliability based on seven pre-treatment days was 0.91. Clinically important difference on the MOS Sleep Disturbance domain and the Sleep Quality Scale were estimated to be 7.9 and 0.83, respectively. Mediation models showed that pregabalin directly improved sleep disturbance and sleep quality. Approximately 66 to 80% of the improvement in Sleep Disturbance and 43 to 61% of the improvement in Sleep Quality were the direct result of pregabalin not related to the pain.

Conclusion: The structure of the MOS Sleep Scale is confirmed in patients with FM. In general, this scale's internal consistency reliability is satisfactory except for earlier assessments on the two-item Adequacy domain. The Sleep Quality Scale as measured has high test-retest reliability. On both scales, clinically important differences were identified. The mediation model indicated that pregabalin's effect on sleep is not entirely dependent on the pain treatment effect.

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0918

MEASUREMENT PROPERTIES OF THE DAILY SLEEP QUALITY NUMERIC RATING SCALE IN SUBJECTS WITH FIBROMYALGIA

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Introduction: Sleep disturbance is a characteristic symptom of fibromyalgia (FM). This study evaluated the reliability and estimated the clinically important difference in sleep quality using a daily sleep diary in FM patients.

Methods: Patients meeting ACR criteria for FM for ≥ 3 months and pain VAS score ≥ 40 mm were treated for 13-14 weeks in 2 randomized, double-blind, placebo-controlled trials (Studies 1056 and 1077). 1493 patients received either 300, 450 or 600 mg/d pregabalin or placebo after a 1 week baseline phase. The primary efficacy parameter was change in endpoint Mean Pain Score (MPS). Sleep Quality was assessed on a daily diary using a numeric rating scale (range: 0 [best possible sleep]-10 [worst possible sleep]). Test-retest reliability was based on seven pre-treatment days using intraclass correlation coefficients (ICC). Clinically important difference (CID) was estimated by modeling Sleep Quality (outcome) against Patient Global Impression of Change score (predictor).

Results: Pregabalin treatment at 300, 450 and 600 mg/d showed significant improvement in Endpoint MPS and PGIC. Baseline mean sleep quality was 6.7 and 6.2. In both studies, test-retest reliability was high with mean ICC ≥ 0.90 . Pregabalin treatment was associated with significant improvements in sleep quality and effects were noted within 1 week. The estimated CID was 0.83. The endpoint mean placebo-corrected improvement in sleep quality exceeded 0.83 at all doses except the 300 mg dose group in one study. Adverse events were consistent with the known side effects of pregabalin.

Conclusion: Pregabalin treatment (300, 450 and 600 mg/d) significantly reduced pain in FM patients. The sleep quality diary had high test-retest reliability and an estimated CID of 0.83. Pregabalin treatment led to clinically and statistically significant improvement in sleep quality and effects were seen within one week.

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0919

SLEEP DISORDERED BREATHING IN BREAST CANCER PATIENTS

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Introduction: Studies involving women with breast cancer have shown that fatigue levels are high and sleep is frequently disturbed. These patients experience cancer-related fatigue, a tiredness that is related to cancer or its treatment. This fatigue often results in poor sleep at night and increased daytime napping. Patients with sleep disordered breathing also complain of fatigue and experience poor sleep at night and daytime sleepiness. As part of larger studies examining the relationship between sleep, fatigue and breast cancer, we examined how common sleep disordered breathing might be in women with breast cancer.

Methods: 48 women (mean age 49.8 years, range 34-68 with a mean BMI of 28.8) with newly diagnosed breast cancer scheduled to begin 4 cycles of neoadjuvant or adjuvant anthracycline-based chemotherapy had one night of ambulatory PSG in their home (Embla Flaga Medical Devices/Medcare, Reykjavik, Iceland). Of these patients 2 women had their PSG taken before chemotherapy and 46 women had their PSG taken after chemotherapy. During the PSG recording 32 women were postmenopausal, 10 were pre/perimenopausal and 6 were post hysterectomy. Records were scored for standard sleep parameters and for apneas and hypopneas; the apnea hypopnea index (AHI) was computed.

Results: The mean AHI was 6.4 (SD 7.3; range 0-40.2); however 48% had an AHI ≥ 5 (mean AHI 11.0; SD 8.3) and 15% had an AHI ≥ 10 (mean AHI 19.8; SD 10.8).

Conclusion: In the Wisconsin cohort, only 9% of women in the general population aged 30-60 years old had sleep disorder breathing with an AHI ≥ 5 . In the breast cancer study higher levels of AHI in women may be due in part to the cancer, the chemotherapy or the forced menopause. Further research is needed to understand this high prevalence and determine the relationship between sleep disordered breathing and disturbed sleep and fatigue in these women.

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0920

SLEEP DISTURBANCES IN CHILDREN WITH CENTRAL NERVOUS SYSTEM NEOPLASMS

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Introduction: Primary central nervous system (CNS) tumors are the most common solid tumors in children. Since sleep is regulated by the brain, it is expected that children with CNS tumors will experience sleep disturbances. Possible mechanisms underlying sleep disturbances among these children include local effects of the tumor, effect of the adjuvant therapies and factors that are common in other malignancies. The purpose of this study was to examine sleep characteristics of children with CNS tumors and to investigate possible relationships between sleep disturbances and tumor characteristics, specifically tumor type, tumor location, chemotherapy, and brain irradiation.

Methods: Children who were diagnosed and treated for CNS tumors were enrolled. Charts were reviewed and information on demographics, tumor type and location and therapies was collected. Parents of all participants completed a 28 items sleep questionnaire including the pediatric daytime sleepiness scale (PDSS). Sleep was also objectively evaluated using actigraphy for 5-7 consecutive days.

Results: Thirty-five children (56% male) were studied. Mean age was 9.0 ± 2.7 years (range: 4-17 years). The mean time from diagnosis to questionnaire completion was 4.1 ± 1.4 years (range: 2-8). Posterior fossa tumors composed 56% of the tumors followed by midbrain tumors (24%), temporal and frontal tumors (9% each). 26% of the children had been treated by chemotherapy plus radiotherapy. The mean PDSS score was 9.5 ± 5.5 (range: 1-19). Snoring and disorders of arousals were reported in 18% and 11% of the children respectively. The rate of sleep disturbances was not affected by tumor type, anatomic site, or treatment with chemotherapy or radiotherapy. Age adjusted total sleep time (TST) measured by actigraphy was shorter than TST documented subjectively: 493 ± 60 and 585 ± 60 respectively. TST was also significantly shorter than total sleep duration values previously published for normal children. Time spent awake was 11.3 ± 4.8 min. and mean sleep efficiency was $87\% \pm 4.7$ (range: 79%-95%).

Conclusion: The frequency of sleep disturbances among children with a history of CNS tumors is comparable to the rate reported for healthy children. The shorter sleep duration in this population needs further investigation to conclude whether it results from the CNS disease and therapy or from secondary behavioral and social factors.

0921

MEASURING SLEEPINESS IN THE HEART FAILURE POPULATION

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Introduction: Prior investigations suggest that excessive daytime sleepiness (EDS) is under-reported in patients with heart failure (HF), based largely on the Epworth Sleepiness Scale (ESS). The clinical suspicion of primary sleep disorders in these patients is low, as EDS is commonly ascribed to the underlying heart disease. Yet a substantial number of these individuals have significant sleep disorders. The aim of this study is to investigate the EDS using multiple measures in HF patients.

Methods: Subjects with stable HF treated were invited to participate in a study investigating predictors of sleep apnea in HF. Subjects completed a series of questionnaires including the ESS and underwent PSG followed by MSLT. Self-reported EDS was determined by responding to the question "Based on your experience in the last 6 months, do you feel excessively sleepy during the day?"

Results: Complete data are available for 7 subjects (5 male). Mean age was 45 years (22-59). Self-reported EDS was observed in 2 (29%) subjects. Mean ESS was 11.7 +/- 5.1; five (71%) subjects had ESS of 10 or greater. Mean sleep latency was 6.9 minutes +/- 5.8. The MSLT was normal (MSL >10 min) in 1 subject; MSL ranged from 5 - <10 min in 2 (28%) subjects and was < 5 min in 4 (57%) subjects. Six (85.7%) subjects had sleep apnea.

Conclusion: These preliminary data suggest a marked degree of hypersomnia and discrepancy between self-reported EDS and the MSLT in HF patients. Patient perception of EDS may be reduced and healthcare providers may fail to adequately explore sleep-wake complaints as both focus on treatment of the primary condition. Given the small sample size, our findings require confirmation. However, these findings support the need to routinely incorporate a sleep history in the evaluation of patients with HF.

0922

PERIODIC BREATHING IN WAKEFULNESS IS ASSOCIATED WITH SEVERE SLEEP APNEA IN HEART FAILURE PATIENTS WHO ARE CANDIDATES FOR CARDIAC RESYNCHRONIZATION THERAPY

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Introduction: Sleep apnea is common in patients with advanced heart failure (HF). Recent work has highlighted the occurrence of periodic breathing (PB) during exercise in such patients. However, the relationship between waking PB and sleep disordered breathing is not as clear. We investigated the relationship between PB at rest or 6 minute walk test and sleep apnea and heart failure parameters in HF patients.

Methods: 22 patients (91% Caucasian) undergoing cardiac resynchronization therapy (CRT) for advanced HF were prospectively studied. All were males aged 67.9±8.8. All patients underwent breathing pattern assessment with a nasal airflow monitor (Apnealink, Resmed) under the following conditions: supine wakefulness (10 minutes), standing wakefulness (3 minutes) and 6 minute walk testing. Full polysomnography in the sleep laboratory was also performed within 24 hours. Periodic breathing was assessed by qualitative visual analysis of the recordings

by 2 physicians. Disagreements were adjudicated by consensus. For purposes of this analysis, PB in any of the wake test conditions was considered to be positive.

Results: All patients had NYHA class III HF and evidence of ventricular dyssynchrony. Eighty-six percent of patients had underlying ischemic cardiomyopathy. Ejection fraction (EF) was 29.3±9.4. The following comorbidities were assessed: hypertension (86%), diabetes (63%), peripheral vascular disease (36%), history of smoking (95%), renal disease (43%), and dyslipidemia (95%). Eight/22 patients (36%) demonstrated PB during wakefulness under at least one condition of testing. Patients demonstrating PB had similar age, weight, EF's, left ventricular end diastolic dimensions, Minnesota Living with HF Questionnaire scores, and BPs. Demographics, cause of HF, and comorbid conditions were not different between the groups. Patients with PB showed a trend toward higher brain natriuretic peptide (BNP) (854.3±350.2 vs. 276.7±210.9 pg/ml, p=0.08). Apnea-hypopnea index (AHI) was significantly higher in patients demonstrating waking PB (31.9±16.4 vs. 14.1±14.4, p=0.024). Central sleep apnea (CSA) did not differ between the groups.

Conclusion: PB during wakefulness is prevalent in a cohort of patients with advanced HF. Patients with PB are more likely to have a significantly elevated AHI and higher BNP levels. Our results did not support a relationship between waking PB and CSA in patients who are CRT candidates, although the small sample size may have affected the ability to detect a relationship.

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0923

HEART DISEASE AND RISKS OF SLEEP APNEA IN A CARIBBEAN SAMPLE

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Introduction: Few studies have investigated associations between physical health measures and sleep apnea (SA) among Blacks. To our knowledge, no studies have assessed these associations in Caribbean-American populations. Using a community-based sample of Caribbean Americans, we examined which physical health characteristics were predictive of SA risk.

Methods: A total of 554 patients (mean age: 48.17 ± 16.75yrs) participated in the study; 55% were women. Data were collected in four primary-care clinics in Brooklyn, NY. Eligible patients completed questionnaires available in both English and Haitian Creole. A health educator explained the purpose of the study to consenting patients and assisted them in completing questionnaires, which required 15min to complete. Participants reporting habitual snoring, excessive daytime sleepiness, and sleep fragmentation were considered at high SA risk. Data were entered in SPSS 15.0 for statistical analysis.

Results: Rates of SA symptoms were: snoring (45%), excessive daytime sleepiness (33%), and difficulty maintaining sleep (34%). Many reported falling asleep while watching television (47%) or while driving (14%). The average BMI of the patients was 29.15 ± 7.16kg/m². Of the sample, 35% reported a history of hypertension, 16% a history of heart problems, and 13% were at high risk for SA. Fewer individuals at low SA risk reported insomnia complaints (17% vs. 35%, $\chi^2 = 12.35$, p < 0.001). Logistic regression analysis showed that a history of heart disease was the most important predictor of the likelihood of expressing SA symptoms, with a corresponding multivariate-adjusted odds ratio of 11 (95% CI = 3.03--40.63).

Category N—Sleep in Medical Disorders

Conclusion: Findings are consistent with previous studies showing associations between heart disease and SA among Whites and African Americans. Caribbean patients with a history of heart disease should be a prime target for interventions that promote screening and diagnosis of sleep apnea. Future studies should assess sleep patterns of Caribbean Americans using epidemiologic methodology.

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0924

ADULT GROWTH HORMONE DEFICIENCY IS ASSOCIATED WITH MAJOR ALTERATIONS IN ENDPOINTS CHARACTERIZING SUBJECTIVE MEASURES OF SLEEP

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Introduction: Adults with growth hormone deficiency (GHD) often complain of excessive daytime sleepiness and fatigue, however their nocturnal sleep remains poorly characterized. The aim of the present study was to examine free-living sleep log records as surrogate measures of sleep quality in patients with untreated GHD in comparison to that of age, gender, and body mass index matched (BMI) healthy subjects.

Methods: Twenty GHD patients ages 19-71yr and twenty gender-, age- and BMI-matched controls recorded their activity using the Karolinska Sleep Log during six consecutive nights with usual bedtimes at home. The analyzed data is presented as mean \pm SD.

Results: The time spent in bed (417 \pm 60 min vs. 435 \pm 78 min for week nights and 454 \pm 87 vs. 446 \pm 62 for week-end nights) was similar in GHD subjects and matched controls, respectively ($p > 0.05$). However, GHD patients reported more fragmented sleep with increased number of awakenings 3 \pm 1 vs. 1 \pm 1 controls ($p = 0.002$) and more time spent awake after sleep onset 31 \pm 28 min vs. 16 \pm 18 controls ($p = 0.02$). GHD subjects had significantly decreased sleep quality score 3.2 \pm 0.9 vs. 3.9 \pm 0.8 controls, $p = 0.02$ (1 =very poor and 5= very well). GHD patients scored their sleep as less refreshing than controls with a score of 2.9 \pm 0.8 vs. 3.9 \pm 1 min ($p = 0.001$), with a score of 1 =being not refreshed and 5=completely refreshed). These differences were associated with a lower score for sound sleep on a 1-5 scale (3.3 \pm 0.9 in GHD subjects vs. 3.9 \pm 0.6 in controls; $p = 0.02$). Sleep efficiency was worse in GHD than in controls (3.1 \pm 0.8 vs. 4.1 \pm 0.8, p level 0.001).

Conclusion: Our results indicate that GHD patients have reduced subjective measures of quality of sleep compared to matched controls, despite spending a similar time in bed. The reported disturbances consist of increased sleep fragmentation with increased number of awakenings. Thus, GHD appears associated with deterioration of sleep, which may result in excessive daytime sleepiness and may decreased quality of life.

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0925

SLEEP IN PATIENTS WITH MULTIPLE MYELOMA

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Introduction: Cancer-related insomnia is a prevalent and distressing symptom among many newly-diagnosed patients with cancer. However, the nature of sleep disturbance in specific cancer groups has not been well-characterized. Possible increases in daytime sleep may contribute to the development of chronic insomnia, although daytime sleep characteristics have not been reported for many specific types of cancer. The purpose of this presentation is to describe the nocturnal and daytime sleep of adults with multiple myeloma (MM).

Methods: Actigraphy data were collected from 178 adults (41% female), predominantly Caucasian (91%), mean age of 56 years (25-76 years; S.D. =9.8), and newly diagnosed with MM, as part of an experimental study of exercise and sleep. All patients were newly enrolled for aggressive treatment at an international MM institute for research and therapy.

Results: Mean sleep onset latency was 29 minutes (S.D.=38.9), nocturnal sleep time was 414 minutes (S.D.= 98.5), per cent of time asleep was 80% (S.D.= 14.2), number of wake episodes were 12 times (S.D.= 5.7). Daytime sleep episodes were 10 times (S.D.=10), daytime sleep time was 98 minutes (S.D.= 98.6), and total sleep time (per 24 hours) was 512 minutes (S.D.= 157.1).

Conclusion: Although total sleep time appears adequate, nocturnal sleep time comprises only 81% while daytime sleep time accounts for 19% of the 24-hour total. These findings support screening for sleep disturbance in patients with MM, and further research on insomnia and related sleep interventions in this cancer population.

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0926

RESTLESS LEGS SYNDROME AND FIBROMYALGIA: A CASE-CONTROL STUDY

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Introduction: Fibromyalgia (FM) is a chronic disorder of diffuse pain. Restless legs syndrome (RLS) is a sensorimotor disorder characterized by an urge for leg movement. We investigated the association between these two sleep disrupting disorders.

Methods: Fibromyalgia cases, recruited from the University of Washington Chronic Fatigue Clinic, met the American College of Rheumatology diagnostic criteria. Pain and fatigue free controls were recruited from the greater Seattle metropolitan area. RLS was ascertained by self-administered modified Hopkins Telephone Diagnostic Interview. Sleep quality was determined using the Pittsburgh Sleep Quality Index (PSQI), the Insomnia Severity Index (ISI), and the Epworth Sleepiness Scale (ESS). Prevalence estimates were age and gender adjusted using the regression adjustment approach and compared with a Wald test. Logistic regression determined the FM/RLS association. Student's t-test compared mean PSQI, ISI, and ESS scores between FM subjects with and without RLS.

Results: We recruited 169 FM subjects (mean age 50, 93% female) and 61 healthy controls (mean age 41, 56% female). The age and gender adjusted prevalence of RLS in FM was 33.0% (95% CI: 25.9-40.1%), significantly higher than the control group prevalence of 3.1% (0.0%-7.4%; $p=0.001$). For those with FM, the age and gender adjusted odds of RLS were 11.7 (95% CI: 2.6-53.0) times higher than controls. Sleep outcomes among FM subjects were compared according to RLS status. The mean PSQI score was significantly higher for FM subjects with RLS than those without RLS (11.8 vs. 9.9; $p=0.01$). FM subjects with RLS also demonstrated higher ISI (20.1 vs. 18.2; $p=0.07$) and ESS scores (10.3 vs. 8.9; $p=0.08$) than those without RLS, although these differences were not statistically significant.

Conclusion: RLS is highly prevalent in FM patients and the association between these two disorders is strong. A significant portion of sleep disturbance in FM is RLS related. Clinicians should query FM patients regarding RLS symptoms as treatment may improve sleep and quality of life.

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0927

EFFECT OF BRIGHT LIGHT THERAPY ON NAPTIME IN WOMEN WITH BREAST CANCER UNDERGOING CHEMOTHERAPY

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Introduction: Daytime napping is a frequent response to the fatigue experienced in women with breast cancer. Bright light therapy is known to improve sleep and be alerting in other populations. We now examine whether bright light would also decrease naptime in women with breast cancer undergoing chemotherapy.

Methods: 20 women (mean age=52.6 yrs, SD=8.7, range: 32-70) diagnosed with stage I-III breast cancer were randomized into two treatment groups: bright white light (BWL; $n = 10$) or dim red light (DRL; $n = 10$) and instructed to self-administer light therapy (Litebook, Inc) for 30 minutes every morning, during their first 4 cycles of anthracycline-based chemotherapy. Actigraphy (Ambulatory Monitoring, Inc. and Respironics) was used to record sleep/wake activity for 72-hours pre-chemotherapy (baseline, BL) and during the last week of cycle 4 (C4). Mixed models were developed with group, cycle of chemotherapy, and the group-phase interaction included as covariates.

Results: In the BWL group, mean naptime during BL was 1.3 hours (SE=0.5) while during C4 it was 1.0 hour (SE=0.3). In the DRL group mean naptime was 2.0 hours (SE=1.3) during BL and 3.0 hours (SE=1.3) at C4. Thus in the DRL group there was a mean 1 hour increase in naptime compared to a modest 0.3 hour decrease in the BWL group ($p=0.14$).

Conclusion: Preliminary results suggest that bright white light may prevent an increase in naptime in women with breast cancer undergoing chemotherapy. We continue to collect data and will examine the relationship between night time sleep and naptime.

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0928

POWER SPECTRAL ANALYSIS OF THE SLEEP ELECTROENCEPHALOGRAM IN HEARTBURN PATIENTS WITH OR WITHOUT EROSIIVE GASTROESOPHAGEAL REFLUX DISEASE (GERD)

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Introduction: GERD has been shown to adversely affect objective sleep parameters and subjective sleep. The aim of this study was to compare the power spectrum of sleep electroencephalogram (EEG) in heartburn patients with erosive gastroesophageal reflux disease (GERD) and heartburn patients without evidence of erosive GERD.

Methods: Data were prospectively collected from asymptomatic volunteers and symptomatic patients with heartburn. All symptomatic patients underwent an upper endoscopy. Patients without erosive esophagitis on endoscopy underwent 24-hour esophageal pH monitoring. Sleep was polygraphically recorded in sleep laboratory in all subjects. Spectral analysis of the sleep EEG was performed to determine the power spectrum in the following four bandwidths: δ (0.8 - 4.0 Hz), θ (4.1 - 8.0 Hz), α (8.1 - 13.0 Hz) and β (13.1 - 20.0 Hz).

Results: A total of 11 patients were included in the heartburn and GERD group (all had erosive esophagitis), 6 patients in the functional heartburn group (heartburn and no GERD: negative endoscopy, pH test, and response to proton pump inhibitors) and 8 in the normal group. The sleep efficiency and the stage N3 sleep were lower in both the functional heartburn and the GERD groups compared to the normal group. There were no significant differences in the macro-architecture of sleep between the functional heartburn and the GERD groups. Heartburn patients with GERD had evidence of lower average δ -power than the heartburn patients without GERD and the normal subjects. Patients with GERD had a greater overall α -power in the latter half of the night (three hours after sleep onset) than patients without GERD. No significant differences were noted in the spectral power between functional heartburn and normal subjects.

Conclusion: Among heartburn patients with erosive GERD, EEG spectral power during sleep is shifted towards higher frequencies as compared to heartburn patients without GERD. This suggests that GERD is associated with findings consistent with worse objective sleep quality.

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0929

SLEEP DISTURBANCES, FATIGUE AND HEALTH RELATED QUALITY OF LIFE IN ASYMPTOMATIC BRCA1/2 MUTATION CARRIERS

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Introduction: The aim of the current study was to investigate whether increased lifetime risk for developing breast-ovarian cancer negatively impacts sleep, fatigue and health related quality of life (HR-QOL) in asymptomatic BRCA1/2 mutation carriers.

Methods: Asymptomatic BRCA1/2 mutation carriers (n=16) and non-carriers (n=20) previously tested at the oncogenetic clinic at Rambam Medical Center and low-risk controls (n=36) were assessed. Participants completed a battery of demographic, cognitive (Cancer Related Worry, CRW), fatigue (Fatigue Symptoms Inventory, FSI), sleep quality (Pittsburgh Sleep Quality Index, PSQI) and HR-QOL (SF-36) questionnaires. Actigraphs were worn for one week for objective assessment of sleep quality.

Results: Based on the PSQI threshold of >5 for poor sleep quality, 75% of the carriers had poor sleep quality compared to 40% of the non carriers and 36% of the controls. Significant group differences were found for CRW (carriers 0.82±0.51, non-carriers 0.70±0.52, controls 0.45±0.44; p=0.028); PSQI based sleep efficiency (SE) and Total scores (SE: carriers 0.87±1.19, non carriers 0.55±0.89, controls 0.06± 0.33, p=0.002; Total: carriers 6.87±3.94 non carriers 4.25± 2.71, controls 4.39±2.75, p=0.02); and effects of emotional status on role functioning based on the SF-36 (carriers 79.17±31.91, non carriers 91.67± 21.29, controls 97.22±9.34, p=0.013). Based on actigraphy, borderline significance was found for sleep latency in minutes (carriers 12.24±14.86, non-carriers 5.41±5.93, controls 9.44±8.06; p=0.10). In carriers, sleep duration and wake after sleep onset tended to be higher and SE tended to be lower compared to non carriers and controls. Demographic variables (including age, income and education), fatigue and other HR-QOL measures were not significantly different between groups.

Conclusion: These findings indicate that asymptomatic BRCA1/2 carriers are prone to increased sleep disturbances and decreased emotional related role functioning, likely mediated by increased cancer related worry. Early identification and intervention may prevent the development of insomnia and associated health risks.

0930

“ALPHA INTRUSION” IN PURE CHRONIC FATIGUE SYNDROME? PROPORTIONS OF SLEEP EEG POWER SPECTRA DURING SLOW WAVE SLEEP

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Introduction: In a previous study, we reported that pure chronic fatigue syndrome (CFS) patients show a different NREM sleep distribution to what can be observed in primary sleep disorders (PSD). We also previously showed higher alpha-like EEG activity during SWS with an au-

tomated pattern recognition in CFS compared to healthy controls (HC) and patients with PSD. Controversial results reported by others, concerning sleep in CFS could often be linked to selection criteria, recording methods and heterogeneity of patient groups. Recently higher levels of delta power bands on sleep EEG in pure CFS have been mentioned (Guilleminault et al. 2006). We wanted to test the hypothesis about different alpha and delta power proportions during SWS in CFS.

Methods: During a one-year period we recruited a sample of ten treatment-free, pure CFS patients (mean age 30.86 (8.05), only females) without any significant medical co-morbidity, any mental disorder and any PSD. Only the results of the second night’s polysomnographic recording were used. Distribution of EEG power spectra, obtained by fast Fourier transformation, during SWS were compared to ten matched HC (mean age 32.26 (9.84), only females). Intensity of fatigue was measured with the fatigue severity scale.

Results: Global proportion of delta power was higher during SWS in CFS patients (p<0.001). Evolution of alpha power during SWS showed also a significantly higher level (p<0.001). All other power bands did not show significant differences between groups. None of these measures was correlated to the severity of fatigue in our sample.

Conclusion: Delta power was higher during SWS in a pure untreated CFS patients sample than in matched HC. The present results are consistent with recently published data and contribute to the investigation of SWS in CFS. Furthermore we could add quantitative information on repeatedly mentioned abnormal alpha-like activity during SWS in CFS.

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0931

VALIDATION OF ACTIGRAPHY AS COMPARED TO POLYSOMNOGRAPHY IN THE EVALUATION OF SLEEP IN SUBJECTS WITH RETT SYNDROME

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Introduction: Rett Syndrome (RS) is a severe neurodevelopmental disorder which mainly affects females. It is generally caused by genetic mutations in the MECP2 gene. In order to evaluate sleep objectively, and develop treatment strategies, it is necessary to have an accurate measurement of sleep/wake states. Subjects with this disorder have hand stereotypies (hand wringing) during wakefulness as well as seizures (during wake and sleep) which may affect actigraphy data. Actigraphy has not previously been validated in RS but does provide valid measures of sleep/wake patterns for ‘typically developing’ infants, children and adults. Few studies comparing actigraphy to the ‘gold standard’ of polysomnography have been carried out to validate this methodology in children and adults who are not ‘typically developing’ such as those with RS.

Methods: Parents of subjects followed in the Israeli Rett Syndrome clinic were contacted and invited to participate in this study comparing actigraph and overnight polysomnography. Subjects underwent standard polysomnography with expanded EEG montage during a single night recording while wearing an actigraph on the non-dominant wrist (when dominance was established). Actigraph data was scored using the algorithm developed by A. Sadeh. The data was analyzed comparing sleep/wake states between the two sleep measures in one minute epochs.

Results: Five female subjects were studied, 4 subjects between the ages 4-6 years, and one adult subject age 29 years. All were diagnosed with RS with genetic confirmation. The polysomnography duration ranged from 2.5 to 6.5 hours (mean 5.5). Sleep efficiency ranged from 78 to 98% (mean 85). The actigraph accurately detected sleep/wake in 92.5%

of one minute epochs. The actigraph incorrectly scored wake as sleep in 1.4% and sleep was incorrectly scored as wake in 4.8% of epochs.

Conclusion: This is the first study demonstrating the validity of actigraphy in subjects with RS as compared to polysomnography with excellent accuracy. It is significant that the actigraph can be used to accurately detect sleep/wake states in this population despite the presence of frequent hand wringing stereotypies during wake, and possible seizures. Further research of sleep disturbance and treatment options to improve sleep in patients with RS can be done using actigraphy as an objective measurement to detect change in sleep/wake patterns.

0932

THE USE OF ACTIGRAPHY TO DEMONSTRATE FREQUENT SLEEP DISRUPTION IN SUBJECTS WITH RETT SYNDROME

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Introduction: Sleep problems are frequently reported by parents of children with Rett Syndrome (RS), a severe neurological disorder which mainly affects females and is generally caused by mutations in the MECP2 gene. A recent study reported the prevalence of sleep problems in a large cohort with >200 cases included. However this recent study, and others evaluating children with RS or other developmental disorders typically use retrospective parent questionnaires or prospective sleep diaries. The authors of this study have validated the use of actigraphy as compared to polysomnography in RS. In this prospective study, actigraphy was used to objectively measure sleep/wake patterns of girls for one week.

Methods: Parents of children followed in the Israeli RS clinic were contacted and invited to participate in monitoring of their daughters' sleep patterns. The actigraph was worn on the non-dominant wrist (when subjects had established hand dominance) and parent(s) completed both sleep and actigraphy diaries. Actigraph data was evaluated using scoring algorithm developed by A. Sadeh.

Results: 10 subjects were enrolled in the study. In 5 cases, the data was insufficient to analyze due to failure of the actigraph or non-compliance of the subjects. Five subjects, ages 4-6 years who all had genetic mutations associated with RS each had seven days of actigraphy data. Sleep onset latency (SOL) ranged from 0-183 minutes (average 25.9). Sleep efficiency (SE) ranged from 73-86% (mean 79). Average number of nocturnal arousals ranged from 4.4 (range 2-6) to 18 (range 9-22) per night. The average duration of each arousal in all subjects ranged from 5-11.5 minutes.

Conclusion: This study demonstrates the difficulties encountered in attempting to use actigraphy, an objective measurement of sleep/wake activity in girls with RS. Despite the difficulties encountered, in this small series of five girls, the actigraph data documents consistently poor sleep in all subjects with prolonged SOL, reduced SE, frequent and prolonged arousals. These findings are consistent with previous sleep research done using sleep questionnaires and sleep diaries in this population. Seizure diaries were not used in this study but would be important in future research to determine wakings associated with nocturnal seizures. Further research is needed using actigraphy as an objective measurement to evaluate sleep in subjects with RS and develop treatment strategies in this population.

0933

DO SHORTER AND FULL VERSIONS OF THE ASTHMA CONTROL QUESTIONNAIRE HAVE SIMILAR CORRELATIONS WITH OBSTRUCTIVE SLEEP APNEA RISK?

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Introduction: Recently, asthma control as measured on Asthma Control Questionnaire (ACQ-full version) was found to be associated with obstructive sleep apnea (OSA) symptoms, but whether similar relationships exist for two of its shorter versions is not known. We hypothesized that comparable associations will be observed between ACQ full version (symptoms, activity limitation, β_2 -agonist use and bronchoconstriction) (ACQ_f), symptoms plus activity limitation (ACQ_s) or symptoms, activity limitation plus short-acting β_2 -agonist (ACQ_b) scores, and OSA risk. **Methods:** Asthma patients during routine follow-up visits at tertiary Asthma and Pulmonary Clinics completed the ACQ and Sleep Apnea scale of the Sleep Disorders Questionnaire (SA-SDQ). OSA risk was categorized using validated cut-offs (≥ 36 for men and ≥ 32 for women) (Douglass AB, Sleep 1994). Spearman rank and student t-test were used to assess the associations of interest.

Results: Of the 83 asthmatics not on treatment for OSA, 58 (70%) were women, mean (\pm s.d.) age was 48 \pm 14 yrs. Mean ACQ_f score was 1.02 \pm 0.94, ACQ_s 1.03 \pm 1.09 and ACQ_b 0.97 \pm 1.03. Mean SA-SDQ was 29 \pm 8 and 30 (36%) met the high OSA risk. Higher SA-SDQ scores correlated with worse (higher) ACQ_f (Spearman $\rho=0.57$, $p<0.0001$), ACQ_s ($\rho=0.52$, $p<0.0001$) and ACQ_b ($\rho=0.51$, $p<0.0001$) scores. Scores on any of the ACQ versions were similarly higher when comparing those with to those without high OSA risk (ACQ_f 1.51 vs 0.75, $p=0.0008$; ACQ_s 1.64 vs. 0.69, $p=0.0003$; ACQ_b 1.51 vs 0.67, $p=0.0008$).

Conclusion: Comparable associations were observed between the full and two shorter versions of the ACQ and OSA risk. This data suggests that any of these ACQ versions could be used to assess disease-specific changes in prospective studies of OSA in asthma patients.

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0934

EXPERIENCES WITH EXCESSIVE SLEEPINESS FROM PATIENTS' PERSPECTIVES

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Introduction: Excessive sleepiness (ES), a common complaint of many adults in the US, is a symptom associated with sleep disorders (e.g. narcolepsy, obstructive sleep apnea) and non-sleep disorders (e.g., multiple sclerosis, cancer, depression). ES is also associated with certain occupations (e.g. physicians, military personnel, and other night shift workers). The purpose of this study was to gather qualitative information from patients experiencing ES to assess whether sleepiness experiences are similar for patients with different underlying etiologies.

Methods: Semi-structured qualitative interviews were conducted with 20 patients confirmed to have ES (Epworth Sleepiness Scale ≥ 10) recruited through a sleep clinic. Audio-recordings were transcribed and data analyzed using qualitative analysis software.

Results: Patients with ES due to a sleep disorder (n=6) or a non-sleep disorder (n=5), or occupation-associated ES (n=9) were included. Six patients were male and the mean age was 44.1 years. Description of 'a typical night's sleep' varied across the 3 groups. Patients with sleep disorders often described waking up as a result of their treatment while non-sleep disorder patients described waking throughout the night or waking too early in the morning. Other patients described how their changing work schedule affected their ability to fall asleep, stay asleep,

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or have a restful sleep. When describing experiences with sleepiness during waking hours, findings were similar across the groups: participants described feeling tired and sleepy during waking hours and dozing off unintentionally when sitting quietly (reading, watching TV). Many described near-miss car accidents and mistakes at work because of tiredness, and forgetfulness or lack of concentration.

Conclusion: Results suggest that patients with different underlying etiologies describe sleep experiences differently, however, experiences with sleepiness were similar across etiologies. These findings suggest that measurement tools designed to assess excessive sleepiness could be relevant across patient populations experiencing ES.

0935

DEVELOPMENT OF A EXCESSIVE SLEEPINESS DIARY

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Introduction: Excessive sleepiness (ES) is a symptom associated with sleep disorders (e.g. narcolepsy, obstructive sleep apnea), non-sleep disorders (e.g., multiple sclerosis, cancer, depression), and certain occupations (e.g. physicians, military personnel, and other night shift workers). In developing a tool to assess patients' experiences of ES and capture treatment effects, the measure must first show evidence of content validity for the patient populations of interest. The purpose of this study was to assess the content validity of a new daily diary designed to assess sleepiness and its impact among patients experiencing ES across underlying etiologies.

Methods: Initial diary versions were drafted through literature review and interviews with sleep clinicians and researchers. Semi-structured cognitive debriefing interviews were then conducted with 20 patients confirmed to have ES (Epworth Sleepiness Scale ≥ 10) recruited through a sleep clinic. Patients completed the 16-item diary and were then engaged in a standardized retrospective debriefing interview. After 10 interviews, the diary was modified based on patient feedback. Audio-recordings were transcribed and data analyzed using qualitative analysis software.

Results: Patients with ES due to a sleep disorder (n=6) or a non-sleep disorder (n=5), or occupation-associated ES (n=9) were included. Six were male; the mean age was 44 years. The recall period (today) and items were well understood by all patients. Patients reported they could easily remember their experiences with sleepiness over the course of that day. Patients across groups reported items related to excessive sleepiness, concentration, forgetfulness, and accidents/mistakes as relevant to their sleepiness experiences. Patients differentiated between tired versus sleepy and dozing off (accidental) versus napping (intentional).

Conclusion: Results suggest items were easy for patients to interpret and were relevant to patients' experiences across underlying etiologies. Participants were able to reliably report their sleepiness experiences over 'today.' The sleepiness diary demonstrated content validity across patient populations experiencing ES.

0936

POOR SLEEP QUALITY AND MOOD DISTURBANCES IN PATIENTS WITH ADVANCED LUNG CANCER

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Introduction: Depression and anxiety are common responses to a cancer diagnosis and are associated with disturbed sleep. This study exam-

ined the impact of mood disturbances on sleep quality in patients with advanced lung cancer.

Methods: Participants were recruited from VA Oncology Clinics in Philadelphia, PA and Buffalo, NY. The Pittsburgh Sleep Quality Index, Hospital Anxiety and Depression Scale, demographic, disease and treatment information were collected while patients waited for clinic appointments.

Results: Among 38 participants, the mean age was 62 years (SD=9.3, Range= 47-84), with 97% male and 58% African American. The majority of patients were diagnosed with nonsmall cell lung cancer (84%) and 76% received both chemotherapy and radiotherapy. Patients spent 7.6 (SD=1.9) hours in bed, but only 5.6 (SD=1.7) hours asleep; they thus had a markedly low sleep efficiency of 74% (SD=24%). Mean sleep latency was 37 (SD=31) minutes. Mean overall global sleep quality was 8.9 (SD=4.2) with 76% of the sample above the clinically significant cut-off score of five. The majority of patients (76%) rated their sleep quality better than all the component scores except for one-daytime dysfunction- indicating a misperception of poor sleep. Mean anxiety score was 6.1 (SD=4.4) with 8% reporting anxiety >10 indicating at risk for a mood disorder. Mean depression score was 5.4 (SD=3.7) with 8% reporting depression >10 indicating at risk for a mood disorder. There were no significant correlations between sleep quality and demographics/disease/treatments. Marital status was related to anxiety ($r=-0.39$; $p=0.018$). The correlation between Global sleep quality and anxiety was low ($r=0.37$; $p=0.026$).

Conclusion: Preliminary data suggest that the relationship between mood disturbances and sleep quality in advanced lung cancer is limited. Poor sleep quality is quite common but not recognized by patients with advanced lung cancer. Patients with lung cancer underestimate their sleep problems. Further investigation is warranted using more objective measures to examine the nature and impact of sleep problems in this population. Data collection is ongoing.

0937

UNIQUE EEG SIGNATURE IN FIBROMYALGIA PATIENTS TESTED AT HOME

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Introduction: The sleep architecture of fibromyalgia patients during stages of REM sleep has not been well documented. Analysis of REM epochs from five fibromyalgia patients and one control showed similar abnormalities among the fibromyalgia patients.

Methods: Six patients, five diagnosed with fibromyalgia and one control, underwent a virtually attended, home polysomnogram (PSG) study. All were screened for primary sleep disorders and medications. A registered polysomnographic technician (RPSGT) staged and scored the PSGs, and analyzed the percentage of spindles, α -intrusions, β -intrusions, and k-complexes in each epoch of REM. Each waveform appeared in either <20% of the epoch, between 20% and 50% of the epoch, or >50% of the epoch.

Results: REM epochs from our fibromyalgia patients revealed 717 (72% of total) had spindles in the <20% range, and 118 (12% of total) in the 20-50% range. Epochs with α -intrusions, demonstrated 413 (41% of total) in the <20% range, 277 (28% of total) in the 20-50% range, and 201 (20% of total) in the >50% range. For β -intrusions, 536 epochs (54% of total) had <20%, 283 epochs (28% of total) had 20-50%, and 137 epochs (14% of total) had >50%. Finally, 279 epochs (28% of total) had k-complexes appear in <20% of the epoch. By comparison, REM epochs from our control patient showed only 7 (7% of total) had any spindle activity- all <20%. For α -intrusions, 26 epochs (25% of total) had <20%, and 7 epochs (7% of total) had 20-50%. Epochs with β -intrusions were 35 (33% of total) with <20%, and 4 (4% of total) with 20-50%. No epochs had α - or β -intrusions >50%, or any k-complexes.

Conclusion: A greater percentage of REM epochs containing abnormal waveforms appeared in our fibromyalgia patients. While further research is needed, these results suggest that abnormalities in REM may be unique to fibromyalgia patients.

0938

CANCER AND INSOMNIA: PREVALENCE OF INSOMNIA IN A LONGITUDINAL SAMPLE OF CANCER PATIENTS

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Introduction: Insomnia occurs at high rates in patients with cancer. The etiology is unknown, but may be related to psychological factors (anxiety or depression), pain, treatment-related toxicity, or other co-morbid medical conditions. Insomnia has been linked with increased rates of depression, decreased quality of life, and increased fatigue in other patient populations, and is therefore important to understand in the context of cancer.

Methods: Sleep and daytime function were assessed in patients (N=396) with newly diagnosed cancer at several timepoints. Timepoints were baseline (defined as 2-weeks prior to 1st clinic visit), initial clinic visit (occurred the week prior to initial chemotherapy dosing), last week of 1st chemotherapy cycle, last week of 2nd chemotherapy cycle and 2-4 weeks post 2nd cycle. Sleep was subjectively assessed in one week increments with diaries. Insomnia was defined as sleep latency and/or WASO>30 minutes, occurring >2 nights/week in patients who complained of difficulty sleeping. Daytime function measures included: Epworth-Sleepiness-Scale, Insomnia-Impact-Scale, Fatigue-Severity-Scale, Beck-Depression-Inventory; State-Trait-Anxiety-Inventory.

Results: The sample size by tumor site was as follows: breast-29%; GU-24%; GI-10%; lung-8%; other-29%. At baseline, insomnia symptom prevalence was 10%. At the initial clinic visit, prevalence increased to 24%. Prevalence rates rose dramatically during the 1st two cycles of chemotherapy with rates of 45% and 63%, respectively. Rates dropped down to 42% after the completion of the 2nd chemotherapy cycle. Patients exhibiting insomnia symptoms had significantly impaired daytime function on all measures at all timepoints (all p-values <0.0001) compared with those who did not have sleep impairment, with the severity of impairment increasing dramatically during and post-chemotherapy.

Conclusion: Insomnia symptoms occurred commonly in this sample of cancer patients, with prevalence rates rising rapidly across the 1st two chemotherapy cycles. Though prevalence rates dropped after the completion of the 2nd chemotherapy cycle, they nonetheless remained 4-times higher than those at baseline. Daytime function in these patients was also compromised, with severity of impairment decreasing across time.

0939

DAILY SLEEP QUALITY, MOOD, AND ALERTNESS AMONG CHRONIC KIDNEY DISEASE (CKD) PATIENTS VS. HEALTHY CONTROL SLEEPERS

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Introduction: Little is known about the differences in sleep quality, mood and alertness among patients with stage 4-5 CKD or those on hemodialysis (HD) or ambulatory peritoneal dialysis (APD) vs. healthy control sleepers. We characterized sleep quality, mood and alertness of patients with CKD (stages 4-5) and then on dialysis compared to healthy control sleepers, using daily diary methods.

Methods: We assessed symptoms of sleep quality, mood and alertness using the Pittsburgh Sleep Diary and visual analogue scales (VAS: response ranges 0 to 100, higher scores “better”). The sample included 90 patients and 100 healthy control sleepers who completed 14 daily VAS scores. Of the 90 patients, 60 were on in center thrice-weekly HD, 10 were on home APD, and 20 had CKD stage 4-5. The average age was 52.4 years, 63.21% (n=122) were men, and 75% (n= 144) were white. The Pittsburgh Sleep Diary data were analyzed using generalized estimating equations to account for within subject correlations and mixed models for paired case versus control tests.

Results: Compared to healthy control sleepers, those with stage 4-5 CKD demonstrated lower scores in sleep quality, mood, and alertness (p<0.05). Patients on dialysis (CHD or APD) had lower scores than stage 4-5 CKD patients on each of these three domains.

Conclusion: This study demonstrates the feasibility of using diary methods in the CKD population. Furthermore, these findings suggest that: 1) dialysis patients have impaired sleep quality, mood and alertness compared to patients with stage 4-5 CKD and healthy control sleepers, and 2) patients with stage 4-5 CKD have impaired sleep quality, mood, and alertness compared to healthy control sleepers. Measuring and monitoring sleep quality, mood, and alertness among patients with CKD are critical to the patient’s well-being. Further studies should employ frequent analysis to measure diurnal variations.

0940

EFFECTS OF A PULSED MAGNETIC FIELD ON SLEEP DISTURBANCES, FATIGUE, PAIN, AND FUNCTIONAL STATUS IN WOMEN WITH RHEUMATOID ARTHRITIS

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Introduction: Women with rheumatoid arthritis (RA) experience moderate to high levels of symptoms in spite of taking DMARDs and biologics. Women often turn to complementary therapies to further reduce symptom levels. Thus, this study investigated the effects of a low strength pulsed magnetic field (PMF) on sleep disturbances, fatigue, pain, and functional status in women with RA.

Methods: Three group [active PMF pad, sham pad, and usual care alone (UC)] randomized controlled design was used, with PMF and sham groups being double-blinded. The sample consisted of 52 postmenopausal women with mean age of 59.9 ± 7.5, education level of 13.4 ± 2.8 years, and RA duration of 11.6 ± 11.7 years. Pad groups lay on full body pads (looked like yoga mats) twice a day, for eight minutes each time, over 12-weeks. All participants remained on usual care. Measures included wrist actigraphy, General Sleep Disturbance Scale, Lee’s Fatigue Inventory, pain NRS (0-10), and Health Assessment Questionnaire (HAQ). Multilevel models were used to analyze group differences over time.

Results: Baseline sleep measures ranged from 66 to 82% for sleep efficiency, 5.6 to 6.9 hours of total sleep time, and 1.6 to 2.7 hours of wake time during the night. Slopes did not differ over time between groups on either subjective or objective sleep measures. After controlling pain as a time-varying covariate, the slopes of fatigue (p=0.043) and HAQ (trend, p=0.059) improved over time in the PMF group compared to the sham and UC groups. The slope of pain also improved over time in the PMF group compared to either the sham or UC groups (trend, p=0.060).

Conclusion: Pulsed magnetic fields did not improve sleep disturbances over time. Those receiving PMF did experience improvements in pain, fatigue, and functional status compared to sham or UC groups.

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CAM). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of NCCAM, NIH.

0941

POLYSOMNOGRAPHIC STUDY IN PATIENTS WITH CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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Introduction: Sleep related breathing disorders (SRBD) were recognized as a secondary cause of precapillary pulmonary hypertension (PH). Their occurrence is estimated at 20% (17-73%), but there are no studies in particular subgroups of precapillary PH including chronic thromboembolic PH (CTEPH). With regard to pathophysiology, occurrence of SRBD with their negative influence on cardiovascular system is probable in patients with CTEPH. The aim of this study was to determine sleep architecture and occurrence of SRBD in CTEPH patients.

Methods: Eleven patients (9 men, 2 women, average age 57.5 ± 13.2 , average BMI 26.3 ± 3.1) with the diagnosis of CTEPH (average pulmonary artery systolic pressure - PASP - 112.3 ± 33.6 mmHg) participated in our study. They underwent polysomnographic examination (in consideration of sleep architecture, night ventilation and periodic limb movements) and Multiple Sleep Latency Test (MSLT).

Results: Decreased sleep efficiency (71.8 ± 10.8) with mild shortage of NREM2 and REM sleep were measured. Obstructive sleep apnea (OSA) was detected in 7 patients (respiratory disturbance index - RDI 15.24 ± 13.43), periodic hypoxemia was present in all patients (oxygen desaturation index - ODI 24.2 ± 12.6). Periodic limb movements (PLM) were founded in 10 patients (periodic limb movement index - PLMI 44.4 ± 39.3). Neither restless legs syndrome (RLS) nor excessive daytime sleepiness were mentioned by patients. Shortened sleep latency (in agreement with MSLT) was measured in only one patient with severe OSA.

Conclusion: OSA and PLM detected in CTEPH patients show the urgency of polysomnographic examination and subsequent care in patients with CTEPH. Persistent effects of fragmented sleep on cardiovascular system negatively influence the unfavourable course of the disease. Etiology of SRBD is suspected by reason of essential disorder. Etiology of PLM stays obscure. Either like comorbidity within the scope of SRBD or regarding the severity of PLM secondary or comorbid to CTEPH.

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0942

THE EFFECTS OF FIBROMYALGIA IMPACT AND AGE ON DAYTIME ACTIVITY PATTERNS AND CIRCADIAN RHYTHM IN WOMEN WITH FIBROMYALGIA

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Introduction: The aim of this study was to examine the effects of age and fibromyalgia impact on daytime activity and circadian rhythm in women with fibromyalgia (FM).

Methods: Thirty five women with FM (Mean age = 47.5 ± 11.8 years) completed the Fibromyalgia Impact Questionnaire (FIQ) followed by 7 days of wrist actigraphy. Measures of circadian rhythms (periodicity, mesor, amplitude, acrophase, and percent rhythm) and daily activity levels (daily total, peak activity, and average activity per minute) were obtained. The cohort was divided into groups by age: younger (<50 years) and older women (>50 years). Participants were also divided into high (FIQ>58) and low (FIQ<58) FM impact groups based on the mean FIQ score.

Results: Circadian rhythms were highly variable in both younger (n=25) and older women (n=10). There was a significant interaction of

FM impact and age for percent rhythm, $F(1, 31) = 5.67$, $p = .02$. There were no significant effects of age, FM impact or interactions between FM impact and age for periodicity, mesor, amplitude, and acrophase. Post hoc analysis indicated less robustness to circadian rhythm among older women with less FM followed by younger women with less FM impact on days 1 & 7. On days 2 - 6, interactions indicated less robust circadian rhythm in older women with less FM impact followed by younger women with more impact. There was no significant interaction of FM impact and age in predicting daytime activity (peak, total, avg/min) nor were either of the main effects significant.

Conclusion: These findings demonstrate that age and FM activity impact on the robustness of circadian rhythms, but not daytime activity. These results indicate that older women with less FM impact and younger women with more FM impact had less robust circadian rhythm than younger women with less FM impact and older women with more impact. We speculate that occupational schedule affecting free time to sleep when desired may influence the robustness of circadian rhythm in these women of different ages with varying degrees of FM impact.

0943

SLEEP ABNORMALITIES IN PATIENTS WITH EHLERS DANLOS SYNDROMES: RELATED TO CHRONIC PAIN OR AN INDEPENDENT ENTITY?

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Introduction: Patients with Ehlers-Danlos Syndromes (EDS), a group of rare hereditary disorders of connective tissue characterized by joint laxity and tissue fragility, often complain of disturbed and non-refreshing sleep. Since many patients also suffer from chronic musculoskeletal pain, we hypothesized that the reported sleep abnormalities are related to the chronic pain syndrome. Other etiological factors considered relate to laxity of the connective tissues of the pharynx leading to sleep apnea.

Methods: Multiple sleep and pain assessment tools were administered to sixty five consecutive patients with a diagnosis of EDS enrolled in the National Institutes of Aging protocol 2003-086 on the natural history of hereditary disorders of connective tissue. Data was collected utilizing the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Inventory (PSI) as well as a sleep questionnaire designed to elucidate the specific problem areas such as difficulty falling or remaining asleep, snoring, early morning awakening and non-refreshing sleep. Pain was assessed through the Brief Pain Inventory (BPI) and review of systems data focusing on musculoskeletal and generalized pain.

Results: Results indicate that 33/65 (50%) of patients had an ESS scale > 9, and 49/65 (75%) a PSI Quotient > 5, suggesting the presence of a sleep disorder. Almost all patients (62/65; 95%) had pain in at least one location, and 29/65 (44 %) reported chronic generalized pain. Of the patients with ESS > 9, a complaint of generalized pain was present in 15/33 (45 %). Of the 49 patients with PSI > 5, generalized pain was present in 24 (48 %).

Conclusion: The discordance of sleep disturbance with chronic generalized pain in EDS suggests that the pathogenesis of sleep complaints in this disorder may be unrelated to the pain syndrome, at least in part. Further investigation regarding the etiology of this phenomenon in EDS, using formal sleep studies, is warranted.

Support (optional): This study was supported through funds originating at the National Institute on Aging, National Institutes of Health.

0944

SLEEP PROBLEMS FREQUENCY IN A POPULATION WITH PHYSICAL COMPLAINTS IN A PRIMARY CARE UNIT

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Introduction: The relationship between sleep and pain is already known. It is not clear yet, the percentage of patients that goes to the primary care attention with physical complaints but also has sleep problems.

Methods: To check the frequency of sleep problems at the primary care system, we evaluated during ten days all patients with physical complaints that went to the Vila Leonice primary care unit in Curitiba, Brazil. Two hundred and fourteen patients completed the following questionnaires: Patient Health Questionnaire 15 - item Somatic Symptom Severity Scale (PHQ scale) and a sleep questionnaire.

Results: The results showed that patients with higher score in the PHQ scale have more sleep complaints than patients with lower score. We also observed that back pain; headache; pain in the limbs and joints; feeling tired and low energy are the most frequently complaint in these patients.

Conclusion: We concluded that the physician at the primary care attention should always ask patients about sleep problems even when they do not bring the issue immediately because the frequency of these problems is very high in the population that goes to primary care units with physical complaints.

0945

ACTIGRAPHY REVEALS PHASE ADVANCEMENT OF THE SLEEP MIDPOINT IN PATIENTS WITH CHRONIC TEMPOROMANDIBULAR JOINT DISORDER PAIN COMPARED TO HEALTHY PAIN-FREE CONTROLS

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Introduction: Clinical pain often has a disorder specific circadian profile. Recent basic science work has identified opioid receptors in the suprachiasmatic nuclei that when stimulated induce circadian phase advancement. Melatonin has known analgesic properties. Potential circadian dysrhythmia in chronic pain disorders, however, has received little attention. In this exploratory actigraphy study, we sought to evaluate evidence of potential phase advancement in temporomandibular joint disorder (TMD).

Methods: Thirty-nine patients diagnosed according to research diagnostic criteria for TMD and thirty-nine pain-free, healthy controls were matched on age (TMD = 27.82±5.21, Control = 26.10±5.09), sex (28 Females in each group), BMI, education level, and marital status (p > .05). All subjects were free from psychotropic medications narcotics, and recreational drugs. Participants wore Mini-Mitter actigraphs, 24 hour/day for two-weeks. A minimum of 7 complete days was required for inclusion in the analyses. Sleep midpoint was calculated by determining the time between actigraphically derived Sleep End and Sleep Start, divided by 2.

Results: Surprisingly, the groups did not differ on any traditional actigraphic measures of sleep continuity, including total sleep time (p's > .05). However, even after controlling for slight differences in employment status, as hypothesized, the mean sleep midpoint for TMD demonstrated a significant phase advancement [TMD clock time sleep midpoint = 04:02 ± 49 min; Control = 04:31±63 min (p=.039)].

Conclusion: This exploratory study suggests that TMD patients, who experience chronic intermittent, mild to moderate pain, demonstrate on average approximate 30 minute phase advancement in sleep midpoint compared to healthy, well matched pain-free controls. This study supports future work using more complex chronobiologic methods such

as forced desynchrony protocols and dim light melatonin sampling to more directly examine chronobiologic dysregulation in TMD. Future work should determine whether phase advancement is a consequence or cause of chronic pain and whether chronobiologic dysregulation relates to symptom profiles, which may be amenable to chronotherapeutic interventions.

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0946

DECREASED SLEEP EFFICIENCY IS ASSOCIATED WITH REDUCED ENDOGENOUS PAIN INHIBITORY CAPACITY IN PATIENTS WITH CHRONIC TEMPOROMANDIBULAR JOINT DISORDER (TMD) PAIN

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Introduction: We recently reported that experimentally reduced sleep efficiency (SE) via forced awakenings, impaired laboratory tests of pain inhibition in healthy pain-free subjects. Impaired supraspinal pain inhibition is implicated in the pathophysiology of idiopathic pain disorders. We sought to extend our experimental work, to evaluate whether SE is negatively associated with pain inhibition and mechanical hyperalgesia in TMD.

Methods: 46 medication-free TMD patients (age = 34±12.3); 78% female, 76% Caucasian) were studied polysomnographically for two consecutive nights. We conducted quantitative sensory testing each evening and morning. Pressure pain threshold (PPth) was assessed via algometry on the masseter and brachioradialis muscles. We measured pain inhibitory capacity using a diffuse noxious inhibitory controls paradigm, with cold pressor applied to the contralateral hand as the conditioning stimulus. Bivariate correlations were conducted between demographic variables and PSG parameters. Bivariate correlates were entered into simultaneous multivariate regressions.

Results: Pain inhibitory capacity did not differ by time of day and was averaged across all 4 measurements. Mean SE was positively associated with pain inhibition (r= .37, p=.01). SE was negatively associated with age (r= -.43, .003) and periodic limb movement index [PLMI (r=-.28, p=.07)]. Sleep architecture, AHI, and bruxism index were not significant correlates. Multivariate models demonstrated that SE remained a significant (p=.03) correlate of pain inhibition, controlling for age and PLMI. With respect to mechanical pain sensitivity, evening PPth was reduced compared to morning ratings (p<.0001). Sleep Latency was the only sleep parameter associated with PPth's (p's<.05), but it did not remain significant after controlling for sex, age and BMI.

Conclusion: These data extend our experimental work. We demonstrate here, novel findings that reduced sleep efficiency is associated with reduced pain inhibitory capacity in TMD. These findings support future investigations aimed at treating insomnia in TMD to determine whether sleep consolidation enhances pain inhibition and improves clinical pain.

Support (optional): This work was supported by NIH/NINDS: K23NS047168 (MTS).

