

# SLEEP

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Associated Professional Sleep Societies, LLC

A joint venture of the  
American Academy of Sleep Medicine  
and the Sleep Research Society

**SLEEP 2006**

**20th Anniversary Meeting of the  
Associated Professional Sleep Societies, LLC**

**June 17-22, 2006**

**Salt Lake City, Utah**

**Scientific Highlights/Abstracts of Original Investigations**

**SLEEP**  
**SALT LAKE CITY**  
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The SLEEP 2006 meeting abstract supplement unites the journal SLEEP and the science of the Associated Professional Sleep Societies in a convenient format. This special issue includes all abstracts to be presented at the SLEEP 2006, 20th Anniversary Meeting of the Associated Professional Sleep Societies, June 17-22, in Salt Lake City, Utah. The supplement provides all AASM and SRS members, including those unable to attend the meeting, a brief glimpse into the new ideas and latest research taking place in the sleep medicine and sleep research field.

Of the 1,111 abstracts accepted, 224 will be presented in oral presentation format and the remainder as poster presentations. Similar to prior meetings, the Program Committee elected to:

- 1) Group posters into thematic categories;
- 2) Dedicate a 90-minute block of time each day for poster presentations;
- 3) Display each poster on one of the three scheduled poster days (June 19, 20, 21).

Each poster has a unique 4 digit number and is assigned to one of the 20 categories listed below, to facilitate identification and location.

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

Attendees of the SLEEP 2006 Meeting will experience a forum for the discussion of new ideas and key research in the field 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 in the sleep field, further promoting 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, Ph.D.  
Interim Editor-in-Chief

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0001

**SODIUM OXYBATE CONSOLIDATES WAKEFULNESS IN OREXIN KNOCKOUT MICE***Mochizuki T, Clark EL, Scammell TE*

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**Introduction :** Sodium oxybate (Á-hydroxybutyrate) reduces cataplexy and daytime sleepiness in people with narcolepsy, but its neuronal mechanisms are unknown. We studied the effects of sodium oxybate in narcoleptic orexin knockout (KO) mice to determine whether orexin is necessary for sodium oxybate's beneficial effects and to establish a model to better define the mechanism of sodium oxybate.

**Methods :** Male orexin KO mice were implanted with EEG/EMG electrodes, a temperature/activity transmitter (TA-F20, DSI), and an intraperitoneal catheter. Beginning immediately after surgery, saline was infused via the catheter at a rate of 1  $\mu$ l/min. Two weeks later, EEG/EMG recordings were performed on a 12:12 LD cycle. Three different doses of sodium oxybate were administered via the catheter for 7 days each; 200 mg/kg/day over days 2-8, 400 mg/kg/day over days 9-15, and 800 mg/kg/day over days 16-22. Behavioral states were scored in 10 sec epochs using SleepSign (Kissei Comtec) followed by manual correction.

**Results :** Chronic infusions of sodium oxybate at these doses did not induce an abnormal EEG pattern or reduce body temperature as often occurs with bolus injections. The mean duration of wake bouts during the 12 hr dark period was lengthened by 60% and the number of wake bouts was decreased by 30% on day 15 (day 7 of 400 mg/kg/day). No additional consolidation of wakefulness occurred with the 800 mg/kg/day dose. In addition, sodium oxybate increased the amount of wakefulness by 7% in the dark period. Neither the number nor duration of cataplexy episodes changed significantly over 21 days of sodium oxybate treatment.

**Conclusion :** Chronic treatment with sodium oxybate consolidated wakefulness in orexin KO mice, suggesting that sodium oxybate improves wakefulness via an orexin-independent mechanism. Future studies may establish whether other dosing regimens improve cataplexy and whether sodium oxybate acts through GABA-B receptors.

**Support (optional):** The American Sleep Medicine Foundation (#29-CA-04) and Orphan Medical Inc/Jazz Pharmaceuticals.

0002

**SLEEP DEPRIVATION REDUCES HIPPOCAMPAL EXPRESSION OF THE TRANSCRIPTION REGULATORY PROTEIN ZIF-268***Havekes R, Kuipers I, Roman V, van der Zee EA, Meerlo P*

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**Introduction :** One theory about the function of sleep is that it plays an important role in neuronal and synaptic plasticity necessary for memory formation. In line with this hypothesis, the expression of various genes appear to change with behavioral state, including the immediate early gene zif-268 (also known as Egr-1, Krox-24, NGFI-A). The zif-268 gene encodes for a transcription factor protein that controls various other genes with important roles in neuronal function and synaptic plasticity. Furthermore, studies with knockout mice have shown that deletion of zif-268 impairs learning and memory in a variety of tasks. In the present study, we examined the daily profile and effect of sleep deprivation on zif-268 protein expression in the hippocampus and other brain regions involved in learning and memory.

**Methods :** The experiments were performed with adult male C57BL/6J mice. In one group of animals brains were collected at 3h intervals throughout the 12h light /12h dark cycle. In a second series of animals, brains were collected after 12h of sleep deprivation by gentle handling

during the light phase (the circadian resting phase). The brains were processed for immunocytochemistry with a polyclonal antibody against zif-268.

**Results :** The data show that the 24h pattern of zif expression in the dentate gyrus of the hippocampus parallels the pattern of sleep, with higher numbers of zif-268 positive cells during the light phase than during the dark phase. Sleep deprivation during the light phase caused a significant reduction in the number of zif-positive cells in various hippocampal regions, including the dentate gyrus.

**Conclusion :** The results suggest that sleep promotes the hippocampal expression of the transcription regulator zif-268. A decrease in the expression of zif-268 due to sleep loss may eventually result in reduced neuronal plasticity and cognitive function.

**Support (optional):** This work is supported by the Graduate School of Behavioral and Cognitive Neurosciences and the Netherlands Organization for Scientific Research (grant 016.021.017 to EAvdZ and grant 864.04.002 to PM).

0003

**CHRONIC PARTIAL SLEEP DEPRIVATION INCREASES SEROTONIN-1A RECEPTOR-ASSOCIATED GI-PROTEIN NUMBERS IN THE AMYGDALA***Roman V, Keijsers JN, Luiten PG, Meerlo P*

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**Introduction :** Chronic partial sleep loss is a growing problem in modern society. Frequent sleep loss may have adverse effects on functional outputs of the brain such as emotionality and stress-responsivity. Since these functions are under control of the serotonergic system, chronically restricted sleep may increase the sensitivity to stress-related diseases and mood disorders by gradually altering changes in serotonergic neurotransmission. In the present study, we examined whether chronic partial sleep deprivation alters the serotonin-1A receptor signaling cascade in brain areas involved in stress and emotionality.

**Methods :** Adult male Wistar rats were subjected to a schedule of partial sleep deprivation for 2 or 8 days. The schedule consisted of 20h sleep deprivation and 4h of rest per day. Sleep deprivation was achieved by placing the animals in slowly rotating wheels. Since this method of sleep restriction involves forced physical activity, we included control rats that were placed in wheels rotating at double speed for half the time. Thus, these rats had to walk the same distance but had sufficient time to sleep. A third group of rats served as home cage controls. After 2 or 8 days of sleep restriction, brain material was collected and processed for autoradiographic analysis of serotonin-1A receptors and serotonin-1A receptor-associated Gi-proteins.

**Results :** In the brain areas that were examined, 2 and 8 days of sleep restriction did not lead to changes in serotonin-1A receptor numbers. However, 8 days of sleep restriction significantly increased serotonin-1A receptor-associated Gi-protein numbers in the amygdala. The forced activity control procedure had no effect on either serotonin-1A receptor numbers or Gi-protein numbers.

**Conclusion :** Whereas restricted sleep for one or two days may not have noticeable effects, chronic partial sleep deprivation for over a week gradually alters serotonin-1A receptor-mediated signaling cascades in the amygdala, a brain structure involved in the regulation of mood and stress-reactivity.

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0004

**EFFECTS OF CARBACHOL ON ELECTRICAL COUPLING IN THE SUB-COERULEUS NUCLEUS**

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**Introduction :** Multiple studies have implicated ponto-geniculo-occipital (PGO) waves in the generation of rapid eye movement (REM) sleep. PGO waves are paroxysmal bursts of neuronal firing associated with critical aspects of REM sleep. Rodent equivalent P-waves can be induced by local injections of the muscarinic agonist carbachol (CAR) into the rat dorsal Subcoeruleus (SubC) nucleus. We investigated the possibility that these paroxysmal bursts could be mediated by electrical coupling in SubC neurons. **Methods :** Intracellular current clamp recordings were conducted on 12-21 day old rat brainstem neurons maintained in artificial CSF. After basic physiological properties were determined, CAR (40 $\mu$ M), atropine (ATR-10 $\mu$ M), and tetrodotoxin (TTX-30 $\mu$ M) were administered. Neurobiotin was injected upon completion of recordings.

**Results :** CAR had a direct depolarizing effect on some SubC neurons, which was blocked by pretreatment with ATR but persisted after TTX. CAR also had an excitatory effect as shown by the induction of spikelets, a physiological marker for the probable presence of gap junctions. Additionally, neurobiotin injection into single SubC neurons demonstrated intercellular connections manifested by the presence of multiple labeled neurons.

**Conclusion :** These results show that CAR had a direct excitatory effect on some SubC neurons. Furthermore, the existence of multiple labeling and spikelets are indications of electrical coupling and the presence of gap junctions. This study suggests the presence of electrotonic coupling in at least some SubC neurons, which may be activated by CAR. The generation of synchronized, electrically coupled bursts of activity by the SubC may be one potential mechanism behind PGO waves.

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0005

**EXPRESSION OF C-FOS IN THE PREOPTIC AREA DURING DIFFERENT LEVELS OF SLEEP DRIVE**

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**Introduction :** Recent studies implicate the median preoptic nucleus (MnPN) and the ventral lateral preoptic area (vlPOA) of the hypothalamus in sleep regulation. The present study examined c-fos expression in these nuclei during different levels of sleep propensity/pressure. Sleep-pressure was hypothesized to be low during the dark/active period, moderate during the light/rest period and high in response to sleep deprivation (SD) during the light period.

**Methods :** Sleep-waking diurnal organization was assessed in 23 Sprague-Dawley rats. Rats exhibiting 60-70% sleep during the light period and 15-25% sleep in the dark were permitted 2h spontaneous sleep-waking behavior either during the light (ZT1-3; n=6) or dark (ZT13-15; n=6) periods; six rats were subjected to 2h-SD during ZT1-3 (SD1). Five rats with weaker diurnal rhythms in sleep-waking were also subjected to 2h-SD during ZT1-3 (SD2). Sleep-pressure in SD2 rats was hypothesized to be lower compared to SD1 animals. Brain tissue was immunostained for c-Fos protein and for glutamic acid decarboxylase (GAD), a marker

of GABAergic cells.

**Results :** Dark-recorded rats exhibited 28.8 $\pm$ 2.1% sleep; light-recorded rats had 83.3 $\pm$ 1.6% sleep; SD1-rats accumulated 5.6 $\pm$ 1.1% sleep. The number of Fos+GAD-immunoreactive (IR) neurons in rostral MnPN was highest in SD1 (36.6 $\pm$ 2.9), moderate in light-sleep (20.7 $\pm$ 0.9) and least in dark-sleep (13.5 $\pm$ 0.9) rats. Fos+GAD-IR cell counts in vlPOA cluster were highest in light-sleep (20.6 $\pm$ 0.9), moderate in SD1 (10.4 $\pm$ 0.9) and least in dark-sleep (6.8 $\pm$ 0.6) rats. Cell counts in caudal MnPN and extended vlPOA showed a similar pattern across groups. Compared to SD1 rats, SD2 animals manifested lower degree of sleep-pressure defined by the number of attempts to enter sleep during SD-procedure (49 $\pm$ 5.9 versus 83 $\pm$ 2.2 attempts). Fos+GAD-IR cell counts in SD2-rats were lower than cell counts in SD1-rats.

**Conclusion :** Activation of MnPN GABAergic neurons reflects homeostatic sleep-pressure while activity of vlPOA GABAergic neurons is more strongly related to sleep amount than to sleep drive.

**Support (optional):** Supported by the Department of Veterans Affairs and MH 63323

0006

**HYPOCRETIN/OREXIN DEFICIENT MICE DISPLAY REDUCED METABOLIC RATE**

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**Introduction :** Studies have identified interrelationships between sleep duration, body weight regulation and energy expenditure. A critical component of energy regulation that can be influenced by sleep is the hypocretin/orexin neuropeptide system. We have observed a significantly higher body weight in female rodents lacking functional hypocretin transmission compared to normal females. In this study, we explore the function of hypocretins in energy expenditure using orexin/ataxin-3 transgenic (TG) mice.

**Methods :** TG (N8, backcrossed to C57BL/6) mice and their wild-type littermates (WT) were maintained under a 12h:12h light/dark cycle at 21-22 $^{\circ}$ C with food and water ad libitum. Metabolism, feeding, drinking, locomotor activity, body temperature and electroencephalography were continuously monitored in Plexiglas chambers (Columbus Instruments, OH; Data Science International, MN).

**Results :** Both WT and TG mice displayed significant diurnal rhythm in metabolism, with values higher during the night. Respiratory quotient (RQ, ratio of carbon dioxide production to oxygen consumption) was lower during the day, suggesting an increased fat consumption when the animals are not feeding. A 24-hour food deprivation eliminated the RQ rhythm. Upon entering the metabolic chambers, WT mice responded with nocturnal hyperactivity lasting 2-3 days, while TG mice displayed little hyperactivity. As a result, the initial metabolic rate of TG mice was significantly lower than that of WT mice. The steady-state metabolism (corrected by body weight) of WT mice was slightly higher than that of TG mice, especially during the dark period, correlating with significantly higher level of locomotor activities in wild type mice. The metabolic difference reaches significant level in females. Simultaneous monitoring of sleep and metabolism at 10-second epochs allowed detailed analyses at stage transitions. WT and TG mice showed similar patterns in metabolism: active wake >> quiet wake > rapid-eye-movement sleep > slow-wave sleep.

**Conclusion :** Although hypocretin-deficient mice consume less food compared to their wild-type littermates, their reduced metabolism likely leads to overweight.

**Support (optional):** Supported by the Howard Hughes Medical Institute and National Institutes of Health (MH073435).



0007

**MULTIPLE NEUROTRANSMITTER SYSTEMS CONTROL THE ACTIVITY OF GABAergic NEURONS IN THE NPO**Zhang J,<sup>1</sup> Sampogna S,<sup>1</sup> Morales F,<sup>1,2</sup> Chase M<sup>1,2,3</sup>

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**Introduction :** Microinjections of either GABA or agonists of GABA receptors into the nucleus pontis oralis (NPO) of cats immediately produce prolonged periods of wakefulness. In addition, GABAergic neurons in the NPO are activated during wakefulness. In the present study, using adult cats and guinea pigs, we investigated putative inputs to GABAergic neurons in the NPO that are responsible for the induction of wakefulness.

**Methods :** Immunofluorescent techniques were used to stain frozen sections with anti-GAD or anti-GABA antibody. Double staining was carried out with anti-GABA and 1) anti-ChAT, 2) anti-5-HT, 3) anti-MCH, or 4) anti-hypocretin-1 antibodies. Selected sections were stained with antibodies against GABA and hypocretin receptor 1 or receptor 2.

**Results :** Abundant GABA or GAD positive fibers and terminals as well as positive neuronal somata were observed in the NPO. GABA positive neurons were relatively small (12-18 mm in diameter) and their somata were round or oval. Fibers and terminals, that were stained by antibodies against ChAT, 5-HT, MCH or hypocretin-1, were also present in the NPO; some of these stained terminals were located in close apposition to GABA-containing somata. Double staining with antibodies against GABA and hypocretin receptor 1 or receptor 2 revealed colocalization within the same neurons.

**Conclusion :** The close apposition of terminals containing ChAT, 5-HT, MCH or hypocretin with GABAergic neuronal somata in the NPO suggests that these GABAergic neurons are controlled by multiple neurotransmitter systems. In addition, the colocalization of GABA and hypocretin receptors 1 and 2 indicates that the hypocretinergic control of GABAergic neurons is mediated through both hypocretin receptors. We hypothesize that the preceding diverse inputs modulate the activity of GABAergic neurons that control the occurrence of wakefulness and active sleep.

**Support (optional):** This research was supported by grants AG 04307, NS 23426, NS 09999 and MH 43362.

0008

**INFLUENCE OF RAPID EYE MOVEMENT SLEEP DEPRIVATION (REMSD) ON HIPPOCAMPAL MATURATION**

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**Introduction :** In young rats, maintenance of long-term potentiation (LTP) in hippocampus is susceptible to disruption by low-frequency stimulation (LFS). With development, however, LTP becomes more robust and stable, making it harder for LFS to reverse it. We tested for effects of early life REMSD on LTP stability in the CA1 region of hippocampus.

**Methods :** Young (postnatal day, PN16) and adult (PN44) rats begin REMSD for 4hrs/day during 3 consecutive days (total 12hrs). REMSD by gentle cage-shaking is started remotely by the experimenter at every visually and electrophysiologically identified REMS onset. Then, residing undisturbed for another 3-7days in home cages, the now PN21-25 and PN49-53 REMS-deprived animals, and their corresponding age-matched non-REMSD and normal-control are sacrificed. Brain slices from hippocampus are prepared for in vitro LTP reversal experiments. A stable baseline of 20min is recorded before high-frequency stimulation (HFS) is

applied to induce LTP. After 30min of stable LTP, LFS is applied to attempt reversal of LTP.

**Results :** HFS produced a criterion increase in the slope of the field Excitatory Postsynaptic Potential (fEPSP; % change from baseline) in all tested animals. LFS temporarily eliminated LTP in all groups. LTP recovered in all groups except in the young-REMSD animals, in whom it remained at baseline level. A two-way ANOVA for the difference between the slopes of the last 10min of baseline and the final 10min of recording post-LFS revealed a statistically significant age-by-treatment interaction ( $p < 0.05$ ).

**Conclusion :** Our results suggest that molecular processes involved in maintenance and stability of hippocampal LTP are susceptible to disruption by REMSD. REMSD early in life appears to prevent or slow down synaptic events that usually lead to the formation and stabilization of synapses during development. These data in hippocampus constitute additional support for the role of REMS in brain maturation and synaptic plasticity regulation.

**Support (optional):** NIH/NINDS NS31720

0009

**SELECTIVE 5HT2A AND 5HT6 RECEPTOR ANTAGONISTS PROMOTE SLEEP IN RATS**Moirarty S,<sup>1</sup> Hedley L,<sup>2</sup> Flores J,<sup>1</sup> Martin R,<sup>2</sup> Kilduff TS<sup>1</sup>

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**Introduction :** Serotonin has long been implicated in the control of sleep and wakefulness. Whereas 5HT1 receptors are known to be involved in REM sleep (REMS) and 5HT2 receptors are thought to be involved in NREMS, the role of other 5HT receptors in sleep/wake regulation has been little studied. In the present study, we investigated the effects of the selective 5HT2A receptor antagonist MDL-100,907 (MDL) and the novel 5HT6 antagonist RO4368554 (RO) on sleep in rats.

**Methods :** Eight Wistar rats were implanted with telemetry devices for recording EEG, EMG, core body temperature and locomotor activity. Using a repeated measures design, three concentrations of RO (1.0, 3.0, and 10.0 mg/kg) and MDL (0.1, 1.0 and 3.0 mg/kg) were tested in Wistar rats and compared to the effects of zolpidem (ZOL, 10.0 mg/kg) and vehicle. Drugs were administered IP in the middle of the active period (at the start of ZT hr 19).

**Results :** Both test compounds produced significant increases in sleep and decreases in waking compared to vehicle control. All three concentrations of MDL produced increases in NREMS, more consolidated sleep and increased delta power during NREMS. MDL 3.0 mg/kg had the longest lasting effect with significant hourly increases in sleep occurring for 5 h after dosing. MDL 0.3 and 1.0 mg/kg produced significant increases of sleep through hour 3 after dosing. The highest concentration of RO (10.0 mg/kg) produced significant increases in sleep and decreases in waking during hour 2(ZT20) following dosing. This increased sleep was more consolidated and associated with greater delta power during NREMS. Zolpidem also produced significant increases in NREMS but produced significant decreases in REMS. Neither RO nor MDL produced REMS suppression.

**Conclusion :** These results support a role for 5-HT6 receptors in sleep/wake regulation in rats. In addition, they confirm and extend previous reports linking 5HT2A receptor modulation with NREMS using a 5HT2A antagonist that is currently in Phase 2 clinical trials for insomnia. The role of the 5-HT6 and 5-HT2A receptors in humans remains to be determined. However, the rodent data generated herein suggest that their inhibition may play clinically important roles in sleep. This is especially important since selective antagonists for these receptors are under development for psychiatric indications where disruption in sleep is known to occur.

**Support (optional):**

0010

**DIALYSIS ADMINISTRATION OF THE ADENOSINE A1 RECEPTOR AGONIST N6-P-SULFOPHENYLADENOSINE INTO THE PREFRONTAL CORTEX OF C57BL/6J MOUSE DECREASES PREFRONTAL CORTEX ACETYLCHOLINE RELEASE AND DELAYS ANESTHESIA WAKE-UP TIME**

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**Introduction :** Acetylcholine (ACh) is essential for cognitive function and increases during tasks requiring attention. Cognitive performance decreases with prolonged wakefulness. During prolonged wakefulness, adenosine levels increase within basal forebrain regions that provide ACh to the cortex. The mechanisms by which cortical function declines with prolonged wakefulness are unknown. This study is testing the hypothesis that dialysis delivery of N6-p-sulfophenyladenosine (SPA) to the prefrontal cortex (PFC) decreases PFC ACh release and delays anesthesia wake-up time.

**Methods :** Adult male C57BL/6J mice (n=11) were anesthetized with isoflurane. A CMA/7 dialysis probe was aimed unilaterally for the PFC. The probe was perfused continuously (2  $\mu$ l/min) with Ringer's (control) followed by Ringer's containing SPA (0, 1, or 10 mM). ACh release was quantified by HPLC with electrochemical detection. Time required to resume righting reflex after anesthesia (wake-up time) also was recorded. Data were analyzed using one way analysis of variance (ANOVA) and Tukey-Kramer multiple comparisons test.

**Results :** SPA significantly altered PFC ACh release ( $F(3,128)=66.23$ ,  $p<0.0001$ ). ACh release was decreased ( $p<0.01$ ) by 1 mM SPA (-18.8%) and by 10 mM SPA (-34.3%). SPA also significantly delayed ( $p<0.02$ ) wake-up time by 96.9% (1 mM SPA) and by 362.5% (10 mM SPA). Histology confirmed dialysis probe placement in the PFC.

**Conclusion :** The finding that SPA decreased ACh parallels the decrease in PFC ACh release caused by morphine. CMA/7 dialysis probes deliver only ~5% of the perfused SPA concentration. Thus, unilateral delivery of  $\mu$ M amounts of SPA to the PFC also caused a significant delay in wake-up time. Ongoing studies will determine whether the effects of SPA are blocked by co-delivery of an adenosine A1 receptor antagonist, and vary as a function of SPA concentration.

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0011

**SLEEP HOMEOSTASIS, SLOW WAVES AND CORTICAL SYNCHRONIZATION: I. MODELING HOW SYNAPTIC STRENGTH DETERMINES SLOW WAVE SYNCHRONY**

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**Introduction :** According to a recent hypothesis, waking is associated with synaptic potentiation and sleep with synaptic downscaling. The hypothesis predicts that synaptic downscaling leads to a reduced synchronization of cortical neurons, which in turn underlies the well known decrease of slow wave activity (SWA, 0.5-4Hz) during sleep. We evaluated these predictions in a large-scale computer model of the thalamocortical system that reproduces detailed neurophysiological features of slow wave sleep.

**Methods :** The model consists of over 65,000 excitatory and inhibitory spiking neurons representing thalamic and reticular nuclei as well as pri-

mary and higher-order cortical areas, connected by over 5,000,000 AMPA, NMDA, GABAA and GABAB synapses. The model was first run in the sleep mode with 100% connection strength. Then the strength of excitatory corticocortical connections was scaled down progressively to 70% of the starting value, leading to a proportional reduction of postsynaptic currents. Membrane potentials were recorded for all units. The local field potential (LFP) was derived by averaging 1,600 intracellular membrane potentials from cortical layers 2-3.

**Results :** An analysis of single unit membrane potentials revealed that decreasing synaptic strength led to: i) a decreased synchronization of cell membrane potentials and spiking activity during the transition between the up- and down-states of the slow oscillation; ii) a decreased hyperpolarization level during the down-state; iii) an increased duration of the up-state; and iv) emergence of local clusters of synchronized multicellular activity. These changes were reflected in the LFP as: i) a decreased incidence of high-amplitude slow waves; ii) a decreased slope of up- and down-swings; iii) an increased slow wave duration; and iv) a higher proportion of waves with more than one peak. Finally, spectral analysis confirmed that these LFP changes were associated with a decrease in SWA.

**Conclusion :** The simulations show that decreasing synaptic strength reduces the synchronization of the intracellular slow oscillation, alters the incidence and shape of sleep slow waves, and reduces SWA in the LFP. Experimental results from rat LFP recordings and human high density EEG during sleep show similar changes in slow wave parameters with decreasing sleep pressure, suggesting that the underlying mechanism may be a net decrease in synaptic strength.

**Support (optional):** Supported by the NIH Director's Pioneer Award.

0012

**NOCICEPTION IS DECREASED BY CHOLINOMIMETICS AND THE ADENOSINE A1 RECEPTOR AGONIST N6-P-SULFOPHENYLADENOSINE, BUT NOT MORPHINE, MICROINJECTED INTO THE PONTINE RETICULAR FORMATION OF C57BL/6J MOUSE**

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**Introduction :** Sleep and pain are inversely related and the neurochemical basis underlying this relationship remains to be clarified. In C57BL/6J (B6) mouse, REM sleep is significantly enhanced by pontine reticular formation (PRF) microinjection of cholinomimetics and adenosinergic agonists. No previous studies have determined whether nociceptive behavior in B6 mouse is altered by PRF microinjection of cholinomimetics, N6-p-sulfophenyladenosine (SPA), or morphine. This study is testing the hypothesis that cholinergic and adenosinergic neurotransmission in the PRF of B6 mouse modulate nociception.

**Methods :** Adult male B6 mice were implanted with microinjection guide tubes aimed for the PRF. Hind paw withdrawal latency to a thermal stimulus was quantified in sec using an IITC Model 336T Hargreaves Paw Withdrawal system. The PRF was injected with 50 nL of saline (control) and 10 mM morphine sulfate, neostigmine bromide, carbachol, nicotine base, or SPA. Paw withdrawal measurements were taken 10, 20, 30, 60, 90, and 120 min post-injection. All data were evaluated by two-way ANOVA (drug and time) and Tukey-Kramer multiple comparisons test.

**Results :** Paw withdrawal latency (PWL) was significantly increased by microinjection of neostigmine ( $F(1,161)=58.4$ ;  $p<0.0001$ ), carbachol ( $F(1,161)=71.3$ ;  $p<0.0001$ ), nicotine ( $F(1,161)=60.6$ ;  $p<0.001$ ), and SPA ( $F(1,161)=38.1$ ;  $p<0.0001$ ). PWL was increased by neostigmine (44.2%), carbachol (44.6%), nicotine (40.2%), and SPA (31.0%). The time effect on PWL was significant following microinjections of neostigmine ( $F(5,161)=3.3$ ;  $p=0.0076$ ) and SPA ( $F(5,161)=2.6$ ;  $p=0.0025$ ). PRF injection of morphine did not alter PWL. Histology confirmed that all microin-

jections were in the PRF.

**Conclusion :** Cholinergic and adenosinergic neurotransmission in the PRF modulates nociceptive behavior and sleep in B6 mouse. Ongoing studies are determining whether the effects on nociceptive behavior are concentration dependent and blocked by muscarinic, nicotinic, and adenosine A1 receptor antagonists.

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### 0013

#### NEUROPEPTIDE S MODULATES HYPOCRETIN/OREXIN NEURONS VIA PRE- AND POST-SYNAPTIC MECHANISMS IN THE MOUSE HYPOTHALAMUS

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**Introduction :** Two wake-promoting neuropeptides, hypocretin (Hcrt) and neuropeptide S (NPS) were recently identified. Although NPS is predominantly expressed in a cluster of cells located between the locus coeruleus and Barrington's nucleus, NPS fibers contact a small population of Hcrt neurons in the lateral hypothalamus. Both peptides potently increase wakefulness and locomotion but they differentially modulate anxiety-like behavior. To test the hypothesis that some of the biological actions of NPS are mediated by direct interaction with the Hcrt system, we investigated the neurophysiological effects of NPS on defined Hcrt neurons.

**Methods :** Hypothalamic slices (230  $\mu$ m) were prepared from neonatal transgenic mice in which the enhanced green fluorescent protein was linked to the Hcrt promoter. Slices were perfused (2ml/min) with physiological solution containing (mM): NaCl 135, KCl 5, CaCl<sub>2</sub> 1, MgCl<sub>2</sub> 1, NaHCO<sub>3</sub> 25, glucose 10. Whole-cell recordings were made using an Axopatch 1D amplifier.

**Results :** In current-clamp mode, NPS (0.1 - 1  $\mu$ M) produced either no detectable (8/14 cells) or excitatory effects (6/14 cells), manifested as membrane depolarization, decreased input resistance and increased firing rate. In voltage-clamp mode, NPS (0.5  $\mu$ M) increased the frequency of spontaneous inhibitory postsynaptic currents by 357 $\pm$ 142 % (n=4) but did not significantly increase the amplitude of these events. In contrast, an increase in the frequency of spontaneous excitatory synaptic currents by NPS was only observed in 2 out of 6 cells recorded.

**Conclusion :** These results indicate that, although NPS directly activates only a subset of Hcrt neurons, NPS may also play an important role in modulating input to Hcrt neurons. Moreover, NPS may differentially modulate excitatory and inhibitory inputs to Hcrt neurons. This interaction may allow NPS to fine-tune Hcrt neuronal activity and allow for the biological functions of NPS and Hcrt to be coordinated in the modulation of complex neurobehaviors, such as arousal and anxiety.

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### 0014

#### EFFECTS OF CAFFEINE ON ESTROGEN-INDUCED INCREASES IN RUNNING WHEEL ACTIVITY

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**Introduction :** Estradiol (E2) modulates lipocalin-type prostaglandin D synthase (L-PGDS) expression in a region-dependent manner in mouse

brain. This links sex hormones with sleep-wake cycle regulation. The somnogenic effects of PGD2 are thought to be mediated via increases in adenosine and sleep-active VLPO neurons are activated by adenosine 2A (A2A) agonists. We hypothesize that increased arousal after E2 treatment is mediated by a reduction of L-PGDS and lowered A2A-ergic neurotransmission. We investigated whether chronic administration of the A2A receptor antagonist, caffeine, could also elicit increased running-wheel (RW) activity in oil-treated animals

**Methods :** 48 ovariectomized mice were implanted with an E2 or oil capsule, and were placed in RWs under a 12:12h light-dark cycle. RW activity per 3h was calculated and averaged for each week. Week 1: baseline, week 2: E2 or oil and week 3: caffeine. Caffeine was administered to half of the animals diluted in water at 2 concentrations: 0.4 and 1 mg/ml. Daily drinking amounts were recorded from all animals.

**Results :** Average RW activity was increased in E2-treated mice compared to oil. 1 mg/ml Caffeine: Both oil and E2-treated mice had significantly lowered RW activity during the caffeine week. Caffeine abolished the E2-induced increases in RW activity. Caffeine-treated animals consumed 48% less liquid than controls. 0.4 mg/ml Caffeine: RW activity was decreased in oil, but not E2-treated mice. Liquid consumption was similar in both caffeine and water groups.

**Conclusion :** These unexpected findings could be due to the fact that at a high dose, caffeine is able to completely block A2A receptors, thus preventing the changes in A2A-ergic neurotransmission due to the effects of E2 from being registered. On the other hand, the lower dose was still capable of suppressing RW activity in oil-treated mice, but not in E2-treated mice.

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### 0015

#### SLEEP AND REST REGULATION IN YOUNG AND OLD ESTROGEN-DEFICIENT FEMALE MICE

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**Introduction :** Sleep and rest are homeostatically regulated. Little is known about effects of hormonal changes related to gender and age on sleep regulation. The effects of circulating estrogen deficiency on sleep regulation and locomotor activity was investigated in aromatase cytochrome P450 deficient mice (ArKO) and wild type (WT) littermate controls.

**Methods :** EEG and EMG were recorded in 3-month old mice (24-h baseline, 6 h sleep deprivation (SD: hours 0-6 after light onset), 18 h recovery), and motor activity was recorded at 3, 9 and 12 months.

**Results :** Both genotypes had the same amount of sleep. However, in ArKO mice sleep was more fragmented, and the light-dark difference was reduced compared to WT controls. This redistribution of sleep and waking resulted in a smaller diurnal change in the time course of slow-wave activity (SWA; power between 0.75 - 4.0 Hz) in nonREM sleep, suggesting that mechanisms maintaining the homeostatic balance between sleep amount and sleep intensity are intact despite the estrogen deficiency. In support of this notion, slow wave energy (cumulative SWA), and the homeostatic compensatory increase in sleep and SWA in nonREM sleep after SD was similar between the genotypes. Motor activity was lower in ArKO mice compared to WT at all three ages, and decreased with age in both genotypes. Under increased sleep pressure after SD, behavioural rest in 3-month old WT mice increased above baseline during recovery, and was more consolidated. These effects of SD were less pronounced in ArKO mice of the same age, and absent when compared to older mice within each of the genotypes, reflecting genotype differences in their

baseline, as well as age differences.

**Conclusion :** The data indicate that despite the pronounced redistribution of sleep and motor activity in estrogen deficient mice, the basic homeostatic mechanisms of sleep and rest regulation in ArKO mice remained intact.