0947

TOTAL SLEEP TIME IN END STAGE RENAL DISEASE: EFFECTS OF HEMODIALYSIS

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Introduction: Patients with End-Stage Renal Disease (ESRD) have more sleep complaints than the general population, but the effects of hemodialysis are less clear. We assessed the extent to which hemodialysis is associated with total sleep time (TST) measured by actigraphy, by comparing non-dialysis kidney patients and participants undergoing thrice-weekly hemodialysis.

Methods: For 14 consecutive days, 36 chronic kidney disease patients (CKD) and 51 HD patients wore wrist actigraphs and completed sleep diaries. Groups were compared on race, age, gender, body mass index, Charlson score, prevalence of depression and diabetes, serum albumin, hemoglobin and ferritin levels, and dialysis shift start times. TST was generated from the actigraphy data for each night. Average TST over the study period was compared between groups. In the HD group, we also examined the difference in TST between HD nights and non-HD nights.

Results: Average TST was 410 minutes in CKD vs. 344 minutes in HD ($p < 0.05$). In the HD group, 28 (55%; subgroup A) had a mean change in TST > 60 min between HD and non-HD nights and 23 (45%; subgroup B) had a change in TST < 60 min. Subgroups differed significantly ($p < 0.05$) in race (61% African American subgroup A vs. 32% subgroup B), prevalence of depression (32% vs. 20%), and dialysis shift start time before 8am (79% vs. 40%). Other variables were not significantly different in the subgroups.

Conclusion: HD patients had significantly shorter average actigraphic TST compared to CKD patients. The majority of participants in the HD group had a highly variable TST between HD and non-HD nights. These results suggest that more often than thrice weekly HD or later HD shifts may provide more balanced and stable night sleep with less TST variability in HD patients with sleep problems.

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0948

SLEEP, SLEEPINESS, FATIGUE AND PSYCHOLOGICAL OUTCOMES FOR PARENTS OF CRITICALLY ILL HOSPITALIZED CHILDREN

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Introduction: Many health care professionals believe that parents' sleep is affected by their child's hospitalization; however, no prior studies have used objective determinations of parental sleep.

Methods: Parents with a child in a pediatric critical care unit wore an actigraph and completed a sleep diary including fatigue and sleepiness measures for 5 days and nights. Sleep quantity, fatigue and sleepiness scores were averaged over days of enrollment. After the final night, parents completed measures of anxiety, depressive and physical symptoms and decisional conflict.

Results: From April-September 2007, 204 eligible participants were approached and 118 parents (73 mothers; 45 fathers) of 91 children consented. Mean age of the child was 2.94 years and reason for admission included chronic illness (27%), acute illness/trauma (31%) and planned surgery (42%). Median length of hospital stay at enrollment was 2 days. Parents slept at home (38% of 497 parent nights), in a nearby hotel/residence or a designated parent room in the hospital (41%), at the child's bedside (13%), and in a lounge/waiting room (8%). Mean morning fatigue scores (possible range 0-100) were 44.2 (SD 18.8), mean morning Stanford Sleepiness Scores were 3.0 (SD 1.0). Mean nighttime sleep

was 423 (SD 56) minutes for mothers and 398 (SD 64) minutes for fathers and mean length of longest stretch of nighttime sleep was 172 (SD 93) minutes for mothers and 126 (SD 93) minutes for fathers; both these differences were statistically significant ($p < 0.042$). Mean WASO was 52 (SD 37) minutes and mean number of awakenings was 6.1 (SD 4.0); there were no significant differences between mothers and fathers. Parents had high anxiety, depressive symptom, decisional conflict and physical symptom scores; relationships between these psychological variables and sleep outcomes will be presented.

Conclusion: Parents experience sleep loss and significant fatigue, sleepiness and psychological difficulties during their child's hospitalization.

0949

THE FEASIBILITY AND POTENTIAL BENEFIT OF HYPNOTIC RELAXATION TO REDUCE STRESS AMONG INDIVIDUALS WITH DIABETES MELLITUS: THE NEED TO ADDRESS SLEEP PROBLEMS IN THIS POPULATION

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Introduction: The current study utilized a single-arm design in order to examine the feasibility and potential benefit hypnosis to reduce stress among individuals diagnosed with diabetes mellitus, Type 1 (T1DM) or Type 2 (T2DM).

Methods: There were 10 participants, recruited as part of a larger study, who had a formal diagnoses of DM, T1DM ($n = 2$) or T2DM ($n = 8$). Their mean age was 44.63 (SD = 4.33) and their race/ethnicity was 70% Caucasian, 20% Hispanic, and 10% African American. There were 9 females and 1 male. Participants wore a wrist actigraph at home for approximately a week and collected saliva samples (using passive drool) at five different time points in one 24-hour period (immediately upon waking, 45 minutes after awakening, noon, before dinner, at bedtime). Participants also completed the Pittsburgh Sleep Quality Index (PSQI), Perceived Stress Scale (PSS), Positive and Negative Affect Scales (PAS/NAS). The intervention consisted of three face-to-face sessions and an audio-taped induction to practice self-hypnosis.

Results: All participants attended every session and completed all assessment procedures. Paired sample t-tests revealed significant reductions on primary self-reported outcome measures of negative affect ($t(9) = 4.49$, $p = .002$) and perceived stress ($t(9) = 3.52$, $p = .007$) and an increase in positive affect ($t(9) = -3.31$, $p = .009$). There were no pre-post differences in sleep onset latency (SOL), sleep efficiency (SE), total sleep time (TST), and percent of wake (%wake). There was a trend ($p = .089$) for participants to sleep fewer hours post-treatment, with an average of 6.44 hours at baseline and 6.06 at endpoint. However, there was a trend for participants' sleep duration to be more consistent across nights post-treatment as evidenced by the coefficient of variation (CV) ($p = .054$). PSQI scores also did not differ following treatment, but the item measuring sleepiness indicated a significant improvement at endpoint compared to baseline ($t(9) = 3.00$, $p = .017$).

Conclusion: There is emerging evidence that inadequate sleep may contribute to obesity and metabolic dysfunction. Given the prevalence of sleep problems amongst these participants, particularly in regards to TST, which declined post-treatment, the intervention would be strengthened by adding cognitive-behavioral techniques, such as stimulus control, sleep hygiene education, and cognitive restructuring. Findings will be interpreted in the context of clinical meaningfulness of the outcome measures.

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0950

CHRONIC SLEEP-DEPENDENT CARDIOVASCULAR DYNAMICS PREDICTED BY SYMPATHOVAGAL BALANCE

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Introduction: The pharmacoeconomic impact of sleep-sensitive cardiovascular disease is a burgeoning problem. Autonomic tone balance is critical to both late-stage sleep and to hemodynamic regulation during normal wakefulness. However, the role of sleep architecture in non-sleep cardiac mechanics is incompletely understood.

Methods: We studied sleep parameters in 20 patients (age 45.7±14.2 years, mean±SD) with abnormally high sympathovagal ratio. None of the patients we studied had sinoatrial or atrioventricular dysrhythmias, cardiomyopathy, renal disease or cerebrovascular disease. We quantitated sympathovagal ratio by spectral analysis of heart rate variability and measured such sleep parameters as rapid eye movement sleep and arousal index by multi-channel polysomnography. Further, we determined such cardiovascular parameters as ventricular work and cardiac index via transthoracic bio-impedance.

Results: Respiratory disturbance altered tightly with a low sympathovagal ratio in REM sleep (Spearman, $\rho=0.79$, $p<0.001$) and not at all in non-REM sleep (Spearman, $\rho=0.33$, $p=0.27$). Cardiac contractility measured by the hemodynamic velocity and acceleration indexes correlated intensely to delta (Spearman, $\rho=0.84$, $p<0.001$) and REM sleep (Spearman, $\rho=0.84$, $p<0.001$), as did left cardiac work (delta sleep, Spearman, $\rho=0.91$; REM sleep, Spearman, $\rho=0.97$, $p<0.001$). Interestingly, the effect on cardiac mechanics was not related to changes in the sympathovagal ratio.

Conclusion: These data suggest that the observable effects of sympathovagal balance on cardiovascular mechanics might primarily be exerted via a putative sleep architecture mechanism. We plan to study this phenomenon further by observing discrete populations of patients with sympathovagal and sleep architecture lesions.

0951

SUBJECTIVE PERCEPTION OF SLEEP, BUT NOT ITS OBJECTIVE QUALITY, IS ASSOCIATED WITH POSTPARTUM BLUES IN HEALTHY WOMEN

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Introduction: Existing literature supports a bi-directional linkage between sleep disruption and affective disorders. Women sleep less with poorer quality during pregnancy and postpartum periods, and are particularly vulnerable to a number of affective disturbances including postpartum blues (PPB) and antenatal/postpartum depression. This study tested whether there was a relationship between PPB and sleep disruption, using both objective and subjective measurements of sleep.

Methods: During the third trimester (Time-1), 44 healthy, low-risk women completed questionnaires on mood and sleep (i.e. the Depression Anxiety Stress Scale, the Hospital Anxiety Depression Scale, the Positive Negative Affect Schedule, and the Pittsburgh Sleep Quality Index). 41 of these women wore actigraphy continuously for 7 days. All participants were contacted again two weeks before due days. 37 completed the same mood and sleep questionnaires at one week postpartum (Time-2), and 28 wore actigraphy during the first postpartum week. Attrition was caused by the demands of the research protocol, early deliveries, and restrictions of hospital procedures.

Results: After delivery, mood generally improved across all scales, although there was some deterioration of mood in 45.95% of the sample, among whom 75% were nulliparas. Both objective and subjective nighttime sleep significantly worsened after delivery while daytime napping behaviour significantly increased. Multiparas slept more and better during postpartum nights while nulliparas took more naps during the day. Multiple regression analyses showed little relationship between Time-1 or Time-2 objective nighttime sleep and postpartum mood. Poorer subjective nighttime sleep at both Time-1 and Time-2 was consistently associated with poorer mood reports at Time-2, R^2 ranges .25-.49. Linear regression analyses showed that greater actigraphically measured nap numbers and higher sleep related daytime dysfunction at both Time-1 and Time-2 were also significant predictors of poorer Time-2 mood (R^2 ranges .11-.28 and .11-.24 respectively). Both variables were affected by participants' daytime sleepiness, which depended largely on nighttime sleep quality, and a conscious awareness of the need to make up for subjectively perceived poor sleep.

Conclusion: Compared to actual sleep quality or quantity, the perception of poor sleep, and the conscious awareness of its impact during wake-time, might play a more active role in the occurrence of PPB in a group of healthy, low-risk women.

Support (optional): Funded by the School of Behavioural Science, University of Melbourne, Australia. Participants recruited through the Antenatal Clinic, Northern Hospital, Australia.

0952

CIRCADIAN MISALIGNMENT CORRELATES WITH SYMPTOM SEVERITY IN NON-SEASONAL DEPRESSION

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Introduction: One of the first circadian theories for major depressive disorder (MDD) posited that the biological clock (endogenous circadian pacemaker) is set abnormally early with respect to the timing of sleep. However, studies have not consistently found that the pacemaker is set either abnormally early (phase advanced) or late (phase delayed) in individuals with depression. Nevertheless, it remains possible that a misalignment between the timing of sleep and the pacemaker in either direction may be depressant in vulnerable individuals. We sought to determine if misalignment between the timing of sleep and the pacemaker

correlated with symptom severity in MDD as we have found in seasonal affective disorder (SAD).

Methods: Subjects were 14 women (19-60 y.o.) with MDD, a score of 7 or greater on the 21-Item Hamilton Depression scale (HAM-D), and poor sleep. No changes in antidepressant medications were allowed during the 6 weeks before, and week of, study. Subjects kept a regular sleep/wake schedule for one week (eight hours in bed, bedtimes and wake times within $\pm 1/2$ an hour) verified with sleep diaries and wrist actigraphy. They were then admitted to the Clinical and Translational Research Center at Oregon Health & Science University in the late afternoon. Symptom severity was assessed using the HAM-D and blood was then drawn every 30 minutes for 6 hours in dim light (<10 lux). Plasma melatonin concentrations were measured by RIA (ALPCO, Ltd., Windham, N.H.) and the plasma dim light melatonin onset (DLMO) was assessed using a 10 pg/ml threshold. Circadian misalignment was defined as the time interval between the DLMO and average midsleep during the prior week (phase angle difference, PAD).

Results: The average HAM-D score (\pm SD) was 16.5 ± 4.1 . Average bed and wake times were $23:22 \pm 1:32$ and $07:35 \pm 1:13$, respectively. The average DLMO time was $21:14 \pm 2:07$. Subjects had an average PAD of $6:14 \pm 1:39$ h. Among the 7 phase-delayed subjects ($PAD \leq 6$), depression severity correlated ($r = 0.86$, $p = 0.012$) with PAD: the more phase-delayed, the more severe the symptoms. There was no correlation between symptom severity and PAD in the phase-advanced subjects ($PAD > 6$).

Conclusion: The results suggest that there may be a component of circadian misalignment that contributes to symptom severity in some individuals with non-seasonal MDD.

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0953

REM PHASIC ACTIVITY IN PTSD-DISCORDANT MONOZYGOTIC TWINS

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Introduction: The pathophysiology of the sleep disturbance in post-traumatic stress disorder (PTSD) has yet to be determined. However, several studies have shown increases in REM sleep (REM) phasic activity, a possible indicator of exaggerated alerting in PTSD. We studied monozygotic twins discordant for PTSD to determine whether increases in REM phasic activity are explained by trauma and its effects or by genetic factors.

Methods: We obtained two nights of laboratory polysomnography from 10 male Vietnam War veterans (mean age 54.8, SD 1.4) with lifetime PTSD and from each veteran's twin, without PTSD. Data from the second night were analyzed. The EOG was recorded using orthogonal horizontal and vertical bipolar electrode placements and digitally filtered (0.5 - 7 Hz). Rapid eye movements were scored both manually and using a computer-based algorithm. Computer-scored eye movements were counted as the number of movements per 30-sec REM epoch. Paired t-tests were used to compare the two groups.

Results: Computer-based and manually derived eye movement measures were highly correlated (ρ 's = 0.60 to 0.71, p 's $< .01$). With the former method, the PTSD group displayed increases in horizontal (Mean = 1.87, SD = 0.78 vs. Mean = 1.59, SD = 0.69, $p < .05$) and vertical (Mean = 1.37, SD = 0.64 vs. Mean = 1.07, SD = 0.50, $p < .05$) eye movements exceeding 100 μ v. No differences were observed using

manual eye movement scoring or for standard sleep macro-architecture measures.

Conclusion: REM phasic activity was increased in the men with PTSD compared to their twins. These differences can be attributed to environmental factors, probably exposure to trauma and the long-term consequences. Elevated REM phasic activity likely indicates the PTSD phenotype, not a genetic predisposition. Compared to manual rapid eye movement scoring, computerized scoring was more sensitive to PTSD diagnosis.

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0954

OBJECTIVE SLEEP DISTURBANCES IN RETURNING VETERANS WITH PTSD: PRELIMINARY FINDINGS

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Introduction: Complaints of sleep disturbances are a primary reason for psychiatric referral in troops serving in ongoing conflicts, and often become chronic in military veterans. The goal of this preliminary study was to compare polysomnographic sleep parameters and quantitative EEG parameters (absolute delta and beta power) in combat-exposed returning veterans of Operations Iraqi/Enduring Freedom (OIF/OEF) and age-matched good sleepers (GS).

Methods: Eleven medication-free OIF/OEF veterans (M age = 28.7 ± 6.7 years old) slept in the laboratory prior to randomization into an ongoing clinical trial. All reported more than one combat exposure, and nine met full criteria for current moderate-to-severe posttraumatic stress disorder (PTSD). Only two met criteria for current major depression. Eleven medication-free and healthy GS (M age = 28.3 ± 5.4 years old) completed the same laboratory procedures. None of the participants had sleep apnea or periodic leg movements during sleep. Cohen's *d* effect sizes were computed to assess group differences. Small, medium, and large effect sizes are indicated by *d* values of .20, .50, and .80, respectively.

Results: Sleep efficiency was lower in veterans compared to GS ($d = .81$), and was related to moderate increases in sleep latency ($d = .35$), duration and number of nocturnal awakenings ($d = .49$ and $d = .62$), and reduced total sleep time ($d = .34$). REM sleep variables did not differ in OIF/OEF veterans and GS. During NREM sleep, OIF veterans showed decreased absolute delta power ($d = .46$) as well as beta power compared to GS ($d = -.99$). Sleep efficiency was strongly and negatively correlated with PTSD severity ($\rho = -.65$, $p < .001$).

Conclusion: Returning veterans with full and partial PTSD show evidence of objective sleep disruption. Sleep neuroimaging techniques are required to identify the neurobiological underpinnings of sleep disturbances associated with posttraumatic stress.

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0955

DURATION OF FIRST REM EPISODE IN NEVER-DEPRESSED ADOLESCENTS: EARLY INDICATOR OF AFFECTIVE DISTURBANCE?

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Introduction: Early night REM sleep and depression are associated in adults, but the direction of association is unclear. This analysis assessed whether early REM sleep could predict the first signs of affective disturbance in never-depressed adolescents.

Methods: Fifty-two medication-free never-depressed adolescents (31 female; mean age 15.96, SD=1.2, range =14-18 years) underwent polysomnographic sleep studies (Time 1) and 43 returned 8 weeks later to complete a second PSG study (Time 2). Participants also completed the Youth Self Report (YSR) and the Positive and Negative Affect Scale (PANAS) at each time point.

Results: The proportion of REM sleep in the first REM episode to total REM sleep time (REM1p) ranged from .01 to .75, mean=.21, SD=.18. REM1p was correlated with YSR depression/anxiety, attention problems, and internalizing problems at both time points ($p < .05$). REM1p at Time 1 was also highly predictive of internalizing problems 8 weeks later ($r = .58$, $p < .00005$). Adolescents with greater than 20% of their total REM sleep allocated to the first REM episode (REM1p > .20) at Time 1 ($n = 17$) had significantly higher YSR withdrawal, depression, attention, thought, internalizing and internalizing problems, (and a trend toward YSR higher somatic and social problems, $p < .10$) and higher PANAS negative mood scores at Time 2 ($p < .05$). To determine if REM1p was a predictor of future internalizing problems, rather than just a correlate, REM1p from both time points were entered into a simultaneous regression as independent variables. REM1p at time 1 accounted for 34% of the variance of internalizing problems at time 2, while REM1p at Time 2 did not contribute to variance explained.

Conclusion: These data indicate that a high proportion of REM sleep in the first REM episode may be an early indicator of affective disturbance.

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0956

NOCTURNAL BP IN YOUNG ADULT AFRICAN AMERICANS; RELATIONSHIPS TO PTSD AND SLEEP VIGILANCE

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Introduction: Posttraumatic Stress Disorder (PTSD) is associated with medical including cardiovascular conditions. The persisting sleep disturbances that accompany PTSD likely contribute to physical health risk, however, this possibility remains unstudied. The studies that have found a relationship between PTSD and hypertension have substantial representation of African Americans (AA). AAs have elevated rates of HTN and are more likely to exhibit an absence of the normal “dip” of blood pressure (BP) at night. Nocturnal BP “non-dipping” is an established risk factor for HTN and its end-organ complications. Increased arousal and vigilance are hallmarks of PTSD. Nocturnal BP non-dipping and sleep disturbances of PTSD have both been linked to sympathetic nervous system (SNS) activity. We hypothesized that there would be associations of nocturnal BP with PTSD and vigilance related to sleep.

Methods: We are recruiting healthy young adult AAs. Over 100 have filled out surveys regarding trauma exposure, PTSD symptoms, sleep, and health history. To date, 28 participants (18 female; mean age - 20.1, SD = 2.2; 9 with lifetime PTSD, an additional 8 meeting subthreshold criteria, 6 with current symptoms) received 24 hour BP and actigraphy monitoring, and structured clinical assessment of PTSD.

Results: The difference between nocturnal and day mean values for mean arterial pressure correlated with current (Spearman $\rho = -.40$, $p < .03$) and lifetime ($\rho = -.50$, $p < .01$) PTSD severity. Endorsements of “feeling on guard” and being “concerned for safety” while going to sleep were significantly related to PTSD and insomnia severity, and having been traumatized in the sleep environment. “Feeling on guard” correlated with nocturnal BP ($\rho = .40$, $p < .04$).

Conclusion: Elevated nocturnal BP may be a link between PTSD and cardiovascular morbidity in AAs. The roles of vigilance in relation to sleep and other remedial factors have implications for preventive intervention.

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0957

SLEEP HEART RATE AND RESPIRATORY SINUS ARRHYTHMIA DISTINGUISH PTSD AND PANIC DISORDER

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Introduction: Persons with posttraumatic stress disorder (PTSD) and panic disorder (PD) evidence disturbances of waking arousal likely tied to alteration of central fear mechanisms that are, in turn, richly interconnected with sleep regulatory systems. Both groups complain of sleep disturbances that can include prominent dysphoric arousals (nightmares and nocturnal panic attacks). Here, we report the results of extended in-home mattress actigraphic recordings that point to important divergences in sleep autonomic function between these two groups as indexed by heart rate (HR) and respiratory sinus arrhythmia (RSA).

Methods: Mattress actigraphic recordings lasting from 5 to 30 nights, all nights containing at least two hours of quantifiable kinetocardiogram (KCG), were obtained from 67 community-residing participants as they slept in their homes. Thirteen subjects were diagnosed with PD, 24 with PTSD, 15 with comorbid PD+PTSD, and 15 as free of Axis I mental disorder. Groups did not differ in gender distribution (~67% female), mean age (~41), BMI (~24) or AHI (~2.5). Sensitive accelerometers embedded in a mattress “topper” transduced thoracic movements induced by cardiac contractions which were recorded and quantified off-line. KCG-based estimates of HR and RSA have been extensively validated against ECG-based criteria (Woodward et al., 2007).

Results: Both HR ($F(3,64) = 2.90, p < 0.05$) and RSA ($F(3,64) = 3.00, p < 0.05$) exhibited main effects of diagnosis. Post-hoc tests (Tukey’s L.S.D.) found that participants with PTSD and PTSD+PD exhibited elevated sleep HR relative to controls (p ’s < 0.05). PTSD was associated with attenuation of sleep RSA magnitude relative to PD and controls (p ’s < 0.01 , and 0.05 , respectively).

Conclusion: Despite sharing prominent features of waking arousal dysregulation and sleep disturbance, PTSD and PD clearly diverged in extended in-home sleep recordings. PTSD but not PD was associated with elevated HR and reduced RSA.

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0958

INSOMNIA AND POOR SLEEP QUALITY AS PREDICTORS OF SUICIDAL SYMPTOMS IN A NONCLINICAL SAMPLE

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Introduction: A growing body of research suggests that poor sleep quality and insomnia symptoms are associated with depression, as well as an increased risk for suicide. Sleep disturbances are also now listed among the top 10 warning signs of suicide by SAMHSA. Even so, few investigations have reported on symptom relationships between sleep disturbances, depression, and suicidal ideation among nonclinical samples, or among populations that may not be traditionally screened or assessed for suicide risk.

Methods: Data were collected among 322 undergraduates (aged 19-24) at a large university. The following symptom measures were administered: Pittsburgh Sleep Quality Index (PSQI); Insomnia Severity Index (ISI); Beck Depression Inventory (BDI); Beck Scale for Suicide Ideation (BSS). Poor self-reported sleep quality and elevated insomnia symptoms were hypothesized to be significantly associated with depressive and suicidal symptoms. Hierarchical linear regression analyses were employed to test study predictions.

Results: Consistent with past research, PSQI [$t=5.14, \beta=.64, p<.01$] and ISI total scores [$t=3.74, \beta=.27, p<.01$] were significantly associated with greater BDI scores. As hypothesized, elevated scores on the BSS were significantly predicted by higher scores on the ISI [$t=2.48, \beta=.53, p<.05$] and the PSQI, although the latter emerged only as a nonsignificant (ns) trend [$t=2.07, \beta=.54, p=.065$]. Importantly, after BDI scores were entered into the model as a covariate, ISI and PSQI scores jointly predicted greater BSS scores [$F(1,3)=11.7, p<.01$], though they failed to significantly predict these symptoms independently at the $p < .05$ level.

Conclusion: Similar to results among more severe clinical samples, poor sleep quality and insomnia were significantly associated with suicidal symptoms among a large sample of college undergraduates. These relationships were not statistically significant after controlling for depression, although jointly, insomnia and poor sleep quality significantly predicted suicidality. Results indicate that the assessment of sleep among young adults may be an important opportunity for intervention when screening for depression and suicide risk.

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0959

ASSOCIATION BETWEEN SLEEP DISTURBANCES AND SUICIDAL THOUGHTS IN WOMEN WITH DEPRESSION: A CROSS-SECTIONAL SURVEY USING PHQ-9

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Introduction: Major depressive disorder (MDD) is a common illness with a life time prevalence of around 15%. Sleep disturbances are also very common with a prevalence of 30-40%. The interaction between MDD and sleep disturbances is bi-directional. Sleep disturbance is one of the diagnostic features of MDD and patients with insomnia are at a higher risk for MDD. Suicide, the most common cause of death in MDD, is difficult to predict, and attempts to correlate with symptoms of MDD have not been successful. Although MDD is twice as common in women, insomnia is 1.5 times more common in women, and women are 4 times more likely to attempt suicide, no studies have assessed the association between sleep disturbances and suicidal thoughts in women with depression.

Methods: Patient Health Questionnaire (PHQ-9) is a validated subjective instrument to screen for MDD. It is a 9 item questionnaire with questions on symptoms of depression including sleep and suicide. A score of > 10 and > 20 are suggestive of moderate and severe depression, respectively. Data was collected from 193 women between the ages of 18 and 84 years during the Women’s Health Day.

Results: The prevalence of moderate to severe depression (PHQ > 10) was 21%, and 87.5% of these subjects reported sleep problems and 25% reported suicidal thoughts. Pearson Chi-Square analysis showed a significant correlation between depressed mood and sleep problems ($\gamma = 0.45, p < 0.001$). Among subjects with moderate to severe depression and suicidal thoughts, all subjects reported sleep problems and 60% of them reported sleep problems over half of the days to nearly everyday.

Conclusion: MDD and sleep disturbances are both more common in women and associated with increased morbidity and mortality. Women with depression and sleep disturbances are at a much higher risk of having suicidal thoughts than those without sleep disturbances. It remains to be seen if targeted treatment of insomnia in MDD will decrease the suicide risk.

0960

ASSOCIATION OF PITTSBURGH SLEEP QUALITY INDEX AND ADVERSE CHILDHOOD EXPERIENCES IN A COLLEGE SAMPLE

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Introduction: Sleep patterns and quality have not often been explored in college students. In addition, the long-term consequences of childhood trauma on adult sleep quality have not been fully investigated. The goals of the current study were 1) to examine sleep quality in a university sample, and 2) to examine the association of adverse childhood experiences with adult sleep quality.

Methods: The Pittsburgh Sleep Quality Index (PSQI) and the Childhood Trauma Questionnaire (CTQ) were administered to university students, $N = 70$, as part of a larger battery. Participants (mean age = 18.54, $SD = 2.77$) were divided into mild and moderate/severe trauma groups on each of five CTQ subscales; emotional abuse (EA), physical abuse (PA), sexual abuse (SA), emotional neglect (EN), and physical neglect (PN). PSQI sleep quality indices were examined in these groups. Chi-square tests were used to examine childhood trauma rates in poor sleepers ($n = 29$) versus good sleepers ($n = 41$).

Results: Mean self-reported sleep latency on the PSQI was 21.57 minutes ($SD = 16.80$), mean total sleep time was 6.99 hours ($SD = 1.43$), sleep efficiency was 92% ($SD = 13\%$), and mean total PSQI score was 5.65 ($SD = 3.12$). Participants in the moderate/severe EA group reported significantly more daytime dysfunction on the PSQI than those in the mild group, and the moderate/severe PN group had poorer sleep duration and daytime dysfunction. Approximately half of poor sleepers (51.7%) indicated that they had experienced some form of childhood abuse, whereas significantly fewer good sleepers (26.8%) endorsed childhood physical, sexual, or emotional abuse on the CTQ.

Conclusion: The current findings add to the modest literature on sleep in college students. With regard to adverse childhood experiences, the current study suggests that effects on sleep may extend into early adulthood.

0961

ACADEMIC ACHIEVEMENT PREDICTED FROM SLEEP, NEUROPSYCHOLOGICAL VARIABLES, AND IQ

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Introduction: Significant associations between sleep disturbance and impaired neuropsychological, behavioral, emotional and academic functioning have been reported in some previous studies, although the findings have been inconsistent and often contradictory. In this study, we examined the relative importance of sleep, IQ, neuropsychological test scores, and ADHD symptoms in predicting reading and math achievement in a large community sample of children.

Methods: We assessed 412 elementary school students from a general population epidemiologic study of the prevalence of sleep disorders. All children underwent a full night polysomnography and comprehensive neuropsychological testing. Parents completed multiple rating scales and sleep questionnaires.

Results: A stepwise linear regression analysis was performed that included sleep, IQ, neuropsychological, and ADHD scores as predictors. The most powerful combined predictors of achievement were IQ and some neuropsychological test scores. Subjective parent reported sleep problems and objective polysomnograph scores did not contribute significantly more to the prediction of achievement. Further, IQ, neuropsychological test scores and ADHD parent ratings were all significantly related to achievement, but correlations between achievement and objective and subjective sleep scores were all nonsignificant. Children with and without sleep problems did not differ from each other in achievement.

Conclusion: These data suggest that IQ is the best single predictor of reading and math and objective and subjective measures of sleep disturbance did not contribute significantly to the predictors of achievement in a general population sample of children.

0962

ADHD SUBTYPES AND COMORBIDITIES: DIFFERENCES IN SLEEP PROBLEMS

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Introduction: Sleep disturbances are common in children with ADHD. Our study investigated differences in frequency and type of sleep problems as a function of ADHD subtype, comorbidity, and medication.

Methods: The parents of 681 children with ADHD (combined type) or ADD (inattentive type) and 594 general population children completed the Pediatric Behavior Scale (PBS). The PBS is a 165 item norm referenced rating scale that assesses sleep, ADHD, behavior, mood, and health problems. All children had an IQ > 80 and were age 6-16. For those children with ADHD, 100% agreement on the diagnosis was obtained from two independent clinicians.

Results: PBS Sleep Problems T scores were significantly greater in children with ADHD when comorbid anxiety or depression was present, whereas oppositional-defiant disorder did not affect sleep. Children with ADD alone had the fewest sleep problems and did not differ from controls. Children with ADHD had significantly more sleep problems than controls, and sleep problems increased as the severity of ADHD increased. Daytime sleepiness was greatest in children with ADD. Children with ADHD did not have increased daytime sleepiness, even though they slept less and had more sleep problems than controls. Daytime sleepiness was not significantly correlated with sleeping less than normal, but was associated with sleeping more than normal. Differences in sleep problems between medicated and unmedicated children with ADHD were nonsignificant when ADHD severity was controlled.

Conclusion: Comorbid anxiety and depression intensify sleep problems in children with ADHD, whereas oppositional-defiant disorder does not. Sleep problems are associated with ADHD and not ADD. Children with ADD have few sleep problems, but experience daytime sleepiness, suggesting a neurophysiologic underarousal in ADD. Our study shows that daytime sleepiness is not due to parent reported sleep problems, and instead, is associated with sleeping more than normal. Therefore, some children are sleeper day and night.

0963

SLEEP AND BODY MASS INDEX IN DEPRESSED CHILDREN AND HEALTHY CONTROLS

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Introduction: Major depressive disorder (MDD) is associated with subjective sleep disturbances in over 90 % of children and adolescents. Moreover, there is also an association between higher body mass index (BMI) and early onset MDD. Recent studies also suggest that higher BMI is associated with greater objective sleep disturbance. Thus, one might expect that the relationship between BMI and sleep disturbance would be stronger in children with MDD than in healthy controls. The purpose of the present study was to evaluate the relationship between BMI and sleep polysomnography in children and adolescents with MDD, compared to healthy non-MDD controls.

Methods: The sample included 74 children 8-17 years of age who met criteria for MDD. They were symptomatic and unmedicated at the time of study. Seventeen healthy controls with no personal or family history

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of psychopathology were also recruited. Each participant maintained a regularized sleep/wake cycle for one week followed by 2 consecutive nights in the sleep lab. Night 1 served as adaptation and as a screening for independent sleep disorders. BMI was adjusted using the CDC formula for percentiles by age. Data were coded for group, sex and age and correlational and regression analyses were conducted.

Results: The MDD group showed significant correlations between BMI percentiles with sleep efficiency and awake time after sleep onset. Higher BMI was associated with lower sleep efficiency, more time awake, less REM and more Stage 1 sleep, although age and sex moderated these relationships. By contrast, none of these variables correlated significantly with BMI in controls.

Conclusion: These findings indicate that there is greater sleep disturbance in MDD children and adolescents who have a higher BMI. The relationship between BMI and sleep is stronger in MDD than in controls.

0964

PERIODICITY OF BETA ACTIVITY DURING NON-RAPID EYE MOVEMENT SLEEP IN MAJOR DEPRESSIVE DISORDER

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Introduction: Previous work has revealed quantitative sleep EEG differences between individuals with major depressive disorder (MDD) and healthy controls. Individuals with MDD have shown lower delta (0.5-3.9 Hz) activity and enhanced beta (12-32 Hz) during sleep and all-night temporal coherence is lower in those with MDD, perhaps indicative of hyper-arousal associated with MDD. The present study evaluated short duration ultradian rhythms in beta activity within NREM sleep episodes.

Methods: The sample included 26 individuals with MDD (11 female, 15 male) and 55 healthy controls (30 female, 25 male) that spent 2 consecutive nights in the lab after following an 11pm-6am sleep schedule. The first night served as adaptation and screening for primary sleep disorders. All data analysis were based on the second lab night. FFTs quantified sleep EEG recorded from left and right central, parietal and occipital electrodes. Time series analysis determined the period length of ultradian rhythms within NREM sleep in each individual.

Results: Preliminary results indicated rhythmic beta activity during NREM sleep in the MDD group with a period of 8-13 minutes. Overall, beta rhythms were stronger in women than in men. No predominant ultradian beta rhythm was found within NREM sleep in healthy controls.

Conclusion: Short duration ultradian rhythms in beta activity are evident in those with depression but not in healthy controls. The findings are not inconsistent with hyper-arousal during sleep in depression.

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0965

THE ROLE OF PERCEIVED ANXIETY CONTROL IN SLEEP AND WORRY

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Introduction: General sleep disturbance has been associated with worry. Specifically, sleep deprivation has been found to result in increased emotional consequences (i.e., anxiety, depression, paranoia) among healthy adults. Perceived anxiety control may influence the extent to which an individual experiences worry. This study investigated the relation between anxiety control, and sleep quality. Greater worry and less perceived anxiety control were expected to be associated with worse sleep in younger adults.

Methods: The current sample was recruited from the undergraduate and graduate student population at West Virginia University. Participants completed several questionnaires as part of a larger study. Per-

ceived anxiety control was measured by scores on the Anxiety Control Questionnaire, on which higher scores suggest greater perceived anxiety control. Problematic worry was assessed by the Penn State Worry Questionnaire on which higher scores represented more uncontrollable worry. Sleep quality was measured by scores on the Pittsburgh Sleep Quality Index, with higher scores indicating more sleep disturbance.

Results: The current sample of (N = 27) younger adults was 51.9% female and 96.3% Caucasian with a mean age of 20.5 years (SD±1.7). A negative correlation was found between perceived anxiety control (105.4 [SD±20.7]) and sleep quality (7.7 [SD±3.5]): $r = -.495$, $p < 0.01$. Anxiety control was correlated with worry (50.4 [SD±14.7]): $r = -.522$, $p < 0.01$, but worry was not correlated with sleep quality.

Conclusion: As was expected, lower perceived control over anxiety was associated with worse sleep quality. Less anxiety control was also associated with increased worry. However, the relation between worry and sleep was not found to be significant. These results suggest that treating one's sleep disturbances may affect one's perceived control over anxiety and that this may be an important factor to consider during treatment of both sleep and anxiety disorders. Additionally, acceptance based therapies aimed at improving anxiety control may improve one's sleep as well.

Support (optional): West Virginia University Alumni Fund

0966

CARDIAC VAGAL CONTROL, DEPRESSION, AND INSOMNIA

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Introduction: Cardiac vagal control (CVC), as indexed by respiratory sinus arrhythmia (RSA), is a measure of parasympathetic nervous system function. Lower CVC during wake has been associated with mood and sleep disturbances in various populations. Here, we examined the relationship between nocturnal RSA and the severity of depression and insomnia in participants with both disorders.

Methods: Data were obtained from 24 participants (15 females) aged 25-69 (Mean age = 46.6). Depression was diagnosed using the Structured Clinical Interview for DSM-IV Disorders and the Hamilton Rating Scale for Depression (HRSD). Insomnia was diagnosed based on the Duke Screening Interview and baseline daily sleep diaries. Severity of insomnia was measured with the Insomnia Severity Index (ISI). Participants' sleep was recorded at home using ambulatory polysomnography, which included heart rate (sampled at 256 HZ). Sleep stages were scored according to standard criteria. RSA was calculated for ten minutes of wake before sleep onset, stage 2 of the first sleep cycle, and REM of the second sleep cycle.

Results: RSA during wake and stage 2 sleep were negatively correlated with the HRSD ($r = -.43$, $p = .04$ and $r = -.62$, $p = .04$, respectively). RSA during wake was also negatively correlated with mid-night awakenings as measured by the ISI ($r = -.51$, $p = .01$) and showed a trend correlation with total ISI scores ($r = -.35$, $p = .09$). RSA during REM sleep, although in the same direction, was not significantly correlated with either depression or insomnia ($p > .10$).

Conclusion: Past results pertaining to depression and daytime RSA have been replicated and extended to include RSA measured during stage 2 sleep and pre-sleep wakefulness. Lower cardiac vagal control during stage 2 sleep, as well as during wake, appear to be psychophysiological markers of severity of depression and insomnia.

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0967

THE IMPACT OF ANXIETY COMORBIDITIES AND MIGRAINE ON THE SLEEP QUALITY AMONG PATIENTS WITH MAJOR DEPRESSIVE DISORDER

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Introduction: Sleep disturbance, depression, anxiety, and migraine are closely related and interactive. The aim of this study was to investigate the impact of anxiety disorders and migraine on sleep quality among patients with major depressive disorder (MDD).

Methods: Consecutive psychiatric outpatients with MDD in a medical center were enrolled. MDD and seven anxiety disorders were diagnosed using the Structured Clinical Interview for DSM-IV-TR. Migraine was diagnosed based on the International Classification of Headache Disorders, 2nd edition. The Chinese version of the Pittsburgh Sleep Quality Index (PSQI) and Hamilton Depression Rating Scale (HAM-D) were used to evaluate the sleep quality and the severity of depression, respectively.

Results: There were 135 participants (34 M, 101 F) with MDD. The mean total PSQI score was 13.61±3.96 and nearly all participants (98.8%, 133) had poor sleep quality (PSQI global score greater than 5). Panic disorder and agoraphobia were the two most important comorbid anxiety disorders with significant negative impacts on sleep quality among patients with MDD. MDD patients with anxiety disorders and migraine have a higher severity of depression. Subjects with panic disorder and agoraphobia had a poorer sleep quality in four components of the PSQI. Subjects with migraine, chronic depression, and obsessive compulsive disorder also had a poorer sleep disturbance. A higher severity of depression in subjects with panic disorder, agoraphobia, and migraine might be partially resulted from a worse sleep problem.

Conclusion: The impacts of some anxiety disorders and migraine on MDD were not limited on anxiety severity or pain, respectively, but also on sleep quality. Future studies should further explore the interactions among sleep disturbance, depression, anxiety, and migraine.

0968

SLEEP DISTURBANCE INDUCED BY AMPHETAMINE IN A RODENT MODEL OF MANIA

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Introduction: We assessed the effects of acute and chronic amphetamine (AMPH) administration on sleep pattern in an induced rat model of mania.

Methods: Sleep was monitored continuously after a single or repeated injections (7 daily administration; 2 mg/kg, ip) of AMPH or saline in adult Wistar rats.

Results: Electrophysiological findings demonstrate acute injection of AMPH suppressed sleep for the first two hours, followed by a gradual increase in the amount of sleep. Both slow wave sleep (SWS) and paradoxical sleep (PS) were compromised. Repeated exposure to AMPH led to a drastic disruption of sleep-wake cycle, mainly decreasing PS during all time-points recorded in comparison to saline group due to lower number of PS episodes in the AMPH group. Further, acute and chronic AMPH-injected to rats presented longer latency to SWS and PS compared with saline group. Taken together, these results suggest that AMPH produces disturbances in sleep, and the decreased PS sleep time.

Conclusion: Disturbance in sleep is a key feature in manic states, which adds to the face validity of the use of AMPH injections as a means to model mania in rats. In addition, these findings open up an avenue to explore the relationship of changes in the sleep architecture as a means to trigger and/or contribute to the emergence of the manic syndrome.

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0969

AN OPEN PILOT OF A COGNITIVE-BEHAVIORAL GROUP TREATMENT FOR COMORBID INSOMNIA AND COMBAT-RELATED NIGHTMARES IN VETERANS WITH PTSD

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Introduction: Up to 90% of combat veterans with posttraumatic stress disorder (PTSD) experience sleep disruption and 52% report frequent nightmares, yet no efficacious treatments exist for these patients. In an open pilot study, we evaluated the efficacy of a cognitive-behavioral group treatment for comorbid insomnia and nightmares (CBTI-N) in combat veterans with PTSD.

Methods: Nine male combat veterans (mean age 57.9±10.5 years), who met diagnostic criteria for PTSD and reported chronic nightmares and insomnia (mean insomnia duration 17±12.6 years), were recruited from the Ann Arbor VA to participate in 12 sessions of group CBTI-N. All participants had comorbid psychiatric and medical disorders and were prescribed psychopharmacological agents to treat their PTSD. CBTI-N consisted of 4 sessions of cognitive-behavioral insomnia treatment, 6 nightmare reduction sessions, and 2 relapse prevention sessions. Participants kept daily sleep and dream diaries (rating nightmare frequency and level of nightmare distress on a 10 point scale). Measures of sleep (Insomnia Severity Index; ISI, Pittsburgh Sleep Quality Index) and daytime functioning (Multidimensional Fatigue Inventory; MFI-20, State-Trait Anxiety Inventory, Quick Inventory of Depressive Symptomatology) were completed pre- and post-treatment.

Results: Paired-sample t-tests indicated sleep diary-rated improvements in wake after sleep onset (73.52 ± 58.70 to 47.89 ± 48.25, p = 0.03) and sleep efficiency (73.56 ± 58.70 to 80.11 ± 15.99, p = 0.02). Sleep and daytime functioning improvements were reflected in the ISI (21.5 ± 4.31 to 15.38 ± 6.61, p = 0.02) and Mental Fatigue subscale of the MFI-20 (17.38 ± 2.56 to 14.38 ± 3.89, p = 0.01). Dream diaries from 5 participants documented non-significant reductions in weekly nightmare frequency (10.70 ± 11.22 to 4.60 ± 8.11, p = 0.27) and nightmare distress (6.14 ± 3.45 to 5.15 ± 4.72, p = 0.45).

Conclusion: In this small, uncontrolled pilot study of combat veterans with PTSD, chronic nightmares, and insomnia, improvements in subjective reports of insomnia severity, sleep consolidation, and mental fatigue were evident following 12 weeks of group CBTI-N. Although mean reductions in weekly nightmares were noted, frequency and distress ratings did not achieve statistical significance. We are continuing to refine the nightmare component of this treatment in anticipation of conducting a controlled trial.

0970

THE IMPACT OF SMOKING CESSATION ON SLEEP

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Introduction: Subjective sleep disruption is a common consequence of quitting smoking. However, polysomnography (PSG) studies over the course of smoking cessation are rare and none have been conducted to

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evaluate bupropion (BUP) and nicotine replacement therapy (NRT) effects in conjunction with smoking cessation. We report data from a randomized, double-blind placebo controlled trial of NRT and BUP treatment for smoking cessation.

Methods: 27 smokers (15 men, 40.9 ± 13.9 years) underwent full night PSG on a baseline night (still smoking) and the first night following quitting. Participants smoked 18.8 ± 6.4 cigarettes per day and had a mean expired CO of 28.9 ± 11.2 ppm at the start of the study. The mean Fagerström Test for Nicotine Dependence score (FTND) was 4.6 ± 1.5. BUP and NRT were administered as per current clinical practice guidelines. Data are presented unblinded as to treatment condition and variables were compared using Wilcoxon signed ranks tests.

Results: Relative to baseline, participants showed a 4.8 ± 8.6 % decrease in sleep efficiency ($Z = -2.756$, $p < .01$), a 21.9 ± 33.9 minute increase in wakefulness after sleep onset (WASO) ($Z = 3.244$, $p < .01$) and a 5.2 ± 9.7 increase in the number of wake periods ($Z = 2.502$, $p < .01$) on the quit night. There were no significant differences in sleep onset latency, or the percentages of stage 1, stage 2, SWS or REM sleep. FTND was significantly correlated with the baseline-quit night difference in WASO ($\rho = -0.38$, $p < .05$), and baseline expired CO was significantly correlated with the baseline-quit difference in number of wake periods ($\rho = -0.45$, $p < .01$) and in the percentage of stage 1 sleep ($\rho = -0.43$, $p < .05$).

Conclusion: Sleep continuity is negatively impacted on the first night of quitting smoking with preliminary evidence that the disruption is greater in those with higher levels of nicotine dependence.

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0971

SLEEP QUALITY IN FEMALE UNDERGRADUATES WITH AND WITHOUT POSTTRAUMATIC STRESS SYMPTOMS

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Introduction: Sleep complaints have been consistently documented in women diagnosed with Posttraumatic Stress Disorder (PTSD) after sexual assault. However, few studies have examined sleep quality in assault survivors endorsing non-clinical levels of posttraumatic stress symptoms. The purpose of this study is to compare sleep quality between sexual assault survivors with clinical and non-clinical levels of PTSD symptoms and female undergraduate students without a history of sexual assault.

Methods: Female undergraduates (N=700, mean age=19.2) completed the self-report Pittsburgh Sleep Quality Index (PSQI) and a screening measure for lifetime history of sexual assault. The 104 women reporting prior assault completed the self-report PTSD Symptom Scale and were divided into two groups based on the DSM-IV-TR diagnostic cutoffs for PTSD symptoms. Global PSQI scores were compared across three groups (clinical PTSD symptoms, n=27; non-clinical PTSD symptoms, n=77; no assault history, n=596).

Results: A one-way ANOVA was used to compare the three groups' PSQI scores, with higher scores indicating poorer sleep quality. Results revealed a significant difference between the groups, $F(2, 697)=5.79$, $p<.01$. Tukey's post hoc analysis revealed the clinical PTSD group ($M=8.37$, $SD=3.14$) scored significantly higher on the PSQI than the group with non-clinical PTSD symptoms ($M=6.52$, $SD=2.62$) and the group with no assault history ($M=6.31$, $SD=3.14$).

Conclusion: Sexual assault survivors with clinical levels of PTSD symptoms reported significantly worse sleep quality than survivors with non-clinical symptoms and women with no assault history. Results also show that even in a relatively healthy sample of young adults, poor sleep is a common problem. These findings highlight the importance of assessing sleep disturbance among those with non-clinical PTSD symptoms, as untreated sleep problems may worsen over time and place the individual at risk for increased psychopathology.

0972

THE INTERACTION BETWEEN DEPRESSION AND SLEEP COMPLAINTS AFFECTS EMOTIONAL REACTIONS TO STRESSFUL EVENTS AND OBJECTIVE SLEEP

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Introduction: The goal of the current study was to explore the relations between depression and subjective sleep on stress and negative affect reactions to a stressful event, and determine if those reactions could predict sleep disruption the night of that event.

Methods: Fifty-two adults with a history of recurrent depression in full or partial remission completed the Beck Depression Inventory, three weeks of sleep diaries and an adaptation night prior to returning to the laboratory for testing. Participants underwent the Trier Social Stress Test (TSST), a standardized laboratory stressor that involved a simulated public speaking and oral subtraction task. Before and after the stressor, each participant completed the Spielberger State Anxiety Inventory and the Positive and Negative Affect Scale. The participants then spent the night in the laboratory for a polysomnographic sleep study.

Results: Multiple regression tested whether the interactions between current depression and perceived sleep rating (split into sleep complaints [CS] or no sleep complaints [NCS]) significantly affected change in state anxiety (SA) and negative affect (NA). In the NCS group, a significant interaction indicated that the greater the depression scores the stronger the reaction to the TSST in terms of both SA and NA. In the CS group, higher depression scores were associated with a blunted response to the TSST in terms of NA, and had no effect on SA levels. A sequential regression revealed that change in SA was able to predict total awakenings and arousals better than NA change such that the greater the anxious reaction to the TSST, the less awakenings that night.

Conclusion: Negative affect and anxiety in reaction to psychosocial stressors are dependent on the interaction between depressive symptomatology and perceived sleep quality. Strong anxiety reactions then protect against awakenings the night following the stressful event.

0973

NO FIRST-NIGHT EFFECT IN HOME POLYSOMNOGRAPHY OF METHADONE MAINTENANCE PATIENTS WITH SUBJECTIVE SLEEP COMPLAINTS

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Introduction: Approximately 85% of patients in methadone maintenance treatment (MMT) for opiate addiction report sleep disturbances. The current study is part of an investigation of the contribution of poor sleep to relapse in patients undergoing MMT. The present analysis examined first-night effects (FNE) on sleep in at-home polysomnographic (PSG) studies of patients in MMT.

Methods: 64 patients were recruited from 7 MMT clinics in Rhode Island from January 2006 to October 2007. Patients with a Pittsburgh Sleep Quality Index score > 5 received home PSG recordings using a portable Safiro unit (Compumedics, Charlotte, NC) on two consecutive nights. Sleep was scored in 30-sec epochs according to Rechtschaffen and Kales criteria. 46 participants (50% female; mean age = 37.6 ± 8.7 years; median methadone dose = 100 mg) completed 2 consecutive nights of home PSG. Non-independent t-tests examined night-to-night differences in sleep variables selected from previous studies that have shown FNE.

Results: No significant ($p < .05$) differences were found for the selected sleep parameters (mean \pm SD): Sleep Period Time (minutes; N1 = 395 \pm 123; N2 = 376 \pm 149), Total Sleep Time (minutes; N1 = 334 \pm 113; N2 = 317 \pm 136), % Sleep Efficiency (N1 = 84.5 \pm 10.7; N2 = 83.4 \pm 12.1); Wake After Sleep Onset (minutes; N1 = 60.8 \pm 40.9; N2 = 58.2 \pm 43.8), % Stage 1 (N1 = 2.3 \pm 1.7; N2 = 2.2 \pm 1.3), % Stage 2 (N1 = 66.6 \pm 11.0; N2 = 65.8 \pm 23.0), % Slow Wave Sleep (N1 = 14.6 \pm 8.8; N2 = 16.7 \pm 10.5), % REM (N1 = 16.5 \pm 8.4; N2 = 15.2 \pm 8.6), REM Latency (minutes; N1 = 97.0 \pm 75.4; N2 = 83.8 \pm 68.4), % Wake (N1 = 15.5 \pm 10.7; N2 = 16.6 \pm 12.1), Arousal Index (events/hr; N1 = 11.3 \pm 11.6; N2 = 11.6 \pm 12.9).

Conclusion: No first-night effects on sleep were demonstrated in 46 MMT patients on two consecutive nights of home PSG. FNE may not have been observed because PSGs took place in a familiar environment. Nevertheless, several sleep parameters, e.g., REM percent and wake after sleep onset, were abnormal compared to normal adults in this age range, providing corroboration of sleep complaints. Future home PSG studies in MMT subjects may not require an adaptation night.

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0974

SLEEP DISORDERS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) RECORDED OVER NIGHT BY VIDEO-POLYSOMNOGRAPHY

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Introduction: During the past ten years, attention was drawn to the possible role of co-morbid sleep disorders in the clinical managing of attention-deficit/hyperactivity disorder in children. We tried to assess the prevalence and contributing role of sleep disorders in a cohort of ADHD children referred to our Sleep Center by Pediatric Neurology and Psychiatry.

Methods: 55 ADHD children adolescents (7 female, mean age 8.9 years) consecutively referred upon first diagnosis to our centre from 2004 to 2006 were included. Subjects diagnosed with other psychiatric or neurological diseases were excluded. All 55 patients underwent a sleep questionnaire, video-PSG including 18 EEG leads and a behavioural/neuropsychological assessment, including cognitive profile. Polysomnographic data were compared with those obtained from a group of 20 healthy controls matched for age, gender, and IQ. Resulting data have been examined using the Mann-Whitney Test for comparison between the two groups. Moreover Spearman coefficient ($p < 0.05$ criterion level) was used to assess the association between behavioral and sleep continuous variables.

Results: Sleep disorders were found in 83.4% of ADHD children: PLMS in 40%, disorders of arousal (DOA) 36.3%, bruxism in 32.7%, RLS in 25.4%, Sleep Related Rhythmic Movement Disorders in 21.8%, Sleep Related Breathing Disorders in 18.1%, DSPS in 5.4%, pre-clinic RBD in 1.8%. Mean score IRLS-RS within the RLS+ group was 19.1. There is a significant difference in almost all studied sleep variables (SE%, N2%, N3%, REM%, TST, REM latency, MA index) between ADHD children and controls. RLS positive children had a significantly higher score on SNAP-H than RLS negative. Similarly DOA positive ADHD children had an higher arousal index than DOA negative.

Conclusion: An high prevalence of sleep disorders was found in our sample of ADHD children, especially DOA and SRMD. ADHD children showed consistently, fragmented sleep albeit an increased percentage of SWS. The presence of RLS significantly affected behavioural scores.

0975

SLEEP QUALITY DEPRESSION AND ANXIETY AMONG HISPANICS OF MEXICAN DESCENT AND NON-HISPANIC WHITES IN SAN DIEGO COUNTY

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Introduction: The association of sleep quality with depression and anxiety is well known. However, this association has not been extensively studied among Hispanics. We investigated the association of sleep quality and depression in Hispanics of Mexican descent (HMD) and in Non-Hispanic Whites (NHW) living in San Diego County.

Methods: We performed a population-based telephone survey using the Waksberg random digit dialing procedure and the Kish intra-household selection method to administer a questionnaire dealing with sleep health. A global sleep quality score was calculated from responses to six different questions dealing with sleep quality from the Sleep Habits Questionnaire. The prevalence of depression or anxiety was determined by the subject's report of having received a diagnosis by a physician. Chi-Square tests were used for comparisons of sleep quality and depression by ethnicity and logistic regression to determine predictors of depression or anxiety.

Results: A total of 1333 adults were interviewed (47.6% HMD and 52.4% NHW). NHW were significantly older than HMD (40.9 \pm 15.5 Vs 52.6 \pm 16.8, $p < 0.001$), and had a higher prevalence of ever being told by a doctor that they had depression or anxiety (34.4% Vs 28%, $p = 0.013$). Non-Hispanic Whites also reported sleep quality complaints more frequently than HMD (75.1% Vs 68%, $p = 0.036$), and took sleeping aids more often than HMD (31.7% Vs 18% $p < 0.001$). Adjusting for age, gender, sleep quality, ethnicity and use of sleeping aids as covariates, worse sleep quality, being a woman and the use of sleeping aids were significant independent predictors of depression or anxiety.

Conclusion: In a population-based survey, NHW report worse sleep quality, use of sleeping aids and depression or anxiety more frequently than HMD. However, ethnicity was not an independent predictor of having a diagnosis of depression or anxiety.

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0976

COMPARISONS BETWEEN OBJECTIVE AND SUBJECTIVE MEASURES OF SLEEP BETWEEN GOOD SLEEPERS, PARADOXICAL AND PSYCHOPHYSIOLOGICAL INSOMNIA SUFFERERS AND BORDERLINE PERSONALITY DISORDER INDIVIDUALS

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Introduction: Recent findings suggest few differences in sleep continuity and quality between borderline personality disorder individuals (BPD) and good sleepers (GS). Nonetheless, BPD individuals show marked discrepancies between subjective and objective sleep measures. The objective of this study is to document sleep in BPD, insomnia sufferers (paradoxical, Para-I; psychophysiological, Psy-I) and GS.

Methods: 12 BPD reporting insomnia, 15 Para-I, 15 Psy-I and 15 GS, underwent three consecutive nights of standard PSG recordings (Night 1 to Night 3). All participants completed a clinical interview (SCID and Insomnia Diagnostic Interview), and two weeks of sleep diaries. Participants did not suffer from any other psychopathology and were drug-free.

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Results: MANOVAs were computed and post-hoc analyses applied. On Night1, GS and BPD had less awakenings than Para-I ($ps < .01$) while Para-I had more than Psy-I ($p = .04$); BPD slept more than Psy-I ($p = .04$) and showed higher % of stage 4 (S4) than Para-I ($p = .03$) as well as spent more time in S4 (in minutes) than both Para-I and GS ($ps < .05$). On Night2, BPD had higher % of S4 than Para-I and GS ($ps < .01$) as well as more S4 than GS ($p = .03$). On Night3, BPD had higher % of S4 and spent more time in S4 than Para-I, Psy-I and GS ($ps < .01$). Compared to Psy-I and GS, BPD reported having slept more and better in the sleep laboratory than at home while reporting feeling less restored upon awakening.

Conclusion: The subjective sleep of BPD is similar to the one of Para-I. However, while they reported feeling less refreshed upon awakening, BPD spent more time in stage 4 than any other individual. As BPD are very sensitive to loneliness and interpersonal stressors, laboratory settings might provide a secure context facilitating sleep, and not representative of 'home' sleep. Results might also reflect psychobiological mechanisms peculiar to BPD.

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0977

SLEEP PATTERNS OF RESIDENTIALLY-BASED ADOLESCENTS WITH AUTISM

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Introduction: Sleep problems are highly prevalent in children and adolescents and occur more frequently in those with developmental disabilities. The most common sleep problems are difficulties with sleep onset, sleep maintenance, and early morning waking. A highly structured sleep schedule may improve these difficulties. The purpose of this study was to assess the sleep patterns of adolescents with autism living in a highly structured residential setting.