**Support (optional):** Swiss National Science Foundation and European Union grant QLK6-CT-2000-00499.

### 0016

#### THE EFFECTS OF A SINGLE DOSE OF DIETHYL-LACTAM ON RAT SLEEP

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**Introduction :** An investigational anticonvulsant, diethyl-lactam (3,3-diethyl-2-pyrrolidone), has been shown to modulate GABAA receptors. Other well-studied compounds that bind with GABAA receptors are barbiturates and benzodiazepines, which have soporific properties. Previous work at higher doses has shown to increase High Voltage (HS) sleep. The present study investigated the dose-response of lower doses on diurnal sleep in rats.

**Methods :** Sixteen Sprague-Dawley rats weighing approximately 450 grams received either a 200mg/kg or 300mg/kg dose of diethyl-lactam dissolved in saline or a vehicle injection of saline. Each animal served as its own control. Sleep was recorded and analyzed for the 12-hour light cycle immediately following drug or saline administration.

**Results :** Four 2x(2x2) repeated measures ANOVAs were conducted for each sleep parameter (Wake (W), HS, Paradoxical (PS) and Low Voltage (LS)) with post hoc as needed. Results showed the 300mg/kg group had more W ( $F=8.552$ ,  $p=.011$ ) and more HS scored in the 200mg/kg group ( $F=11.522$ ,  $p=.004$ ) across both conditions (control/treatment). More PS was scored in the control versus treatment condition and more PS in the second 6-hours of recording ( $F=12.157$ ,  $p=.004$  and  $F=41.180$ ,  $p<.001$ ). There was a greater change in W from the first 6-hours compared to the second 6-hours for treatment versus control condition, however, more W is noted in the 300mg/kg group in the second compared to the first 6-hours when combining both conditions across time. More HS was scored for the second 6-hours in the 200mg/kg compared to 300mg/kg group. Less PS was scored during the first 6-hours of treatment groups. Results also found more LS scored during the first 6-hours ( $F=5.550$ ,  $p=.034$ ) versus the second 6-hours.

**Conclusion :** It seems that 300mg/kg may have disrupted sleep rather than inducing it. PS sleep appears to be suppressed, especially during first six hours. The lower dose was sufficient to increase HS into the second 6-hours.

**Support (optional):**

### 0017

#### GABA MEDIATES SUANZAORENTANG, A TRADITIONAL CHINESE COMPOUND MEDICATION, -INDUCED SLEEP ALTERATION

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**Introduction :** The sedative-hypnotic medications, including benzodiazepines and non-benzodiazepines, are the most common treatments for

insomnia. However, concerns regarding patterns of inappropriate use (abuse), dependence, and adverse effects such as impairment of memory or movement, and next-day "hangover" have led to caution in prescribing benzodiazepines. On the other hand, suanzaorentang has been efficiently used in clinic for insomnia relief without severe side effects since the ancient China. This study is designed to elucidate the effects of suanzaorentang on sleep and its relative mechanism.

**Methods :** Male Sprague-Dawley rats were surgically implanted with EEG recording electrodes and ICV cannula. Rats were allowed a minimum of one-week recovery period, and kept on a 12:12h Light:Dark cycle at  $23 \pm 1$  °C. Locomotion was recorded by infrared motion detector. After recovery, 24-h baseline recording and pyrogen-free saline (PFS)-treated recording were obtained as control. Sleep EEG was recorded after oral administration of suanzaorentang, prior to the dark onset, in the dose of 1 g/Kg. ICV administration of GABA-A or GABA-B antagonists, bicuculline (2.5 microgram) or 2-hydroxysaclofen (2.5 microgram), combined with oral administration of suanzaorentang was then given, and sleep EEG was recorded.

**Results :** Slow wave sleep (SWS) increased from  $20.8 \pm 5.3$  % obtained after control to  $38.9 \pm 3.7$  % after oral administration of 1g/Kg suanzaorentang during the first four-hour of the dark period. Rapid eye movement sleep (REMS) was not significantly altered. GABA-A antagonist bicuculline significantly blocked suanzaorentang-induced enhancement in SWS during the dark period, but GABA-B antagonist 2-hydroxysaclofen has no effect. The time spent in SWS during the first four-hour of the dark period was  $27.3 \pm 3.5$  % after bicuculline, and  $35.8 \pm 4.0$  % after 2-hydroxysaclofen.

**Conclusion :** These results suggest that this tradition Chinese compound medication, suanzaorentang increases sleep activity and its effects may be mediated through the GABA-A receptor.

**Support (optional):**

### 0018

#### IS THERE A PONTINE SITE INVOLVED IN THE CONTROL OF QUIET (NREM) SLEEP?

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**Introduction :** The ventro-lateral preoptic area has been proposed to participate in the generation of quiet (NREM) sleep (QS). In the present report, we present data demonstrating that the caudolateral peribrachial area (C-PBL) of the pons plays an important role in the transition from QS to active (REM) sleep (AS).

**Methods :** Chronic cats were prepared for monitoring the following sleep and waking states which were present for 1-2 hours preceding euthanasia: QS (n = 4); quiet wakefulness (QW, n = 4); active wakefulness (n = 4); AS induced by carbachol (n = 6). Additional data were obtained from animals that spent this period in QS and QW (n = 2), or AS-rebound after a deprivation paradigm (n = 1). After euthanization, immunohistochemical techniques were utilized to detect Fos and GABA. Subsequently, the number and distribution of immunostained neurons were determined.

**Results :** Small (14  $\mu$ m) oval-shaped Fos+ neurons were observed in the C-PBL of QS animals. The number of Fos+ neurons was greater ( $P < 0.0001$ ) during QS than during the other behavioral states. In addition, there was a positive correlation between the percentage of time the animals spent in QS and the number of Fos+ neurons in the C-PBL. The majority of the QS-Fos+ neurons were GABAergic.

**Conclusion :** These data indicate that GABAergic C-PBL neurons play a role in the regulation of QS. This conclusion is supported by anatomical

studies that demonstrate that the C-PBL is connected with areas involved in the control of QS. The C-PBL is also a source of PGO-waves and is part of the rhombencephalic component of the autonomic network, where-in there is a shift from forebrain to rhombencephalic dominance in the transition from QS to AS. Consequently, we hypothesize that C-PBL neurons play an important role in promoting the transition from quiet to active sleep.

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## 0019

### SLEEP AND FATIGUE DURING CHRONIC VIRAL INFECTION

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**Introduction :** Infections with human gammaherpesviruses (GHVs), such as Epstein Barr virus (EBV), are associated with chronic fatigue. During EBV infection, cytokines that induce fatigue and alter sleep are chronically elevated. Murine GHV-68 (MuGHV) has been used as an animal model of human GHV due to similarities in immune responses, viral genetics, ability to cause an active infection, and subsequent development of life-long latency. We hypothesized that infection with MuGHV will induce fatigue and alter sleep of mice.

**Methods :** Male C57BL/6J mice (25 g, n = 6) were surgically implanted under isoflurane anesthesia with transmitters to record core body temperature and EEG. Mice were held under a 12:12 h L:D cycle at a temperature of  $29 \pm 1$  °C. They were inoculated intranasally at dark onset with vehicle to obtain control recordings. Mice were then inoculated with 400 PFU of MuGHV and recorded for 30 days post-infection. Fatigue was operationally defined as a decrease in wheel running and general cage activity.

**Results :** Wheel running decreased during MuGHV infection. This reduction in wheel running was most evident during the second half of the dark period. Infection reduced core body temperature during the dark period, which did not always coincide with decreased activity. Transitions between arousal states increased and theta frequencies in the EEG during wakefulness were reduced.

**Conclusion :** Results indicate that mice become fatigued during chronic viral infection. Hypothermia may be only partially attributed to decreases in activity, suggesting effects of MuGHV on thermoregulatory mechanisms. Though sleep of mice was not greatly altered, sleep quality suffered. Thus, this animal model mimics some facets of human chronic fatigue, in which energy levels are lower during the subjective afternoon and sleep quality is poor.

**Support (optional):** NIH MH64843 and the University of Michigan Department of Anesthesiology.

## 0020

### EYE MOVEMENTS AND EXTRAOCULAR MOTONEURONS ACTIVITIES DURING THE SLEEP-WAKE CYCLE OF THE CAT

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**Introduction :** Fifty years ago rapid eye movements (REM) were described during sleep giving rise to a new sleep state. Although REM have constituted the main element for the recognition of this state, there are few precise studies about REM and the behaviour of extraocular motoneurons during sleep remains unknown.

**Methods :** Eight female adult cats were chronically implanted with bipolar electrodes in both VIth nerves for electrical stimulation and teflon-coated stainless-steel coils for chronic recording of eye movements by the scleral search coil technique. Abducens motoneurons (ABDMn) were antidromically identified and their extracellular activity along with binocular eye movements and ponto-geniculo-occipital waves (PGO) were recorded continuously during spontaneous sleep-wake cycle.

**Results :** During REM sleep the eyes rotated downward and nasally and tended to maintain this deviation. However, in coincidence with each PGO the eyes performed a fast horizontal rotation sometimes accompanied by another upward eye movement of smaller amplitude. No rapid eye movements were observed in absence of PGO. During REM sleep the firing rate of ABDMn correlated with eye velocity but not with eye position. In coincidence with PGO, ABDMn showed two unusual patterns of activity. Whereas in one abducens nucleus motoneurons discharged one or two very close action potentials followed by a silence, the contralateral ABDMn showed a silence followed by a burst-tonic firing frequency. These activities of ABDMn fully explain the complex horizontal eye movements that occur during REM sleep.

**Conclusion :** Tonic and phasic motor signals seem to be segregated in the oculomotor system during REM sleep. Tonic signals are not coded by ABDMn, whereas velocity signals responsible for eye movements are inexorably paired to PGO. The inhibition-activation profile of extraocular motoneurons remembers the behaviour of other non-oculomotor motoneurons; so, eye movements are not a consequence of the exploration of the oneiric images.

**Support (optional):** Supported by MCYT-BFI2002-01378-BFU2005-01579

## 0021

### RECURRENT APNEA-INDUCED POTENTIATION OF HIPPOCAMPAL CA3/CA1 SYNAPSES IS ASSOCIATED WITH APOPTOTIC DAMAGE TO CA1 NEURONS

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**Introduction :** Obstructive sleep apnea (OSA) results in the damage of hippocampal CA1 pyramidal cells which eventuates in neurocognitive deficits (Macey et al., Am. J. Respir. Crit. Care Med. 166:1382-7, 2002). To test the hypothesis that apnea-induced potentiation of the hippocampal glutamatergic CA3/CA1 pathway precedes excitotoxic processes and irreversible damage to CA1 neurons, we examined synaptic and structural changes in CA1 pyramidal neurons following recurrent apnea in the *in vivo* guinea pig preparation.

**Methods :** Adult guinea pigs were anesthetized with  $\alpha$ -chloralose (60 mg/kg, i.v.) and immobilized with Flaxedil (1 mg/kg, i.v.). Apnea was induced by ventilatory arrest to produce a decrease in SpO<sub>2</sub> to the 75% level of oxygen saturation; recovery to >95% SpO<sub>2</sub> occurred prior to the initiation of each succeeding apneic episode. This process was repeated for a period of three to six hours. The effect of stimulation of CA3, which evoked a field EPSP (fEPSP) in CA1, was examined prior to and following recurrent apnea. Immunoreactivity for single strand DNA was scored in experimental (recurrent apnea) and control (normoxic) animals.

**Results :** Recurrent apnea potentiated the CA1 fEPSP response to CA3 stimulation. Typically, the slope of the EPSP initially increased 25-30% after the onset of apneic episodes. Potentiation of the CA1 fEPSP declined after three to six hours of recurrent apnea. In contrast to normoxic guinea pigs, CA1 neurons of animals that were subjected to extended

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periods of recurrent apnea exhibited positive immunoreactivity for fragmented DNA strands.

**Conclusion :** Our results indicate that recurrent apnea-induced potentiation of the CA1 synaptic response is associated with apoptotic damage to CA1 neurons. We hypothesize that these synaptic and structural changes contribute to the neurocognitive deficits that are present in OSA patients.

**Support (optional):** This research was supported by USPHS grants NS69372, HL60296, NS23426, NS09999 and AG04307.

### 0022

#### MICROINJECTION OF THE GABA-A RECEPTOR ANTAGONIST BICUCULLINE INTO THE PONTINE RETICULAR FORMATION OF C57BL/6J MOUSE DECREASES WAKEFULNESS AND INCREASES SLEEP

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**Introduction :** The pontine reticular formation (PRF) plays a key role in REM sleep generation. In cat and rat, PRF microinjection of bicuculline increases REM sleep. This study is testing the hypothesis that GABAergic transmission in the PRF of C57BL/6J (B6) mouse modulates sleep and wakefulness.

**Methods :** Adult male B6 mice (n=6) were implanted with recording electrodes to objectively quantify arousal states and with a microinjection guide tube aimed for the pontine reticular nucleus, oral part (PnO). The PnO is the rostral portion of the PRF. After one week of recovery from surgery, mice were conditioned to the recording chamber. Microinjections (50 nl) of bicuculline methiodide (0.01, 0.1, 1 mM; 0.25, 2.5, 25 ng) and saline (vehicle control) were made during wakefulness, and EEG and EMG were recorded continuously for 4 h. Sleep and wakefulness were scored manually in 10 s bins. Statistical significance was evaluated by ANOVA and Dunnett's test.

**Results :** Histological examination confirmed that all microinjection sites were localized to the PnO. Bicuculline significantly decreased the amount of wakefulness below control levels during the first 2 h post-injection ( $F(3, 38)=3.7$ ;  $p=0.02$ ). NREM sleep time was increased significantly during the first 2 h post-injection ( $F(3, 38)=3.1$ ;  $p=0.04$ ) and remained significantly increased during the third and fourth h ( $F(3, 38)=3.5$ ;  $p=0.03$ ). Increases in REM sleep time ranged from 43-146% during the first two h post-injection and from 16-97% during the third and fourth h post-injection. The decreases in wakefulness and increases in NREM sleep were not significantly different between the bicuculline concentrations tested to date.

**Conclusion :** Microinjection of the GABAA antagonist bicuculline into the PnO of B6 mice enhanced sleep and decreased wakefulness. These findings support the interpretation that endogenous GABA in B6 mouse PnO promotes wakefulness.

**Support (optional):** National Institutes of Health grants MH45361, HL65272, HL57120, HL40881, and the Department of Anesthesiology

### 0023

#### ACETYLCHOLINE RELEASE IN THE PRE-BÖTZINGER COMPLEX OF WISTAR RAT IS INCREASED BY MICRODIALYSIS DELIVERY OF MORPHINE SULFATE

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**Introduction :** The medullary pre-Bötzinger complex (pre-Bötzc) contains respiratory neurons that are crucial for maintaining and generating the respiratory rhythm. The pre-Bötzc receives cholinergic projections from the rostral ventrolateral medulla (RVLM) and contains both muscarinic and nicotinic cholinergic receptors. Opioids depress breathing and

decrease acetylcholine (ACh) release in brain regions known to modulate respiratory and arousal state control. No previous studies have reported the effects of opioids on pre-Bötzc ACh. This study is testing the hypothesis that morphine alters ACh release in the pre-Bötzc.

**Methods :** Adult male Wistar rats (n=13) were anesthetized with isoflurane and microdialysis probes were aimed for the pre-Bötzc. Dialysis samples were collected and quantified as pmol ACh/12.5 min using HPLC-EC. ACh release was measured while dialyzing with Ringer's (control) followed by Ringer's containing 10  $\mu$ M morphine or 10  $\mu$ M morphine and 1  $\mu$ M naloxone. Additional experiments evaluated blocking of the opioid effect by systemic naloxone (1 mg/kg).

**Results :** Delivery of morphine to pre-Bötzc caused a significant ( $t=8.63$ ;  $df=29$ ;  $p<0.01$ ) increase (54%) in ACh release compared to control. Co-administration of naloxone with morphine to the pre-Bötzc failed to block the morphine-induced increase in ACh release ( $t=4.98$ ;  $df=28$ ;  $p<0.01$ ). Systemic naloxone blocked the increase in pre-Bötzc ACh caused by morphine.

**Conclusion :** The morphine-induced increase in pre-Bötzc ACh release is consistent with microdialysis data showing that morphine increased ACh in the RVLM (Biol Pharm Bull 26:1548, 2003). The finding that systemic, but not local, naloxone blocked the opioid-induced increase in ACh supports the conclusion that pre-Bötzc ACh is modulated by brain regions outside the pre-Bötzc. Ongoing studies aim to specify the presynaptic mechanisms regulating opioid-induced changes in pre-Bötzc ACh.

**Support (optional):** National Institutes of Health grants HL57120, HL40881, HL65272, MH45361, and the Department of Anesthesiology.

### 0024

#### STATE-SPECIFIC ASYMMETRIES IN EEG SLOW WAVE ACTIVITY INDUCED BY LOCAL APPLICATION OF (S)-AMPA

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**Introduction :** AMPA-type glutamate receptors may be involved in sleep regulation. The Krueger-Obal theory of use-dependent local sleep posits that sleep begins as a localized targeted event driven within neuronal assemblies by sleep regulatory substances (SRSs). In this study, we examined whether an AMPA receptor agonist, (S)-AMPA, is capable of inducing local state dependent sleep responses, as determined by electroencephalogram slow wave activity (EEG SWA) within the cerebral cortex.

**Methods :** Six male Sprague-Dawley rats weighing 300-350 g were implanted bilaterally with guide cannula in the somatosensory cortex. Before any injections were performed, EEG and EMG baseline data were recorded for a 23 hour period started from the light onset, 0900h. On an experimental day, 16ng (s)-AMPA dissolved in 2  $\mu$ l pyrogen-free saline (PFS) were injected unilaterally at light onset. The injected side was chosen randomly. On a control day, 2  $\mu$ l of vehicle (PFS) were injected into the same side at the same time. The sequence of (S)-AMPA and PFS injections were randomized and there was one day rest between the two consecutive injections. Data were collected for 23 hours after each injection.

**Results :** (S)-AMPA significantly enhanced EEG SWA on the injected side during the first hour after injection. The effects were confined to the 0.5-4.5 Hz frequency band and were state-dependent occurring only during non-rapid eye movement sleep (NREMS).

**Conclusion :** Our findings suggested that AMPA receptors play a role in cortical generated slow-wave oscillations and are consistent with the notion that sleep can be a localized targeted event.

**Support (optional):** Supported by NIH NS 31453

0025

**GHRELIN INTRAHYPOTHALAMIC ADMINISTRATION SUPPRESSES SLEEP IN RATS***Szentirmai E,<sup>1,2</sup> Krueger JM<sup>1</sup>*

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**Introduction :** Ghrelin is an endogenous ligand of the growth hormone secretagogue receptor. Ghrelin plays a role in a food intake regulatory circuit which also involves orexinergic and NPYergic mechanisms. Orexinergic mechanisms promote wakefulness and previous experiments in our laboratories revealed that intracerebroventricular injection of ghrelin suppresses sleep in rats. In order to find the possible wake-promoting target sites of ghrelin, we studied the effects of intrahypothalamic microinjections of ghrelin on sleep in rats.

**Methods :** Groups of rats received bilateral microinjections of isotonic NaCl (all rats) and 0.04 µg, 0.2 µg or 1 µg ghrelin (volume 100 nl) into the lateral hypothalamus or medial preoptic area (MPA) (n = 8-10 per dose). Injections were carried out 10-15 minutes before light onset and sleep-wake activity was recorded for 23 hours.

**Results :** The lowest dose of ghrelin had no effect at any injection sites. Lateral hypothalamic microinjection of 0.2 µg ghrelin induced 60 % decrease in non rapid-eye-movement sleep (NREMS), 1 µg ghrelin suppressed NREMS by 65 % in the first hour after the injections. Rapid-eye-movement sleep (REMS) almost completely disappeared in the first hour after both doses of ghrelin injections. The effects of MPA injections were similar although less pronounced (35 % decrease in NREMS and 87 % in REMS after 0.2 µg ghrelin and 53 % decrease in NREMS and 94 % decrease in REMS following 1 µg ghrelin injection). NREMS suppression was accompanied by decreases in NREMS delta power with a subsequent increase in the following hours.

**Conclusion :** Results are in agreement with the hypothesis that ghrelin has a role in the integration of feeding, metabolism and sleep regulation.

**Support (optional):** NIH (USA) grant No. NS27250

0026

**NEUROPEPTIDE Y PROMOTES WAKEFULNESS AFTER CENTRAL ADMINISTRATION IN RATS***Krueger JM,<sup>1</sup> Szentirmai E<sup>1,2</sup>*

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**Introduction :** Neuropeptide Y (NPY) is a well-characterized neuromodulator in the central nervous system. It is mainly implicated in the regulation of feeding. Neurons containing NPY, orexins and ghrelin form a hypothalamic food intake regulatory circuit. Orexinergic and ghrelinergic mechanisms are also involved in sleep-wake regulation. In the present study, we investigated the sleep responses to central administration of NPY in rats.

**Methods :** Rats received intracerebroventricular (icv) injections of isotonic NaCl (all rats), 0.4 µg (n = 8), 2 µg (n = 9) or 10 µg (n = 8) NPY in a volume of 4 µl at light onset. Another group of rats (n = 8) received bilateral microinjections of isotonic NaCl or 2 µg NPY (200 nl) into the lateral hypothalamus. Sleep-wake activity was recorded for 23 hours. Food intake after the control and treatment injections was also measured on separate days.

**Results :** Icv injection of 0.4 µg NPY had no effect on sleep. Two µg NPY induced a 52 % decrease in non rapid-eye-movement sleep (NREMS) and about a 98 % suppression in rapid-eye-movement sleep (REMS) in the first h after the injection. The highest dose, 10 µg NPY, induced 55 % and 95 % suppressions in NREMS and REMS, respectively. Lateral hypothalamic injections had similar effect on sleep: 62 % decrease in NREMS and

82 % decrease in REMS in the first h after the injection. In addition, NPY stimulated food intake in the first h after both routes of administration.

**Conclusion :** Data are consistent with the hypothesis that NPY has a role in the integration of feeding, metabolism and sleep regulation.

**Support (optional):** NIH (USA) Grant No. NS27250

0027

**GROWTH HORMONE RELEASING HORMONE RECEPTOR-IMMUNOREACTIVE CELLS INCREASE IN THE BARREL FIELD IN RESPONSE TO WHISKER DEFLECTION IN RATS***De A, Fix C, Hall S, Churchill L, Krueger JM*

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**Introduction :** The homeostatic regulation of sleep involves several sleep regulatory substances including growth hormone releasing hormone (GHRH). Previous studies showed that microinjection of GHRH onto the surface of the cortex increases EEG delta power during non-REM sleep and that cortical GHRH receptor mRNA levels increase after 6 h of sleep deprivation during the dark. These studies suggest that the GHRH receptor may be sensitive to stimulation of whiskers that are mainly used during the dark. Whisker deflection increases fos expression within specific barrels of the primary somatosensory cortex providing an anatomical localization for a specific neuronal activation without invasion into the brain. We hypothesized that activation of neuronal circuits enhances release of sleep regulatory substances locally and such use-dependent molecules provide a mechanism for state-specific EEG slow wave power and for micro circuitry connectivity processes such as synaptic scaling.

**Methods :** Six male Sprague-Dawley rats (200-300g) were stimulated unilaterally by brushing with fingers the long whiskers along the caudal edge of the whisker field for 2 h in the afternoon. After 2 h of stimulation, the rats were perfused with 4% paraformaldehyde, the brains post-fixed for 2 h, sunk in 20% sucrose and immunoreactivity (IR) for GHRH receptor (GHRHR), fos and nerve growth factor (NGF) were analyzed.

**Results :** In layer IV (the primary sensory input to the barrel field) as well as in layers II-III, the number of GHRHR-IR cells increased in the barrel columns that showed fos activation in an adjacent section. No changes in IR for NGF were observed in adjacent sections.

**Conclusion :** These data suggest that afferent activation of a cortical column enhances the number of GHRH receptors in these cortical cells. These data support our hypothesis that the GHRH receptor is functionally sensitive to neuronal activation and are consistent with the Krueger-Obal theory of use-dependent local sleep.

**Support (optional):** NIH (USA) NS 27250

0028

**INCREASED REGIONAL EEG SYNCHRONIZATION AFTER STIMULATION OF GABAA RECEPTORS WITH 3 MG/KG MUSCIMOL IN MICE***Vyazovskiy VV, Vesely M, Tobler I*

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**Introduction :** In mice THIP, a GABAA agonist, induced an abnormal EEG pattern characterized by high-amplitude sporadic waves. These waves may reflect hypersynchronization of neocortical neuronal circuits. We investigated the occurrence of the waves and their phase relationship between two cortical derivations after a challenge with a high dose of muscimol, a GABA analogue with potent agonistic effects.

**Methods :** A parietal and frontal cortical EEG (cerebellum as reference), EMG, infra-red (IR) - and running-wheel (RW)-activity were recorded in male C57BL6 mice (n=8) after 3 mg/kg muscimol i.p. 3 h after light onset.

**Results :** Muscimol suppressed motor activity and induced cataplexy for approximately 1.5 h followed by hyperactivity, with vigorous running. During the "hyperactivity phase", prominent theta-activity, typical for running behavior, was evident in the parietal derivation, while the frontal derivation was dominated by slow waves. Two mice, which showed a seizure event after the hyperactivity phase, had the longest cataplexy period and the lowest intensity of RW-activity during "hyperactivity". During cataplexy, EEG power was enhanced in low frequencies, while higher frequencies were dramatically suppressed compared to NREM sleep before injection. Consistently, the EEG of both derivations was characterized by high amplitude waves on a low amplitude background. While during pre-injection NREM sleep there was no consistent phase-relationship between slow waves of the frontal and parietal derivation, during cataplexy the waves in the frontal EEG were time locked to the occurrence of waves in the parietal derivation.

**Conclusion :** Muscimol elicited a stereotypic succession of a highly depressed and a highly activated behavioral state, associated with profound alterations of the EEG. The close phase relationship in the occurrence of high-amplitude waves between the frontal and parietal derivation suggests that overstimulation of GABAA receptors causes a shift in cortical activity towards a highly-synchronous mode that can lead to seizures. The data indicate that GABA-ergic mechanisms play an important role in spatial synchronization of neuronal activity, underlying the generation of slow EEG waves.

**Support (optional):** Swiss National Science Foundation

### 0029

#### MODELING THE EFFECTS OF HOMEOSTATIC DRIVE, CIRCADIAN TIME, LOCOMOTOR ACTIVITY, AND HPA AXIS ACTIVATION ON HYPOCRETIN-1 (OREXIN A) CONCENTRATIONS IN THE SQUIRREL MONKEY

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**Introduction :** Studies have shown that hypocretin activity correlates with wakefulness per se and with other concomitants of wakefulness such as locomotion, stress or feeding. Importantly, however, much of this work has been conducted in species where sleep is polyphasic and in many cases nocturnal. Such mammals exhibit wakefulness that can be consolidated in response to stimuli such as stress, food restriction, and locomotion. Humans, however, have consolidated wakefulness without any needed external stimulation. We hypothesized that the regulation of hypocretin may differ between species to accommodate these ecological differences. As hypocretins are only consistently found in cerebrospinal fluid (CSF) and brain tissue, its study in humans is difficult. We have therefore developed a squirrel monkey model, a primate with consolidated sleep/wake cycles like humans, to examine the normal physiologic regulation of hypocretins. The goal of the current project is to examine the factors that contribute to hypocretin regulation in a sleep/wake consolidating mammal.

**Methods :** Male and female squirrel monkeys (*Saimiri sciureus sciureus*) were examined using a variety of protocols. Monkeys (n=10) were examined over the course of a diurnal cycle, following a single (n=10) or multiple (n=6) sleep deprivations, and after manipulation of locomotion (n=10). CSF and blood samples were collected, as was collar-based actigraphy. CSF samples were assayed for hypocretin-1 and cortisol and blood samples were assayed for leptin and total ghrelin.

**Results :** Multivariate modeling and univariate correlations indicate that both time of day and homeostatic pressure significantly influence hypocretin-1 concentrations while cortisol, leptin, ghrelin, and locomotion had no effect on hypocretin-1.

**Conclusion :** Our results suggest that hypocretin-1 increases reactively to increased sleep pressure, but is also modulated by the circadian clock. There is only limited, if any, effects of cortisol, locomotor feedback, ghrelin or leptin (under normally fed conditions) on CSF hypocretin-1 in this species.

**Support (optional):** NARSAD (JMZ), MH47573 (DML), HHMI (EM), NS232724 (EM)

### 0030

#### THE ROLE OF CHANGES IN LOCAL CBF IN THE EFFECTS OF SLEEP DEPRIVATION ON THE BOLD RESPONSE

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**Introduction :** A growing number of studies demonstrate that sleep deprivation causes changes in the blood oxygenation level-dependent (BOLD) response associated with several behavioural tasks. Such changes are interpreted to reflect fatigue related differences in the underlying neural response. However, a valid interpretation of such findings relies on the assumption that the BOLD response is similar in the sleep deprived and rested brain. There is reason to question this assumption. The BOLD signal is inversely related to local deoxyhemoglobin content because increases in local cerebral blood flow (ICBF) and blood volume occur without an equivalent magnitude of increase in local oxygen consumption. The increase in ICBF is mediated by several neurochemical signals including neuropeptide Y (NPY), neural nitric oxide (NO), and eicosanoids (product of arachidonic acid) secreted from depolarized astrocytes. The concentration in the cortex of at least some of these substrates (e.g., NO, NPY) are also known to change after sleep deprivation, thus possibly affecting the coupling of the BOLD response to the underlying neural activity. Here we tested whether sleep deprivation affects the ICBF concomitant with BOLD.

**Methods :** Subjects were scanned twice: after a 36hr sleep deprivation and fully rested. In a 4T Varian scanner, subjects were presented with a drifting grated annulus in a block design of 30s on 30s off. This stimulus induces retinotopic positive BOLD in early visual cortex and negative BOLD in adjacent, unstimulated cortex. Two types of functional imaging data were acquired: BOLD (TR=1s, TE=28ms); and a measure of ICBF - FAIR (flow-sensitive alternating inversion recovery; TR=3s, TE=11ms).

**Results :** Preliminary findings show that sleep deprivation increased positive and decreased negative BOLD in primary visual areas, with the opposite effects in FAIR (i.e., increased negative decreased positive blood flow) in equivalent regions.

**Conclusion :** These preliminary findings suggest that sleep deprivation may affect the coupling of neural activity to the BOLD response differently for inhibitory and excitatory processes, due to changes in ICBF.

**Support (optional):** American Psychology Association Postdoctoral Fellowship; National Science Foundation Graduate Fellowship; Berkeley Brain Imaging Center.

### 0031

#### VARIATION IN SLEEP, EEG POWER AND ACTIVITY IN AN OUTBRED RAT STRAIN

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**Introduction :** Humans show a wide range of individual differences in habitual sleeping time. Compared to long sleepers (LS), short sleepers (SS) spend less time in light sleep, have shortened sleep latency after an awakening, and show higher EEG theta power during wakefulness. These



characteristics have led to suggestions that SS may live under high homeostatically regulated sleep pressure. We examined outbred Wistar rats for the presence of SS, LS and intermediate sleepers (IS) and compared their sleep across groups and across days.

**Methods :** EEG and activity were recorded via telemetry in Wistar rats (n=29) over 2 days in well-habituated conditions. Rats were sorted based on total sleep time on day 1 (SS, 580±6.2, n=10; IS, 627±5.5, n=9 and LS, 694±10.6, n=10). We then examined consistency of sleep amounts, EEG power and activity levels across days and between groups.

**Results :** Significant cross day correlations in all selected sleep measures, in activity, and in EEG power in selected frequency bins (1, 7, 14 Hz) suggested consistency across days within individual rats. 24 h amounts of total sleep and NREM were significantly less in SS rats (SS < IS < LS) whereas REM did not differ between groups. SS rats were also more active (SS > LS). NREM EEG power at 0.5-2.0 Hz did not differ among groups, but was less in SS rats in the 2.5-6.0 Hz band, particularly at the 4.0 Hz peak (SS < LS). EEG theta (5.5-9.0 Hz) was greater in SS rats during wakefulness (SS > LS) and REM (SS > IS = LS).

**Conclusion :** Individual differences in sleep, EEG parameters and activity were stable across days indicating the existence of SS and LS in Wistar rats. Increased theta in wakefulness suggests that SS rats have increased sleep pressure and waking activity compared to LS, findings that parallel comparisons of SS and LS in human studies. Reduced NREM EEG power in the upper delta range (around 4.0 Hz) in SS rats may also reflect a difference in sleep pressure compared to LS rats.

**Support (optional):** NIH grant MH64827

### 0032

#### THE NUMBER OF TUMOR NECROSIS FACTOR-IMMUNOREACTIVE CELLS INCREASES IN LAYER IV OF THE BARREL FIELD IN RESPONSE TO WHISKER DEFLECTION IN RATS

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**Introduction :** Relatively little is known about the homeostatic regulation of sleep. Several sleep regulatory substances, such as interleukin1, (IL1,) and tumor necrosis factor · (TNF·), are likely involved in homeostatic processes. We hypothesized that neural use enhances release of sleep regulatory substances locally within the activated neuronal network and such use-dependant molecules provide a mechanism by which the brain keeps track of sleep-wake history and thus represent a key component of a homeostatic sleep mechanism.

**Methods :** Six male Sprague-Dawley rats (200-300g) were stimulated unilaterally by brushing with fingers the long whiskers along the caudal edge of the whisker field for 2 h in the afternoon. After 2 h of stimulation, the rats were perfused with 4% paraformaldehyde, the brains post-fixed for 2 h, sunk in 20% sucrose and immunoreactivity (IR) for TNF·, fos, and IL1, was analyzed using antibodies from R&D Systems. Quantitative analyses of 0.4 by 0.2 mm rectangular areas, one from each layer, were completed using digital pictures of coronal sections of the somatosensory cortex. The number of darkly labeled cells was counted manually by an investigator blind to the experimental conditions.

**Results :** In layer IV (the primary sensory input to the barrel field) as well as in layers II-III, the number of TNF·-IR cells increased in the barrel columns that showed fos activation in an adjacent section. No changes in IR for IL1, were observed in adjacent sections. Double-labeling with fluorescent probes demonstrated that fos-immunoreactive nuclei were present in TNF·-IR cells.

**Conclusion :** Collectively, these data suggest that afferent activation of a cortical column enhances TNF· production. These data support our hypothesis that sleep is activity-dependent and initiated within local net-

works.

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

### 0033

#### SPECTRAL EEG POWER AFTER UNCONTROLLABLE SHOCK (US) AND FEARFUL CONTEXT (FC): VARIABILITY AMONGST MOUSE STRAINS

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**Introduction :** Training with US and exposure to FC decrease REM in mice. Decreases in REM after either US or FC are greater and more persistent in reactive BALB/c (C) mice compared to less reactive C57BL/6 (B6) and to CB6F1 (CB6, F1 hybrid, C x B6) mice. The effects on NREM amounts are more variable across strain, but potential changes in EEG have not been examined. This may be important as social and restraint stress increase EEG slow wave activity (SWA, 0.5-5 Hz) during NREM in rats. We examined EEG power in mice trained in contextual fear.

**Methods :** EEG and activity were recorded via telemetry in B6 (n=15), C (n=19) and CB6 (n=17) mice. After baseline sleep recording, mice received 15 trials of US on 4 consecutive days followed by an FC exposure on a separate day. Control mice received identical handling but never received US. Relative density of EEG power was calculated in 0.5 Hz bins from 0.5 to 20.0 Hz for light period wakefulness, NREM and REM after US or FC.

**Results :** Compared to time-matched baseline, US and FC increased SWA and decreased amplitude at higher EEG frequencies (5.5-20.0 Hz) during NREM in B6 and CB6 mice. US also increased SWA during wakefulness in B6 mice. By comparison, neither US nor FC altered EEG power in C mice. Control mice did not show significant changes in EEG power. EEG power during REM was not significantly altered in any condition.

**Conclusion :** B6 and CB6 mice show increased SWA after US and FC, and these strains exhibit smaller decreases in REM. By comparison, C mice did not show increased SWA and have larger decreases in REM. These strain differences suggest that the magnitude and persistence of stress-induced reductions in REM may be correlated with stress-induced changes in SWA of NREM, and perhaps even of wakefulness.

**Support (optional):** NIH research grant MH61716

### 0034

#### CHOLINERGIC REGULATION OF THE CENTRAL NUCLEUS OF THE AMYGDALA (CNA): EFFECTS ON SLEEP AND EEG IN RATS

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**Introduction :** Microinjections of the cholinergic agonist carbachol (CARB) into CNA increase wakefulness in rats and decrease tonic immobility in guinea pigs suggesting that cholinergic stimulation of the amygdala is arousing in rodents. We examined sleep and EEG following microinjections into CNA of CARB, the acetylcholinesterase inhibitor, neostigmine (NEO), the muscarinic antagonist, scopolamine (SCO) and the nicotinic antagonist, mecamylamine (MEC).

**Methods :** Wistar rats were implanted with electrodes for recording sleep, and with cannulae aimed into CNA. Rats (n=9) received bilateral microinjections (0.2  $\mu$ l) of CARB (CARBL: 0.3  $\mu$ g; CARBH: 3.0  $\mu$ g) and NEO (NEOL: 0.3  $\mu$ g; NEOH: 3.0  $\mu$ g). Different rats (n=8) received SCO (SCOL: 0.3  $\mu$ g; SCOH: 1.0  $\mu$ g) and MEC (MECL: 0.3  $\mu$ g; MECH: 1.0  $\mu$ g). Saline was microinjected as control. Microinjections were counterbal-

anced and given at 5-day intervals. Wakefulness, REM and NREM were scored for 8 h after injection and a Fourier analysis of the EEG was conducted for each state. Comparisons of 8 h totals were made to saline using paired t-tests.

**Results :** Both doses of CARB and NEO significantly reduced REM, but did not significantly alter NREM. SCOH significantly increased NREM. CARBH and NEOH decreased REM EEG power in the 5.5 -10.0 Hz band and NEOL and NEOH decreased NREM EEG power in the 0.5 to 5.0 Hz band. CARBL decreased waking EEG power in the 0.5-5.0 Hz band and NEOH decreased waking EEG power in the 5.0-10.0 Hz band. Both doses of SCO significantly increased waking EEG power in the 5.5-10.0 Hz band. MEC did not significantly alter sleep or EEG power.

**Conclusion :** The reduction of REM by CARB and NEO and the promotion of sleep by SCO are consistent with findings that cholinergic stimulation of the amygdala promotes arousal in rodents. However, CARB microinjections into CNA apparently increase REM in cats, though the reasons for the species differences are not known.

**Support (optional):** NIH research grant MH64827

### 0035

#### EFFECTS OF BRIEF MANUAL RESTRAINT (MR), UNAVOIDABLE SHOCK (US) AND NOVEL ENVIRONMENT (NE) ON SLEEP AND EEG IN RATS

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**Introduction :** Sleep patterns and amounts vary with different types of stressors. For example, though all stressors appear to produce an initial period of arousal, restraint and exposure to NE are followed by a subsequent increase in REM, whereas US may not be. Brief MR, such as handling necessary for experimental manipulations (e.g., drug administration), may also be stressful, though how it may interact with other stressors is not known. We examined the effects of MR on sleep and its influence on sleep after US and NE.

**Methods :** EEG and activity were recorded via telemetry in Wistar rats (n=8). After recovery and recording of baseline sleep, recordings were made (8-h light and 12-h dark period) following a series of manipulations: 1) three 5-min sessions of MR (MR1-3) at 2-day intervals; 2) 30-min exposure to NE with and without prior MR (NEMR); 3) 20 US applied via grid floor with or without prior MR (USMR). Experiments 1 and 2 were counterbalanced and conducted at 5-day intervals. All comparisons were made relative to baseline.

**Results :** Light and dark period total sleep and NREM, and dark period REM were increased after MR1-3. NE and NEMR increased dark period total sleep, NREM and REM whereas NEMR also increased light-period total sleep and NREM, but not REM. US and USMR increased light period total sleep and NREM and dark period total sleep, NREM and REM. However, US significantly decreased light-period REM whereas it did not differ from baseline after USMR. Significant increases in NREM EEG delta power were observed after MR1, NEMR and USMR, but not after MR2-3, and NE and US alone.

**Conclusion :** Repeated sessions of MR continue to alter sleep amounts relative to baseline though delta power may return to baseline levels. MR also can influence the effects of other stressors on sleep and EEG delta power.

**Support (optional):** NIH research grant MH64827

### 0036

#### GABA ANTAGONISM OF THE CENTRAL NUCLEUS OF THE AMYGDALA (CNA) ATTENUATES REDUCTIONS IN RAPID EYE MOVEMENT SLEEP (REM) AFTER FOOTSHOCK STRESS

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**Introduction :** Footshock stress can produce a relatively selective decrease in REM. CNA has a central role in stress and is a strong modulator of REM. Microinjections into CNA of the GABA agonist muscimol (MUS) selectively decrease REM, whereas microinjections of the GABA antagonist bicuculine (BIC) selectively increase REM. We evaluated the effects of MUS and BIC in CNA on footshock-induced reductions in REM. Fos was used to determine the potential involvement of the locus coeruleus (LC), a REM regulatory region that is activated by footshock and receives input from CNA.

**Methods :** Male Wistar rats were implanted with transmitters for recording sleep and with cannulae aimed into CNA. After recovery, the rats were placed in one of four microinjection and footshock groups: SC (saline [0.2 µl] with no footshock, n=5); SS (saline [0.2 µl] plus footshock, n=4); MS (MUS [1.0 µM/0.2 µl] plus footshock, n=5); BS (BIC [333 pM/0.2 µl] plus footshock, n=5). Sleep was recorded for two h after footshock (0.2 mA, 15 trials, 1.0 min interstimulus interval). Afterwards, the animals were sacrificed for Fos immunohistochemistry.

**Results :** In the hour before sacrifice, REM in SS ( $1.02 \pm 0.28$ ) and MS ( $0.58 \pm 0.41$ ) rats was significantly less than in SC ( $5.05 \pm 0.68$ ;  $p < 0.01$ ) and BS ( $5.18 \pm 0.9$ ;  $p < 0.01$ ). There was no significant difference in REM between SC and BS. Fos expression in LC was greater in SS ( $40.25 \pm 1.84$ ) and MS ( $48.20 \pm 2.35$ ) compared to SC ( $7.20 \pm 1.32$ ;  $p < 0.001$ ) and BS ( $19.00 \pm 1.81$ ;  $p < 0.001$ ). Fos expression in LC was greater in BS than in SC ( $p < 0.01$ ). NREM sleep did not differ among groups.

**Conclusion :** Footshock alone and MUS plus footshock selectively reduced REM and enhanced Fos activation in LC. By comparison, BIC attenuated the reduction in REM and attenuated Fos activation by footshock. The results suggest that the effects of footshock stress on REM may involve local GABA in CNA and activation of LC.

**Support (optional):** NIH research grant MH64827.

### 0037

#### TUMOR NECROSIS FACTOR INCREASES SURFACE EVOKED POTENTIALS IN THE BARREL FIELD BY WHISKER DEFLECTION DURING SLEEP IN RATS

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**Introduction :** Somatosensory barrel columns oscillate between functional states as evidenced by the amplitude of surface evoked potentials (SEPs) to a whisker deflection. SEPs are higher during those functional states that correlate with whole organism sleep. When the sleep regulatory substance tumor necrosis factor (TNF) is unilaterally microinjected into the cortex, EEG delta power increases unilaterally during non-REM sleep, but not during REM sleep or waking, on the injected side only. We hypothesized that TNF microinjection onto the surface of a barrel stimulated by whisker deflection would also increase the SEPs during sleep.

**Methods :** Five rats were trained to tolerate physical restraint 6 days a week for 2 h/day. Bilateral electrode microarrays with microinjection cannula in the center of each were surgically implanted over the primary somatosensory cortex and the rats' whiskers were mapped. For 1-2 months after surgery, the rats were adapted to bilateral deflection of a

selected whisker. Rats were microinjected unilaterally with either heat-inactivated TNF $\cdot$  or TNF $\cdot$  (150 ng/2  $\mu$ l) one week apart and SEPs to whisker stimulation determined. We calculated the ratio of the SEP responses after TNF $\cdot$  to the responses after treatment with the control heat-inactivated TNF $\cdot$ , for both the injected and non-injected sides, during wake and quiet sleep episodes.

**Results :** After TNF $\cdot$  whisker deflection-induced SEPs were higher in amplitude than those SEP values obtained after heat-inactivated TNF $\cdot$ . The time course was biphasic with an initial enhancement during the first 0.5 hr followed by a second period of enhanced SEPs 1 hour after the injection. These effects were independent of whole animal state.

**Conclusion :** TNF $\cdot$  alters barrel column SEPs suggesting that functional states of cortical columns are in part TNF-dependent. Other data indicated that cortical TNF levels are neuronal use-dependent and sleep-dependent suggesting a role for TNF in local sleep.

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

### 0038

#### 5-HT<sub>2A</sub> ANTAGONIST EFFECTS ON NREM AND REM SLEEP PARAMETERS IN RATS

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**Introduction :** The hypnotic efficacy of a subset of antidepressants and antipsychotic medications, such as ritanserin, trazodone and quetiapine, has been attributed in part to 5-HT<sub>2A</sub> antagonism, consistent with increased sleep in clinical trials with the 5-HT<sub>2</sub> antagonists MDL-100,907 and eplivanserin. These compounds, however, are less than 100-fold selective for 5-HT<sub>2A</sub> over 5-HT<sub>2C</sub>, and have high affinity for other receptors, including H<sub>1</sub> and alpha-adrenergic receptors. To clarify the role of 5-HT<sub>2A</sub> in sleep/wake profiles, we compared a novel, selective 5-HT<sub>2A</sub> antagonist EMD-281014 (5-HT<sub>2A</sub> IC<sub>50</sub>: 0.4 nM, 5-HT<sub>2C</sub> IC<sub>50</sub>: 1334 nM) with MDL-100,907 and ritanserin on sleep measurements in rats.

**Methods :** Male CD rats were instrumented for telemetry-based EEG/EMG recordings (Data Sciences/Transoma Medical). Antagonists and respective vehicle controls were administered i.p. (0.3-3.0 mg/kg) in the middle of the active (dark) phase of the 12:12 h LD cycle. EMD-281014 was also administered p.o. Recordings were analyzed for NREM and REM amounts and NREM spectral analysis for 6 hours after compound administration. MDL-100,907 and EMD-281014 were synthesized according to published procedures. Ritanserin was obtained commercially.

**Results :** Each compound, at the minimally effective tested doses, increased NREM sleep during the 6-hour analysis period by 140-180% compared to vehicle controls. Each compound increased average NREM sleep bout lengths, with EMD-281014 administered orally the most efficacious. Both EMD-281014 and MDL-100,907 increased delta power (0-4 Hz) within NREM sleep. Ritanserin reduced % REM, overall, while MDL-100,907 and EMD-281014 delayed REM onset without net reductions in the 6-hour analysis period.

**Conclusion :** EMD-281014, a 5-HT<sub>2</sub> antagonist with 4000-fold selectivity for 5-HT<sub>2A</sub> over 5-HT<sub>2C</sub>, retained the NREM sleep-promoting and continuity properties observed with the less selective comparison compounds. EMD-281014 and MDL-100907 did not suppress REM sleep amounts, although delayed onset was apparent. These results support the hypothesis that 5-HT<sub>2A</sub> receptors are sufficient for increasing slow-wave sleep, and may contribute to hypnotic effects in sedating psychiatric medications with a 5-HT<sub>2A</sub>-antagonist component.

**Support (optional):**

### 0039

#### INFLUENZA VIRUS INCREASES THE NUMBER OF TUMOR NECROSIS FACTOR $\cdot$ (TNF $\cdot$ )- IMMUNOREACTIVE CELLS IN THE OLFACTORY BULB FOLLOWING INTRANASAL INOCULATION

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**Introduction :** Influenza virus is usually diagnosed on the basis of its severe systemic symptoms, such as fever and excess sleep. Viral symptoms are generally assumed to be regulated in part by cytokines made in the respiratory system communicating with the brain. We previously demonstrated replicating viral RNA in the olfactory bulb (OB) of influenza-infected mice as early as 4 h post-infection (PI). Consequently, we hypothesized that the presence of the virus will increase the production of the proinflammatory cytokines TNF $\cdot$  and IL-1, in the infected tissue.

**Methods :** Mature C57BL/6 mice were inoculated intranasally with the PR8 strain of influenza virus or boiled virus. Mice were anesthetized and perfused with 4% paraformaldehyde at 15 h PI to collect the brains. Brains were post-fixed, sunk in 20% sucrose and frozen prior to microtome sectioning (30 microns). OB sections were stained for viral antigen, TNF $\cdot$ , or IL-1, or were double-labeled for TNF $\cdot$  and the neuronal marker NeuN. Sections were examined and photographed using light and confocal microscopy.

**Results :** Viral antigen was concentrated in the OB glomerular layer. The majority of TNF $\cdot$ -immunoreactive-cells were found in the external plexiform layer (EPL) particularly in the vicinity of the mitral cell layer. Double labeling demonstrated the presence of TNF $\cdot$  immunoreactivity in cells also staining with NeuN, indicating that neurons are producing this cytokine. IL-1, immunoreactive cells were observed both in the glomerular layer and the EPL. After quantification, the number of TNF $\cdot$ -immunoreactive cells was significantly higher in the infected group. No significant changes in the number of IL-1, immunoreactive cells were observed.

**Conclusion :** An increase in the production of TNF $\cdot$ , a somnogenic cytokine, in the olfactory bulb may be part of the initial signaling to the brain to induce sleep and fever following influenza infection.

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### 0040

#### EFFECT OF ENVIRONMENTAL TEMPERATURE ON SLEEP IN C57BL/6J MICE

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**Introduction :** Ambient temperature exerts a prominent influence on sleep. In rats and humans, low ambient temperatures generally impairs sleep, whereas higher temperatures tends to promote sleep. The current study evaluates sleep patterns of mice under baseline conditions and after sleep deprivation (SD) at different temperatures.

**Methods :** C57BL/6J mice were surgically implanted for recording EEG and EMG. After recovery from surgery, mice were housed individually in cages placed in sound attenuating chambers with a 12:12 hour light-dark cycle and ambient temperatures of 22C, 26C, or 30C (n=7 per group). After a temperature acclimation period of 21 days, data were collected for 24h without disturbing the mice and then during and for 18h after a 6h period of SD that began immediately after light onset.

**Results :** C57BL/6J mice maintained at 30C spent significantly more

time in SWS during the light phase (47.1 +/- 0.3%) than did mice maintained at 22C (44.3+/-0.5%) or 26C (40.5+/-0.4%). During the light phase, delta wave amplitude during SWS (S-DWA), as compared to the 24h average baseline, was significantly higher at 22C (101.5+/-0.6%) than at 26C (98.4+/-0.5%) or 30C (99.4+/-0.4%). During the initial 2h after SD, mice housed at 22, 26, and 30C respectively spent 69.0+/-3.9%, 64.8+/-5.8%, and 72.8+/-2.4% of their time in SWS. During that time, S-DWA, were 105.9+/-1.9%, 105.8+/-1.1%, and 114.7+/-2.6%, for mice housed at 22, 26, and 30C, respectively. The duration of enhanced sleep after SD was also longer in mice housed at 30C vs. 22C or 26C.

**Conclusion :** Higher environmental temperatures promote spontaneous SWS and lower S-DWA in C57BL/6J mice, but increase both SWS time, S-DWA after SD. Thus, higher temperatures reduce sleep depth under normal conditions, but augment recuperative responses to sleep loss.

**Support (optional):** Supported by NIH grants NS40220, HL70522, and RR17543.

### 0041

#### EFFECT OF LIPOPOLYSACCHARIDE ON SLEEP AND SLEEP REGULATORY SUBSTANCES IN B6129PF2/J AND P50 KO MICE

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**Introduction :** The heterodimeric transcription factor, nuclear factor (NF) - kappa B, regulates several somnogens, including A1 adenosine receptor (A1AR) and TNF-. Lipopolysaccharide (LPS) alters vigilance states in numerous species and also activates NF- $\kappa$ B. p50/p65 heterodimer is the most common form of NF- $\kappa$ B expressed. To assess, the participation of NF- $\kappa$ B in sleep modulation after LPS administration, we evaluated sleep, TNF- and A1AR expression in mice lacking the p50 subunit of NF- $\kappa$ B (p50 KO).

**Methods :** p50 KO and control B6129PF2/J mice were surgically implanted with electrodes for recording of EEG and EMG. After recovery from surgery, mice were housed in individual cages on a 12:12 hour light-dark cycle at 22C. Mice were monitored for 24 hours before and after intraperitoneal administration of either pyrogen free saline (0.2 ml) or LPS (10ug/0.2ml), at light onset. Mice were sacrificed 4h after LPS administration, and serum and cerebral cortex were collected for measurement of TNF- concentrations (ELISA) and A1AR (radioligand binding), respectively.

**Results :** After LPS administration, both strains increased time spent in SWS and decreased time spent in REMS, but changes were greater in magnitude in KO mice and did not develop in saline treated mice. As compared to saline treated mice of the same strain, LPS administration increased cortical A1AR binding in F2 mice but not in KO mice. Serum TNF- was almost 5-fold higher in LPS treated KO mice as compared to F2 mice.

**Conclusion :** As compared to F2 mice, LPS treated KO mice showed higher serum TNF- concentrations and spent more time in SWS, consistent with TNF- involvement in mediating LPS-induced changes in somnolence. However, LPS administration did not induce A1AR binding in KO mice, as it did in F2 mice. Thus, p50 dependent mechanisms appear to be involved in A1AR induction, but this induction is not essential to promoting enhanced SWS.

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### 0042

#### MICRODIALYSIS PERFUSION OF CLONIDINE IN THE OREXINERGIC PERIFORNICAL HYPOTHALAMUS REDUCES REM SLEEP IN FREELY BEHAVING RATS

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**Introduction :** In vitro studies of postsynaptic effects of noradrenaline (NE) on orexin neurons are controversial. Li et al., (2005) have shown a postsynaptic  $\alpha$ 2 receptor mediated inhibitory input whereas Grivel et al., (2005) have shown that NE directly excites orexin neurons via postsynaptic  $\alpha$ 1 receptors in normally sleeping animals but inhibits them by postsynaptic  $\alpha$ 2 receptors after sleep deprivation. To evaluate the role of NE in orexinergic regulation, we performed microdialysis perfusion of clonidine ( $\alpha$ 2 agonist) in the orexinergic perifornical hypothalamus (PFH) and monitored its effect on sleep-wakefulness (W) in rats.

**Methods :** Adult Sprague-Dawley rats (300-400 g) were implanted with sleep recording electrodes and bilateral guide cannulae targeted toward the orexinergic PFH. After post-operative recovery, the microdialysis probes (CMA/11, 2 mm membrane; 0.24 mm O.D) were inserted. After 12 hours of probe insertion recovery, bilateral perfusion of artificial cerebrospinal fluid (ACSF) and/or clonidine (0.1, 1 and 3 mM) was carried out (flow rate= 2.0  $\mu$ l/min). Separate experiments were conducted for the light and dark period. On the control days ACSF was perfused from 10.00 to 16.00 (light period) and 16.30 to 22.30 (dark period). The protocol used on the experimental days was as follows: Light period experiments : Clonidine perfusion (12.00-14.00 hr) was preceded (10.00-12.00 hr) and followed by ACSF perfusion (14.00-16.00 hr). Dark period experiments: Clonidine perfusion (18.30 - 20.30 hr) was preceded (16.30 - 18.30) and followed by ACSF perfusion (20.30 - 22.30 hr). On completion, the animals were sacrificed, brains removed and processed for immunohistochemistry.

**Results :** Bilateral perfusion of clonidine in the histologically confirmed orexinergic PFH decreased REM sleep significantly during the dark (N=5; p<0.01) and light period (N=6; p<0.01 Friedman RM ANOVA on Ranks). W and nonREM sleep were unaffected during the dark period. While nonREM sleep was unchanged, W showed a significant decrease during the light period

**Conclusion :** Our data suggests that clonidine application in the PFH reduces REM sleep in freely behaving rats. To further determine whether clonidine perfusion activates orexin neurons, we are in the process of examining Fos-IR following clonidine perfusion.

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### 0043

#### DESCENDING GABAERGIC INNERVATION OF THE CAUDAL, ORAL PONTINE RETICULAR FORMATION IN THE RAT

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**Introduction :** Pharmacological manipulations of GABAa 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. Other than the local GABAergic interneurons, sources of GABA to the PnOc that could interact with GABAa receptors have not been explored. We report here immunochemical identification of several GABAergic neuronal populations innervating the PnOc.

**Methods :** Long-Evans Hooded rats were injected with 50 nl of a 0.5% solution of cholera toxin subunit B (CTb) in the PnOc and sacrificed by

transcardial perfusion 7 days later. Coronal sections at, and rostral to, the injection site 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 :** The distribution of retrogradely labeled CTb+ neurons conformed well with past reports utilizing tracer-injections in the pontine reticular formation. Of the neurons projecting to the PnOc, CTb+/GAD+ neurons were found scattered through the midbrain and pontine reticular formation on both sides of the brain. At higher density, double-labeled cells were found in the ipsilateral, dorsal zona incerta and fields of Forel, HI in the subthalamic area. In addition, many double-labeled cells were distributed in the region of the contralateral, rostral pole of the pedunculo-pontine tegmental nucleus intermingled with cholinergic neurons and extending medially into the midbrain extrapyramidal area.

**Conclusion :** The finding of extra-reticular sources of GABA to the PnOc implicates new mechanisms in state-control that will require future investigation.

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## 0044

### STIMULUS DEPENDENT AROUSAL LIKE BEHAVIOR UNDER ISOFLURANE ANESTHESIA

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**Introduction :** An electroencephalogram (EEG) burst-suppression pattern can be recognized during isoflurane anesthesia, where periods of nearly silent EEG are followed by short high amplitude bursts. EEG-based monitoring devices digitize, process and report anesthesia depth by incorporating the degree of suppression, relative power in several frequency ranges, and other components. We hypothesize that the temporal characteristics of cortical burst suppression states may be dependent on external stimuli. Since external stimuli could drive thalamic activation and elicit the appearance of bursts, external stimuli could elicit arousal like EEG signatures and result in an abnormally low value of anesthesia depth from monitoring devices.

**Methods :** EEG, and electrocardiogram (EKG) were recorded from isoflurane anesthetized rats during external auditory stimulation, and without stimulation (sham). The average latency of the burst occurrence after the stimuli and the burst suppression ratio (BSR) were calculated.

**Results :** Total time of near silent cortical EEG decreased when auditory external stimulation was applied. Burst activity was synchronized to external auditory stimuli. BSR values were lower during periods of external stimulation.

**Conclusion :** These results show that burst suppression ratio is dependent on external stimulation. Since auditory external stimulation can synchronize the burst activity, we speculate that external stimuli might bring cortical membrane potentials to an up (aroused) state. Under these conditions, monitoring devices will report lower values of anesthesia depth, and there is a danger of giving an overdose of anesthesia.

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## 0045

### ELECTROPHYSIOLOGICAL RECORDINGS FROM BRAINSTEM GABAERGIC NEURONS IN GAD67-GFP KNOCK-IN MICE AND REM SLEEP CONTROL BY CHOLINERGIC AND OREXINERGIC MECHANISMS

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**Introduction :** Gamma-amino-butyric-acid (GABA) is the main inhibitory neurotransmitter in the mammalian central nervous system. Different groups of GABAergic neurons in the basal forebrain, hypothalamus, mid-brain and brainstem control waking, slow-wave sleep and rapid-eye-movement (REM) sleep. Previously technical difficulties hampered the identification of intrinsic membrane properties and modulation by neurotransmitters of these neurons. Here, we used novel genetically modified mice which express green fluorescent protein (GFP) under the control of the glutamic acid decarboxylase (GAD67) promoter (GAD67-GFP knock-in mice) to perform electrophysiological recordings from identified GABAergic neurons that may play a role in REM sleep control.

**Methods :** Thin (200 micron) brain slices were prepared from heterozygous GAD67-GFP knock-in animals. Neurons expressing GFP in the area of interest of the 'living' slice were identified using a Hamamatsu ORCA-AR low light level CCD camera. Cell-attached or whole-cell patch-clamp recordings were made using a Multiclamp 700A amplifier. Drugs were bath-applied.

**Results :** Recordings were made from over 30 GFP+ neurons in areas of the brainstem reticular formation (subcoeruleus (SubC), pontine nucleus oralis (PnO) and ventral tegmental area (VTg)) important in controlling REM sleep. The neurons were spontaneously active, firing action potentials at a low rate (4-12 Hz) in the absence of injected current. Orexins (500 nM) uniformly excited GFP+ neurons in the SubC, PnO and VTg areas. In contrast, the cholinergic agonist carbachol (10 microM) had either excitatory (SubC or PnO) or inhibitory actions (PnO, VTg) on different GFP+ neurons.

**Conclusion :** Previous studies showed that injection of GABA-A receptor antagonists into the SubC or PnO promotes REM sleep. Thus, a reduction in GABAergic tone may be necessary to trigger this state. This reduction may be caused by acetylcholine since a significant proportion of GFP+ neurons were inhibited by carbachol. Orexin excitation of these same GABAergic neurons is likely to be important in suppression of REM.

**Support (optional):** Supported by NIMH R01 MH062522 and R37 MH039683 (to RWM) and VA.

## 0046

### EFFECTS OF CARBACHOL ON ELECTRICAL COUPLING IN THE PEDUNCULOPONTINE NUCLEUS

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**Introduction :** We previously reported the presence of spikelets, indicators of electrical coupling, in posterior pedunculo-pontine nucleus (PPN) neurons. We investigated the possibility that the muscarinic agonist carbachol (CAR) would affect the manifestation of spikelets.

**Methods :** Intracellular current clamp recordings were conducted on 12-21 day old rat brainstem neurons maintained in artificial CSF. After basic physiological properties were determined, CAR (40<sup>o</sup>M), atropine (ATR-10<sup>o</sup>M), and tetrodotoxin (TTX-30<sup>o</sup>M) were administered. Neurobiotin was injected upon completion of recordings.

**Results :** CAR had a direct depolarizing effect on type I and type III PPN neurons, which was blocked by pretreatment with ATR but persisted after TTX. CAR also had an excitatory effect as shown by the induction of spikelets, a physiological marker for the probable presence of gap junctions. Additionally, neurobiotin injection into single PPN neurons demonstrated intercellular connections manifested by the presence of multiple labeled neurons. All of the neurons labeled were non-cholinergic, and

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some were located posterior to cholinergic PPN cells.

**Conclusion :** These results show that CAR had a direct excitatory effect on type I and III PPN neurons, leading to depolarization as well as increased spikelet frequency. The presence of spikelets and of multiple cell labeling after injection of a single cell are indications of electrical coupling and the presence of gap junctions. This study suggests the presence of electrotonic coupling in at least some, usually non-cholinergic, PPN neurons, which may be activated by CAR. The generation of synchronized, electrically coupled bursts of activity by the PPN may be one potential mechanism behind bursting activity during REM sleep.

**Support (optional):** USPHS grants NS020246 and RR020146.

### 0047

#### EFFECTS OF EARLY SOMATIC OR VISCERAL PAIN ON PARAFASCICULAR NEURONS

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**Introduction :** Early painful experience is known to lead to chronic changes in pain threshold as well as arousal, attentional and cognitive deficits. A model of early somatic pain (paw formalin injection) leads to sensory and behavioral disturbances in adulthood in all those treated, whereas a model of early visceral pain (colonic distention) leads to such deficits in most of those treated. One potential mechanism for the origin of chronic neurogenic pain is intralaminar thalamic low threshold spiking (LTS) leading to thalamocortical dysrhythmia. Lesion of such LTS-generating regions is known to abolish neurogenic pain.

**Methods :** Rat pups were treated with somatic pain (days 4-7) or visceral pain (days 6-10), and intracellular recordings were performed in parafascicular (Pf) neurons in 12-21 day rat brainstem slices in artificial CSF.

**Results :** Of 21 Pf neurons recorded from the somatic pain model, 95% (n=20) displayed LTS activity. LTS bursts were blocked with Ni or Cd (n=4), both non-specific Calcium channel blockers, and mibefradil (n=4), a selective T-type Calcium channel blocker. Resting membrane potential was significantly different (df=40, F=15.444, p=0.0003) in treated animals -60.5 +/- 1.3mV (n=21) compared to intact animals -54.6 +/- 0.7mV (n=21). Of 19 Pf neurons recorded from the visceral pain model, 64% (n=12) displayed LTS activity. LTS bursts were blocked with Ni (n=5). Resting membrane potential was significantly different (df=38, F=7.144, p=0.01) in treated animals -59.8 +/- 1.9mV (n=19) compared to intact animals -54.6 +/- 0.7mV (n=21).

**Conclusion :** Early pain experience induced LTS activity in Pf neurons that normally do not exhibit LTS, which may explain lasting changes resulting from early somatic or visceral pain. Such changes may account for some of the sleep, arousal and attentional deficits observed after early pain experience.

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### 0048

#### PRE AND POSTSYNAPTIC EFFECTS OF HYPOCRETIN ON NEURONS OF THE NUCLEUS PONTIS ORALIS (NPO), AN IN VITRO STUDY

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**Introduction :** The nucleus pontis oralis (NPO), which plays a key role

in the generation of active sleep (AS), is controlled by diverse structures and different neurotransmitters. In the present study, an in vitro preparation was employed to assess the pre and postsynaptic effects of hypocretin on NPO neurons in adult guinea pigs.

**Methods :** Intracellular recordings were obtained from NPO neurons in brain stem slices. The spontaneous activity of these neurons, as well as their response to intracellularly applied current pulses, were examined prior to, during and after hypocretin application. In selected experiments, the recorded neurons were labeled by the intracellular injection of biocytin.

**Results :** Hypocretin increased the excitability of NPO neurons; there was a decrease in the rheobase and an increase in the frequency of action potentials evoked by depolarizing pulses. Input resistance increased by approximately 30%, which suggests a decreased potassium conductance. Hypocretin also induced action potential discharges in neurons that were silent during control conditions and increased the frequency of spikes in those neurons that were already spontaneously active. Synaptic activity was increased in conjunction with hypocretin application. High-gain recordings revealed an increase in the frequency and the amplitude of depolarizing postsynaptic potentials. As a working hypothesis we suggest that these postsynaptic potentials are glutamatergic, cholinergic and/or hypocretinergic. Therefore, hypocretin may facilitate the induction of AS by promoting, postsynaptically, the discharge of NPO neurons and, presynaptically, the release on NPO neurons of other excitatory neurotransmitters, thus synergistically increasing their excitability.

**Conclusion :** The present data reveal that hypocretin exerts excitatory effects on NPO neurons acting via pre- as well as postsynaptic mechanisms.

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### 0049

#### A NEURAL LOCUS INVOLVED IN SLEEP IN DROSOPHILA

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**Introduction :** The fruit fly *Drosophila melanogaster* exhibits many of the cardinal features of sleep, yet the neuroanatomical loci regulating its sleep have not been identified.