Methods: Two weeks of archival data were collected on 16 males (11 to 18 years) with autism living in the same residential center. Sleep data were collected every 5 to 15 minutes. Data extraction included sleep onset latency, sleep onset time, number and duration of nightwakings, rise time, total sleep time, and sleep efficiency.

Results: The usual bedtime was 9:00, with residents experiencing prolonged sleep latency ($M = 69.00$ minutes, $SD = 26.82$) and usual sleep onset time of 10:11 ($SD = 27.00$ minutes). There were few nightwakings ($M = .32$) of minimal duration ($M = 10.13$ minutes; $SD = 9.29$). Total sleep time averaged 483.27 minutes ($SD = 40.19$), with an average sleep efficiency of 80.5%. However, sleep efficiency increased to 93.97% if calculated from sleep onset time to their 7:00 scheduled wake time. The average rise time was 6:38 ($SD = 23.00$ minutes), however only 3 of the 16 residents woke before this scheduled wake time 75% or more of the time.

Conclusion: This study is the first to examine the sleep patterns of adolescents with autism living in a highly structured residential setting. Most striking was the extended sleep onset latency, however normal sleep efficiency and minimal sleep disruption was observed once asleep. A more age-appropriate bedtime may lead to even better sleep. Results suggest that a structured setting may be an appropriate non-pharmacological approach to sleep issues in this population.

0978

NOCTURNAL EATING: PREVALENCE, FEATURES AND NIGHT SLEEP AMONG BINGE EATING DISORDER AND BULIMIA NERVOSA PATIENTS IN ISRAEL

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Introduction: Nocturnal Eating Syndrome (NES) is a rare clinical syndrome comprising both eating and sleep disorders. BED (Binge Eating Disorder) and BN (Bulimia Nervosa) have similar clinical features characterised by uncontrolled binge eating episodes. Nocturnal Eating Syndrome (NES) among BED and BN patients entails binge eating episodes after sleep onset. The aim of this study was to examine differences between BN and BED patients with respect to nocturnal sleep-related eating disorders.

Methods: Twelve BED and ten BN patients referred to the Eating Disorders Clinic of Rambam Medical Center suffering from NES participated in the study. Twenty BED and twenty-nine BN age and BMI matched patients with no NES participated as controls. Patients were monitored by the actigraph (Mini-Act, AMA-32, and AMI, Ardsley, NY) for one week and completed the Mini-Sleep Questionnaire (MSQ) in addition to providing demographic and clinical data.

Results: Objective sleep monitoring presented no significant differences between BN and BED despite differences in demographic and clinical data. Both groups had low sleep efficiency relative to their respective control groups. The mean number of night eating episodes, as monitored by actigraph, was 3.9 ± 2.2 for the BED group and 3.0 ± 2.2 for the BN group. The MSQ revealed severe subjective sleep disorders, and clinical data revealed that traumatic life events as well as levels of psychiatric comorbidity and sexual abuse coincided closely with NES onset.

Conclusion: Approximately 5% of the outpatients presenting annually in the clinic were self-identified as having problems with night eating. The results may indicate that NES in BED and BN cluster together as a discriminate subgroup of eating disorders. It may be considered as a new diagnostic subgroup of the DSM-IV, namely, Nocturnal Binge Eating Disorder.

0979

BASILINE POLYSOMNOGRAPHY AND MOOD RESPONSE TO SLEEP DEPRIVATION IN MINOR DEPRESSION: PRELIMINARY RESULTS

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Introduction: We compared baseline polysomnography (PSG) and mood response to sleep deprivation (SD) in Minor Depression (Min D) with major depression (MD) patients and normal controls (NC). We hypothesized that Min D patients would exhibit PSG features similar to Major Depression but less pronounced.

Methods: 4 MD patients, 4 Min D patients, and 2 NCs (all unmedicated) spent 3 nights (adaptation, baseline, and total SD (TSD)) in the sleep laboratory with standard montage and Rechtschaffen & Kales scoring. They completed the 17-item Hamilton Depression Rating Scale (HDRS17) at standard times during the baseline and sleep deprived days. Mood response was measured by percent decrease in the HDRS17 (omitting sleep and weight loss items) (HDRS17Mod) between baseline and the minimum after TSD.

Results: MD patients' (baseline HDRS17 13.5 ± 3.5) HDRS17Mod decreased from 8.8 ± 5.2 (baseline) to 6.3 ± 4.1 (TSD). Min D patients' (baseline HDRS17 6.5 ± 1.7) HDRS17Mod increased from 3.5 ± 2.4 (baseline) to 4.3 ± 2.6 (TSD). Min D patients were intermediate between MD patients and NC's on total sleep time (401.0 ± 57.1 vs. 349.0 ± 127.4 vs. 416.3 ± 4.6 minutes), sleep efficiency (81.5 ± 8.6 vs. 69.2 ± 22.5 vs.

87.0 ± 11.9 percent), REM latency (61.9 ± 23.5 vs. 49.8 ± 26.8 vs. 65.5 ± 0.0 minutes), and REM minutes (99.3 ± 35.7 vs. 88.4 ± 43.3 vs. 114.0 ± 22.6). Min D patients had less slow wave sleep minutes (25.4 ± 33.7) than MD patients (32.1 ± 19.2) or NC's (49.5 ± 28.3).

Conclusion: Reasons the Min D group's mood did not improve with TSD are not clear. Further subject accrual will be necessary to see if this pattern persists and will help clarify possible baseline PSG differences in Min D responders vs. nonresponders. This is the first study of baseline PSG and mood response to TSD in a group consisting entirely of Min D patients.

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0980

COGNITIVE BEHAVIORAL SOCIAL RHYTHM THERAPY FOR VETERANS WITH COMORBID PTSD AND DEPRESSION: INITIAL RESULTS FROM A PILOT STUDY

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Introduction: Sleep problems are highly prevalent in both Posttraumatic Stress Disorder (PTSD) and Major Depressive Disorder (MDD). Patients with PTSD, MDD and insomnia have more severe psychopathology and worse treatment outcomes than patients with only one of these disorders. Although cognitive behavioral interventions are acceptable, tolerable, and highly effective treatments for each of these problems, few studies to our knowledge have used an integrative approach targeting both sleep and psychiatric symptoms. The purpose of this study was to develop and test a new cognitive behavioral group therapy designed specifically to target mood and sleep symptoms in veterans with these disorders.

Methods: Cognitive Behavioral Social Rhythm Therapy (CBSRT) is a 12-week, 2 hour group therapy designed to improve sleep and increase the frequency and regularity of daily habitual behaviors. To date, 7 male Vietnam veterans with PTSD and MDD have completed this ongoing pilot program. Pre- to post-treatment symptom scores were measured via the Daily Sleep Diary (DSD), Pittsburgh Sleep Quality Index (PSQI), PTSD Checklist (PCL), and Beck Depression Inventory (BDI).

Results: Mixed linear modeling analyses indicated improvements in sleep (number of awakenings, $\gamma_{10} = -.08$, SE = .03, $p = .003$, global PSQI scores, $\gamma_{10} = -.89$, SE = .42, $p = .08$), depression (global BDI scores, $\gamma_{10} = -.70$, SE = .25, $p = .03$; M scores reduced 10 points), and PTSD symptoms, although this change was not statistically significant due to high variability between patients (global PCL scores, $\gamma_{10} = -.99$, SE = .61, $p = .16$; M scores reduced 13 points). Examination of individual scores indicated that 6 of 7 patients experienced improvement on both sleep and depression scores. Moreover, the majority of patients experienced a reliable clinically significant change on subjective sleep or depression scores.

Conclusion: Preliminary results support the effectiveness of CBSRT, especially given the tendency for Vietnam veterans to over-report symptoms on self-report measures. Overall, these preliminary data demonstrate that CBSRT is both feasible to administer and effective for sleep and depression symptoms in veterans with PTSD, MDD, and sleep problems. The logical next step is to test the efficacy of CBSRT via a randomized controlled trial.

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0981

SLEEP DISTURBANCES AMONG INDIVIDUALS CONSULTING EMERGENCY DEPARTMENTS FOR NONCARDIAC CHEST PAIN AND HAVING PANIC DISORDER: PRELIMINARY RESULTS

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Introduction: Panic disorder (PD) is encountered in 20 to 30% of patients consulting emergency departments (ED) with noncardiac chest pain. In psychiatric settings, around two thirds of PD patients report sleep disturbances, and more than half has experienced nocturnal panic attacks (NPA). This study explored the nature and magnitude of sleep problems among PD patients consulting ED with noncardiac chest pain.

Methods: We present the data from 15 consecutive patients (8 women; mean age 37.20, SD = 11.34) consulting an ED 1) with noncardiac chest pain; 2) diagnosed as having PD by a research assistant; and 3) accepting to participate in a PD treatment study. Patients were assessed with the ADIS-IV, Insomnia Interview Schedule, and self-report questionnaires (Insomnia Severity Index, ISI; Dysfunctional Beliefs and Attitudes about Sleep Scale, DBAS). Sleep diaries were completed during one week.

Results: Data drawn from the Insomnia Interview Schedule indicated that, out of 13, 3 participants met criteria for Insomnia without experiencing NPA, 3 had NPA without reporting Insomnia, and 4 had both Insomnia and NPA. These results were confirmed by sleep diaries. Mean ISI scores were 3.00 for PD patients without Insomnia or NPA; 11.50 for PD patients with Insomnia; 8.00 for PD patients with NPA; and 17.00 for PD patients with both Insomnia and NPA. Mean DBAS scores were 0.83 for PD patients without Insomnia or NPA; 3.90 for PD patients with Insomnia; 3.90 for PD patients with NPA; and 5.43 for PD patients with both Insomnia and NPA.

Conclusion: The majority (77%) of patients consulting ED for noncardiac chest pain and having PD displayed sleep disturbances. There may be two distinct forms of sleep disturbances in this population, namely NPA and comorbid Insomnia. Data are currently being collected to increase sample size and test these hypotheses statistically.

0982

IMPACT OF SLEEP DISTURBANCE ON PTSD SYMPTOMS AND PERCEIVED HEALTH

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Introduction: More than two thirds of individuals with Posttraumatic Stress Disorder (PTSD) report significant sleep difficulties. This study aimed to assess the influence of sleep disturbances on PTSD symptom severity and perceived health. A second goal was to explore clinical correlates of sleep disturbances in PTSD.

Methods: Ninety-two volunteer treatment-seeking adults with PTSD were administered a Structured Clinical Interview for DSM-IV and a series of questionnaire assessing PTSD symptom severity, perceived health, sleep, and alcohol use. To assess the impact of sleep difficulties on PTSD symptom severity, perceived physical health and perceived mental health, three sets of hierarchical multiple regression analyses were performed.

Results: Sleep quality had an impact on PTSD severity, still accounting for 10% of the variance associated to PTSD symptoms after the effect of other potential confounding variables (sociodemographic data, trauma-related characteristics, psychiatric comorbidities and alcohol and medication use) was statistically accounted for. Sleep explained a significant 5% of the variance associated with perceived mental health, but did not account for a significant portion of the variance associated with perceived physical health. More severe sleep difficulties were ob-

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served among individuals suffering from both comorbid Major Depression Disorder and one or more comorbid Anxiety Disorder in addition to PTSD, and among those using psychotropic medication. Gender, age, time interval since trauma, trauma type and alcohol use had no incidence on sleep quality.

Conclusion: Sleep appears to have a unique contribution in accounting for the severity of PTSD symptoms. Sleep also impacts how individuals with PTSD perceive their own mental health. Most individuals with PTSD present significant sleep difficulties regardless of their clinical presentation. Knowing the specific features of sleep in PTSD, as well as assessing the need to address sleep problems in PTSD treatment will help refine interventions with individuals suffering from this distressing disorder.

0983

THE RELATIONSHIP BETWEEN POOR SLEEP QUALITY AND PPMD RECURRENCE IS NOT MEDIATED BY IL-6

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Introduction: Postpartum major depression (PPMD) is a serious health concern affecting approximately 14.5% of women. No risk factor has proven superior at predicting who will develop PPMD. We recently found that poor sleep quality, as defined by the Pittsburgh Sleep Quality Index (PSQI), was a better predictor of recurrence after 4 weeks postpartum than traditionally assessed risk factors, including depressive symptomatology. One mechanistic pathway that may mediate this relationship is inflammation, as evidence indicates that depression is linked to dysregulation of inflammatory cytokines. We evaluated the mediating role of IL-6, a pro-inflammatory cytokine, in the relationship between sleep quality in late pregnancy and PPMD recurrence.

Methods: Participants were pregnant women (N = 33, 31 ± 4 yrs) with past histories of PPMD but not depressed at enrollment. The PSQI was completed at week 36 gestation and the 21-item Hamilton Rating Scale for Depression (HRSD-21) at week 4 postpartum. Circulating IL-6 levels were assayed from blood drawn at week 2, 3 or 4 postpartum. Recurrence was determined by two consecutive HRSD scores > 15 and clinician interview.

Results: Eleven (33.3%) women recurred within 6 months postpartum. No relationship was found between PSQI scores and IL-6 levels or between IL-6 levels and PPMD recurrence (p 's > .20). Poor sleep quality in late pregnancy, but neither HRSD scores in late pregnancy nor IL6 at week 4 postpartum, was related to a recurrence of PPMD.

Conclusion: The current relationship between poor sleep quality and PPMD recurrence is not mediated by IL-6. Although these findings support previous reports that poor sleep quality is a prodrome for recurrent depression (Perlis et al., 1997), the biological mechanism mediating this relationship remains unclear. Further exploration of the degree to which cytokine dysregulation is involved in this relationship and the pathophysiology of PPMD is warranted.

0984

IMPROVED INSOMNIA SYMPTOMS AND DAILY FUNCTIONING IN PATIENTS WITH COMORBID MAJOR DEPRESSIVE DISORDER AND INSOMNIA FOLLOWING ZOLPIDEM EXTENDED-RELEASE 12.5MG AND ESCITALOPRAM CO-TREATMENT

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Introduction: This study evaluated the effect of zolpidem extended-release (Ambien CR®), with concurrent escitalopram therapy, on sleep and daytime functioning in patients with comorbid insomnia and major depressive disorder (MDD).

Methods: Multicenter, double-blind, parallel-group, randomized, placebo-controlled trial in adults (n=385, age 21-64) with comorbid insomnia and MDD. Patients received escitalopram 10mg/day (open-label) and either nightly zolpidem extended-release 12.5mg or placebo. After 8 weeks of treatment (Phase 1), depression responders (≥50% HAM-D17 reduction) entered 16 additional treatment weeks (Phase 2). Daily morning questionnaires for sleep and next-day functioning were evaluated bi-weekly (Phase 1) and every 4th week (Phase 2). Safety was assessed by AEs and evidence for rebound insomnia.

Results: 119/193 and 67/96 zolpidem extended-release/escitalopram, and 125/192 and 60/95 placebo/escitalopram patients completed Phase 1 and Phase 2 respectively. Phase 1 sleep measures improved from baseline for zolpidem extended-release/escitalopram patients versus placebo/escitalopram for total sleep time (TST; Wk. 8 primary endpoint: +101.4 vs +64.0 min; $P < 0.0001$), wake time after sleep onset (WASO), nocturnal awakenings (NAW) and sleep latency (SL; $P \leq 0.0003$ each measure/timepoint). Zolpidem extended-release/escitalopram also improved next-day morning energy, morning concentration, sleep quality and sleep impact on daily activities ($P \leq 0.0092$). In Phase 2, improvements with zolpidem extended-release/escitalopram group occurred for TST (Wk. 12, 16); NAW (Wk. 12-24), WASO (Wk. 16, 20), sleep quality (Wk. 12-24), morning energy (Wk. 12-24) and sleep impact on daily activities (Wk. 12-24; $P < 0.05$ each measure/timepoint cited), but not for SL and morning concentration. Zolpidem extended-release did not significantly augment depressive symptoms compared with placebo. No evidence of rebound insomnia. Most frequent AEs (>10%) in zolpidem extended-release/escitalopram vs placebo/escitalopram groups were headache (14.1%/17.9%) and nausea (10.9%/8.4%).

Conclusion: Zolpidem extended-release and escitalopram co-therapy was a well tolerated and effective treatment of multiple insomnia symptoms in patients with comorbid insomnia and MDD, over 24 weeks.

Support (optional): Funding for this study was provided by sanofi-aventis

0985

ZOLPIDEM EXTENDED-RELEASE 12.5 MG CO-ADMINISTERED WITH ESCITALOPRAM IMPROVES INSOMNIA SYMPTOMS AND NEXT-DAY FUNCTIONING IN GENERALIZED ANXIETY DISORDER COMORBID WITH CHRONIC INSOMNIA

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Introduction: To examine the effect of zolpidem extended-release 12.5mg (Ambien CR®), taken concomitantly with escitalopram on insomnia and next-day functioning in patients with chronic insomnia comorbid with generalized anxiety disorder (GAD).

Methods: 8-week, multicenter, double-blind, parallel-group, placebo-controlled trial; adults with comorbid insomnia and GAD (n=383, age 21-64) received nightly zolpidem extended-release 12.5mg or placebo; all patients received open-label escitalopram 10mg/day. Sleep and next-day functioning were assessed at Week 1 and every other week by daily morning questionnaires. The Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire (MGH-CPFQ; Week 4 and 8 only) was given. GAD symptoms were assessed with the Hamilton Rating Scale for Anxiety (HAM-A) and Beck Anxiety Inventory (BAI). AEs throughout and end-study rebound insomnia were assessed.

Results: 116/192 zolpidem extended-release/escitalopram and 126/191 placebo/escitalopram patients completed the study. Patients reported significant improvements from baseline with zolpidem extended-release/escitalopram treatment versus placebo/escitalopram, for total sleep time (primary endpoint), nocturnal awakenings, wake time after sleep onset and sleep latency (P<0.0001 for each measure/timepoint assessed). Compared with placebo/escitalopram, zolpidem extended-release/escitalopram treatment significantly improved from baseline in next-day morning energy, morning concentration, sleep impact on daily activities and sleep quality (P<0.0001 for each measure/timepoint assessed). On the MGH-CPFQ, the zolpidem extended-release/escitalopram group improved, versus placebo/escitalopram, on motivation/interest/enthusiasm (P<0.005; Week 4 only), wakefulness/alertness (P<0.02; Week 4 and 8), and energy (P<0.02; Week 4 and 8). No group differences occurred for improvements on attention, memory, word-finding and mental acuity scales. Zolpidem extended-release did not significantly augment the anxiolytic response measured by the HAM-A and BAI. Most frequent AEs: zolpidem extended-release /escitalopram vs placebo/escitalopram: nausea (21.5%/16.8%), dizziness (14.1%/6.8%), headache (12.6%/15.3%), fatigue (10.5%/5.3%), dry mouth (7.3%/10.5%). No rebound insomnia was observed upon discontinuation.

Conclusion: Zolpidem extended-release/escitalopram improved multiple measures of sleep and next-day functioning versus placebo/escitalopram and was well-tolerated in patients with comorbid insomnia and GAD.

Support (optional): Funding for this study was provided by sanofi-aventis.

0986

IMPROVED SLEEP IMPACT IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER TREATED WITH ZOLPIDEM TARTRATE EXTENDED-RELEASE IN COMBINATION WITH ESCITALOPRAM

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Introduction: Insomnia associated with Major Depressive Disorder (MDD) can further exacerbate the impact of the disease on the patient's day to day life. To evaluate the benefits of effective treatment, the Sleep Impact Scale (SIS) was included in a randomized clinical trial (RCT) of insomnia associated with MDD to evaluate the impact of zolpidem tartrate extended-release

Methods: Efficacy data of the SIS were collected alongside a RCT of escitalopram+placebo or escitalopram+zolpidem tartrate extended-release in adults with insomnia associated with MDD. Subjects were administered the SIS at baseline and every 4 weeks for 24 weeks. Phase I included all subjects to Week 8; Phase II included only Phase I subjects who responded to escitalopram. Change from baseline to each assessment was performed using ANCOVA with treatment, gender and baseline SIS domain score as covariates. Longitudinal analyses were performed using mixed-effects ANCOVA for repeated measures with SIS change from baseline scores as the dependent variable with fixed-effects of treatment, visit, treatment-by-visit interaction, gender and SIS domain at baseline. Subject was treated as a random effect. Analyses were performed separately for Phase I and Phase II for each SIS domain.

Results: 379 subjects were included in the modified intent-to-treat population. Change scores in Phase I were significant for all SIS domains at Week 4 and for all domains except Mental Fatigue at Week 8. The longitudinal analysis in Phase I found zolpidem tartrate extended-release was significantly superior on all domains. Change scores in Phase II were significant for all SIS domains at Week 24 except Mental Fatigue. The longitudinal analysis in Phase II found zolpidem tartrate extended-release was significantly superior on all SIS domains except Mental Fatigue.

Conclusion: The SIS was responsive to treatment effects in this clinical trial and able to demonstrate improvements in patient reported outcomes, favoring zolpidem tartrate extended-release.

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0987

THE EFFECT OF SUBSTANCE USE/ABUSE ON SLEEP-DISORDERED BREATHING AND CONTINUOUS POSITIVE AIRWAY PRESSURE COMPLIANCE

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Introduction: The exact rate of different substance use/abuse syndromes in Obstructive Sleep Apnea (OSA) patients or the effect of these syndromes on Continuous Positive Airway Pressure (CPAP) compliance are unknown. Our goals are to explore the relationships between alcohol, nicotine and caffeine use/abuse and both OSA severity, and CPAP acceptance and compliance.

Methods: A retrospective review of medical records was conducted for all subjects who had a diagnosis of OSA and followed with available compliance card. The database was reviewed for subject's demographic data, the use/abuse of alcohol, nicotine and caffeine, and compliance card report. If patient was using substances, the degree of use was evaluated.

Category O—Sleep in Psychiatric Disorders

Results: Out of 600 charts reviewed, 228 were included in the final analysis. 79.2% of the patients reported no alcohol use/abuse and only 2.3% had been diagnosed with alcohol abuse disorder. 78.9% of participants reported no current nicotine use and 19.9% reported no caffeine use. None of the three substances were related with any of the OSA severity measures (AHI, Lowest Sao₂, or CPAP pressure needed). The CPAP compliance was lower (percent of days the device was used) in patients with alcohol abuse compared to patients who reported no alcohol abuse ($t = -2.034$, $df = 212$, $p = 0.043$). Similarly, for the caffeine users the percent of days the device was used was lower than for non-users ($t = 1.773$, $df = 212$, $p = 0.025$). Nicotine use/abuse was not related to any of the compliance measures.

Conclusion: Contrary to our expectation that nicotine use/abuse may affect lowest SaO₂, and caffeine use/abuse may be related to the severity of OSA, we found that alcohol, nicotine or caffeine use/abuse did not predict OSA severity. We found that alcohol and caffeine use/abuse predicted lower CPAP compliance. Larger studies are needed to confirm our findings.

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0988

SLEEP PATTERNS IN ADOLESCENTS WITH BIPOLAR DISORDER OR BORDERLINE PERSONALITY DISORDER

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Introduction: In bipolar disorder (BD) and borderline personality disorder (BPD), not only emotional instability is found but also sleep disorders. The aim of this research was to compare sleep patterns in adolescents with BD and BPD.

Methods: Seven adolescents with euthymic BD (2M; 5F; 16.02 (SD=0.6) years) and five with BPD (5F; 15.3 (SD=1.0) years) wore wrist actigraphy device and filled a sleep agenda for an average of nine days. All participants were under psychopharmacological treatments. Actigraphy data was computed using one-minute epochs and groups were compared using Mann-Whitney U-tests.

Results: Actigraphy results in BPD adolescents showed that during weekdays, compared to weekends, the active period was significantly longer ($p < .02$) and sleep was significantly shorter ($p < .05$), with a tendency for increased wake time between the final morning awakening and rise time. Such differences were not found in BD adolescents and group comparisons yielded no significant differences. On the other hand, weekday agendas showed significantly longer sleep onset latencies in BD compared to BPD ($p < .05$).

Conclusion: It appears that weekdays are more sensitive than weekends to indicate differences in sleep patterns between adolescents with BPD and euthymic BD. When both groups are compared to each other, actigraphy reveals a sleep maintenance problem in adolescents with BPD while agendas filled by euthymic BD adolescents seem to demonstrate longer sleep onset latencies. Further research would determine whether these differences are due to affective symptoms, poor sleep hygiene or a circadian rhythm disorder. We are continuously enrolling new patients in the protocol in order to replicate the present results with larger groups.

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0989

TWINS SLEEP MORE ALIKE ON NIGHT 2 THAN ON NIGHT 1

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Introduction: Ten male monozygotic twin pairs (mean age 54.8, SD 1.4) discordant for Vietnam combat exposure and lifetime posttraumatic stress disorder (PTSD) were studied for two nights in the laboratory. Quantitative analyses of polysomnographic (PSG) data were performed in addition to manual sleep staging. As quantitative analyses have perfect intra-rater reliability, this design enabled preliminary analysis of cross-twin versus within-twin correlations of PSG indices in a small sample.

Methods: Quantitative polysomnographic measures were numbers of vertical and horizontal eye movements during REM sleep, slow wave sleep delta power, stage 2 sigma power, non-REM alpha power, REM beta power, NREM heart rate, respiratory sinus arrhythmia, and respiratory frequency, and numbers and amplitudes of peri-orbital integrated potentials during REM. There was no human intervention in these analyses except in the manual classification of sleep epochs as belonging to one of the conventional sleep stages. As the values extracted were medians over all similarly classified epochs, they were insulated from all but large aggregate "errors" in manual staging.

Results: Quantitative PSG values obtained on night 1 were highly correlated with those obtained on night 2 (mean $r \sim 0.79$, $p < 0.01$). Similar correlations were calculated across monozygotic twins (mean $r \sim 0.81$, $p < 0.01$). However, for 9 of 11 quantitative variables, the cross-twin correlations were higher on night 2 than on night 1. The probability of this outcome is $p = 0.033$ (binomial test or one-sample chi-square.) These results were not likely due to elevated levels of artifact on night 1, as numbers of epochs scored artifactual, movement, or wake did not differ over nights.

Conclusion: Though preliminary due to the small size of the sample, this result suggests that PSG data obtained from an adaptation night and a post-adaptation night are differentially reflective of environmental and heritable influences.

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0990

USE OF AND ATTITUDES ABOUT SLEEP MEDICATIONS IN A TERTIARY SLEEP CLINIC

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Introduction: The aim of this study was to evaluate use of medications for sleep and the prevalence of psychological dependence on these medications in a sample of insomnia patients attending a group Cognitive Behavioral Therapy for Insomnia (CBTI).

Methods: The sample consisted of 123 patients diagnosed with psychophysiologic insomnia, 57% female and a mean age of 51 years (SD=14), who completed a baseline questionnaire on medication use and consented to participate in this study. The questionnaire also asked about attitudes concerning the use of these medications.

Results: 83% of participants were taking a medication for sleep. Of those, 14% took a benzodiazepine, 80% a non-benzodiazepine (88% took either benzodiazepines or non-benzodiazepines), 15% took an antidepressant or antipsychotic medication (for sleep), 11% took over the counter medications/herbs, and 13% took medications from another class. Among medication users 22% were taking medications from more

than one class. Among medication users, 30% reported that the medication was “not helping as much as before”, 51% worried they would not be able to sleep if they did not take medications, 57% worried that they had “become too dependent on the medication,” and 46% tried to stop taking medications and failed. Compared with those who took one medication for sleep, those who took multiple medications were significantly more likely to believe the medications were not helping ($p=.001$), to worry that they will not sleep without medication ($p=.002$), and to worry that they “have become too dependent” ($p=.006$).

Conclusion: The majority of insomnia patients participating in a group CBT take hypnotics, and approximately 25% take medications from multiple classes. Approximately 50% evidence psychological dependence, which is significantly greater among those who take medications from multiple classes. The construct of psychological dependence on medication taken for sleep is understudied and deserves future attention.

0991

SUBJECTIVE BUT NOT OBJECTIVE MEASURES OF SLEEP ARE ASSOCIATED WITH INCREASED DEPRESSIVE SYMPTOMS IN OLDER ADULTS

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Introduction: Obstructive Sleep Apnea Syndrome (OSAS) is characterized by sleep-related decreases (hypopneas) or pauses (apneas) in respiration. Recent evidence suggests OSAS is associated with an increased risk of depression (Peppard et al., 2006). OSAS is very common among the general population, but its prevalence drastically increases to 45%-62% in older adults. Depressive symptomatology also increase with age. We investigated whether increased severity of OSA was associated with higher levels of depressive symptoms in community-dwelling, older adults.

Methods: A total of 110 older adults participated, aged 55 to 90 years, mean age 70.90 years. All were assessed with in-home full ambulatory polysomnography. We employed the Apnea-Hypopnea Index (AHI), i.e. the average number of apneas and hypopneas per hour of total sleep time (TST), as our measure of OSA severity. We assessed mean oxygen saturation during TST, the minimum SaO₂ level, and the time spent below a threshold of 90% of oxygen saturation. Self-reported daytime sleepiness and sleep quality were measured using the Epworth Sleepiness Scale and the Pittsburgh Sleep Quality Index (PSQI). All participants were assessed with the Geriatric Depression Scale (GDS).

Results: No significant associations were observed between the GDS and severity of OSAS or any measure of hypoxia, even after controlling for age and BMI. However, significantly poorer sleep quality, as measured by the PSQI was significantly associated with increased depressive symptomatology ($P<.001$).

Conclusion: GDS scores were mild in this sample, and the lack of any relationship with OSAS may have reflected the fact that very few subjects met diagnostic criteria for depression. The positive association of the PSQI with depressive symptoms may simply reflect the fact that subjective sleep problems are a symptom of depression. Alternatively, poor sleep quality, but not OSAS per se, may be more important in leading to increased depressive symptoms in older adults.

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0992

SLEEP PROBLEMS AND DEPRESSION IN A PRIMARY CARE UNIT

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Introduction: The relationship between sleep and depression is already known. It is not clear yet, the percentage of patients that goes to the

primary care attention with physical complaints but also has sleep problems and depression symptoms.

Methods: To check sleep problems frequency in the population of one primary care system, we evaluated during ten days all patients that went to the primary care unit in Curitiba, Brazil, with physical complaints. They completed the following questionnaires: CES-D, and a sleep questionnaire. We divided the patients in two groups, one with score at CES-D above 15 ($G>15$), and the other below 15 ($G<15$).

Results: A total of 214 patients answer the questionnaires. The group above 15 had a total of 123 patients with median age of 40,7 years old (15-65), 28 men and 95 women. The group below 15 had a total of 91 patients with median age of 37,5 years old (18-65), 28 men and 63 women. When we compared the two groups, we found in the group $G>15$ more physical (13,11 and 6,47 respectively) and sleep complaints (38,42 and 25,58 respectively) then in the group $G<15$.

Conclusion: We concluded that the physician should always ask patients about sleep problems and symptoms of depression at the primary care attention because the frequency of these problems is very high in the population that goes to primary care units with physical complaints.

0993

SLEEP RELATED COGNITION AND BEHAVIOR OF CHRONIC INSOMNIAC PATIENTS COMORBID WITH DEPRESSION OR ANXIETY

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Introduction: Depression, anxiety and insomnia share high comorbidity. Previous researches focus on sleep related cognition and behavior in primary insomnia patients. However, there are fewer researches focused on cognition and behavior in insomnia patients' comorbid with depression and anxiety. Sleep related cognition and behavior are the important perpetuating factors in chronic insomnia. This study aim to clarify comorbid insomnia patients' sleep related cognition and behavior.

Methods: This is a cross-sectional study. Total 271 subjects were divided into five subgroups which are Primary Insomnia group (PI, $n=66$), Anxiety Insomnia group (AI, $n=15$), Depression Insomnia group (DI= 36), Anxiety and Depression with Insomnia group (ADI= 57), and Good Sleeper (GS= 97). The Insomnia Severity Index (ISI), Dysfunctional Beliefs and Attitudes about Sleep Questionnaire (DBAS) and Sleep Hygiene Practice Scale (SHPS) were applied to compare the differences in sleep related cognition and behavior among each subgroups of insomnia patients.

Results: There is no significant difference of insomnia severity between primary and comorbid insomnia patients. However, the pathological level of sleep related cognition and behavior are significantly higher in comorbid insomnia patients. In DBAS, AI and DI are significant higher than GS ($p=0.00$), ADI is significant higher than PI and GS ($p=0.00$). In SHPS, DI is significant higher than GS ($p=0.00$), ADI is significant higher than PI and GS ($p=0.00$).

Conclusion: Comorbid insomnia patients shared similar insomnia severity with primary insomnia patients; therefore, the insomnia symptoms of comorbid insomnia patients deserved more clinical attentions. Besides, the sleep related cognition and behavior of comorbid insomnia patients have pathological specificity. Strategies designed to correct dysfunctional sleep related cognition and behavior may be included in the intervention of comorbid insomnia patients to prevent the further consequences.

Support (optional): Department of Health, Executive Yuan, ROC

0994

THE EPWORTH SLEEPINESS SCALE: SELF-ADMINISTRATION VS. ADMINISTRATION BY THE PHYSICIAN, AND VALIDATION OF A FRENCH VERSION

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Introduction: The Epworth sleepiness scale (ESS) is often used to measure sleepiness in patients with obstructive sleep apnea (OSA) and others. Questionnaires are usually self-administered, but can be obtained by questioning by the physician. We set out to ascertain whether those 2 methods of administering the ESS are equivalent, and also to validate a French version of this widely used scale.

Methods: 188 consecutive patients presenting to the sleep clinic at a tertiary care center answered a questionnaire containing the ESS. During the medical interview on the same day, one of 3 respirologists specialised in sleep medicine, unaware of the result, filled out a second questionnaire with the patient. Also, a prior ESS was available in the chart of 124 OSA patients and was compared to the current results.

Results: For all subjects, the ESS score obtained by the physician was inferior to that of the self-administered version (9.4 ± 5.9 vs. 8.5 ± 5.8 ; $p < 0.0001$ (paired t test)). The intraclass correlation (ICC) was 0.835. In OSA patients, the ESS score decreased with treatment by CPAP (12.4 ± 6.8 to 7.6 ± 5.0 , difference 4.8 ± 5.6 ; $p < 0.0001$; $n = 64$). For patients who remained untreated between the 2 evaluations (test-retest), the average score was unchanged (10.3 ± 6.0 to 10.8 ± 6.5 ; $p = 0.35$; $n = 56$) after a median of 7 months, with $ICC = 0.847$. The correlation between ESS and AHI in OSA patients was $r^2 = 0.08$ ($p = 0.01$).

Conclusion: The French version of the ESS has good reproducibility in sleep clinic patients, and responds well to treatment in OSA patients. It correlates poorly with the AHI, similar to the English one. However, although there is a strong correlation between the auto-questionnaire and the physician-administered test, the systematic underscoring by physicians may be of importance in the research setting.

0995

RACIAL DIFFERENCES IN THE EPWORTH SCORE

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Introduction: African-Americans have been reported to be sleepier than Caucasians as assessed by the Epworth Sleepiness Scale (ESS) but the reason for this difference is unclear. We sought to assess which components of the ESS vary by race.

Methods: Responses to the ESS were assessed in 336 consecutive patients referred to a hospital-based sleep clinic and laboratory. Analyses were restricted to those reporting either Caucasian or African-American race. All analyses were adjusted for age, gender, marital status, and level of education.

Results: After controlling for demographic differences, African-Americans had a significantly greater ESS score than Caucasians (11.3 vs. 9.8 , $p = 0.039$). African-Americans scored significantly higher on 4 out of the 8 ESS questions. After accounting for differences in total ESS score, only 2 questions remained significantly elevated in African-Americans: "How likely are you to doze while sitting and watching TV?" ($p = 0.007$) and "How likely are you to doze while sitting and talking to someone?" ($p = 0.002$). Controlling for total ESS score, African-Americans were 3.4 times more likely to report a moderate or high chance of dozing while watching TV ($p = 0.002$) and 6.5 times more likely to report a moderate or high chance of dozing while sitting and talking ($p = 0.008$).

Conclusion: The elevated ESS score among African-Americans is due primarily to increased scores on questions related to sleepiness while

watching TV or sitting and talking. Further research is needed to better understand the differential response to these questions.

Support (optional): NIH HL081385

0996

ARTIFICIAL NEURAL NETWORK SCORING OF HUMAN SLEEP-WAKE STAGES COMBINING SHORT-EPOCH FEATURE EXTRACTION AND POST-PROCESSING INFERENCE RULES

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Introduction: The use of learning machines in the automatic analysis of human sleep-wake stages has shown performance near to inter-expert agreement. However, automatic classifiers are sensitive to small differences in the signal conditioning inherent to the existence of various polysomnographic collection systems and digital file formats. In addition, automatic analysis yields some incoherent results and doesn't always provide the requested flexibility in time resolution, which may vary between countries and species.

Methods: Using candidate features selected for their relative independence to biosignal collection parameters, we have developed a new method allowing 1) to train artificial neural network (ANN) from a database of short duration prototypic sleep/wake stage epochs and 2) to infer final scores at a variable duration using a set of implemented expert rules. The PRANA biosignal processing software was used to compute and extract a set of 16 different features from the electroencephalographic and electromyographic signals collected during 48 night recordings performed in 11 healthy adults using ambulatory recorders. Two independent human experts scored sleep/wake stages into 20-s epochs according to the conventional criteria. A database of 1 029 125 2-s epochs including the expert scores and the computer-extracted features was created. Five hundred and six 2-s epochs representative of each sleep/wake stage were manually selected by one expert from a subset of 7 individuals and further used for ANN learning.

Results: Simulation of the automatic scoring system using 20-s epochs showed a $30 \pm 10\%$ error rate as compared to consensual expert scores and a Cohen's kappa of 0.56 ± 0.16 . The global performance of the sleep-wake stage classification system ranges slightly below inter-scorer agreement ($82.8 \pm 3.3\%$).

Conclusion: This new classification method can perform automatic sleep/wake staging with various epoch durations. Improved performance can reasonably be expected by selecting a larger amount of learning epochs and by introducing additional rules mimicking expert decision-making strategies.

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0997

THE VALIDITY AND RELIABILITY OF WRIST ACTIMETRY ASSESSMENT OF SLEEP WITH AND WITHOUT SLEEP APNEA

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Introduction: It is unclear whether actimetry can be reliably used to measure sleep in severe obstructive sleep apnea (OSA) patients. We compared polysomnography (PSG) with actimetric assessment of sleep on an epoch-by-epoch basis in subjects with and without OSA. We hy-

pothesized that the validity and reliability of actimetry decreases with increased sleep apnea severity.

Methods: 21 subjects were recorded with simultaneous overnight standard PSG and actimetry (AW64, Mini-Mitter, Respironics).

Results: 10 subjects with $RDI < 10$ ($6.5 \pm 2.8/hr$) were classified as non-OSA subjects and 11 subjects with $RDI > 10$ ($42.0 \pm 27.3/hr$) were classified as OSA patients. The overall sensitivity and specificity for actimetry to identify sleep was 94.6% and 40.6%, respectively, with an overall mean sleep/wake simple agreement of 84.6% and Kappa of 0.38. There was no difference in agreement between non-OSA and OSA subjects (simple agreement: 83% vs. 86%, $p=0.43$; Kappa: 0.35 vs. 0.40, $p=0.64$). The Kappa agreement did not correlate with PSG arousal index ($r=-0.21$, $p=0.36$) but declined with reduced sleep efficiency ($r=0.66$, $p=0.001$). Although substantial differences were found in some individuals, there was no group difference (all $p > 0.40$) between actimetry and PSG in sleep latency, total sleep time and sleep efficiency in non-OSA and OSA subjects. However, while fragmentation index measured by actimetry tends to overestimate arousal index measured by PSG in non-OSA subjects (19.6 ± 11.9 vs. 14.8 ± 3.0 , $p=0.20$), fragmentation index significantly underestimated PSG arousal index in OSA patients (23.9 ± 17.8 vs. 33.1 ± 18.5 , $p=0.04$).

Conclusion: Contrary to prior reports, epoch-by-epoch comparison of sleep/wake scoring showed similar fair agreement between actimetry and PSG in subjects with or without OSA. The agreement does not correlate to respiratory arousals but significantly declines as the sleep efficiency is reduced. Fragmentation index by actimetry may underestimate arousals caused by respiratory events, and may offer misleading results in severe OSA patients.

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0998

ERRORS IN ESTIMATING TIDAL VOLUME FROM THE NASAL PRESSURE SIGNAL

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Introduction: Montserrat et al. have shown that the nasal pressure signal can be linearized to pneumotach flow via a square-root transform. Additionally, Thurnheer et al. have surmised that the asymmetrical flow between the nares induces errors in quantifying breath values over long periods of time. We hypothesized that we could quantify the degree of error the current nasal cannula pressure systems would produce in computing Tidal Volume (TV), during bilateral flow (BF) versus unilateral flow (UF) scenarios, as expected to occur during the Nasal Cycle. We compared the FloChannel (FC) with a specialized bifurcated nasal cannula, to a Braebon Pressure transducer (NP) with a common-plenum Pro-Tech cannula.

Methods: We created a bifurcated symmetrical apparatus to simulate the nasal pathway. We took each device with their respective cannula, securely placed in the simulated nose, and created sinusoidal breaths utilizing a computerized artificial lung (ASL-5000). All breaths were 0.5 liter TV. Five breaths at the following breaths per minute (BPM) were produced: 5, 10, 12, 15, 20, 25. Additionally, we reproduced the breaths with BF and UF. Prior to analysis, each signal was corrected via square-root transformation. Customized software was used to identify inspiration and expiration, and compute the area under the curve (TV). The resulting time points were visually inspected for accuracy. We took the average of all breaths during the BF scenario in each BPM group, and averaged among all BPM group averages, to compute a linear factor to ensure the relative volume of the BPM groups were set to 0.50 Liters. We then applied the same linear factor for each device to re-compute TV in the UF scenario.

Results: TV changed from 0.5001 (BF) to 0.5129 (UF) for the FC device, a 2.56% difference. The NP device changed from 0.5025 (BF) to 0.7112 (UF) for the NP device, a 41.53% difference.

Conclusion: With the traditional nasal cannula pressure system, we determined that a degree of error of approximately 40% for tidal volume is expected in a switch from BF to UF nasal flow, or similarly vice-versa. This error is due to the flow from each nare not being isolated and measured independently.

Support (optional): Chad Therapeutics

0999

IMPAIRED DAYTIME FUNCTIONING RELATED TO SLEEP: PSYCHOMETRIC PROPERTIES OF THE INSOMNIA IMPACT SCALE

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Introduction: For people with insomnia, the relation between sleep and daytime functioning is complex. Evidence exists that indicates perceived sleep related distress is an important factor in understanding this relation. The Insomnia Impact Scale (IIS) is a potentially valuable measure of perceived sleep related distress that has not received psychometric attention in its current form. The goal of this study was to examine the factor structure of the IIS and determine its reliability in a diverse sample.

Methods: Participants were recruited through a random dialing procedure as part of a large epidemiological study of sleep and daytime functioning. At least 50 men and 50 women in each age decade from 20 to 89 completed the IIS as part of this process. The IIS consists of 40 items rated from strongly agree to strongly disagree on a 5 point scale.

Results: Data from 400 participants was submitted to principle components analysis with oblique rotation. Examination of item mean and variance eliminated 12 poorly performing items. The solution ($\alpha = 0.90$) reduced total items to 21 and explained 48.3% total variance. Three components, labeled daytime functioning impairment, sleep preoccupation, and distorted beliefs, were correlated between 0.36 and 0.49 with α ranging from 0.70 to 0.88. Data from 372 participants was submitted to confirmatory factor analysis. Goodness of fit statistics indicated the data fit the proposed solution from the previous analysis, GFI = 0.94, RMSEA = 0.04, NFI = 0.97; $\alpha = 0.89$.

Conclusion: The analyses reduced the number of IIS items and determined strong reliability in a diverse sample. The IIS-R is a 21 item scale measuring sleep preoccupation, distorted beliefs, and impaired daytime functioning; important elements of perceived sleep related distress. The IIS-R fills a need for an assessment tool specifically measuring the extent an individual connects their daytime functioning deficits to their sleep pattern.

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VALIDATION STUDY OF AN ECG BASED SLEEP DIAGNOSTIC SYSTEM

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Introduction: Recent algorithms developed at the Medical Physics Department at Tel Aviv University enable determination of sleep/wake architecture, cardiorespiratory activity and autonomic tone from stan-

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standard ECG and pulse oximetry signals. In this study we defined levels of agreement between these ECG-derived values of sleep-wake architecture and cardiorespiratory parameters with those calculated from manually scored polysomnographic (PSG) recordings.

Methods: Polysomnographic recordings from 54 subjects were randomly selected from those obtained from a cohort of 254 subjects participating in a study of Chronic Fatigue Syndrome. All participants underwent standard PSG with all studies being scored manually by the same individual, according to Rechtschaffen & Kales criteria. The ECG and pulse oximetry signal were analyzed by the Hypnocore HC1000P to determine values for sleep time, sleep efficiency, % time awake, in NREM and REM sleep, and respiratory disturbance index (RDI).

Results: 53 of 54 PSG 's contained technically acceptable ECG and pulse oximetry signals. There was no significant (t test) difference between ECG and PSG derived values of total sleep time (396.5 ± 48.0 vs 387.9 ± 29.2 minutes), sleep efficiency ($88.7\% \pm 7.6\%$ vs $82.6\% \pm 4.3\%$), wake ($15.6\% \pm 9.4$ vs $15.6\% \pm 4.1$), NREM ($65.9\% \pm 7.8$ vs $67.2\% \pm 4.9$), and REM sleep ($18.6\% \pm 6.3$ vs $15.2\% \pm 4.8$). Comparisons between RDI values yielded a correlation coefficient of $R=0.96$, providing a positive predictive value (PPV) of 90.6% and a negative predictive value (NPV) of 95.2%. Further comparisons between the two methods revealed a kappa of 0.84 for a RDI cutoff at 5, with a PPV of 93.8%, NPV 100%; for a RDI cutoff at 15, the kappa was 0.95. Using the Bland and Altman technique the level of agreement (mean ± 1 SD) between ECG & oximetry based RDI and manually scored RDI was PSG's 4.1 ± 3.9 .

Conclusion: We assessed a novel algorithm that derives values of sleep/wake architecture, cardiorespiratory activity and autonomic tone from standard ECG and pulse oximetry signals. We found no difference between values of wakefulness, sleep, NREM, REM sleep and RDI calculated with this algorithm versus those derived from manually scored PSG recordings. We propose this unique algorithm will facilitate high throughput analysis of sleep/wake parameters and RDI that, when combined with clinical information, provides reliable and reproducible diagnosis of sleep disordered breathing as well as disorders of initiating and maintaining sleep.

Support (optional): Chronic Viral Diseases Branch, Coordinating Center for Infectious Diseases, Centers for Disease Control & Prevention, Atlanta, GA, USA

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ECG DERIVED RESPIRATION AS A VALID RESPIRATORY SIGNAL FOR DETECTION OF APNEA/HYPOPNEA EVENTS

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Introduction: Surface ECG is a robust, easy to acquire physiological signal. Many studies have used ECG derived parameters, mainly heart rate variability, as a measure of central autonomic control during sleep. Our objective is to demonstrate that additional variables derived from the ECG signal provide valuable information on respiration during sleep. The purpose of this study is to show that is as effective as any other measure of respiratory activity, in detecting apnea events.

Methods: ECG derived respiration (EDR) is extracted by measuring the effect of slight anatomical displacements (which accompany normal and abnormal the respiratory movements) on the morphology of the ECG complexes. This concept was introduced by Moody et al (1985). 128 whole night polysomographs, including SpO₂, abdomen and thorax effort signals, and oronasal airflow (thermistor), were analyzed using gold standard manual scoring and an automatic score based on EDR and SPO₂ signals.

Results: EDR was calculated and yielded a signal that resembles effort signal during normal and abnormal breathing. The linear correlation

between the results of manual score of apnea events and the automatic score was very good ($R=0.88$). The replacement of the EDR signal with any one of the recorded respiratory signals (thorax, abdominal movement and flow), in the automatic score, resulted in similar RDI results ($R=0.87$, $R=0.85$, $R=0.86$ respectively). The correlation between the total number of respiratory events automatically detected using EDR and SPO₂ and any respiratory signal (thorax, abdomen and flow) and SPO₂ ($R_2=84$, $R_2=91$, $R_2=85$ respectively). The breathing frequency calculated minute by minute for each signal, was identical (difference was below 1 breath per minute) for all signals for 90%, 89%, 90% of the time for abdomen, thorax, and flow respectively.

Conclusion: Respiration measured by means of thorax/abdomen effort or flow yield similar results to those obtained when EDR is used, concerning respiratory frequency, total respiratory events and RDI. The use of EDR is limited to patients with sinus rhythm. The use of EDR as an alternative respiratory signal is based on a signal with an excellent signal to noise ratio, may be more comfortable for the patient.

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COMPARISON OF SCORING OF PORTABLE PSG RECORDING - MANUAL VERSUS AUTOMATIC SCORING

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Introduction: Portable polysomnography (PSG) devices and corresponding software have been developed to meet the increasing need for sleep studies. The objective of this study is to compare the PSG results between automatic scoring by a software system and manual scoring by a certified PSG technologist.

Methods: After hospital ethics approval, preoperative patients over 18 years old were recruited. The patients were invited to PSG studies preoperatively at home, first and third night postoperatively at hospital with a portable PSG device (Embletta x100). All PSGs were set up by PSG technicians. The PSG recording was first automatically scored by Somnologia Studio 5.0 and then scored by a certified PSG technologist, who was blind to the results of the automatic scoring.

Results: A total of 101 PSG recordings from 51 patients were included in the study. The age was 62 ± 11 ; 22 males, 29 females; BMI 32 ± 6 kg/m² and the neck circumference was 37 ± 8 cm. Compared to manual scoring, the automatic scoring produced significantly lower apnea hypnea index (AHI) (8.6 ± 13 vs 24.8 ± 29 , $p<0.0001$) and oxygen desaturation index (ODI) (13.5 ± 20 vs 16.3 ± 22 , $p=0.0113$). The total apnea episodes and hypopnea episodes were also significantly under-scored, 27.9 ± 52 vs 45.4 ± 88 ($p<0.0001$) and 25.2 ± 43 vs 66.5 ± 89 ($p<0.001$) respectively. In terms of sleep architecture, automatic scoring presented a longer total sleep time (382 ± 129 vs 275 ± 110 min, $p<0.0001$), a shorter stage 1 sleep (2.4 ± 4 vs 4.1 ± 4 %, $p=0.0154$) and stage 2 sleep (27.2 ± 22 vs 48.7 ± 17 %, $p<0.0001$), and a longer stage 4 sleep (13.1 ± 8.7 vs 1.5 ± 3.6 %, $p<0.0001$).

Conclusion: Due to the under-detection of apnea and hypopnea episodes, and failure to recognize sleep-wake status and sleep stages accurately; the AHI and ODI were significantly under-scored in automatic scoring versus manual scoring.

1003

COUPLING OF RESPIRATION AND HEART BEAT DIFFERS BETWEEN SLEEP STAGES

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Introduction: Coupling between respiration and the heart rhythm at rest is known as respiratory sinus arrhythmia. Heart rate increases during inspiration and lowers during expiration. Independent of this modulation of heart rate, intrathoracic pressure changes during respiration cause periodic movements of the chest and this causes R peak amplitude changes in the ECG. This can be used to derive respiration from the ECG itself.

Methods: Cardiorespiratory polysomnography with a chest wall ECG and three channels for respiration (oronasal airflow, chest and abdominal movements) was obtained in 112 healthy subjects (SIESTA study). We derived an additional respiratory signal from the ECG using heart rate and the modulation of R wave amplitudes. The reliability of this trace was checked using cardiorespiratory polysomnography [1]. Then we calculate the synchronisation of the respiratory waveform and the heart beat by calculating the instantaneous phase shift using the Hilbert transformation.

Results: The reconstruction of breathing from the ECG was reliable in most subjects. Based on this we reconstructed the breathing patterns from the ECG without additional signals. In healthy subjects we found 3.8% of the time in non-REM with coupled respiration and heart beat and only 0.6% of the time spent in REM sleep. During wakefulness within the sleep recording we found 1.6% of the time with coupled respiration and heart beat. This amount of time decreases with increasing age and decreases with body mass index. There is no gender difference.

Conclusion: It is possible to derive respiration from a combination of R-R interval analysis and R peak amplitude variability. The varying synchronization between the heart beat and respiration changes with sleep stage and can give indications for the severity of sleep related breathing disorders because it relates to the cardiorespiratory regulation responsible for pathophysiology.

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ARE THE PITTSBURGH SLEEP QUALITY INDEX (PSQI) AND THE EPWORTH SLEEPINESS SCALE (ESS) RELATED? FINDINGS FROM A COMMUNITY SAMPLE

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Introduction: The PSQI and ESS are widely used self-report measures, but their relationship to each other and to other clinical and sleep measures have not been carefully studied. We examined these relationships in a representative adult sample.

Methods: Participants were recruited from a community-based cohort study of nontraditional risk factors for cardiovascular disease. The current sample (n=187; M=59.5±7.2 years) included men (n=99), women (n=88), African-Americans (n=77), and Caucasians (n=110). Participants completed self-report questionnaires; sleep diary and actigraphy (10 days); home PSG (two nights); ambulatory blood pressure monitoring (48 hours); and overnight urine collection. Pearson correlation and exploratory factor analysis (EFA) were used to examine PSQI-ESS

relationships. Sleep phenotypes were defined by PSQI/ESS categories. Differences between phenotypes were examined with MANOVA and ANCOVA.

Results: Mean PSQI score was 6.3±3.4 (50.8% with scores >5), and mean ESS was 8.2±3.9 (25.7% with scores >10). PSQI and ESS scores were significantly but weakly correlated (r=0.16, p=.025, 2.6% of variance explained). EFA on the seven PSQI component scores and eight ESS items resulted in seven factors; PSQI and ESS items loaded on different factors. Four phenotypes were identified by cross-tabulation of PSQI scores (<5=PSQI-; >5=PSQI+) and ESS scores (<10=ESS-; >10=ESS+). Women comprised a larger proportion of the PSQI+/ESS- phenotype. Phenotypes differed significantly on quantitative and qualitative sleep diary measures and self-report measures of psychological symptoms and stress. PSQI+ phenotypes generally had the worst scores, and the PSQI-/ESS- phenotype the best. Nocturnal diastolic blood pressure dipping was most abnormal in the PSQI-/ESS+ group. PSQI/ESS phenotypes were unrelated to actigraphy, PSG, or urinary catecholamine measures.

Conclusion: The PSQI and ESS measure different constructs, and have different patterns of association with demographic and self-report measures. Individuals can apparently distinguish sleep quality and daytime sleepiness, but what they report is different from what is measured with PSG or actigraphy.

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1005

CORRELATES OF PLMS VARIABILITY OVER MULTIPLE NIGHTS AND IMPACT UPON RLS DIAGNOSIS

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Introduction: Two-night variability of periodic leg movements (PLMs) in Restless Legs Syndrome (RLS) has been described previously. We examined variability over an extended number of nights and examined its clinical correlates.

Methods: Twenty RLS subjects (mean IRLSSG Rating Scale = 20.8, SD = 3.0) were monitored for 10-15 nights (mean = 13.7, SD = 1.9) using PAM-RL actigraphy. We calculated individual Coefficients of Variation (COVs, SD/mean (x 100)) and repeated measures ANOVA (with one repeated measure (time) and one individual difference factor (subject)). Percentage of nights for which PLMI ≥ 10/hr was calculated for each subject. We performed correlations between individual COVs and clinical features, including age, body mass index, Clinical Global Impression, IRLSSG Rating Scale, Epworth Sleepiness Scale and scales of Medical Outcomes Study SF-36 and Profile of Mood States. COVs by gender were compared with a two-group t-test.

Results: Mean PLMI difference between lowest and highest night for each case was 25.1/hr (range: 3.9 - 73.8). For each case the percentage of nights with PLMI ≥ 10.0 varied from 0 to 100 with a mean of 51.9 (SD = 34.4). Effect sizes for subjects (Eta2 = 0.140) were nearly five times those for nights (Eta2 = 0.027). PLMI of 10/hr was attained in 51.9% of single nights, 66.8% of night pairs, and 83.5% of five night recordings. Three subjects (15%) never reached a PLMI of 10/hr. Women had significantly higher COVs relative to men (64.2 vs 43.1, t = 2.16, p < 0.05).

Conclusion: Variability in PLMs within RLS subjects was substantial yet individuals' PLMI represented a quantitative trait. Five recording nights were sufficient for determination of PLMs status, which was positive in 85%. Higher variability was related to female gender.

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VALIDATION OF CHANGES IN FOREHEAD VENOUS PRESSURE AS A MEASURE OF RESPIRATORY EFFORT

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Introduction: Measurement of respiratory effort is important in differentiating central from obstructive breathing during sleep and distinguishing sleep disorder breathing (SDB) from normal changes in ventilation.

Methods: Thirteen patients underwent a laboratory-PSG which included an esophageal catheter and chest-wall and abdomen piezoelectric belts to measure respiratory effort. Respiratory effort by Forehead Venous Pressure (FVP) was derived from simultaneous recording that combined photoplethysmography and surface pressure of the reflectance SpO₂ sensor, and accelerometers. Only nasal pressure and esophageal signals were used to select 200 events with changes in airflow consistent with flow-limited SDB, obstructive apneas, ventilation change or central events (n=132,25,33,10, respective). Two scorers (S1,S2), blinded to the signal type, independently rated the four effort signals as superior, equivalent, inconclusive or inferior relative to the others in detecting effort changes consistent with the airflow event. RMANOVA was used to identify main and interactive effects and test for scorer/signal/event differences.

Results: Main effects were observed for rater (F=4.04)(S2 gave lower scores) and signal type (F=4.32), while interactions between scorer/signal (F=3.03), event/signals (F=2.96) and scorer/signal/events (F2.37) were noted. FVP trended superior to chest (p=0.11), inferior to esophageal (p=.16), with no apparent difference between FVP vs. chest+abdomen. Both scorers rated FVP superior twice as often as any of the others signals. S1 and S2 agreed FVP was inferior in only 6 cases (3% of all events). In a three way interaction between scorer, signal, and flow-limited SDB events, S1 rated esophageal superior with FVP second while S2 rated chest inferior. Both scorers found FVP superior in the small sample of central apnea events. Of the 22 events S2 rated FVP inferior, 11 were apneic events, with S1 in agreement in only four cases.

Conclusion: These findings suggest FVP provides an alternative to conventional respiratory belts in recognizing changes in respiratory effort associated with SDB.

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ACCURACY OF AUTOMATED SLEEP STAGING USING SIGNALS FROM A SINGLE FOREHEAD SITE

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Introduction: Portable devices have been increasingly used for the diagnosis of obstructive sleep apnea (OSA) but are limited by the inability to measure and stage sleep. This is a preliminary report on the accuracy of automated algorithm for staging sleep using a forehead portable recorder (ARES™ Unicorder).

Methods: Five healthy subjects and 15 OSA patients underwent concurrent overnight recording with PSG and ARES. The AASM scoring criteria were applied to the PSG recordings. Automated algorithms classified wake, non-REM and REM using a differential signal from two electrodes positioned approximately at Fp1 and Fp2, plus actigraphy. Epoch-by-epoch comparisons (n=14,755) were made to assess sensitivity and specificity by category; Kappa statistics were used to assess sig-

nificance. Differences in sleep latency (SL), total sleep time (TST) and sleep efficiency (SE) were tested by Wilcoxon signed rank test.

Results: The sensitivity/specificity across all subjects was Wake=0.74/0.86, non-REM=0.81/0.82, REM=0.75/0.95 with an overall agreement of 79% (Kappa=0.54). For those with an RDI <20(n=10), the results were Wake=0.79/0.88, non-REM=0.83/0.86, REM=0.74/0.95, overall agreement=0.81. For those with an RDI >20(n=10), the results were Wake=0.71/0.84, non-REM=0.78/0.78, REM=0.76/0.95, overall agreement=0.76. Sleep latency did not differ significantly between ARES and PSG (median=1.5min, range=-24 to+7 min, R=73, p=0.37), but ARES tended to underestimate TST (median=-16min, range=-112 to +37 min, R=40.5, p=0.016) and SE (median=-4.8%, range=-28 to+21%, R=42, p=0.018). The differences in TST and SE moderately increased with RDI but the relation was not statistically significant (TST: r=0.27, p=0.26; SE: r=0.37, p=0.17).

Conclusion: The feasibility of staging sleep using two forehead sensors that require no preparation in combination with actigraphy was established. These findings should be supported with a cross validation using an independent data set.

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SPECTROGRAPHIC CHARACTERISTICS OF SLEEP IN STABLE HEART FAILURE

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Introduction: Chronic heart failure (HF) is associated with sleep disordered breathing. However, standard scoring approaches may not fully capture the stability of sleep - a characteristic that may be associated with pathophysiologic and functional consequences. The electrocardiogram (ECG)-derived sleep spectrogram is a new technique for characterizing sleep stability that measures the coupling of two signals encoded within the continuous ECG - heart rate variability and ECG-derived respiration (related to the variation of R-wave amplitudes with respiration).

Methods: We retrospectively matched a sample of 156 chronic HF patients (age: 60.6 ± 16.6 yrs; gender: n = 55/35% female; LVEF: 33.3 ± 15.6%; NYHA Class III/IV: n = 70/44.9%; BMI: 30.9 ± 8.2) from structured HF management programs and matched them by age, BMI, gender and sleep apnea-hypopnea index (15.9 ± 17.8 vs.14.7 ± 11.8) to a sample of NHLBI Sleep Heart Health Study (SHHS) participants who did not have clinical heart disease. PSG variables were obtained for the HF and SHHS participants using ambulatory recordings for one night and scored using Rechtschaffen & Kales and AASM criteria. Sleep spectrograms were generated using the raw continuous ECG signals.

Results: HF patients had poorer sleep efficiency (80.6 ± 9.8 vs. 71.8 ± 15.7%, p < 0.001), more N1 and less N2, N3, and REM sleep than the comparison group (all p < 0.001), despite matching on AHI. High frequency coupling, the ECG-spectrographic biomarker of stable sleep state that is independent of conventional stages, was markedly reduced in HF patients, 42.7 ± 21.5 vs. 30 ± 20.7, p < 0.001. Low frequency coupling, the biomarker of unstable sleep state, was not significantly different (39.6 ± 18.2 vs. 42 ± 20.8, p = 0.21).

Conclusion: HF patients have more fragmented and less stable sleep than matched patients without heart disease. The ECG-derived sleep spectrogram offers a potentially unique, inexpensive and repeatable way to characterize and monitor sleep quality in HF patients.

Support (optional): NR008022

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VISUAL AND SEMI-AUTOMATIC SLEEP STAGE SCORING USING ONLY ELECTRO-OCULOGRAPHYVirkkala J^{1,2}, Velin R¹, Lapveteläinen N¹, Himanen S², Värri A³, Sallinen M¹, Härmä M¹, Hasan J¹¹Brain Work Research Center, Finnish Institute of Occupational Health, Helsinki, Finland, ²Department of Clinical Neurophysiology, Pirkanmaa Hospital District, Tampere, Finland, ³Institute of Signal Processing, Tampere University of Technology, Tampere, Finland

Introduction: We have recently demonstrated the possibility of automatic sleep stage scoring using only standard two-channel sleep electro-oculography (EOG). The method could be self-applicable with self-adhesive electrodes. Although substantial agreement with standard visual scoring was obtained, human supervision is still needed. In this study visual sleep scoring using only electro-oculography channels was compared to standard sleep scoring based on EEG, EOG and EMG. Also a semi-automatic method using only electro-oculography channels with automatic separation between S2 and SWS was studied.

Methods: Eleven sleep recordings (females, age 20-54 years) were visually scored four times by two experienced sleep technicians. Besides repeated standard visual sleep scoring, visual sleep scoring was conducted twice based on two electro-oculography channels only (EOG Right-M1, EOG Left-M1). This scoring with a reduced set of electrodes was done using standard criteria with reduced alpha, spindle and EMG activity visible on traces. In all analysis stages, S3 and S4 were combined to SWS.

Results: The intrarater agreements (Cohen's Kappa) between standard visual scoring and visual scoring using only electro-oculography were 87% (0.81) and 83% (0.76). With automatic separation between S2 and SWS, the obtained agreements were 85% (0.79) and 84% (0.77). Repeated interrater agreements were 91% (0.87) and 90% (0.86) for standard visual scoring and 85% (0.79) and 89% (0.84) for scoring using only electro-oculography. Intrarater agreements were 93% (0.90) and 91% (0.87) for standard visual scoring and 92% (0.89) and 89% (0.84) for scoring using only electro-oculography.

Conclusion: Agreement between standard visual scoring and visual scoring using only electro-oculography channels was high. If separation between S2 and SWS was done automatically (to reduce human work), the agreement was essentially the same. In conclusion, high accuracy of sleep stage estimation could be obtained using self applicable two-channel electro-oculography and at least part of the scoring can be automated without major effects on the results.

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A SINGLE CHANNEL WAKE-SLEEP DETECTION SYSTEMWang Y¹, Kaplan RF¹, Bootzin RR², Loparo KA¹¹Consolidated Research of Richmond, Inc., Euclid, OH, USA,²Department of Psychology, University of Arizona, Tuscon, AZ, USA

Introduction: A multi-year effort has been dedicated to the development of an automated wake-sleep detection system that uses a single differential-mastoid EEG channel. Previous abstracts reported on the use of the system in the treatment of insomnia. The present analysis focuses on the system's validity in discriminating wake from sleep.

Methods: The automated, single channel system determines sleep state, awake or asleep, every 30 seconds using high and low frequency EEG information in the time and frequency domains. 100 paid volunteers underwent an overnight laboratory PSG. One subject dropped out of the study and was excluded from analysis. PSG studies from the 99 remaining subjects (52F/47M, 18-60 years, median age 32.7) were independently scored by three or four certified polysomnographic (PSG) technologists whose results were combined into a single score file, called a virtual scorer.

Results: The results of a detailed comparison between the automated wake-sleep detection system and the virtual scorer were: The correlation for detecting wake epochs between the virtual scorer and the automated detection system was 0.993. 5.7% (sd=5.6%) of epochs scored as wake by the virtual scorer were scored as sleep by the automated detection system. The correlation for detecting sleep epochs between the virtual scorer and the automated detection system was 0.985. 3.2% (sd=3.2%) of epochs scored as sleep by the virtual scorer were scored as wake by the automated detection system.

Conclusion: The wake-sleep detection performance of the automated system appears to have promise for a number of application areas. The system is suitable for both off-line and real-time wake-sleep detection and may be used in a variety of in-home ambulatory applications.

1011

THE 20-ITEM PITTSBURGH INSOMNIA RATING SCALE (PIRS20) AND PITTSBURGH SLEEP QUALITY INDEX (PSQI) STUDIED AS A SINGLE SCALE

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Introduction: The PIRS20 is an insomnia severity scale derived from the original 65-item PIRS. It contains items concerning nighttime symptoms of insomnia, daytime consequences, and selected sleep quantity items. Its score range is from 0 to 60. Its relationship to the components of the PSQI has not been assessed. We combined the PIRS20 and PSQI to study their common factors and relative item characteristics.

Methods: Subjects who simultaneously completed the PIRS and PSQI in clinical trials numbered 260 (195 with insomnia, 64 controls; 155 females; 50±19 years) and ranged across a full spectrum of scores (PSQI:0-20; PIRS20:0-56). PIRS20 item responses were obtained from the original PIRS psychometrics study, and combined with PSQI component responses to form a scale. Principal components analysis with varimax rotation explored the factors of this combined scale. Item response theory (IRT) modeling using MULTILOG 7 estimated its item-level parameters.

Results: The first factor of the modeled scale explained 47% of total variance describing sleep quality. The second and third factors represented daytime impairment and sleep quantities such as sleep length (9% and 5% variance, respectively). In the IRT analysis, sleep quality items across both questionnaires provided the most item-level information for the subjects, especially the PIRS20 Sleep Satisfaction item and the PSQI Sleep Quality component. Items pertaining to daytime consequences of insomnia contained moderate item-level information. Sleep latency items provided less information. The PSQI Sleep Disturbance and Needs Meds to Sleep components provided little information.

Conclusion: The combined scale suggested 3 main factors related to insomnia across both questionnaires. Factor and IRT analyses both pointed to sleep quality as the key issue for patients. PSQI and PIRS items relating to daytime consequences and sleep quantity variables performed less robustly. For insomnia patients, selected PSQI components did not speak to their symptoms.

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VIGILANCE EVALUATION WITH THE OXFORD SLEEP RESISTANCE TEST IN APNEIC PATIENTS

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Introduction: Vigilance evaluation in the apneic patient may be difficult but remains essential in some situations. The maintenance wakefulness test (MWT), which is the usual test used to quantify vigilance, necessitates continuous recording of an electroencephalogram (EEG)

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to determine sleep onset latency. The OSLER test (Oxford SLEEp Resistance) is a simplified version of the MWT which does not require recording of an EEG. The goal of this study was to compare the OSLER test to a simultaneous EEG recording using different sleep onset scoring criterias in apneic patients.

Methods: For 37 apneic subjects, most of which were under treatment, the sleep onset latency was determined with the OSLER test and with a simultaneous EEG. Three scoring techniques to determine sleep onset were used: (a) usual scoring technique: three 30-s epochs of stage one non-rapid eye movement sleep (non-REM), or a single 30-s epoch of any other sleep stage (b) one epoch of sleep (c) 6 seconds of sleep.

Results: The mean sleep onset latency for the three scoring techniques was, in the same order, 34.7, 30.8 and 27.2 minutes while it was 28.9 minutes for the OSLER test. If the definition of an abnormal OSLER test was to be set at below 26 minutes the sensitivity of the test would be 100% and its specificity 78%. The first two sessions were sufficient to preserve the same sensitivity and a comparable specificity when compared to an EEG scored by the usual criterias for a MWT.

Conclusion: The OSLER test is a good test to detect pathologic sleepiness in apneic patients using the usual MWT scoring technique. Two sessions in morning give results that are comparable to four sessions.

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DIFFERENCES IN SWAI SUBSCALE SCORES BY ADHERENCE TO CPAP

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Introduction: This study assessed changes in Sleep-Wake Activity Inventory (SWAI) subscale scores with varying levels of adherence to CPAP among persons with obstructive sleep apnea (OSA).

Methods: This was a prospective study assessing CPAP utilization at one month after treatment implementation. Participants completed the SWAI at baseline, followed by diagnostic and titration polysomnography to confirm clinical suspicion of OSA and determine optimum pressure for CPAP therapy. Participants returned after one month with CPAP for follow-up. Thirty-two participants, 22 males and 10 females, completed the study (mean age 45.4±4.6). Participants were divided into thirds based on adherence: the low adherence group had <5 average hours of use/night (n=13), the moderate adherence group had 5 to <6.3 hours (n=10), and the high adherence group had ≥6.3 hours (n=9). Groups were comparable on age and gender. The low adherence group had significantly lower BMI (31.8±5.2 vs. 41.4±7.6 and 39.4±7.1, respectively) and diagnostic AHI (38.9±25.4 vs. 77.2±30.6 and 72.4±25.9) than the other two groups.

Results: The groups were comparable at baseline on all subscale scores. The high adherence group had a significantly greater sleepiness decrease (37.1±8.8) as measured by SWAI-Excessive Daytime Sleepiness scores than the low (15.8±13.6) and moderate (19.2±16.7) adherence groups (p<.01; 31.3±13.2 vs. 41.5±10.5 and 34.5±10 at baseline, respectively). The high adherence group also had a significantly greater increase (13.1±3.5) in SWAI-Energy scores than the low adherence group (4.3±7.5; p=.02; 26.2±3.6 vs. 21±6.1 at baseline) but not the moderate adherence group (7.6±8.3, 26.5±6.8 at baseline). There was a trend (p=.075) for greater adherence to have increasingly greater SWAI-Relax subscale scores. There was no difference in change on SWAI-Nocturnal Sleepiness, SWAI-Social Desirability, and SWAI-Psychological Distress subscale scores.

Conclusion: CPAP adherence not only improves daytime alertness, but also subjective perceptions of feeling energetic and relaxed. Thus, the multi-dimensional nature of the SWAI provides for a more complete picture of therapeutic effects.

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AUTOMATED SIGNAL PROCESSING OF EEG IN PRIMARY INSOMNIA PATIENTS

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Introduction: Assessment of automated analysis of PSG recordings in sleep provides insights into insomnia disease states. This study compares signal processing outcomes using adaptive segmentation with traditional sleep parameters in adults identified with primary insomnia. Morpheus TM is a system that performs automated analysis of sleep staging using a multidimensional mathematical analysis of EEG applying adaptive segmentation and fuzzy logic with Markov models. Fundamental frequency values below 4 Hz are believed to represent increased EEG synchrony.

Methods: 40 adults were selected with a diagnosis of primary insomnia. A post-hoc analysis compared R&K analysis to adaptive segmentation studying 2 nights using a cross-over design with 4 compounds. Each patient received 3 different medications or placebo denoted by A, B, C and P(placebo). This represents first night analysis. Total sleep time (TST), latency to persistent sleep (LPS), wake after sleep onset (WASO), sleep efficiency (SE), % of slow wave sleep (SWS), and % of REM sleep were analyzed for each group and compared with the placebo group. One parameter of adaptive segmentation, fundamental frequency below 4 Hz, is calculated. Duration as a function of minutes of TST, % of TST, and mean segment duration were analyzed for each group and compared with the placebo group.

Results: Results with means and standard deviations are measured in minutes. For TST: P=365(84); A=423(42); B=418(43); C=398(65) and LPS: P=50(63); A=36(28); B=22(21); and C=49(46). For WASO: P=74(64); A=26(34); B=44(39); and C=39(37). For SE: P=88(9); A=89(7); B=87(9); and C=83(14). Fundamental frequency below 4Hz for TST is: P=126(48); A=203(61); B=162(46); and C=164(52). %TST is: P=34%(12); A=47%(13); B=39%(10); and C=40%(11). Mean segment duration (seconds) is: P=3.08(0.36); A=3.88(0.46); B=3.30(0.06); and C=3.42(0.41). T-tests of TST, LPS, and WASO comparing the placebo group with groups A, B, C were statistically significant at p<0.05 level with the following exceptions: LPS comparing placebo to group A and to group C. Fundamental frequency of TST (min), %TST, and mean segment duration were significant at p<0.05 comparing the placebo group with groups A, B, and C. A significant signal statistically was the duration of modal frequency below 4 Hz for compound A= p<0.000006. For R&K SWS% for compound A= p<0.00001.

Conclusion: Adaptive segmentation assesses sleep state in insomnia patients with enhanced resolution of EEG signals.

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COMPARATIVE VALUE OF ACTIGRAPHY VERSUS SLEEP LOGS

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Introduction: Current practice parameters suggest a need to address the relative contributions of actigraphy and sleep logs in the evaluation of hypersomnolent patients. A recent military study demonstrated that subjective estimates of total sleep time (TST) preceding PSG/MSLT were significantly greater than those predicted by actigraphy, and that the latter data correlated with decreased mean sleep latency on the MSLT (Bradshaw 2007). We sought both to explore the generalizability of this discrepant TST data, and to ascertain whether gleaned information affected clinicians' decisions to proceed with further testing.

Methods: A retrospective review of patients with actigraphy data during a 1.5-year period was conducted. Completion of logs are routinely requested in this setting. In cases where both were available in complete form (n=40), blinded TST comparisons were performed, utilizing written responses for logs, and ruler measurements for actigraphy. We

subsequently reviewed charts with usable actigraphy data (regardless of whether complete log information was available, $n=76$), to determine the frequency of postponement of anticipated PSGs/MSLTs.

Results: 15% of patients did not return logs. Among 40 patients for whom comparative analyses were performed, mean differences were insignificant on weekdays (7.65 ± 1.85 vs. 7.90 ± 1.54 , $p=0.301$) and weekends (7.42 ± 2.10 vs. 8.07 ± 2.06 , $p=0.161$) for actigraphy and logs. Of 76 patients who underwent actigraphy, testing was postponed in 17% (10% with hypersomnia) based on actigraphic data (\pm logs).

Conclusion: There were no significant differences in TST as measured by logs and actigraphy within our patient population. Nevertheless, actigraphy was more reliable when considering the proportion of patients who did not complete logs as instructed. Longitudinal TST information clearly influences clinicians' decisions to proceed with further testing, particularly among patients with hypersomnia. Future MSLT Practice Parameters should include more detailed requirements for sleep logs or actigraphy during the week prior to the anticipated studies.

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A PILOT STUDY OF QUANTITATIVE ASSESSMENT OF EXTERNAL MANDIBLE DEVICE FOR HEAD-TILT AND CHIN-LIFT AGAINST UPPER AIRWAY OBSTRUCTION DURING SEDATION

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Introduction: It has been well accepted that "head-tilt and chin-lift" is the most effective maneuver for upper airway obstruction. We have newly developed and tested the effect of external semi-automated mandible device against upper airway obstruction using the analysis of critical closing pressure (P_{crit}) during propofol sedation.

Methods: Five subjects (male=3, female=2) (age 22.5 years, BMI 21.0 kg/m²) were studied. The device was constructed with different part of air-inflatable pneumatic artificial muscles on the head strap. We used a pressure-flow relationships to evaluate critical closing pressure (P_{crit}) and upper airway resistance (R_{ua}) in propofol sedation. The pressure and inspiratory flow at subjects nose mask were recorded and Polysomnographic parameters (electroencephalograms, submental electromyograms, plethysmogram) were also recorded. P_{crit} was measured in each subject during propofol sedation (target blood concentration = 1.5~2.0 μ g/ml). The level of sedation was assessed by Ramsay OASS score (level 3~4) and BIS value (40~60).

Results: During neutral mandible position in supine position, P_{crit} was -5.8 ± 3.9 and R_{ua} was 30.1 ± 18.5 cmH₂O/l/s. When we have applied head-tilt and chin-lift using external device, P_{crit} significantly decreased to -11.2 ± 5.1 cmH₂O without changing R_{ua} (29.8 ± 17.8 cmH₂O/l/s).

Conclusion: We found that the external semi-automated device for "head-tilt and chin-lift" may be useful method for upper airway obstruction during sedation and sleep.

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TWO INTEGRATED SENSORS IN A SMALL DEVICE FOR THE MEASUREMENT OF BODY POSITION AND SNORING DURING SLEEP STUDIES

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Introduction: The gold standard to measure body position and snoring in a sleep lab is a video recording of the patients' position and a Db-meter device, respectively. For the ambulatory setting, the method most commonly used is an electro-mechanical body position sensor made of moving elements that switch positions attached to the patient's body and a microphone positioned on the patient's supra clavicle notch. We have developed a new device that integrates both a highly sensitive micro-

phone and a 3-axis accelerometer in a small housing. Both sensors are driven by a miniaturized electronic circuit. The accelerometer measures the acceleration in each axis and a small microprocessor integrated in the device transforms the projection of the gravity in the direction of the body position in a 3 axis system. From the gravity vector the body position is computed with high precision. In addition, the microprocessor utilizes a transfer function that provides db level equal to that of a DB-meter positioned 1 meter from the patient's bed.

Methods: Eight patients were tested awake while maneuvering positions in a documented controlled manner ($n=5$) and during sleep in a sleep lab ($n=3$) with simultaneous recordings of the tested device and video-camera. An epoch by epoch comparison of the position was performed between the two methods.

Results: The total agreement between the tested device and video-camera was 82% for a total accumulated 2798 epochs in the sleep lab and 512 epochs in the controlled maneuvering. The agreement for each position was 78%, 79%, 87%, 55% and 90% in the sitting, left side, right side, prone and supine postures respectively. Snoring was detected in 2 of the 3 patients in the sleep lab studies. For a total recording time of 15 hours the mean error between a dB meter positioned 1 meter from the patient bed and the device was 0.4 ± 5 db. The total agreement for detecting snoring over or under 45, 50, and 60 DB was 80%, 95 % and 96% respectively ($P<0.05$).

Conclusion: We conclude that the new sensor can detect the five basic postures with a higher accuracy than the conventional sensor (for which we recently reported less than 70% total agreement). In addition snoring level is detected adequately. Future studies should test the ability to measure mixed ("in between") positions that are undetectable with the standard sensors.

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CORRELATION BETWEEN POLYSOMNOGRAPHY AND ACTIGRAPHY IN DETECTING CHANGE IN MACRO SLEEP VARIABLES DURING TREATMENT OF PERSONS WITH BOTH DEPRESSION AND INSOMNIA

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Introduction: Insomniacs often report a degree of sleep disturbance that is not reflected in polysomnography (PSG), and may report improvements that are not supported by PSG. PSG is encumbered by high cost, patient inconvenience, and the artificiality of the laboratory setting. Actigraphy is emerging as an alternative to PSG in the measurement of treatment effects in sleep.

Methods: The Actiwatch by Mini Mitter Co., Inc. is an actigraph with a sensitivity of 0.5 grams, bandwidth between 3-11 Hz, and it samples at 32 Hz. We examined its performance in detecting treatment effects in 24 persons with both depression and insomnia who received 8 weeks of open-label fluoxetine coupled with blinded eszopiclone versus placebo. The sample was $39.6 + 11.5$ years with 75% women. All participants completed one night of PSG at baseline, repeated after 9 weeks of treatment. Actigraphy was simultaneously recorded from the non-dominant wrist, using 30-second epochs. Mini Mitter's proprietary software produced estimates of sleep latency (SL), wake after sleep onset (WASO), and total sleep time (TST).

Results: We computed the Pearson's r correlations between actigraphy and PSG for change scores in SL, WASO, and TST, and these were 0.17, 0.35, and 0.38, respectively.

Conclusion: We conclude from this preliminary experience that actigraphy may be a suitable, low-cost surrogate for PSG in the long-term, continuous measurement of WASO and TST, but the correlation for SL sleep onset was poor. While the correlations for TST and WASO were modest, the precision of measurement with actigraphy may be vastly

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enhanced by nightly measurement, with a resulting ‘smoothing’ of the data, and better signal-to-noise ratios than could be achieved with single pre-post nights of PSG. Furthermore, the ability to measure sleep/activity in the home enhances the ecological validity of measurement.

Support (optional): NIH MH70821; M01-RR07122; Sepracor, Inc; and Mini Mitter Co, Inc (Respironics)

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ACTIGRAPHY AS A COMPONENT OF SCREENING FOR SLEEP APNEA AND PERIODIC LIMB MOVEMENTS

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Introduction: Clinical trials of primary and secondary insomnia may exclude persons with sleep apnea (SA) and periodic limb movement disorder (PLMD). Polysomnography (PSG) may identify SA and PLMD, but is encumbered by high cost. We examined the value of actigraphy in classifying insomniacs with and without SA and PLMD.

Methods: Forty patients (42 +13 y.o.; 27 women) in a depression/insomnia clinical trial underwent one week of baseline home actigraphy followed by one night of full, in-lab PSG. Patients had been pre-screened to exclude BMI > 35 and RLS. Patients wore the Actiwatch (Mini Mitter Co., Inc.) on the non-dominant wrist, with data stored in 30 second epochs. Data were averaged across the week for each actigraphic variable. We created a new summary variable called the Mega index, which is the sum of the apnea/hypopnea index and PLM arousal index. Ten persons had a Mega index >10 (MI+).

Results: We calculated receiver operating curves (ROC) to examine the value of actigraphy in predicting MI+, after accounting for demographic and clinical variables. MI+ patients were older than MI- patients (49 versus 39 y.o.) Age alone was a significant predictor of MI+ versus MI- ($p < 0.05$), but the area under the curve (AUC) was only 0.70, indicating that age alone was only a “fair” model. Furthermore, the age-only model misclassified 17 patients. Gender, BMI, severity of insomnia and severity of depression did not differ between MI+ and MI-, and did not improve the ROC model. In contrast, the creation of a complex model that added 9 actigraphy variables to age produced a highly significant model ($p < 0.005$) with AUC of 0.94, indicating an excellent predictive model. Moreover, only 4 patients were misclassified by this model.

Conclusion: We conclude from this preliminary experience that actigraphy may be a useful component of screening for SA and PLMD patients in insomnia clinical trials.

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AROUSAL DISTRIBUTION/DURATION AS A NEW MEASURE OF SLEEP DISTURBANCE

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Introduction: Arousal index (AI) is the traditional measure of sleep disturbance. Arousals that occur at a high frequency produce non-restorative sleep while infrequent arousals do not. This suggests that the amount of time during the night containing frequent arousals (duration) may also be a useful measure of sleep disturbance. The current study compared AI with arousal duration (AD) in middle-aged apnea patients.

Methods: Based on RDI, 17 patients with severe OSA and 14 patients with moderate OSA who had separate baseline and CPAP nights were identified. Patients with other significant sleep disorders or medical illness were excluded. Sleep studies were rescored by the same well-

trained scorer. AD was calculated by totaling the sleep time between all arousals that occurred within 2 minutes of another arousal and dividing that time by the total sleep time for the night. AD is presented as the percent of the night with this pattern.

Results: CPAP treatment produced a significant decline in AI (from 61 to 24 arousals/ hour) and in AD (from 64% to 15% of the night) compared with baseline nights. When AI and AD were entered into an ANOVA, a significant interaction was found between baseline and CPAP nights. No difference was found between AI and AD at baseline, but a significantly shorter AD was found during CPAP treatment ($F = 12.95$, $p < 0.001$ with Neuman-Keuls pairwise test) compared with AI. Baseline AD and AI were strongly correlated ($r = 0.86$, $p < 0.0001$), but the correlation decreased on CPAP nights ($r = 0.48$, $p < 0.005$).

Conclusion: As expected, both AI and AD decreased with initiation of CPAP. AD was highly correlated with AI at baseline due to large arousal variability. However, CPAP treatment resulted in a significantly greater decrease in AD than AI. This suggests that measures of AD are different from AI and could provide a more sensitive predictor of sleepiness.

Support (optional): Supported by the Dayton Department of Veterans Affairs Medical Center, Wright State University School of Medicine, and the Sleep-Wake Disorders Research Institute

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RELIABILITY AND VALIDITY OF ARABIC VERSION OF EPWORTH SLEEPINESS SCALE

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Introduction: The Epworth Sleepiness Scale (ESS) is a self-administered eight-item questionnaire that is widely used in English speaking countries for assessment of daytime sleepiness in adults, but there is no Arabic version from ESS. The aim of this work was to translate the ESS into Arabic and to evaluate reliability and validity of the Epworth Sleepiness Scale (ESS) in the Arabic language as a diagnostic method among patients suspected to have obstructive sleep apnea syndrome (OSAS) and Arabic population.

Methods: The Arabic version of the ESS (ESSar) was applied to 98 healthy controls (78 normal persons answer the ESSar in two sets with 5 months interval, and 18 chest physician answers the ESS by both Arabic and English languages with 4 weeks interval and 80 consecutive subjects attending the sleep Unit chest department with symptoms of sleep-disordered breathing. Test-retest reliability of the ESSar was tested in a separate group of 78 subjects and bilingual of 18 chest physician. The ESSar scores of 80 subjects with high suggestion of obstructive sleep apnea (OSA) were doing full night polysomnography.

Results: The mean +/- SD of ESSar scores in normals was (2.95 +/- 2.71), in patients it was (9.79 +/- 5.19). In patients Ess Scores were not correlated with age, sex, snoring index and arousal index but strongly correlated with the BMI and AHI ($r = 0.310$, $p < 0.005$ and $r = 0.314$, $p < 0.005$). Items analysis confirmed internal consistency of the ESSar scale (Cronbach $\alpha = 0.59$ & 0.61 in 78 normal persons test-retest, and 0.58 & 0.59 in bilingual chest physicians patients). The test-retest intraclass correlation coefficient were ranged from $r = 0.70$ to $r = 1.0$ and $p = 0.000$ in normal persons). There were significant correlations between the ESSar subscales and total ESSar. The ESSar is a reliable and valid measure of daytime sleepiness.

Conclusion: The Arabic version of the ESS (ESSar) is reliable and valid scale for evaluation of daytime sleepiness among Arabic speaking population. The performance of the Arabic version of the ESS in patients with obstructive sleep Apnea Syndrome is similar to that of the original English ESS. Therefore, this questionnaire may be employed for assessment of subjective daytime sleepiness in Arabic individuals and populations.

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ENGLISH/SPANISH CROSS VALIDATION OF A SLEEP MEASURE

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Introduction: Sleep disturbances have been well-described for English-speaking non-Hispanic white and African Americans; however, little is known about sleep problems of Spanish-speaking Southwestern U.S. Latinos due to the lack of translated and validated sleep measures.

Methods: Psychometric data were compiled on a newly developed Spanish version of the Sleep Heart Health Study (SHHS) Sleep Habits Questionnaire (SHQ). Bilingual participants residing in the Southwestern U.S. completed English and Spanish versions one week apart in randomized order. Reliability, scale equivalence, and criterion validity were evaluated using Cronbach α , Spearman-Brown r , t -tests, and cross-tabulations of frequencies.

Results: Of the 50 participants, 52% were women and 92% self-identified as Latino. Mean age was 39 \pm 12 years and education was 15 \pm 3 years (range 6 to 22). Cronbach α was 0.82 and 0.85 for English and Spanish versions respectively for the 12-item SHHS SHQ sleep symptoms scale, 0.71 and 0.81 for the combined 3-item SHQ difficulty initiating and maintaining sleep (DIMS; insomnia) scale, and 0.83 and 0.81 for the 8-item Epworth Sleepiness Scale (ESS). Spearman-Brown correlation between English and Spanish versions was >0.90 for each of the three scales indicating scale equivalence. T -tests indicated that participants with English ESS scores >10 scored higher on an English fatigue measure ($p < 0.01$), as did participants with Spanish ESS scores >10 ($p < 0.01$). Women were more likely than men to have insomnia (English 46% vs. 29%; Spanish 46% vs. 33%). Participants 40 to 62 years old were more likely to have insomnia than participants 18 to 39 (English 48% vs. 31%; Spanish 52% vs. 31%).

Conclusion: English and Spanish versions of the SHHS SHQ demonstrated equivalent reliability and validity in a Southwestern U.S. Latino sample. Additional psychometric data are being collected on 210 Spanish-speaking individuals. Findings will also be compared with data collected from participants residing in Mexico to determine instrument generalizability.

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EVALUATION OF A PORTABLE DRY SENSOR BASED AUTOMATIC SLEEP MONITORING SYSTEM

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Introduction: The development and validation of low cost, easy to use, portable sleep recording devices, with algorithms to distinguish between sleep stages and wakefulness, has important implications for sleep medicine and research. A comfortable wireless system has been developed for assessing sleep. The system utilizes dry fabric sensors that require no preparation. The sensors are integrated into a headband that acquires a single channel from the forehead, and transmits to a base station for processing. Sleep stages are scored automatically by a neural network. The aim of the current study was to compare sleep measures derived from polysomnography (PSG) and from the wireless system.

Methods: Three healthy female volunteers (ages 25, 33 and 38) were co-monitored in a sleep lab for two nights each by the wireless system

and standard PSG recordings. Wireless system data were sampled with a 12 bit A-D converter and captured at 128 samples per second. Sleep records were visually scored by a trained technician according to Rechtschaffen & Kales, and simultaneously scored automatically by the wireless system. Sleep onset latency (SOL) to 3 continuous epochs of sleep, wakefulness after sleep onset (WASO), total sleep time (TST), and sleep efficiency (SE) were derived from the records for comparison.

Results: Preliminary findings from this ongoing study suggest that sleep measures were reasonably similar for PSG vs. the wireless system: SOL 26.6 \pm 9.3 vs. 26.8 \pm 3.7min, WASO 59.9 \pm 12.7 min vs. 69.8 \pm 21.8 min, TST 326 \pm 22.5 min vs. 307.9 \pm 30.1 min, SE 81 \pm 3% vs. 76 \pm 5%, respectively (Mean \pm SEM). The wireless device was well tolerated by subjects.

Conclusion: Ongoing and additional data collection and analyses are needed to further evaluate and validate the wireless system. The wireless system shows promise as a low cost, portable, easy to use, sleep monitoring technology.

Support (optional): Support for this study provided by Axon Labs, Inc.

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PREDICTORS OF QUALITY OF LIFE IN PATIENTS WITH SLEEP DISORDERS

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Introduction: Sleep disorders can have a powerful influence on health related quality of life (QOL). Few published reports elucidate the relationship between sleep disorders and QOL. This investigation evaluated self-reported health indicators, health risk behaviors and socioeconomic (SES) variables as predictors of QOL in a sample sleep disordered patients.

Methods: A convenience sample of 85 patients referred to the Sleep Disorders Center was recruited for the study. Subjects were administered surveys before beginning sleep-related therapy, including: Health Utilities Index (HUI)3, Functional Outcomes of Sleepiness Questionnaire (FOSQ), Epworth Sleepiness Scale, a socioeconomic survey, and health risk behavior survey.

Results: Subjects included 30 (36%) females and 54 (64%) males, 60% Caucasian and 33% African American. Age was 45.7 \pm 13.6 years; range 19-78. Ten percent had a household income of less than \$25,000. Sleep diagnoses included obstructive sleep apnea (85%), periodic limb movement disorder (31%) and narcolepsy (6%). Comorbidities were present in 44%, including 27 (32%) reporting psychiatric conditions. Mean (SD) survey scores included: FOSQ (sleep specific) total score 15.3 (3.6) and HUI3 (general QOL) 0.68 (0.3). Two or more days of poor physical health or poor mental health in the last month were reported by 46% and 53% of subjects, respectively. Using backwards stepwise regression, significant independent predictors of QOL included self-rated general health (for HUI3: $p = .007$; for FOSQ: $p = .037$), self-reported days of poor mental health (for HUI3: $p = .003$; for FOSQ: $p = .030$) and number of co-morbid conditions (for HUI3: $p = .001$).

Conclusion: Poor physical and mental health are common among sleep disordered patients, and were significant predictors of poor QOL. Indices of SES and health risk behaviors did not correlate with QOL.

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REAL-TIME AUTOMATIC WAKE/SLEEP SCORING BASED ON A SINGLE EEG CHANNEL

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Introduction: Facing the increasing demand for diagnosis of sleep-associated pathologies, especially respiratory sleep breathing disorders, ambulatory polygraphy was developed. However, with such devices the apnea-hypopnea index (AHI) is often underestimated due to overestimation of total sleep time. With the aim of providing accurate sleep analysis with minimal required equipment, the single-channel based automatic scoring algorithm ASEEGA was developed and validated (SLEEP 2007;30(11):1587-95). The aim of the present study was to evaluate its ability to distinguish, in real-time, wake and sleep states in patients with Sleep Apnea Syndrome (SAS).

Methods: 54 patients (aged 61.7 ± 11 years, 11 women) with SAS had polysomnography (PSG) and were scored, both manually (full PSG) and automatically (EEG CzPz). The real-time analysis was mimicked by providing the algorithm with incremental EEG data, and by preventing the algorithm from updating its decision on earlier data samples. Sleep stage assignment was delivered with a one-epoch-long lag compared to the available data. The epoch by epoch comparison presented here focusses on the simple Wake-Sleep classification that is of interest in AHI monitoring.

Results: Statistical comparisons were computed based on the total of 56,696 recorded epochs. Among these, 1,795 (3.2%) and 100 (0.2%) epochs were classified as artefact or movement time respectively, either by the automatic or the human expert. Results showed an automatic/manual agreement of 90.4% in the sleep-wake classification task. Cohen's kappa coefficient reached 0.74. Finally, the sensitivity and positive predictive value for wake detection obtained 79.3% and 81.3% respectively.

Conclusion: This feasibility study assessed that the algorithm is accurate for real-time sleep/wake classification. This shows that, once implemented into a hardware device, ASEEGA could be used for real-time applications such as the online split-nights or AHI monitoring.

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QUALITY CONTROL OF ACTIGRAPH DATA USING PRINCIPAL COMPONENTS ANALYSIS

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Introduction: The actigraph, a battery-operated watch-sized device, measures frequency-of-movement (FOM) over an allocated epoch. Clinical and research settings use actigraphs to convert FOM to estimates of sleep and wake times/durations (Sadeh & Acebo, 2002). However, little is known about inter-actigraph reliability when measuring the same set of motion. Therefore, this study examined a methodology for statistically testing the reliability of the actigraphs, using both the raw FOM data and the sleep variables.

Methods: Study I: To assess similar motion detection across units, 41 actigraphs (AMI) were wrapped in bubble wrap and taped to the back of a swivel office chair. Study II: Using the swivel chair method, 41 actigraphs recorded FOM at the same time point. The chair was set in a location of constant use to allow for more frequent movement. Study III: The data from Study II were analyzed using Action-W2 software (AMI) and a validated algorithm to estimate the following variables: Sleep minutes and Wake minutes. These variables produced a secondary method for testing inter-actigraph reliability. Statistical Methods: Princi-

pal Components Analysis (PCA) was used to produce test statistics from an F-distribution under a 95% confidence interval.

Results: Study II: The FOM data showed actigraph 2030 exceeded the 95% confidence interval threshold ($F = 33.45 > F(.05) = 18.89$). Study III: Actigraph 2030 exceeded the 95% confidence interval threshold ($F = 13.62 > F(.05) = 9.01$) just as in study II. We also found actigraph 2039 to be an outlier ($F = 10.83$).

Conclusion: The study derived an objective method to test actigraphs for quality control purposes. Our results found that only one actigraph recorded measurements statistically different from the others under both conditions. However, the sleep/wake variables found another strong outlier. This leads us to question how the sleep/wake variables produce an extra outlier, and which of these two methods provides greater reliability. Ultimately, this methodology may be useful when utilizing many actigraphs simultaneously in both research and clinical settings.

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AN EFFICIENT PROCEDURE FOR FINDING THE 95% CONFIDENCE INTERVAL OF PERFORMANCE PREDICTIONS BASED ON THE TWO-PROCESS MODEL

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Introduction: Sleep/wake-based biomathematical models of performance have limited value without quantification of the accuracy of the predictions they make. Prediction accuracy can be estimated by calculating 95% confidence intervals (CIs), but high computational burden has prohibited broad implementation of such calculations. For performance prediction with the five-parameter Two-Process Model, currently used 95% CI algorithms are of order N^5 , which means that for every tenfold increase in calculation precision 100,000 times as many calculations are needed. Here we present a novel method for calculating 95% CIs much more efficiently.

Methods: We first proved mathematically that the boundary of the smallest 95% confidence region in a multidimensional probability density function (pdf) constitutes a level contour. In a nested procedure, this contour can be expressed in terms of standard deviations from the mean in a coordinate system rotated for each parameter or pair of parameters. After projecting back onto the original coordinate system, the 95% confidence region is represented in closed form using elliptical splines. The closed form is then used as a constraint equation in the Lagrange multiplier procedure, in order to maximize and minimize the prediction over the boundary of the smallest 95% confidence region. This yields the boundaries of the 95% CI of a performance prediction.

Results: By reducing the calculation of 95% CIs to a nested series of operations on single parameters or pairs, the computational burden was reduced from order N^5 to order N^2 . Monte Carlo simulations confirmed that the algorithm yields correct results.

Conclusion: We improved the efficiency of 95% CI calculations for performance predictions with the Two-Process Model by as much as three orders of magnitude, making real-time assessment of prediction accuracy feasible for the first time. Our novel algorithm can also be applied to performance models with more than 5 model parameters, as long as each separate term in the model contains at most two mathematically distinct variables. Under that condition, the order of the computational cost involved does not increase.

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COGNITIVE PERFORMANCE TEST FOR DETECTING SLEEPINESS-INDUCED IMPAIRMENT

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Introduction: The detection of dangerous impairment levels induced by poor or insufficient sleep can be of benefit in certain situations, such as the screening of workers with safety-critical jobs. The present study was conducted to evaluate a new cognitive performance test as a potential tool for impairment detection. The BLT test (developed by Bowles-Langley Technologies, Inc.) is a brief, simple computerized shape recognition test that requires the user to make a Yes/No decision about whether all items in a given screen are the same. After a series of 50 screens the resulting speed/accuracy-based score is compared to the user's baseline.

Methods: Fifteen subjects (aged 25-50 years) participated in a sleep restriction study. They stayed in the lab for two consecutive days and nights and were only allowed to sleep for three hours in the morning before the second test day. On each test day, they completed ten bi-hourly test sessions (starting at 1200). Each test session included several subjective tests (e.g., Visual Analog Scales, Thayer Activation-Deactivation Adjective Checklist, Karolinka Sleepiness Scale), 5-min simple reaction time test (PVT), 25-min driving simulation task, 50-screen four-choice reaction time test, and four shape recognition tests (SRT).

Results: The various testbed measures (subjective tests, PVT, four-choice test and driving task) showed the expected circadian trend with consistently impaired levels at night. SRT scores were significantly lower at night (0200, 0400, 0600) as compared to the two highest-score test sessions of the same test day (paired t-tests). On the group level, the SRT score (standard scoring algorithm 1.0) correlated well with many of the testbed measures (Spearman $R > 0.8$, separate analysis for each test day). However, on the individual level, correlations were less strong and varied greatly between subjects.

Conclusion: The aim of further analysis is to refine the SRT scoring algorithm in order to improve the intra-individual correlations between the score of the shape recognition test and other testbed measures, and to define impairment thresholds.

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CAN SLEEP DIARIES BE ACCURATELY COMPLETED RETROSPECTIVELY?

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Introduction: Sleep diaries are commonly used in research in which quantitative measures of sleep are of interest. Sleep diaries yield accurate and reliable estimates of sleep and wake times. In many psychosocial studies there is an interest in assessing sleep to ascertain possible relationships between sleep and other psychosocial factors. However, at times it is impractical to have participants complete daily diaries. These studies often rely on qualitative measures of sleep. These types of measures are not able to provide researchers with specific quantitative descriptors of sleep but rather estimates. Other areas of behavioral research have shown that individuals are able to accurately report past behaviors over a specified period of time. The purpose of this study is to evaluate the accuracy of individuals' abilities to provide (in a one-time evaluation) their nightly estimates of sleep activity over the preceding week.

Methods: Participants responded to a recruitment ad requesting volunteers for an activity study and were unaware of the true purpose of the study. Participants wore an actigraphy monitor for one week and

received minimal instructions so as to not sensitize them to the study's real purpose. They were instructed to wear the watch 24 hours a day and press the event marker at bedtime and waketime to separate sleep from waking activity. At the end of the week, participants completed a 7-day sleep diary and answered additional questions.

Results: Preliminary analyses have been completed on 11 participants (5 males). Intraclass correlations between actigraphy and diary data were calculated per night for total sleep time, sleep onset latency, WASO, time in bed and sleep efficiency. Consistency varied across variables. Time in bed yielded the highest intraclass correlations and the greatest number of significant correlations (significant r 's ranged between .56 and .95, with 6 of 7 days having values with p 's < .05). Total sleep time was second with 5 of 7 days showing significant intraclass correlations that ranged from .43 to .70. Sleep efficiency showed the least consistency with no significant intraclass correlations.

Conclusion: Preliminary data suggest that individuals may have the capacity to accurately estimate some aspects of their sleep retrospectively, although the data must be interpreted cautiously as consistency varies across sleep variables. Research in this area should further examine these relationships and establish which variables are best recalled retrospectively.

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POINCARÉ ANALYSES PROVIDE NOVEL INSIGHTS INTO THE TEMPORAL ORGANIZATION OF SLEEP

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Introduction: Poincaré analyses provide a method to display cyclic data as discrete points within two time dimensions and extend characterization derived from inferential statistics. Poincaré analyses have been used to characterize heart rate variability (Sleep 14:526, 1991; 19:117, 1996) and EEG (Sleep 16:586, 1993) during sleep. We have demonstrated (Sleep 31: Abstract in press, 2008) that rats bred for low intrinsic aerobic running capacity (LCR) exhibit decreased and disrupted sleep compared to rats bred for high intrinsic aerobic running capacity (HCR). This study is testing the hypothesis that Poincaré analyses offer unique insights into the temporal organization of sleep.

Methods: Six HCR and six LCR rats (Science 307:418, 2005) were implanted with electrodes for recording states of arousal. Every 10 seconds of each 24 h recording (n=12) was scored as REM sleep, NREM sleep, or wakefulness. Poincaré graphs of REM sleep were generated by plotting the length of each REM episode as a function of its immediate antecedent value. Measurements of standard deviation in relation to the line of identity (SD1) and a line perpendicular at the mean (SD2) quantified short-term (epoch to epoch) and long-term (24 h) variability, respectively.

Results: LCR rats had an SD1 15.4% larger than HCR rats, indicating that low aerobic capacity is associated with more short-term variability in REM epoch length. LCR rats also displayed a 19.7% larger SD2 value ($p < 0.05$) than HCR rats, showing that low aerobic capacity is associated with greater variability in REM epoch length for the entire recording.

Conclusion: Poincaré analyses unmasked REM sleep variability not visible using inferential statistics. These analyses provide new insight into the stability of sleep architecture across time by directly comparing each REM episode to its predecessor. Poincaré analyses quantify subtle changes in sleep architecture.

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HEMISPHERIC PHASE AND AMPLITUDE SYNCHRONY DIFFERENCES BETWEEN SLEEP AND WAKE CONDITIONS

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Introduction: Changes in hemispheric synchrony have been observed during the transition from wakefulness to sleep using coherence and correlation measures. The purpose of the present study is to assess differences in hemispheric synchrony between sleep and wakefulness using more sensitive measures in the phase and amplitude domains.

Methods: Data for this analysis came from 21 patients (mean age 45) who underwent a Multiple Sleep Latency Test for evaluation of their hyper-somnolence. The first nap was segmented in 2.5s epochs for spectral decomposition (FFT). Epochs were sleep/wake classified using a sleep index ($\alpha + \beta$) / ($\theta + \delta$), and values $<.30$ were classified as waking and those $>.30$ as sleep. Several synchrony measures were calculated from O1-A1 and O2-A2 derivations as follows: The twelve Hz signal was extracted from both EEG channels using a first-order complex Gaussian continuous wavelet transform (CWT). Complex CWT results were angular transformed and unwrapped to produce phase time series. Synchrony Index (SI) the averaged normalized phase distances between both EEG channels was calculated; Synchrony Entropy Index (SEI), the deviation of phase differences from the uniform distribution was quantified using an approach based on Shannon's entropy. The Hilbert transformation of the real component of the CWT results yielded the demodulated amplitude. The Synchrony Amplitude Index (SAI), the entropy estimation of the demodulated amplitude differences, was calculated.

Results: ANOVA demonstrated that phase synchrony measures increased from wake to sleep, SI, (wake=0.179, sleep=0.224, $p<.001$), SEI (wake=0.39, sleep=0.6, $p<.001$). In contrast the amplitude synchrony measure decreased during this transition, SAI (wake=0.232, sleep=0.181, $p<.001$).

Conclusion: Previous findings that have shown increased hemispheric synchrony in the wake to sleep transition may have conflated phase and amplitude domains. We propose that wake to sleep transitions are represented differently in the phase and amplitude synchrony domains.

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EFFECTS ON MAINTENANCE OF WAKEFULNESS TEST OF RECOVERY SLEEP DOSE FOLLOWING SLEEP RESTRICTION

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Introduction: Little is known about the sensitivity of the Maintenance of Wakefulness Test (MWT) to differing sleep period lengths (TIB) following chronic sleep restriction. This study investigated the effect of varying TIB sleep doses on a night following 5 nights of sleep restriction (SR).

Methods: N=118 healthy subjects (age=30.12±6.98yr, 64f) participated in a controlled laboratory protocol. Subjects underwent 2 nights of baseline sleep (TIB=10h) followed by 5 nights of SR (TIB=4h) and a night of varying time in bed for recovery sleep (R1). On R1 subjects were randomized to one of six TIB sleep doses (0h n=13; 2h n=18; 4h n=24; 6h n=16; 8h n=17; 10h n=21 TIB). Modified single trial (30min) MWTs were conducted between 1430h-1600h on the day after the second baseline night, after the fifth SR night (SR5) and after R1. Sleep latency was defined as time to the first appearance of a brief sleep (10sec microsleep). N=9 served as 10h TIB per night control subjects.

Results: MWT sleep latency (\pm SD) after 5 nights of SR was 10.48±8.6min, which differed significantly from baseline 19.12±10.3min ($p<0.001$). At SR5, sleep latency was shorter in the sleep restricted group

(10.48±8.6min) versus the control group (22.26±9.32min; $p<0.01$). R1 sleep doses of ≤ 6 h TIB (0h, 2h, 4h, 6h) yielded MWT sleep latencies significantly below those at baseline (all $p<0.05$). R1 0h and 2h TIB decreased ability to stay awake significantly below that on SR5 ($p<0.05$). R1 10h TIB improved ability to stay awake significantly above SR5 ($p<0.05$), however 8h TIB did not ($p>0.05$).

Conclusion: The MWT was sensitive to SR and to the dose of subsequent TIB for sleep. However, MWT showed significant recovery only after a sleep dose of 10h TIB. Analyses are underway to determine the nature of physiological sleep obtained in the 10h TIB.

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A CLASSIFICATION SCHEME FOR MEDICATION USE IN CLINICAL RESEARCH SAMPLES

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Introduction: Medication use data is usually collected in clinical research. However, there exists no standardized method for categorizing these data, either for sample description or for the study of medication use as a variable. We developed a simple, empirically based classification scheme for medication use. Here we describe the development technique and to illustrate its potential, we apply it to samples where sleep disorders are prominent.

Methods: The development sample included 480 participants (45 men: mean age=56.56; 18 women: mean age=58.11, S.D.=12.97), recruited for a large, multi-stage study on daytime functioning in sleep disorders. As part of the questionnaire battery, participants provided information on medication use. Participants also underwent polysomnographic assessment of their sleep. Based on the Canadian Compendium of Pharmaceuticals and Products (CPS) and subsequent consensus grouping, medications were coded into 16 specific therapeutic classes. A principal components factor analysis was carried out to reduce the number of classes into usable categories. Hypotheses were developed and tested on: 63 individuals with Sleep Apnea/Hypopnea Syndrome (SAHS), 24 with Chronic Fatigue Syndrome (CFS), and 48 Healthy Controls.

Results: The factor analysis yielded 5 categories: 1) Psychoactive medication, 2) Metabolic syndrome/pain related medication, 3) Respiratory/gastric/urologic related medication, 4) Infection/skeletal/lifestyle related medication, and 5) Hormonal medication. As a preliminary test of validity of the classification scheme for medication use we tested and confirmed the hypotheses (a) that participants with SAHS use significantly more Cardiovascular medication than do CFS or Control participants and (b) that CFS participants use significantly more Psychoactive medication than do SAHS or Control subjects.

Conclusion: The categorization system we developed is easy to use and appears to discriminate some populations. We believe that a standardized classification scheme for medications commonly found in clinical populations could be of great benefit to researchers by allowing (1) better sample descriptions and (2) clearer conceptualizations of the role of medications in the etiology, maintenance, and treatment of illness.

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A NEW INSTRUMENT FOR RAPID CLINICAL SCREENING OF EXCESSIVE DAYTIME SLEEPINESS

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Introduction: Excessive daytime sleepiness is a common symptom encountered in primary care and sleep medicine practices. The ability to provide an appropriate diagnostic work up in such patients is sometimes difficult since pathological sleepiness can be caused simply by poor sleep hygiene in the form of insufficient sleep time. A brief screening tool that assists in the assessment of pathological sleepiness could help make the diagnostic process more efficient. The Glidewell Rapid Sleep Screen (GRSS) is a brief semi-structured interview developed to enable primary care clinicians to rapidly screen for sleep disorders as a source of daytime sleepiness.

Methods: 60 new patients presenting to a private AASM accredited sleep center completed the Epworth Sleepiness Scale (ESS) prior to being administered the interview by a staff nurse. The interview consists of four sleepiness questions. Positive response to any sleepiness item results in a classification of EDS. Sensitivity and specificity analysis was completed to evaluate the ability of interview items to correctly classify high (ESS score equal to or greater than 9) and low (ESS score less than 9) scorers on the ESS.

Results: Concurrent use of the four interview sleepiness items resulted in a sensitivity of 92% and specificity of 48% for the classification of high and low scorers on the ESS. Analysis of individual items reveals that a single sleepiness item querying sleepiness at “inappropriate or unwanted times or places” results in a sensitivity of 84% and specificity 48%.

Conclusion: 1) It appears that these sleepiness questions provide good sensitivity, but relatively poor specificity. 2) Using the GRSS, clinicians can use a positive response to a single question as a guide to the presence of significant daytime sleepiness. 3) The low specificity of these questions implies that a negative response should not preclude other lines of questioning regarding the presence of daytime sleepiness.

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PILOT EVALUATION OF A PORTABLE MONITOR FOR DIAGNOSIS OF OBSTRUCTIVE SLEEP APNEA IN A CONSECUTIVE SERIES OF PATIENTS COMPARED WITH POLYSOMNOGRAPHY

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Introduction: Validated portable monitors (PM) are a viable tool to assist in the diagnosis of obstructive sleep apnea (OSA) in the estimated 93% of middle-aged women and 82% of men with moderate to severe OSA who remain undiagnosed. We assessed the utility of a Level 3 PM for OSA, Medibyte® (BRAEBON® Medical Corporation) by pairing it with attended overnight polysomnography (PSG) in the sleep laboratory (Level 1).

Methods: A consecutive series of patients, not all of whom were suspected to have OSA, wore the PM with PSG. Hypopneas were scored based on a reduction in airflow on the nasal cannula pressure transducer signals of 50% or more from baseline and a reduction in oxygen saturation of $\geq 3\%$ on the PM record, and/or associated with arousals on PSG. The number of apneas and hypopneas were calculated per hour of recording time between lights off and on for the PM, called the respiratory disturbance index (RDI), and per hour of sleep time for the PSG-based apnea-hypopnea index (AHI).

Results: For 30 patients (10M/20F) aged 19 to 70 years (mean \pm SD: 51 \pm 12) and BMI 35.1 \pm 8.1 kg/m² (range 21.4 - 49.9), the AHI was 29.6 \pm 32.8 while the RDI was 19.2 \pm 22.5. The mean difference AHI-RDI showed under-reporting by the PM of 10.4 \pm 14.5. There was good correlation between the RDI and AHI, Pearson correlation $r = 0.93$, which accounted for 86% of the variance ($R^2 = 0.865$). For an AHI above 5 the sensitivity of the PM was 88%. For severe OSA (AHI ≥ 30), the PM sensitivity was 88% and specificity 100%.

Conclusion: Tested in the laboratory, all cases of severe OSA had an RDI > 15 on this PM which showed very good accuracy in identifying patients with OSA.

Support (optional): Three portable monitors and associated consumables were provided by Braebon.

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EVALUATION OF IMMOBILITY TIME FOR SLEEP LATENCY IN ACTIGRAPHY

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Introduction: Actigraphy has become an important tool in sleep research. However, most actigraphic models have had little validation of their sleep scoring software. Some reports have described poor agreement of actigraph and PSG results. In this study, we examined the validity of Actiwatch-L with Actiware® software version 5.0 (Minimitter-Respiroics, Bend, Oregon).

Methods: We analyzed the sleep latencies and the total sleep times in 33 actigraph recordings (24 men, 9 women, mean age of 54 \pm 8.7 years, 20 with OSA, 13 with OSA and PLMS), and compared performance to simultaneous polysomnography. For scoring sleep latency, the default parameter for scoring sleep onset (10 minutes of immobility) was compared with 4, 5, 6, and 15 minutes of immobility.