**Methods :** We exploited a dominant temperature sensitive blocker of synaptic transmission (shibirets) to manipulate the activity of neural circuits. Using the GAL4/UAS system, we drove shibirets expression in multiple adult brain regions defined by 97 distinct GAL4 lines and assayed the consequences on sleep.

**Results :** We identified three "short-sleep" (SSL) GAL4 lines that in combination with shibirets inhibited sleep at the restrictive temperature (29oC) in an assay where temperature was cycled between the restrictive and permissive (21oC) temperatures. While these lines had diverse anatomical expression patterns within the brain, they shared expression in the mushroom bodies (MB), a region of the brain involved in learning and memory. Two additional GAL4 lines selected for high levels of expression throughout the MB were then identified as SSL lines using this assay, and were used for all further studies. When SSL flies were maintained at the restrictive temperature, total sleep was dramatically reduced in all lines, and measures of sleep consolidation were reduced, including average sleep bout length. In addition, sleep reductions were correlated with reduced lifespan. When SSL flies were maintained at the permissive temperature sleep and sleep consolidation were largely unaffected. Chemical ablation of the MB resulted in an SSL phenotype with similar effects on sleep consolidation. Additionally, MB ablation in a SSL line did not enhance the SSL phenotype, indicating MB inhibition is primarily

responsible for its phenotype.

**Conclusion :** Our results strongly implicate a specific and central role for the MB in promoting sleep. These studies set the stage for the identification of sleep regulatory loci within the MB as well as the elucidation of genetic pathways regulating MB-induced sleep.

**Support (optional):**

## 0050

### PROKINETICIN-2 AFFECTS SLEEP RHYTHMS

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**Introduction :** Diffusible factors released from the SCN are thought to mediate key aspects of circadian rhythm control. Three putative output factors have been identified: vasopressin, TGF- $\beta$  and prokineticin-2 (PK2); ICV PK2 injection was previously shown to suppress running wheel activity in rats. We sought to determine the effects of ICV PK2 administration on sleep in rats.

**Methods :** Pairs of rats received injections into the third ventricle of 1, 5 or 10 $\mu$ g of synthetic rhesus PK2 and aCSF at ZT2 and ZT 14 (n=5 pairs, each condition). EEG and EMG activity, core body temperature and heart rate were monitored.

**Results :** ICV PK2 injections at both ZT2 and ZT14 caused a potent dose-dependent suppression of REM sleep for 10 hours following injection, compared to aCSF injections. REM sleep was nearly eliminated for 10 hours following 10 $\mu$ g PK2 injection at ZT14 and for 6 hours following 10 $\mu$ g PK2 injection at ZT2. PK2 injections at both ZT2 and ZT14 also caused a potent dose-dependent suppression of total and NREM sleep and a corresponding increase in active waking for 4 hours following injection, compared to aCSF injection. Sleep amounts were reduced overall for the remainder of the light or dark period (10h) following injection without rebound in the following 12h light or dark period.

**Conclusion :** Acute injections of PK2 suppress sleep and increase active waking amounts.

**Support (optional):** This work was supported in part by funding from Kinexis.

## 0051

### REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION DURING WAKEFULNESS INDUCES A LOCAL INCREASE IN EEG SLOW WAVE ACTIVITY DURING SUBSEQUENT SLEEP

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**Introduction :** Recent work has shown that repetitive transcranial magnetic stimulation (rTMS) applied to motor cortex can produce changes in muscle motor evoked potentials lasting up to one hour. We have shown that rTMS of left motor cortex induces a localized potentiation of TMS-evoked cortical responses (Esser et al., 2005). Here we investigate whether rTMS induced potentiation performed during wakefulness produces lasting effects on EEG spontaneous activity recorded during subsequent sleep.

**Methods :** We performed an rTMS potentiation protocol (1500 rTMS pulses, at 5 Hz, block design, 90% of motor threshold, left motor cortex hand area, 20 minutes session in the evening, n=5 subjects) using a 60-channel TMS/EEG system with infrared stereotaxic positioning. TMS test stimuli showed an increase in the magnitude of cortical responses (40.4 $\pm$ 7.5%) for a cluster of electrodes located slightly anterior to the site of stimulation. Immediately after the rTMS session, subjects were reclined and allowed to sleep while the EEG was continuously recorded for 1-h. Separated by at least 1 week we performed a sham stimulation (coil angled

and spaced) and recorded subsequent control sleep. The sleep EEGs were staged, subjected to semi-automatic artifact removal and processed using power spectral analysis (4-s epochs, FFT routine, Hanning window).

**Results :** When the first hour of sleep was compared between the potentiation and the control condition, all subjects showed a prominent increase of EEG power (26.6 $\pm$ 16.5%) in the slow-wave activity (SWA) frequency range in a cluster of left central electrodes. MRI-aided electrode co-registration localized the increase in SWA to Brodmann area 6, near the site of maximum potentiation during wakefulness.

**Conclusion :** Together with our recent demonstration that SWA homeostasis could be triggered by a learning task involving specific brain regions (Huber et al., 2004), these results provide further evidence for the local regulation of SWA homeostasis and support a role for sleep at the cellular level.

**Support (optional):** SSMBS and NIMH

## 0052

### SOCIAL DEFEATS INDUCE MODEST CHANGES IN SLEEP AND OPEN FIELD BEHAVIOUR IN RATS

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**Introduction :** Depression in humans is associated with affective changes, sleep alterations (e.g. altered rapid eye movement (REM) sleep, reduced delta sleep and fragmented sleep) and psychomotor disturbance. Similar symptoms are also observed in animals after exposure to unpredictable stressors. Social defeat (SD), resulting from the fight for a territory, has been used as an animal model of depression and anxiety. The model is based on the resident-intruder paradigm in which a male rat 'intruder' is placed in the territory and defeated by an older, bigger and more aggressive male resident. We investigated whether SD, an animal model of depression and anxiety, would cause changes in sleep, emotionality locomotor activity in the defeated rat.

**Methods :** Male Wistar rats were implanted with EEG and EMG electrodes. Rats were divided in a SD group (n=8) exposed to 1h SD on two subsequent days and a control group (n=8). In all animals sleep was recorded the day before, 13h and 4 days after last SD confrontation. Behaviour of all animals was quantified in the open field test on four consecutive days starting at day 8 after last SD.

**Results :** Defeated rats showed more fragmented sleep day 4 compared to baseline (F(1,6)=23.897, p=0.003) due to an increased amount of slow-wave-sleep-1 (p<0,001) and slow-wave-sleep-2 episodes (p<0.001). However, the SD procedure did not produce any changes in REM sleep amount, REM sleep latency, or delta sleep. Defeated rats showed less activity in the central sector of the open field (F(1,14)=8.106, p=0.013) and had no significant decrease in defecation rate across days. This suggests that defeated animals had become more emotional. However, total locomotor activity in the open field was not affected by the SD procedure.

**Conclusion :** The SD procedure resulted in modest sleep alterations and increased emotionality in rats.

**Support (optional):**

## 0053

### ON THE ROLE OF CGMP IN NITRIC OXIDE-MEDIATED REGULATION OF RECOVERY SLEEP IN THE BASAL FOREBRAIN

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**Introduction :** We have shown recently that release of nitric oxide (NO) in the basal forebrain (BF) may be a key mechanism underlying develop-

ment of recovery sleep after sleep deprivation (SD). Both SD and infusion of NO donor into the BF induce increases in subsequent sleep as well as in extracellular adenosine suggesting that NO-induced sleep might be mediated through adenosine release. cGMP is intracellular messenger involved in most of NO actions. To study the possible role of cGMP in regulation of recovery sleep by NO we: 1) pharmacologically increased cGMP level (by infusion of 8-pCPT-cGMP, a cGMP analogue, or zaprinast, an inhibitor of cyclic nucleotide phosphodiesterases), and compared changes in adenosine level and sleep to those observed after SD; 2) blocked cGMP-mediated effects during SD (by infusion of RP-8-Br-cGMPS, an inhibitor of cGMP-dependent protein kinase) and compared sleep response to the effect induced by SD alone.

**Methods :** Male rats were implanted with electrodes for EEG/EMG recording and guide cannulae for microdialysis probes aimed at the BF. The experimental schedule for each rat included: recording of natural sleep-waking cycle; SD for 3h; infusion of 8-pCPT-cGMP or zaprinast for 3h; SD combined with infusion of RP-8-Br-cGMPS. Adenosine concentrations were measured by HPLC coupled to UV detector. Polysomnograms were continuously recorded for 30h.

**Results :** Zaprinast at 0.1mM induced increase in sleep comparable with recovery sleep after SD and also increased adenosine level. 8-pCPT-cGMP at 1mM and 10mM also increased sleep in a dose-dependent manner but this effect was not preceded by increase in adenosine. Infusion of RP-8-Br-cGMPS at 0.5mM and 5mM during SD induced partial suppression of recovery sleep.

**Conclusion :** Regulation of recovery sleep by NO in the BF is only partially mediated by cGMP. This pathway may be distinct from that involving adenosine release.

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## 0054

### A NEW ROLE FOR HYPOCRETIN IN DRUG RELAPSE

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**Introduction :** Hypocretin neurons receive afferents from corticotropin release factor (CRF)-containing neurons from the bed nucleus of the stria terminalis, central amygdala and medial septum. Since CRF is a key factor in the stress response that also drives relapse for drug seeking, we hypothesized that hypocretin neurons might have a role in addiction processes. Here we have tested the effects of central administration of hcrf on acquisition of cocaine self administration and relapse.

**Methods :** We implanted catheters on the jugular vein of Male Wistar rats for self administration studies. Rats (n=56) were trained for cocaine self administration as described elsewhere. Lever presses were recorded using a personal computer setup. Data was analyzed using ANOVA, followed by planned comparisons among means adjusted using False Discovery Rate procedure.

**Results :** Intracerebral infusion of hypocretin reinstated extinguished cocaine seeking behavior in a dose dependent manner (0.3-1.5 nmoles). Hypocretin-induced reinstatement was prevented by blockers of CRF and noradrenergic signaling. Footshock-induced reinstatement of cocaine seeking behavior could be blocked by a systemic injection of SB-334867 (30 mg/kg), a hypocretin receptor 1 antagonist.

**Conclusion :** The hypocretins may be important modulators of the neural circuitry involved in drug relapse. These results may yield to therapeutic interventions to prevent relapse.

**Support (optional):**

## 0055

### CANNABIDIOL, A CONSTITUENT OF CANNABIS SATIVA, INDUCES WAKING IN RATS

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**Introduction :**  $\psi$ -9-tetrahydrocannabinol ( $\psi$ 9-THC) and cannabidiol (CBD) are 2 major constituents of the Cannabis Sativa.  $\psi$ 9-THC modulates sleep but not clear evidence about the role of CBD was available. Here we evaluated the effects of CBD on sleep, as well as c-Fos expression.

**Methods :** Wistar male rats (250-300g) housed (21 + 10C) under a controlled light-dark cycle (lights on: 07:00-19:00h) were implanted for sleep recordings as well as a cannula placed into lateral ventricle. All experiments were conducted with food and water ad libitum. CBD was dissolved in vehicle (PEG/saline; 5:95 v/v) and injected (10 $\mu$ g/5 $\mu$ l, icv) during either the lights-on or lights-off period of the rats. The EEG/EMG was scored in wakefulness (W), slow wave sleep (SWS) and rapid eye movement sleep (REMS). At the end of all the experiments, animals were sacrificed 60 min after receive either vehicle or CBD (10 $\mu$ g/5 $\mu$ l, icv) with a lethal dose of pentobarbital.

**Results :** CBD injected during the lights-on period increased W and decreased REM sleep. No changes were observed in SWS as well as during the lights-off period. Additionally, CBD increased the c-Fos expression in lateral hypothalamus and dorsal raphe nucleus (RDR).

**Conclusion :** CBD modulates W via activation of neurons in hypothalamus and DRD. Since CBD induced alertness, it might be considered to treat excessive somnolence.

**Support (optional):** This work was supported by Fideicomiso UNAM to R. D-C.

## 0056

### SEPSIS-INDUCED ALTERATIONS IN SLEEP OF RATS

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**Introduction :** Infection-induced alterations in sleep have been demonstrated for several pathogens. In hospitals, polymicrobial infections remain a serious problem; diagnosis of sepsis confers a 0.3 to 0.4 probability of death. Little effort has been made to determine the impact of sepsis on CNS processes. As an initial study, we hypothesized that sleep of rats would be altered during sepsis.

**Methods :** All studies were approved by the University of Michigan Committee on Care and Use of Animals. Male rats (300 g, n = 16) were surgically implanted under isoflurane anesthesia with EEG recording electrodes and a thermistor to measure brain temperature. After recovery, each animal was subjected to an abdominal surgery. Half the rats were subjected to cecal-ligation and puncture (CLP), and half had the cecum exposed without puncture (SHAM). Broad-spectrum antibiotics and an analgesic were administered. Abdominal surgeries were performed during the early part of the light period. Recordings began at dark onset on the day of surgery and continued for 96 h.

**Results :** NREMS and REMS were differentially impacted by CLP-



induced sepsis. Relative to SHAM animals, CLP rats spent more time in NREMS during dark periods, and less time in REMS during light periods. Diurnal temperature rhythms returned in SHAM rats by day 4, but did not normalize in CLP rats during the recording period.

**Conclusion :** This is the first study of which we are aware to demonstrate alterations in sleep during CLP-induced sepsis. Reductions in REMS during immune challenge are a consistent finding, but the response to sepsis is unique in that these reductions are limited to the light period. The pattern of changes in sleep and temperature suggest a flattening of diurnal rhythms, which may implicate the SCN as a target. This clinically-relevant model provides a framework within which to explore infection-induced alterations in sleep and CNS function.

**Support (optional):** HL080972, GM067189, and the University of Michigan Department of Anesthesiology

## 0057

### THE INHIBITION OF THE FATTY ACID AMIDE HYDROLASE VIA CYCLOHEXYL CARBAMIC ACID 3'-CARBAMOYL-BIPHENYL-3-YL ESTER (URB597) MODULATES WAKING IN RATS

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**Introduction :** The Fatty acid amide hydrolase (FAAH) catalyzes the hydrolysis of the endocannabinoid anandamide (ANA). Our group has reported that the FAAH inhibitor named Cyclohexyl Carbamic Acid 3'-Carbamoyl-biphenyl-3-yl Ester (URB597) increases the brain levels of ANA. We additionally have demonstrated that ANA increases sleep in rats.

**Methods :** In order to evaluate the pharmacological properties of URB597 on the sleep of rats, male adult Wistar rats (230-250g) were implanted for sleep recordings (EEG and EMG) as well as cannulae aimed to the lateral ventricle. Rats were allowed to recover for 7 days. They were housed under a controlled light-dark cycle (12:12; lights-on at 07:00h) with access to food and water ad libitum. Animals received either vehicle of URB597 (10µg/5µl, icv) at the beginning of the lights-on or lights-off period. After injections, animals were recorded during 4h. The sleep-wake cycle was divided into wakefulness (W), slow wave sleep (SWS) and rapid eye movement sleep (REMS).

**Results :** We found that the injection of URB597 increased significantly W and decreased SWS during the lights-on period. On the other hand, no statistical changes on sleep after administration of URB597 during the lights-off period were observed.

**Conclusion :** Our results suggest that inhibition of the FAAH, as an element of the endocannabinoid system, plays an active role in the modulation of the sleep.

**Support (optional):** This work was supported by Fideicomiso UNAM to R. D-C.

## 0058

### NEURONAL SUBSTRATES OF THE ASCENDING RETICULAR ACTIVATING SYSTEM (ARAS)

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**Introduction :** Moruzzi and Magoun first articulated the concept of an ascending reticular activating system (ARAS) originating in the mesopontine reticular formation that controls cortical arousal and awareness. However, the neurons of origin and course of this pathway have never been established. We decided to reexamine the ARAS, by a top-down approach, i.e. by identifying the key ascending relays that maintain an

activated cortex, and from there retrogradely tracing inputs from the mesopontine tegmentum.

**Methods :** To identify the key relay for cortical activation, neurotoxins ibotenic acid and orexin-saporin were used to lesion the thalamus or the basal forebrain (BF), and then retrograde tracing was used to identify the potential inputs from the brainstem. Finally, we lesioned the identified brainstem source and examined sleep-wake behaviors.

**Results :** Ibotenic acid lesions of the thalamus or selective immunolesions (192-saporin) of the BF cholinergic neurons or selective lesions of non-cholinergic neurons by orexin-saporin (low dose, 0.32 microgram) did not affect baseline amounts of sleep and wakefulness or EEG activity. After two hours of wakefulness, these lesioned rats and sham controls were perfused and Fos expression was seen in the neocortex and ascending arousal systems in both lesioned and control groups. By contrast, lesions in the BF by orexin-saporin (high dose, 0.4 microgram) destroyed virtually all non-cholinergic neurons and 85% of cholinergic neurons, and caused coma with EEG slowing so that it was indistinguishable from EEG during sleep. Fos expression was seen in the subcortical arousal systems but not in the cerebral cortex during the usual wake cycle. Retrograde tracing from the BF demonstrated inputs from the precoeruleus region (PC) and the parabrachial nucleus (PB) in the mesopontine tegmentum. Large lesions of the PB caused a 40% of increase in sleep over controls and coma; lesions of the PC abolished hippocampal theta EEG.

**Conclusion :** (1) Both cholinergic and noncholinergic (possibly GABAergic) BF neurons contribute to cortical arousal. (2) The PB-BF-neocortex axis is a critical component of the ARAS that maintains cortical arousal; the PC-MS-hippocampus axis is important in ARAS control of hippocampal function. (3) The reticulo-thalamo-cortical pathway may play a very limited role in the regulation of overall level of arousal or EEG activation during wakefulness.

**Support (optional):** NH NS051609 and MH 55772,

## 0059

### SURVIVAL OF HYPOCRETIN NEURONS GRAFTED INTO YOUNG HOST

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**Introduction :** Narcolepsy is a chronic disorder characterized by excessive daytime sleepiness, premature transitions to rapid eye movement sleep and cataplexy. Recent studies have concluded that narcolepsy is associated with a decrease in the number of HCRT neurons. Transplantation has been suggested as a promising approach in order to replace the loss of HCRT cells in narcolepsy. We have reported recently that HCRT cells survive after grafting into the pons of an adult rat. In the present study we studied the survival rates of HCRT grafted neurons into an adult host at different 36 days after transplantation.

**Methods :** A suspension of HCRT-containing cells from the lateral hypothalamus (8- 10-day old) rat pups was grafted into the pons of adult host rats. Control rats received cells from the cerebellum (tissue with no presence of HCRT neurons). All host rats were sacrificed 1, 3, 6, 9, 12, 24, or 36 days after grafting. The presence of HCRT neurons at the target area was characterized by immunohistochemistry.

**Results :** At day 1 after transplantation, HCRT cells were present in the target area the (55%). At day 3 post-grafting, we found the 40% of HCRT grafted neurons in targeted area. Six days after transplantation, 37% of HCRT transplanted neurons were still present. Following 9 days after transplantation, HCRT-immunoreactive cells were present at the implantation site (30%) whereas at 12 days, a significant decrease was observed (25%). Finally, at 24 days post-grafting 15% of the HCRT transplanted

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neurons were observed whereas at 36 days cells were present but greatly reduced (5%).

**Conclusion :** Our results demonstrate that through time the number of HCRT grafted neurons diminished significantly within the target area. Cell replacement as a therapy for narcolepsy, should not be overlooked.

**Support (optional):** This work was Supported by Fideicomiso UNAM to R. D-C.

### 0060

#### INTRACEREBROVENTRICULAR ADMINISTRATIONS OF MODAFINIL PROMOTE WAKEFULNESS AND DECREASES SLEEP REBOUND AFTER TOTAL SLEEP DEPRIVATION IN RATS

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**Introduction :** Modafinil is a wake promoting drug that has been used in the treatment of excessive daytime sleepiness associated with narcolepsy. However, no evidence is available about its pharmacodynamic properties on sleep after icv administration in rats.

**Methods :** Male adult Wistar rats (230-250 g) were implanted with electrodes for sleep recordings as well as cannulae aimed to the lateral ventricle. Rats were housed under a controlled light-dark cycle (12:12; lights-on at 07:00h) with food and water ad lib. Animals received either vehicle or modafinil (10 g/5 l) at 07:00h. The sleep-wake cycle was divided into wakefulness (W), slow wave sleep (SWS) and rapid eye movement sleep (REMS).

**Results :** Modafinil increased W whereas sleep remained diminished. To test the role of modafinil on sleep homeostasis, on Experiment 2, animals were kept awake using gentle manipulation (total sleep deprivation [TSD]) for 6h starting at 07:00h. At the end of the TSD, rats received either vehicle or modafinil (10 g/5 l, icv) and were recorded. Surprisingly, modafinil increased W even after TSD. Additionally we found that the SWS and REMS were diminished as well.

**Conclusion :** Our results show that modafinil is a strong W-promoting drug and modulates the sleep homeostasis.

**Support (optional):** This work was supported by Fideicomiso UNAM to R. D-C.

### 0061

#### NEURONAL SUBSTRATES OF THE DESCENDING RETICULAR ACTIVATING SYSTEM-MESENPHALIC LOCOMOTION REGION AND CATAPLEXY

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**Introduction :** In 1946, Rhines and Magoun first proposed that a descending reticular activating system that originates roughly within the pontine reticular formation is involved in control of locomotion behaviors. Twenty years later, Shik, Orlovsky, and colleagues identified a confined area, the mesencephalic locomotion region (MLR) located in the region of the "cuneiform nucleus," which was later identified with the pedunculopontine tegmental nucleus (PPT). Electrical stimulation of the MLR triggers locomotion in decerebrate cats on a treadmill. To this day, the cells making up the MLR and mechanism of the MLR are not well defined.

**Methods :** To identify the MLR, we did a series of experiments to determine cellular phenotypes of the MLR, its neurotransmitters, projections to the spinal cord and association with cataplexy and orexin (also called hypocretin) receptors, by means of combinations of anterograde and retrograde tracing, in situ hybridization, Fos, chemical stimulation and cell lesions.

**Results :** The MLR has been widely assumed to include the cholinergic neurons of the PPT, but we found that sites where chemical stimulation caused walking and standing behavior in rats were concentrated nearby in the lateral pontine tegmentum, near the region where inhibition by GABA agonists causes atonia (Devor). Lesions in this site produced cataplexy, suggesting that it plays a key role in producing motor tone by suppressing atonia. The pontine motor system was assumed by Rhines and Magoun to relay via the medial medullary reticular formation, but large lesions of the medial medulla failed to block the MLR-triggered rhythmic walking. Finally, we found that neurons in the MLR project directly to the spinal cord, and that they contain mRNA for the vesicular glutamate transporter as well as orexin 2 receptors, but not choline acetyltransferase immunoreactivity

**Conclusion :** (1) The MLR generates motor tone by inhibiting atonia pathways as well as by directly activating spinal pattern generators that control locomotion and posture. This same pathway may be important in preventing cataplexy during wakefulness and REM atonia during NREM sleep. (2) Orexin inputs from the lateral hypothalamus may act on orexin 2 receptors on MLR neurons, and this may be a key mechanism for preventing cataplexy.

**Support (optional):** NS 051609, MH 55772

### 0062

#### EFFECTS OF CARBACHOL ON DIFFERENT TYPES OF PEDUNCULOPONTINE NEURONS

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**Introduction :** The PPN is known to modulate waking and REM sleep. REM sleep decreases between 10 and 30 days postnatally in the rat. PPN neurons are known to receive cholinergic inputs from the contralateral PPN and bilaterally from the LDT. We investigated the potential contribution of cholinergic PPN inputs to the developmental decrease in REM sleep.

**Methods :** We recorded intracellularly from PPN neurons in 12-21 day rat brainstem slices maintained in artificial CSF to study the responses induced by the mainly muscarinic agonist carbachol (CAR).

**Results :** Of 33 PPN neurons recorded, 4 were type I, 26 type II and 3 type III. Superfusion of CAR resulted in hyperpolarization of all (100%) type II cells, and depolarization of all (100%) type I and type III cells. Both hyperpolarizing (type II, n=20) and depolarizing (type I and III, n=7) responses persisted in the presence of TTX and CAR, suggesting that the location of the muscarinic cholinergic receptors was postsynaptic. The reversal potential of the response to CAR was close to the potassium equilibrium potential (~-90 mV, n=5). CAR effects were completely blocked by scopolamine (n=12) and partially by atropine (n=7), the remainder were blocked by the nicotinic antagonist mecamylamine, indicating the activation of both muscarinic and nicotinic receptors by CAR on the same cells.

**Conclusion :** All type II PPN cells appear inhibited by muscarinic cholinergic inputs while all type I and III cells appear to be excited. There was no change in these responses across the developmental decrease in REM sleep.

**Support (optional):** USPHS grants NS020246 and RR020146.

## 0063

## NICOTINIC ACTIONS ON DEVELOPING PEDUNCULOPONTINE NUCLEUS (PPN)

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**Introduction :** The PPN is known to modulate waking and REM sleep. REM sleep decreases between 10 and 30 days postnatally in the rat. PPN neurons are known to receive cholinergic inputs from the contralateral PPN and bilaterally from the LDT. We investigated the potential contribution of cholinergic PPN inputs to the developmental decrease in REM sleep.

**Methods :** We recorded intracellularly from PPN neurons in 12-21 day rat brainstem slices maintained in artificial CSF to study responses induced by the non-desensitizing nicotinic agonist DMPP.

**Results :** Of 58 PPN neurons recorded, 86% responded to DMPP, and 2 were type I, 52 type II and 4 type III. There was a change in type II cells (ANOVA,  $df=44$ ,  $F=13.7$ ,  $p<0.0001$ ), such that from days 12 to 15 the effect was depolarizing, after which time it was either depolarizing or hyperpolarizing, with the majority after 15 days hyperpolarizing. Superfusion of the nicotinic antagonist mecamylamine (MEC) prior to DMPP suppressed the effect of DMPP ( $n=9$ ), while MEC superfusion on its own ( $n=4$ ) did not alter the membrane potential of PPN neurons. In 15 cells tested with TTX and DMPP, their responses persisted after blockade of sodium-voltage gated channels (i.e. had nicotinic receptors located postsynaptically), whereas 11 had their effects abolished (i.e. had nicotinic receptors located presynaptically). Applying the drug at various holding potentials in the presence of TTX suggested a reversal potential between -30 and -45mV ( $n=6$ ). Blockade of glutamatergic, serotonergic, gabaergic and muscarinic receptors did not affect postsynaptic nicotinic inhibition of most PPN cells.

**Conclusion :** These results suggest the involvement of postsynaptic nicotinic receptors in the hyperpolarization of some type II PPN cells, and in the depolarization of other type II PPN cells.

**Support (optional):** USPHS grants NS020246 and RR020146.

## 0064

## EFFECTS OF THE GABA-A RECEPTOR AGONIST THIP ON THE SLEEP EEG OF GABA-A RECEPTOR DELTA SUBUNIT KNOCKOUT MICE

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**Introduction :** THIP (Gaboxadol), is a selective GABA-A receptor agonist, described by *in vitro* studies as being more potent at delta-subunit containing receptors. GABA-A receptors containing the delta subunit are located extra-synaptically. To further elucidate the mechanism of action of THIP *in vivo*, as well as its effects on sleep and the EEG, we performed EEG recordings in GABA-A receptor delta-subunit knockout mice (delta  $-/-$ ) to investigate the effects of THIP (4 and 6 mg/kg dose) treatment versus saline control.

**Methods :** Recordings were performed in delta  $-/-$  mice and wild-type (WT) littermates. Parietal and frontal EEG electrodes, as well as two EMG electrodes were implanted. THIP (4 mg/kg) and vehicle were injected 3 h after light onset, following a crossover design with at least one week between each treatment. A third injection, THIP 6 mg/kg, was administered at least 7 days after the crossover treatment. Continuous EEG and EMG recording were obtained throughout the 12-h light period.

**Results :** Preliminary analyses of the EEG recordings in  $n=4$  mice of each genotype showed similar effects of THIP 4 mg/kg on the nonREM sleep

EEG in WT mice as published previously. A massive increase in EEG power lasting approx. 1.5 hours was observed in both EEG derivations, especially in the waking EEG. Similar changes occurred in the EEG spectrum in subsequent nonREM sleep. All changes were more prominent in the frontal EEG. Compared to the EEG effects in WT mice, THIP (4 mg/kg) elicited only minor effects on the EEG of the delta  $-/-$  mice both during waking and nonREM sleep.

**Conclusion :** Our results support the *in vitro* data that THIP acts preferentially via GABA-A receptors containing the delta subunit. The large effects of THIP on the EEG spectrum in waking indicate that its effects do not correspond to specific mechanisms regulating sleep and the sleep EEG.

**Support (optional):** Research supported by the European Union Marie Curie (MCRTN-CT-2004-512362)

## 0065

## EFFECT OF NEUROPEPTIDE "S" ON SLEEP AND WAKEFULNESS: ROLE OF HYPOCRETIN NEURONS

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**Introduction :** We recently described the identification and characterization of Neuropeptide S (NPS), a wake-promoting peptide with anxiolytic properties. Here we have analyzed the effect of local injections of NPS on different brain areas. To determine whether the wake-promoting effects of NPS are mediated by hypocretin-containing neurons in the lateral hypothalamus we analyzed the effect of NPS on sleep in wild-type and hypocretin-deficient transgenic mice.

**Methods :** Mice (C57BL6J;  $n=4$ ) were implanted with EEG and EMG electrodes to score the states of vigilance and with intracerebral cannulas in different brain regions, including the lateral hypothalamus. States of vigilance were scored using Sleep Sign software during 6 hours after local injection of NPS (10-100 pmol). Orexin-ataxin mice (kindly provided by Dr. Takeshi Sakurai, University of Tsukuba;  $n=4$ ) were implanted with icv cannulas in addition to EEG and EMG electrodes. NPS (1 nmol) was injected in the lateral ventricles during the light period and EEG and EMG were recorded 6 hours after injection. Data was analyzed using ANOVA.

**Results :** Local injection of NPS in the lateral hypothalamus dramatically increased wakefulness during the first hour after injection, suggesting that at least some of the wake promoting effects of NPS are mediated through this brain region. The effect of intracerebroventricular infusion of NPS (1 nmol) in orexin ataxin mice was undistinguishable from that of wild-type mice, suggesting that activation of hypocretin neurons is not essential for the wake promoting activity of NPS.

**Conclusion :** Neuropeptide S promotes wakefulness by activating hypocretin and other hypothalamic neurons. Hypocretin neurons do not seem to be essential for the wake-promoting activity of Neuropeptide S. Other hypothalamic neurons, including those containing MCH, and extrahypothalamic targets of NPS may mediate its arousal-inducing effect.

**Support (optional):**

0066

**DIFFERENTIAL EFFECTS OF MODAFINIL DURING THE EARLY POSTNATAL PERIOD IN RATS**

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**Introduction :** During the first postnatal week in rats, the lengths of sleep bouts increase significantly. Utilizing precollicular transections and electrolytic lesions, we recently showed that this elongation is influenced by hypothalamic structures, including the GABAergic preoptic area (POA), which promotes sleep in adult rats by inhibiting wake-promoting areas of the brain. We found that POA lesions in infants had wake-promoting effects similar to those seen in adults, suggesting that the POA is similarly performing an inhibitory function at this early age. However, during this early postnatal period, GABA has been reported to be primarily excitatory, rather than inhibitory. To investigate this apparent discrepancy, we administered the drug modafinil at different postnatal ages and examined the resulting sleep patterns. Modafinil has been hypothesized to promote wakefulness in part by potentiating inhibition of GABAergic POA neurons, thereby allowing us to estimate the possibly differential amounts of inhibition provided by these neurons across the postnatal period.

**Methods :** Postnatal day (P)2 and P9 Sprague-Dawley Norway rats (*Rattus norvegicus*) were injected intraperitoneally with modafinil or methylcellulose vehicle, and sleep/wake behaviors were measured using nuchal muscle electromyography and observation of associated motor behaviors.

**Results :** At both ages modafinil produced a significant increase in wake bout durations, but only at P9 did it also produce a significant decrease in sleep bout durations.

**Conclusion :** This suggests that POA inhibitory control over wake-promoting regions of the brain increases during the early postnatal period.

**Support (optional):** Supported by NIMH grants MH50701 and MH66424 to M.S.B.

0067

**CART PEPTIDE PROMOTES WAKE AND SEIZURE ACTIVITY IN THE RAT**

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**Introduction :** CART peptides are putative neurotransmitters implicated in feeding, reward, and neuroendocrine integration. Reciprocal neuronal interactions between CART and dopamine (DA) have been suggested based on: 1) immunomicroscopy; 2) extracellular DOPAC and HVA increases in nucleus accumbens after icv CART infusion; and 3) upregulation of CART mRNA following traditional psychostimulants and in mice lacking the DA D3 receptor. DA, and the mesolimbic DA system in particular, is increasingly viewed as a key substrate that promotes wakefulness. Thus, we investigated the hypothetical wake promoting effects of CART.

**Methods :** Rats (n = 9) were implemented with EEG and EMG electrodes and a guide cannula for icv administration. Following baseline recording, rats received icv injections of either saline, 0.5, 1.0, or 2.0 µg/2µl of active CART 55-102 peptide within 1 hour of lights-on, the beginning of the rats' normal sleep period. A separate control group of rats (n=7) received delivery of either saline or inactive CART peptide, CART 1-27.

**Results :** Injections of active CART peptide produced a dose-dependent increase in the amount of subsequent wake time within all rats. Continuous wakefulness of up to 4 hours was observed at the 2µg dose. This increase in wake was followed by rebound sleep not unlike that observed following psychostimulant administration. These effects were specific to the active peptide as infusion of inactive CART peptide did not

produce changes on subsequent behavioral state. Separately, 3 rats were given 5µg of active CART which consistently resulted in seizure activity as demonstrated by spike-wave activity in the EEG and tonic body tremors and prostrate posturing.