Results: Of 4, 5, 6, 10 and 15 minutes of actigraphic immobility, 5 minutes of immobility yielded sleep latencies best correlated with those of polysomnography ($r=0.44, 0.65, 0.22, 0.29, \text{ and } 0.39$ respectively). Correlation coefficients for total sleep time between actigraphy and polysomnography were also better using 4 or 5 minutes of immobility than with 10 minutes of immobility in low, medium and high threshold algorithms; 0.79, 0.85, 0.85 (4 minutes: low, medium, high threshold) vs. 0.79, 0.85, 0.86 (5 minutes: low, medium, high threshold) vs. 0.76, 0.80, 0.80 (10 minutes: low, medium, high threshold) respectively. Mean total sleep time with low and medium thresholds using 4 or 5 minutes of immobility produce minimal bias.

Conclusion: We found that a default 10 min. immobility parameter for sleep onset was not as valid as 5 minutes for scoring sleep latency and total sleep time in this clinical sample. In ongoing work, we will expand our sample, further evaluate algorithm scoring parameters, and search for superior alternatives.

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OBSTRUCTIVE SLEEP DISORDERED BREATHING: A SIGNAL ANALYSIS APPROACH

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Introduction: Obstructive sleep disordered breathing can be identified by signals which reflect the airflow through nose and mouth and expansions of thorax and abdomen. These respiratory signals are robust for detection of apneas during the night. Besides apneas, breathing is irregular due to hypopneas and periodic breathing.

Methods: In order to identify breaths, Period Amplitude Analysis (PAA) [1,2] was adapted for the analysis of the respiratory signals. Each sig-

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nal is divided into half waves, i.e. the upward and downward parts of a signal. They are characteristic for a specific breathing pattern and were used to discriminate between quiet breathing and apneas and hypopneas. The features were evaluated relative to a moving reference interval, describing the ongoing breathing pattern. The hypothesis was that obstructive breathing is related to asynchrony between thoracic and abdominal movements. Therefore, in this study a phase angle (ϕ) was estimated and evaluated in order to classify apneas and possibly also hypopneas.

Results: Six recordings were used to validate the algorithm. For a selection of one hour data of each recording, normal half waves were detected with a sensitivity of 95.8%. Apneas and hypopneas were detected with a sensitivity of 87% and a positive prediction of 56%. Our analysis systematically detected more hypopneas. Moreover, ϕ proved to be sleep-state dependent and decreased from $-13(41)^\circ$ in wakefulness to $-40(11)$ in NREM sleep. ϕ was highly variable in REM sleep $-31(28)^\circ$.

Conclusion: PAA appeared to be successful for the analyses of the respiratory signals measured during the night. The half waves are the basis for further analyses and enable the extraction of all relevant information. Furthermore, this method is able to detect apneas and hypopneas successfully and to take artifacts into account. References [1] Feinberg, I. et al. Period and amplitude analysis of 0.5-3 c/sec activity in NREM sleep of young adults. *Electroencephalogr. Clin. Neurophysiol.* 44,202-213, 1978 [2] Gotman, J. and Gloor, P. Automatic recognition and quantification of interictal epileptic activity in the human scalp EEG. *Electroencephalogr. Clin. Neurophysiol.* 43, 513-529, 1976.

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DEFINING THE MINIMALLY IMPORTANT DIFFERENCE FOR THE INSOMNIA SEVERITY INDEX

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Introduction: The minimally important difference (MID) is an important consideration in evaluating changes in patient-reported outcome instruments. The purpose of this analysis was to determine the MID for the Insomnia Severity Index (ISI) by evaluating the association between ISI and health-related quality of life (HRQOL), productivity, and fatigue.

Methods: Analyses used data from a clinical trial evaluating the long-term efficacy of eszopiclone in primary insomnia (N=828). Dichotomized outcome variables at baseline selected from the SF-36v1 Health Survey, Work Limitation Questionnaire (WLQ), and Fatigue Severity Scale (FSS) were regressed onto baseline ISI scores. At 6-months post-treatment, outcome variables were regressed onto ISI change-from-baseline scores.

Results: Improvement in ISI scores was significantly associated with reduced risks of negative outcomes in HRQOL, WLQ, and FSS in both the baseline and change-score models. Deterioration in ISI scores was significantly associated with increased risks of negative outcomes. The magnitude of the regression coefficients was larger in the baseline model versus the change-score model. Odds ratios (ORs) of reduced risk in outcomes improved with ISI improvements (reductions of 2, 4, and 6 points) from the population means: in baseline models, both “feeling worn out” and “unable to think clearly” (ORs=0.67; 0.45; and 0.30, respectively), “feeling fatigued” (ORs=0.64; 0.41; 0.26); in change score models, “feeling worn out” (ORs=0.80; 0.65; 0.52), “unable to think clearly” (ORs=0.82; 0.67; 0.54), “feeling fatigued” (ORs=0.78; 0.61; 0.48).

Conclusion: Based on these results, an MID of 4 points for the ISI is proposed when comparing group means among insomnia patients (baseline model). For individual responder analyses, a 6-point difference is proposed (change-score model).

Support (optional): Support for this study provided by Sepracor Inc.

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RELATIONSHIP BETWEEN LABORATORY POLYSOMNOGRAPHY AND SIMULTANEOUS ACTIGRAPHY IN HEALTHY SUBJECTS

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Introduction: Actigraphy is widely used to estimate sleep time in both clinical populations and experimental protocols. There is controversy, however over the reliability of actigraphy to accurately predict polysomnography (PSG) variables. The aim of this study was to examine the relationship between PSG and actigraphy in healthy subjects.

Methods: For initial analysis N=21 subjects aged 22-44 y, participated in a laboratory controlled sleep restriction protocol. All participants wore an actigraph (Mini-Mitter Actiwatch AW64) during a 10h TIB sleep period at baseline (2200-0800), following an adaptation night. Simultaneously sleep was recorded with PSG using a standard montage (C3-A2, EOG and EMG; portable Sandman system). The actigraphs have a motion detector that counts the amount of movement in one minute epochs. A high threshold algorithm was applied to the actigraphy data that scored an epoch as wake if it exceeded a threshold of activity (defined as >80 activity counts per epoch). The actiware software provided estimations of sleep variables. To examine the relationship between the two measures, PSG and actigraphy derived sleep variables - total sleep time (TST), sleep efficiency (SE), sleep latency (SL), and number of awakenings (#Awake) were correlated.

Results: Statistically significant relationships were found between variables: SL ($r=0.90$, $p<0.001$), TST ($r=0.44$, $p=0.04$) and SE ($r=0.47$, $p=0.03$). However, actigraphy defined #Awake did not show a significant correlation with PSG ($r=-0.12$, $p=0.60$).

Conclusion: Preliminary analysis suggests that there is a relatively poor relationship between actigraphy and PSG in healthy individuals. Actigraphy is not a substitute for PSG, when precision regarding TST, SE, and #Awake is important.

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1040

DROPS IN PULSE WAVE AMPLITUDE: A RELIABLE CORTICAL REACTIVATION SURROGATE

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Introduction: During sleep, sudden drops in pulse wave amplitude are commonly observed simultaneously with microarousals. Their presence is thought to result from a vasoconstriction induced by a central autonomic activation. We sought to determine if pulse wave amplitude drops are associated with cortical reactivation as quantified by the EEG spectral analysis.

Methods: EEG spectral analysis was performed over 5 consecutive epochs of 5 seconds before (#1+2), during (#3) and after (#4+5) the pulse wave amplitude drops (> 20%). A total of 1084 events, from 10 consecutive sleep polygraphic recordings were analysed. The presence or absence of visually scored EEG arousals was also determined (according to AASM criteria) by an investigator blinded to pulse wave signal. EEG spectral analysis was performed over five frequency bands: (beta 17-30 Hz, alpha 8-12 Hz, theta 4-8 Hz, sigma 12-16 Hz, and delta 0.75-4 Hz). The power density in each frequency band was compared between the five epochs using repeated measures ANOVA with a Tukey post hoc test.

Results: The global analysis of all drops in pulse wave revealed a significant increase in EEG power density of all frequencies for the epoch #3 (during) in comparison to the preceding (#1-2) and subsequent (#4-5) ones ($p < 0.001$). Further analysis of pulse wave drops not associated with visually recognized microarousals also revealed a significant increase in EEG power in all frequency bands during the pulse wave drops (epochs #3; $p < 0.001$).

Conclusion: Pulse wave amplitude drops, observed on polygraphic sleep recordings, are associated with a brief increase in the EEG power density. This suggests that drops in pulse wave amplitude are concomitant to cortical reactivation, even in the absence of visually scored microarousal.

Support (optional): Swiss Pulmonary Society Fund for Research

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FURTHER VALIDATION OF THE CLAYTON DAYTIME FUNCTIONING SCALE

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Introduction: Although impairments to daytime functioning are routinely reported as a consequence of sleep disorders, the most commonly used subjective measures focus on daytime sleepiness and not fatigue or cognitive impairments. The Clayton Daytime Functioning Scale (CDFS) has previously demonstrated effectiveness in discriminating between a normal and clinical sleep disordered population. The goal of this study was to further validate and demonstrate reliability of the CDFS.

Methods: From November 2006 through June 2007, a total of 360 patients presenting for clinical polysomnography completed subjective sleep measures, including the CDFS, Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS), and the Pittsburgh Sleep Quality Index (PSQI). Factor analysis was performed on the full version of the CDFS, followed by validation comparison of the subjective daytime functioning scales with the PSQI.

Results: A total of 206 patients completed the CDFS. Factor analysis of the full version CDFS (20 questions) revealed one factor, primarily loading questions related to fatigue, cognitive/performance deficits, and less so for sleepiness. A total of 11 questions were included in the final version (all $r > .07$). Validation comparison to the PSQI revealed significant relationships with all three measures, with the CDFS demonstrating the strongest correlation ($r = .432$, $p < .001$), suggesting the CDFS possesses a stronger relationship with subjective estimates of poor sleep quality than other subjective sleepiness or fatigue measures. Reliability analysis was performed on 40 patients who returned for subsequent testing, resulting in a significant test-retest correlation ($r = .91$, $p < .001$), and a Cronbach's $\alpha = .93$.

Conclusion: The final version of the CDFS (11 items) is a quick, easy to use, and reliable scale that demonstrates a strong linear relationship in estimating the degree of daytime functioning to subjective estimates of poor sleep quality.

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CAUTION IN INTERPRETATION OF DAYTIME FUNCTIONING SCALES: CONSIDERATION OF AGE AND GENDER

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Introduction: Daytime functioning impairments are often reported consequences of disrupted sleep. Subjective estimates of sleepiness and fatigue are used as clinical tools aiding in the interpretation of functional impairments, and often as qualification criteria for treatments. However,

the relationship between subjective daytime functioning estimates and objective polysomnography (PSG) data are not well defined. This study attempts to look at this relationship in a large sample of patients undergoing polysomnography.

Methods: A total of 550 patients who presented to a Midwestern metropolitan sleep center for diagnostic PSG from November 2006-June 2007 also completed subjective sleep measures including the Epworth Sleepiness Scale (ESS), Fatigue Severity Scale (FSS), and the Pittsburgh Sleep Quality Index (PSQI). Inclusion criteria were ages 18-79, no shift work, no prior sleep disorder diagnosis, and no split-night studies.

Results: There was a significant positive correlation between the ESS and the PSQI ($r = .32$, $p < .001$) and the FSS and the PSQI ($r = .14$, $p < .01$). However, all subjective measures had a nonsignificant, negative correlation with the PSG arousal index and apnea/hypopnea index. Comparing groups using a one-way ANOVA according to severity of arousal index (mild < 15 /hr, moderate 15-30/hr, severe > 30 /hr) yielded an interesting negative trend in all subjective measures as well as significant differences according to gender, with females typically scoring higher on subjective measures across age groups. A MANOVA analysis showed a trend for younger patients to score higher on the ESS, FSS, and PSQI as the arousal severity increased. Conversely, older patients tended to score higher on subjective measures with lower arousal severity and lower on subjective measures as the arousal severity increased.

Conclusion: Subjective estimates can be useful tools to aid in the clinical significance of sleep related disorders. However, consideration should be given to the interpretation of the results, especially with age and gender.

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CONTINUOUS MICRODIALYSIS MEASURES OF HISTAMINE WITH SLEEP RECORDINGS IN FREELY MOVING MICE

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Introduction: Microdialysis is a powerful method to monitor the extracellular levels of various neurotransmitters (such as monoamines, acetylcholine, and peptides) in behaving animals. With this technique and simultaneous sleep recordings, the fluctuation of these neurotransmitters can be correlated with homeostatic and circadian sleep/wake changes in relatively high time resolutions (10 minutes to 30 minutes). The use of this technique for mice are limited, especially for long hour monitoring, since maintaining inlet and outlet tubes and EEG cables are difficult in small and actively moving animals. We made a smaller version of a floor rotating cage specifically for mice microdialysis experiments, and the results will be presented.

Methods: EEG/EMG electrodes and one microdialysis probe (Bregma -0.26, L = 0.5, D = -5) were implanted in 3 mice. After 3 days of accommodation period, microdialysis perfusate was collected in a 30-minute sampling bin while sleep was continuously monitored over 96 hours in automated floor rotating cages (Osakamicro, Suita, Osaka). This rotation cage does not require a commutator or swivel, and when large torque was detected from the twists of fluid lines and wires for EEG and EMG recordings, the floor of the chamber automatically rotates in the opposite direction to disentangle the lines. For this study, histamine contents in microdialysis perfusate were measured by HPLC.

Results: We have succeeded in collecting microdialysis perfusate of freely moving mice with sleep recordings for over 72 hours. As we have previously reported in rats, histamine contents exhibit clear diurnal fluctuation patterns, and contents were high during dark (active) periods and low during light (resting) periods. Furthermore, histamine contents were significantly correlated with the amount of wakefulness scored during the same 30 minutes time bins.

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Conclusion: Our results demonstrate that our microdialysis method does not disturb the sleep/wake patterns of mice and allows us to collect the perfusate for neurotransmitter measures (with simultaneous sleep monitoring) for several days. This method is very useful for evaluating neurochemical changes associated with sleep changes in various mice with genetically engineered and/or disease models.

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TOTAL SLEEP, OPTIMAL SLEEP AND PERCENT OF OPTIMAL SLEEP MEASUREMENTS

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Introduction: Individual differences in sleep need (Van Dongen et al., 2003) and frequent sleep restriction (National Sleep Foundation, 2005) results in broad individual differences in experienced sleep. While self-reported total sleep time reflects sleep obtained, it does not account for individual sleep need. The present study assessed whether percent of optimal sleep was a better overall measure of sleep than total sleep time.

Methods: 67 undergraduates at Baruch College maintained a sleep diary for 8 nights. The variables of interest were total sleep time (TST), optimal sleep time (OPT) and a composite of sleep quality (satisfaction, feeling refreshed, general evaluation of sleep).

Results: TST and OPT differed significantly in general ($M_s = 7.04$ and 8.41 hrs, $t(66) = 12.52$, $p < .001$), and for 7 of the 8 nights. Inspection of the overall SDs revealed greater fluctuation in TST than OPT ($M_s = 1.49$ and 0.81 hrs, $t(66) = 7.54$, $p < .001$). This was reinforced by a significant quadratic trend for TST, $F(1, 58) = 7.68$, $p = .007$, and lack of comparable polynomial trends for OPT. Percent of optimal sleep (POS), equal to $(TST \div OPT) \times 100$, was compared with TST. POS and TST were correlated with the sleep quality composites for each night and statistically compared (Warner, 2007). For 6 of the 8 pairs, correlations with POS were stronger in magnitude than those with TST. Further, 2 of these 6 pairs differed significantly. This is a preliminary indication of POS's advantage over TST.

Conclusion: Sleep diaries revealed that individuals obtained less sleep than they needed. Given the variability in total sleep time, a new variable accounting for optimal sleep termed percent of optimal sleep (POS), may be a better self-report measurement. These findings need replication and extension to performance variables before POS can be used in assessments.

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THE DIFFERENCE IN SLEEP LATENCY IF SLEEP ONSET IS DETERMINED BY SLOW EYE MOVEMENTS COMPARED TO ALPHA RHYTHM ATTENUATION

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Introduction: Polysomnography is used in the diagnosis and the management of many sleep disorders. One of the main functions of Polysomnography is to establish sleep onset and sleep latency. The AASM Manual for the Scoring of Sleep and Associated Events recommends that in subjects who generate alpha rhythm, to score stage N1 if alpha rhythm is attenuated and replaced by low amplitude, mixed frequency for more than 50% of the epoch, and in subjects who do not generate alpha rhythm to score stage N1 with the earliest commencing of slow eye movement as one of the phenomena to determine sleep onset in these subjects. As slow eye movements often commence before attenuation of alpha rhythm, sleep latency may be slightly shorter for some individuals

who do not generate alpha rhythm. The aim of this study is to evaluate if the difference in sleep latency is significant if slow eye movements were used to establish sleep onset as compared to the attenuation of alpha rhythm.

Methods: We studied the nocturnal polysomnography of 57 adult patients (35 M, 22 F), age between 18-75 years, who had sleep studies at an accredited sleep laboratory affiliated with university hospital. All these patients had good alpha rhythm. We reviewed the EEG (C4-A1, C3-A2, O1-A2, O2-A1) to determine sleep onset as the first epoch of sleep using alpha rhythm attenuation and using the commencement of slow eye movements. We calculated sleep latency from the time of light out till the time of the first epoch of sleep using these two rules.

Results: Using the alpha rhythm attenuation rule, the mean sleep latency for these patients was 20.66 minutes (20.66 ± 15.41); whereas the mean sleep latency was 18.09 minutes (18.09 ± 13.97) by using the slow eye movements commencement. And using the t-test, there was extremely statistically significant difference between sleep latency using the alpha rhythm attenuation and sleep latency using slow eye movements commencement rule (2.64 ± 2.32 , P value < 0.0001). The difference in sleep latency between these two rules ranged from 0-9 minutes. Six patients who had sleep latency more than 5 minutes by the alpha rhythm attenuation rule, their sleep latencies were less than 5 minutes using the slow eye movements rule.

Conclusion: Sleep latency is significantly shorter if sleep onset is determined by using slow eye movements compared to alpha rhythm attenuation.

Support (optional): Further studies with larger numbers are warranted to evaluate this finding, and whether this difference in sleep latency should be considered in clinical practice, especially when shortened sleep latency might affect the social and professional lives of some patients such as commercial drivers.

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SLEEP DISTURBANCE IN RETT SYNDROME AS DOCUMENTED BY POLYSOMNOGRAPHY

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Introduction: Rett Syndrome (RS) is a severe neurodevelopmental disorder, which mainly affects females. It is generally caused by specific genetic mutations in the MECP2 gene. There is a high prevalence of sleep problems in subjects with this disorder. A recent report evaluating using sleep questionnaires noted that sleep problems were highest in cases with the particular genetic mutations associated with RS. No previous study has evaluated a cohort of subjects with RS using objective sleep measurement with polysomnography.

Methods: Parents of subjects followed in the Israeli RS Clinic were contacted and invited to participate in a study with overnight polysomnography to evaluate sleep architecture in RS. Parents completed sleep questionnaires and children were prospectively enrolled. Polysomnography included a single night with expanded EEG montage and video-monitoring.

Results: Ten females with Rett Syndrome (7 with genetic confirmation) were evaluated. Nine were between 2 to 6 years, and one was 29 years old. The data from two subjects was not included due to the inability of these subjects to sleep during the evaluation. Eight subjects had sufficient sleep duration (5.5 to 6.5 hours) to evaluate sleep architecture. In these subjects sleep efficiency ranged from 78 to 98% (mean 88.5). Sleep architecture was normal in 3 subjects, abnormal but without a consistent pattern in 5 subjects. Obstructive sleep apnea was detected in 5 of the 10 subjects; mild in 4 and moderate in 1. Three subjects had epileptiform activity during sleep. In subjects with sleep apnea, parents had not recognized or sought medical attention for this problem. No con-

sistent abnormality was detected based on specific genetic mutations in this small series.

Conclusion: It is difficult for children with severe neurodevelopmental disorders such as RS to comply with overnight polysomnography due to the need to sleep in an unfamiliar environment. In this study, sleep efficiency was reduced to <88% in half the subjects. Sleep architecture was abnormal in 5 of 8 subjects. The most common abnormality detected was OSAS in half of the subjects. Sleep-related breathing disturbance, if undetected by parents may be further contributing to the subjects' poor sleep, increased seizure activity and daytime fatigue. Further research is needed to determine the role of detecting and treating OSAS in this population and to confirm previous findings of the relationship between sleep problems and subjects with RS and confirmed genetic mutations.

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SEX DIFFERENCES IN HUMAN ADOLESCENT NOCTURNAL ACTIVITY: IMPLICATIONS FOR ACTIGRAPHIC SLEEP MEASUREMENT

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Introduction: Current data show discrepant findings for sex effects on activity patterns of humans, and few studies investigate adolescents. One study that examined sex effects on activity in adolescence (13- and 14-year-olds) found that girls have less nocturnal activity than boys (Gaina et al., 2005). Here we examine sex differences for actigraphic night-time activity levels in high-school students.

Methods: 56 students (at least 10 from grades 9-12, 61% female) kept sleep logs and wore actigraphs (AMI Mini-motionlogger) for 16 weeks and had polysomnographic (PSG) studies near weeks 8 and 16.

Results: Boys had significantly more activity counts per 1-minute epoch than girls during night-time actigraphy (M [SD]: 12.9 [5.5] vs. 10.2 [3.6], $p = .027$). As estimated by actigraphy (Sadeh algorithm), boys had significantly more time awake (M [SD]: 55 [39] vs. 36 [26] minutes, $p = .037$), less time asleep (M [SD]: 401 [47] vs. 440 [36] minutes, $p = .001$), and lower sleep percentage (M [SD]: 88.6 [7.6] vs. 92.6 [5.2], $p = .025$) than girls. In contrast, sleep interval (actigraphic sleep onset to wake time and sleep diary time in bed) showed no significant sex differences. PSG recordings also showed no sex differences for sleep onset latency, wake after sleep onset, total sleep time, total dark time, or sleep efficiency at either week 8 or week 16.

Conclusion: The major finding of this analysis is that adolescent boys move more during the night than girls, and this difference is reflected in the actigraphic estimates of sleep and wake during the night. Sleep diary records indicate that the sex difference in sleep is not due to boys allowing less time for sleep, given that both girls and boys averaged around 8 hours in bed by self-report. Furthermore, no sex differences in sleep were measured by PSG at 2 time points. Taken together, these data indicate that sleep scoring algorithms may need to account for sex differences in nighttime activity levels.

Support (optional): MH045945

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INCREASED USE OF ACTIGRAPHY FOR SLEEP RESEARCH

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Introduction: Actigraphy is used to estimate sleep-wake duration, circadian patterns, nap periods during normal activity times, and movement during periods of normally low activity. Because a large number of studies using actigraphy were noted in the 2007 APSS abstracts, we evaluated the extent to which the use of wrist actigraphy by our sleep research community is increasing.

Methods: A search of the APSS abstracts (Sleep; 2000: Volume 23, Abstract Supplement #2 and Sleep; 2007: Volume 30, Abstract Supplement) was conducted searching for "actigraph" and for various PSG related terms (PSG, EEG, Sleep Stages, REM etc.). Each abstract was scanned to determine if actigraphy, PSG, or both were used in human research. Also, CRISP, an NIH database, was searched for "human sleep" research, and additionally for keyword "actigraph", for awards in the years 2000 and 2007.

Results: Of the 780 APSS 2000 Abstracts, 258 abstracts reported human sleep recording, 214 (83%) using PSG alone, 32 (12%) using actigraphy alone, and 12 (5%) using both. Of the 1124 APSS 2007 Abstracts, 393 abstracts reported human sleep recording, 302 (77%) using PSG alone, 60 (15%) using actigraphy alone, and 32 (8%) using both. In 2000, CRISP listed 25 awards for research on human sleep using actigraphy; by 2007 the number had grown to 55. In the interval from 2000 to 2007, total NIH CRISP listings with keywords sleep and human (including actigraphy grants) dropped about one third from 760 to 505.

Conclusion: In the interval from 2000 to 2007 the percentage of sleep recording abstracts containing actigraphy has increased from 17% to 23%. Over the same period, NIH funded actigraphy research grants increased from 25 to 55 despite a sharp reduction in the total number of human sleep projects funded, from 760 to 505. The role of actigraphy in human sleep research has increased in the interval between 2000 and 2007.

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SIGNAL AND INFORMATION LOSS IN LEVEL 1 AND LEVEL 2 POLYSOMNOGRAPHIC EVALUATIONS

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Introduction: Sleep disordered breathing (SDB) is common health condition adversely effecting 2-11% of the general population. Diagnosis has traditionally been performed in laboratories under constant observation by a technician (Level 1). Polysomnography has undergone significant revolution with increased micro-processing capabilities, miniaturization of mass storage devices, and sensor miniaturization. This investigation assessed ambulatory polysomnography (Level 2) as a method for diagnosing various sleep disorders.

Methods: For this investigation, patients were separated into three groups: patients undergoing complete polysomnography under direct technician observation (Level 1), patients undergoing ambulatory polysomnography without direct technician observation (Level 2), and patients who undergoing Level 2 recordings who slept in the laboratory setting without technician interaction (Level 2a). Subjects were matched by sex and body mass index (BMI). Each recording was a minimum of 6 hours. Signal loss and scoring capability were tabulated epoch by epoch for each physiologic channel.

Results: Analysis demonstrated that, with the exception of abdominal effort and chin EMG, no statistical differences were detected in the number of signal loss periods comparing Level 2, Level 2a, and Level 1 recordings. Level 2 and Level 2a recordings demonstrated significantly more epochs of signal loss ($P < 0.05$; X²) than did the Level 1. Epochs which lost the ability to score respiratory events were significantly greater among Level 1 recordings compared to Level 2 and Level 2a recordings. This was related to the loss of airflow through 70, 87, and 157 epochs, respectively and oximetry. These 157 epochs represented only 5.4% of the sleep time among Level 2 recordings, however. Sleep staging was not significantly different, with 16, 28, and 34 epochs respectively, being lost. A high prevalence of chin lead loss occurred among all the groups (59, 66, and 67 loose leads). The total number of epochs with chin EMG signal loss was significantly less among Level 1 recordings

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(344, 328, and 597, respectively). This loss did not significantly affect the ability to sleep stage recordings.

Conclusion: Maximum information loss was 5.5% among Level 2 recordings versus 1.9% for Level 1 recordings. Level 2 recordings can adequately serve as a cost-efficient alternative to laboratory based Level 1 recordings.

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THE SLEEPDEST MSLT PATIENTS SLEEP MORE ON PRE-MSLT POLYSOMNOGRAMS WHILE MEDICATIONS SHOW NO EFFECT ON MSLT RESULTS

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Introduction: Ideally, Multiple Sleep Latency Testing (MSLT) is conducted in drug free patients following eight hours of sleep. However, medication withdrawal may not be practical and patients may not sleep eight hours on prior polysomnogram. We hypothesized that medications and preceding night's sleep in clinical patients would alter MSLT results.

Methods: Following IRB approval, we examined 205 patients completing diagnostic polysomnography and MSLTs between January 2005 and June 2007. We grouped then into five medication categories: none, sedating, stimulating, combination (stimulating and sedating), or mixed-effects medications. The combination group included patients taking, for example, modafinil and temazepam. The mixed group included, for example, patients taking antidepressants with potentially sleep disruptive or sedating effects. The MSLTs followed prior night polysomnography.

Results: Patients' drugs did not obviously affect the MSLT, which varied from 6.5±4.2 (mean±SD) for stimulating drugs group to 9.7±4.8 minutes for the combination drug group ($F=1.8$, $df=4$, 200 , $p=ns$). The number of drugs taken by patients in the different MSLT categories (0 to <5 minutes, $n=65$; 6-10 minutes, $n=71$; >10 minutes, $n=69$) varied from 3.1±3.5 to 3.2±3.4 to 3.1±2.9 from the sleepiest to most alert groups ($F=0.035$, $df=2$, 202 , $p=ns$). Controlling for BMI and age did not result in a significant effect for either analysis. In contrast, polysomnographic total sleep time (TST) was related to MSLT scores with the sleepiest group sleeping the most and the most alert group sleeping the least. Means were 420±66, 393±74, and 374±72 minutes respectively ($F=8.59$, $df=2$, $p<0.001$). Controlling for age, BMI, and number of medications did not change this relationship.

Conclusion: Chronic medication use by sleep disorders center patients did not show a relationship to MSLT scores. In contrast to sleep manipulation in normal subjects, clinical patients who slept more the night before, fell asleep more quickly on the MSLT indicating a pervasive sleepiness.

Support (optional): Internal

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VALIDATION OF A COMMERCIALY AVAILABLE RODENT POLYSOMNOGRAPHIC SCORING ALGORITHM

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Introduction: We have assessed the sensitivity and specificity of a commercially available rodent electroencephalography (EEG) scoring program. This algorithm derives sleep-wake state through spectral analysis (SA) of cortical and hippocampal EEG and electromyography (EMG) signals as well as physical activity /movement. An additional feature enables the user to manually adjust the sensitivity of the software's decision algorithm to optimize determination of sleep-wake states.

Methods: Polysomnographic data was collected from 7 rats and 3 mice, each over a 24-hour period. A single observer then scored each record using 10-second epochs to define states of wake (W), non-rapid eye movement (NREM), or REM sleep. Wake was defined by the presence of low amplitude fast frequency EEG in conjunction with moderate to high amplitude EMG. NREM was defined by the presence of high amplitude low frequency delta wave activity that occupied at least 20%, but no more than 50%, of the epoch in conjunction with low amplitude EMG. REM sleep was defined by the presence of hypersynchronous theta wave activity centered near 6.5 Hz, low amplitude fast frequency EEG and EMG activity at its nadir. Once each polysomnographic record had been manually scored, the rodent EEG scoring program (Neuro-score) was used to score each file. Kappa coefficients determine levels of agreement between these two scoring methods for each rat's 24-hour data file.

Results: Hand scoring was compared with automated scoring in 10 rodents that had undergone continuous EEG recordings for at least 24 hours, yielding 93,497 ten second epochs. Levels of agreement between the 10 hand-scored and automatically scored files were: 1) 83.7%, 2) 83.1%, 3) 89.8%, 4) 91.4%, 5) 89.7%, 6) 87.5%, 7) 89.3%, 8) 89.9%, 9) 90.6%, 10) 92.0%, yielding a mean agreement level of 88.7%.

Conclusion: Significant levels of agreement were achieved between polysomnographic variables scored manually and then automatically with the rodent scoring plug-in module. We conclude that this automated scoring algorithm, can detect and score the states of wake, NREM and REM sleep in both rats and mice. Ongoing validation of newly developed features such as: a) batch processing, 2) epileptiform spike activity, and 3) analysis of EEG and EMG power/frequency components, will better define the applicability of this automated analysis program for scoring rodent polysomnographic data.

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COMPARISON OF VISUAL AND AUTOMATED ANALYSIS OF ESOPHAGEAL PRESSURES DURING POLYSOMNOGRAPHY

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Introduction: Analysis of esophageal pressure (Pes) data generally has relied on time-consuming quantification by visual inspection of a limited number of respiratory cycles selected from a polysomnogram. We developed and sought to validate a new automated method to quantify esophageal pressure swings (Δ Pes).

Methods: Retrospective data was obtained from 40 patients (14 men, 26 women aged 43 ± 11 [s.d.] years) who underwent full-night diagnostic polysomnography between October 2005 and March 2006. The sample reflected a wide range of SDB severity, with apnea/hypopnea indices ranging from 0.3 to 88.1 (mean 11.2 ± 16.7). Esophageal monitoring had been requested by the referring clinician and was used successfully without technical complications. The Pes signal was low pass filtered to remove cardiovascular artifact. Δ Pes was then calculated as the difference between a local minimum following a local maximum. For comparison, visual scoring followed our clinical laboratory guidelines, which require representative samples from all sleep states and generate at least 30 samples per record.

Results: The mean Δ Pes that was automatically computed for each subject correlated well with that derived by human eye (Spearman rho = 0.86, $p < 0.0001$). A Bland and Altman analysis comparing the automatically computed variable to the results of human scoring showed reasonable accuracy with only a small bias: differences between the visual and automated methods were within one standard deviation of the mean difference for 37 of the 40 subjects. On average over all subjects, the human scoring was 4 cm of water lower than the automated scoring.

Conclusion: Automated Δ Pes values, in comparison to those generated manually by trained technologists, show good accuracy, incorporate

nearly all possible data points, save time, and may facilitate continuous quantitative analysis of work of breathing trends and variation.

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A NOVEL WIRELESS PSG SYSTEM FOR INPATIENT SLEEP EVALUATION

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Introduction: Wireless PSG devices in the hospital are expected to grow as they greatly facilitate critical sleep assessment on the ward. Users of wireless inpatient PSG, however, are often faced with a number of technical challenges that include radio frequency (RF) interference, equipment size, and others. Here, we describe a novel wireless PSG system that is highly portable and configurable, which greatly simplifies implementation in the hospital environment.

Methods: A new wireless PSG system dedicated for inpatient sleep evaluation was developed. It consists of three components: patient module, “gateway”, and review module. The patient module is wearable; it collects and transmits up to fourteen channels to the “gateway”. The wireless transmission protocol is flexible and can use either the 2.4 GHz or 900 MHz frequencies making it adaptable to multiple RF environments. The “gateway” is a small tablet PC mounted on an easy-to-move IV pole; it receives the data from the patient’s module and relays it to the review module via either wireless or wired hospital connectivity. The review module, which can be located many floors away, allows real time review and scoring.

Results: An analysis of the RF environment in three major hospitals (two in Cleveland and one in Baltimore) showed busy 2.4 GHz band in two hospitals (Cleveland) and occupied 900 MHz in the third (Baltimore). To avoid interference, patient modules with data transmission bands that fell outside the used frequencies were selected: 900 MHz for Cleveland hospitals, 2.4 GHz for Baltimore. Assigning transmission frequency within the occupied bands resulted in slower or interrupted review of PSG data. System is currently being used preoperatively in a large clinical study on cardiac surgery inpatients.

Conclusion: Expanding the reach of sleep evaluation into the hospital room will require wireless inpatient PSG solutions that are configurable to best suit the demanding radio frequency environments.

Support (optional): This research was supported by NIH.

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VALIDATION OF THE EPWORTH SLEEPINESS SCALE IN THE BRAZILIAN PORTUGUESE LANGUAGE

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Introduction: The Epworth Sleepiness Scale (ESS) is widely used for the assessment of daytime sleepiness in patients with sleep disorders. The aim of this study was to validate a Brazilian Portuguese version of ESS.

Methods: The Brazilian Portuguese version (ESS-BR) was developed according to the following steps: a) translation; b) back-translation; c) test and retest in bilinguals; d) comparison between translation and back-translation performed by group of experts. Over a 22 month study period, the ESS-BR was then applied in a group of consecutive patients who were submitted to overnight polysomnography with a clinical suspicion of Obstructive Sleep Apnea Syndrome (OSAS), insomnia and primary snoring. A control group was composed of subjects with a history of normal sleep habits, without noticed snoring.

Results: A total of 114 patients and 21 controls completed the scale and had overnight polysomnography done. The 8 item scores of the ESS-BR had an overall reliability coefficient (Cronbach’s alpha) of 0.83, indicating a high degree of internal consistency. Total number of subjects in the groups was: 21 normal controls, 34 primary snoring, 21 insomnia and 59 OSAS. The mean (\pm SD) ESS-BR score was: 5.24 ± 2.98 for control subjects; 8.82 ± 3.37 for primary snoring; 5.29 ± 2.61 for insomnia; 13.51 ± 5.06 for OSAS. One-way ANOVA demonstrated significant differences in ESS-BR scores among the four diagnostic groups ($p < 0.001$). Posthoc tests between paired groups showed that the ESS-BR scores for insomniacs did not differ from controls ($p = 0.999$), as noticed in the original study. Scores for OSAS and primary snorers were significantly higher than controls ($p < 0.001$ and $p = 0.001$, respectively). The ESS-BR scores for OSAS were significantly higher than primary snorers ($p < 0.001$).

Conclusion: Our data validate the ESS-BR for application in Brazilian Portuguese-speaking populations. No major cultural adaptations were necessary during the process of validation. Despite relevant influences of language and cultural background, ESS-BR is a valuable tool for clinical management and research.

Support (optional): FIPE/HCPA, PPGCM/FAMED

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VALIDATION OF THE PITTSBURGH SLEEP QUALITY INDEX IN THE BRAZILIAN PORTUGUESE LANGUAGE

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Introduction: The Pittsburgh Sleep Quality Index (PSQI) is a questionnaire which assess sleep quality and disturbances during a month time period. It is a valuable tool for research purposes. The aim of this study was to validate a Brazilian Portuguese version of PSQI.

Methods: The Brazilian Portuguese version (PSQI-BR) was developed according to the following steps: a) translation; b) back-translation; c) test and retest in bilinguals; d) comparison between translation and back-translation performed by group of experts. Over a 22 month study period, the PSQI-BR was then applied in a group of consecutive patients who were submitted to overnight polysomnography with a clinical suspicion of Obstructive Sleep Apnea Syndrome (OSAS) and insomnia. A depression group was composed of patients from mood disorders unit of the Psychiatry Department. A control group was composed of subjects with a history of normal sleep habits, without noticed snoring.

Results: A total of 83 patients and 21 controls completed the questionnaire and had overnight polysomnography done. The 7 component scores of the PSQI-BR had an overall reliability coefficient (Cronbach’s alpha) of 0.82, indicating a high degree of internal consistency. The groups were composed of 43 OSAS, 21 insomnia, 19 depression and 21 normal controls. The mean (\pm SD) PSQI-BR score was: 2.48 ± 1.99 for control subjects; 8.14 ± 3.97 for OSAS; 12.81 ± 3.68 for insomnia; 14.53 ± 3.67 for depression. One-way ANOVA demonstrated significant differences in PSQI-BR scores among the four diagnostic groups ($p < 0.001$). Posthoc tests between paired groups showed that scores for OSAS, depression and insomnia were significantly higher than for controls ($p < 0.001$). PSQI-BR scores for insomnia did not differ from depression ($p = 0.602$), but both were higher than for OSAS ($p < 0.001$).

Conclusion: Our data validate the PSQI-BR for application in Brazilian Portuguese-speaking populations. No major cultural adaptations were necessary during the process of validation.

Support (optional): FIPE/HCPA, PPGCM/FAMED

1056

HOME SLEEP TESTING WITH A TYPE III PORTABLE MONITOR

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Introduction: SleepScout offers up to 9 channels of data exceeding the Portable Monitoring guidelines issued by AASM. This simple, compact tool allows for monitoring of sleep disordered breathing to be made outside the traditional sleep lab, suitable for the patient's home or hospital setting.

Methods: Nine subjects were given the device with an instruction sheet for self-hook up sensor placement. On the following day the patients returned the system, a registered polysomnographic technologist imported and scored the data from an SD Memory Card. After scoring, a standardized report using was generated. Patients were asked to complete a brief questionnaire on the ease of use and degree of complexity for self hook-up using the instruction sheet.

Results: The average hook-up time was 20 minutes, including all EMG and ECG sensors. The subjects were asked to hook-up all of the channels by themselves including ECG and leg EMG. All volunteers clipped the system to the thoracic effort belt, ensuring collection of body position sensors, located within the device. Some early subjects had difficulty placing the cannula. The instruction sheet was modified and later subjects reported no difficulties and had improved data quality. Throughout these studies the majority of sensors stayed in place, allowing high quality recording. During one study, the cannula was displaced, resulting in no airflow or snore recording for a portion of the night. All other signals produced excellent quality readings. The respiratory disturbance index (RDI) ranged from 3.3 events/hour to 14.4 events/hour. Successful reports were generated for all studies with imported data.

Conclusion: This study has demonstrated an easy-to-use home monitor for the detection of primary sleep disorders. Subjects were able to hook themselves up with the help of simple instructions. The same system can be used for home testing as well as hospital inpatient testing.

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REMOTELY ATTENDED PSG STUDY WITH A 22-CHANNEL WIRELESS SYSTEM

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Introduction: Remotely attended sleep studies were recorded using a wireless 22-channel PSG system and a home monitoring gateway. The home monitoring gateway uses mobile broadband internet service to transmit patient data and video in real time from a subject's home. The Sapphire PSG 22-channel system was used to collect PSG data.

Methods: The subjects were hooked up by a registered PSG technologist. Collodion was used on the six EEG electrodes. Snap leads were used for the EOG, EMG and ECG electrodes. Respiratory Inductance Plethysmography (RIP) effort belts were used. The subjects were sent home with the sleep testing equipment. The subject called the technologist fifteen minutes before lights out. The technologist conducted bio-calibrations and verified the integrity of the signals over the remote connection. During the virtually attended study the technologist was able to view and annotate the study.

Results: Home studies were recorded on two subjects. Both studies were of excellent quality. The sensors stayed in place throughout the night. The mobile broadband connection was good for the first study allowing the technologist to annotate the data and view the video throughout the study. The signal strength of the broadband network was low at the second subject's home, causing the remote connection to be lost a few times during the night. The data was successfully recorded locally and the remote technologist was able to check the data periodically. Both studies were successfully scored and reports were generated.

Conclusion: This study has demonstrated an easy-to-use home monitor that allows for full remotely attended PSG studies to be conducted almost anywhere. This system is ideal for testing patients who may have difficulty coming to the sleep lab such as pediatric patients or those that are elderly or in chronic pain.

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AUTOMATIC DETECTION OF ELECTROENCEPHALOGRAM (EEG) SLEEP DISCONTINUITY

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Introduction: Sleep fragmentation is associated with a range of health conditions including day-time sleepiness. The visual detection of sleep fragmentation, specifically arousals, relies on manually identifying discrete changes in EEG frequency. Although, to maximize reliability, 3-secs is conventionally used as a minimal duration criteria, manual scoring may be still unreliable. Additionally, this restriction may reduce sensitivity to detect clinically important sleep fragmentation. The aim of this work is to develop an automated EEG discontinuity detection method to reliably identify episodic changes in EEG frequency of short duration. This may provide a useful tool for researchers studying the association of EEG discontinuity with other PSG derived events and clinical correlates. We evaluate the method in terms of its ability to predict sleepiness.

Methods: Analyses were based on 15 studies selected to be representative of a range of sleep apnea. An automated discontinuity detection algorithm based on localizing EEG in time and frequency is developed to detect transient and abrupt changes in the EEG (i.e., Automatically detected Discontinuity Index, ADI). A Filtered Discontinuity Index (FDI) was additionally derived from ADI by aggregating all events that are less than one second apart with at least 2 second durations for the aggregated events. The correlations among the automatic results of this algorithm are compared with the discontinuity index derived from visual scoring using standard criteria (VDI). The correlation of each index with sleepiness, assessed by the Epworth Sleepiness Score (ESS) is also assessed.

Results: Since the frequency of NREM abrupt changes in EEG are prominent in stage 2, the analysis was restricted to this stage. The VDI and ADI were strongly correlated ($r=.88$; $p<.01$). The correlation coefficients of the ESS with ADI was 0.52 ($P<.03$). The correlation coefficients with ESS were somewhat higher for the VDI ($r=0.63$; $p<.01$), and were highest for the FDI ($r=0.68$; $p<.01$).

Conclusion: Our data suggest that the aggregated EEG discontinuities (quantified by automated, novel measures) during sleep with duration that exceeds a given minimum threshold (e.g. 2 second) may be useful as measures of clinically significant outcomes, such as sleepiness. Although further validation is needed, the proposed automatic algorithm may provide a useful tool for detecting such EEG discontinuities that is both sensitive and reliable.

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1059

GENDER DIFFERENCES IN OBJECTIVE MEASURES OF SLEEPINESS IN NARCOLEPSY

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Introduction: Daytime consequences of sleep disorders can be measured with objective (physiological and behavioral) methods. The multiple sleep latency test (MSLT) remains the most well-established objective measurement of excessive daytime sleepiness. The pupillometric sleepiness test (PST) is another measure of the intrusion of sleepiness into waking tendency and, unlike the MSLT, can potentially quantify alertness.

Methods: We studied 19 patients previously diagnosed with narcolepsy (13 Female, 6 Male) and 57 healthy controls with no sleep complaint and no diagnosed sleep disorder (30 Female, 27 Male). All subjects underwent overnight polysomnography followed by alternating sessions in the PST and the MSLT (four trials each). Sleepiness was quantified according to the mean sleep latency (SL) derived from the MSLT and the mean pupillary unrest index (PUI) computed from the PST. We computed ROC curves to compare the sensitivity and specificity of SL and PUI in discriminating narcoleptic subjects from normal controls.

Results: At fixed sensitivities to detect narcolepsy of 30%, 50%, 75% and 90%, the following specificities were achieved, respectively: PUI-Female = 96.7%, 93.3%, 83.3%, 50%; PUI-Male = 92.3%, 71.2%, 65.4%, 57.7%; SL-Female = 96.7%, 91.7%, 90%, 83.3%; SL-Male = 92.3%, 63.5%, 55.7%, 41.2%. The specificity for detecting narcolepsy at all sensitivity levels up to 90% was significantly greater than chance level for both measures ($p < 0.05$ for each). The specificity of SL was greater than PUI for detecting narcolepsy in female subjects, while the PUI achieved better specificity for detecting narcolepsy in male subjects.

Conclusion: We conclude that the PST performed better than the MSLT in detecting narcolepsy in male subjects while the MSLT performed better than the PST in detecting narcolepsy in female subjects.

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A CO-MORBIDITY MODEL TO IDENTIFY SEVERITY OF OBSTRUCTIVE BREATHING DURING SLEEP - PHASE II RESULTS

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Introduction: Obstructive Sleep Apnea (OSA) has been associated with increased risk of hypertension, stroke and heart failure. It has been associated with increased risk of traffic accidents. OSA may influence breathing during anaesthesia. These events increase the incidence of morbidity and mortality and contribute to an increase in healthcare cost. Currently there is no cost effective, efficacious and validated model of identifying patients at risk of OSA in the general population. The prevalence of OSA was approximately 2-4% of men and 1-2% of women, aged between 30-65 (Young, 1993). There is growing concern among clinicians regarding the identification of OSA patients 'at risk' and to improving clinical outcomes through appropriate airway management. There is a need for an inexpensive, time effective model to identify OSA. This study determines the accuracy and efficacy of a new questionnaire - Identification of Sleep Apnea Questionnaire (ISAQ).

Methods: 102 consecutive male and female subjects were recruited through a non-psg testing facility. Subjects were currently not treated for OSA. Each subject underwent overnight diagnostic at home ambulatory

study and completed the Epworth Sleepiness Scale (ESS) and the 16-item Identification of Sleep Apnea Questionnaire (ISAQ). Completed questionnaires were correlated with ambulatory results for each subject. All physiological measurements and ESS were compared to individual ISAQ items and the ISAQ total score. Both ESS and ISAQ scores range between 0 - 24.

Results: 30% = Female, 70% = Male. Males had significantly higher RDI than females. The most significant questions were affirmative answers to 'snoring' (87%) 'witnessed apneas' (47%), 'hypertension' (50%) and nocturnal gastric reflux (29%). Severity of sleep disordered breathing increased with an increase of affirmative answers in any of these items. The total score of the questionnaire increased as the severity of SDB increased. The ESS had no correlation to severity of SDB.

Conclusion: The 16-item co-morbidity questionnaire accompanied by simple physiological measurements, can indicate moderate to severe sleep disordered breathing. Further studies in Phase III are planned to check the weightings applied to each item.

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COMMON INPUT - DIFFERENT OUTPUT: PSA AS CONDUCTED ACROSS TWO WELL ESTABLISHED PLATFORMS

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Introduction: There are many dedicated Power Spectral Analysis (PSA) packages available, however no cross validation studies have, to our knowledge, been published. Even with identical input data the output may vary between software packages, partially because of program set-up. In this study identical data was used to compare the PSA analytic output of two different commercially available software packages.

Methods: Four nights of PSG data were collected from different subjects using Grass Gamma software and Grass Model 15 amplifiers. EDF data from these acquisitions were submitted to two PSA packages (Stellate Harmonie Luna and Delta Software Pass Plus). The PSA settings in both analysis packages were matched as closely as possible (e.g., spectral window size, overlap between PSA windows, tapers, pre-processing routines, etc. - Note: band definitions were discordant by 0.25Hz). PSA analyses were conducted for a single EEG channel (C3-A2), and statistical comparisons were performed in SAS.

Results: Power values were computed and compared for the following bands: Delta (0.5-2.0Hz), Theta (2.0-7.5Hz), Alpha (7.5-12Hz), Sigma (12-14Hz), Beta1 (14-20Hz), Beta2 (20-35Hz), Gamma (35-45Hz), and Omega (45-125Hz). Significant differences ($p < .05$) in both absolute and relative power were found for all spectral bands except Sigma, with the largest differences appearing in the lower frequency bands.

Conclusion: The fact that the two packages assessed yielded significantly different absolute and relative power profiles suggests investigators need to be cautious when considering cross-laboratory QEEG findings. The lack of standardization within the sleep field for PSA setup parameters (e.g., PSA window size, bin definition, type of taper, pre-processing detrends, etc.), along with each package varying with respect to the available user-definable setup parameters, may help explain some of the inconsistent findings in the literature. Importantly, these results do not suggest that either of the programs evaluated produces superior or more veridical data.

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RELIABILITY OF CYCLIC ALTERNATING PATTERN (CAP) DETECTED BY MONOPOLAR DERIVATIONS

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Introduction: Cyclic alternating pattern (CAP) refers to periodic EEG activity occurred in non-REM sleep. It may indicate sleep instability and/or sensitive sleep fragmentation, and also be expected for the sleep parameter related to subjective sleep quality. We evaluated the reliability of CAP visual scoring conducted under the standard polysomnography (PSG) montage which is monopolar derivations to be able to use CAP sleep evaluation for clinical trial.

Methods: We used 17 examples recorded under standard EEG montage (Fp1-F3, F3-C3, C3-P3, P3-O1, Fp2-F4, F4-C4, C4-P4, P4-O2, C3-A2, C4-A2) for CAP scoring. 9 examples of those have scored it by CAP standard derivations first and scored it only in monopolar derivations method (C3-A2, C4-A1) successively. Remaining 8 examples have scored it by inverse order.

Results: Mean CAP rate scored by monopolar derivations was 50.9±12.2%, which is significantly lower than that of scored by CAP standard derivations; 54.6±12.9%. As for CAP rate, a high correlation was accepted in both monopolar and CAP standard derivations.

Conclusion: Because high correlation in a CAP rate was found, it was thought that even monopolar derivation could review a change of CAP rate relatively. About clinical application of CAP evaluation, there are still several problems, for example association with CAP and subjective sleepiness and shortening of time to score visually.

1063

EMOTION REGULATION AND SLEEP IN MEDICAL STUDENTS: A PRELIMINARY EXAMINATION

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Introduction: Both sleep deprivation and emotional suppression may contribute to the development of emotional disorders. Previous research has found that sleep deprivation predicts emotional reactivity to negative images. No previous research to our knowledge has looked at the relationship between sleep deprivation and emotional regulation in medical students. We hypothesized that sleep deprived medical students would be less likely to cognitively reappraise emotions given previous research indicating that sleep deprived students choose to engage in tasks requiring less cognitive effort.

Methods: This study made use of a cross-sectional design to assess sleep and emotional regulation in 3rd year medical students on the Psychiatry rotation. The independent variable was sleep, and the dependent variable is emotional regulation. The Pittsburgh Sleep Quality Index (PSQI) was administered, then participants were asked to listen to sad instrumental music to induce depressed mood. Following the mood induction task, participants completed the Emotional Regulation Scale (ERQ). One-way ANOVA techniques were used to examine sleep in the following three groups: (1) students with high suppression and low reappraisal scores, (2) students with low suppression and high reappraisal scores, and (3) students with high suppression scores.

Results: First, those with high suppression spent more hours in bed on weekends, $F(1,21) = 5.02, p < .05$. The second group of students had high suppression and low reappraisal, and spent more time in bed on weekdays, $F(1,21) = 3.2, p < .10$, but felt they did not receive enough sleep, $F(1,10) = 4.6, p < .10$, as compared with other students. The third, mostly female, group employed the most healthy regulation skills, high reappraisal and low suppression, and had a later bedtime in general than desired, $F(1,19) = 11.3, p < .05$.

Conclusion: Initial findings indicate that medical students who suppress emotions report spending more time in bed and feeling sleep deprived, although they do not report receiving less sleep than their peers. One possible interpretation is that medical students who suppress emotion may retire to bed as a coping strategy. We are currently gathering additional data from new students, and we believe assessing during different rotations or employing objective sleep measures would be beneficial future directions for this research.

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A COMPARISON OF GENDER DIFFERENCES ON THE EPWORTH SLEEPINESS SCALE AND BED PARTNER'S RATINGS IN THE ABILITY TO IDENTIFY OF OSA

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Introduction: The Epworth Sleepiness Scale (ESS) is typically used to identify sleepiness. This retrospective chart review study evaluated potential gender-related differences vis-à-vis ESS cutoff scores.

Methods: Consecutive patients completed the ESS and, when available, bed partners' ratings were also requested prior to diagnostic polysomnography (PSG). There were 202 males (age 47.8±13.5) and 99 females (age 46.9±13.2). BMIs were 32.4±7.3 and 33.2±11.1; ESS was 10.6±5.5 and 10.6±5.6, respectively. Males had a mean apnea/hypopnea index (AHI) of 38±33.2, and females had a significantly lower AHI of 24.1±31.7 ($p < .05$). 154 male and 64 female patients had a partner available. Cutoff scores were determined where sensitivity approximated .80. ROC analyses were run in SPSSv12.

Results: Using an AHI of >5 on the PSG as the diagnostic criteria, male patients had an area under the curve (AUC) on the ESS of .68; female AUC was .53. These areas were significantly different ($p = .04$) using Hanley and McNeil's formula (1983). For male patients, a cutoff of 8 yielded a sensitivity of 80%, specificity of 41%, and positive predictive value (PPV) of 90.7%. For females, a cutoff of 8 yielded a sensitivity of 78%, specificity is 19%, and PPV of 74.3%. For male patients' partners a score of 8 yielded sensitivity of 80%, specificity of 25%, and PPV of 90.6%. For female patients' partners, sensitivity was 71%, specificity 38%, and PPV 77.3%.

Conclusion: Among sleep clinic patients, ESS scores of 8 or above were found to yield sensitivities of approximately 80% or above. ROC curves between males and females differ despite similar percentages of positive ESS scores among both genders (using the same cutoff 67% of males and 69% of females). Thus, while female patients rate themselves equally sleepy as males, their scores (and those of their partners) are less likely to indicate presence of OSA.

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DIAGNOSIS-DEPENDENT CIRCADIAN FLUCTUATIONS IN PUPILLOMETRIC SLEEPINESS

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Introduction: The pupillary unrest index (PUI) has been suggested as an alternative to multiple sleep latency testing (MSLT) for objective assessment of sleepiness in health and disease. Sleepiness assessed by mean sleep latency (SL) on MSLT is well-known to vary according to circadian phase, but circadian influences on PUI have not been well-studied. We compared SL, PUI and subjective sleepiness by visual analog scale (VAS) in healthy control volunteers (C) and patients with narcolepsy (N) or OSA (O).

Methods: Following overnight polysomnography to verify diagnosis and inclusion criteria, O (N = 9), N (N = 19) (removed from treatment

for at least 2 weeks) and C (N = 54) subjects completed a 4-nap MSLT, pupillometry and VAS (4 trials each).

Results: SL demonstrated the expected circadian variation with a minimum at 2 PM and a maximum at 4 PM ($p < 0.0001$). SL was similar in O and N ($p > 0.2$); both were shorter than C ($p < 0.0001$), and showed minima and maxima at the 2 PM and 4PM naps, respectively. PUI also demonstrated significant circadian variation ($p < 0.0001$), but this effect differed by group ($p = 0.05$ for group*time interaction term); PUI was significantly elevated in association with minimum SL (2 PM) only in N, while PUI was at a minimum in association with SL maximum (4 PM) in all groups. VAS demonstrated greatest alertness at 4PM in O, but, unexpectedly, at 2PM in C ($p < 0.05$ for each). Circadian fluctuations in VAS were not significant in N.

Conclusion: We conclude that PUI, an alternative physiological measure of sleepiness, demonstrates significant circadian fluctuations consistent with maximal alertness in late afternoon and minimal alertness in early afternoon. The neural substrate for this effect remains to be determined.

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A COMPARISON OF RETROSPECTIVE AND PROSPECTIVE ASSESSMENTS OF SLEEP

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Introduction: Retrospective reports of sleep are mediated via cognitions and perceptions and therefore, may be biased. We analyzed retrospective and prospective subjective measures of sleep parameters and quality in two groups of cancer patients and a comparison group matched by age, gender, and race to examine the degree of correspondence and influencing factors.

Methods: The sample included 80 outpatients (27 lung, 24 colorectal, 29 comparison) with a mean age of 62.20 ± 10.86 years. Thirty nine subjects (48.8%) were female and 81.3% were White. All subjects completed the Pittsburgh Sleep Quality Index (PSQI) and a 14-day sleep diary (SD). Sleep quality on the SD was recorded on visual analogue scales of sleep depth, continuity, and restfulness which were averaged each day. Because SD variables were highly correlated across the 14 days, summary measures were used in the analysis. We examined total sleep time (TST), sleep latency (SL), and quality of sleep on each of the measures. Correspondence between TST and SL, correlation between sleep quality measures, and the influence of demographic and clinical variables were examined by Wilcoxon Signed Rank tests, nonparametric correlations, and logistic regression.

Results: Estimates of TST were lower on retrospective assessment ($p < 0.0001$); the difference in SL was not statistically significant. Group membership, demographic factors (age, gender, race, education), and clinical factors (depressive symptoms, functional status) were not associated with differences in sleep parameters. However, poor sleep quality (PSQI > 5) was significantly associated with differences in TST > hour and SL > 10min. SD measures of sleep quality were associated with PSQI global scores ($p < 0.0001$). Correlations remained significant when controlling for demographic and clinical factors.

Conclusion: Stability between retrospective and prospective assessments of sleep parameters was greater among subjects reporting good quality sleep suggesting that retrospective reports may be biased in poor sleepers. PSQI global sleep quality scores reflect general assessments of sleep quality on prospective measures.

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A META-ANALYSIS OF THE FIRST NIGHT EFFECT (FNE) IN POLYSOMNOGRAPHY - ITS IMPLICATIONS FOR BASELINE MEASUREMENTS

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Introduction: On the first night in a sleep laboratory, subjects often sleep qualitatively and quantitatively worse than they do on subsequent nights of study. This phenomenon is referred to as the first night effect (FNE). The presence of a FNE in different age and clinical population groups (insomnia, depression) remains undefined. Hence a meta-analysis of published literature related to this phenomenon was performed.

Methods: Online searches were performed using databases of Ovid MEDLINE, PubMed, PsycBOOKS, and PsycINFO; and meta-analysis with SPSS for Windows 15.0 (Chicago, IL, USA).

Results: Normal sleepers on the second night had shorter SOL ($p = 0.002$) and REML ($p < 0.001$) and more REM ($p < 0.001$) and SWS ($p = 0.004$) sleep compared to night one. However, data for the changes in consecutive nights showed variability (SOL $R^2 = .660$, REML $R^2 = .777$, REM% $R^2 = .683$, and SWS% $R^2 = .985$). Insomniacs showed a shorter REML ($p = 0.002$) but an increased SWS% ($p = 0.009$) between nights 1 and 2 ($R^2 = .823$ and $.957$ respectively). Depressives: SOL decreased ($p = 0.008$, R) and REM% ($p = .023$) increased significantly. All other clinical groups including narcolepsy, epilepsy, PTSD, RLS, Psychiatric Disorders, Chronic Fatigue Syndrome, Cystic Fibrosis, Rheumatoid Arthritis, Irritable Bowel Syndrome, and Pregnant (1st trimester): FNE for REML and REM% only (both $p < 0.001$). Children: SOL ($p = 0.046$), REML ($p < 0.001$), and REM% ($p < 0.001$).

Conclusion: First night PSG data from normal sleepers showed consistent FNE, whereas insomniacs often show reverse FNE. Variability seen within the groups could not be accounted for by age or sleep setting (laboratory vs. home). Despite shorter REML and more SWS on night two and variable SOL, it is recommended that for normal sleepers first night data should not be included for data analysis and for insomniacs an average of two nights to account for changes in SOL be taken accounted for; especially for the investigation of sleep initiation insomnia.

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SUCCESSFUL LONG-TERM SLEEP MONITORING IN THE INTENSIVE CARE UNIT USING A TEAM APPROACH

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Introduction: Sleep deprivation is one of the most frequent complaints of intensive care unit (ICU) survivors. Research using long-term sleep monitoring is needed to investigate the potential effects of sleep quality on clinical outcomes. This represents a significant challenge as polysomnography (PSG), which is expensive and labor intensive, is considered the only reliable method to monitor the quantitative and qualitative aspects of a critically ill patient's sleep. We present the prevalence of success and failure of a collaborative, team effort to collect long term PSG data in ICU patients.

Methods: Adult, critically ill, mechanically ventilated patients were monitored in the ICU setting utilizing continuous PSG. PSG was initiated within 48 hrs of the initiation of mechanical ventilation and continued for up to 100 hrs or until extubation. Techniques for electrode placement conformed to the international 10-20 system of electrode placement. Electrode placement included: two central (C4/A1, C3/A2), two occipital (O1/A2, O2/A1) channels for EEG, electrooculogram (EOG), and submental EMG. The Nihon Kohden Air-EEG system with remote access monitoring was used for each long-term monitoring session. The research team consisted of sleep technologists, research nurses, physician investigators, and ICU nursing staff. Sleep technologists performed the initial hookup and routine electrode checks. The sleep technologists and the principle investigator had the ability to access the study remotely and real-time. ICU nursing staff and research personnel were trained in the use of the system. Nurses, technicians and physicians input data relating to the patient's neurocognitive condition and maintained electrode integrity.

Results: 22 patients had long-term PSG's totaling 1356.13 hrs of recording time. Mean recording time per patient was 61.6 hrs. Study downtime related to system failure or shutdown was 64.23 hrs (4.74%); downtime secondary to dislodged electrodes or technical artifacts was 12.27 hrs (0.9%). The combined all cause downtime was 76.5 hrs (5.6%). Thus, using a team approach, successful PSG data acquisition was achieved 94.4% of the total test time.

Conclusion: Long-term PSG is needed to evaluate the effects of sleep quality on clinical outcomes in ICU patients. Bedside monitoring by a sleep technician during these studies can often be cost prohibitive. We found that long-term PSG can be performed with a high degree of success using a collaborative effort of researchers and bedside nursing staff.

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1069

EFFECT OF SLEEP MEDICINE SPECIALISTS AND AMERICAN ACADEMY OF SLEEP MEDICINE ACCREDITATION ON MANAGEMENT OF OBSTRUCTIVE SLEEP APNEA

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Introduction: The central objective of this ongoing study is to determine the effect of American Academy of Sleep Medicine Accreditation of sleep centers and sleep-medicine certification of physicians on the management of patients with obstructive sleep apnea (OSA).

Methods: Prospective, multi-center, observational study that included 4 participating sleep centers and 243 patients. All patients underwent polysomnography at participating locations and completed validated questionnaires regarding education received from physicians and sleep centers, timeliness of the initial sleep study, and overall satisfaction of care received from physicians and centers. Subsequently, a 3-month follow-up questionnaire was administered via telephone and in patients receiving positive airway pressure (PAP) therapy, adherence to PAP therapy was measured.

Results: Interim analysis based upon 243 patients (age 55 ± 12 [SD] years; 16% women; and body mass index 34.0 ± 6.6 Kg/m²) is reported. Patients at accredited centers were more likely to report having received adequate education regarding obstructive sleep apnea (100%) than patients at non-accredited sites (83.5%; P<0.001). After adjusting for covariates, lack of accreditation or certification status of providers was independently associated with greater likelihood of not receiving adequate education regarding OSA (odds ratio [OR] 1.9, 95% confidence interval [CI], 1.1-3.6; p = 0.035). During their initial visit for polysomnography, overall patient satisfaction ratings for physician or center were not influenced by accreditation status of centers or certification status of physicians (P>0.53). Time delays between initial evaluation by physician and polysomnography were not different between accredited and non-accredited sites: median 19 days; inter-quartile range [IQR] 10, 25 days and median 17 days; IQR 10, 40 days, respectively (P=0.36; Mann-Whitney test).

Conclusion: In this multi-center, prospective, observational study, interim analysis revealed that patients cared for by accredited centers and certified physicians received better education than patients cared for by non-accredited centers and non-certified physicians. Whether such favorable effects on patient education translates into greater adherence to PAP therapy or other outcome measures may be revealed by this ongoing study.

Support (optional): American Sleep Medicine Foundation of the American Academy of Sleep Medicine

1070

OSA SCREENING - A TEAM APPROACH

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Introduction: In accordance with the newest patient safety goal, initiation of an OSA screening process has been on the agenda of many hospitals across the country. A team approach is necessary in order to provide maximum benefit to the patient population while minimizing the impact on staff.

Methods: Edward Hospital assembled a team of specialists in order to provide comprehensive screening services to their patients. Team members were recruited from medical staff, nursing, respiratory care, information systems, risk management, pre-admission testing, and quality excellence. Specialty physicians in the areas of anesthesia, sleep, fam-

ily practice, and pulmonology were also an integral part of the team. Based on screening questions and physical assessment, both the medical and surgical patient populations received additional OSA-related care when warranted. Anesthesiologists provided interventions for surgical patients, while nursing and RCPs worked together to provide interventions for medical patients. Potential OSA populations were identified by reports generated by information systems based on nursing admission database items. Algorithms and standing order sets were developed in order to provide consistency throughout the hospital. The OSA bundle provided additional stability and effectiveness by bringing together the OSA order set, narcotic screening, oxygen therapy, remote telemonitoring, and CPAP therapy.

Results: As a result of this team approach, Edward Hospital was able to identify and treat a significantly larger OSA patient population, eliminate unplanned ICU admissions, decrease OSA-related intubations, and improve patient compliance related to CPAP equipment. In addition, morbidity and mortality was significantly reduced by the elimination of OSA adverse events and OSA cardio-respiratory arrests. Despite identifying a larger OSA population, the CPAP average LOS was decreased by 7 percent after initiation of the OSA bundle.

Conclusion: An interdisciplinary team approach provides the most effective outcome when implementing a new OSA process. Each team member must know their role, and how their piece fits into the overall care plan. An effective OSA intervention team receives contributions from many areas of the hospital, and results in superior outcomes for both the patient and the institution.

1071

AN EPIDEMIOLOGICAL ANALYSIS OF THE NATIONAL HIGHWAY TRAFFIC SAFETY ADMINISTRATION REPORT TO IDENTIFY RISK GROUPS FOR ACCIDENTS AND FATALITIES

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Introduction: National estimates of motor vehicle crashes reveals that on average a person is killed every 12 minutes and injured every 12 seconds. Fatigue plays a significant role in such accidents but is frequently under-recognized and under-reported. In the last decade, significant efforts have been initiated at impacting fatigue related accidents. The aim of this research is to better identify and understand risk groups.

Methods: The Traffic Safety Facts 2005 Report (U.S. Department of Transportation) was used for this analysis. Rates for persons killed or injured during 1975-2005 per 100,000 registered vehicles, based upon type of vehicle were compared. Fatality rates per 100 million vehicle miles traveled were analyzed to identify differences between large and light truck crashes. Comparisons of fatal crashes based upon rural or urban highways were also performed. Statistical tests included developing the General Linear Model to identify differences in trends, ANOVA to identify differences between multiple groups, and Mann Whitney and Kruskal Wallis tests to evaluate differences for non-parametric data.

Results: Fatalities and injuries decreased during 1975-2005 ($p < 0.0001$). This decreasing trend for injuries is less for large trucks as compared to cars ($p = 0.023$). There was a decrease in light and large truck crashes ($p < 0.0001$). However, incremental analyses showed plateauing of this decrease in the last five years ($p > 0.05$). Further, there is a trend towards an increase in crashes involving large trucks. Fatal crashes on rural highways strongly trended higher than crashes on urban highways ($p = 0.06$).

Conclusion: 1) Fatigue is not explicitly measured in national highway safety reports. 2) Decrease in crashes secondary to road safety initiatives, laws, and better equipment, is now slowing. 3) Role of fatigue as a factor resulting in the plateauing of decrease in crashes, particularly

in high risk groups - large trucks and rural highways needs to be further evaluated.

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POVERTY EFFECTS ON POPULATION SLEEP

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Introduction: Sleep in the general population (referred to as 'population sleep') and its determinants are poorly understood. We hypothesized that socioeconomic (SES) factors play a significant but underinvestigated role in sleep quality in addition to race/ethnicity.

Methods: 9714 subjects were randomly surveyed in a cross-sectional study. Poor sleep quality (outcome), measured by self-report on a 5-point scale (poor quality=1, good quality=5) was dichotomized by combining scores 2-4 and modeled using logistic regressions. SES predictors included poverty, level of education, and employment status. All analyses employed weights to reflect the target population.

Results: Of 9714 subjects 9.1% reported poor sleep quality, 30.5% reported good sleep quality. 25.6% were below the poverty threshold. Education level (OR=0.32, 95% CI 0.22-0.49 for post college education versus less than high school) and employment status (OR=2.32, 95% CI 1.85-2.31 for unemployed/disabled versus employed) predicted sleep quality adjusted for age, sex, race, and poverty. Race/ethnicity differences in sleep quality were observed in unadjusted analysis: Blacks and Latinos are more likely to have poor sleep quality: OR=1.66, 95% CI 1.38-2.0, and OR=1.61, 95% CI 1.25-2.06, respectively compared to Whites. However, poverty significantly moderated the effect of race/ethnicity on sleep quality for Whites, Blacks, and Latinos. Adjusted for age and sex, poverty effects were greatest in Whites (OR=4.27, 95% CI 3.36-5.44) compared to Blacks (OR=1.56, 95% CI 1.14-2.13), and Latinos (OR=1.71, 95% CI 0.85-3.41). After adjusting for age, sex, education level, and employment status, poverty effects persisted only in Whites (OR=2.67, 95% CI 2.05-3.48) and not Blacks or Latinos.

Conclusion: To our knowledge this is the largest US sample investigating poverty's effect upon sleep quality. Poor sleep quality was strongly associated with poverty. Poverty significantly moderated race differences in sleep quality. Interestingly, impoverished Whites had the highest likelihood of poor sleep. This may have public health policy implications in targeting higher risk groups.

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1073

RESCUE CPAP IN A VULNERABLE POPULATION: DOES INTENSE SERVICES IN AN AASM ACCREDITED SLEEP CENTER MATTER?

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Introduction: Nasal CPAP is effective in treating OSAS although resistance and intolerance to it pose limitations to its use. Studies have indicated that early CPAP use, as early as 3 days-identifies long term adherence to CPAP therapy. Predictors of long term CPAP usage in this population remain unclear. We sought to determine the impact of a goal driven protocol on long term CPAP compliance in patients with OSAS.

Methods: We studied 55 (36 males and 19 females) consecutive patients in an AASM accredited center with OSAS whose CPAP compliance was < 4 hours at their 1 month follow up visit. All subjects were evaluated

Category Q—Healthcare Services, Research & Education

and counselled by a board certified sleep specialist and a certified respiratory therapist and were educated about OSA. CPAP desensitization and mask fittings were conducted if indicated and patients had access to specialized CPAP clinic. All patients were offered follow up with their downloadable compliance card.

Results: Of the 55 patients (mean age 55.7 ± 13.7 years, BMI 34.5 ± 7.8 , ESS 12 ± 5 AHI 25 ± 18 and PSQI 10 ± 4) 34 patients (61%) were compliant and were followed up for 6 months. CPAP compliance improved from 138.6 ± 52.0 minutes to 259.0 ± 103.5 minutes ($p < 0.001$) in those 34 patients and more patients availed of mask changes and desensitization in the compliant group ($p = 0.006$). Older age was related to increasing compliance ($r = 0.38$; $p = 0.02$) and in a multivariate stepwise model including age, gender, BMI, AHI, ESS, PSQI, CPAP pressure, mask changes and desensitization, older age was the most important predictor of compliance ($p = 0.009$).

Conclusion: Access to specialized services with close follow up in an AASM accredited center improves long term CPAP compliance in patients with high risk of CPAP failure. Patients in the older age group are particularly responsive to multimodal CPAP rescue services and are a model for development in sleep centers.

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A FATIGUE COUNTERMEASURES PROGRAM FOR HOSPITAL STAFF NURSES: AN INTERVENTIONAL APPROACH

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Introduction: Recent studies have shown that extended shifts worked by hospital staff nurses are associated with significantly higher risk of errors. Long work hours coupled with insufficient sleep are even riskier. Although other industries have developed programs to reduce fatigue-related errors and injury, a fatigue countermeasures program for nurses (FCMPN) is lacking. The purpose of this study is to evaluate the potential of a FCMPN for reducing fatigue among hospital staff nurses. The NASA Ames Research Center's Fatigue Countermeasures provided the framework for intervention development.

Methods: This pilot study uses a one-group pretest-posttest approach, with 30 participants serving as their own control. Data were collected using a demographic questionnaire, the Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, and a daily logbook to assess sleep and work variables and health care errors. Participants completed the instruments during the two weeks prior to the FCMPN, four weeks after receiving the intervention, and again at three months.

Results: Data analysis is in progress. The results will provide preliminary information concerning the feasibility of the FCMPN, as well as its potential for minimizing health care errors and maximizing patient safety in acute care hospitals. It will also test the hypothesis that adoption of a standardized fatigue intervention program used in many other industries will improve nurses' sleep quality, sleep duration, and alertness at work, while decreasing daytime sleepiness, drowsiness at work, and health care errors.

Conclusion: High patient acuity levels, increasing complexity of care, and a shortage of nurses pose serious challenges for health care delivery. Findings from this study can be used by nurses, health care administrators, and legislators, to develop infrastructures that may ensure a more alert workforce, minimize health risks for nurses, and maximize the safety of those in their care.

Support (optional): Financial support for this study was provided by Blue Cross Blue Shield of Michigan Foundation.

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CORRELATION BETWEEN SLEEP DURATION, BODY MASS INDEX AND ROTATING SHIFT WORK

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Introduction: Obesity is becoming a global epidemic in both children and adults. It is associated with numerous comorbidities such as cardiovascular disease, type 2 diabetes, hypertension, certain cancers, and sleep apnea/sleep-disordered breathing. Recent studies have correlated the short sleep duration in the shift work population with the increase of the body mass index. The aim of this study was to analyze the correlation between sleep duration, body mass index and rotating night shifts in Brazilian workers.

Methods: A group of 282 male rotating shift workers of the Brazilian Nuclear Power Plant (18-60 years) was analyzed. Body mass index was calculated by dividing weight in kilograms by height in meters squared. Subjects were asked about the total years of rotating night shifts and sleep duration was measured by self-report. Pearson's correlation coefficient was used and $p < 0.05$ was considered as statistically significant.

Results: It was found a significant correlation between body mass index and years of rotating night shifts ($r = 0.24$; $p < 0.05$). However, no significant correlation was found between sleep duration and body mass index.

Conclusion: Years of rotating night shift work seem to be a factor involved in obesity and should be better studied in this population.

Support (optional): AFIP, FAPESP (CEPID 98/14303-3), FADA/UNIFESP, CEMSA, CNPQ.

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WHY TREAT OBSTRUCTIVE SLEEP APNEA? GRAPHIC TOOLS TO EDUCATE PATIENTS AND CAREGIVERS ABOUT PATHOPHYSIOLOGY OF OBSTRUCTIVE SLEEP APNEA

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Introduction: Patients and medical professionals outside of the sleep community sometimes question the importance of treating obstructive sleep apnea (OSA) due to the perceived obtrusiveness of treatment options, and/or to ignorance about how OSA causes or exacerbates other disease. Many people are "visual learners" and thus absorb information more readily when presented as images instead of in written text or speech. Therefore, we sought to develop visual tools to help explain OSA pathophysiology and co-morbidity to patients and caregivers.

Methods: We developed a set of diagrams (flow charts) that illustrate demonstrated or suspected relationships between OSA and other disease. To do this, we compiled the salient, peer-reviewed literature concerning OSA pathophysiology and specific co-morbidities. Cause-effect relationships were identified and presented as specifically as possible. In addition, where the collective literature suggested existence of a "vicious cycle", we portrayed this visually. When flow charts are viewed on a computer, the peer-reviewed article citations concerning specific relationships appear when you select (click on) that relationship.

Results: Flow charts were developed to present detailed pathophysiologic relationships between OSA and: obesity, hypertension, congestive heart failure, cerebrovascular disease, diabetes, gastroesophageal reflux, sexual dysfunction, and depression/anxiety. For example, one diagram depicts details of the vicious cycle between OSA and obesity (brief overview: obesity --> OSA --> somnolence --> inactivity --> dysmetabolism --> obesity --> ...). Our experience with these diagrams indicates they are substantially more effective than lecturing or written handouts to help patients understand how untreated OSA may contribute

to other medical problems they confront. CME for caregivers has been well-received.

Conclusion: Graphic illustration of OSA-related pathophysiology improves patient education. This in turn should help motivate treatment by giving patients a good understanding of how treatment may benefit them. Caregivers may be more interested than patients in the literature references for specific relationships shown on flow chart diagrams. The diagrams are easily modified and updated based on the most recent literature. Also, they are fractal, in that the depth and detail of information they present is limited only by the available literature.

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EFFECTIVENESS OF INTEGRATION OF SLEEP DISORDERS KNOWLEDGE COMPARING INNOVATIVE ONLINE METHOD WITH TRADITIONAL EDUCATION METHOD

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Introduction: Electronic formats allow students access to educational materials at their convenience while freeing the physician-educator for other activities. We undertook to create enduring electronic based education in 4 key areas of sleep medicine. We measured effectiveness compared to traditional teaching methods and the integration of this knowledge into patient care situations.

Methods: We developed curriculum on Sleep Process and Circadian Rhythms, Sleep Disordered Breathing, Parasomnias, and Hypersomnia. Third year medical students entering the pediatric clerkship were randomized to either a 2.5 hour workshop on sleep disorders (F2F) or to view four 40-minute online modules (online). A 20 multiple choice question test with Pre-Post comparison for initial sleep knowledge acquisition was used to measure immediate retention. Integration of sleep knowledge into patient care was measured using 1. a sleep focused OSCE at end rotation, 2. chart audit for sleep history and assessment done 2-8 months after completing the sleep education. Each student could score 8 points for write-ups. Online and F2F participants audit results were grouped to compare the method's effectiveness.

Results: 68 students completed both the pre and post MCQ tests. There was a significant improvement in the test scores post education. The RMANOVA omnibus F-test was significant ($F(1, 66) = 137.717; p < 0.001$). There was no significant difference between the online and F2F methods. 76 students in F2F and 81 students in online groups completed a sleep OSCE and averaged mean scores of 23.14 and 23.85 respectively out of high score of 35. There were no significant differences in OSCE performance between groups. 32 students from the F2F and 26 students from the online education completed ambulatory medicine after the pediatric clerkship. The mean score per student averaged over 4 writes per student was 0.89 for the F2F and 0.92 for the online groups. There was no significant difference by Levene's test for equality of variances between the F2F and online groups ($p=0.083$).

Conclusion: Sleep Medicine education regardless of format for delivery improves immediate post-education test scores. The formats were equal in providing the students with the ability to integrate this new knowledge in patient care setting as evidenced by the OSCE scores and the patient write-ups. Online formatted education can provide effective integration of sleep medicine for medical students.

Support (optional): American Sleep Medicine Foundation

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NURSE PRACTITIONERS (NPS) AND SLEEP EDUCATION

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Introduction: NPs frequently encounter patients with sleep symptoms, and are critical to recognition and management of sleep disorders. Since many NPs lack formal training in sleep, they may not recognize or feel comfortable managing sleep disorders. This study aims to better understand NPs sleep education and continuing education (CE) needs.

Methods: 658 NPs with email addresses were identified by the Illinois Society of Advanced Practice Nursing membership database; 529 were valid, 168 responded anonymously via SurveyMonkey. Data were analyzed with unpaired, 1-tail tests.

Results: NP practice areas were 69.4% primary care and 30.6 % specialty care. 81.3% screened for sleep disorders. Interest levels in sleep CE: 31.2% very interested, 37.9% somewhat interested, 9.3% neutral, 17.9% mildly interested, 3.6% not interested. Sleep education in school averaged 2.1 hours; 27.9% had none. CE hours averaged 9, and 31.4 % had none. Preference for CE programs included 30.7% half-day, 25% web-based, 22.1% 1 hour, 10% full day, 9.3% written, 2.1% none. Areas of greatest CE interest included insomnia (73%), sleep apnea (70.8%), and restless leg syndrome (RLS) (59.9%). NPs were comfortable/very comfortable in diagnosing insomnia (43.5%), sleep apnea (37.1%), and restless legs syndrome (29%). NPs were comfortable/very comfortable treating/managing insomnia (39.2%), sleep apnea (29.4%), and RLS (24.7%). NPs with a higher comfort level in diagnosing sleep apnea were more likely to order a polysomnogram ($p < 0.0001$).

Conclusion: Each year more patients are evaluated and managed by NPs, many of whom know little about sleep. This lack of sleep education is similar to that found among medical students and physicians. NPs interest in sleep CE is high. The areas in which they express interest -- insomnia, sleep apnea and RLS -- are common; patients would benefit greatly from NPs recognition and management of these.

Support (optional): OSF Saint Francis Medical Center Illinois Society for Advanced Practice Nursing

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NURSE PRACTITIONERS (NPS) PRACTICE BEHAVIORS WITH SUSPECTED OBSTRUCTIVE SLEEP APNEA (OSA)

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Introduction: NPs frequently encounter patients with OSA symptoms and are critical to recognition and management of this sleep disorder. Untreated OSA can result in serious consequences affecting cardiovascular, cognitive, emotional, and psychosocial functioning. This study analyzed selected NP practice behaviors related to suspected OSA.

Methods: 658 NPs with email addresses were identified by the Illinois Society of Advanced Practice Nursing membership database; 529 were valid, 168 responded anonymously via SurveyMonkey. Data were analyzed with unpaired 1-tail tests.

Results: 81.3% screened patients for sleep disorders; 84.4% asked about snoring/pauses in breathing, 83.9% about feeling sleepy or tired. When OSA was suspected, 71.1% ordered a polysomnogram, 21.5% overnight oximetry, 3% not sure, 2.2% multiple sleep latency test and 20% no testing (many indicated referral to a physician). 37.1% were comfortable/very comfortable with diagnosing OSA. Those with a greater comfort level were more likely to order a polysomnogram ($p=0.0001$). Usual actions to treat OSA included refer to a sleep specialist (69.3%), weight loss (57.7%), order CPAP (34.3%), refer to ENT (30.7%), sleep hygiene (26.3%), would not treat (10.2%), prescribe medication (3.6%).

Category Q—Healthcare Services, Research & Education

Responses to the most appropriate treatment for mild/moderate/severe OSA (respectively) with excessive sleepiness were as follows: CPAP 27.5%, 75.4%, 59.8%; weight loss 45%, 3.7%, 0.8%; mandibular advancement device 3.1%, 1.5%, 0.8%; palatal surgery 0%, 1.5%, 9.1%; not sure 16.8%, 17.2%, 29.5%; avoid sleeping supine 7.6%, 07%, 0%. NPs comfort levels with treating OSA included 10.3% very comfortable, 19.1% comfortable, 24.3% neutral, 22.8% uncomfortable, 23.5% very uncomfortable.

Conclusion: Since OSA has important health, economic and social consequences, NPs should be prepared to recognize and manage patients at risk. Many NPs report low comfort levels in diagnosing and treating OSA, which is reflected in their testing and treatment choices. Clearly, there is continued opportunity to increase NPs knowledge in recognition and management of OSA.

Support (optional): OSF Saint Francis Medical Center Illinois Society for Advanced Practice Nursing

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NURSE PRACTITIONERS (NPS) PRACTICE BEHAVIORS WITH INSOMNIA

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Introduction: NPs frequently encounter patients with insomnia, and are critical to recognition and management. Untreated insomnia can result in serious consequences affecting cognitive, emotional, and psychosocial functioning. This study analyzed selected NP practice behaviors related to insomnia.

Methods: 658 NPs with email addresses were identified by the Illinois Society of Advanced Practice Nursing membership database, 529 were valid, 168 responded anonymously via SurveyMonkey. Data were analyzed with unpaired 1-tail tests.

Results: 81.3% screened patients for sleep disorders; 78.8% asked about the amount of sleep, 85.6% about problems falling or staying asleep. When insomnia was suspected, 72.9% did no testing, 13.2% ordered a polysomnogram, 8.5% not sure, 7.8% overnight oximetry, 1.6% multiple sleep latency test. 43.5% were comfortable/very comfortable with diagnosing insomnia. There was not a significant relationship ($p=0.9709$) between comfort level and testing. Usual actions to treat insomnia included sleep hygiene (83.2%), prescribe medication (67.2%), refer to sleep specialist (26.3%), weight loss (21.2%), refer to psychiatry (13.9%), would not treat (4.4%), refer to ENT (3.6%), order CPAP (0.7%). Responses to the most appropriate treatment for acute insomnia, chronic insomnia, early morning awakenings, nonrestorative sleep (respectively) with daytime impairment were as follows: sleep hygiene 55.9%, 10.2%, 20.5%, 10.6%; CBT 6.6%, 25.5%, 11.4%, 10.6%; hypnotic 9.6%, 16.8%, 3.8%, 6.8%; other medication 5.9%, 14.6%, 15.2%, 7.6%; other treatment 2.2%, 6.6%, 8.3%, 16.7%; not sure 19.9%, 26.3%, 40.9%, 47.7%. NPs comfort levels with treating insomnia were 39.2% comfortable/very comfortable.

Conclusion: Since insomnia is the most common sleep disorder and has important health, economic and social consequences, NPs should be prepared to recognize and manage these patients. Over one-half of NPs report low comfort levels in diagnosing and treating insomnia, which is reflected in testing and treatment choices. Clearly, there is opportunity to increase NPs recognition and management of insomnia.

Support (optional): OSF Saint Francis Medical Center Illinois Society for Advanced Practice Nursing

1081

DOES THE SRS-SPONSORED TRAINEE SYMPOSIUM SERIES FOSTER PUBLICATION AND RESEARCH FUNDING IN SLEEP?

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Introduction: For the past 13 years, the Sleep Research Society has sponsored a one-day Trainee Symposium Series (TSS) at the APSS meeting. The TSS provides an opportunity for trainees at the undergraduate through post-doctoral level to attend lectures and workshops on topics related to sleep research and professional development. The SRS Trainee Education Advisory Committee (TEAC) is undertaking a program evaluation of the TSS.

Methods: TSS event attendance records were available for 2004-2007. Lists of SRS supported travel awardees were available for 2001-2007. For those receiving travel awards, the following information was obtained: (1) number of years attended; (2) total SRS travel award funds provided for attendance; (3) number of sleep-related publications indexed in PubMed, and (4) number of sleep-related NIH-funded grants (from CRISP database). Descriptive statistics were computed and t-tests comparing those who received travel support to those who did not on years of attendance, publications, and grants were calculated.

Results: From 2004-2007, an average of 210 individuals attended the TSS each year (606 unique individuals attended an average of 1.1 times). For trainees who received travel support (2001-2007), the mean (SD) number of sleep-related publications was 4.1 (4.6); 77% had >1 publication. 22 former award recipients (9%) had ≥ 1 funded grants. From 2004-2007, those who received travel support attended more years ($p=.01$), published more papers ($p=.02$), and tended to have more sleep-related grants ($p=.06$) than those who did not.

Conclusion: The results demonstrate that the TSS has reached a large audience over the past 4 years, although most trainees only attended a single year. We are continuing to gather data on involvement in sleep research by past attendees. The results of this program evaluation will be used to determine if changes in TSS are needed.

1082

APPLICATION OF BEHAVIOR CHANGE PRINCIPLES TO SLEEP

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Introduction: Sleep, like diet and exercise, is a health behavior. The literature on health behavior change can be applied to understanding the process through which individuals maintain or change their current sleeping patterns. One model that can be directly applied is the Stages of Change, which characterizes behavior change as a process consisting of distinct stages. Another related construct is that of self-efficacy, which related to an individual's confidence in their ability to change their behavior. The goal of this study is to examine self-efficacy and stage of change as they relate to sleep, and to make comparisons with other health behaviors.

Methods: 38 undergraduate students were recruited to complete a health behavior survey. This survey contained standard measures of self-efficacy and stage of change for smoking, exercise, and alcohol use. These measures were also adapted to ask about sleeping. At this stage of data collection, basic descriptive statistics have been computed.

Results: The modal sleep self-efficacy rating was “somewhat confident”, indicating that the students are not very confident in their ability to obtain a night of quality sleep. When compared with the other health behaviors, sleep had a similar self-efficacy rating with exercise, and lower self-efficacy than smoking and alcohol use. For the stages of change, the highest frequency of responses (31.6%) fell in the preparation stage suggesting that students were planning to improve their sleep in the near future. This placed sleep further along the process of change than alcohol use but not as far as exercise and smoking.

Conclusion: Undergraduate students were actively thinking about changing their sleep, but were not as far in the process as they were for smoking and exercise. Most of the students also showed low levels of self efficacy for achieving a night of quality sleep, especially when compared with smoking and alcohol use.

1083

SCREENING FOR UNDIAGNOSED AND UNTREATED OBSTRUCTIVE SLEEP APNEA IN PATIENTS UNDERGOING ELECTIVE SURGERY

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Introduction: Obstructive sleep apnea (OSA) may increase the risk of peri-operative complications. As a part of an ongoing quality improvement initiative, we report preliminary data on the prevalence of undiagnosed and untreated OSA in patients undergoing elective surgical procedures.

Methods: OSA screening questionnaire was administered as a part of a routine evaluation to 290 patients preparing for elective surgery.

Results: The mean age (\pm SD) of the population was 52 (\pm 18) years; 126 (43%) of the patients were females. Total of 24 (8%) patients screened positive for OSA, with estimated 95% confidence intervals for prevalence 5-11%. There was no difference in age or gender in patients who screened positive for OSA compared to those who screened negative ($p = \text{NS}$). Out of the 24 patients that screened positive, 18 patients had previous diagnosis of OSA, and 10 of these patients were non-adherent to the previously recommended OSA therapy. The remaining 6 patients were newly identified patients with high likelihood of OSA based on the screening questionnaire, and further sleep evaluation was recommended. Elective surgery did not have to be postponed in any of these 290 screened patients.

Conclusion: OSA was prevalent among patients preparing for elective surgery. In patient with prior diagnosis of OSA, non-adherence to previously recommended OSA therapy was frequently encountered. Screening for OSA should be considered as a part of routine pre-surgical evaluation, and streamlined algorithm for evaluation of OSA in this setting doesn't appear to delay elective surgical procedures.

1084

IS FULL-NIGHT CONTINUOUS POSITIVE AIRWAY PRESSURE TITRATION MORE ADVANTAGEOUS THAN SPLIT-NIGHT CONTINUOUS POSITIVE AIRWAY PRESSURE TITRATION

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Introduction: Increasingly, sleep centers are performing diagnostic and therapeutic modalities of Continuous Positive Airway Pressure (CPAP) titration in one night (split night-titration). We hypothesized that full-

night titration studies would be more likely to result in adequate set pressure, and less likely to result in the initiation of AutoPAP.

Methods: A retrospective review of 227 consecutive polysomnographic reports collected in 2007 was performed in order to compare full-night titrations with split-night titrations for adequacy of established CPAP pressures and prevalence of Auto-PAP initiation.

Results: Out of the 227 patients, 139 patients underwent full night-PAP titration and 88 underwent split-night titration, as per our protocol (threshold for initiation of CPAP=20 respiratory events per hour during the diagnostic portion of the study). 67% (n=93) of full-night titrated patients were adequately titrated by CPAP or BiPAP. However, 33% (n=46) were placed on Auto-PAP. Of the 88 split-night titrations, 69% of patients were adequately titrated by either CPAP or BiPAP (n= 66). 31% (n=27) of split-night titrated patients were placed on AutoPAP. No statistically significant difference in the prevalence of AutoPAP use was detected in two groups ($P>0.5$).

Conclusion: The results suggest no particular advantage of full night titrations over split-night titrations, despite the assumption that full-night titration would provide more opportunity for the fine-tuning of effective pressure. Further analysis of the role of variable contributory factors, such as positionality and REM/NonREM apnea distribution is required. This is particularly important in view of the cost, inconvenience, and delayed initiation of treatment in patients subjected to full-night diagnostic polysomnography. This study had departmental support.

1085

CAN TRIAGING UTILIZING A PHYSICIAN EXTENDER EXPEDITE DIAGNOSIS AND TREATMENT OF OBSTRUCTIVE SLEEP APNEA?

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Introduction: Lengthy wait times for evaluation by a sleep specialist has led to decreased access to polysomnography. We hypothesized that the addition of a physician extender (PE) to triage patients for direct admit (bypassing the initial consultation) may decrease wait times for polysomnography and the subsequent treatment of obstructive sleep apnea (OSA).

Methods: A screening questionnaire was administered to established patients of the medical center who were referred to the sleep center between January 2007 and September 2007. The PE reviewed the charts of all patients with a high probability of OSA. Based on the likelihood of sleep-disordered breathing they were triaged to direct admission for a sleep study or consultation by a sleep specialist. Patients with a high probability of OSA, as measured by questionnaire and chart review, were directly referred to the sleep clinic while patients with low probability were directed to a consultation with a sleep specialist.

Results: Eighty-six patients were triaged. Forty-one (47.7%) were triaged directly to the sleep center while 45 (52.3%) were triaged to a sleep specialist. Seventy-three (85%) were appropriate for polysomnography. Thirty-seven patients received positive airway pressure treatment. Patients triaged directly to the sleep center had significantly reduced wait times for polysomnography compared to patients who first consulted with a sleep physician, (16 days vs. 33 days, $p<0.01$). Triaging patients directly to the sleep center as opposed to a sleep specialist did not significantly affect the time from first contact to treatment (52 days vs. 70 days, $p>0.05$).

Conclusion: Triaging patients on first contact decreased wait times for an initial sleep study. An initial PE evaluation in high-risk patients may be a cost effective method to reduce initial polysomnography wait times.

1086

NON-COMPLAINT CPAP USERS EXPERIENCE MORE SLEEP-RELATED PATHOLOGY

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Introduction: Continuous positive airway pressure (CPAP) is accepted as the gold standard for managing obstructive sleep apnea-hypopnea syndrome (OSAHS). It is assumed effective provided patients are “compliant.” While measures of compliance remain obscure, less is known about the affects of the comorbidity of other sleep disorders on CPAP use and resolution of sleepiness. This investigation surveyed 172 patients using conventional CPAP therapy who had undergone Level 1 polysomnography.

Methods: A standardized questionnaire was provided and symptom indices were created for restless legs, snoring, sleep apnea, transmandibular joint disease (TMJ), Epworth Sleepiness Scale (EPWSS), and Fatigue Severity Scale (FSS); periodic limb movement rate was obtained from the polysomnogram. Each patient underwent a 30 follow-up which incorporated the above survey and a download of their CPAP device. Eighty-one patients were included in these analyses. CPAP users were categorized as responders (RESP) if their EPWS and FSS fell 50% or fell to within normal limits. Non-responders (nRESP) failed to demonstrate.

Results: Statistically, RESP did not differ from nRESP with respect to age (43.6 vs 46.4), body mass index (37.9 vs 36.0), or diagnostic AHI (30.6 vs 31.5). Therapeutic CPAP pressures were not significantly different (9.7 vs 9.4). RESP had less days with < 4 hours of use (4.6 vs 7.5; $p = 0.003$) with less mask leak ((20.3 vs 28.3; $p < 0.001$). Apnea symptoms were less among RESP (22.3 vs 25.1; $p = 0.037$) while snoring was greater for RESP (21.3 vs 17.4; $p < 0.001$). Symptoms associated with TMJ (5.1 vs 7.2; $p = 0.002$), RLS (5.6 vs 7.7; $p = 0.002$), and PLMS (19.7 vs 27.3; $p < 0.001$) were less frequent among RESP. TMJ and RLS symptoms adversely affected compliance. PLMS, however, did not significantly differ between compliant and non-compliant CPAP users.

Conclusion: Patients whose sleepiness and fatigue resolved with CPAP use after 30 days demonstrated less sleep related comorbidity, more nightly use, and less mask leak. Patients with TMJ and RLS symptom acclimated poorly to CPAP and remained sleepy. PLMS patients remained sleepy but were compliant to CPAP.

1087

SLEEP EDUCATION IN GRADUATE LEVEL TRAINING OF PSYCHOLOGISTS

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Introduction: Psychologists are integral members of multidisciplinary sleep centers, providing behavioral interventions and treatment for an array of sleep related issues, including insomnia, narcolepsy, and adherence to CPAP. Furthermore, all psychologists should understand normal sleep and sleep disorders given the high prevalence of sleep disturbances in the general population and that sleep problems are commonly associated with psychiatric disorders. Thus, the purpose of this study was to evaluate the current education on sleep provided to doctoral students and interns in clinical psychology.

Methods: The directors of 743 APA-accredited PhD, PsyD, and internship were contacted via email to participate in a web-based survey on sleep education. Questions focused on the number of faculty specializing in sleep, the availability of sleep education, and beliefs about the effectiveness of programs in training students about sleep and sleep disorders.

Results: Overall, 16% of the programs reported at least one faculty member who specialized in at least one area of sleep. Graduate programs (29%) were more likely to offer didactic sleep education as part of other courses when compared to internships (5%) ($X^2=22.06$, $p<.001$), while internship sites were more likely to offer clinical training in the diagnosis (26%) and treatment of sleep disorders (36%) than doctoral programs (10% and 20%, respectively) ($X^2=5.52$, $p=.012$; $X^2=4.38$, $p=.025$, respectively). Internships were more likely to report being interested in the development of a standard sleep curriculum (doctoral programs=22% and internships=46%; $X^2=9.42$, $p=.001$). Few programs offered training or experience with actigraphy (3.3%) or polysomnography (5.7%). Overall, 43% of all programs reported that they provide no experience in the diagnosis or treatment of sleep disorders.

Conclusion: There are few opportunities for trainees in clinical psychology to gain didactic or clinical experience with sleep and sleep disorders. Although graduate programs are more likely to have course-related material than internships, internships provide students more opportunities to learn about the assessment and treatment of sleep disorders. Clearly, sleep education needs to be incorporated more into the training of clinical psychologists.

1088

OSA RISK ASSESSMENT IN THE PRE-SURGICAL POPULATION

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Introduction: Up to this point, little emphasis has been given to sleep disordered breathing during a preoperative assessment. The American Society of Anesthesiologists(ASA) has recently suggested that all surgical patients be screened for obstructive sleep apnea (OSA) risk factors. This observation study evaluates the prevalence of OSA among adult surgical patients.

Methods: 2877 adult patients undergoing elective surgery have been screened for this study. All patients were asked to complete a questionnaire to assess their OSA risk level. 2778 subjects completed the Apnea Risk Evaluation System OSA Screening Questionnaire(AQ). This tool assesses daytime somnolence, snoring frequency, witnessed apnea, body mass index and neck circumference. All patients that scored in the high risk category were asked to be evaluated by a home testing device for 2 consecutive nights. Respiratory events were scored as defined by the ARES insight software. Apneas were defined as a complete cessation of breathing for at least 10 seconds. Hypopneas required a 50% airflow reduction, 3% desaturation, and an arousal.

Results: 661(23.7%) participants (age 52.9±13.4, neck circumference 17.3±1.6, BMI 38.4±7.2) were screened as high risk OSA candidates per the AQ. Of those, 534 (81%) had not been previously diagnosed with sleep disordered breathing. 233 valid home sleep studies were performed, of which, 207 of the subjects were previously undiagnosed. In this population, 170 (82%) were found to have OSA (AHI >5). OSA severity was categorized using the ASA criteria. 47% were found to have mild OSA (6-20 AHI), 19% had moderate OSA (21-40 AHI), and 16% had severe OSA (>40 AHI).

Conclusion: Over 20% of all preoperative patients screened high risk. Home sleep studies confirmed that OSA screening questionnaires may be a useful tool in the prescreening assessment for surgical patients.

Support (optional): This work was supported by the Barnes Jewish Foundation.

1089**INTEGRATING SLEEP MEDICINE INTO EXISTING MEDICAL SCHOOL CURRICULA***Bae CJ^{1,2}, Suh TT^{3,2}*¹Neurological Institute, Cleveland Clinic, Cleveland, OH, USA,²Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, OH, USA, ³Geriatric Medicine, Cleveland Clinic, Cleveland, OH, USA

Introduction: Sleep disorders are common in all age groups. A recent survey of four-year medical school curricula showed that the average amount of time devoted to sleep medicine is two hours. Most medical students graduate with little knowledge about the diagnosis or treatment of common sleep disorders.

Methods: At the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, sleep medicine is introduced in the second year neurosciences module. A two-hour seminar is designed to teach the basic neurophysiology of sleep, along with a case-based discussion of four typical sleep disorders (sleep apnea, insomnia, restless legs syndrome, narcolepsy). Sleep medicine is next covered in the third or fourth year during one week of a month long Aging Adult rotation. A two-hour case-based small group discussion about sleep disorders in the elderly starts the week. During the session, the neurophysiology of sleep is reviewed along with changes related to normal aging. A case-based discussion about sleep disorders in the geriatric population concludes the session. Selected articles about various sleep disorders are provided to students prior to the session via an internet portal designed for this rotation. During the rest of the week, students see patients in an outpatient clinic at the Cleveland Clinic Sleep Disorders Center. Students are also required to observe the set-up process for a polysomnogram, and to have a continuous positive airway pressure (CPAP) education to experience CPAP.

Results: Medical students have over 12 hours of sleep medicine education in a four-year curriculum.

Conclusion: Given scarcity of time in four-year medical school curricula and the multidisciplinary nature of Sleep Medicine, integrating sleep medicine education into existing medical school curricula may be an effective and efficient way to increase the amount of sleep medicine education. A future goal is to create a two-week Sleep Medicine elective.

1090**SEASONAL VARIATION OF SLEEP COMPLAINTS***Rowlands S, Knight C*

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Introduction: The current study aims to investigate whether the time of year patients were referred to a sleep disorders clinic would have an effect on they types of disorders that were reported.

Methods: A stratified random sample of 30 initial patients from each of the four seasons (spring, summer, fall, winter) was taken from the clinic database. Spring was defined as the months of March, April and May; summer was defined as June, July and August; fall was defined as September, October, and November; winter was defined as December, January and February. Complaints were taken from patients self reports of primary reason for referral to the sleep disorders clinic. The complaints were categorized into four areas: apnea/snoring, insomnia, hypersomnolence, and other.

Results: Comparison of primary sleep complaints from the four different seasons using a one way ANOVA showed a significant difference (Fobs = 27.41, Fcrit = 3.49, alpha= .05).

Conclusion: Therefore, the season in which the patient was referred to the sleep disorders clinic had an effect on the reason for seeking medical attention.

1091

SLEEP DEPRIVATION MODULATES THE IMMUNE RESPONSE THROUGH NFκB IN *DROSOPHILA MELANOGASTER*

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Introduction: Sleep interacts with several physiological processes including the immune response. However, reports on the effect of sleep deprivation on immune response have been controversial. We used *Drosophila melanogaster*, a powerful genetic tool, to characterize the interaction between sleep and the immune response. We found that sleep deprivation modulates the immune response and NFκB activity in a manner that was dependent on the amount of sleep loss.

Methods: The immune response was measured by quantifying the colony forming units (cfu) remaining in flies 24 h after infection with *E. coli*. Sleep deprivation was conducted right after infection via pharmaceutical method for 24 h or mechanical method for 4, 8, 16 and 24 h. To investigate the role of NFκB in the regulation of sleep and the immune response, transgenic flies containing a luciferase reporter gene under promoter of NFκB binding sequences (ceckB-luc) were generated and used for in vivo and real-time NFκB activity measurement during infection and sleep deprivation.

Results: Sleep deprivation via both pharmaceutical and mechanical methods influenced bacterial resistance as indicated by a change in cfu/fly relative to a non-deprived control. Long term sleep deprivation by pharmaceutical (24 h) or mechanical (16-24 h) methods decreased bacterial resistance. In contrast, short term (4 h) mechanical sleep deprivation increased bacterial resistance consistent with previous observations. In vivo luciferase assay in living flies indicates that NFκB is activated with sleep deprivation. Short term (4 h) mechanical sleep deprivation enhanced peak NFκB activity during infection. Long term (16-24 h) mechanical sleep deprivation also enhanced peak NFκB activity but peak levels were sustained for the duration of the deprivation period. This sustained NFκB activity during sepsis is detrimental for bacterial clearance.

Conclusion: Long and short term sleep deprivation periods differentially affect the immune response in *Drosophila* via an NFκB dependent mechanism.

Support (optional): Supported by the UMDNJ foundation.

1092

HOMER1A IS A CORE BRAIN MOLECULAR CORRELATE OF SLEEP LOSS

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Introduction: Sleep is regulated by a homeostatic process that determines its need and a circadian process that determines its timing. A highly reliable index of the homeostatic process is provided by the amplitude and prevalence of EEG delta oscillations (delta power). We have shown that the homeostatic regulation of sleep need, quantified as delta power, varies with genetic background and is associated with a locus on mouse chromosome 13. Here we show that *Homer1a*, localized within this locus, is the best transcriptional index of sleep need.

Methods: Sleep deprivation and transcriptome profiling was performed in 3 inbred mouse strains with differential delta power response to sleep deprivation. A transgenic mouse model was generated that expresses a Flag-tagged poly(A) binding protein under the control of the *Homer1* gene enabling us to study gene expression in *Homer1* expressing cells.

Results: We show that genetic background affects susceptibility to sleep loss at the transcriptional level in a tissue-dependent manner. In the brain, *Homer1a* expression best reflects the response to sleep loss. Time course gene expression analysis suggests that 2032 brain transcripts are under circadian control. However, only 391 remain rhythmic when mice are sleep deprived at four time points around the clock. Using our transgenic mouse line we show that in *Homer1*-expressing cells specifically, apart from *Homer1a*, three other activity-induced genes (*Ptgs2*, *Jph3*, and *Nptx2*) are over-expressed after sleep loss.

Conclusion: Our findings suggest that most diurnal changes in gene transcription are sleep-wake dependent rather than clock dependent. The four genes identified play a role in recovery from glutamate-induced neuronal hyperactivity. The consistent activation of *Homer1a* suggests a role for sleep in intracellular calcium homeostasis and in the protection from neuronal activation imposed by wakefulness.

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SLEEP CHANGES AFTER REPEATED SMALL INTERFERING RNA INJECTIONS TARGETING VESICULAR GABA TRANSPORTER IN THE RAT BASAL FOREBRAIN

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Introduction: We recently reported the use of small interfering RNAs (siRNAs) to decrease the prepro-orexin mRNA levels by almost 60% in the lateral hypothalamus of rats that resulted a corresponding REM sleep increase during the dark period. Here, we employed the same technique to functionally inhibit GABAergic neurons of the rat basal forebrain, and then evaluated effects on spontaneous sleep and the homeostatic sleep drive.

Methods: A pool of 4 siRNAs against rat vesicular GABA transporter (vGAT) was used (siRNA-vGAT). A corresponding pool of 4 siRNAs with no homology to known rat genes (siRNA-ctrl) was used as control. For verification of effective target gene knockdown, siRNA-vGAT was microinjected into one side of the basal forebrain area, while siRNA-ctrl was injected into the contralateral side. Basal forebrain tissue was removed and processed for RNA extraction after 2 days, followed by quantification with Taqman real-time PCR. Another group of rats that received the same treatment were examined for vGAT immunoreactivity. For sleep studies, baseline sleep was first recorded for 24hr. One group of rats then received bilateral microinjections of siRNA-vGAT into the basal forebrain twice for two consecutive days, while a separate group of rats received siRNA-ctrl. Polysomnographic data were recorded for 6 days post-injection, and scored visually offline.

Results: A single injection of siRNA-vGAT decreased the vGAT gene expression by 30%, whereas the GAD67 mRNA, that colocalizes in the same cells, was not affected. Rats treated with siRNA-vGAT increased their waking time by about 1.4 hours (5.8%) during a 24 hr period following the last injection and the effect was diminished by day 4. However, the amount of sleep rebound was unaffected after a 6-h sleep deprivation both before and after siRNA-vGAT injections. To increase the coverage area of siRNA, double injections (0.5mm apart) on each side of the basal forebrain were performed. Initial data showed that this increased rats' wakefulness by over 2 hours (8.4%) a day.

Conclusion: Our results imply that GABAergic neurons in the basal forebrain facilitate sleep, and increasing the spread area of siRNA injection may boost its effectiveness.

Support (optional): Support: NIMH grants 062522, 39683, 01798 and VA Merit Award

1094

A NOVEL METHOD FOR IDENTIFYING GENES INVOLVED IN SLEEP HOMEOSTASIS

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Introduction: The increase in sleep following a night of sleep deprivation is a defining feature of the state and is observed throughout the animal kingdom. Unfortunately, the underlying mechanisms remain unknown. We have identified an environmental manipulation, starvation, in which flies spontaneously exhibit periods of waking that are not compensated by a homeostatic response and which are not associated with learning deficits. By comparing waking induced by sleep deprivation with waking induced by starvation it is possible to identify genes that are involved in sleep homeostasis. Indeed, flies mutant for the clock gene *cycle* (*cyc⁰¹*) are extremely sensitive to sleep deprivation but easily withstand waking induced by starvation making them uniquely suited to identify genes involved in sleep homeostasis. Once identified, the role of these genes can be evaluated using genetic tools.

Methods: Three day old female *cyc⁰¹* flies were monitored for sleep according to standard procedures. Immediately following sleep deprivation or starvation, mRNA was extracted from whole heads and assessed using cDNA and Affymetrix arrays. This analysis yielded 109 genes, 90 of which were confirmed using real-time quantitative PCR. These genes fell into multiple categories, including energy metabolism, defense response, transcription factors, and signaling molecules. Mutants were obtained and their response to sleep deprivation was evaluated by examining sleep homeostasis, levels of a biomarker of sleepiness (*Amylase*) and learning.

Results: Flies mutant for *Lipid Storage Droplet 2* (*Lsd2⁵¹*) have altered lipid metabolism and exhibit a starvation-like phenotype. Consistent with starved *cyc⁰¹* mutants, *Lsd2⁵¹* mutants show no rebound after sleep deprivation, do not respond to sleep loss with an increase in *Amylase* levels, and do not exhibit a learning deficit after sleep deprivation compared to genetic controls.

Conclusion: These results validate our approach and emphasizes that the identified genes may be useful for identifying additional pathways important for sleep regulation.

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GENE EXPRESSION IN THE RAT BRAIN DURING PROSTAGLANDIN D2- AND ADENOSINERGICALLY-INDUCED SLEEP

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Introduction: Extensive evidence suggests that prostaglandin D2 (PGD2) is an endogenous sleep regulatory substance, the effects of which are dependent on adenosine A2a receptor-mediated signaling. We compared gene expression during PGD2- and adenosinergically-induced sleep to recovery sleep (RS) after sleep deprivation (SD) because pathways common to both natural and chemically-induced sleep may provide insights into the function of sleep.

Methods: Wistar rats were instrumented with electroencephalogram, electromyogram electrodes, and stainless steel cannulae in a midline position for drug infusions. Rats were randomly assigned to one of three groups (n=5-7/group): (1) Saline infusion group; (2) PGD2 infusion (200 pmol/min) group; (3) CGS21680, a selective adenosine A2a agonist (20 pmol/min) group. All animals were sacrificed at ZT14, after a

2-h infusion period, and brains were dissected into cortex (Cx), basal forebrain (BF), and hypothalamus (Hy). Total RNA was extracted from each Cx, BF, and Hy and combined into 9 RNA pools (3 brain regions x 3 groups). cRNA probes were prepared for hybridization to duplicate Affymetrix rat U34 Neurobiology arrays. Candidate genes from the arrays were verified by quantitative real-time PCR.

Results: Using a small panel of mRNAs whose expression in the Cx increases during RS, we found that gene expression during PGD2- and CGS21680-induced sleep showed surprisingly limited similarity to that observed during RS. In the BF and Hy, there was widespread activation of immediate early genes not seen during RS, likely due to local action of these chemicals on adenosine A2a signaling pathways. In all three brain regions, PGD2 and CGS21680 reduced the expression of *arc*, a transcript associated with synaptic plasticity whose expression is elevated during SD. Using Affymetrix GeneChips®, we also screened for other genes whose expression changed during PGD2- and CGS21680-induced sleep and found that the majority of genes induced by either agent were induced by both, supporting the contention that these molecules activate the same regulatory pathways in the brain.

Conclusion: These results indicate that these two agents converge on a common regulatory pathway, one that is likely activated by the buildup of endogenous adenosine that occurs during extended wakefulness.

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ENTRAINMENT OF TEMPERATURE AND ACTIVITY RHYTHMS TO RESTRICTED FEEDING IN OREXIN KNOCK OUT MICE

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Introduction: Ablation of the SCN, an established circadian clock, does not abolish food entrainment, suggesting that the food-entrainment oscillator must lie outside the SCN. Signals from this oscillator would converge onto arousal neurons so that the animal might forage for food. Here we investigate whether the neuropeptide orexin, which has been linked to arousal, might transduce the arousal signal.

Methods: Orexin-knockout (orexin-KO; n= 7) and wildtype (WT; n= 11) mice (both C57/Bl/6J derived) were implanted with MiniMitter transmitters that recorded core temperature and activity (12h LD cycle). After a week of ad-libitum feeding, the mice were given access to food for 4h (ZT 4-8) for nine days followed by 2-days of fasting.

Results: When orexin-KO mice were placed in a restricted feeding schedule core body temperature and activity entrained to the feeding schedule. In these mice gross locomotor activity was severely blunted during the nine day period of restricted feeding (-79.4 ± 6.3%) from the WT, but they showed an increase in core body temperature in anticipation to the meal time similar to the WT mice. There was no difference in the amount of food intake between the genotypes.

Conclusion: We conclude that orexin is not required for entrainment of activity and temperature to a restricted feeding schedule, but is required for the robust expression of gross locomotor activity in anticipation of the scheduled feeding.

Support (optional): NIH grants (NS030140, NS052287), and Medical Research Service of the Department of Veterans Affairs

1097

SLEEP FRAGMENTATION IN RATS INCREASES ENDOPLASMIC RETICULUM STRESS IN BASAL FOREBRAIN NEURONS AS SHOWN BY EXPRESSION OF P-eIF2 α

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Introduction: Sleep fragmentation (SF) is a symptom of several human sleep disorders. Like sleep deprivation, SF increases homeostatic sleep drive as indicated by daytime sleepiness. Increased brain protein synthesis has been hypothesized to be a function of sleep. Sleep homeostasis may be induced by an increased demand for brain protein synthesis. Protein folding in the endoplasmic reticulum (ER) is a key step of the synthetic pathway; ER stress, corresponding to arrest of protein folding, is induced by short term sleep deprivation in fly, mouse and rat (Naidoo et al., 2005). Arrest of sleep synthesis and folding is caused by phosphorylation of eIF2 α . We hypothesized that SF would induce p-eIF2 α in homeostatic pathways including in basal forebrain cholinergic neurons.

Methods: Four pairs of rats were subjected to 96 hrs of either SF or SF control (SFC) by the intermittent treadmill method. SF rats had their sleep interrupted for 3 seconds after every 30 seconds, whereas sleep of SFC rats was interrupted for 30 min every 5 hrs. After treatment, rats were euthanized and their brains stained for ChAT and p-eIF2 α immunofluorescence. The number of single labeled (ChAT or p-eIF2 α) and double labeled neurons (ChAT + p-eIF2 α) were counted in defined BF regions.