**Conclusion :** This is the first preliminary report of the effects of CART peptide on EEG and sleep/wake architecture in the rat. The robust nature of the 2µg active CART dose on wake promotion is consistent with known functional anatomy of CART/DA, but will require additional experiments to decipher the cellular and subcellular mechanisms mediating this response.

**Support (optional):** Support contributed by NS43374, RR00165, DA00418, DA10732.

0068

**DISINHIBITION OF PERIFORNICAL HYPOTHALAMIC NEURONS BLOCKS THE ABILITY OF PONTINE CARBACHOL TO PRODUCE REM SLEEP-LIKE STATE IN ANESTHETIZED RATS**

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**Introduction :** The perifornical (PF) region of the posterior hypothalamus was identified by von Economo (1930) as important for the maintenance of wakefulness. The subsequent discovery that the region contains cells that synthesize orexins, the peptides with wake-promoting properties and actions that prevent narcolepsy/cataplexy, suggested that neuronal activity generated in the PF region suppresses REM sleep. We tested this prediction in anesthetized rats in which REM sleep-like state can be produced pharmacologically and PF hypothalamic cells, including those that contain orexin, can be activated by the GABAA receptor antagonist, bicuculline.

**Methods :** In 6 urethane-anesthetized, paralyzed and artificially ventilated rats, carbachol injection (10 nl, 10 mM) were made into the dorsomedial pons before and at different times after unilateral microinjections of bicuculline (20 nl, 1 mM) into the PF region.

**Results :** As in our earlier studies, pre-bicuculline pontine carbachol injections elicited 2-4 min-long REM sleep-like episodes of cortical and hippocampal activation, suppression of hypoglossal (XII) nerve activity (by 75±5% (SE); p<0.01) and slowing of the respiratory rate (from 45±2 to 36±1 min<sup>-1</sup>; p<0.01). Following hypothalamic bicuculline injections, XII nerve activity was increased by a maximum of 100±24% (p<0.05) for 34±3 min, respiratory rate increased from 45±2 to 48±2 min<sup>-1</sup> (p<0.05), and distinct changes occurred in the cortical and hippocampal signals. In 4 rats in which carbachol injections were made during the first 10-50% of the total period of the response to bicuculline, all REM sleep-like effects of carbachol were abolished. They could be elicited again at 50-125% of their original magnitude by carbachol injections made after termination of the effects of hypothalamic bicuculline.

**Conclusion :** These results demonstrate that disinhibition of neurons located in the hypothalamic PF region results in suppression of REM sleep-like phenomena at multiple levels, including the cortical, hippocampal, motoneuronal, and respiratory rhythm generator.

**Support (optional):** HL-071097.

0069

**TWO-PORE DOMAIN POTASSIUM CHANNEL TASK-1: EFFECTS ON SLEEP OF INTRACORTICAL INJECTIONS OF AN ANTI-TASK-1 ANTIBODY**

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**Introduction :** During NREM sleep, the membrane potential of all cells

in the cerebral cortex undergoes slow oscillations (<1 per second), which includes a hyperpolarization phase characterized by the interruption of neuronal firing. Under natural conditions, the transition between waking and sleep is governed by the reduced firing of brain neuromodulatory systems with diffuse projections, which produces changes in several ion currents that influence cell excitability. One such current is a potassium (K<sup>+</sup>) conductance, whose increase results in a 10 to 20 mV hyperpolarization of the resting membrane potential. The nature of this K<sup>+</sup> current is still debated, but two-pore domain K<sup>+</sup> channels could be involved since 1) they are highly expressed in the thalamocortical system and 2) their opening is affected by neuromodulators and by general anesthetics. Here, we studied the effect on sleep of blocking one of these channels, TASK-1.

**Methods :** Male Wistar Kyoto rats (7-8 week old; 200-250g) were implanted for chronic polygraphic recordings and kept in a 12:12 light:dark cycle (lights on at 10am). Local field potentials (LFPs) were measured in the left and right parietal and occipital cortices using bipolar electrodes. Drugs were injected in the right occipital cortex (1ul/min, up to 2 ul) using a CMA 400 Syringe Pump System (>= 3 injections/rat, spaced apart at least 4 days; onset of injections between 1 and 2PM). Sleep stages were scored visually based on 4-s epochs. EEG power spectra of consecutive 4-s epochs (FFT routine, Hanning window) were calculated for the parietal and occipital derivations of both sides within the 0.25-25.0 Hz frequency range. For behavioral analysis, real-time 24-h video recordings were obtained for all rats.

**Results :** An antibody designed against the extracellular portion of the rat TASK-1 channel abolished EEG signs of NREM sleep on the right (injected) occipital cortex for up to 3 hours after the injection. The effect was dose-dependent, reversible, and site-specific. The behavior of the rat was unchanged after the injection, and remained consistent with the EEG on the left hemisphere. Injections of an antibody against the extracellular portion of NCAM (n=3), anti-Kv1.3 (mainly microglial; n=3), of anti-rabbit IgG (n=3) did not affect the sleep EEG, nor the behavioral state of the animal. EEG power spectrum analysis is in progress.

**Conclusion :** The two-pore domain potassium channel TASK-1 antibody injection affects the sleep EEG in a dose-dependent, reversible, and site-specific manner.

**Support (optional):** Supported by a grant from the United States Defense Advanced Research Projects Agency.

## 0070

### SLEEP PRESSURE AFFECTS EARLY AND LATE COMPONENTS OF ELECTRICALLY INDUCED CORTICAL RESPONSES IN THE RAT

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**Introduction :** According to a recent hypothesis, waking is associated with synaptic potentiation and sleep with synaptic downscaling (Tononi and Cirelli, 2003). A corollary of the hypothesis is that the amplitude and slope of cortical evoked responses (ERs), which are established indicators of synaptic strength, should increase during wakefulness and decrease after sleep. We therefore investigated effects of preceding sleep-wake history on cortico-cortical ERs in the rat.

**Methods :** Male adult Wistar rats (n=3,4 per group) were used. Cortical local field potentials (LFP) were recorded with bipolar concentric electrodes from left frontal and right parietal derivations while the right frontal cortex was stimulated (0.5 ms duration, 500 µA). Waking ERs were collected during an undisturbed baseline at 4 or 6 h intervals and after 4 h sleep deprivation (SD) starting at light onset. EEG was continuously recorded to quantify vigilance states and slow wave activity (SWA) in NREM sleep before and after ERs sessions.

**Results :** Average ERs consisted of an early component (latency approximately 15 ms) with two peaks, followed by a large late component (latency approximately 100 ms). Both the slope and the amplitude of the first component increased after SD, and declined progressively during subsequent recovery. The second component had a shorter duration and faster build up both after SD and under naturally elevated sleep pressure at the beginning of the light period. The time course of these ER parameters paralleled that of SWA. Similar effects were observed for both the frontal (transcallosal) and the parietal (ipsilateral) ERs. Under high sleep pressure, additional late components in the theta range (5-6 Hz) were observed. These evoked theta-bursts resembled spontaneous theta-bursts observed during undisturbed quiet wakefulness.

**Conclusion :** As predicted by the synaptic homeostasis hypothesis, two established indicators of synaptic strength - the amplitude and slope of cortical evoked responses (ERs) - increase during wakefulness and decrease after sleep. As indicated by the SD experiment, the observed effects are related to sleep-wake history rather than to circadian time.

**Support (optional):** Swiss National Science Foundation, NIH Director's Pioneer Award

## 0071

### DEVELOPMENT OF STATE-DEPENDENT NEOCORTICAL ACTIVITY IN INFANT RATS

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**Introduction :** In infant rats, state-dependent neocortical activity is absent during the first two postnatal weeks. Exactly why and how state-dependent neocortical activity emerges at this time is unknown. In infant humans, however, before the onset of state-dependent neocortical activity, there is evidence of slow activity transients (SATs) that are related to the slow oscillation (<1 Hz). In order to investigate whether similar waveforms exist in infant rats we recorded EEG activity using one of two filtering methods: AC (.1-500 Hz) or DC (open band pass).

**Methods :** Subjects were 9, 11, and 13-day-old rats. Cortical EEG electrodes and nuchal EMG electrodes were implanted in all subjects. Subjects were allowed to move freely in a testing chamber maintained at thermoneutrality. EEG signals were filtered in one of two ways: AC (.1 - 500 Hz), or DC (open band pass). We examined EEG records for the emergence of delta activity and the frequency of SATs.

**Results :** Preliminary data indicate that, in agreement with previous studies, state-dependent neocortical activity (specifically delta waves) emerges at around P11 in the infant rat and there is an increase in delta power between P11 and P13. Interestingly, much like in human infants, we found evidence of SATs before the onset of state-dependent neocortical activity, and the frequency of SATs decreased with the onset of delta activity.

**Conclusion :** The presence of SATs in the EEG before the onset of state-dependent neocortical activity could shed light on the mechanisms responsible for the emergence of delta activity.

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## 0072

### SLEEP HOMEOSTASIS, SLOW WAVES AND CORTICAL SYNCHRONIZATION: II. A LOCAL FIELD POTENTIAL STUDY IN THE RAT

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**Introduction :** According to a recent hypothesis, waking is associated with synaptic potentiation and sleep with synaptic downscaling. Computer simulations show that synaptic downscaling leads to a decreased incidence

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and slope of cortical slow waves, to an increase in their duration, and to the occurrence of multipeak waves. These changes are reflected in a decrease of sleep slow wave activity (SWA, 0.5-4 Hz). We examined these predictions under high and low sleep pressure in the rat.

**Methods :** Cortical local field potentials (LFP) were recorded with bipolar concentric electrodes from the frontal, parietal and occipital derivations in two groups of male adult Wistar rats ( $n=3,6$ ), during baseline and after 2 h sleep deprivation (SD) starting at light onset. LFP signal was bandpass filtered [0.5-4 Hz (stopband frequencies 0.1-10 Hz)], and slow waves were detected as positive signal deflections between two consecutive negative peaks.

**Results :** During 12-h light period SWA in the LFP signal showed well-known homeostatic decline. Concomitantly, high-amplitude ( $>$ median +1 std dev) slow waves exhibited: i) a pronounced decrease in their incidence ( $n/\text{min}$  of NREMS), with only a minor change in mean amplitude; ii) a decrease in the slopes of the up- and down-swings; iii) an increase in wave duration; iv) a higher proportion of waves with more than one peak. These changes were evident in all three derivations. Homeostatic changes in SWA were strongly correlated with the time course of slow wave incidence. After SD, high-amplitude slow wave incidence and their slopes increased further, while wave duration and the number of multipeak waves decreased.

**Conclusion :** Several parameters of LFP slow waves during sleep changed with decreasing sleep pressure. As indicated by computer simulations, these changes were consistent with a progressive decrease in the strength of corticocortical synapses leading to reduced synchronization of sleep slow waves.

**Support (optional):** Swiss National Science Foundation, NIH Director's Pioneer Award

### 0073

#### SLEEP HOMEOSTASIS, SLOW WAVES AND CORTICAL SYNCHRONIZATION: III. A HIGH-DENSITY EEG STUDY IN HUMANS

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**Introduction :** According to a recent hypothesis, waking is associated with synaptic potentiation and sleep with synaptic downscaling. Computer simulations show that synaptic downscaling leads to a decreased incidence and slope of cortical slow waves, to an increase in their duration, and to the occurrence of multipeak waves. These changes are reflected in a decrease of sleep slow wave activity (SWA, 0.5-4 Hz). We examined these predictions under high and low sleep pressure in humans.

**Methods :** High-density EEG (Geodesic Sensor Net, 256 channels) was recorded across an entire night of sleep in 5 subjects. The EEG was visually scored (20s epochs) for the first 3 cycles and artifacts rejected (4s epochs). The signal was ear-referenced and bandpass filtered (0.5 - 4 Hz). Slow waves were detected as negative signal deflections between two consecutive positive peaks.

**Results :** During the first 3 cycles of NREM sleep, SWA in the EEG signal showed well-known homeostatic decline. Concurrently, high-amplitude ( $>$ median +1 std dev) slow waves exhibited: i) a pronounced decrease in their incidence ( $n/\text{min}$  of NREMS), with only a minor change in mean amplitude; ii) a decrease in the slopes of the up- and down-swings; iii) an increase in wave duration; iv) a higher proportion of waves with more than one peak. These changes were independent of channel location. Homeostatic changes in SWA were strongly correlated with the time course of slow wave incidence. Furthermore, high-amplitude slow waves propagated from distinct origins and were detected in a varying

subset of channels, with higher amplitude waves affecting more channels. Furthermore, multipeak waves appeared to have multiple origins and may be the result of wave interaction.

**Conclusion :** Several parameters of EEG slow waves during sleep changed with decreasing sleep pressure. As indicated by computer simulations, these changes were consistent with a progressive decrease in the strength of corticocortical synapses leading to reduced synchronization of sleep slow waves.

**Support (optional):** This research was supported by National Research Service Award (NRSA) T32 GM07507, Swiss National Science Foundation, and NIH Director's Pioneer Award.

### 0074

#### EFFECTS OF MICRODIALYSIS OF ANISOMYCIN INTO LATERAL PREOPTIC AND PERIFORNICAL AREAS ON SLEEP IN RATS

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**Introduction :** Sleep is a restorative process which promotes brain protein synthesis. Although the effects of systemic inhibition of protein synthesis on sleep has been investigated, no study has investigated the effects of localized inhibition of protein synthesis in a sleep or wake promoting area. Therefore, we compared the effects on sleep of microdialysis of a protein synthesis inhibitor, anisomycin (ANI), into the lateral preoptic area (IPOA) and perifornical area (PF) in free moving rats.

**Methods :** Eleven male Sprague-Dawley rats were implanted with EEG and EMG electrodes; 6 had guide cannula directed at the IPOA and 5 had cannula directed at the PF. After 5-7 days of recovery, microdialysis probes were inserted. Sleep recording started 18 hrs after probe insertion. In a random order, 2 doses of anisomycin (500 nM or 5  $\mu\text{M}$ ) or artificial CSF were microdialyzed for 2 hrs followed by 18 hrs of ACSF perfusion, beginning at either ZT 3 (IPOA) or ZT 15 (PF). On any given day, each rat received only one of the three treatments. Data from the first 4 hours of recording after beginning of treatments were analyzed with ANOVA.

**Results :** In the IPOA, compared to ACSF, 5 $\mu\text{M}$  of anisomycin significantly ( $p < 0.05$ ) reduced active wake (ACSF:52.41  $\pm$  6.61; ANI:29.86  $\pm$  4.72) and increased SWS2 (ACSF:11.12  $\pm$  3.13; ANI:32.03  $\pm$  2.15) without affecting other stages. In the PF, 5 $\mu\text{M}$  of anisomycin significantly ( $p < 0.05$ ) increased REM (ACSF:6.21  $\pm$  1.62; ANI: 12.06  $\pm$  2.87) and did not alter other stages.

**Conclusion :** The findings suggest that protein synthesis inhibition facilitates the activity of sleep-promoting neurons in the IPOA, but suppresses the activity of REM inhibiting neurons in the PF, either directly or indirectly. Since inhibition of protein synthesis in sleep-wake regulatory sites increases sleep, a need for protein synthesis may normally promote sleep.

**Support (optional):** This work was supported by the grants: MH 47480, NS-050939

### 0075

#### RAPID CHANGES IN GLUTAMATE LEVELS DURING SLEEP DEPRIVATION, WAKING AND REM SLEEP

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**Introduction :** Glutamate is the most ubiquitous excitatory neurotransmitter. The recent development of glutamate biosensors allows for the first time an assessment of the time course of glutamate release across the

sleep-wake cycle.

**Methods :** Electrodes for the measurement of sleep-wake parameters were chronically implanted in male Sprague-Dawley rats. A guide cannula was also implanted 1 mm above the target areas. One week after surgery the glutamate sensor (Pinnacle Technology Inc., Kansas) with 1-mm long active area was inserted through the guide cannulae. This glutamate sensor, is an enzyme based biosensor designed for the measurement of rapid changes in the extracellular concentrations of brain glutamate level in freely behaving rats. This enzymatic biosensor (Platinum-Iridium electrode) with integrated Ag/AgCl reference electrode is designed for the *in vivo* glutamate measurements.

**Results :** There was a progressive increase in glutamate level in the cortex and perifornical area during active waking/ grooming. The level of glutamate increased up to 10 nmoles in perifornical area and 7 nmoles in cortical region. The latency to the peak level of glutamate levels changed (20-400 sec) depending on episode duration. In quiet waking and slow wave sleep glutamate level remain unchanged. An immediate (<5sec) and progressive increase in glutamate levels during REM sleep (to 7 nmoles) was also observed in PH-TMN region (n=3). Sleep deprivation or extended periods of spontaneous prolonged waking produced increases in glutamate levels in the cortex (n=2), PH-TMN (n=2) and perifornical hypothalamic region (n=2). An increase in the basal level of glutamate level was also seen in the dark phase (active period) as compared to the light phase.

**Conclusion :** Glutamate levels in a variety of brain areas increase in proportion to waking and REM sleep durations and may drive or be driven by processes regulating sleep need.

**Support (optional):** HL41370, 1P50, HL060296, VA Medical Research Services.

## 0076

### PONTINE CHOLINERGIC AND NORADRENERGIC PROJECTIONS TO THE HYPOGLOSSAL NUCLEUS

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**Introduction :** By acting on different receptors, cholinergic agonists increase or decrease the activity of hypoglossal (XII) motoneurons which innervate the genioglossus, an important upper airway dilator. Since pontine cholinergic cells have increased activity during wakefulness and/or REM sleep, they could contribute to some aspects of sleep-wake dependent changes in upper airway motor tone. However, the data about the projections of pontine cholinergic neurons to cranial motor nuclei are contradictory. Our goal was to determine the source(s) of such projections to the XII nucleus.

**Methods :** Retrograde tracer, fluoro-gold (FG; 4%, 5-10 nl) was injected into the XII nucleus of Sprague-Dawley rats (n=5). After 7 days, the animals were perfused and every 5th brainstem section immunohistochemically processed for nitric oxide synthase (NOS), a marker for pontine cholinergic neurons, or tyrosine hydroxylase (TH), a marker for catecholaminergic neurons.

**Results :** In all 5 rats, we found 215 NOS-positive pontine neurons retrogradely labeled with FG; this corresponded to ~1.3% of the total number of pontine cholinergic neurons. The projections were bilateral, with 72% of double-labeled cells located in the ventral portion of the pedunculopontine tegmental nucleus pars compacta (PPT-pc) and the remaining 28% in the laterodorsal tegmental nucleus pars alpha (LDT). In the same animals, we found 310 neurons in the A5, A7 and sub-locus coeruleus regions that were both TH- and FG-positive; this corresponded to ~7% of the total number of noradrenergic neurons in these three groups combined.

**Conclusion :** Cholinergic cells of the PPT-pc and LDT project to the XII nucleus, but the projection is relatively weak compared to the input from

pontine noradrenergic neurons. Whereas the withdrawal of noradrenergic excitation makes an important contribution to sleep-related decrements of XII motoneuronal activity, pontine cholinergic projections may contribute to wakefulness and/or REM sleep-related increases of that activity.

**Support (optional):** HL-47600.

## 0077

### SPATIO-TEMPORAL CHARACTERISTICS OF FMRI SIGNAL FLUCTUATION DURING LIGHT SLEEP

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**Introduction :** During rest, a number of physiologic processes remain active in the human brain, some of which are observable with fMRI. Measurements performed in the absence of stimuli presentation have revealed temporally correlated signal fluctuations within functionally related regions. However, it is still unknown whether this correlated activity continues during sleep. To investigate this, we performed fMRI during an extended resting state and early sleep while monitoring alertness using EEG.

**Methods :** Eleven volunteers participated in this study. Simultaneous fMRI and EEG were collected on a 3.0T scanner. The experimental paradigm was composed of a 50-minute rest period, followed by a 10-minute visual task. During the rest period, the subjects were instructed to close their eyes and encouraged to fall asleep. EEG datasets were visually scored in 30 s epochs (by TJB). To detect and characterize spatio-temporal patterns of correlated activity, we applied spatial independent component analysis (ICA) to awake and sleep periods separately. After ICA, inter-subject consistency of ICs was evaluated by determining spatial overlap.

**Results :** During both awake rest and stage 1 and 2 sleep, we found a large number of ICs that involved almost exclusively gray matter regions. We found 18 (awake rest) and 18 (sleep) ICs that showed high spatial consistency across subject groups, and resembled functionally connected regions. The spatial extent and anatomical location of consistent ICs were very similar between awake rest and sleep. These results suggest that spatially correlated activity during rest is not specific to the wake state.

**Conclusion :** Accurate mapping of resting state activity patterns indicates an involvement of most brain regions that continues during early sleep. This suggests that this phenomenon may not represent conscious mentation.

**Support (optional):**

## 0078

### PONTOMEDULLARY REGIONS EXHIBITING C-FOS ACTIVATION FOLLOWING REM SLEEP-LIKE EFFECTS ELICITED IN ANESTHETIZED RATS BY PONTINE INJECTIONS OF CARBACHOL OR CARBACHOL WITH BICUCULLINE

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**Introduction :** In anesthetized rats, both carbachol (CARB) and bicuculline (BIC) elicit REM sleep-like episodes from overlapping pontine sites. The effects include cortical and hippocampal activation and suppression of hypoglossal nerve activity. We recently determined that, by injecting the two drugs together repeatedly, one can maintain a steady REM sleep-like state for at least 30 min. We combined this approach with c-fos protein detection to localize brainstem cells activated following pon-

tine injections of CARB and BIC.

**Methods :** In 3 urethane-anesthetized, paralyzed and artificially ventilated rats, 4 successive 10 nl pontine injections of CARB (10 mM) + BIC (2 mM) were made at 8-12 min intervals; they produced a REM sleep-like episode lasting 36-39 min. In 2 rats, similarly timed successive microinjections of saline were made at a site at which one CARB injection made 80 min earlier elicited a REM sleep-like episode lasting 3-4 min. In another 2 rats, we made similarly localized and timed successive microinjections of saline only. About 15 min after the last injection, the animals were perfused and brainstem sections subjected to immunohistochemistry for c-fos alone or c-fos and nitric oxide synthase, a marker for pontine cholinergic cells.

**Results :** Compared to the rats with saline injections only, those with single CARB injections exhibited increased c-fos expression in multiple pontomedullary sites, and those with multiple CARB+BIC injections had even more c-fos-expressing cells in the same locations. The effects of CARB and CARB+BIC were particularly strong in non-cholinergic cells of the dorsolateral parabrachial region, the medial vestibular nucleus, reticular region located ventrolateral to the nucleus prepositus hypoglossi, and medullary intermediate reticular region (IRt).

**Conclusion :** The sites with c-fos expression in this animal model are similar to those previously identified as c-fos-expressing following periods of intense natural REM sleep. The activation in the IRt region may originate in inspiratory hypoglossal premotor cells that are activated during REM sleep.

**Support (optional):** HL-47600.

### 0079

#### NEONATAL INTERMITTENT HYPOXIA IN RATS INDUCES SEX-SPECIFIC INCREASES IN DOPAMINE LEVELS IN THE NUCLEUS ACCUMBENS

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**Introduction :** Increased sleep, cognitive dysfunction, and increased locomotor activity characterize post hypoxic male rats. These traits are postulated to reflect reduced extracellular dopamine (DA) within nigrostriatal circuitry, hippocampal apoptosis, or oxidative damage to forebrain neurons. Recently, we demonstrated that male post hypoxic rats exhibited increased DA content in the striatum; an observation leading us to examine the dopaminergic activity within the mesolimbic circuit.

**Methods :** 10 male and 12 female Sprague-Dawley rats were studied. Between post natal (PN) days 7-11, pups were randomly assigned to either an intermittent hypoxia inducing chamber, or a normoxic chamber, where they received either 6 hours of intermittent hypoxia per day or only bursts of room air. At the conclusion of the protocol on PN 11, all pups were permitted to mature without further intervention. On PN 80, rats were sacrificed and the nucleus accumbens dissected. Accumbens tissue was homogenized and total DA content determined with high performance liquid chromatography.

**Results :** Total tissue content of dopamine (mean  $\pm$ 1 SEM picograms DA/ng protein) was significantly increased in the nucleus accumbens of post hypoxic (N=6) male rats compared to normoxic (N=4) littermates ( $232.9 \pm 47.9$  vs  $156.8 \pm 38.97$ ,  $p = 0.030$ ). However, no differences existed between post hypoxic (N=6) female rats compared with normoxic (N=6) littermates ( $222.8 \pm 90.5$  vs  $219.05 \pm 62.7$ ).

**Conclusion :** We demonstrate impaired integrity of the mesolimbic dopamine system in post hypoxic male but not female rats. This vulnerability of the dopaminergic system to intermittent hypoxic insults thus appears to be sex-specific. Ongoing studies are aimed at delineating the behavioral significance of these novel findings.

**Support (optional):** HL 72722 (Decker) and NS 40221(Rye)

### 0080

#### POLYSIALYLATED NEURAL CELL ADHESION MOLECULE IMMUNOREACTIVITY IN THE RAT SLEEP/WAKE-REGULATORY SYSTEM: A POSSIBLE ROLE IN SLEEP-WAKE REGULATION

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**Introduction :** The neural cell adhesion molecule is a cell-surface glycoprotein, and its highly sialylated form, PSA-NCAM, has been shown to be involved in axonal growth during development and synaptic plasticity in adult (e.g., during LTP). A recent study demonstrating that synaptic rewiring is involved in regulation of food intake led us to hypothesize that the regulation of sleep-wake cycles may also involve synaptic plasticity. PSA-NCAM may have a role in such synaptic reorganization. The specific goal of this study was to examine whether PSA-NCAM immunoreactivity is present in brain areas involved in the regulation of sleep and wake.

**Methods :** Adult male Wistar rats were perfused during the light phase. Dual immunofluorescence labeling was performed using a monoclonal antibody to PSA-NCAM and antibodies to neurotransmitter markers of main sleep/wake-promoting cell groups. Immunostained sections were examined using confocal microscopy.

**Results :** Dense PSA-NCAM immunoreactivity was observed in the locus coeruleus and surrounding regions, as well as in the dorsal raphe nucleus. Noradrenergic and serotonergic perikarya were surrounded by PSA-NCAM immunoreactive elements. Moderate PSA-NCAM immunoreactivity was found in the laterodorsal tegmental nucleus, ventral tuberomammillary nucleus, and respectively adjacent areas. Light PSA-NCAM staining was seen in the ventral tegmental area and perifornical region. In addition, PSA-NCAM-immunoreactive cell bodies were observed in a number of brain regions, including the hippocampus, as previously reported, but also selected cortical regions and zona incerta.

**Conclusion :** We have shown that PSA-NCAM immunoreactivity is present in a number of wake-promoting regions, with particularly dense expression in the locus coeruleus and dorsal raphe nucleus. The immunoreactivity often appears to surround noradrenergic and serotonergic neurons in these regions. These results suggest that PSA-NCAM, which has been shown to play a role in synaptic plasticity, may also play a role in sleep-wake regulation. Possible changes in PSA-NCAM immunoreactivity after sleep deprivation are currently under investigation.

**Support (optional):**

### 0081

#### INVESTIGATING A DOPAMINERGIC MECHANISM OF ACTION FOR MODAFINIL IN DROSOPHILA

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**Introduction :** Available evidence suggests that modafinil, a novel wake-promoting drug, is a dopamine transporter (DAT) antagonist which increases dopaminergic (DA) neurotransmission in mammals. *Drosophila melanogaster* also respond to modafinil with decreased rest and disruption of sleep consolidation. We tested whether modafinil acts via DAT in *Drosophila* by examining the response of fumin flies (fmm; DAT null flies who display increased baseline activity levels and decreased sleep) to modafinil.



**Methods :** The locomotor activity of wild type and fmn flies was monitored, using the Trikinetics DAM system, before and after exposure to modafinil and nisoxetine (a noradrenaline transporter antagonist with a high affinity to *Drosophila* DAT). Changes in total activity and sleep (defined as at least five consecutive minutes of zero activity counts) were compared within flies and between lines.

**Results :** Fmn flies are hypersensitive to modafinil and hyposensitive to nisoxetine compared to wild type. The decrease of sleep seen in fmn lines on modafinil was greater than in controls. However, whereas nisoxetine also decreases sleep in wild type lines, the response of fmn flies to nisoxetine was greatly attenuated. Fmn flies were also resistant to the lethal effects of higher doses of nisoxetine seen in wild type, but more sensitive to those of high modafinil doses.

**Conclusion :** Our preliminary evidence suggests that modafinil does not act via the DAT in *Drosophila*. This is an opposite result to that from DAT-null mice, who are unresponsive to modafinil, although they also have altered responses to caffeine and hence there may be developmental alterations. Our results question whether modafinil acts through DAT or the dopaminergic system, and indicates that *Drosophila* may be a useful model to investigate modafinil's as yet unknown mechanism of action.

**Support (optional):** This research was supported by Cephalon, Inc.

## 0082

### LARGE-SCALE MODELING OF THE CORTICAL RESPONSE TO TRANSCRANIAL MAGNETIC STIMULATION DURING WAKEFULNESS AND SLEEP

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**Introduction :** During wakefulness, transcranial magnetic stimulation (TMS) of specific cortical targets produces an evoked EEG response that reverberates amongst distant cortical sites. During NREM sleep early in the night, the same perturbation produces a response that is initially larger than during wakefulness, but rapidly decays without propagating to other sites. It has been hypothesized that this breakdown in effective connectivity may be related to the fading of consciousness during sleep. To investigate the neural mechanisms underlying the observed disruption of signal propagation, we developed a large-scale computer model of the cortical evoked response to TMS during wakefulness and sleep.

**Methods :** Building upon previous modeling work, we constructed a large-scale simulation that incorporates key anatomical and physiological features of the motor thalamocortical system and includes over 30,000 spiking, integrate-and-fire neurons containing several intrinsic currents. These neurons are arranged in a primary motor area and a premotor area and are connected by over 5 million AMPA, NMDA, GABAA and GABAB synapses. The simulation also includes a diffuse neuromodulatory system that regulates whether the model is in a waking or sleep mode.

**Results :** The model produced spontaneous firing rates and membrane potential levels similar to those generated in vivo during quiet wakefulness and NREM sleep. In the waking mode, TMS perturbation of the primary motor area produced strong firing at the site of stimulation for 5 ms. This activity propagated to the premotor area, resulting in a wave of spiking approximately 15 ms following stimulation. In the sleep mode, TMS delivered to the primary motor area typically produced a strong, but brief wave of activation at the site of stimulation that did not propagate to the premotor area. Further simulations are examining to what extent the observed disruption of signal propagation during sleep can be accounted for by the bistability of cortical circuits in the slow-oscillation mode and by the effects of thalamic hyperpolarization.

**Conclusion :** We developed a large-scale thalamocortical model that reproduces the breakdown of cortical effective connectivity during sleep recently observed in humans with TMS/EEG and permits the detailed investigation of the underlying neural mechanisms.

**Support (optional):** NIH Pioneer Award

## 0083

### CHANGES IN CSF HYPOCRETIN-1, BLOOD GLUCOSE AND INSULIN LEVELS AFTER LOCOMOTOR ACTIVITY IN NORMAL DOGS

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**Introduction :** Hypocretin (Hcrt) levels in the CSF are greatly elevated following periods of waking activity. It is unclear, however, whether this increase is due to motor activity per se or correlated changes in emotion and arousal. In this study we measured CSF Hcrt-1 level in dogs after treadmill exercise of varying speed. We also measured blood glucose and insulin levels before and after exercise to see if changes in Hcrt level are correlated with changes in the levels of glucose and insulin.

**Methods :** Normal adult Doberman pinschers were trained to locomote at varying speeds on a treadmill. Five treadmill speed conditions were used, from 0 to 160 m/min over a 30 min period. Rectal temperature, heart rate, blood pressure and respiration were measured immediately before and after the treadmill procedure. Three ml of blood was collected immediately before and after treadmill for blood glucose and insulin measurements. Two ml of CSF was collected thirty or sixty min after treadmill under thiopental anesthesia from cisterna magna with a spinal needle. Insulin and Hcrt-1 were analyzed using RIA kits.

**Results :** Intense (105 and 160 m/min) but not light (25 and 65 m/min) locomotor activity on treadmill produced a small to moderate increase in CSF Hcrt-1 (16 and 25% over baseline). This increase was much smaller than the increase we have previously reported in the same dogs after they were released into a yard allowing exploration and play. Glucose levels did not change with exercise. On the other hand, insulin was increased significantly with the speed of the treadmill. But insulin increases were not correlated with Hcrt increases.

**Conclusion :** We conclude that intense locomotor activity does activate Hcrt neurons but to a lesser extent than spontaneous play.

**Support (optional):** Supported by NS14610, MH64109 and the Department of Veterans Administration.

## 0084

### NORADRENERGIC CONTROL OF AIRWAY MOTONEURONS DURING NATURAL SLEEP IN RATS

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**Introduction :** One of the hallmarks of sleep is a potent suppression of skeletal muscle tone which occurs in a predictable pattern across the sleep-wake cycle. Understanding the physiological mechanisms that regulate muscle activity during sleep is important as dysregulation of these processes underlies a number of major sleep disorders including obstructive sleep apnea, narcolepsy and REM-sleep behavior disorder. The neurophysiological mechanisms that regulate sleep-related changes in muscle activity are currently unclear. It is hypothesized that withdrawal of excitatory, noradrenergic inputs onto motoneurons reduces muscle tone during sleep (and cataplexy). Accordingly, this study aims to understand the role that the noradrenergic system plays in regulating motoneuron excitability and hence muscle tone across the sleep-wake cycle.