Results: Ninety six hrs of SF increased the number of p-eIF2 α expressing neurons in both rostral and medial BF [Rostral:- 164 \pm 38 (SF) vs 131 \pm 21 (SFC); Medial:- 244 \pm 69 (SF) vs 96.25 \pm 31 (SFC)]. SF also increased the proportion of ChAT cells that co-localized p-eIF2 α [Rostral:- 21.0 \pm 4.7 (SF) vs 14.8 \pm 2.4 (SFC); Medial:- 20.3 \pm 2.9(SF) vs 12.9 \pm 4 (SFC)].

Conclusion: The build up of an ER stress molecule following SF in the POA/BF neurons could be a cellular correlate of the mechanism underlying increased sleep drive induced by SF.

1098

THE EFFECTS OF PARADOXICAL SLEEP DEPRIVATION AND SLEEP REBOUND ON GLOBAL GENE EXPRESSION IN THE RAT BRAIN

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Introduction: Paradoxical sleep deprivation promotes a number of behavioural, physiological, as well as cellular functioning alterations. Recent data has demonstrated that PSD can also influence the expression of genes in specific brain regions.

Methods: To better understand the effects of PSD at a molecular level, equivalent mass amounts of total RNA from the right cerebral cortex of Wistar rats assigned to the following groups: Control (n=3), PSD-96h (n=3) and rebound 24h (n=3), were used to hybridize nine independent sets of GeneChip® Rat Genome 230 2.0 arrays, comprised of more than 31,000 probe sets.

Results: A total of 55 genes were found to be differently expressed after 96 hours of sleep deprivation. These include genes related to cellular and metabolic process (BDNF, Glycerol-3-phosphate dehydrogenase), regulation of biological process (HtrA serine peptidase), response to stimulus (Metallothionein, Heat shock 27kDa protein, Hypocretin and Glutamate receptors2), rhythmic process (Period-2) and reproduction (VGF nerve growth factor inducible). Interestingly, after 24 hours of sleep recovery, ~50% (n=25) of the PSD genes had their expression returned to control levels and 200 transcripts, such as, Adenosine A2B receptor, Insulin receptor substrate2, Corticotropin releasing hormone, Homer1,

Early growth response 1,2,4, were specifically altered when compared to sleep deprivation condition. Moreover, when the sleep rebound group was compare to control animals, only 4 transcripts showed significantly different expression levels.

Conclusion: Together, these results suggest that prolonged sleep deprivation promotes a specific pattern of gene expression that is likely to affect a series of cellular and physiological processes. In addition, a number of potential candidates for the molecular basis of homeostatic mechanism of sleep regulation could be identified, suggesting that sleep rebound state can also be reflected at gene expression levels.

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GENE EXPRESSION PROFILING IN BASAL FOREBRAIN OF MICE FOLLOWING SLEEP FRAGMENTATION

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Introduction: In mammalian brain, sleep and wakefulness are associated with widespread changes in gene expression. Obstructive sleep apnea (OSA) is a complex disorder and sleep fragmentation (SF) is one of its primary characteristics. We hypothesized that changes in gene expression would occur in the basal forebrain of mice subjected to a recently developed, stress-free SF procedure.

Methods: Adult CB57BL mice (n=7) were exposed to SF (arousals every 2 min for 6 h) using a custom designed instrument and 5 timed-control mice were also studied. Animals were quickly decapitated under general anesthesia, basal forebrains were harvested and snap frozen in liquid nitrogen, total RNA was extracted, and hybridized onto whole mouse genome long-oligonucleotide microarrays (Agilent). Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses were used to identify significant functionally-related groups of genes, and hierarchical cluster analyses were used to visualize expression changes between control and SF conditions.

Results: Of the 41,411 viable transcripts, 4,336 transcripts were differentially expressed in SF mice using initial scrutiny based on p-values <0.05. GO and biological pathways were constructed and revealed that the major molecular functions consisted of catalytic activity, molecular transducer activity, transcription regulator activity, and transporter activity. The KEGG pathway database was also used to characterize the enrichment of specific pathway components into functionally regulated genes groups. The 4 significantly modulated pathways were MAP kinase signaling; focal adhesion; calcium signaling; and cytokine-cytokine interactions.

Conclusion: Patterns of gene expression in murine basal forebrain are extensively altered following acute SF. Initial analytical procedures lend support to the use of systems biology approaches to increase our understanding of potential mechanisms that underlie SF-associated adaptations and consequences. Further analyses should allow for identification biologically-relevant gene clusters and pathways and gene-gene interactions that may be functionally relevant in sleep fragmentation.

Support (optional): SCOR 2P50HL60296, HL 69932 and Children's Foundation for Sleep and Neurobiology Research

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DIURNAL RHYTHM OF MICRORNA EXPRESSION IN THE BRAIN

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Introduction: MicroRNAs (miRNAs) are regulators of mRNA translation. They are small (~22 nucleotide) strands with the capacity to hybridize with the RISC protein complex and target mRNA leading to its degradation or inhibiting its translation. Because gene and protein levels

are altered by sleep/wake state we hypothesized miRNA levels in the brain would be affected by time-of-day.

Methods: Male Sprague-Dawley rats 275-325 g were acclimated to a 12/12 hr L/D cycle and sacrificed at two time points, light or dark onset. Immediately following decapitation, hippocampus, prefrontal cortex, somatosensory cortex and visual cortex were dissected and frozen in liquid nitrogen. RNA isolation, fractionation, labeling and array hybridization were performed as previously described (Neurosci Lett 422:68-73).

Results: In the somatosensory and visual cortex, twenty miRNAs decreased in the dark with respect to corresponding values obtained from rats sacrificed in the light. Let-7b, miR-132, miR-138 and miR-13232 were among the miRNAs that decreased from dawn to dusk in the prefrontal cortex, while let-7c, miR-29a, miR-128a and miR-191 increased. In contrast, twenty-two hippocampal miRNAs manifest up-regulation and only five showed down-regulation, including miR-138 and miR-13232.

Conclusion: These findings are important to the idea that miRNAs are involved in sleep regulation. Recently we reported that sleep loss alters miRNA expression in the hippocampus, cortex and hypothalamus. The majority of those miRNAs affected by sleep loss also fluctuated across the day. Currently we are investigating the targets of select miRNAs that change with sleep propensity. It seems likely that miRNAs, as key components of gene expression, are important intermediates in the regulation of sleep.

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DIURNAL VARIATIONS IN PURINE P2X7 AND P2Y1 RECEPTORS CORRELATE WITH THE SLEEP-WAKE CYCLE IN THE CORTEX

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Introduction: ATP is co-released with glutamate and other neurotransmitters during synaptic transmission. ATP binds to purine P2X7 receptors on microglia to release tumor necrosis factor (TNF) and interleukin-1 (IL1). These cytokines are implicated in sleep regulation and act on nearby neurons to alter their expressions of the adenosine A1 receptor and the gluR1 component of the AMPA receptor and thereby scale their responsiveness to subsequent inhibitory or excitatory signals in proportion to prior activity. Further, the TNF receptor forms a complex with the P2Y1 receptor on astrocytes and this complex is involved in glutamate release from the astrocytes. Through these actions we posited that these mechanisms provide a means by which the brain can track past activity and hence time spent in sleep and wakefulness on a local scale. As a first test of this hypothesis we determined P2X7 and P2Y1 mRNA levels in cortical samples.

Methods: Rats were acclimated to a 12:12 h L/D cycle at 24°C. Every 3 h 6 rats were sacrificed, somatosensory cortical samples dissected, RNA extracted, cDNA prepared and real time RT-PCR performed as previously described (Taishi et al Brain Res 1156:125, 2007) to determine P2X7, P2Y1, TNF and IL1 mRNA levels.

Results: mRNA levels of both purine receptors were highest during the last 3 h of the light period, just before the transition to dark hours. Their values at that time were about 2-fold higher and significantly different from their corresponding lowest values observed. In contrast, TNF and IL1 mRNA highest levels were at the beginning of the light period as previously reported.

Conclusion: Results are consistent with the hypothesis that extracellular ATP provides a mechanism via somnogenic cytokines to keep track of prior sleep/wake history.

Support (optional): NINDS (NS25378 and NS31453)

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FOOD ANTICIPATORY ACTIVITY IN PREPROGHRELIN KNOCKOUT MICE

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Introduction: Diurnal rhythms can be entrained by daily feeding schedules suggesting the existence of a food-entrainable oscillator. The signals that entrain this oscillator in accordance to the feeding schedule are not known. Ghrelin could serve as such a signal, since fluctuations in plasma ghrelin levels closely follow feeding activity and ghrelin receptors are expressed in the dorsomedial hypothalamus, a brain region implicated in the regulation of food-entrainable rhythms. In the present study we determined whether mice lacking the preproghrelin (Ppg) gene are able to develop food anticipatory behavior.

Methods: Baseline values of sleep-wake activity, food intake, body weight, body temperature and locomotor activity of Ppg knockout (KO, n = 8) and wild-type (WT, n = 8) mice were collected during a three-day period. Mice were kept on 12-12 hour dark-light cycle; lights went on at 9 am. Beginning from the fourth day mice were allowed to eat only during the light period in hours 5-8. Data were collected for two weeks.

Results: Restricted feeding to a 4-h period in the light phase induced characteristic changes in all measured parameters within 7 days. In the second half of the night NREMS and REMS started to increase and were significantly elevated for 6 hours compared to baseline. One hour before the scheduled feeding period wakefulness increased and stayed above baseline for the 4-hour feeding period. These anticipatory increases in wakefulness were accompanied by elevated locomotor activity and increases in body temperatures. The responses in WT and KO mice were not statistically different.

Conclusion: Present findings indicate that preproghrelin KO mice are able to mount food anticipatory activity when kept on a restricted feeding protocol. Thus, products of the preproghrelin gene are not essential for food anticipatory behavior in mice.

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1103

A MOUSE MODEL FOR FAMILIAL ADVANCED SLEEP PHASE SYNDROME

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Introduction: Recently, we reported "early-runner" behavior in a subset of mice derived from a backcross of two genetically diverse strains -- CAST/EiJ (CE) x C57BL/6J (B6) (Wisor et al., 2007). These "early-runners" typically initiate wheel-running 4-6 hours prior to dark onset, whereas most mice begin at dark. We identified a QTL on chromosome 18 that accounts for a substantial portion of the genetic variance in this trait. In this study, we tested similar mice under a wider range of conditions.

Methods: Daily rhythms of activity or sleep were assessed in CE, B6, and progeny by wheel-running or in a piezoelectric system that scores sleep and wake (AE Flores et al., 2007). A 12h:12h Light:Dark (LD) cycle was followed by several weeks in DD. Conditions in this present study utilized green lights at 100-lux, whereas our earlier report utilized more intense fluorescent light.

Results: All B6 mice displayed normal activity onsets at dark, while CE mice displayed activity onsets several hours earlier. This was observed

in both wheel-running activity and by percentage of sleep and wake using the piezoelectric technology. This result was observed in three independent laboratories (at UK, SRI, and NWU). In both backcrosses and intercrosses, progeny displayed onsets ranging from eight hours before dark onset to the time of dark onset. The median phase of activity/wake onset for CE mice and early runner progeny was about four hours before dark. Upon release to DD, all mice maintained the phase determined by the prior LD cycle.

Conclusion: CE mice, and a high percentage of progeny from CE crosses, display an advanced activity and sleep-wake pattern similar to humans with Advanced Sleep Phase Syndrome (ASPS). The chromosome 18 QTL, described in Wisor et al. 2007, contains two casein kinase I genes similar to the gene responsible for one form of Familial ASPS (Xu et al, 2005).

1104

NEURAL SUBSTRATES OF AWAKENING PROBED WITH OPTOGENETIC CONTROL OF HYPOCRETIN NEURONS

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Introduction: The neural underpinnings of sleep involve interactions between sleep-promoting areas such as the anterior hypothalamus, and arousal systems located in the posterior hypothalamus, the basal forebrain and the brainstem. Hypocretin (Hcrt, also known as orexin)-producing neurons in the lateral hypothalamus are important for arousal stability, and loss of Hcrt function has been linked to narcolepsy. However, it is unknown whether electrical activity arising from Hcrt neurons is sufficient to drive awakening from sleep states or is simply correlated with it.

Methods: Here we directly probed the impact of Hcrt neuron activity on sleep state transitions with *in vivo* neural photostimulation, genetically targeting channelrhodopsin-2 to Hcrt cells and using an optical fibre to deliver light deep in the brain, directly into the lateral hypothalamus, of freely moving mice. We measured the latencies of Non Rapid Eye Movement sleep (NREM)- and Rapid Eye Movement sleep-to-wake transitions after a single optical stimulation at different frequencies in ChR2-transduced wildtype and Hcrt knockout animals. We further used a long-term optical stimulation protocol to study behavioral transitions under sustained optical stimulations of the Hcrt neurons.

Results: We found that direct, selective, optogenetic photostimulation of Hcrt neurons increased the probability of transition to wakefulness from either slow wave sleep or rapid eye movement sleep. Notably, photostimulation using 5-30 Hz light pulse trains reduced latency to wakefulness, whereas 1 Hz trains did not. Interestingly, Hcrt KO animals did not exhibit a reduction of latency to wakefulness after repeated long term optical stimulation.

Conclusion: This study establishes a causal relationship between frequency-dependent activity of a genetically targeted Hcrt neurons and behavioral transitions. Alternative optical stimulation protocols should define the implication of the Hcrt neurons in wakefulness maintenance.

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METABOLIC GENE VARIANTS, SLEEP QUALITY AND CIRCADIAN RHYTHMS IN COMMUNITY-DWELLING OLDER MEN

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Introduction: Previous studies suggest a link between sleep dynamics and metabolic control including steroidogenesis, glucose/insulin metabolism, growth hormone, and appetite regulation. We assessed the association between polymorphisms in these pathways and rest-activity rhythms measured by actigraphy in a population based cohort.

Methods: Activity patterns were measured using wrist actigraphy for an average of 5.2 nights in a cohort of 3053 community-dwelling men aged 67 and older from the Osteoporotic Fractures in Men Study. Parameters of interest included sleep performance (total sleep time, efficiency, latency, wake after sleep onset) and rest-activity rhythms (amplitude, mesor, acrophase, F-value). Genotyping of tagging (HapMap phase I) and potentially functional SNPs was performed in 454 men with wrist actigraphy data. Analyses were multivariate adjusted for age, clinic site and BMI.

Results: Regression analysis for sleep disturbance (wake after sleep onset, efficiency, latency) showed nominally significant associations with SNPs in IGF1 (p=0.007), PPARg (p=0.006), PPARGC1a (p=0.008), LEPR (p=0.007), HSD17B4 (p=0.004) and PPARa (p=0.002). The IGF1 SNP along with SNPs in IGF1R (p=0.006) and IGF2R (p=0.007) were associated with reduced total nighttime sleep duration and increased daytime sleep. Analyses for rest-activity parameters revealed significant associations between SNPs in IGF1 (p=0.009) and RXRa (p=0.003) for acrophase (time of peak activity) and amplitude (height of peak). Polymorphisms in IGF1R (p=0.005) and HSD17B4 (p=0.003) were associated with reduced mesor (mean activity) and F-value (circadian robustness). Haplotype analysis revealed stronger associations for several of genes and outcomes including IGF1, IGF2R, and HSD17B4 and daytime sleep, PPARa and total nighttime sleep, and IGF1R and sleep latency.

Conclusion: Our results suggest that polymorphisms in genes controlling steroidogenesis, glucose/insulin metabolism, and appetite control are associated with increased sleep fragmentation, shorter sleep duration and desynchronized rest-activity rhythms. Future research will involve replication of findings in another large cohort and additional genotyping/sequencing to identify the putative causal variants underlying these associations.

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1106

SEQUENCE POLYMORPHISM OF THE HOMER 1 GENE DETERMINES DIFFERENTIAL ACCUMULATION OF SLEEP NEED AFTER SLEEP DEPRIVATION

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Introduction: Analysis of the QTL for accumulation of delta power after sleep deprivation in inbred strains of mice indicates that the Homer 1 gene is a likely candidate responsible for this phenomenon. Homer proteins form scaffolds that connect receptors such as the metabotropic glutamate to downstream signaling molecules. In this experiment, we performed sequence analysis of the Homer 1 gene promoter in recombinant inbred strains of mice used for the QTL mapping. We determined the expression pattern of the Homer 1 gene and its isoform, Homer 1a, in sleep and after sleep deprivation.

Methods: The nucleotide sequence of the promoter region of Homer 1 gene containing G/C polymorphism in c-Ets-1 and E-box domains was established in twenty-seven inbred/parental strains of mice. This polymorphism is defined by the SNP rs29874758. We question whether sequence polymorphism in the promoter of Homer 1 gene is predictive of the time course of accumulation of delta power after sleep deprivation. The expression pattern of the Homer 1 gene and its isoforms was determined by RT-PCR and the levels of Homer proteins by Westerns.

Results: We established that recombinant inbred strains carrying the C allele exhibited long time courses of accumulation of delta power after sleep deprivation that was characteristic of DBA/2J mice. Strains carrying the G allele in promoter region of the Homer 1 gene accumulated delta power faster with characteristics of that of C57BL/6J mice. DBA/2J and C57BL/6J differ significantly in their abilities to up-regulate the Homer 1a; when compared to C57BL/6J, DBA/2J mice are unable to increase levels of Homer 1a after sleep deprivation.

Conclusion: We postulate that sequence polymorphism of Homer 1 promoter, and as a consequence the differential expression of Homer 1a isoform, determines the time course of accumulation of delta power after sleep deprivation in inbred strains of mice.

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GENETIC POLYMORPHISM IN CLOCK PREDICTS TIMING OF CIRCADIAN LIGHT SENSITIVITY IN HUMANS

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Introduction: A negative feedback loop of genes and proteins lies at the core of the circadian clock. One of its molecular components is *circadian locomotor output cycles kaput* (*CLOCK*), disruption of which causes a lengthening of circadian period and a diminution of circadian amplitude in mice. A known single nucleotide polymorphism (SNP) of human *CLOCK* (T3111C) has been associated with differences in morningness/eveningness (M/E) preference.

Methods: We determined the relationship between the *CLOCK* T3111C SNP and M/E in a cohort of older individuals (31 female, 14 male, 64.0±7.00 years old, 87% Caucasian) with primary insomnia. We also determined the relationship between this SNP and the phase angle of entrainment (ψ), the time between the midpoint of habitual sleep and the midpoint of the plasma melatonin rhythm. Plasma melatonin concentrations were assessed during an overnight protocol at the Stanford General Clinical Research Center (GCRC). Sleep during the week prior to entry into the GCRC was quantified using wrist actigraphy and sleep

logs. Blood was collected for determination of the *CLOCK* T3111C SNP status. M/E was determined using the Horne-Östberg questionnaire.

Results: The C allele was associated with less morningness: CC (n=5, M/E=59±9.1), CT (n=17, M/E=65±8.8), TT (n=21, M/E=68±8.4) (*n.b.*, higher M/E scores are associated with more morningness). The C allele was also associated with a larger ψ (*i.e.*, melatonin peak occurring earlier in sleep cycle): CC (n=5, ψ =0.84±0.61h), CT (n=17, ψ =0.53±0.87h), TT (n=22, ψ =0.55±0.76 h).

Conclusion: While the C allele in the *CLOCK* T3111C SNP is associated with less morningness, we find that individuals homozygous for the C allele have a larger ψ , suggesting that the phase response curve (PRC) is shifted earlier in the sleep episode in these individuals. The PRC represents the light sensitivity of the circadian clock. Thus, a SNP in the *CLOCK* gene was associated with the timing of circadian light sensitivity.

Support (optional): R01 AG 12914 (NIH), VA, MIRECC, RR-00070 (NCRR-NIH)

1108

CYTOKINE GENE VARIATIONS ARE ASSOCIATED WITH SLEEP DISTURBANCE IN HIV-INFECTED ADULTS

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Introduction: Previous research implicates cytokine function in sleep pathology, and yet the role of innate gene variation in this relationship is largely unknown. This study examines genetic variations of three cytokines: Interleukin (IL)-1 β , IL-6, and tumor necrosis factor (TNF) α as predictors of sleep time (TST) and wake after sleep onset (WASO).

Methods: Fasting bloods were collected from 174 HIV-infected men and women (ages 22 to 65) for genetic analyses. Most were either White (41%) or Black (40%), with 9% Latino, 9% other/mixed, and 1% Asian. Genotypes were determined using Pre-Developed Taqman[®] Assays for allelic discrimination. Wrist actigraphy (Ambulatory Monitoring, Inc.) and sleep logs were used to monitor sleep for 72 consecutive weekday hours.

Results: Single nucleotide polymorphisms (SNPs) from the cytokines examined were associated with sleep parameters. Two of the seven IL-1B SNPs were associated with WASO. The rs1143634 minor A allele carriers (p=.037) and rs1071676 minor C allele carriers (p=.039) had WASO that was higher than non-carriers (mean difference \pm SE for both SNPs was 5.7% \pm 2.7%). Two of the five IL-6 SNPs examined were associated with TST. The IL-6 rs2069845 major A allele carriers and rs35610689 major T allele carriers had shorter total sleep time by 49 \pm 23 minutes (p=.034) and 81 \pm 36 minutes (p=.041), respectively. One of the five TNFA SNPs was associated with WASO. The TNFA rs2239704 major C allele carriers had higher (23.0% \pm 17.0%) mean WASO values than non-carriers (14.6% \pm 11.3%; p=.033).

Conclusion: These results provide preliminary evidence of genetic association of three cytokines with sleep disturbance in a sample of HIV-infected subjects and suggest that the inflammatory pathway is involved in sleep/wake regulation in this clinical population. Analyses are currently in process to examine associations with anthropometrics as well as covariates that include gender, race, duration of HIV infection, and medication use.

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CYTOKINE GENE VARIATIONS ARE ASSOCIATED WITH CIRCADIAN RHYTHM IN HIV-INFECTED ADULTS

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Introduction: Previous research implicates cytokine function in sleep/wake cycles, and yet the role of innate gene variation in this relationship is largely unknown. This study examines genetic variation in three cytokines, Interleukin (IL)-1 β , IL-6, and tumor necrosis factor (TNF) α as predictors of circadian rhythm strength (autocorrelation), acrophase, and chronotype.

Methods: Fasting bloods were collected from 166 HIV-infected men and women (ages 22 to 65) for genetic and metabolic analyses. Most of the sample was either White (42%) or Black (39%), with 9% Latino, 1% Asian, and 9% other or mixed ethnicity. Genotypes were determined using Pre-Developed Taqman[®] Assays for allelic discrimination. Wrist actigraphy (Ambulatory Monitoring, Inc.) and sleep logs were used to monitor sleep for 72 consecutive weekday hours. Subjects also completed the 19-item Morningness-Eveningness Questionnaire (MEQ; Horne & Ostberg), but due to subjects' difficulty completing the full scale, only the last item ("which type do you consider yourself to be?") was used to estimate chronotype. The last item had a correlation of .72 with the full-scale score.

Results: Each of the cytokines had at least one single nucleotide polymorphism (SNP) associated with self-reported chronotype ($p=.004$ to $.038$). In addition, two of the seven IL-1B SNPs were associated with circadian rhythm strength. The IL-1B rs16944 minor A allele carriers and rs1143629 minor G allele carriers had weaker 24-hr rhythms ($p=.038$ and $.047$, respectively). TNFA rs2239704 minor A allele carriers had later acrophases ($p=.014$) and TNFA rs1800683 minor T allele carriers had weaker 24-hr rhythms ($p=.020$).

Conclusion: These results provide preliminary evidence of the association of three cytokine gene variations with circadian rhythm parameters in a sample of HIV-infected men and women. Analyses are currently in process to examine associations between circadian rhythm parameters and cytokine analytes as well as covariates such as gender, race, duration of HIV infection, and medication use.

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1110

THE FORAGING/PKG LOCUS PROMOTES SLEEP/WAKE TRANSITIONS IN DROSOPHILA

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Introduction: Recent studies in *C. elegans* identified the cGMP-dependent protein kinase (PKG) gene *egl-4* as a regulator of sleep-like behavior (Raizen et al, '08). In *Drosophila*, changes in activity of the *foraging* locus, which also encodes a PKG, were associated with changes in total sleep. In this study, we describe sleep architecture differences that are associated with differences in foraging gene activity.

Methods: To accurately measure *Drosophila* sleep, we used video analysis (Zimmerman et al, '08). Following 3 days of acclimation in a 25-deg incubator under 12-hr:12-hr light:infrared conditions, we recorded for 48-hours the behavior of 20-28 virgin females of each genotype housed in glass monitor tubes containing 1% agar and 5% sucrose at one end and a yarn plug at the other. We analyzed the video data as described (Zimmerman et al, '08). Strains used include the R, s, and s2 strains. The R strain has higher PKG activity than both the s and s2 (Osborn et al, '97). The s2 strain was derived from the R strain (Pereira et al, '93).

Results: R flies slept more than s2 flies during both the day ($p=0.04$) and the night ($p=0.04$) and slept more than the s flies only during the day ($p=E-13$). When compared to its s2 genetic control, R flies showed shorter sleep and wake bouts, in particular during the day ($p=E-5$, $p=0.003$, respectively).

Conclusion: As in *C. elegans*, greater PKG activity is associated with more sleep in *Drosophila*, suggesting a conserved sleep-regulatory role for this gene. Sleep architecture analysis suggests that PKG promotes sleep-wake transitions in *Drosophila*.

1111

MARITAL HAPPINESS AND SLEEP QUALITY IN WOMEN: RESULTS FROM THE STUDY OF WOMEN'S HEALTH ACROSS THE NATION

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Introduction: Divorced individuals have higher rates of insomnia, particularly among women. However, divorce is an imperfect proxy for relationship functioning. Unhappy marriages may similarly confer increased risk for sleep problems, but little is known about the association between marital quality and sleep. Thus, the present study examined the association between marital happiness and sleep in women.

Methods: Participants were 2,148 married women from the Study of Women's Health Across the Nation (SWAN), a multi-site study of midlife women (M age=45.9 years). The cohort included Caucasian (n=1085), African American (n=439), Hispanic (n=198), Chinese (n=199), and Japanese (n=227) women. Participants reported their marital happiness, sleep quality (SQ) and frequency of difficulty falling asleep (DFA), staying asleep (DSA), or early morning awakenings (EMA). DFA, DSA, and EMA were scored 0 (< 3 times per week) or 1 (≥ 3 times per week). SQ was coded as 1 (restless or very restless) or 0 (average, restful, or very restful). A composite sleep disturbance score was calculated by summing the 4 binary sleep items (range 0 to 4). Ordinal logistic regression examined whether higher levels of marital happiness were associated with lesser risk of having multiple sleep complaints after statistically adjusting for medication usage, and sociodemographic, psychosocial, and general health characteristics.

Results: Higher levels of marital happiness were associated with lesser risk of having multiple sleep complaints in the fully adjusted model (OR=.90; 95%CI:.83,.98), but only among the Caucasian women (OR=.85; 95%CI:.76,.95). Analysis of the individual sleep items revealed that greater marital happiness was associated with lesser risk of DFA, DSA, EMA, and restless SQ.

Conclusion: Marital happiness may attenuate the risk of sleep problems in Caucasian women. Alternatively, marital strife may potentiate the risk. Assessing relationship quality may yield important information regarding the etiology or maintenance of sleep problems in midlife women.

1112

PERFORMANCE ON A LETTER VERBAL FLUENCY TASK IS BETTER, NOT WORSE, AFTER SLEEP DEPRIVATION

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Introduction: Previous studies have found that sleep deprivation impairs verbal fluency. As part of a larger study investigating executive function during sleep deprivation, we examined performance on a letter verbal fluency task. This task involves in 1min generating as many novel words as possible that begin with a certain probe letter. Switching between phonemic word clusters during the task to avoid repeating previous responses involves effortful executive control.

Methods: 24 healthy native English speakers (aged 22-40y; 12 females) spent 7 consecutive 24h days in a sleep laboratory with continuous behavioral monitoring. 12 subjects were randomized to 62h total sleep deprivation (TSD) preceded and followed by two nighttime sleep periods with 10h TIB; 12 controls had 10h TIB for sleep each night. The letter verbal fluency task was administered at 11:00 during baseline, 52h TSD, and recovery. During each test bout, subjects received three equivalent 3-letter versions of the task (F,A,S; P,R,W; or C,F,L) in randomized, counterbalanced order. Mixed-effects ANOVAs were performed to examine condition, session and interaction effects. Analyses were repeated with probe letter and version order as covariates.

Results: A significant practice effect across test bouts was observed; from the first to the last test bout the number of correct words generated increased from 37.5±2.1 to 44.5±2.1 (F=19.4, P<0.001). There were significant condition by bout interaction effects for number of correct words (F=5.8, P=0.004) and number of switches between word clusters (F=8.32, P<0.001). Pre-planned contrasts revealed that specifically for the second (i.e., sleep deprivation) test bout, subjects in the TSD condition displayed a relative improvement of 7.7±2.3 more correct words and 8.5±2.2 more cluster switches compared to controls. These results were robust to inclusion of covariates.

Conclusion: Sleep-deprived participants generated more words and displayed more switching between phonemic word clusters on a letter fluency task than did rested controls. Performance on this task has been linked to cognitive flexibility. Earlier research suggested that cognitive flexibility is specifically vulnerable to impairment during sleep deprivation, but such a conclusion may be overly generalized. We hypothesize that sleep deprivation, through impairment of working memory, may reduce interference from prior responses in the letter verbal fluency task, thus leading to improvement in word generation and cluster switching ability.

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1113

THE IMPACT OF MOOD AND SLEEP DISTURBANCE ON EMOTIONAL MEMORY IN REMITTED DEPRESSED PARTICIPANTS

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Introduction: We earlier reported that sleep disturbance plays a significant role in emotional memory in remitted depressed participants. It has been shown that mood state can also influence the type of stimuli most likely to be recalled. The current analysis seeks to differentiate the roles of sleep disturbance and mood in recall of emotional stimuli.

Methods: Medication-free subjects with partially remitted Major Depressive Disorder (n=17) were shown 30 slides from the International Affective Picture System (with positive, negative, and neutral valences) prior to an overnight sleep study. In the morning, subjects were asked to recall as many pictures as possible, and to complete the Positive and Negative Affect Scale. Sleep was assessed by overnight polysomnography. Linear regressions were used to determine the relative contribution of sleep disturbance and mood to recall.

Results: Sleep disturbance accounted for a significant proportion of the variance in recall for neutral pictures (p<.10), while measures of mood at the time of recall did not (p>.05). This pattern was also observed for recall of positive pictures, but did not reach statistical significance. Recall for negative pictures was predicted by mood measures (p=.08), but not by sleep disturbance (p=.96). Sleep disturbance and mood measures were unrelated to one another (p>.10).

Conclusion: Sleep disturbance and mood showed differential patterning on memory of emotional images. Sleep disturbance was the primary predictor of recall of neutral and positive pictures, while mood accounted for nearly all of the variance in recall of negative pictures.

1114

REM SLEEP, PREFRONTAL THETA, AND HUMAN EMOTIONAL MEMORY CONSOLIDATION

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Introduction: Memory can be modulated by emotion, leading to enhanced consolidation across hours/days. Sleep also modulates memory processing, resulting in offline performance enhancements. Most sug-

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gestive, a remarkable overlap exists between the known neurobiological mechanisms that orchestrate emotional memory consolidation, and the complimentary neurobiology that REM-sleep provides. Using a nap paradigm, here we test this hypothesis, demonstrating the selective REM-sleep facilitation of emotional memory consolidation and its associated with prefrontal theta power during REM.

Methods: Thirty subjects (18-30yr) were assigned to either a Nap or a No-Nap group. Subjects performed two study sessions, in which they learned emotionally negative and neutral picture stimuli; one 4hr prior, and one 15min prior to a recognition memory test. The Nap group (n=15) obtained a 90-minute midday nap after the first study session, while the No-Nap group (n=15) remained awake.

Results: Within the No-Nap group, no significant enhancement of either emotional or neutral stimuli occurred across the offline period. In contrast, a significant and selective offline enhancement of emotional (but not neutral) memory was observed in the Nap group ($p < 0.05$). Furthermore, within the Nap group, the amount of emotional memory consolidation was strongly correlated with the amount of REM sleep ($r = 0.62$, $p = 0.02$), and negatively correlated with the REM latency ($r = -0.63$, $p = 0.02$). Most striking, power spectrum analysis demonstrated that right-dominant prefrontal theta-power (4.0-7.0Hz) during REM exhibited a significant and positive relationship with the amount of emotional memory facilitation ($r = 0.61$, $p = 0.03$).

Conclusion: Together, these findings demonstrate 1) that negative emotional memories are preferentially consolidated by the neurophysiology of REM sleep, and 2) that characteristics of theta activity within the right prefrontal cortex during REM (a region associated with negative affective processing, and with reciprocal connectivity to the amygdala), may modulate these neuroplastic memory processes; findings of clinical relevance and translation implications for affective mood disorders.

1115

VIRTUAL MAZE LEARNING IS ENHANCED BY A SHORT DAYTIME NAP CONTAINING ONLY NREM SLEEP

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Introduction: Animal studies demonstrate that, following performance of spatial tasks, learning-related brain activity is re-expressed in the hippocampus and in cortical networks, during NREM sleep. Though similar learning-dependent hippocampal reactivation has been observed during human sleep, the effects of sleep vs wakefulness on spatial memory performance across time have not yet been fully described. Here, we examined the effect of a daytime nap on changes in virtual maze performance across the day.

Methods: Participants (n=35) were trained on a 3D-style virtual maze task at 12:30pm. Following training, subjects either immediately lay down to begin a 1.5 hr nap opportunity (n=17), or else remained awake (n=18). Nap participants were awoken prior to entering REM. All subjects were retested on the maze at 5:30pm. Nap EEG was analyzed by examining power spectral density in the spindle (11-15Hz), slow oscillation (<1Hz), and delta (1-4Hz) bands, using Welch's method.

Results: Post-training sleep provided a clear performance benefit, but only for those participants who had relatively greater prior experience navigating a virtual environment. In these participants (n=26), maze performance improved significantly more across sleep than across wakefulness ($p = .02$). In contrast, novice game players (n=9; reporting playing 3D-style games < once per year) improved substantially across time ($p = .02$), but equivalently across periods of wake and sleep. The effect of sleep on performance improvement was strongly dependent on prior game experience (ConditionxTimexExperience interaction, $p = .005$). Frontal slow oscillation power, as well as delta power during Stage 2, predicted the extent of performance improvement in experienced game players.

Conclusion: These observations suggest that reactivation of learning-related brain activity during NREM sleep, similar to that seen in rodents, confers a performance advantage for spatial memory in humans. Furthermore, the performance improvements seen here were related to low-frequency (slow oscillation, delta) EEG power, thought to support hippocampal-cortical communication during sleep.

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SLEEP AND EPISODIC MEMORY CONSOLIDATION

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Introduction: Post-training sleep has previously been shown to be critical for improvement on explicit memory tasks. Here, we examined the role of sleep in consolidation of episodic memory using a task that allowed us to dissociate the effects of sleep on memory for objects (pure factual information), their spatial locations, and the order in which the objects were presented (temporal information).

Methods: Forty-one healthy 18-25 year olds were trained on an episodic memory task and tested the following morning. They were randomly assigned to either a sleep group (n = 22), which had an 8-hour period of sleep during the retention interval, or a control group (n = 19), which remained awake during the retention interval.

Results: The sleep and wake groups did not differ at baseline in their memory for objects, object locations, temporal order of objects, or on composite episodic memory score. To provide an overall test of whether sleep versus wake produced differences in episodic memory, a MANOVA was calculated across 3 dependent variables. There was a significant overall effect of group on episodic memory performance ($p = 0.030$). Memory for objects was improved with sleep, and deteriorated in the wake condition ($p = 0.006$). We report trend-level correlations between improvements in memory for objects and a decreased percentage of stage 2 NREM sleep ($r = 0.371$, $p = 0.089$) and an increased percentage of slow-wave sleep ($r = 0.379$, $p = 0.082$). We did not find that sleep had a beneficial effect on memory for spatial information. Sleep preserved memory for temporal order information, while the wake group showed a trend toward a decline in performance ($p = 0.072$).

Conclusion: We obtained an overall effect of sleep for episodic memory consolidation. We had hypothesized that the wake group would perform less well than the sleep group, and for two out of the three trial types, this was the case. Sleep had a beneficial effect on performance, a finding that is consistent with other literature suggesting that sleep is involved in explicit memory.

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1117

THE RELATIONSHIPS AMONG STRESS, SLEEP DURATION, AND SLEEP QUALITY AT THE TRAIT AND STATE LEVEL

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Introduction: The deleterious effects of poor sleep on neurobehavioral and physiological outcomes have been well documented. However, there is a paucity of research looking at how restricted sleep duration and poor sleep quality contributes to daily affective experiences, such as stress. Study objectives were to examine the relationship between stress, sleep duration, and sleep quality at the trait and state levels over the course of one week.

Methods: Participants consisted of 42 college undergraduates at a Midwestern university. Participants completed initial trait level measures of

stress (tST), and reported typical sleep quality (tSQ), and sleep duration (tSD). Daily surveys of state level stress (sST), sleep duration (sSD), and sleep quality (sSQ) were completed for five consecutive days beginning on a Monday during the semester.

Results: Correlations revealed that tST significantly correlated with tSD and tSQ ($p < .001$). One-way ANOVAs demonstrated those with lower sSQ reported significantly greater tST ($p < .001$), and lower sSD ($p < .05$). Using a repeated-measures ANCOVA over the five days, controlling for tSD, those with high tST reported significantly lower sSQ on days 1 and 3 ($p < .05$), while maintaining high sST even though reporting increased sSD. Of note, those with low tST demonstrated a trend of decreased sSD on days 1 through 3 with a corresponding increase in sST. Whereas high tST participants demonstrated no sST variability due to sSD. Linear regression showed that cumulative sleep loss over the week predicted state stress on day five.

Conclusion: Results suggest high tST has a strong relationship with poorer tSD and tSQ, although this study did not determine the direction of the relationship. There was an interesting trend in those with low tST toward increased vulnerability of an adverse stress response due to sleep changes, although an insufficient sample size limited statistical power. Further work is needed to understand the potential cyclical relationship between sleep and stress, especially as state varies from trait measures.

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DELAYING SCHOOL START TIME BY ONE HOUR: EFFECTS ON COGNITIVE PERFORMANCE IN ADOLESCENTS

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Introduction: Adolescents tend to stay up late and sleep late the next day. This shift in the sleep/wake pattern reflects changes in the brain's biological timing system. As adolescents need about 9.25 hours of sleep to function well, they often don't meet their sleep need. Consequently, they are sleep deprived, resulting in school absences, decreased motivation, inattention, and difficulty controlling emotions and behavior. The purpose of this current research was to evaluate the effect of school start times and sleep duration on cognitive performance functioning.

Methods: Forty-seven eighth graders from two classes, divided into experimental and control groups participated for two weeks. On week one, the experimental class began their school day one hour later than usual (at 08:30), and the control class began at the regular time (07:30). On week two, both classes began at 07:30. Subjects were requested to maintain their habitual sleep-wake pattern. Actigraphs were worn (Mini-Act, AMA-32, and AMI, Ardsley, NY) to objectively monitor sleep-wake patterns. On the fifth day of each week, students performed the following attention and concentration tests: (1) The MATH-CPT computerized test, (2) The d2 paper and pencil test.

Results: During the first week, the experimental class subjects woke up at 07:05±16, fifty one minutes later on average than the control class (06:25±23). During the second week, the experimental class woke up at (06:14 ± 13). Bedtime and sleep efficiency remained the same. Both cognitive tests showed better performance with the experimental group in comparison to the control group on the first week. On the MATH-CPT, the experimental group had better overall attention score (-1.13±0.64 vs. -0.17±1.03; $F=6.54$, $p<.05$) and on the d2 test, the experimental group had less total mistake responses (14±9 vs. 23.3±16; $F=7.79$, $p<.01$).

Conclusion: The results demonstrate that longer sleep duration positively affects cognitive functioning. An additional 51 minutes of sleep each day significantly improved attention and concentration.

1119

NAPPING ENHANCES ASSOCIATIVE STRENGTH IN CREATIVITY TASK

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Introduction: Creative problem solving has been observed to require an incubation period. Anecdotally, highly creative people report periods of drowsiness before sleep during which problem-relevant associations drift into consciousness, followed by the solution appearing upon waking. An associative explanation of the creative process proposes that this incubation period involves a rearrangement of preexisting, otherwise disparate and remote associative elements into new and useful combinations. We hypothesize that pre-incubation priming of correct answers on the Remote Associates Test (RAT) will increase the associative strength of primed words. Furthermore, sleep will be necessary to improve performance on the primed items of the RAT.

Methods: Well-rested adults were tested at 0930 on Form1 of the RAT(baseline), followed by a stem completion task, which provided the priming for RAT Form2. Between 1300-1500, nappers had a polysomnographically recorded nap, while non-nappers listened to Mozart with EEG. At 1730, subjects were tested on RAT Form2. Half of the Form2 items were previously primed. We calculated difference scores that compared baseline to primed and non-primed items and compared nap and non-nap groups on these change scores.

Results: There was a significant interaction between nap group and priming. Nappers showed a significant increase in performance for the primed items, relative to the unprimed items. Non-nappers showed no difference between primed and unprimed items.

Conclusion: Implicit priming increases the associative strength of specific words. Naps may, in turn, facilitate the associative connections related to these words, thereby improving performance on the RAT. An eight-hour delay occurred between priming and test. In future studies, we will vary the period between priming and testing, as well as the timing and length of the nap. These results have implications for domains that require creative strategizing and solution formation during daytime work.

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THE MEMORY-ENHANCING EFFECTS OF SLEEP

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Introduction: After learning information, what happens to those newly forged memories? How do they change over time and what are the determinants of those changes? Does sleep play a meaningful role? We recently presented data, using an A-B, A-C interference paradigm, that unmasked a large benefit of sleep for verbal memory (Ellenbogen et al, *Current Biology*, 2006). Here we further refine this experimental paradigm and repeat these novel findings with a different subject population.

Methods: Participants learned a list of 60 word-pair associates (A-B). Twenty pairs were randomly selected and tested 5 minutes after learning (baseline condition). The next randomly selected 20 pairs were tested after a 12-hour period of sleep, at night, or wake, during the day (no interference conditions). Then subjects learned an interfering list (A-C) for the remaining 20 A-B pairs. Finally, they were tested on their ability to retain these B words (interference conditions). For all conditions, the primary outcome was mean percent recall of the target words (B).

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Results: A two-way, mixed ANOVA ($N = 45$) demonstrated a significant main effect of Sleep [$F(1,43)=12.5, p=.001$] and Interference [$F(1,43)=38.1, p<.0001$], and a Sleep-by-Interference interaction [$F(1,43)=4.7, p=.035$]. In the no-interference conditions, mean recall was higher in the Sleep group ($M=81\%$, $SD=18$), than the Wake group ($M=65\%$, $SD=22$), $t(43)=2.63, p=.01$. In the interference conditions, this benefit of sleep for memory was even more pronounced: Sleep-Interference ($M=71\%$, $SD=21$) and Wake-Interference ($M = 44\%$, $SD = 24$), $t(43)=3.96, p < .0001$.

Conclusion: Memory evolves. When we sleep, newly formed memories strengthen, becoming resistant to interference in the day to come.

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COMPARISON OF THE EFFECTS OF 24-HOURS OF TOTAL SLEEP DEPRIVATION AND SLEEP INTERRUPTION ON VIGILANCE PERFORMANCE IN THE RAT-PSYCHOMOTOR VIGILANCE TASK

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Introduction: Sleep disturbance results in impairments in tasks requiring sustained attention. Although animal studies of sleepiness tend to employ total sleep deprivation (SD), sleep interruption/fragmentation (SI) is a more common condition in humans. Here we compare the effects of 24-hours of SD and SI on the rat-Psychomotor Vigilance Task (rPVT), a test of vigilance in rats highly analogous to the human PVT, which is widely used in sleep research to assay attention.

Methods: Water-restricted rats were trained to respond to short (0.5s), but unpredictable, light flashes at a central location with a nose-poke into the water delivery port mounted directly below the light, in return for water-reward. Different schedules of movement of an activity wheel were used to produce SD (3s on: 12s off for 24h) and SI (4s on: 56s off). An exercise control (EC) condition for both SD and SI provided the same overall amount of locomotor activity during each 3-hour of the 24, but provided the opportunity for long periods of uninterrupted sleep (SD-EC: 36min on 144min off; SI-EC: 12min on 168min off). A baseline condition (rats in the wheels for 24-hours without wheel movement) was also used. Each rat experienced all conditions in a repeated-measures counter-balanced design.

Results: In preliminary findings ($N=5$) both SD and SI increased the number of lapses when compared to baseline and EC. However, rats made more lapses after 24h of SI, than after 24h of SD. Similarly, response latencies increased after both SD and SI, but there was little difference between the effect of SI and SD. Premature response errors and the number of total responses were not affected by either condition.

Conclusion: Although both 24 hours SD and 24 hours SI produced vigilance impairments analogous to those seen in sleepy humans, 24 hours SI produced greater impairments when compared to 24 hours SD, baseline, and the exercise control conditions.

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DOES DAYTIME NAPPING PROTECT ALL DECLARATIVE MEMORY AGAINST FORGETTING?

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Introduction: Studies have suggested that overnight sleep has differential effects on the memory of related and unrelated word pairs. This implies that sleep may play a different role in the consolidation of re-

cently acquired and recently re-encountered, long established, knowledge. However, until recently, the effects of sleep and waking retention intervals on memory for differing degrees of pre-existing association had not been compared within the same experiment. Doing so revealed that overnight sleep, compared with a waking retention interval, protects the memory of related word pairs against forgetting and reduces the memory loss of unrelated pairs (Lo, Dijk, & Groeger, submitted). Here, in order to extend these findings further, we examined the effect of daytime napping on cued recall of related and unrelated words pairs.

Methods: Participants ($n = 18$) attended two laboratory sessions: remaining awake or having the opportunity of taking a nap for 90 minutes, after learning 40 semantically related and 40 unrelated word pairs.

Results: Average total sleep time was 72 ± 15 minutes (mean \pm SD) and consisted of $14.0\pm 9.5\%$ S1 sleep, $37.5\pm 19.0\%$ S2 sleep, $6.7\pm 3.7\%$ S3 sleep, $21.4\pm 20.0\%$ S4 sleep, and $14.6\pm 15.6\%$ REM sleep. We found that change in recall performance across the retention interval was moderated by both the type of retention and the semantic relatedness of the word pairs ($F(1,17) = 4.40, p = .05$). While forgetting of related word pairs was minimal after both waking retention (0.11 ± 2.42) and napping retention (-0.61 ± 1.58), more unrelated words pairs were forgotten after waking retention than after napping retention (-2.17 ± 3.05 vs. -0.78 ± 2.00).

Conclusion: Recently encountered, well established knowledge, as represented by closely related word pairs, is robust against the effects of retention intervals, whether these involve sleep or waking. In contrast, over similar intervals, recently learned word-pairings are lost more rapidly, but daytime naps protect such newly acquired knowledge against forgetting.

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REDEFINING THE PVT LAPSE IN TERMS OF DURATION, AND WHETHER THE EYES ARE OPEN OR CLOSED

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Introduction: Studies utilising the Psychomotor Vigilance Task (PVT) usually define a lapse as a response longer than 500ms. This cut-off is rather arbitrary, and an assessment of what a participant is doing during lapses may reveal a better discrimination of the processes of participant 'disengagement' during these events, and provide further criteria for categorising PVT responses in relation to sleepiness-impaired performance.

Methods: Sixteen healthy, young adult ($24.4y\pm 3.6$) normal healthy sleepers ($8h\pm 1h$), without complaint of daytime sleepiness (< 2 naps/wk; $ESS\leq 10$; bihourly KSS) underwent two extended 30minute PVT sessions, at 22.00h (ALERT) and again at 04.00h (SLEEPY). Video-data (birds-eye and frontal-view) was used to classify each lapse ($\geq 500ms$) as occurring with eyes open (EO) or eyes closed (EC). Other lapses due to distraction were excluded (2.4%).

Results: Repeated measures three-way ANOVA for lapse (EO vs EC), sleepiness (Alert vs Sleepy), and PVT epoch (3x10min bins) showed significant main effects ($p\leq 0.005$) together with a significant lapse x sleepiness x time ($p=0.013$) interaction. EO lapses remained stable over PVT epochs, whereas EC lapses increased. Further analysis of lapse duration showed: no reaction time effect of sleepiness for EO (Av. 728ms for alert vs 744ms for sleepy), significant effect for EC (Av. 3061msec vs 4207ms). There were clear changes in the EO vs EC nature of lapses: those above 3200ms were 95% likely to be EC, whereas those between 500-600ms were 95% likely to be EO. We provide probabilities of EC/EO for the transition between these two extremes of lapse durations.

Conclusion: Notwithstanding different time of day effects between the conditions and that sleep loss was not severe, these findings point to the potential usefulness of a further sub-division of lapses beyond the usual dichotomy of lapse/no lapse, based only on a 500ms criterion, which can provide further insight into developing sleepiness.

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PERFORMANCE ON A DECLARATIVE MEMORY TASK CORRELATES NEGATIVELY WITH SLOW-WAVE SLEEPPayne JD^{1,2}, Schacter D², Stickgold R¹¹Department of Psychiatry, Harvard Medical School, Boston, MA, USA,²Department of Psychology, Harvard University, Cambridge, MA, USA

Introduction: Evidence suggests that declarative memory performance is supported specifically by time spent in slow-wave sleep (now referred to as stage N3). However, in two separate experiments investigating memory for semantically associated words, we found a negative correlation between memory performance and slow-wave sleep. Although this is the opposite of what has been found in the literature to date, we suggest that the two major subtypes of declarative memory - episodic and semantic - may have different relationships to slow-wave sleep.

Methods: Participants studied eight 12-word lists at 9AM or 9PM in Experiment 1. They recalled these words (1) after 12 daytime hours spent awake, (2) after 12 nighttime hours containing sleep, (3) twenty minutes after learning in the morning, or (4) twenty minutes after learning in the evening. These last two conditions were included as circadian controls. In Experiment 2, all participants studied the lists at noon and were tested at 6pm (1) with or (2) without a 90min nap opportunity at 1PM.

Results: In Experiment 1, participants recalled significantly more words after a night of sleep than after a 12-hour period of daytime wakefulness ($p < .01$). Participants in the “sleep” group were also significantly more likely than those in the “wake” group to falsely recall “critical lure” words that were semantically associated to the theme of the list but never presented for study. This same difference was seen in Experiment 2 between the nap and no-nap groups ($p < .05$). In both experiments, word recall was negatively correlated with minutes spent in slow-wave sleep ($ps < .05$). In Experiment 1, the negative correlation also emerged with percent of slow-wave sleep ($p < .01$).

Conclusion: We have shown that a period of sleep elevates recall of semantically related words compared to equivalent periods spent awake. Performance on this declarative memory task, which draws heavily on semantic processing and memory for “gist”, is negatively associated with slow-wave sleep. This is the opposite of what has been found in other experiments, which have routinely tested spatial or episodic forms of declarative memory. Together, these findings suggest that the two major subtypes of declarative memory are differentially affected by slow-wave sleep, which may facilitate contextually-specific memory but impair memory for gist and semantic generalities.

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SLEEP-RELATED PROCEDURAL SKILL ENHANCEMENT IN ELDERLY INDIVIDUALSTucker M¹, McKinley S², Stickgold R^{1,2}¹Psychiatry, Harvard Medical School, Boston, MA, USA, ²Harvard

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Introduction: Motor sequence memory is enhanced by post-training sleep in healthy young subjects. The present study assessed whether this sleep-related enhancement is observed in healthy elderly subjects.

Methods: Fifteen subjects (5 males, 10 females, mean age=68, age range, 60-79) participated in the study. Subjects reported no sleep complaints, and were not taking medications known to affect sleep architecture. Each subject completed two training-retest sessions. During one session they were trained on one sequence (e.g., 4-1-3-2-4) in the morning and retested after 12hrs of wakefulness, and in another session they were trained on a second sequence (e.g., 2-3-1-4-2) in the morning and tested 24hr later, after a night of sleep. Session and sequence order were counterbalanced across subjects.

Results: Measuring improvement as the difference between the average of the last 6 trials of the training session and the last 6 trials of the retest

session we observed that 12hrs of wakefulness imparts no performance enhancement (mean=0.2 sequences; $p=.32$), whereas a 24hr period containing sleep results in a 1.4 sequence (12.3%; $p < .005$) improvement (paired t-test for sleep-wake difference, $p=.03$). Unlike previous findings showing that young subjects start the retest session (first 3 trials) with a 17% post-sleep performance boost, elderly subjects start at the same point they left off at the end of training (0% change), while performance declines (-21%; $p < .005$) after 12hrs of wakefulness (paired t-test for sleep-wake difference, $p < .01$). While the shape of the learning curves is similar for elderly and young subjects during training, the average number of completed sequences is appreciably diminished in elderly subjects, who average 12 completed sequences during training, compared to 21-23 sequences completed by young subjects.

Conclusion: Despite a general decline in motor skill performance, the results clearly suggest that sleep continues to play a role in the enhancement of motor skill over the life span.

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INDIVIDUAL DIFFERENCES IN CHILDHOOD SLEEP PROBLEMS PREDICT COGNITIVE EXECUTIVE FUNCTIONING IN LATE ADOLESCENCEFriedman NP¹, Wright KP²¹Institute for Behavioral Genetics, University of Colorado at Boulder,Boulder, CO, USA, ²Department of Integrative Physiology, Sleep

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Introduction: There is considerable evidence that sleep problems impair cognitive functioning. We examined the influence of developmental patterns of sleep problems on later cognitive abilities. Specifically, we evaluated whether individual differences in growth trajectories of sleep problems from ages 4 to 16 predicted three separable but related executive functions—inhibiting dominant responses, updating working memory, and shifting task sets—at age 17.

Methods: Participants were 916 individual twins (465 female, 451 male) from the Colorado Longitudinal Twin Study with complete or partial sleep problems data from ages 4, 5, 7, and 9-16 years ($n=897$) and/or cognitive data at age 17 ($n=568$). The sleep problems measure was a 7-item scale from the parent-report Child-Behavior Checklist (nightmares, being overtired, sleeping less or more than others, sleeptalking/sleepwalking, trouble sleeping, and bedwetting). Each executive function was measured as a latent variable with three indicators. Developmental trajectories of sleep problems were modeled with a latent variable growth curve model.

Results: Sleep problems declined over time, with ~70% of children having one or more sleep problems at age 4 and ~30% of children at age 16. However, there were significant individual differences in both the initial levels of problems (the intercept of the growth model), and changes across time (the slope). The intercept did not significantly correlate with the later executive function latent variables; however, the nonlinear slope variable significantly ($p < .05$) negatively correlated with inhibiting ($r=-.27$) and updating ($r=-.21$), but not shifting ($r=-.10$) abilities. Further analyses suggested that the slope variable predicted the variance common to the three executive functions.

Conclusion: Early levels of sleep problems, as reflected by the intercept, do not seem to have appreciable consequences for later executive functioning. However, individuals whose sleep problems decreased more across time, as reflected by the slope, showed better general executive function ability in late adolescence.

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SLEEP EFFECTS ON CONDITIONED FEAR AND ITS EXTINCTION - PILOT RESULTS

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Introduction: PTSD patients suffer both poor sleep quality and putatively deficient ability to consolidate extinction memories that compete with conditioned fear memories. Because sleep loss can impair extinction recall in animals, we hypothesized that sleep would promote consolidation of extinction memory in healthy humans.

Methods: Twenty healthy volunteers (9 female), mean age=24.6 (range=19-35) underwent a 5-phase protocol. Habituation, Conditioning, and Extinction phases occurred sequentially in either morning (“Wake”) or evening (“Sleep”) groups (N=10 each). Following 12 hours of waking (Wake) or a normal night’s sleep (Sleep), Extinction Recall and Fear Renewal phases occurred sequentially. During Conditioning only, a mild, 0.5-sec shock reinforced conditioned fear to two differently colored lamps (CS+’s) within the computerized image of a room (“conditioning context”). A third lamp color was never reinforced (CS-). Square-root transformed skin conductance response (SCR) was measured as conditioned response. Immediately after Conditioning, one CS+ was extinguished (CS+E) by presentation, without shocks, within the image of a different room (“extinction context”). The other CS+ was not extinguished (CS+NE) and did not reappear until the CS+E, CS+NE and CS- were presented 12 hours later, first in extinction context (Extinction Recall) and then conditioning context (Fear Renewal). Percent fear recall (and renewal)=100 x mean-SCR to the first two CS+E or CS+NE presented divided by their respective maximum SCR generated during Conditioning. Extinction recall=100 minus %fear recall to the CS+E.

Results: Sleep and Wake groups did not differ in percent fear or extinction recall or in contextual renewal of conditioned fear. However, the difference in percent fear recall between the CS+E and CS+NE conditions tended to be smaller following sleep than following wake (N=20, p=.26, Cohen’s d=.52), an effect driven by male subjects (N=11, p=.13, d=1.02) and resulting from greater fear recall to the CS+NE among Wake-group males (p=.04, d=1.45).

Conclusion: Pilot results do not support extinction retention superiority following sleep. Sleep, however, may promote generalization of extinction memory from extinguished CS+’s to similar, unextinguished CS+’s, especially among males.

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PARENTAL RATINGS OF PROBLEMATIC CHILD BEHAVIOR AS THEY RELATE TO AMOUNT OF STAGE 2 SLEEP AND REM LATENCY

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Introduction: Percent of time spent in stage 2 sleep and latency to rapid eye movement (REM) sleep have both been associated with problematic cognitive and behavioral patterns in children. The purpose of this study was to determine if parental report of child behavior patterns was associated with amount of time spent in stage 2 sleep and latency to REM sleep as measured by in-home polysomnography.