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**Methods :** Male, Sprague-Dawley rats (330-444g; n=6) were implanted with EEG and EMG (masseter and neck muscles) electrodes to record sleep states. Microdialysis probes were placed into the left trigeminal motor nucleus for dialysis of artificial cerebral spinal fluid (ACSF) or candidate noradrenergic agonists. Phenylephrine (PE), an  $\alpha$ -1-noradrenergic receptor agonist was infused into the trigeminal motor nucleus while masseter muscle activity was monitored during waking and sleep in freely behaving rats.

**Results :** Application of 10mM PE onto trigeminal motoneurons had minimal effects on basal masseter muscle tone during waking, NREM and REM sleep (2-way ANOVA;  $P=0.089$ ; n=6). However, this same intervention significantly increased phasic masseter muscle activity (twitches) during REM sleep (paired t-test;  $P=0.006$ ).

**Conclusion :** We conclude that the noradrenergic system plays a negligible role in mediating basal muscle tone during sleep or waking. Rather, we suggest that it may act to facilitate phasic reflex behaviors such as the masseteric reflex or other rhythmic activities like mastication.

**Support (optional):**

### 0085

#### GENDER DIFFERENCES IN SUSCEPTIBILITY TO OXIDATIVE INJURY AND SLEEPINESS FROM INTERMITTENT HYPOXIA

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**Introduction :** Adult male mice exposed to long-term intermittent hypoxia (LTIH), modeling sleep apnea oxygenation patterns, develop NADPH oxidase-dependent residual hypersomnolence and oxidative injury in select brain regions, including wake-active regions. Pre-menopausal females are less susceptible to selective oxidative brain injuries. We sought to determine whether female mice exposed to LTIH would confer resistance to LTIH-induced wake impairments and oxidative injuries.

**Methods :** Young adult male and female C57Bl/6J mice (8-10 wks old) were studied in a university laboratory. Mice were randomized to either LTIH or sham LTIH for 8 weeks. Total (24hr) wake time and mean sleep latency were measured under two conditions: rested and following 6 hours of enforced wakefulness. NADPH oxidase activation (membrane translocation), carbonylation (ELISA), and lipid peroxidation (mass spect) assays were also performed to assess gender differences in oxidative responses to LTIH.

**Results :** In contrast to the significant LTIH-induced wake impairments observed in male mice, females following LTIH showed normal wake times and sleep latencies. Female mice revealed less baseline carbonylation and less carbonylation following LTIH, but showed robust NADPH oxidase activation and lipid peroxidation. In contrast to the female relative resistance to LTIH sleepiness, female mice showed more pronounced sleepiness and delta response after enforced wakefulness.

**Conclusion :** Despite a robust oxidative response to LTIH, age-matched female mice may be protected, at least temporarily, from LTIH wake impairments by lower basal carbonylation. In contrast, females show greater wake impairments after sleep deprivation. We hypothesize gender differences in polysomnographic predictors of sleepiness and residual sleepiness in humans with sleep apnea.

**Support (optional):** NIH grants HL65225 and HL080492 to S.C. Veasey

### 0086

#### EEG RESPONSES TO MAGNETIC CORTICAL STIMULATION DURING REM SLEEP

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**Introduction :** In a previous study we used a combination of navigated transcranial magnetic stimulation (TMS) and high-density electroencephalography (HD-EEG) to measure the changes in cortical excitability and connectivity occurring during the progression from wakefulness to deep NREM sleep. These results suggested that a breakdown of cortical effective connectivity may be responsible of the fading of consciousness during NREM sleep early in the night. The aim of the present study is to test whether cortical effective connectivity recovers, at least in part, during late-night sleep, especially during REM sleep, a time at which conscious reports become longer and more vivid.

**Methods :** Subjects were allowed to sleep for 3 hours and then were requested to stay awake for another 3 hours before the experiment started at 7:00 am. Low frequency (<1 Hz) TMS was delivered to premotor cortex while subjects (n=9) lied on a reclining chair. An infrared positioning system and a 60-channel TMS-compatible EEG amplifier were used to target precisely and reproducibly the cortical region of interest while recording TMS-evoked potentials over the entire scalp.

**Results :** All subjects progressed from wakefulness to NREM sleep while stimulation was delivered. Four subjects entered a stable period of REM sleep during which at least 200 trials could be collected. In all subjects, during wakefulness, TMS induced a sustained response made of recurrent waves of activity. Specifically, a sequence of time-locked high-frequency (20 to 35 Hz) oscillations occurred in the first 100 ms and was followed by a few slower (alpha band, 8 to 12 Hz) components that persisted until 300 ms. During NREM sleep the initial fast oscillations were replaced by a high-amplitude, slower component and all TMS-evoked activity extinguished before 150 ms. With the onset of REM sleep, TMS evoked a high-frequency early response, similar to the one observed in wakefulness, but failed to induce the later (alpha band) components. A preliminary source modeling analysis revealed that, during REM sleep, the propagation of TMS-evoked activity was intermediate between wakefulness and NREM sleep.

**Conclusion :** These results suggest that i) REM sleep differs from NREM sleep due to a partial recovery of effective connectivity, associated with the presence of early fast oscillations ii) REM sleep differs from wakefulness due to a reduction of the long-range, long-lasting recurrent activations associated with later alpha components.

**Support (optional):** NIH Pioneer Award, NARSAD

### 0087

#### THE EFFECTS OF A HYDROGEN SULFIDE DONOR, NAHS, ON SLEEP IN RATS

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**Introduction :** There is a growing body of evidence that gaseous messengers play an integral role in brain function. The role of nitric oxide in sleep regulation is under intensive investigation. Another gas that is produced by the brain and present in high concentrations is hydrogen sulfide (H<sub>2</sub>S). In the brain, H<sub>2</sub>S is formed from cysteine by cystathionine beta-synthase, an enzyme which is expressed in various structures, including the hippocampus. Physiologic concentrations of H<sub>2</sub>S elicit a variety of

neuronal effects, such as the facilitation of LTP and modulation of CRH release. It has been suggested that H<sub>2</sub>S may serve as a neuromodulator in the brain. The aim of the present experiments was to test the effects of systemic and icv injections of a H<sub>2</sub>S donor, NaHS, on sleep-wake activity in rats.

**Methods :** Male Sprague-Dawley rats were implanted with EEG, EMG electrodes and icv guide cannulae. The animals were injected at dark onset with isotonic NaCl (4  $\mu$ l icv or 2 ml/kg ip) on a baseline day and NaHS (in saline) on the test day. Sleep-wake activity was monitored for 23 h after the injections.

**Results :** Icv injection of 10 and 50  $\mu$ g NaHS (n = 5 and 7, respectively) induced slight increases in NREMS and decreases in REMS. The lowest dose, 2  $\mu$ g (n = 7), did not affect NREMS amounts but decreased REMS. The same dose also suppressed EEG power in the 0.5 to 10 Hz frequency range during REMS for at least 3 h after the injection. Systemic injection of 10  $\mu$ g/kg NaHS (n = 8) induced increases in NREMS in the first 2 h.

**Conclusion :** Administration of a H<sub>2</sub>S donor affects sleep and EEG power during REMS. These observations are in line with the hypothesis that H<sub>2</sub>S may have a neuromodulator role in the central nervous system.

**Support (optional):**

## 0088

### GAMMA ACTIVITY IN EEG DURING POLYSOMNOGRAMS - COMPARISONS OF WAKE AND SLEEP STAGES

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**Introduction :** The gamma frequency range from 30 - 60 Hz has been thought to represent synaptic activity related to higher cognitive functions such as object representation and thought processes. This frequency range has been difficult to study in the past until digital EEG allowed adequate sampling rates and filtering which can faithfully reproduce the signals at these higher frequencies. The signal is generated in the primary and higher order association cortices where cognitive processing takes place. These rhythms, like other frontotemporal activity such as theta activity, apparently are under the influence of the thalamic reticular spindle generator in stage 2, 3 and 4 of NREM. Theoretically this rhythm should be present in REM.

**Methods :** 5 normal overnight polysomnograms were studied using full EEG montages but otherwise standard sleep study protocols. The sampling rate was greater than 200 Hz and the filters were open to beyond 70 Hz. Artifact-free data was then analyzed off-line using the Persyst EEG Software for gamma activity in wake, stage 1, 2, 3, 4 and REM Sleep. Gamma spectral data was extracted and analyzed.

**Results :** The polysomnograms EEGs were studied and showed substantial gamma activity with highly dynamic peaks in wake and stage 1 NREM with amplitudes in the range of 0.4 - 0.8  $\mu$ V<sup>2</sup>. These values fell to less than 0.05  $\mu$ V<sup>2</sup> squared in stages 2, 3, and rose only slightly in REM.

**Conclusion :** The gamma activity represents high frequency cortical synaptic signaling, which is dominant in wake and stage 1 and highly attenuated in stages 2, 3, 4 and to a lesser extent in REM. These findings suggest that the gamma activity reflects differences in cognitive processing between wakefulness and sleep states, both REM and NREM.

**Support (optional):** This research was supported by a grant from the Ontario Mental Health Foundation

## 0089

### THE EFFECT OF LEPTIN ON SLEEP IS ABSENT IN HISTAMINE-3 RECEPTOR DEFICIENT MICE

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**Introduction :** Histamine is an important neurotransmitter in the regulation of sleep and wakefulness. Interestingly, histamine has a prevalent role in energy metabolism and promotes satiety as well as increases energy expenditure. Histaminergic neurons have a diverse afferent and efferent projection system and are in a position to provide a link between various physiological processes. It has been shown leptin, an adipose tissue-derived hormone that regulates long-term energy homeostasis, interacts with histamine signaling in the hypothalamus. In this study, we investigated the effects of leptin on sleep-wake patterns in mice lacking the histamine-3 (H<sub>3</sub>)receptor. These mice have reduced histamine levels, and we hypothesized they would have attenuated responses to leptin administration.

**Methods :** All mice were derived from a breeding colony at Northwestern University and maintained on a 12:12 L:D (lights on 06:00) schedule with free access to regular chow and water. At 10 weeks of age, wild-type (N=8) and H<sub>3</sub> receptor deficient (N=9) mice were surgically implanted with EEG/EMG electrodes for sleep-wake recordings. Three hours after lights on (09:00) mice were given an intraperitoneal injection of vehicle (saline, 0.3 mL) or recombinant murine leptin (1.3 mg/kg, 0.3 mL) in a counter-balanced manner, separated by 3 days. Sleep-wake recordings were analyzed for 3 hours following the injection. Statistical comparisons between vehicle and leptin conditions were made using dependent sample t-tests.

**Results :** In wild-type mice, leptin (1.3 mg/kg) decreased REM sleep time by 21% in the first 3 hours after injection (vehicle, 11.5 $\pm$ 1.8 vs. 9.5 $\pm$ 1.5 minutes, p<.01). In contrast, leptin had no effect on REM sleep time in H<sub>3</sub> receptor deficient mice (vehicle, 10.4 $\pm$ 2.0 vs. 10.2 $\pm$ 1.7 minutes, NS). Leptin had no effect on NREM sleep time or on EEG power spectral values.

**Conclusion :** In wild-type mice, acute leptin administration had a significant effect on REM sleep time in mice. These data indicate that the effect of leptin on sleep involves an interaction with the histaminergic system, as H<sub>3</sub> deficient mice were resistant to the effect of leptin. Histamine may represent an important mechanistic link between sleep regulation and energy metabolism.

**Support (optional):**

0090

**THE SOMNIFICITY OF DIFFERENT ACTIVITIES DESCRIBED IN THE EPWORTH SLEEPINESS SCALE**

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**Introduction :** The somnificity of a posture, activity and situation is a measure of its capacity to induce sleep-onset in the majority of subjects. This is not a characteristic of subjects. Our aim was to demonstrate that this concept, introduced by Johns in 2002, has widespread application.

**Methods :** A population-based sample of 614 subjects (male and female, black and white, 36-48 yr) from USA, and a group of 990 patients, students and industrial workers from Australia (male and female, 17-78 yr) were studied separately. Their item-scores reported in the Epworth Sleepiness Scale (ESS) were ranked from highest (8) to lowest (1) within each subject, with ties given their mean rank.

**Results :** In the US group, item-ranks were significantly different (Wilcoxon's -T,  $p < 0.001$ ) for all items except 3 and 7. In the Australian group, all item-ranks differed significantly ( $p < 0.001$ ), except for items 3 and 7 on the one hand and 6 and 8 on the other. Activities described in the ESS formed an ordinal scale of somnificities with at least 6 levels. Item 5 (lying down to rest) had the highest somnificity, items 2,1,4,7,3, were intermediate, items 8 and 6 (sitting and talking to someone) were lowest.

**Conclusion :** This ordinal scale of somnificities is widely applicable, at least in these countries, across age, gender and race. It enables major influences on sleep propensity (posture, mental and physical activity, and environmental stimulation) to be quantified in general terms for the first time. These influences are in addition to the time of day and the duration of prior wakefulness. The results highlight the fact that sleep propensity is not a characteristic of subjects that can be accurately measured independently of their posture and activity at the time. Somnificity helps to explain why we are more likely to fall asleep when lying down than sitting.

**Support (optional):**

0091

**PERIPHERAL VASODILATION DOES NOT PREDICT DRIVING SIMULATION PERFORMANCE IN OBJECTIVELY SLEEPY DRIVERS**

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**Introduction :** Peripheral vasodilation and skin temperature increase at sleep onset. Sleepy drivers are involved in a significant proportion of automobile accidents and perform poorly on driving simulation tasks (DS) compared to alert drivers. We hypothesized that peripheral vasodilation (skin temperature) and lane variability would correlate positively on a driving simulation task.

**Methods :** From our Sleep Disorders Center population of patients completing a Multiple Sleep Latency Test (MSLT), 15 patients with mean sleep latencies  $\geq 8$  minutes (control) and 15 patients with mean sleep latencies  $< 8$  minutes (abnormal) enrolled (ages 18-64 years). We excluded patients with peripheral neuropathy, peripheral vascular disease, and those using narcotics, hypnotics, or stimulant medications. In the afternoon, usually between the third and fourth MSLT naps, participants completed a 60-minute DS task while wearing a temperature monitor on their right ankle. The DS setup is similar to that of an actual car with a computer-generated highway scenario projected on a screen. Driving performance, measured by lane variability, and skin temperature were recorded continuously.

**Results :** Over all 30 patients, there was a tendency for increased ankle

skin temperature to accompany increased lane variability ( $r = 0.33$ ,  $p = 0.079$ ). The correlation was significant for the control group ( $r = 0.56$ ,  $p = 0.029$ ) but not for the abnormal MSLT group ( $r = 0.12$ ,  $p = 0.672$ ). Mean MSLT sleep latencies were 12.4 and 4.1 minutes for the control and abnormal group, respectively. Age, sex, subjective sleepiness, initial temperature, and initial lane variability did not differ significantly between the control and abnormal groups. The abnormal MSLT group did have higher mean lane variability than the control group ( $p = 0.033$ ).

**Conclusion :** Lane variability of patients with MSLT scores  $\geq 8$  minutes increased with increasing ankle temperature as expected although the abnormal MSLT group did not. These results suggest a dissociation between performance and autonomic nervous system activity in the sleepest patients. Although this dissociation is interesting, it limits the usefulness of skin temperature to detect driver sleepiness.

**Support (optional):** This research was supported by Ambulatory Monitoring, Inc.

0092

**CYCLIC HEART RATE PATTERNS ARE VARIABILITY ASSOCIATED WITH REM AND WAKE CYCLES IN THE ELDERLY**

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**Introduction :** We have observed clear cycles of increased and decreased heart rate (HR), reflecting changes in cardiac autonomic modulation, during sleep. A consistent relationship between increased HR and REM sleep or periods of wake has been hypothesized, suggesting that there should be a strong correspondence between HR peaks and REM and wake cycles.

**Methods :** A random sample of 40 overnight polysomnograms from the second wave of the Sleep Heart Health Study was selected. Subjects (age  $81 \pm 3$ , range 76-91 yrs, 15M, 25F, RDI= $18 \pm 16$ , range 1-71/hr) were also participants in the Holter cohort of the Cardiovascular Health Study. A minimum of 6 hours of data with at least 2 REM cycles was required for inclusion. HR was determined for every 2-min segment after sleep onset that had a usable ECG and that was consistently scored as being in REM, non-REM or wake. Two-min averaged HRs were plotted for the entire night. The total number of HR cycles and the correspondence between cycles of increased HR and periods of wake or REM sleep was determined. Participants were categorized as having an RDI of  $\leq 20$  ( $N=28$ ) or having an RDI of  $>20$  ( $N=12$ ), and results compared between groups.

**Results :** Clear cycles of increased and decreased HR were seen for participants ( $N=9.6 \pm 2.5$ , range 4-15 cycles). During REM sleep,  $71 \pm 33\%$  of epochs had corresponding HR cycles (range 0-100%), meaning that, on average, 29% of REM cycles did not have an associated cyclic increase in HR. Correspondence with HR cycles was larger for wake ( $94 \pm 14\%$ , range 43-100%), so that, on average, only 6% of wake periods were not associated with an increase in HR. On the other hand, 87.5% of subjects had at least one HR peak that did not correspond to either REM or wake (mean  $40 \pm 20\%$ , range 0-83%,  $>2$  non-corresponding cycles for 50% of subjects, range 0-6). When results were compared by RDI group, the percent of REM cycles with corresponding HR cycles was significantly higher ( $80 \pm 28\%$  vs.  $60 \pm 35\%$ ) among those with a lower RDI ( $p < 0.001$ ), but no other differences were found.

**Conclusion :** Heart rate cycles, reflecting changes in cardiac autonomic modulation and present during sleep, are variably associated with REM sleep and wake periods in the elderly. Discrepancies between REM and heart rate patterns may partly be explained by sleep-disordered breathing. Analysis of heart rate patterns by themselves will not reliably identify REM/wake periods in most elderly subjects

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### 0093

#### CHANGING THE AMBIENT TEMPERATURE IN A VEHICLE: EFFECTS ON DRIVER VIGILANCE LEVEL

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**Introduction :** The purpose of this study was to explore the physiological modifications reflecting a change in a driver vigilance contemporary to a modification of the ambient temperature in the vehicle.

**Methods :** Subjects were 52 healthy males, 20 to 35 years old, with standard weight and height. Each subjects participated to two driving sessions of 90 min each, at the same time of the day and separated by a one-week interval. During the sessions, the ambient temperature was maintained at 22°C for 15 min. Then, ambient temperature was linearly decreased during 30 min to reach 18°C (cold condition) or increased during 30 min to reach 28°C (warm condition), and this new temperature was then maintained during 45 min. The experiment was made on our moving-base driving simulator PAVCAS. Measures performed during the whole driving session included Karolinska Sleepiness Scale, 4 EEGs, vertical and horizontal EOGs, EKG, and 7 skin temperatures.

**Results :** Subjective decrease in vigilance occurring during driving was more pronounced in the warm than in the cold condition. Spectral analysis of EEG content allowed us to calculate indices showing a significant progressive deterioration of the vigilance level of the driver in the warm condition, while such a deterioration appeared to be well attenuated in the cold condition. Similarly, the increase in eye closure frequency and mean duration was significantly more pronounced in the warm than in the cold condition. Driving performance was globally unchanged, except for the number of trajectory adjustments, significantly increased in the cold condition, reflecting a better control of the car in this environmental condition.

**Conclusion :** The results of this study confirm that a cold environment inside a vehicle is associated to a smaller degradation of driver vigilance level than a warmer environment.

**Support (optional):**

### 0094

#### HYPOCRETIN/OREXIN EFFECTS ON CARDIOVASCULAR REGULATION DURING SLEEP

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**Introduction :** Cardiovascular physiology changes across rapid eye movement (REM) and non-REM sleep. Blood pressure “dipping”- the decrease that occurs with sleep onset-, is a known marker of cardiovascular risk. Similarly, the increased occurrence of sudden cardiac death in the early morning hours suggests a connection between sleep and cardiovascular function. In diurnal animals, hypocretin release decreases sharply at sleep onset and is minimal in the early morning hours. Hypocretin (orexin) injections in the central nervous system reduce sleep, activate the sympathetic nervous system activity and increase body temperature. We hypothesize that hypocretin has a role in mediating cardiovascular and temperature changes at sleep onset and during sleep stage transition.

**Methods :** To test this hypothesis, we simultaneously studied on-line EEG, EMG, blood pressure, heart rate, locomotor activity, tail and abdominal temperatures in freely moving Sprague-Dawley rats for 24 hours.

**Results :** Expected sleep stage specific effects on blood pressure, temper-

ature and heart rate were found - for example, a decrease in blood pressure was noted at sleep onset, similar to blood pressure dipping in humans, after a transient . We also observed significant diurnal fluctuation for these parameters. The specific contribution of hypocretin to these effects was next evaluated by comparing wild type and hypocretin/ataxin3 transgenic rats, which are partially hypocretin deficient (20% of control CSF hypocretin-1 levels). Core body and tail temperature, systolic and diastolic blood pressure was reduced across the 24 hrs. The core body temperature decrease was most pronounced at the beginning and the end of the active period (0.6°C and 3°C respectively). A small but significant decrease was also seen in heart rate, and in locomotor activity. Sleep stage transition effects are currently analyzed.

**Conclusion :** These results suggest significant effects of hypocretin on many physiological parameters. We conclude that the transgenic rat is a useful model to isolate hypocretin effects on whole animal physiology.

**Support (optional):** This study is supported by the grants MH-073435 and HL-62252 to E. Mignot

### 0095

#### MOTOR UNIT ACTIVITY IN GENIOGLOSSUS DURING AROUSAL FROM SLEEP

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**Introduction :** Motor units (MU) in human genioglossus have a range of discharge patterns. The most frequently observed patterns are inspiratory phasic (peak inspiratory activity, with or without activity during expiration) or tonic (absence of respiratory modulation). We have previously reported that phasic units dramatically reduce their activity at sleep onset, while tonic units are not affected by the transition. We now report the effect of arousal from sleep on the discharge rate and pattern of phasic and tonic MUs in human genioglossus.

**Methods :** Data were collected on three young healthy subjects (1F) for one night each. Sleep-wake state, ventilation and airway mechanics were measured. MU activity in GG was assessed by monopolar intramuscular 112µm Teflon coated wire electrodes (0.5mm exposed tip) referenced to a common surface electrode positioned over the bony mandible. Three electrodes were inserted into the muscle using a percutaneous approach, guided by ultrasonography. MUs that were active throughout pre-arousal sleep and the arousal were identified. Arousals were selected if they met ASDA criteria and if they did not activate a sufficiently large number of additional MUs to conceal the action potentials of the target MUs. Phasic behavior was identified by visual inspection and by the maximum cross correlation value between ventilation and the MUs discharge rate. 48 arousals were analysed and 60 (20 phasic and 40 tonic) MUs were subsequently identified.

**Results :** 18 of the 20 phasic units present during pre-arousal sleep increased their firing frequency at the arousal. Peak frequency increased by 3.5 Hz (p<.05). Further, 31 of the 40 tonic units showed a decrease in firing frequency. Mean frequency decreased by 2.5 Hz (p<.05). Both effects were transitory (1 to 3 breaths) and were most apparent on the first arousal breath. A chi square test indicated the difference in distribution to be highly significant (p<.001). (The discharge patterns of MUs recruited at the arousal are not presented in this abstract.)

**Conclusion :** As with sleep onset, the behaviour of a MU at an arousal from sleep is dependent on its discharge pattern. The differential change in activity for phasic and tonic units suggests a coordinated alteration in the motor control of different MUs at the transition from sleep to wake-

fulness.

**Support (optional):**

**0096**

### CASTE-DEPENDENT CHANGE IN THE SLEEP OF A WORKER HONEY BEE

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**Introduction :** The study of insect sleep has begun to offer tractable, evolutionarily significant perspectives on the behavior of sleep. Honey bees (*Apis mellifera*) have a long history of sleep research. Workers experience a division of labor that is largely determined by age, beginning adulthood as cell-cleaners, later tending immatures as nurse bees, then storing food, and ending their lives foraging for food. This temporal succession of tasks (cell-cleaner, nurse, food-storer, forager) correlates, at least in part, with changing sleep patterns. Honey bee foragers sleep at predictable times during the night, but the younger nurse bees do not show periodic bouts of relative immobility. No one has explicitly documented the sleep dynamics of non-foraging bees, including the remaining two worker castes (cell-cleaners and food-storers), leaving gaps in our understanding of sleep's role across members of a colony. I examined a colony of worker honey bees for caste-dependent sleep signs.

**Methods :** A collaborator and I individually marked members of a freely-foraging colony of honey bees and recorded the frequency of superficial sleep signs of individuals from different castes throughout a 72h period (3sec/h x 40 bees) and a series of 24h periods (30min/h x 1 bee of each caste). To examine change throughout individual bees' lifetimes, we recorded superficial sleep signs for periods of 48h (15min x 2 bees/h x 3weeks) as workers aged and changed tasks, to determine to what degree sleep habits differ among the 4 worker castes. States of (relative) immobility were categorized by posture (body either lifted above substrate or prone), or antennal motility (none, small flicks, or large movements).

**Results :** All four honey bee worker castes exhibited superficial sleep signs as adults. As bees aged and performed different tasks, however, they spent more time in a sleep-state (7%, 9%, 13%, 29%). Rhythmic patterns of immobility-mobility were not found in the young cell-cleaners or in the nurse bees, but began to take shape in the food-storers ( $P=.0013$ ), and rhythmicity was obvious in the foragers ( $P<.0001$ ).

**Conclusion :** Honey bee workers differ in duration and rhythmicity of sleep signs with respect to their caste. Understanding the frequency and degree to which individuals of different castes within a society sleep is the starting point from which one can test and understand the nature of sleep and its impact on the behavior and ecology of societies, and the societally-based purpose(s) of sleep.

**Support (optional):** Environmental Science Institute, The University of Texas at Austin, Department of Ecology, Evolution and Behavior

**0097**

### INHERITANCE OF A SLEEP-RELATED EPILEPSY PHENOTYPE IN THE MOUSE

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**Introduction :** Clinically evident seizures during sleep occur in human epilepsy, but is rarely described in rodent models. We have previously reported by abstract (Strohl et al, SfN 2003) a phenotype of spontaneous spike and wave activity (SWD) predominantly during sleep in the A/J

mouse (Jackson Laboratory me); in contrast, SWDs were not observed in A/J mice from Harlan (Indianapolis, IN) or in C57BL/6J (B6) mice. The hypothesis was that inheritance plays a role in the development of such sleep-related SWDs.

**Methods :** Using EEG monitoring, we studied chromosomal substitution strains (CSSs) in which one A/J chromosome is bred onto a B6 background to determine if a given chromosome conferred risk of SWDs, and intercrossed A/J JAX and B6 mouse strains as well as those CSSs showing SWDs to determine the mode and manner of inheritance. Linkage studies were performed on CSS second generation (F2) progeny.

**Results :** In an A/J JAX x B6 first generation intercross, the trait was not dominantly expressed. The A/J JAX trait was observed in chromosome substitution strains (CSSs) B6a4 and B6a7. Of 113 male and female second generation offspring derived from an intercross of these two CSSs, six animals were observed to clearly manifest SWDs (>3 SWDs; 4 males, 2 females); two were "probable" (<4 SWDs; 1 male, 1 female); and five exhibited isolated spikes (2 males, 3 females). Linkage analysis revealed evidence for gender-specific loci on chromosome 4.

**Conclusion :** We conclude that this unique sleep related epilepsy phenotype exhibits a low penetrance, oligogenic pattern of gender-specific inheritance.

**Support (optional):** NIH HL64278 (Strohl), NCR grant RR12305 to CWRU (Nadeau) and MIT Whitehead Institute (Lander), and the Research Service of the Department of Veterans Affairs.

**0098**

### DIFFERENTIAL EFFECTS OF PEPPERMINT AND LAVENDER ODORS ON SLEEP IN YOUNG HEALTHY ADULTS

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**Introduction :** In two separate experiments, exposure to lavender, a soporific, or peppermint, a stimulant, significantly modified polysomnographic (PSG) sleep. These studies used water as a control, however, rather than an active odor comparison; thus, the sleep changes may be due to expectancy or nonspecific effects rather than specific odor qualities. Therefore, this study directly compared the effects of peppermint and lavender presented before bedtime on subsequent PSG sleep and self-rated sleepiness.

**Methods :** Twelve healthy sleepers (mean age  $\pm$  SD, 22.0  $\pm$  2.4 y) completed 3 consecutive overnight laboratory sessions (adaptation, peppermint or lavender nights; odor order was counterbalanced). Subjects received an intermittent presentation (first four minutes of each ten-minute period) of either odor from 2310h-2340h. Subjects rated the perceptual qualities of the odors using Likert scales at 2314h and 2344h. Karolinska Sleepiness Scale (KSS) and Stanford Sleepiness Scale (SSS) measured self-rated sleepiness at 2355h and 0815h. PSG sleep was recorded from 0000h-0800h. Records were scored in 30-second epochs using Rechtschaffen and Kales' standard scoring criteria. Repeated measures ANOVA examined differences in measures between the peppermint and lavender sessions.

**Results :** Lavender significantly increased slow-wave sleep % sleep period time (SPT) and stage 2 %SPT, and increased sleep efficiency and WASO latency compared with peppermint. By contrast, peppermint significantly increased sleep onset latency and WASO %SPT, and decreased sleep efficiency. Peppermint significantly reduced nighttime sleepiness (on the SSS) compared with lavender, and was rated as more stimulating and elating.

**Conclusion :** Peppermint and lavender presentation before bedtime differentially affected PSG sleep variables. Lavender produced PSG changes consistent with a sedating odor, while peppermint produced changes consistent with a stimulating odor. Such changes were not due to expectancy

or nonspecific effects. Presentation of nighttime peppermint or lavender odor may serve as a non-pharmacologic approach for producing significant alterations in sleep in young adults.

**Support (optional):**

## 0099

### CARBON DIOXIDE STIMULATES BREATHING AND PERHAPS SLEEP

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**Introduction :** Carbon dioxide is a known respiratory stimulant used experimentally to treat sleep apnea. CO<sub>2</sub>-mediated arousal has been demonstrated, however, the effects of different CO<sub>2</sub> concentrations on sleep parameters are unclear. In this study, we sought to determine the effect of hypercapnia on sleep architecture and breathing.

**Methods :** Three cats were studied during 3h sessions while breathing carbon dioxide added to room air. The animals breathed different concentration of carbon dioxide (0%, 2%, 4% and 6% CO<sub>2</sub>) each day over 4 wks according to a 4 x 4 Latin Square design. The animals breathed through a tube inserted into the trachea via a surgically created fistula. Respiration was measured using pneumatography, and electroencephalograms and pontogeniculo-occipital waves were recorded from implanted electrodes to discriminate states of sleep and wakefulness.

**Results :** When breathing 2% inspired CO<sub>2</sub>, total sleep duration increased by 16% compared to control (0% CO<sub>2</sub>). Both NREM and REM sleep increased in duration (15% and 19%) and frequency (7% and 23%). Sleep latency decreased by 47%. However, when breathing higher levels of CO<sub>2</sub> (4% and 6%), total sleep duration decreased. Both NREM and REM sleep decreased in duration (14% and 20% with 4% CO<sub>2</sub>; 42% and 80% with 6% CO<sub>2</sub>) and frequency (10% and 42% with 4% CO<sub>2</sub>; 27% and 77% with 6% CO<sub>2</sub>). Tidal volume, minute ventilation, effort (tidal volume/duration of inspiration) and inspiratory duration increased proportionally in all states with increasing levels of CO<sub>2</sub>. Tidal volume increased by 52.9%, 133.2% and 196.2% with 2%, 4% and 6% inspired CO<sub>2</sub>, respectively.

**Conclusion :** We conclude that a mild hypercapnic stimulus can stimulate breathing and sleep.

**Support (optional):**

## 0100

### TRAIT INDIVIDUAL DIFFERENCES IN SLEEP ARCHITECTURE

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**Introduction :** Individual differences represent a trait if they are stable (over time) and robust (to an experimental challenge). This study is the first to use these criteria to investigate traits in sleep architecture.

**Methods :** 21 healthy subjects (age 28.5 ± 5.5; 11 females) spent 11 consecutive days in a laboratory: two baseline days with 12h TIB, and three 36h sleep deprivation episodes, each followed by two recovery days with 12h TIB. The eight sleep periods were recorded polysomnographically and scored visually. Slow-wave activity (SWA; 0.75-4.5Hz) was determined from the NREM sleep EEG (Fz/C3/C4/Oz). Across all subjects, 33

sleep records were discarded because of equipment failure. For each of the remaining 135 records, sixteen sleep variables were examined. These were subjected to principal components analysis (PCA; varimax rotation) to determine which variables covaried over subjects and across nights. For each factor retained based on the scree plot, variables with absolute factor loadings >0.5 were noted. To estimate trait-like between-subjects variability, factor scores were subjected to mixed-effects regression controlling for first-night and deprivation effects (which were as expected but are not reported here). Intra-class correlation coefficients (ICCs) were calculated to quantify trait individual differences.

**Results :** Three factors were retained in the PCA. The first captured sleep duration (TST, sleep efficiency, S2, number of sleep cycles; negative loadings for sleep latency and wake); ICC=45% (P=0.007). The second represented SWS/SWA; ICC=92% (P=0.002). The third appeared to reflect sleep continuity (S1, movement time, density of sleep stage transitions); ICC=52% (P=0.005). REM sleep did not load >0.5 on these factors.

**Conclusion :** At least three aspects of sleep architecture varied independently among subjects: total sleep obtained (during 12h TIB); slow waves (indicative of sleep homeostasis); and sleep continuity. Individual differences in these factors, particularly the slow wave factor, were significantly trait-like. The functional significance of these traits remains unknown.

**Support (optional):** Supported by NIH grants HL70154 and RR00040.

## 0101

### COMPLEX SLEEP DISORDERED BREATHING AND ATRIAL OVERDRIVE PACING

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**Introduction :** In certain cases of complex sleep disordered breathing, central and obstructive patterns may shift or overlap. Central SDB is typically unresponsive to continuous positive airway pressure. Atrial overdrive pacing (AOP) may have an effect on central but not obstructive SDB. We report two cases of SDB in which AOP substantially reduces CSDB while increasing OSDB. This effect of AOP may help provide insight into underlying mechanisms of complex SDB.

**Methods :** Patients screened by polysomnogram were enrolled in a trial of atrial overdrive pacing for SDB. Patients were assigned, in random order, to no AOP (P0), AOP at 10 beat/min above the average nocturnal heart rate (P10) and AOP at 20 beat/min above (P20). Circulation delay (CD) was taken as the elapsed time from the end of apnea to the following nadir of O<sub>2</sub> desaturation. Brain natriuretic peptide (BNP) and norepinephrine (NE) spillover were assessed at the end of each night.

**Results :** Only 2 of 18 (11%) enrolled patients were found to be CSDB patient at P0 night. Patient 1 (pt 1): 74 y/o M, BMI=42, EF=65%, NYHA I and mild hypertension, central AHI=59, and overall AHI=83. Patient 2 (pt 2): 82y/o M, BMI=28, EF=60%, NYHA I and mild hypertension, central AHI=32, and overall AHI=56. Central AHI was reduced to 36 (pt 1) and 17 (pt 2) with at P10 night and was reduced to 0 (pt 1) and 1 (pt 2) at P20 night, while OSDB increases commensurately to keep overall AHI 81 (pt 1) and 47 (pt 2) at P10 night, overall AHI 64 (pt 1) and 39 (pt 2) at P20 night. AOP decreases CD as well as BNP level and hourly NE spillover for both patients.

**Conclusion :** Both patients are elderly and overweight and thus vulnerable to multiple mechanisms of SDB. AOP decreases CD as well as BNP level and hourly NE spillover. Such responses may be attributed to an effect on undiagnosed heart failure (HF) or diastolic dysfunction. With increased AOP levels CSDB is decreased and eliminated while OSDB increases commensurately. HF related CSDB may have masked a propen-

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sity to OSDB. AOP may affect CSDB by improving CD and reducing cardiac overload. In cases of complex SDB with predominant CSDB, possibly in presence of mild HF, AOP may change SDB pattern. This effect may prove to be therapeutically advantageous when used in conjunction with CPAP.

**Support (optional):**

### 0102

#### ANTI-DEPRESSANT MEDICATIONS, NEUROLEPTICS AND PROMINENT EYE MOVEMENTS DURING NREM SLEEP

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**Introduction :** Eye movements during stage 2, 3, and 4 sleep have been associated with several specific serotonin reuptake inhibitor (SSRI) medications. This activity has been postulated to be a serotonin effect. We identified all cases of NREM eye movements and then correlated this with the patient's active and past medications.

**Methods :** The polysomnogram (PSG) studies of 2,959 consecutive adults, with 2,959 diagnostic PSGs and 2,310 CPAP titrations, studied during 36 months were reviewed prospectively to identify all patients with atypical eye movements during NREM sleep. All PSG studies were reviewed regardless of the indication for the study or the diagnosis identified with the study. Standard recording, staging and arousal scoring methods were used. The use of anti-depressants and neuroleptic medications was recorded for each patient.

**Results :** Eye movements in NREM sleep were detected in fluoxetine (54%), paroxetine (47%), sertraline (40%), citalopram (26%), escitalopram (20%), amitriptyline (5%), nortriptyline (3%), imipramine (0%), desipramine (50%), protriptyline (8%), mirtazapine (5%), venlafaxine (16%), bupropion (7%), duloxetine (0%), trazadone (5%), clonazepam (1%), zolpidem (2%), olanzapine (0%), quetiapine (5%), risperidone (11%). These groups had similar mean ages and gender distributions. SSRI's were most prominently associated with eye movements in NREM sleep ( $p < 0.0001$ ).

**Conclusion :** SSRI's caused the most prominent NREM eye movements, even when discontinued prior to the study. Mirtazapine was rarely related to NREM eye movements. Clonazepam and zolpidem were not associated with atypical eye movements unless used in combination with SSRI medications. In some cases, there were complicated medication combinations. Dopamine blocking agents were not strongly associated with NREM eye movements. Atypical NREM eye movements appear to be related primarily to serotonin and less prominently to dopaminergic medication effects. There appears to be a trend toward increased chin EMG activity during times of increased eye movement.

**Support (optional):**

### 0103

#### THERMOREGULATORY DISSOCIATION OF ALERTNESS AND PSYCHOMOTORIC VIGILANCE

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**Introduction :** The circadian time course of core body temperature

(CBT) is positively correlated with alertness and psychomotoric vigilance (PV). In the evening, when body heat loss increases via distal skin regions, CBT declines together with alertness and PV. Unfortunately, studies demonstrating effects of changes in body temperatures on alertness and PV are sparse. Our aim was to test whether mild core body cooling or warming could differentially change alertness and PV.

**Methods :** In a randomized crossover study, 8 healthy subjects (age:  $31y \pm 3$  s.e.m., 21-52y; 4 women) reported twice (1-3 days between) to the lab at 11:00 and remained supine in bed from 11:20 until 14:10h. At 12:50h they drank 250ml crushed ice/water mixture (= 'ice') or 250ml 55°C warm water (= 'tea') within 5min. Rectal temperature (CBT) and skin temperatures (ST, 8 probes) were continuously measured (20sec-intervals), together with subjective sleepiness ratings (KSS; 20min-intervals) and PV using an acoustic reaction time test (60-100db, 3min, 4 tests before and after ice or tea -intake). The results were analyzed by two-way-ANOVAs for repeated measures (ice vs. tea; 8 time segments). The threshold for significance level was set at  $p=0.05$ .

**Results :** In the first 1.5h after lying down ST increased and CBT decreased, as has been previously reported. During the first 30min after intake of ice hand ST ( $-1.11^{\circ}\text{C} \pm 0.33$ ), CBT ( $-0.10^{\circ}\text{C} \pm 0.02$ ), PV (reaction time:  $+23 \pm 9$ ms) decreased, and alertness increased ( $-1.3 \pm 0.4$  KSS units); the converse was observed after tea intake (hand ST:  $+0.74^{\circ}\text{C} \pm 0.20$ ; CBT:  $+0.06^{\circ}\text{C} \pm 0.02$ ; alertness:  $+0.8 \pm 0.6$  KSS units, n.s.; reaction time:  $-15 \pm 8$ ms, n.s.).

**Conclusion :** Although alertness and PV follow a similar circadian time course, they are not always linked. Mild core body cooling or warming leads to their dissociation, alertness being negatively correlated with distal ST, but PV remaining closely linked with CBT.

**Support (optional):**

### 0104

#### AUTONOMIC REGULATION AND WEIGHT LOSS DURING SLEEP: PRELIMINARY STUDY

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**Introduction :** Different epidemiologic studies showed an inverse association between sleep hours and obesity. A possible explanation is that sleep deprivation causes increased sympathetic response during sleep that is related to multiple endocrine and metabolic consequences. There are no studies, up to present date, relating weight loss during sleep, sleep structure and autonomic response assessed by polysomnography.

**Methods :** Thirty healthy volunteers, 22 females and 8 males, ageing 18-30 were included. Volunteers received a 487 kcal meal and 200 ml water at night. During the experiment weight and height were measured before sleep and after sleep period, before breakfast. Volunteers did not eat, drink, urinate or defecate between both measures. Room temperature was constant around 22°C. Direct and relative weight indices were calculated. Time and frequency domain analysis of heart rate variability (HRV) were calculated for each 5-minute during stage 2, 4 and REM. Linear regression analysis was performed between night weight loss parameters, polysomnographic and HRV variables. HRV time domain parameters: mean RRI, SDNN, RMSSD, SDDSD, NN50, PNN50. Frequency domain parameters: VLF, LF, HF, TP, LFHF.

**Results :** LF correlated negatively with relative weight loss ( $R=-0.67$ ) and relative weight loss rate ( $R=-0.67$ ) during stage 2. SDDSD showed a negative correlation with weight loss rate ( $R=-0.61$ ), relative weight loss ( $R=-0.65$ ) and relative weight loss rate ( $R=-0.67$ ) during stage 4. VLF correlated positively with body mass index reduction rate ( $R=0.65$ ) during REM sleep.

**Conclusion :** Results suggest that weight loss is inversely proportional to



sympathetic component of HRV (LF); however, it is not possible to eliminate an eventual contribution of parasympathetic component of ANS. The authors conclude that increased sympathetic tone may be involved in the mechanism of weight loss during sleep.

**Support (optional):** AFIP and FAPESP/CEPID

## 0105

### AGING: ASYMPTOTIC SLEEP DURATION DURING EXTENDED SLEEP OPPORTUNITIES

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**Introduction :** Many older persons report sleep problems but it remains unclear whether these relate to changes in the circadian regulation of sleep, in the homeostatic “drive” for sleep, changes in sleep “ability” or lifestyle. We studied sleep duration during extended bedrest opportunities in younger and older individuals.

**Methods :** Eighteen younger (18-27 years) and 18 older (60-76 years) volunteers passed a physical exam and clinical sleep screen. Habitual bedrest durations (HBD) of older subjects, as assessed during a three week period, were 7 - 9 hours. For this report, younger subjects with HBD in this range were used as comparison. Subjects were scheduled to 16 hours of sleep opportunity per 24-hr day: 12 hours centered at mid-habitual nocturnal sleep episode and 4 hours centered 12 hours opposite this. This schedule was repeated for three days (5 younger, 4 older); four days (7 younger, 10 older); or seven days (6 younger, 4 older). Sleep was recorded. Asymptotic sleep durations were computed using PROC SAS NLMixed with random effects.

**Results :** During the first 16-hr sleep opportunity (ED1), both younger and older subjects had more TST (12.6 and 9.7 hrs, respectively) than during the first inpatient sleep episode (length = HBD). There was an exponential decay of sleep measures from ED1 through ED7 for younger subjects for TST, NREM sleep S2, and REM sleep. For TST, the predicted asymptotic value was 9.2 hours for younger subjects and 7.5 hours for older subjects ( $p=0.004$ ).

**Conclusion :** Both older and younger subjects will increase their sleep over their HBD when given the opportunity. The amount of increased sleep decreases over days of increased sleep opportunity, demonstrating that a recovery occurs. The increased sleep seen in older persons is less than that seen in younger, suggesting that older persons have less homeostatic pressure given the same bedrest history.

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## 0106

### SLEEP ARCHITECTURE IN BIRDS: AN AVIAN PERSPECTIVE ON ZEPELIN AND RECHTSCHAFFEN (1974)

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**Introduction :** Many comparative studies of sleep architecture exist in mammals. Such studies have found that larger mammals with bigger brains and higher absolute basal metabolic rates (BMR) tended to engage in less SWS and REM sleep. Species experiencing a greater risk of predation also exhibited less SWS and REM sleep. In all cases, however, published studies lacked a formal phylogenetic framework that accounted for shared evolutionary history among taxa. Given the similarities between the sleep architecture of mammals and birds, similar relation-

ships among sleep and constitutive/ecological variables might also be expected in birds.

**Methods :** Following earlier mammalian analyses, we gathered data on avian sleep (SWS time, REM sleep time), and morphological (adult body and brain mass), physiological (BMR, incubation period), and ecological (predation risk index) variables from the primary literature for 24 avian species. Phylogenetic trees were also taken from the literature. Data were transformed into a set of independent contrasts and analyzed with simple correlation.

**Results :** We identified a strong negative relationship between SWS time and predation risk index ( $r = -0.563$ ,  $P = 0.006$ ). All other relationships with SWS time were markedly nonsignificant; however, the trends in sign between SWS time and body mass ( $r = -0.136$ ,  $P = 0.546$ ), brain mass ( $r = -0.151$ ,  $P = 0.503$ ), and BMR ( $r = -0.121$ ,  $P = 0.593$ ) were comparable to those of mammals. Relationships between REM sleep and constitutive variables were also nonsignificant, but were negative nonetheless. Incubation period did not correlate significantly with REM sleep ( $r = -0.072$ ,  $P = 0.752$ ).

**Conclusion :** Many of the “traditional” relationships identified in previous mammalian analyses are not apparent in our avian analysis. Nevertheless, we found that birds sleeping in riskier (i.e., more open) environments engage in less SWS. Both avian and mammalian sleep architecture appears to be strongly influenced by predation risk. However, the constitutive determinants of sleep architecture in birds may not necessarily reflect those identified in mammals.

**Support (optional):**

## 0107

### IMPULSIVE RESPONDING IN THE MIGRATING WHITE-CROWNED SPARROW (ZONOTRICHIA LEUCOPHRYS GAMBELII)

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**Introduction :** We previously found that cognitive performance in White-crowned sparrows remained intact during migration, when sleep is reduced, although the number of responses on the task increased profoundly. The present study attempted to clarify whether increased responding during migration was a function of heightened general activity or increased motivation for food using a procedure designed to selectively reinforce low response rates, more typical of those observed during non-migratory periods.

**Methods :** Migratory sparrows (*Zonotrichia leucophrys gambelii*), collected from Northern California, were housed individually in laboratory cages under a titrating light:dark cycle that simulated natural photoperiods, ranging from 9.5:14.5 to 22.5:1.5. Eight birds were trained to key peck for food reward according to a Differential Reinforcement of Low Rate (DRL) behavior schedule that reinforced pecks separated by at least 20 seconds. Thus, only paced, low-rate response patterns were reinforced. Sessions lasted 30 minutes and were conducted 4 times per week. Home cage activity was recorded continuously using infrared motion to detect migration. Birds were also intentionally sleep deprived for 36-hour periods in the winter and spring; experimenters kept them awake by entering the housing room every 3 - 5 minutes.

**Results :** All birds increased their key pecking during spring and fall migrations, some to such an extreme extent that their reward rates were drastically reduced. However, when sleep deprived for 36 hours, response rates either decreased or were unaffected. Increased responding during sessions corresponded with increases in home cage activity.

**Conclusion :** With endogenous sleep loss during migration, responding increased regardless of consequence, even if it resulted in the loss of food reinforcement. However, exogenous sleep deprivation did not have this

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effect. The increased responding observed during migration is characteristic of impulsive behavior documented in studies mania and drug administration (e.g., amphetamine), and it seems to result from heightened activity concomitant with migration.

**Support (optional):** Supported by NIMH.

### 0108

#### BOLD FMRI DURING AWAKE REST AND LIGHT SLEEP

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**Introduction :** During non-REM sleep, conscious awareness and vigilance are reduced. However, the brain remains electrically active. Imaging studies with positron emission tomography (PET) suggest that some brain regions remain active during light sleep. In this work, we used functional magnetic resonance imaging (fMRI) with concurrent EEG, to further investigate brain activity during light sleep at high spatial and temporal resolution.

**Methods :** Sixty-minute studies were performed on normal volunteers (n=11). Session consisted of 1 min eyes open, 49 min in which subjects were allowed to sleep and 10min. of visual stimulation. EEG was collected on a Synapsms2-Maglink system running Scan4.3 (Compumedics). BOLD fMRI was collected on a 3T (GE) scanner (single-shot EPI, TE:43ms, TR:6s, burst mode, 28 slices, 1.7x1.7x3mm<sup>3</sup>, gap 0.5mm). Sleep was scored (by TB) for each subject based on the EEG data in 30s epochs. fMRI activity was derived by measuring the level of low-frequency (<0.1Hz) signal fluctuations, after correction of cardiac and respiratory artifacts. For each subject that showed wake and sleep periods of at least 2min., the fMRI activity was computed during wake (W) and stage 1 and 2 sleep (S) conditions. This was done by calculating the standard deviation on a pixel-by-pixel basis. A pooled variance t-test was performed.

**Results :** In the six subjects that showed enough W/S, significant increases in BOLD-fMRI fluctuations were observed bilaterally in visual cortex and precuneus while decreases were seen in medial frontal gyri. A mostly lateralized effect -on the left hemisphere- was observed in STG, Inferior frontal gyrus and supramarginal gyrus.

**Conclusion :** Increased activity is evident in several brain regions during early sleep as evaluated by the amplitude of the low frequency fluctuations, while decreases were observed only in prefrontal areas.

**Support (optional):**

### 0109

#### CHARACTERIZATION OF A SLEEP-LIKE STATE IN ADULT ZEBRAFISH

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**Introduction :** Zebrafish are commonly used in developmental genetics as they have a short generation time and a well understood and easily manipulated genome. Furthermore, as vertebrates, they share many of the same neuroanatomical and neurophysiological underpinnings as mammals. Given this, defining sleep in zebrafish may better enable us to discover genes related to vertebrate sleep.

**Methods :** Adult fish behavior was monitored using an infrared video recording system. Recordings were done in either a light:dark cycle or continuous darkness. Video images were acquired and movements were analyzed with FishWatch2 (custom software). Arousal thresholds (mini-

mum stimuli inducing movement) were measured using electric pulses (0-2V) delivered every 30 minutes for 24-hours. We also maintained continuous wakefulness during ZT6-12 (last 6 hours of dark during an LD cycle) by stimulating (2-6V) fish when they exhibited a sleep-like state; control fish were stimulated simultaneously by the same electric pulse.

**Results :** All fish had clear, prolonged states of immobility with a characteristic posture (caudal fin pointed downward). This state could be quickly reversed after strong stimulation (2V), while a more moderate stimulus (0.38V) inconsistently (35%) reversed the immobile state. If already active, most fish (87%) exhibited the capacity to respond to this moderate electric stimulus. Using these data, we determined that a sleep-like state was best defined as an activity level <6 units that lasted at least 6 sec. Enforcing wakefulness for the final 6 hours of darkness resulted in increased sleep time the following dark period, but not the following light period, likely due to the masking effects of light.

**Conclusion :** The stereotypic nature of the immobile posture, its reversibility after stimulation and homeostatic regulation are suggestive of a sleep-like state similar to mammalian or *Drosophila* sleep. This work provides the basis for future genetic and pharmacological studies in this species.

**Support (optional):**

### 0110

#### VOLTAGE-DEPENDENT POTASSIUM CHANNEL KV1.2: EFFECTS ON SLEEP AND EEG POWER SPECTRUM OF INTRACORTICAL INJECTIONS OF AN ANTI-KV1.2 ANTIBODY

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**Introduction :** By performing mutagenesis screening in *Drosophila melanogaster* our laboratory recently identified minisleep (mns), a mutant fly line that sleeps only 4-5 h/day rather than 9-15h like most fly lines. The decrease in daily sleep amount is mainly due to a decrease in the duration of sleep episodes rather than their number, and is not associated with changes in the homeostatic or circadian regulation of sleep. The mns phenotype is caused by a null mutation in Shaker, a gene encoding the alpha subunit of a tetrameric voltage-dependent potassium channel. Shaker-like channels are highly conserved across species but it is currently unknown whether they can affect sleep in mammals as powerfully as Shaker does in flies. As a first attempt to clarify this issue, we studied Kv1.2, a voltage-dependent potassium channel with high expression levels in the rat thalamocortical system.

**Methods :** Male Wistar Kyoto rats (7-8 weeks old; 200-250g) were implanted for chronic polygraphic recordings and kept in a 12:12 light:dark cycle (lights on 11AM). EEG was measured in the left and right parietal and occipital cortices using local field potentials. Drugs were injected in the right occipital cortex (2ul, max 1ul/min) using a CMA 400 syringe pump (max 3 injections/rat, spaced apart at least 4 days; onset of injections 2PM).

**Results :** An antibody raised against the extracellular portion of the Kv1.2 channel, and previously shown to block the Kv1.2 current by up to 70%, abolished or reduced EEG signs of NREM sleep on the right (injected) occipital cortex for up to 12 hours after the injection (n=12). The effect was dose-dependent, reversible, and site-specific. The behavior of the rat was unchanged after injection of all but the highest doses (which triggered a generalized seizure), and remained consistent with the EEG on the right parietal cortex and on the left hemisphere. Control injections were made with antibodies at doses equivalent to the highest dose of extracellular Kv1.2 antibody. Injection of an anti-Kv1.2 specific for the intracellular portion of the channel (n=3), anti-NCAM (n=3), anti-Kv1.3 (mainly microglial; n=3), and anti-rabbit IgG (n=3) did not affect the sleep EEG, nor the behavioral state of the animal. EEG power spectral

analysis is in progress.

**Conclusion :** Blockade of the voltage-dependent potassium channel Kv1.2 can affect the NREM sleep EEG in a dose-dependent, reversible, and site-specific manner.

**Support (optional):** Supported by a grant from the United States Defense Advanced Research Projects Agency, Swiss National Science Foundation, NIH Pioneer Award.

## 0111

### VOLTAGE-DEPENDENT POTASSIUM CHANNEL KV1.2: EFFECTS ON SLEEP AND EEG POWER SPECTRUM OF A NULL KV1.2 MUTATION IN MICE

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**Introduction :** Shaker minisleep (mns) is a null mutation of the Drosophila voltage-dependent potassium channel Shaker. Shaker flies sleep 4-5 h/day instead of 9-15h like wild-type flies. Shaker-like channels are conserved across species but it is unknown whether they affect sleep in mammals as powerfully as Shaker does in flies. To address this issue, we studied sleep in Kv1.2 knockout (-/-) mice. Kv1.2 is a Shaker-like voltage-dependent potassium channel with high expression in the rat thalamocortical system.

**Methods :** Pups (P16; +/+, +/-, -/-) and adult mice (P60, +/+, +/-) were implanted for chronic EEG and EMG recordings and kept in a 12:12 light:dark cycle. Sleep stages were scored visually based on 4-s epochs. EEG power spectra of consecutive 4-s epochs were calculated within the frequency range of 0.25-20.0 Hz. Continuous video recordings verified behavioral states.

**Results :** At P17 (n=13 +/+, 20 +/-, 7 -/-) and P19 (n=11 +/+, 20 +/-, 2 -/-), ANOVA reveals genotype- (p<0.01,) and LD- (p<0.01,) main effects on vigilance state. At P17, -/- pups have significantly less (-23%; p<0.01) NREM sleep and significantly more (+21%; p<0.05) waking than +/+ and +/- pups with no change in REM sleep time. FFT analysis reveals that -/- pups have significantly higher EEG power between 0.5-1.0 Hz than +/+ and +/- pups during NREM. At P19 (n=11 +/+, 20 +/-, 2 -/-), -/- pups show reduced 24-h values of NREM sleep relative to +/+ mice (-26%) and relative to +/- pups (-24%) with only a trend toward increased waking. REM sleep is unaffected by genotype at P19. The decrease in NREM is due, at least in part, to a decrease in sleep episode duration, while episode number was unchanged. Mutant pups appear healthy and gain weight similarly to wild-type mice, but die suddenly by P28 from an isolated episode of generalized seizure. Seizures are absent in +/- mice, and occur rarely in -/- pups before the terminal episode. No abnormal EEG activity is present in -/- pups, except during the seizure. At P67, +/- adults (n=6) show reduced 24-h values of NREM sleep (-23%) relative to +/+ (n=2) mice, with the most significant change during the light period (-27%). REM sleep and waking increase over the 24-h period by 12% and 14%, respectively.

**Conclusion :** Mice lacking one or two copies of the gene encoding the Kv1.2 Shaker-like potassium channel exhibit genotype-specific increases in wakefulness and decreases in NREM sleep with increased EEG power in 0.5-1.0 Hz frequencies during NREM.

**Support (optional):** Supported by a grant from the United States Defense Advanced Research Projects Agency, Swiss National Science Foundation, NIH Pioneer Award.

## 0112

### SLEEP-WAKE PATTERNS OF OCTODON DEGUS

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**Introduction :** Octodon degus are social rodents native to South America. In nature they are diurnal, being active outside the burrow during the day. Degus have been frequently used in circadian rhythms research. Only one laboratory has published findings on the sleep of these animals, and this group suggests degus are crepuscular. Because degus in the wild are diurnal, the aim of our study was to begin systematically determining sleep-wake behavior of these animals in a laboratory setting. If their sleep-wake behavior in the laboratory is diurnal, degus may constitute a rodent model of sleep that more closely resembles the sleep of humans.

**Methods :** Our initial pilot study used three male degus (250 g). Animals were individually housed on a 12:12 light:dark cycle at 18°C. Degus were surgically implanted with EEG electrodes, and thermistors to record brain temperature. Infrared devices were used to detect activity in the cage. After recovery, recordings were made for 24 h. Each animal was videotaped during the recording period. Sleep-wake behavior was assigned to 12 s epochs based on criteria used in the rat.

**Results :** These three degus spent 40 ± 4% recording time in NREMS during the dark period, and 29 ± 3% during the light period. REMS also occurred more during the dark period (5 ± 1% vs. 3 ± 1). Assessment of the videotapes confirmed more behavioral sleep (hunched body posture, no movement, closed eyes) during the dark period. Average brain temperature during the dark period was 34.1 ± 0.1 and during the light period 34.4 ± 0.1.

**Conclusion :** One previously-published study did not demonstrate a clear diurnal pattern of sleep-wake behavior in degus. Our pilot study suggests on the basis of EEG and behavioral data that degus under our laboratory conditions sleep more during the dark period. Future studies will increase samples sizes and examine the neurobiological mechanisms underlying sleep of these animals.

**Support (optional):** Department of Anesthesiology, University of Michigan

## 0113

### BEHAVIORAL SLEEP IN THE WALRUS

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**Introduction :** Pinnipeds can sleep both on land and in water. The phenomenology of sleep has been studied in details in the eared seals (family Otariidae) and true seals (Phocidae). Sleep in the walrus, the only living species of the third pinniped family, Odobenidae, has never been examined.

**Methods :** The behavior of four young (1.5-2 years old) captive walrus was videotaped continuously for 7-17 days. The walrus were housed in a pool with seawater and a platform above the water. The behavior of animals was scored in 1-min epochs as waking, quiet sleep and REM.

**Results :** The walrus were awake on average between 67% and 83% of 24-h spending about 75% of the time in water. Two walrus slept mostly at night on land and swam most of the daytime. Two other animals alternated periods of almost continuous swimming lasted for 40-84 h and periods of rest on land lasted for 16-25 h. While in water they were active on average 96% of the time, while on land they were asleep on average 75% of the time. REM sleep was quantified in two animals. The average amount of REM on land was 0.4% and 1.1% of 24-h with episodes last-

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ed for 5-728 sec. Sleep in water occurred at the surface or on the bottom of pools while the walrus briefly interrupted swimming. Episodes of sleep in water lasted for 10-161 sec. The total duration was less than 0.2% of 24-h. REM in water was observed in only one walrus. Those episodes (15 per 3 days) lasted for 6-118 sec and occurred during one breathing pause while the animal floated with the head submerged below the surface.

**Conclusion :** Behavioral sleep in the walrus appears to be similar to that in Phocidae. Walrus may spontaneously go without sleep for several days, showing almost continuous swimming.

**Support (optional):** Supported by the Utrish Dolphinarium Ltd., NIH, NSF, and the VA.

### 0114

#### HIGH FAT DIET INDUCES CHANGES IN SLEEP-WAKE PATTERNS IN MICE

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**Introduction :** Recent experimental and clinical studies have indicated that sleep loss leads to impairments in energy metabolism, ranging from increased appetite and weight gain to early signs of glucose and insulin dysregulation. In the present study, we tested a reciprocal hypothesis, that altering energy metabolism, by feeding mice a high fat diet, would lead to changes in sleep-wake patterns.

**Methods :** Male C57Bl/6J mice were maintained on a 12:12 L:D schedule with free access to regular chow and water. At 10 weeks of age, all mice were implanted with EEG/EMG electrodes for polysomnographic recording. After a 24-hr baseline sleep-wake recording, half of the mice (N=8) remained on regular chow and half (N=8) received a high fat diet for 6 weeks, followed by another 24-hr sleep-wake recording. Wake, NREM or REM sleep was assigned to 10-second epochs and EEG power spectral analysis was performed. Statistical comparisons were made using t-tests to examine between and within group differences for baseline and week 6 data.

**Results :** In the regular fed group, total sleep time (TST) was similar between the baseline and week 6 recordings. In contrast, after 6 weeks on the high fat diet, TST was significantly increased (baseline, 697±23 vs. week 6, 776±15 minutes, p<.05) due to an increase in the number of sleep bouts (baseline, 201±8 vs. week 6, 247±10, p<.01) and a trend for decreased sleep bout duration (baseline, 3.47±0.1 vs. week 6, 3.16±0.1 minutes, p=.06). The number of arousals from sleep was increased after high fat feeding (baseline, 113±11 vs. week 6, 152±7, p<.05). Both NREM (baseline, 633±21 vs. week 6, 704±13 minutes, p=.07) and REM (baseline, 64±3 vs. week 6, 72±3, p=0.2) sleep times tended to increase after high fat feeding. There were no diet induced effects on EEG power spectral values. Over the 6 week period, regular fed animals gained an average of 0.7±0.2 grams, whereas high fat animals gained 3.1±0.5 grams of body weight.

**Conclusion :** After six weeks on a high fat diet, mice displayed an increased propensity for sleep, however, sleep was more fragmented. Future investigations will be aimed at using such animal models to determine the underlying mechanisms linking sleep and energy metabolism.

**Support (optional):** This work was supported by NIH grants: R01HL075029, P01AG011412, T32HL007909

### 0115

#### CETACEAN SLEEP BEHAVIOR VARIES WITH BODY SIZE

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**Introduction :** Previous studies showed that slow waves occur only uni-hemispherically in dolphins and emphasized that sleep occurs while they are continuously swimming. Here we compare sleep, resting behavior and immobility across 5 cetacean species.

**Methods :** Video and visual observations of behavior were made in a total of 23 cetaceans of 5 different species. EEG recordings were made in 2 freely swimming bottlenose dolphins using digital recorders and measuring fluke movements with actigraphy.

**Results :** Almost continuous swimming appears to be characteristic of all small adult cetaceans (on average 97% of 24-h in Commerson's dolphins) and cetacean calves (96-100% of 24-h in bottlenose dolphin and killer whale neonates) suggesting that they have unihemispheric SWS (USWS) only during swimming. In contrast, long periods of immobility while floating at the surface or lying on the bottom of pools were characteristic of all examined large cetaceans (on average 42-67% of the nighttime in adult belugas and killer whales and 41% of 24-h in one gray whale calf) suggesting that motion is not a necessary feature of cetacean sleep. We recorded USWS in a dolphin while it lay quietly on the bottom of the pool. These episodes lasted 150-210 sec and were interrupted by arousals when the dolphin surfaced to breathe. This data questions the hypothesis that USWS in cetaceans is related to continuous swimming to allow breathing. Monitoring of fluke movements and recording of EEG in dolphins while floating also revealed periods of immobility during USWS lasting for several minutes.

**Conclusion :** Small dolphins, porpoises and cetacean calves, seem to be "obligate" swimmers and have USWS only during swimming, presumably to facilitate thermoregulation, allow "schooling" with the group and preserve buoyancy. USWS in larger cetaceans may occur during swimming, floating at the surface, or lying motionless at the bottom of pools, and, therefore, primarily serving a sentinel function.

**Support (optional):** Supported by NIH, NSF, the Utrish Dolphinarium Ltd. and the VA.

**0116****PHARMACOKINETIC AND PHARMACODYNAMIC EFFECTS OF THE SELECTIVE 5HT<sub>2A</sub> INVERSE AGONIST APD125 IN HEALTHY ADULTS**

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**Introduction :** APD125 is a selective 5HT<sub>2A</sub> inverse agonist that improves sleep consolidation without adversely affecting REM sleep in preclinical models. In the present studies, safety, tolerability, pharmacokinetics (PK), and effects on sleep were evaluated in healthy adults.

**Methods :** Three phase 1 randomized, double-blind, placebo-controlled studies were performed: (1) a single dose (10, 20, 40, 80, and 160 mg) study in 45 healthy men to assess safety, tolerability, PK, and waking EEG; (2) a seven day, repeat-dose (20, 40, or 80 mg each morning) study in 27 healthy men to assess safety, tolerability, and PK; (3) a cross-over study (0, 10, 20, and 40 mg) in 29 healthy volunteers to assess safety, tolerability, and effects on sleep in a post-nap model of insomnia.

**Results :** APD125 was rapidly absorbed after a single dose (t<sub>max</sub>=1-1.5 hr). Plasma half-life was 3.9-10.7 hr at 10-40 mg; exposure was dose-proportional up to 40 mg, with C<sub>max</sub> plateauing at 40 mg and AUC at 80 mg. APD125 decreased EEG alpha-2 power and increased theta power maximally at 40-80 mg. Self-rated sedation was increased 2.5 hrs after dosing at >40 mg. In Study 3, APD125 (10-40 mg) significantly impacted measures of sleep maintenance and consolidation without affecting REM sleep (treatment effect significance: p<0.0001 for SWS, delta power and number of awakenings; p<0.01 for microarousal index). The following morning, no clear dose-related effects on psychomotor testing or subjective sleep quality were observed. APD125 was well-tolerated at all doses. Adverse events were infrequent, and included headache, insomnia and somnolence.

**Conclusion :** APD125 was safe and well-tolerated at single doses up to 160 mg and repeated doses up to 80 mg. APD125 in doses from 10-40 mg increased SWS and decreased the number of awakenings and microarousals, suggesting that it may prove useful for sleep maintenance and consolidation.

**Support (optional):**

**0118****GABOXADOL DOES NOT AFFECT THE SINGLE DOSE PHARMACOKINETICS OF THE R(+) AND S(-) ENANTIOMERS OF WARFARIN AND THE PHARMACODYNAMICS OF WARFARIN**

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**Introduction :** Gaboxadol is a selective extrasynaptic GABA agonist (SEGA) in development for the treatment of insomnia. This study was conducted to determine if there is any interaction between warfarin and gaboxadol.