Methods: 480 children (240 boys and 240 girls, 277 Caucasian and 203 Hispanic) from the Tucson Children’s Assessment of Sleep Apnea Study (TuCASA) (mean age 8.3, SD ± 1.6) underwent in-home polysomnography and parents completed the Conner’s Parental Rating Scales (CPRS). CPRS subscale scores ≥ 65 were considered indicative of problematic behavior. Total minutes of sleep time (TST), percent of TST spent in stage 2 and latency in minutes to onset of 1st REM period were used as indicators of sleep patterns. Children were grouped by t-scores of ≥ 65 or < 65 for each subscale and compared for TST, % Stage 2 and REM latency. Stu-

dent t-test analyses (significance = 0.05) were performed to determine if groups differed on TST, % of stage 2 sleep and REM latency.

Results: Average TST was 487.01(± 79.7) minutes, and did not differ significantly between any CPRS subscale groupings. Children who spent an average of 53% or more of TST in stage 2 sleep were rated as having problematic behaviors on DSM total (t=2.195, p=0.03), DSM inattentive (t=2.23, p=0.03), and social problems (t=2.31, p=0.02) subscales on CPRS. REM latency was longer than 143 minutes on average for children rated as problematic on DSM total (t=2.18, p=0.03), DSM inattentive (t=2.23, p=0.03), and ADHD (t=2.47, p=0.14) subscales.

Conclusion: The present study found evidence that parental ratings of behavior may be reflective of physiological sleep-patterns in children who demonstrate social problems, or ADHD-like behavior patterns.

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RECONSIDERING THE ROLE OF SLEEP FOR MOTOR SEQUENCE LEARNING

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Introduction: Motor sequence performance has been shown to improve after a delay between training and test sessions involving sleep. This finding has been taken as evidence for an active sleep consolidation process that enhances subsequent performance. However, data averaging and circadian factors may have contributed to the sleep enhancement effect.

Methods: Experiment 1: Subjects were trained and tested 12 hours later on a sequential finger-tapping task (FTT). The sleep group trained at 10pm and tested at 10am. The wake group trained at 10am and tested at 10pm. Experiment 2: Subjects were retested after 24-hour delay interval between training and testing and spacing of the FTT within each session was manipulated. Subjects either received 30 seconds of key press per block for 12 blocks at training and test (massed group); or received 10 seconds of key press per block for 36 blocks at training and test (spaced group), controlling for total time of key press.

Results: Experiment 1: The averaged data replicated previous findings; the sleep group showed improvement while the wake group maintained the same performance. Fine-grained analysis, however, revealed a different pattern. Instead, performance was maintained in the sleep group but slowed in the wake group. Circadian factors may also have contributed to the differences between groups. Experiment 2: Consistent with experiment 1, the massed group consistently exhibited within-block fatigue, particularly at the end of training. The spaced group did not reflect this reactive inhibition and showed a faster rate of learning than the massed group during training. There were no differences between groups at the beginning of test. This further suggests that including within-block fatigue in the analyses may taint learning effects.

Conclusion: The present study replicated the sleep enhancement in the motor sequence task in the typical design and analysis, but failed to find any facilitation when both spacing and circadian effects were controlled. These results question the role of sleep on motor sequence learning.

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OVERNIGHT MOTOR SKILLS LEARNING IN CHILDREN WITH AND WITHOUT ADHD

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Introduction: Adults experience enhanced motor skills learning following sleep compared to waking. Here we examine this phenomenon in control children and children with attention deficit hyperactivity disorder (ADHD).

Methods: Participants included 16 healthy children free of ADHD (controls) or who carried the diagnosis or were positive on a structured pa-

rental interview (ADHD). Nine control (ages 10.1 to 12.7 y; mean=11.7; 1 girl) and 7 ADHD (ages 10.3 to 12.9 y; mean=11.8; 3 girls) children kept a stabilized sleep schedule of at least 10-h time in bed for 1 week before the first of two consecutive 10-h laboratory overnights. Training on the finger tapping test of Walker et al., 2002 (5 number sequence, left hand) was completed about 1 h before bed on night 2 (12, 30-sec trials separated by 30-sec rests) and repeated (4 trials) about 1.25 h after rising. Average number of correct sequences (Hits) and Error Rate (number of errors/Hits) were computed for the last 2 evening and first 2 morning trials.

Results: Control children showed significant overnight improvement for Hits (evening mean=10.4, sd=3.5; morning mean=12.8, sd=4.1; $t=-3.56$, $p=.007$) but not for Error Rate (evening mean=.43, sd=.37; morning mean=.30, sd=.27; $t=.96$, $p=ns$). Two ADHD children (1 girl) failed to complete the task (Hits < 1 on all trials). For ADHD children ($n=5$) who could perform the task, overnight improvement was not statistically significant for Hits (evening mean=7.3, sd=5.1; morning mean=10.4, sd=6.0; $t=-2.36$, $p=.078$) and could not be computed for Error Rate due to one child with zero Hits on one evening trial.

Conclusion: Data for this small sample showed improved motor skills performance after a night of sleep in well-slept controls, though not in children with ADHD. Large individual differences were apparent (including 2 ADHD children with performance equivalent to controls), and subsequent work will increase the sample size and examine whether sleep stage variables, sleep disordered breathing, and/or sleepiness (MSLT) affect this process in children.

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SLEEP STAGE ASSOCIATED CHANGES IN DREAM RECALL ACROSS THE DAY ON AWAKENING FROM MSLT NAPS

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Introduction: Variations in waking consciousness occurring though the day include changes in short-term memory, cognitive performance and subjective alertness postulated to occur secondary either to circadian, sleep, or ultradian (REMS) cycles affecting waking. Multiple sleep latency testing (MSLT) is a controlled test of the transition between wake and sleep across the waking day. The frequency of sleep stage associated reports of dream recall on arousal from MSLT naps is likely to reflect variations in waking consciousness.

Methods: This study was conducted during MSLT testing in 84 individuals being clinically evaluated for daytime sleepiness. Technicians queried individuals on awakening from each MSLT nap as to whether they recalled any feeling, thought, or emotion from sleep. MSLT's were done per AASM protocol with naps at 8:00 AM, 10:00 AM, 12:00 Noon and 2:00 PM after polysomnography testing. Results from the 12 4:00 PM naps, are not included in this study. Individuals who did not sleep in at least one nap were excluded as well.

Results: Dream recall from at least one nap was reported by 34.5% (29/84) of the individuals included in this study. Dreams were reported from 51 of 337 naps (15.2%). REMS dreams were reported from 7.4% (25/334) of total naps. Dreaming was reported from 41.7% (25/60) naps with SORP's. Dreams were reported on awakening from non-REM sleep (NREMS) in 7.7% (26/334) of total naps; 9.4% (26/273) of NREMS naps. SORP nap dream recall increased across the day with 6 dreams reported at 8:00 AM, 5 dreams at 10:00 AM, 5 dreams at noon, and 9 REMS dreams reported from the 2:00 PM nap. NREMS dream reports declined across the MSLT day with 11 dreams reported at 8:00 AM, 7 at 10:00 AM, 4 reported at noon, and 5 reported at 2:00 PM.

Conclusion: This study supports previous studies indicating that dream recall occurs at low frequency in hypersomnolent individuals. This study

also supports previous studies suggesting that dream recall is higher in individuals with SORP's. The low dream recall in this population limits our ability to definitively infer whether changes in dream recall based on sleep stage occur across the day. However, this study suggests that REMS dream recall is maintained across the waking day as would be expected if ultradian REMS cycling affects waking as well as sleep. NREMS dream recall declines across the day suggesting that increasing sleep need or circadian sleep drive may negatively affect NREM dream recall.

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PERCEIVED CONTROL OVER SLEEP AND INCONSISTENT SLEEP LATENCIES PREDICT COLLEGE STUDENTS' SLEEP QUALITY BETTER THAN DOES THE REGULARITY OF SLEEP HABITS

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Introduction: Previous studies have shown that irregular sleep schedules are associated with poorer sleep. Apart from studies of shift workers, there has been little research on individual differences in capacity to tolerate irregular sleep schedules. College students are an ideal population to study because irregular sleep habits are common. The present study examined whether college students' sleep quality was predicted better by the regularity of their sleep schedules or by variables that could reflect individual differences in students' ability to tolerate irregular sleep schedules. These variables were regularity of sleep latencies and level of perceived control over sleep. Students who are less tolerant of irregular sleep schedules should have more irregular sleep latencies. Perceived control over sleep differentiates between irregular sleep habits that are voluntary and those that are involuntary.

Methods: Participants were 256 students (181 females) enrolled in introductory psychology. Mean age was 20.75 (SD = 4.40). Participants completed online the Pittsburgh Sleep Quality Index (PSQI) and a questionnaire designed for this study about the regularity of sleep habits and perceived control over sleep.

Results: According to Spearman correlations, poor sleep quality was associated with irregular bedtimes on weekdays ($p < .05$), irregular sleep latencies ($p < .001$), irregular sleep durations ($p < .01$), and a lack of perceived control over sleep ($p < .001$). When variables were entered in a multiple regression analysis, only perceived control over sleep ($\beta = -.33$, $p < .01$) and regularity of sleep latencies ($\beta = .28$, $p < .01$) were significant predictors of sleep quality ($R^2 = .28$).

Conclusion: A lack of perceived control over sleep and irregular sleep latencies were better predictors of college students' poor sleep than were irregular sleep schedules. These results might be explained by individual differences in capacity to tolerate irregular sleep schedules.

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INFLUENCE OF GENDER ON SLEEP-DEPENDENT MEMORY CONSOLIDATION

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Introduction: Recently we reported that the sleep-dependent memory consolidation is a benefit which declines with age. This result provides a provocative and novel explanation of learning deficits observed in older adults. Given that both learning (e.g., Clark et al., 2006; Wolf et al., 2001) and sleep (Park et al., 2001; Prinz et al., 2000) are disproportionately degraded in older women relative to men, a difference attributed to higher cortisol levels in post-menopausal women, I examined whether the age-related decline in sleep-dependent memory consolidation differed by gender.

Methods: Six male and 6 female participants were recruited in each of the following age ranges: 21-30, 31-40, 41-50, 51-60, and 61-70 years.

Category S—Behavior, Cognition & Dreams

Participants were trained on the finger sequence learning task either in the morning or the evening and learning was assessed 12 and 24 hrs later. The sleep benefit on the task was measured as the performance improvement over the 12 hr interval containing sleep relative to performance improvements over the 12 hr interval in which the participant was awake.

Results: Initial learning did not vary with age or gender. Nonetheless, I replicated our previous result demonstrating the age-related decline in memory consolidation with sleep: In older adults (> 40 yrs) performance improvements did not differ for the 12-hr interval awake and the 12 hr interval asleep. Of interest in the present study, this age-related decline was greater in women than men even though there were no gender differences in sleep.

Conclusion: Sleep-dependent memory consolidation is diminished in older adults. This decline is greater in women than in men. Moreover, this age-related decline may not be related to changes in sleep stages with age. Rather, degradation of the hippocampus in older women may directly impact the ability to consolidate memories.

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THE RELATIONSHIP BETWEEN NATURAL SLEEP RESTRICTION AND DISTRESS TOLERANCE IN AN ADOLESCENT POPULATION

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Introduction: NSF statistics suggest that sleep loss is a nationwide epidemic and the problem appears to be of particular concern among adolescents. Both circadian changes and environmental factors (i.e. school start times, academic pressures, social opportunities and rewarding media) impact their ability to obtain adequate amounts of sleep. As a result, daytime impairments have been associated with persistent sleep loss in adolescents. This study examines the specific impact of self imposed naturalistic sleep restriction on adolescent's ability to tolerate/cope with stressful situations. This study is intended to evaluate the sequelae of a pattern of sleep deprivation that has high ecological validity.

Methods: The sleep and psychosocial functioning of 38 Adolescents (mean age = 16 (.90); 47% female) was evaluated over the course of a week with actigraphy, sleep logs, self-report measures, and various behavioral tasks. The association between weekday sleep restriction/weekend recovery sleep and performance on a behavioral measure of distress tolerance is presented here. Specifically, adolescents' ability to persist during a stressful computerized task was assessed following both the sleep recovery and restricted phases.

Results: A paired samples t-test revealed a non-significant trend towards shorter time to quit following the restricted phase. However, when the sample was divided into those that quit vs. those who persisted, a chi square analysis showed that a significantly greater proportion of adolescents (53%) quit following the restricted phase compared to the proportion that quit following recovery [33%; $X^2(1,35) = 10.92, p = .001$]. This association held true independent of age, gender, & race.

Conclusion: Obtaining inadequate amounts of sleep during the week has been linked to significantly lower levels of distress tolerance which may impact an individual's ability to function on a daily basis. The role of distress tolerance needs to be investigated further as it may serve as an important mediator/moderator of daytime impairments related to sleep loss.

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EFFECTS OF EXTENDED WORK HOURS ON OBJECTIVELY MEASURED SLEEP AND PERFORMANCE IN INDUSTRIAL EMPLOYEES

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Introduction: This study was concerned with the work hours of employees of a manufacturing factory where extended hours occur periodically for equipment tear down and rebuild. During this time employees start work earlier and sometimes stay later while the remainder of the facility is shut down. Here we investigate the effect of the extended work hours on objectively measured sleep and performance in this naturalistic setting.

Methods: Ten male employees volunteered for this study. They were each measured for 10 days during normal work hours (NWH) and for 9 days during extended work hours (EWH). Shift duration was determined by self report. Sleep was recorded using an actigraph (Ambulatory Monitoring, Inc.), and performance was measured at shift onset and at shift end using a psychomotor vigilance task (PVT).

Results: Employees worked on average 9.1h/day during NWH and 10.3h/day during EWH; the difference of 1.2±0.3h/day was significant ($t[119]=4.49, p<0.001$). Employees slept on average 6.9h/night following NWH and 6.0h/night following EWH; the difference of -0.9±0.2h/night was significant ($t[119]=-5.34, p<0.001$) and did not significantly deviate from the difference in work hours ($t[247]=0.76, p=0.45$). PVT administration at shift onset and shift end occurred on average at 09:10 and 17:22 during NWH, and at 06:17 and 15:46 during EWH. Mean RT on the PVT was significantly greater during NWH than during EWH, both at shift onset (328±14ms and 307±15ms, respectively; $t[119]=-3.01, p=0.003$) and at shift end (340±23ms and 299±24ms, respectively; $t[116]=-2.02, p=0.045$). The difference between conditions in performance did not vary significantly between shift onset and shift end ($t[244]=-0.85, p=0.40$).

Conclusion: Our PVT results would suggest that performance improved in the extended work hours condition, but caution is needed in the interpretation of this finding. Counterbalancing of conditions was not possible in this field study; and there were differences between conditions in the circadian timing of test bouts due to the difference in shift start and end times. However, using actigraphy we also found that the extension of work by an average of 1.2h was associated with truncation of sleep by an average of 0.9h. Thus, in this naturalistic setting, the increase in work hours occurred primarily at the expense of sleep.

Support (optional): USAMRMC award W81XWH-05-1-0099.

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CORRELATION OF PSYCHOMOTOR VIGILANCE TASK PERFORMANCE WITH PREFRONTAL BOLD SIGNAL MEASURED BY NEAR-INFRARED OPTICAL TOPOGRAPHY

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Introduction: Near-infrared optical topography (NIR-OT) measures the blood oxygen level dependent (BOLD) response, a relative measure of regional brain activation. This technique can be used to record short-term changes in brain activity from the scalp, during the performance of a task. We examined whether NIR-OT recordings of the prefrontal cortex correlated with psychomotor vigilance task (PVT) time-on-task effects.

Methods: 12 healthy young adults (7 males and 5 females, age 22-37) spent 7 consecutive 24h days in a sleep laboratory: two baseline nights

with 10h time in bed (TIB), 62h of total sleep deprivation, and two recovery nights with 10h TIB. Performance was measured using a 10min PVT every 2h during scheduled wakefulness. Bilateral prefrontal brain activity was measured concurrently using BOLD signals recorded with NIR-OT (Hamamatsu NIRO-200) while head position was fixed with a chin rest. Left and right prefrontal oxygenated hemoglobin (O₂Hb-L, O₂Hb-R) were recorded. Linear time-on-task effects in PVT reaction times and in the hemoglobin measures were quantified across the 10min duration of each test bout. The correlation between the slope of the PVT time-on-task effect and the slope of the BOLD signal changes was assessed both within and between subjects.

Results: During the 10min PVT bouts, performance degraded over time while the BOLD signal increased. Within-subject correlations between the slope of the changes in the BOLD signal and the PVT time-on-task effect were not significant due to high noise levels in the NIR-OT data. Between subjects, the PVT time-on-task effect correlated positively with the change in O₂Hb-R ($r=0.60$, $P=0.041$), with a trend for O₂Hb-L ($r=0.52$, $P=0.081$).

Conclusion: Within subjects, the direction of change in the NIR-OT measurements of the BOLD response, as measured from the scalp over the prefrontal cortex, corresponded with the PVT time-on-task effect. Between subjects, linear changes in oxygenated hemoglobin correlated considerably ($r>0.50$) with the PVT time-on-task effect. Further work is needed to reduce the variability in the NIR-OT measurements. However, our results provide preliminary evidence that the prefrontal BOLD response measured by means of NIR-OT may be a neurobiological marker of PVT time-on-task effects.

Support (optional): DURIP grant FA9550-06-1-0281 and the W.M. Keck Foundation.

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SLEEP DEPRIVATION (BUT NOT SLEEP REBOUND) IMPAIRS ACQUISITION, CONSOLIDATION, AND RETRIEVAL OF A DISCRIMINATIVE AVOIDANCE TASK IN RATS: INVOLVEMENT OF CONCOMITANT MODIFICATIONS IN ANXIETY AND MOTOR ACTIVITY

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Introduction: The aim of the present study was to investigate: Effects of paradoxical sleep deprivation (PSD) on the learning/memory processes in rats submitted to the plus-maze discriminative avoidance task (PMDAT).

Methods: 1) Rats were trained in the PMDAT and immediately after the training session they were PSD for 96h. At the end of PSD, the animals were submitted to the test session. 2) Rats were trained in the PMDAT, and allowed to sleep for 24h and then submitted to PSD while other group was sleep-deprived and then, allowed to sleep for 24h. Following this period, were tested again. 3) Rats were PSD or were PSD and given a 24h sleep permission and immediately after submitted to the training session of the PMDAT. 4) Rats were tested 24h after rebound induced by 96h of PSD.

Results: Post-training PSD combined with pre-test PSD induced memory deficits, an increase in the time spent in the open arms and an increase in the number of entries. In experiment 2, both PSD groups showed memory deficits. However, only PSD animals before the training presented an enhancement in the time spent in the open arms and in the number of entries. In experiment 3, PSD rats showed learning deficits and an increase in the time spent and number of entries in the open arms. A 24h sleep permission period after the PSD abolished the learning deficit. Finally sleep rebound did not modify acquisition and retrieval.

Conclusion: Our study contributes to strengthen the critical role of sleep in all the steps of learning and memory formation. In addition, at least

in relation to the PSD effects on acquisition and consolidation such a crucial role is not a consequence of other relevant behavioral alterations induced by sleep deprivation.

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HIGHER INTELLIGENCE IS ASSOCIATED WITH LESS SUBJECTIVE SLEEPINESS DURING SLEEP RESTRICTION

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Introduction: The relationship between intelligence and performance / sleepiness during sleep restriction is unclear. We evaluated the extent to which intelligence confers protective effects on objective performance and alertness and subjective sleepiness during sleep restriction.

Methods: Eleven males and 13 females [mean (SD) age = 25 (6.5) years] slept in the laboratory for one week followed by one baseline, seven sleep restriction [3 hours time in bed (TIB)], and five recovery nights (8 hours TIB - recovery not reported here). Volunteers were administered the Comprehensive Test of Nonverbal Intelligence (CTONI) at baseline and the Psychomotor Vigilance Task (PVT), Maintenance of Wakefulness Test, and Stanford Sleepiness Scale (SSS) throughout all phases hourly from 0800 to 1800. For restriction, slopes were computed for daily average lapses (RTs > 500 ms), speed (1/RT), MWT sleep latency (minutes to 3 consecutive epochs stage 1), and SSS (all scores computed relative to baseline) and then correlated with CTONI Nonverbal (NIQ), Pictorial Nonverbal (PNIQ), and Geometric Nonverbal (G)IQ.

Results: During sleep restriction, higher NIQ was associated with smaller increases in subjective sleepiness relative to baseline ($r = -0.372$, $p < 0.05$), increased objective sleepiness ($r = -0.326$, $p = 0.07$), and greater declines in speed ($r = -0.328$, $p = 0.07$).

Conclusion: Higher intelligence for analogical reasoning, categorical classifying, and sequential reasoning (NIQ) is associated with feeling less sleepy during sleep restriction, with trends for greater physiological sleepiness and worse performance. These results suggest that whereas higher IQ confers protective benefits during sleep restriction on subjective sleepiness, that the converse is true for objective measures.

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BETTER BASELINE OLFACTORY DISCRIMINATION IS ASSOCIATED WITH WORSE PVT AND MWT PERFORMANCE WITH SLEEP RESTRICTION AND RECOVERY

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Introduction: Sleep deprivation adversely affects cognition, with substantial inter-individual variability. The variability in response has been associated with olfactory discrimination (a gauge of prefrontal cortical integrity) under well-rested conditions: better baseline olfactory discrimination is associated with greater behavioral resiliency. The latter is consistent with a “prefrontal reserve” theory of resistance to sleep deprivation (Killgore et al., 2007). Here we examined the relationship between olfactory discrimination capabilities and response to sleep restriction and subsequent recovery.

Methods: Data reported here are from the Rupp et al sleep restriction study (this volume). Volunteers were administered the University of Pennsylvania Smell Identification Test (UPSIT) at baseline and the Psychomotor Vigilance Task (PVT) and Maintenance of Wakefulness throughout baseline, restriction, and recovery between 0800 and 1800. Average daily PVT speed (1/RT), PVT lapses (RTs > 500 ms), MWT

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sleep latency (minutes to 3 epochs stage 1) were calculated relative to baseline and correlated with the total UPSIT score using prior sleep history as a covariate.

Results: During sleep restriction, on Day 7 higher baseline UPSIT scores (indicating better olfactory discrimination) were associated with greater decrements in PVT speed ($r = 0.449$, $p < 0.05$), and on Day 1 with greater decrements in sleep latency ($r = -0.392$, $p < .05$). During recovery, on Day 2 higher baseline UPSIT scores were associated with greater decrements in sleep latency ($r = -0.407$, $p < 0.05$).

Conclusion: In contrast to prior findings during total sleep deprivation, in the present study better baseline olfactory discrimination was associated with worse PVT performance during sleep restriction and greater sleepiness during both restriction and recovery. These data do not appear to be consistent with the “prefrontal reserve” theory of resistance to sleep loss, and suggest potentially different brain mechanisms underlying responses to sleep restriction compared to total sleep deprivation.

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RISK-TAKING BEHAVIOR IS ELEVATED DURING RECOVERY FROM SLEEP RESTRICTION

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Introduction: Total sleep deprivation increases risk-taking propensity (Killgore et al., 2007). Whether chronic sleep restriction - a more common scenario - also impacts risk-taking is not known. We assessed risk-taking propensity across chronic sleep restriction and subsequent recovery.

Methods: Following one baseline night of normal sleep (8 hours TIB), 11 males and 13 females [mean (SD) age = 25 (6.5) years] were sleep-restricted (3 hours TIB) for seven nights followed by five nights of recovery sleep (8 hours TIB). Volunteers were administered three risk-taking assessments: (1) the Iowa Gambling Task (IGT - ratio of risky versus advantageous deck selections across 100 trials) at baseline, on restriction day 7, and recovery day 4; (2) the Balloon Analogue Risk Task (BART - average number of pumps for non-exploded balloons; percent of baseline) and the Evaluation of Risks scale (EVAR - scores on self-control, danger-seeking, energy, impulsiveness, and invincibility scales; percent of baseline) at baseline and once daily thereafter. Variables were analyzed using mixed-model ANOVAs, covarying age, with post-hoc t-tests (Bonferroni corrected).

Results: IGT: During baseline, restriction, and recovery sessions, volunteers made more advantageous deck selections across the first 4 blocks of trials ($p < 0.05$); however, during restriction (n.s. trend) and recovery ($p < 0.05$), volunteers switched to less advantageous decks across the fifth block. BART: Compared to baseline, the average number of pumps increased across restriction and recovery ($p < 0.05$). EVAR: No significant effects were found.

Conclusion: Consistent with total sleep loss effects, IGT and BART showed increased risk-taking with sleep restriction. However, the present results indicate that unlike total sleep deprivation (in which full recovery was found following 12 hours of sleep), risky behavior patterns continued into the recovery phase. The neurophysiology underlying increased risk-taking with sleep restriction may take days to reverse after normal nightly sleep amounts are restored.

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PERSONALITY FACTORS ASSOCIATED WITH PERFORMANCE AND SLEEPINESS DURING SLEEP RESTRICTION AND RECOVERY

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Introduction: Previous studies demonstrated that extraversion and neuroticism are associated with increased sleepiness and worse performance during sleep deprivation (Killgore et al., 2007; Mastin et al., 2005). Whether similar patterns emerge during chronic sleep restriction - and subsequent recovery - is unknown.

Methods: Eleven males and 13 females [mean (SD) age = 25 (6.5) years] slept in the lab for one week followed by one baseline, seven sleep restriction [3 hours time in bed (TIB)], and five recovery nights (8 hours TIB). Volunteers were administered the NEO Personality Inventory-Revised (NEO-PI-R) at baseline and the Psychomotor Vigilance Task (PVT), Maintenance of Wakefulness Test, and Stanford Sleepiness Scale (SSS) throughout from 0800 to 1800. Data were converted to percent baseline, then slopes were computed separately for restriction and recovery phases for daily average lapses (RTs > 500 ms), speed (1/RT), MWT sleep latency (minutes to 3 consecutive epochs stage 1), and SSS. Slopes were then correlated with baseline NEO-PI-R factors neuroticism, extraversion, agreeableness, openness, and conscientiousness.

Results: Higher neuroticism was associated with greater decline in PVT lapses ($r = 0.194$, $p < .05$) and PVT speed ($r = -0.201$, $p < .05$) during restriction and greater extraversion was associated with greater speed declines ($r = 0.194$, $p < .05$). During recovery, higher extraversion was associated with greater improvements in PVT speed ($r = -0.186$, $p < .05$), greater openness was associated with greater physiological and subjective sleepiness ($r = -0.165$, $p < .05$; $r = 0.365$, $p < .05$), and greater conscientiousness was associated with higher subjective sleepiness ($r = -0.372$, $p < .05$).

Conclusion: Like sleep deprivation, neuroticism and extraversion are associated with worse performance and sleepiness with sleep restriction. Improvement during recovery, however, showed an opposite pattern and associations with different personality variables.

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NEGATIVE MOOD ALTERATIONS WITH SLEEP RESTRICTION PERSIST INTO RECOVERY

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Introduction: Mood may be altered with sleep restriction; however, there is individual variability in this response which may relate to prior sleep history. Animal studies show sleep restriction effects on the serotonin system which persist through recovery. We assessed mood changes during chronic sleep restriction and subsequent recovery as a function of prior sleep history.

Methods: Eleven males and 13 females [mean (SD) age = 25 (6.5) years] were assigned to either an Extended [10 hours time in bed (TIB)] ($n = 12$) or Habitual [Mean (SD) = 7.09 (0.7)] ($n = 12$) sleep group for one week followed by one baseline night, seven sleep restriction nights (3 hours TIB), and five recovery nights (8 hours TIB). Volunteers were administered a computerized Neuropsychological Assessment Metrics (ANAM) mood scale (MS) throughout. ANAM mood variables (anger, anxiety, depression, happiness, fatigue and vigor) computed relative to baseline were analyzed using mixed-model ANOVAs, covarying sex, with post-hoc t-tests (Bonferroni corrected).

Results: All mood factors worsened with sleep restriction ($ps < .05$, trend happiness, $p = .059$). Compared to the Habitual group, the Ex-

tended group reported greater anxiety, depression, and fatigue during sleep restriction ($p < .05$), and these group differences persisted into recovery.

Conclusion: In contrast to the protective effects of prior sleep extension on performance during sleep restriction (Rupp et al., this volume), sleep extension did not protect against adverse mood effects; further, these effects persisted into recovery. It is possible that prior sleep extension resulted in more accurate subjective assessment during sleep restriction. Mood changes persisting into recovery highlight the lasting impact and slow recovery of chronic sleep restriction on neurobehavioral processes.

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COGNITIVE PROCESSING IN SLEEP AND WAKEFULNESS VIA SPECTRAL ANALYSIS OF THE EVENT-RELATED ACTIVITY OF THE BRAIN

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Introduction: The present study compares cognitive processing in stages of sleep and wakefulness on the basis of event-related potentials and oscillations (ERPs and EROs, respectively).

Methods: Continuous recording of EEG throughout natural overnight sleep was acquired from 12 healthy, young adult, volunteer males; those on awake stage were obtained from 19 matched males. Auditory stimuli consisted of a series of 2000 Hz deviant ($p = .20$) and 1000 Hz standard ($p = .80$) stimuli (65 dB, 10 ms r/f time, 50 ms duration, 500 ms-1500 ms inter-stimulus interval). In wakefulness, participants counted deviant stimuli (active oddball: OB-a) or performed and irrelevant task while stimulation continued (passive OB: OB-p). Brain activity was recorded from 7 recording sites (10-20 system; reference: linked earlobes). Sampling rate in the 1000 ms pre-stimulus and 1000 ms post-stimulus recording period 512 Hz.

Results: Spectral composition of ERPs were obtained using one-sided Fourier Transform and digital filtering. In Stage 2, the morphological pattern of ERPs and activity in delta and theta bands resembled those obtained under the OB-a paradigm in wakefulness. Meanwhile, the insignificant delta and short-duration theta response under REM sleep resembled the responses obtained under the OB-p paradigm. In both cases amplitudes were significantly higher, ERP and ERO components were significantly later in sleep than in wakefulness.

Conclusion: Albeit via a highly effortful processing (higher amplitudes and longer latencies), there is sensory/perceptual processing and varying degrees of stimulus discrimination in all stages of sleep. In Stage 2, specifically, there is some form of attentional processing (long duration theta response), the allocation of increasingly higher cognitive effort (longest latency in the delta response), and the highest level of stimulus differentiation (highest difference between the deviant- and standard-elicited delta response). REM is a period of shallow processing, analogous to the preattentive and preconscious processing in wakefulness under OB-p.

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IMPAIRED MEMORY CONSOLIDATION DURING SLEEP IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Introduction: Compelling evidence from animal and human studies indicates that healthy sleep facilitates the consolidation of newly acquired memories. The aim of this study was to test the hypothesis that overnight consolidation of procedural and declarative memory is attenuated

in patients with obstructive sleep apnea (OSA) in comparison to healthy subjects.

Methods: General neurocognitive and memory performance (procedural mirror-tracing task, declarative visual and verbal learning task) was assessed before and after one night of polysomnographic monitoring in 15 patients with OSA (10 men, aged 46.4±5.9 years) and 20 sex- and age-matched healthy subjects.

Results: OSA patients showed a significantly reduced sleep period time, increased apnea-hypopnea index, and subjectively disturbed sleep compared to healthy subjects (MANOVA, $p < 0.05$). Memory performance before sleep did not differ between the groups. OSA patients demonstrated a significant attenuation of overnight procedural memory consolidation compared to healthy subjects (MANOVA, $p < 0.05$, large effect size), and a non-significant attenuation of declarative verbal and visual memory consolidation (low to medium effect size).

Conclusion: The results suggest that OSA is associated with a significant impairment of procedural memory consolidation and a less pronounced impairment of declarative memory consolidation during sleep. Future work is needed to determine whether OSA treatment improves or normalizes deficits in memory consolidation during sleep in patients with OSA.

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EMOTIONAL LEARNING THROUGH CYBERTHERAPY INCREASES REM SLEEP

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Introduction: While several sleep components have been linked to learning and memory, REM sleep percentage have only been affected by complex cognitive and psychomotor tasks. We are exploring here the potential relationship between REM sleep and a complex emotional learning situation. Cognitive behavioral therapy (CBT) for specific phobias involves the processing of emotionally charged information and the establishment of new associations between the threatening stimuli and their consequences in addition to learning how to control the anxiety elicited by the feared object.

Methods: So far, the sleep of four subjects suffering from aviophobia has been recorded for five consecutive nights at home with Braebon's MediPalm. EEG, EMG and EOG were recorded and scored according to the new AASM standard method using 30 seconds epochs. The first night was an adaptation night. The second night was the baseline night. On the third and fourth day, the subjects underwent an intensive CBT using virtual reality exposure. Thus, the third and fourth nights were the experimental nights. The fifth night was a follow up night.

Results: All four subjects exhibited a linear increase in REM sleep% from baseline through the experimental nights. Three out of the four continued to increase REM sleep% on the follow up night (overall averages respectively; 22.5%, 27.5%, 29.4% and 31.0%). No systematic changes were noted in the other sleep stages and characteristics.

Conclusion: Eventhough the current sample is very small, the present results support the notion that REM sleep contributes to complex learning which now seems to include the processing of intense emotions such as that involved in CBT with virtual reality exposure. Whether these changes are due to the virtual reality novelty, the increase in visual stimulation, the actual emotional learning occurring during CBT or their combination needs to be verified in further studies.

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COUPLES WITH DIVERGENT DIURNAL PREFERENCES OR SLEEP SCHEDULES SHOW REDUCED AFFECTIVE SYNCHRONY AND LOWER RELATIONSHIP SATISFACTION, ALTHOUGH THE SPECIFIC PATTERNS DIFFER FOR MALE AND FEMALE PARTNERS

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Introduction: Several studies have found that greater similarity in bed-partners' respective sleep schedules is related to greater relationship satisfaction. Accumulating evidence indicates that circadian rhythms are more consistently detectable in positive affect (PA) than negative affect (NA). Accordingly, this study investigated whether greater similarity in sleep patterns is associated with greater synchrony in diurnal patterns of PA, which is in turn associated with higher relationship satisfaction.

Methods: Twenty-nine heterosexual co-sleeping couples completed sleep diaries and wore wrist actigraphs for 7 days. Six times a day, participants individually recorded their momentary affect and the valence of partner contact (since the previous timepoint) on personal data assistants. Measures of morningness-eveningness and relationship satisfaction were completed both at study start and end. A "parallel process" variant of multilevel analysis allowed both simultaneous identification of the affect covariation (i.e., synchrony) in female and male partners of the same couple, as well as the contribution of other variables to that association.

Results: Significant between-partner covariation of PA and NA (both $p < .001$) was present, even after accounting for the variance associated with positive and/or negative partner contact ratings. Diurnal preference and schedule differences were associated with reductions not only in between-partner covariation of PA, but also (contrary to predictions) covariation of NA. Morningness-eveningness differences were associated with reduced between-partner covariation in both PA and NA. Midsleep differences were negatively related to NA covariation exclusively. Some sex differences emerged. Male partners' relationship satisfaction (both Relationship Assessment Scale and Dyadic Adjustment Scale-4 item measures) was positively associated with PA covariation. Finally, sleep onset differences were associated with higher male partners' mean NA ratings and with worse female partners' mean partner contact ratings.

Conclusion: Larger bed-partner differences in morningness-eveningness and sleep times are linked to reduced affective synchrony, which is in turn associated with lower relationship ratings. Overall relationship satisfaction appears more relevant for males while daily partner interaction matters more for females.

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PROBABILISTIC REINFORCEMENT LEARNING AND SLEEP: A PILOT STUDY

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Introduction: Post-training sleep has previously been shown to be critical for improvement on procedural memory tasks. Here, we examined the role of sleep in consolidation of probabilistic reinforcement learning, a procedural learning task that is dependent upon the basal ganglia.

Methods: Eighteen healthy 18-25 year olds were trained on a probabilistic selection task and retested after a delay. They were randomly assigned to a 12-hour wake group ($n = 7$), a 12-hour sleep group ($n = 6$), or a 24-hour sleep group ($n = 5$). The wake group was trained at approximately 9 am, while both sleep groups were trained at approximately 9 pm.

Results: Sleep groups maintained their level of performance on retesting of reinforcement learning training pairs whereas the wake group's performance got worse ($p = 0.06$). However, the wake group, which was trained in the morning, had better performance after initial training than either sleep group ($p = 0.07$).

Conclusion: It is likely that the wake group performed better immediately after training due to the fact that training always occurred in the morning just after the sleep period whereas both sleep groups were trained in the evening before sleep. Our results for the maintenance of learning after sleep suggest that sleep protects memory for probabilistic reinforcement. Sleep may strengthen consolidation and protect against forgetting due to interference.

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IDEAL VERSUS PERCEIVED SLEEP AMONG HEALTHCARE PROFESSIONALS

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Introduction: The national sleep debt is at an all time high, and most people obtain less sleep than they ideally would like. Consequently, adverse health outcomes are often a consequence of sleep deprivation. Less defined is the role personality variables play into the perception of sleep duration and quality, especially among various groups of healthcare professionals. This survey based study assesses the relationship between perceived and ideal sleep and sleep quality.

Methods: A total of 59 attendees to a sleep-related conference completed a packet of questionnaires asking about medical history, stress, personality, health locus of control, and sleep quality. All participants were healthcare professionals including polysomnographic technicians, respiratory therapists, medical residents, and physicians.

Results: A model was used assessing the variance of perceived versus ideal sleep duration, personality variables, and subjective sleep quality. Significant correlations were found between sleep variance and quality ($r = .57, p < .001$); sleep quality and neuroticism ($r = .37, p < .01$), and sleep quality and conscientiousness ($r = -.30, p < .01$). Path analysis regression indicates that neuroticism and conscientiousness mediate the models between sleep variance and quality, accounting for 40% and 34% of the variance, respectively. In addition, a significant relationship exists between external health locus of control measures, history of cardiovascular health and sleep variance, suggesting that those with more sleep duration variance feel less in control of their sleep habits, regardless of when their work shift starts.

Conclusion: The results indicate that individuals who have a higher discrepancy between their perceived and ideal sleep duration report poorer sleep quality, independent of actual sleep duration or circadian factors, when mediated by higher scores of neuroticism and lower scores of conscientiousness. Those with greater variance felt less in control of their health outcomes and were more likely to report adverse health outcomes.

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HEALTH OUTCOMES BASED ON THE BIG FIVE PERSONALITY DIMENSIONS

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Introduction: The Big Five personality traits are five distinctive dimensions of personality that have been widely validated. However, there is minimal data linking the various dimensions with health outcomes, including perceived sleep quality and daytime functioning. Study objec-

tives were to examine differences within each dimension according to various health outcome measures.

Methods: A total of 59 participants ages 19-75 who presented for clinical polysomnography at a Midwestern sleep center participated in the current study. Participants completed measures relating to personality, sleep outcomes, daytime functioning, and other health-related markers. Participants with previously diagnosed sleep disorders, underwent a split night polysomnogram, or perform shift work were excluded. Objective sleep measures were not included in this analysis. Groups were split based on high or low scores of each personality dimension.

Results: Age or gender did not co-vary with the variables. Mann-Whitney U Tests were run for each personality dimension. Increased neuroticism was significant for more anxiety, lower quality of life (QOL) measures on most scales, poorer sleep quality (SQ), and fatigue ($p < .05$). Low extroversion was significant for increased anxiety, pain complaints, fatigue, and poorer SQ ($p < .05$). Low conscientiousness was similar with increased pain complaints, fatigue, and more stress ($p < .05$). Low agreeableness was significant for increased pain and anxiety, and physical limitations ($p < .05$). The dimension of openness did not have any significant differences.

Conclusion: Sleep related complaints tended to come from participants who were introverted and had more neuroticism. Fatigue, anxiety, and pain were also common in these dimensions, possibly suggesting a link with poor perceived sleep and impaired daytime functioning. Interestingly, the adverse health outcome consistent across all dimensions with significance was increased pain complaints, which was accompanied by poorer emotional well-being. Further work is needed to explore the link with other health perception measures and objective sleep data.

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THE EFFECT OF SLEEP EXTENSION ON COGNITIVE FUNCTIONING IN ADOLESCENTS WITH DAYTIME SLEEPINESS AND INSUFFICIENT SLEEP AT NIGHT

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Introduction: Previous research has shown that insufficient sleep during the night contributes to cognitive deficiencies during the daytime in adolescents. The current study examines changes in cognitive functioning after nighttime sleep extension in a sample of adolescents with complaints of daytime sleepiness and insufficient nighttime sleep.

Methods: Participants were 56 adolescents (34 females) aged 14 - 18 (Mean age = 16.46). After one week of baseline, the participants were randomly assigned to either extend their sleep for at least 60 minutes on three consecutive school nights or continue with their normal sleep schedule. Baseline and post-test sleep and cognitive data included daily sleep diaries, the Pediatric Daytime Sleepiness Scale (PDSS), digit span, verbal fluency and trail making.

Results: Nineteen of those assigned to extend their sleep succeeded in doing so with a mean extension time of 80.35 minutes. Repeated measures ANOVAs were performed to evaluate changes in sleep and cognition related to the intervention. Interactions for the sleep diaries found that sleep extenders decreased difficulty in waking in the morning, increased time in bed, total sleep time and sleep efficiency more than non-sleep extenders, (all $p < .05$). Sleep extenders reduced their level of daytime sleepiness on the PDSS more so than controls, ($p < .05$). All participants improved on the forward digit span ($p < .05$), however, only sleep extenders improved on the backward digit span ($p < .05$). All participants improved on the verbal fluency task, ($p < .01$). Everyone improved on trail making part A ($p < .01$), however, only sleep extenders improved on trail making part B, ($p < .01$).

Conclusion: Even a small increase in the duration of nighttime sleep can improve sleep variables, reduce daytime sleepiness, and produce improvement on measures of cognitive ability requiring mental control and flexibility in adolescents.

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SECOND-ORDER PARAMETERS OF SLEEP SPINDLE DISTRIBUTION BEFORE AND AFTER PURSUIT ROTOR LEARNING IN YOUNG AND ELDERLY ADULTS

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Introduction: A 2-state Markov process model was applied to the distribution of sleep spindles (SS) in the Stage 2 sleep of young and elderly adults before and after learning a novel motor task. The Markov state transition probabilities were compared as second-order measures to a conventional first-order measure of SS distribution, sleep spindle density (SSD).

Methods: There were 10 Young (17-23 yrs; 6 female) and 10 Elderly (62-79 yrs; 7 female) adults. In-home polysomnographic sleep recordings were performed on three consecutive nights; the data reported here are from the second (Baseline) and third (Post-Acquisition) nights. Participants performed the pursuit rotor task on the afternoon of the Post-Acquisition day/night using their non-dominant hand. Each night was divided into equal thirds and all Stage 2 SSs were visually identified from a central lead. Inter-spindle intervals (ISIs) were calculated as the number of seconds between 2 successive SSs. "Burst" ISIs were < 5 s and "Isolated" ISIs were ≥ 5 s. 2(Night: Baseline, Post-Acquisition) \times 3(Thirds: First, Second, and Last) repeated-measures ANOVAs were performed separately for each group.

Results: SSD increased significantly across Night, $F(1,9)=8.11$, $p=.019$, and Thirds, $F(2,18)=32.07$, $p<.001$, in the Young group. The probability of transitioning from an Isolated ISI to a Burst ISI increased significantly after learning, $F(1,9)=14.62$, $p=.004$, and across Thirds, $F(2,18)=13.83$, $p<.001$. The probability of transitioning from a Burst ISI to another Burst ISI increased significantly in the Young group across Thirds, $F(2,18)=22.18$, $p<.001$, but not after learning. No significant effects were found in the Elderly group.

Conclusion: Regarding time-of-night effects, SSD and the two Markov transition probabilities increased across thirds of the night. SSD also increased significantly after learning. Regarding the Markov measures, the probability of entering a spindle burst is significantly greater after learning, but the probability of remaining in a spindle burst is not.

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WAKING AND DREAM AFFECT PATTERNS DURING PREGNANCY

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Introduction: The primary goal of the present investigation was to identify and map waking and dream affect longitudinally across the trimesters of pregnancy on an individual and group level. The affect patterns of waking and dreaming states of consciousness were explored from the perspective of the continuity hypothesis, an evolutionary perspective, the disruption-avoidance-adaptation model of the function of dreams and Jung's theory of dream compensation.

Methods: Sixteen primiparae recorded waking experiences and dreams one week per month during gestation and rated them for affect. The amount and intensity of discrete affects (e.g., fear/anxiety; happiness/elation) and affect summary scores (e.g., positive and negative affect; affect in general) were evaluated.

Results: The amount of positive waking affect tended to be higher than amount of negative waking affect, positive dream affect and negative dream affect. Happiness was found to be the predominant waking and

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dream affect and anxiety was the second most predominant affect in dreams, but not in waking. Two stable dream affect patterns were discerned. Either the discrete affects clustered tightly together at a low level or most of the affects fluctuated up and down across the pregnancy.

Conclusion: The findings do not support the continuity hypothesis exploring dreams and waking experiences within the 24-hour cycle, while evaluating mood states across a week, waking and dream affect evidenced positive correlations. The findings were largely not consistent with evolutionary theory in that amount and intensity of Fear/Anxiety did not show positive correlations between waking and dream states, but rather evidenced negative correlations. Affect intensity in the dream material did not consistently oscillate from one night to the other and therefore did not support the disruption-avoidance-adaptation model. Instead of a compensatory relationship between positive and negative affect in waking and dreaming, a stronger positive relationship was found among valences of affects across states of consciousness.

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AGE DIFFERENCES IN SLEEP MACROARCHITECTURE FOLLOWING ACQUISITION OF THE TOWER OF HANOI

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Introduction: Previous studies on sleep and memory in young adults have linked the acquisition of tasks with a strong procedural learning component to REM sleep. However, very little is known how sleep architecture changes following procedural learning in elderly adults. The purpose of this study was to examine age differences in sleep macroarchitecture following acquisition of a procedural learning task (Tower of Hanoi) in young and elderly adults.

Methods: Participants included 8 young adults (19-25 yrs; 3 female) and 8 elderly (65-81 yrs; 5 female) adults. In-home polysomnographic sleep recordings were performed on three consecutive nights; the data reported here are from the second (Baseline) and third (Post-Acquisition) nights. All participants performed five trials of the Tower of Hanoi on the afternoon of the Post-Acquisition day/night. Separate 2(Age: Young, Elderly) by 2(Night: Baseline, Post-Acquisition) mixed ANOVAs were used to determine whether there were age differences in the sleep stages (percentage of total sleep time) before and after learning the Tower of Hanoi.

Results: There was a significant Age by Night interaction for REM sleep, $F(1,14)=13.49$, $p=.003$. Young adults showed a trend toward an increase in REM across the two nights from 21.19% to 24.14%, $t(7)=2.10$, $p=.074$. In contrast, elderly adults showed a significant decrease in REM sleep from 22.75% to 19.35%, $t(7)=3.39$, $p=.012$. The Age by Night interaction for Stage 4 sleep was also significant, $F(1,14)=5.73$, $p=.031$. Elderly adults showed a trend toward an increase in Stage 4 sleep from 0.69% to 2.15%, $t(7)=2.18$, $p=.065$; whereas, the young adults showed a nonsignificant decrease from 5.47% to 4.01% in this stage after learning, $t(7)=1.43$, $p=.195$.

Conclusion: The results of these preliminary data suggest that the changes in sleep macroarchitecture that occur after the acquisition of a procedural learning task are different in young and elderly adults.

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DREAMS DURING PREGNANCY: RELATIONSHIP WITH WAKING DEPRESSION

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Introduction: Pregnancy is a period of major physical changes and is known to be psychologically challenging. Previous studies have shown that dreams during this period of life tend to reflect these upheavals. We

attempted to further explore this phenomenon by looking at the relationship between dreams during pregnancy and waking depressive state. We hypothesized that depressive symptoms would be reflected in dreams by the presence of more negative components in emotions, interactions and outcomes.

Methods: 80 pregnant women maintained a ten-day morning dream diary in their second trimester. In addition, they completed the Edinburgh Postnatal Depression Scale (EPDS), a short screening questionnaire for postnatal depression, which has also been validated for a prenatal use. One dream for each participant was coded by two raters using the Hall & Van de Castle scales (1966). The raters also coded all pregnancy references in dreams (i.e., fetus, baby, delivery, etc.) using a modified version of Maybruck's pregnancy references categories (1986).

Results: A stepwise multiple regression revealed that the best predictors for the score of waking depression were the number per dream of: failures experienced by the dreamer, elements reflecting walls or barriers, aggressions by a familiar character towards the dreamer, and elements related to a dreamer's illness or miscarriage. This combination of variables significantly predicted depression score, $F(4,75) = 10.52$, $p < .001$, with all the four variables contributing significantly to the prediction. The analysis yielded a R^2 of .325, indicating that 32.5% of the variance in depression was explained by this model.

Conclusion: Overall, these results are consistent with previous studies showing that pregnancy has an impact on dream content. They also tend to support the notion that dream content is influenced by the dreamer's emotions and concerns, and that it can reflect depressive and anxious states.

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CLASSIFICATION OF EMOTIONAL TONE OF DREAMS USING MACHINE LEARNING AND TEXT ANALYSES

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Introduction: Until now, most of the studies on dreams have used time consuming coding systems that depend on a rater's judgment. It is of interest to develop a more efficient mean of scoring dreams that can be used with large data banks and reproduced across laboratories. This study stands amongst the first steps toward the exploration of dream's emotional content using automatic analysis tools.

Methods: A sample of 776 dreams, reported by 274 individuals of varied age and sex, was used for dream words correlation extraction and a subset of 477 tagged ones for the training of the software. The dreams were rated by a judge using two 0-3 scales describing respectively the negative and the positive orientation of the dream content. To obtain a linguistically informed representation of dream descriptions, we used certain standard resources, i.e. the CMU Link Grammar Parser and the LIWC dictionary. We also designed a novel, dynamic representation of the change of emotions as the dream description progresses.

Results: We have calculated accuracy of the learned classifier (its performance at predicting the right label, i.e. the label given by the human judge) on the scale 0-3 and the mean-squared error (i.e. difference with human judgment when incorrectly guessing). Multinomial logistic regression model with a ridge estimator classifier outperformed other methods in accuracy and mean squared error, with an accuracy of 59%, which is significantly better than the baseline accuracy (30-33%) and the chance probability (25%). The mean-squared error was 0.37, meaning that almost all errors have only a difference of 1 on the scale.

Conclusion: These results offer a promising perspective for the automatic analysis of dream emotions, which is recognized as a primary

dimension of dream construction. It should facilitate the analysis and mining of large number of dreams.

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CHANGES IN CONTENT OF COMBAT-RELATED NIGHTMARES IN VIETNAM VETERANS WITH PTSD RECEIVING IMAGERY REHEARSAL THERAPY

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Introduction: Combat-related experiences such as being fired upon or firing weapons, witnessing injury and death, and being surrounded by the enemy can all lead to reexperiencing the trauma through nightmares. Imagery Rehearsal (IR) is a psychotherapy that addresses chronic nightmares by mentally rehearsing a changed version of the nightmare that is less traumatic. We are conducting a randomized controlled trial of IR in Vietnam veterans. Here we present preliminary data on changes that have occurred in their nightmares over the course of treatment.

Methods: Veterans have been randomized to receive IR (n=59) or a comparison treatment (n=60). Here we focus on the IR group who, as part of treatment, were asked to write out the content of their most distressing repetitive nightmare and to change the nightmare to make it less distressing using an alternate ending, distancing techniques, or any other way that feels comfortable and safe. We applied content analysis, a qualitative technique, to examine the content of the nightmares before and after the IR changes were made in terms of the levels of: hostility, anxiety, dependency on others, the settings, objects, actions, affects, sounds and color.

Results: The nightmares of 9 veterans have been analyzed thus far. Prior to making changes, veterans described their nightmares as very hostile and provoking anxiety. There was a significant decrease ($p=0.001$) in the level of hostility (6.0(1.0) to 0.5(0.9)) and anxiety (5.8(0.5) to 0.3(0.5)). There were also significant decreases ($p=.05$) in actions (4.9(3.0) to 3.9(2.6)) and affects (6.6(1.7) to 0.9(0.6)).

Conclusion: These data offer preliminary evidence that veterans reduced nightmare distress through reductions in hostile and anxious content, as well as reductions of action and affect. Further analyses will examine the relationship between these changes and daily ratings of nightmare distress, as well as the influence of nightmare changes and treatment outcome.

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NEUROCOGNITIVE DECLINE IN OBSTRUCTIVE SLEEP APNEA

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Introduction: Patients with obstructive sleep apnea syndrome have been reported a wide spectrum of neurocognitive deficits such as attention, memory, executive and motor functions. These spectrums were ranging from almost no effect of OSA on neurocognitive functioning to significant dysfunction in different parameters of cognition. In this study, we aimed to investigate which memory processes are affected by obstructive sleep apnea in clinically suspected OSA patients.

Methods: Sixty six (13 female, 53 male) patients were included to the study. After polysomnographical evaluation, they were divided in to 2 groups according to apnea hypopnea index which was taken 10 per hour as a cut off point. Wechsler Memory Scale, Trial Making Test, Clock Drawing Test, Hospital Anxiety and Depression Scales were given to

all patients by an experienced psychologist. All sleep and respiratory parameters were evaluated. For statistical analysis, student t test was used and $p<0.05$ was accepted for significance.

Results: The number of patients with an apnea hypopnea index above and below 10 per hour is 47 and 19 respectively. The mean apnea hypopnea index is 39.7 ± 22.9 and 4.3 ± 3.3 respectively. There is no significant difference between 2 groups in age, education, depression and anxiety scales. It is found that significant decline in attention ($p<0.001$) and mathematical skills ($p<0.05$) and short term memory ($p<0.05$) in patients with an apnea hypopnea index above 10 per hour.

Conclusion: Cognitive deterioration might be more prominent in moderate to severe patients with OSA.

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DOES EARLY STAGE 2 EQUAL LATE STAGE 2?

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Introduction: The “early sleep” vs. “late sleep” experimental paradigm holds a venerable place in the sleep and memory literature. In this design, early sleep is typically equated with SWS, and late sleep with Stage REM. Because Stage 2 sleep (S2) occupies roughly equal proportions of early and late sleep, it factors out of experimental results. In line with various reports in the literature, the present study asks whether S2 can be regarded as equivalent -- and equivalently sensitive to learning-- in early and late sleep.

Methods: In this ongoing study, baseline digital recordings of nighttime sleep (sampling rate 1000Hz) are divided into early sleep and late sleep. Epochs of early S2 and late S2 are then submitted to fast Fourier transformation (FFT). Various epoch durations, each a power of 2 samples to permit exact FFT, have been investigated. To capture K complexes and sleep spindles, respectively, spectral peaks at 0.6Hz - 2.0Hz and at 12Hz - 14Hz are isolated. A ratio of low frequency peak to spindle frequency peak (K:SPIN ratio) is then computed for each epoch of early and late S2. Thus far, data from 7 subjects in each condition, at FZ and PZ electrodes, have been analyzed.

Results: At FZ, the K:SPIN ratio in early S2 significantly exceeds the K:SPIN ratio in late S2 (2-tailed t-test, $p=0.04$), as does variance in the K:SPIN ratio (F-test for unequal variance, $p=0.00087$). At PZ, the K:SPIN ratio in early S2 does not differ from the K:SPIN ratio in late S2 (2-tailed t-test; $p=0.27$); variances are statistically equal ($p=0.12$). In late S2, neither K:SPIN ratios ($p=0.18$) nor their variances ($p=0.86$) differ between FZ and PZ.

Conclusion: Late S2 is spectrally more homogeneous than early S2. Early and late S2 may differ in their sensitivity to learning. In experiments, S2 may not “factor out” cleanly.

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EVALUATION OF THE PERFORMANCE OF CPAP HEATED HUMIDIFIERS FOR USE IN SLEEP APNEA THERAPY; A COMPARATIVE STUDY OF HUMIDIFICATION EFFECTIVENESS

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Introduction: Heated humidifiers are intended to improve patient comfort and compliance by increasing air temperature and humidity during CPAP therapy. This study compared humidifier performance of four commercial CPAP devices under simulated real-use conditions.

Methods: The devices were evaluated using a side-by-side bench test for seven hours: Fisher & Paykel SleepStyle 608 with ThermoSmart® (FP); Resmed Elite S8 with Humidaire 3i (RS1); Resmed Elite S8 with improved Humidaire 3i labeled “20% MORE humidity” (RM2); and Respirationics RemStar Pro M (RP). Conditions included CPAP pressure 12 cmH₂O, 40 LPM flow, maximum humidifier settings, and ambient temperature of 19-20 °C. Hose-end temperatures were recorded hourly. Humidity was recorded using 1) a modified ISO 8185 moisture output method that also recorded condensation in the tubing, and 2) hose-end hygrometry.

Results: FP delivered highest average humidity and temperature levels: 27.6 mg/L at 29.4 °C. No condensation was observed in FP heated wire tubing. RM1 and RM2 performance differed only 3.1% in humidity and 0.5 °C in temperature. RM2 delivered average humidity and temperature levels: 23.0 mg/L at 25.7 °C. The claimed improvement in humidity for RM2 was not confirmed in this study. RM1 and RM2 resulted in the greatest volume of condensation in the tubing: 3.5 mL and 5.9 mL respectively. RP delivered the lowest average humidity and temperature levels: 19.5mg/L at 24.4 °C. No condensation was detected, due to lower humidity and temperature.

Conclusion: Heated humidifiers in this study increased humidity 10.1 mg/L to 18.3 mg/L and air temperature 4.9 °C to 9.8 °C above ambient levels, sometimes causing condensation in the tubing. FP outperformed other humidifiers in all areas of heat and humidity delivery with zero condensation.

Support (optional): Support provided by Fisher & Paykel Healthcare.

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