**Methods :** Fourteen healthy subjects were randomized in this open-label, multiple-dose, 2 period, crossover study. Subjects received both treatments in the morning: (i) a single open-label dose of 30-mg warfarin on Day 1 plus once-daily open-label dosing with 15-mg gaboxadol on Days

1 to 7 and (ii) a single open-label dose of 30-mg warfarin on Day 1. Blood was collected over 168 hours post dose warfarin for R(+) and S(-) enantiomers of warfarin and for INR (International Normalized ratio for prothrombin time). The 2 treatment periods were separated by at least a 12-day interval. Adverse experiences (AEs) and safety parameters were monitored throughout the study.

**Results :** Gaboxadol did not meaningfully alter the pharmacokinetics of warfarin. For both enantiomers of warfarin, the AUC<sub>0-∞</sub> following warfarin coadministered with 15-mg gaboxadol was similar (90% CI for GMR within 0.80 to 1.25) to the warfarin AUC<sub>0-∞</sub> following warfarin alone: the GMR and 90% CI for the R(+) enantiomer was 0.97 (0.94, 1.00) and for the S(-) enantiomer was 1.00 (0.96, 1.04). Similar results were seen for C<sub>max</sub> (both enantiomers). Gaboxadol did not meaningfully alter the warfarin pharmacodynamics with respect to the INR AUC<sub>0-168 hr</sub>, INR<sub>max</sub>, or mean INR: the GMRs were close to one with 90% CIs within 0.8 to 1.25. The most common drug related clinical AEs included somnolence and vertigo; all were rated as mild in intensity.

**Conclusion :** Seven days of once daily dosing with gaboxadol 15-mg does not affect the single-dose pharmacokinetics of either [R(+)- and S(-)] enantiomer of warfarin 30-mg and does not affect the anticoagulant effect of warfarin 30-mg as measured by the INR. Concomitant administration of gaboxadol 15-mg and warfarin is generally well tolerated.

**Support (optional):** This clinical study was supported by Merck & Co.

**0119****EFFECTS OF CAFFEINE ARE MORE MARKED ON DAYTIME RECOVERY SLEEP THAN ON NOCTURNAL SLEEP**

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**Introduction :** Caffeine is often used to fight sleepiness generated by sleep deprivation, jet lag, and shift-work. Consequently, caffeine is consumed at different times of day and night. However, we know little about the way in which homeostatic and circadian processes influence the effects of caffeine. The aim of this study was to compare the effects of caffeine on sleep at two circadian times.

**Methods :** Thirty-four moderate caffeine consumers (14 men, 20 women, mean age= 38.59±14.80 yrs) participated in both a caffeine (200 mg) and a placebo (lactose) conditions in a double-blind crossover design. Seventeen subjects followed their habitual sleep-wake cycle and slept in the laboratory during the night (Nocturnal) while 17 subjects (sex and age-matched) were sleep deprived for one night (25 hours of wakefulness) and recovery sleep started in the morning (DayRec). All subjects received a capsule of 100 mg of caffeine (or placebo) three hours before bedtime and the remaining dose, one hour before bedtime. The effects of caffeine on polysomnographic sleep were evaluated using mixed ANOVAs.

**Results :** Compared to placebo, caffeine lengthened sleep latency, and reduced stage 2 (p<0.001) and SWS (p£0.05) similarly in the Nocturnal and DayRec groups. Significant interactions between conditions (Caffeine, Placebo) and time of sleep (Nocturnal, DayRec) were found for total sleep time (p£0.04), sleep efficiency (p<0.001) and time spent in REM sleep (p£0.02). Compared to placebo, caffeine reduced sleep efficiency, decreased total sleep time and REM sleep more strongly in the DayRec group than in the Nocturnal group.

**Conclusion :** The effects of caffeine on sleep are more prominent when caffeine is consumed before daytime recovery sleep than before nocturnal sleep. Caffeine showed stronger effects on sleep at an abnormal circadian phase despite the fact that subjects were sleep deprived. These results

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have implications for individuals using caffeine during nighttime to prevent the effects of sleep deprivation.

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### 0120

#### GABOXADOL DOES NOT REQUIRE A DOSE ADJUSTMENT ON THE BASIS OF HEPATIC INSUFFICIENCY

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**Introduction :** Gaboxadol is a selective extrasynaptic GABA agonist (SEGA) in development for the treatment of insomnia. This study was conducted to guide clinicians prescribing gaboxadol for patients with mild or moderate hepatic insufficiency.

**Methods :** This was an open-label study comparing the pharmacokinetics of a single 10-mg dose of gaboxadol in 10 patients (38 to 64 yrs) with moderate hepatic insufficiency (Child-Pugh score of 7 to 9) with 10 healthy (41 to 63 yrs) matched (for age, gender, BMI, race) controls. Each patient/subject received a single 10-mg dose of gaboxadol. Plasma and urine gaboxadol concentrations were collected predose and over 48 hours postdose. The digit symbol substitution test (DSST) and Bond-Lader visual analog scales (VAS) were also evaluated over 24 hrs postdose. Adverse experiences (AEs) and safety parameters were monitored throughout the study.

**Results :** The pharmacokinetics of gaboxadol was not meaningfully altered in patients with hepatic insufficiency. The gaboxadol AUC for patients with moderate hepatic insufficiency was similar (defined a priori as a 90% CI for GMR below 1.5) to the gaboxadol AUC for healthy subjects (GMR of 1.01 with 90% CI of 0.88, 1.15). There were no significant differences between the two populations for either the VAS factors (Alertness, Contentedness, and Calmness) or the mean DSST number correct. Four hepatic patients and 3 healthy controls reported 8 of the 9 drug-related AEs which were nervous system disorders of headache and somnolence. All AEs were rated as mild in intensity.

**Conclusion :** Moderate hepatic insufficiency has no clinically meaningful effect on the pharmacokinetics of gaboxadol. A single 10-mg dose of gaboxadol in patients with moderate hepatic insufficiency, as well as in healthy controls, is generally well tolerated. No dosage adjustment on the basis of mild or moderate hepatic insufficiency is required. These results were expected based on the renal elimination of gaboxadol.

**Support (optional):** This clinical study was supported by Merck & Co.

### 0121

#### GABOXADOL, A SELECTIVE EXTRASYNAPTIC GABA AGONIST (SEGA): SAFETY AND PHARMACOKINETICS IN ELDERLY (> 65 YRS) SUBJECTS WITH BEDTIME DOSING

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**Introduction :** Gaboxadol is a selective extrasynaptic GABA agonist (SEGA) in development for the treatment of insomnia. This study was conducted to determine the safety and PK of gaboxadol in an elderly (> 65 yrs) population.

**Methods :** Twenty-four elderly (65 to 75 yrs) subjects (7 males, 17 females) were included in this double-blind (DB), randomized active- and placebo-controlled 3-period crossover study (gaboxadol 10 mg, zolpidem 5 mg, and placebo orally at bedtime) with a single-blind (SB), nonrandomized 4th period for PK. Adverse experiences and safety parameters were monitored throughout the study. Plasma for gaboxadol PK was obtained over 16 hours postdose. Critical Flicker Fusion (CFF; attention) and Body Sway (equilibrium) were tested at 1.5, 4 and 8 hours post dosing.

**Results :** Fourteen subjects (58.3%) experienced 30 AEs following gaboxadol 10 mg (DB), 7 subjects (30.4%) experienced 12 AEs following zolpidem 5 mg, 9 subjects (39.1%) experienced 18 AEs following placebo, and 6 subjects (27.3%) experienced 7 AEs following gaboxadol 10 mg (SB). Dizziness (20.8%) and fatigue (12.5%) were the most frequently occurring AEs following gaboxadol DB. The geometric mean ratio (elderly females/males) and 95% CI for gaboxadol AUC<sub>0-∞</sub> and C<sub>max</sub> were 1.08 (0.94, 1.23) and 1.19 (0.93, 1.53), respectively. There were no statistical differences between elderly male and females. Body sway: a significant increase for zolpidem treatment relative to placebo at 1.5 and 4 hours postdose and a significant increase (for eyes open) for gaboxadol relative to placebo at 4 and 8 hrs. The increase for zolpidem treatment was significantly greater than the increase for gaboxadol treatment at 1.5 hours, while the increase for gaboxadol treatment was not significantly greater than the increase for zolpidem treatment at any timepoint. CFF threshold: a significant decrease in CFF threshold (descending) at 1.5 hours postdose for zolpidem treatment versus placebo and gaboxadol treatments. No significant decreases for gabaxadol versus placebo treatment.

**Conclusion :** A single oral dose of gaboxadol 10 mg administered at bedtime is generally well tolerated in elderly subjects. Gaboxadol PK is generally similar between elderly male and female subjects. Less acute impairment in equilibrium and attention seem to occur following a single oral dose of 10 mg of gaboxadol administered at bedtime relative to zolpidem 5 mg.

**Support (optional):** This clinical study was supported by Merck & Co.

### 0122

#### ASSESSMENT OF DOSE PROPORTIONALITY, ABSOLUTE BIOAVAILABILITY, AND TOLERABILITY OF GABOXADOL IN HEALTHY YOUNG ADULTS

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**Introduction :** Gaboxadol is a selective extrasynaptic GABA agonist (SEGA) in development for the treatment of insomnia. This study was conducted to evaluate dose proportionality, absolute bioavailability, and tolerability of gaboxadol.

**Methods :** This study was conducted in 2 parts. Part 1 included 8 subjects who received double-blind single i.v. doses of gaboxadol (5 mg and 10 mg) or single i.v. doses of placebo (normal saline) by 1-hr infusion in a fixed sequence, rising dose fashion. Part 2 included 10 subjects in a 5 period, double-blind, randomized, cross-over with a sixth non-randomized period. The 5 oral doses (2.5, 5, 10, 15, and 20 mg) were randomized within Periods 1 through 5; single-dose 10 mg i.v. gaboxadol was

received in Period 6. Plasma and urine samples for PK were obtained over 16 hours post-dose in each period. Summary statistics were computed for  $AUC_{0-\infty}$ ,  $C_{max}$ ,  $T_{max}$ , half-life, clearance, and  $V_{dss}$  as appropriate. Adverse experiences (AE) and safety parameters were monitored throughout the study.

**Results :** All 18 subjects completed the study. The geometric mean  $AUC_{0-\infty}$  (ng-hr/mL) values for the 2.5-, 5-, 10-, 15-, and 20-mg oral doses were 90, 171, 346, 539, and 669, respectively, supporting dose proportionality. Both  $AUC_{0-\infty}$  and  $C_{max}$  were dose proportional in the 2.5 to 20-mg oral dose range. The average bioavailability of a 10 mg dose was ~92%. The clearance averaged ~ 450 mL/min, and  $V_{dss}$  averaged ~ 55 L. The AE profiles following gaboxadol i.v. administration and oral administration were similar. Somnolence and dizziness were the most common AEs.

**Conclusion :** Plasma  $AUC_{0-\infty}$  and  $C_{max}$  of gaboxadol show dose proportionality and appear to be linear over the entire dose range examined, from 2.5 to 20 mg. Bioavailability of gaboxadol is ~92%. Single-dose administration of i.v. gaboxadol doses of 5 and 10 mg, and oral doses of gaboxadol from 2.5 to 20 mg are generally well tolerated.

**Support (optional):** The Clinical Study was funded by Merck & Co., Inc.

## 0123

### ABSORPTION, METABOLISM AND EXCRETION PROFILE OF GABOXADOL IN HUMANS

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**Introduction :** Gaboxadol is a selective extrasynaptic GABAA agonist (SEGA) in development for the treatment of insomnia. The absorption, metabolism and excretion of gaboxadol were investigated after a single oral dose.

**Methods :** Six healthy men (aged 41 to 53) received an oral single morning dose of 15mg 14C-gaboxadol. Urine, faeces and blood were collected up to 96hrs post-dose for determining total radioactivity and gaboxadol levels, protein binding, and metabolite profile. Safety parameters were measured regularly during the study.

**Results :** Absorption of the radioactivity was rapid with a  $T_{max}$  of 0.5hrs (range 0.25 to 0.75hrs), which was comparable to that of gaboxadol measured in plasma (range 0.25 to 0.75hrs).  $C_{max}$  of radioactivity was comparable to gaboxadol (2423nmol-eq/L vs 2190nmol/L). The ratio between  $AUC_{inf}$  of gaboxadol and radioactivity in plasma was 0.54, indicating the presence of one or more circulating metabolites. The apparent elimination half-life was slightly longer for the radioactivity than for gaboxadol (2.17hrs vs 1.58hrs). Radioactivity was primarily renally excreted with a mean of 96.5% (SD:0.4) of the total dose recovered in urine. The overall mean recovery reached 99.5% (SD:0.3) with 3% recovered in faeces. More than 75% of the dose was excreted within 4hrs and more than 93% within 12hrs. The metabolite profiling identified a glucuronide of gaboxadol as the major metabolite in both plasma and urine. In urine, 59% of the total dose was excreted as parent compound and 34% as the glucuronide conjugate. Protein binding was less than 15% for all the subjects. Gaboxadol was well tolerated.

**Conclusion :** The absorption of an oral dose of gaboxadol is fast and almost complete as more than 95% of the dose is excreted in urine. The glucuronide conjugate of gaboxadol is the only metabolite formed in significant amounts. Hence, the CYP450 system does not have significant involvement in the metabolism of gaboxadol.

**Support (optional):** This research was supported by H. Lundbeck A/S

## 0124

### GABOXADOL HAS LITTLE OR NO EFFECT ON COGNITIVE AND PSYCHOMOTOR TESTS COMPARED TO ZOLPIDEM, AND THE TWO COMPOUNDS HAVE LIMITED POTENTIAL FOR INTERACTION IN HEALTHY SUBJECTS

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**Introduction :** Gaboxadol is a selective extrasynaptic GABAA agonist (SEGA) that has demonstrated improvements in both sleep onset and maintenance measures in insomniacs. This study investigated the pharmacodynamic effects of gaboxadol and zolpidem and the interaction potential between the two drugs.

**Methods :** 24 subjects (18-38y) completed a randomized, double-blind, 4-way crossover study with the following treatments given at 8:00am: placebo, gaboxadol 10mg, zolpidem 10mg or a combination of gaboxadol 10mg and zolpidem 10mg. At pre-determined time-points (pre-dose, 0.5, 1.5, 3, 6, 9 and 24hrs post-dose), pharmacokinetic samples were drawn and the following cognitive and psychomotor tests were performed: Simple Reaction Time, Choice Reaction Time, Digit Vigilance, Numeric Working Memory, Immediate and Delayed Word Recall, Word and Picture Recognition, Tracking and Postural Stability. Safety parameters were measured during the study.

**Results :** Gaboxadol alone produced no statistical impairments on the cognitive and psychomotor tests compared to placebo. In contrast, zolpidem alone produced significant impairments relative to placebo on all 14 measures from the 10 tests. These effects often appeared by 0.5hr, with peak effects 1.5 and 3hrs post-dose and had resolved by 6hrs. Compared to the impairment produced by zolpidem alone, a significant extra impairment was produced by gaboxadol when co-administered with zolpidem on: Simple Reaction time(3hrs), Choice Reaction Time(3hrs), Digit Vigilance Targets Detected(1.5hrs), Numeric Working Memory Sensitivity(0.5hrs), Tracking(3hrs) and Postural Stability(0.5 and 1.5hrs). True synergistic interaction was observed for Postural Stability(0.5hrs) and for Simple Reaction Time(3hrs)( $P<0.05$ ). The estimated 90% confidence intervals for  $C_{max}$  and  $AUC_{0-\infty}$  of gaboxadol and zolpidem when co-administered and when administered alone were within 0.8-1.25. All treatments were well tolerated.

**Conclusion :** Gaboxadol alone did not affect the performance in the cognitive and psychomotor tests, whereas zolpidem caused impairments in all tests. Even though there are some indications of interaction between the drugs, these were small and short in duration.

**Support (optional):** This research was supported by H. Lundbeck A/S.

## 0125

### APPROACHING AN ENDOGENOUS MELATONIN SECRETION PROFILE TO IMPROVE DAYTIME SLEEP BY DERMAL MELATONIN DELIVERY

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**Introduction :** Melatonin is widely used as an alternative therapy for insomnia and to enhance sleep during the biological day in night-workers and during jetlag. The short half-life and poor bioavailability of oral melatonin, however, reduce its efficacy in maintaining a prolonged bout of daytime sleep, as desired by night-workers. We therefore tested the feasi-

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bility of dermal delivery to induce sustained elevated melatonin levels and improve daytime sleep.

**Methods :** Eight young, healthy subjects (24-34 years; 4 women) were studied in a randomized double-blind placebo-controlled crossover protocol. Subjects completed two laboratory visits that were 7-16 days apart, each consisting of a nap sleep episode (15:00-19:00 h) on day 1 and a daytime sleep episode (09:00-17:00 h) on day 2. An experimental skin patch (2.1 mg melatonin or placebo; Biotek Inc. Woburn, MA) was applied to the forearm at 08:00 h on day 2 and removed at 18:00 h. Hourly plasma samples were obtained throughout with an indwelling intravenous catheter and sleep was analyzed with polysomnography.

**Results :** After a lag of ~2 h following active patch application, plasma melatonin levels increased steadily, reached statistical significance ( $p < 0.05$ , t-test) over placebo for the first time at 12:00 h, and peaked at 17:00 h. Peak plasma melatonin levels differed ( $p < 0.05$ ) between men (mean  $\pm$  SEM:  $79.9 \pm 24.8$  pg/ml) and women ( $216.9 \pm 29.9$  pg/ml). The active patch increased ( $p < 0.05$ , Wilcoxon) the amount of REM sleep by 20.3 min, and decreased waking after sleep onset by 55.6 min. In the last third of time in bed, coinciding with the highest melatonin levels in the active condition, total sleep time, stage 2 and REM sleep were increased compared to placebo ( $p < 0.05$ ). In addition, melatonin lowered core body temperature by  $\sim 0.1^\circ\text{C}$  between 15:00 and 18:00 h ( $p < 0.05$ ).

**Conclusion :** Dermal delivery of melatonin is effective in producing sustained elevated plasma melatonin levels that approximate the endogenous secretion pattern, and in improving daytime sleep.

**Support (optional):** This research was supported by NIH grants 2R44NS43129-02 to Biotek, Inc., and NCRR-GCRC-M01-RR02635 to Brigham and Women's Hospital.

### 0126

#### SLEEP AND DAYTIME ALERTNESS IN DRUG FREE MDMA USERS

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**Introduction :** Recreational use of 3,4-methylenedioxymethamphetamine (MDMA), an amphetamine derivative with putative serotonergic toxicity, is associated with insomnia. In our previous report MDMA administration reduced sleep time and REM time relative to placebo. Given its serotonergic activity, the sleep-wake function of abstinent MDMA users needs to be more completely characterized.

**Methods :** Seven healthy, 18-25 yrs old, recreational MDMA users and 13 controls without a drug use history, selected from a population-based sample, all without psychiatric disease or drug dependence, were compared. A nocturnal polysomnogram (NPSG) and a standard clinical Multiple Sleep Latency Test (MSLT) the following day were conducted. Bedtime for the NPSG was 8 hrs and the MSLT was done at 1000, 1200, 1400 and 1600 hrs the following day. All were drug free showing negative drug screens prior to the laboratory study.

**Results :** Sleep efficiency was normal and did not differ between MDMA users and controls (89.4 vs 90.3%), nor did sleep latency and wake during sleep. MDMA users had less stage 3-4 sleep (4.8 vs 15.8%,  $p < .01$ ). The groups did not differ in other sleep stage measures. Mean daily sleep latency on the MSLT was elevated in MDMA users relative to controls (15.7 vs 10.7 min,  $p < .01$ ) and the MDMA users had more sleep onset REM periods (SOREMP) on the MSLT than controls (1.0 vs 0.008,  $p < .01$ ). Two MDMA users had 2 SOREMPs, 3 had 1, and 2 had no SOREMPs.

**Conclusion :** Drug free MDMA users, while showing comparable sleep efficiencies to normals, exhibit an elevated MSLT, which is indicative of

hyperarousal. In addition, while not showing differences in REM pressure (i.e., REM latency and REM %), MDMA users did show daytime evidence of impaired REM function. These acute abstinence findings will need to be followed during a more prolonged abstinence, but are consistent with a serotonergic mechanism.

**Support (optional):** NIDA grant #R01-DA14874 awarded to Dr M Tancer

### 0127

#### THE EFFECTS OF STIMULANTS ON RECOVERY SLEEP AND POST-RECOVERY VERBAL PERFORMANCE FOLLOWING 61-HOURS OF SLEEP DEPRIVATION

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**Introduction :** Sleep deprivation (SD) adversely impacts alertness and vigilance, but these deficits can be temporarily reversed by psychoactive stimulant compounds. Such stimulant use, however, can potentially affect the quality of subsequent sleep if the medication is still active in the brain. Previous findings also suggest that dextroamphetamine administered during sleep deprivation may slow cognitive performance upon awakening from a night of recovery sleep. We evaluated the effects of dextroamphetamine, caffeine, modafinil, and placebo on recovery sleep and post-recovery performance.

**Methods :** Fifty-four healthy volunteers (29 men) remained awake for 61 hours, followed by 12 hours of recovery sleep. As a measure of cognitive processing and verbal fluency, the Controlled Oral Word Association Test (COWA) was administered daily. After 44 hours awake, volunteers received a double-blind oral administration of caffeine (600 mg), modafinil (400 mg), dextroamphetamine (20 mg), or placebo. After 61 hours of SD, participants were given 12 hours time in bed to obtain recovery sleep while monitored by polysomnography (PSG).

**Results :** Stimulant medications differentially disrupted the duration and quality of recovery sleep. Volunteers who received dextroamphetamine demonstrated significantly less total sleep time ( $F=4.1$ ,  $p=.01$ ), decreased sleep efficiency ( $F=4.1$ ,  $p=.02$ ), and longer latencies to REM sleep ( $F=5.6$ ,  $p=.001$ ) than volunteers who received caffeine. Although post-recovery performance on the COWA was unrelated to total sleep time, COWA scores were negatively correlated with time in stage 1 ( $r=-.39$ ,  $p=.025$ ) and latency to REM ( $r=-.38$ ,  $p=.025$ ), and positively correlated with time in REM ( $r=.41$ ,  $p=.017$ ).

**Conclusion :** Dextroamphetamine appears to be particularly disruptive to sleep efficiency and post-recovery performance following a period of sleep-deprivation. Findings suggest that impairment of recovery sleep by stimulant medications can adversely impact subsequent cognitive performance. Moreover, this disruption appears to have the greatest impact on cognitive functioning when it affects the quality and duration of REM sleep.

**Support (optional):**

### 0128

#### MODAFINIL IMPROVES HUMOR APPRECIATION DURING SLEEP DEPRIVATION

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**Introduction :** It is well established that alertness, vigilance, and response speed show consistent decrements as a result of sleep loss. In contrast, the effects of sleep deprivation on higher order executive functions such as judgment and affective reasoning remain poorly delineated.



It is also becoming evident that, while stimulant medications are effective at restoring alertness and vigilance, their effects on higher order cognition may be less straightforward. Therefore, we assessed whether a double-blind administration of modafinil, caffeine, dextroamphetamine or placebo could improve the ability to appreciate humor, a complex cognitive-affective ability, following 49.5 hours of sleep deprivation.

**Methods :** Fifty-four, healthy adults (29 male) ranging in age from 18 to 36 years made forced choice judgments of the “funny” of visual (cartoon) and verbal (newspaper headlines) stimuli presented on a computer screen. Volunteers were randomly assigned to one of three stimulant medication groups, including: caffeine, 600 mg (n=12); modafinil, 400 mg (n = 11); dextroamphetamine, 20 mg (n = 16); or placebo (n = 14).

**Results :** Relative to normative data, sleep deprivation impaired the appreciation of humor. For cartoon stimuli, humor appreciation was significantly enhanced by modafinil relative to both placebo (p=.004) and caffeine (p=.011), with scores maintained at levels similar to that of the normative group. None of the stimulants improved the appreciation of verbal humor during sleep loss, however. Psychomotor response speed, in contrast, was enhanced by all three stimulants relative to placebo (all  $p < .05$ ), while only caffeine (p=.03) and dextroamphetamine (p=.004) improved ratings of subjective sleepiness.

**Conclusion :** Although all three stimulant compounds have similar alerting and vigilance promoting effects, only modafinil was effective at normalizing the ability to appreciate humor in cartoon images. These findings suggest that the various stimulant medications may be differentially effective at reversing the detrimental effects of sleep loss on higher order cognitive processes.

**Support (optional):**

## 0129

### THE EFFECT OF CAFFEINE, DEXTROAMPHETAMINE, AND MODAFINIL ON ALERTNESS AND MOOD DURING SLEEP DEPRIVATION

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**Introduction :** Sleep deprivation is known to cause serious decrements in both alertness and mood; therefore, pharmaceutical aids that can counteract the negative effects of sleep deprivation on alertness without exacerbating or producing abnormal alterations of mood are desirable. The current study examined the effects of caffeine, dextroamphetamine, and modafinil on subjective sleepiness, objective alertness, and mood.

**Methods :** Fifty-four volunteers (29 males) were administered the Stanford Sleepiness Scale (SSS), the Psychomotor Vigilance Test (PVT), and the Stern Visual Analog Mood Scales (VAMS) every two hours during 61 hours of total sleep deprivation. After 44 hours, participants were administered a single bolus dose of caffeine (600 mg), dextroamphetamine (20 mg), modafinil (400 mg), or a placebo, followed by regular mood and vigilance testing over the next 17 hours. Data were collapsed into two time periods (6 hours Pre-Drug; 6 hours Post-Drug). A repeated measures ANOVA was calculated between these two periods for each measure.

**Results :** Subjective Sleepiness: All three stimulants significantly reduced SSS scores ( $p < .001$ ). Objective Alertness: All three stimulants enhanced PVT performance relative to placebo ( $p < .05$ ), but did not differ from one another. Mood: Caffeine increased mood ratings of Afraid (p<.001), Confused (p=.002), Energetic (p<.001) and Tense (p<.001), and significantly decreased ratings of Happy (p=.002) and Tired (p<.001). Dextroamphetamine produced significant increases in Energetic (p<.001) and Happy (p<.001) ratings, while ratings of Sadness (p=.004) and Tiredness significantly decreased (p<.001). Modafinil significantly

increased Energy (p=.001) and decreased Tiredness (p=.001).

**Conclusion :** All three stimulants successfully decreased subjective ratings of sleepiness and increased objective alertness. Notably, caffeine produced significant elevations of negative moods, including Afraid, Confusion, and Tension, while dextroamphetamine yielded modest elevation of positive moods such as increased Happiness and reduced Sadness, although within normal levels. Modafinil produced the smallest increase in objective alertness, but was associated with the fewest alterations in mood.

**Support (optional):**

## 0130

### INDIVIDUAL DIFFERENCES IN STRESS MANAGEMENT CAPACITY PREDICT RESPONSIVENESS TO CAFFEINE DURING SLEEP DEPRIVATION

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**Introduction :** It is generally accepted that some individuals are more resistant to sleep loss than others, but the factors that lead to such resistance are poorly understood. One potential factor may involve individual differences in emotional intelligence, which can be defined as the non-cognitive capabilities and skills that influence an individual's ability to cope successfully with environmental pressures and demands. In the present study, baseline scores on the Bar-On Emotional Quotient Inventory (EQ-i) were used to predict sustained vigilance and alertness performance, as measured by the psychomotor vigilance test (PVT), during three successive nights of sleep loss.

**Methods :** Twenty-three subjects (19 male) were sleep deprived for 77 hours. The EQ-i and PVT were administered at rested baseline. In a double-blind administration, subjects received either caffeine (n=12; 200 mg every 2 hours from 0100 to 0700) or placebo (n=11) for the three nights they remained awake. The PVT was then administered 39 times each night from 0015 to 0845.

**Results :** For caffeine, multiple stepwise regression analyses indicated that scores on the Stress Management scale significantly predicted PVT performance during the first night of sleep loss ( $r = -0.85$ ,  $p = 0.001$ ), with poorer stress management scores associated with faster speed on the PVT relative to baseline. After the first night, none of the EQ-i scales were predictive of PVT performance for either drug group.

**Conclusion :** During the first night of sleep loss, caffeine's alerting capacity appears to be amplified in individuals with limited stress management capacities. When administered caffeine, individuals with poor stress management scores demonstrated relatively greater alertness and vigilance performances than individuals with strong in stress management capacities. We interpret these data as suggesting that individuals with poor stress management skills were more likely to experience heightened emotional/autonomic arousal when trying to perform under the influence of caffeine, thus amplifying its alerting effects.

**Support (optional):**

## 0131

### THE EFFECTS OF THE AMPAKINE, CX717, ON SPECTRAL ACTIVITY OF THE EEG DURING RECOVERY SLEEP

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**Introduction :** In clinical medicine there is a need for compounds that

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maintain wakefulness. Ampakines have been observed to enhance performance and cognition in animals and humans, with CX717 shown to abolish behavioural impairments during sleep deprivation in monkeys. The present work assessed effects of CX717 on EEG spectra during sleep following extended wakefulness.

**Methods :** Sixteen subjects ingested CX717 (100, 300 or 1000mg) or placebo, administered double-blind in a four-way crossover design, at 23:00h and then carried out a 10h period of work (00:00-10:00h). This was followed by daytime recovery sleep (10:00-16:00), during which four channels of EEG were recorded (C3-A2, C4-A1, O1-A2, O2-A1). Spectral analysis was carried out, and delta (0.5-3Hz), theta (3.5-7.5Hz), alpha (8-13 Hz), beta1 (13.5-21Hz) and beta2 (21.5-30Hz) power calculated. Only those subjects with four complete PSG recordings without significant artefact were included in the spectral cohort.

**Results :** Key findings from the overall study are presented in the abstract, Boyle et al. The 6 of 16 subjects identified for the spectral cohort did not differ meaningfully from the overall study group. CX717 (1000mg) modified all EEG variables other than theta activity (significant at the  $p < 0.05$  level or less) in a pattern suggestive of increased arousal during sleep. CX717 (100mg and 300mg) produced less marked effects, showing decreased delta activity and some changes in beta activity.

**Conclusion :** Each dose of CX717 modified the spectral content of the EEG, with changes indicative of increased alertness during recovery sleep most evident following the 1000mg dose. The findings were broadly consistent with the findings of visual analysis of the EEG (Boyle et al), although changes in delta activity differed from those seen with slow wave sleep with CX717 (1000mg). These differences may have been due to physiological processes other than slow wave sleep affecting the EEG at delta frequencies.

**Support (optional):**

### 0132

#### EVALUATION OF THE CENTRAL EFFECTS OF CX717 DURING EXTENDED WAKEFULNESS

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**Introduction :** AMPA receptor modulation could be a novel approach to cognitive enhancement. CX717 is a positive allosteric modulator of the AMPA receptor that has shown efficacy in rodent and primate models.

**Methods :** Effects of CX717 (100mg, 300 mg and 1000 mg) and placebo were studied in 16 healthy male volunteers (18 - 45 yrs) in a randomized, four-way crossover design with a 2 week washout between periods. On each occasion subjects were awake from 07.00h on day 1 to 10.00h on day 2. Subjects ingested study medication at 23.00h on Day 1. Cognitive functions were assessed from 00:00h (midnight) to 09:00h, and arousal was assessed using a modified maintenance of wakefulness test at 04:00h. The recovery sleep was studied from 10.00h to 16.00h (day 2) using polysomnography.

**Results :** With placebo there were decrements in cognition over the period of wakefulness with variability between subjects and between the cognitive measures. Analysis of the whole group showed that CX717 (1000 mg) increased alertness, increased sleep latency on the MWT (Cohen's  $d = 0.63$ ), enhanced information processing ability shortly after dosing ( $d = 0.59$ ) and improved attention 1 to 4h post dose ( $d = 0.6$ ). Analysis of those subjects with impaired overnight performance with placebo (corrected for regression to the mean) showed that CX717 (1000 mg) improved alertness (MWT:  $d = 1.25$ ,  $P \leq 0.05$ ), sustained attention ( $d = 2.4$ ,  $P \leq 0.01$ ) and information processing ( $d = 3.8$ ,  $P \leq 0.0001$ ) 4 h post dose. CX717 (100 to 300mg) had minimal effects on recovery sleep, but with 1000mg

there was evidence of continued activity with reduced slow wave sleep ( $P < 0.05$ ,  $d = 0.90$ ).

**Conclusion :** This preliminary study suggests that CX717, primarily at the 1000 mg dose, increases alertness and has the potential to enhance cognitive and psychomotor performance in sleep deprived individuals.

**Support (optional):** This study was supported by Cortex Pharmaceuticals Inc.

### 0133

#### NEXT-DAY DRIVING EFFECTS OF INDIPLON AND ZOPICLONE: RESULTS OF A DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSSOVER STUDY IN HEALTHY VOLUNTEERS

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**Introduction :** The present study evaluated the effect of nighttime administration of indiplon, a novel,  $\alpha 1$  subunit-selective, GABA-A receptor potentiator, on next-day driving performance. Zopiclone was also evaluated to provide a measure of assay sensitivity.

**Methods :** Healthy male subjects ( $N=30$ ) were randomized in a double-blind, crossover design to a single nighttime dose of indiplon 10 mg, indiplon 15 mg, zopiclone 7.5 mg, and placebo. A driving simulation test was performed 8.5 hours post-dose. Driving parameters included: (1) the variability in driving performance as indexed by the standard deviation of the deviations from the ideal route in meters (the primary, a priori, endpoint); (2) the mean of the absolute speed (km/h); and (3) the mean of the deviation from the speed limit.

**Results :** On the primary endpoint, the standard deviation of the deviations from the ideal route were comparable for indiplon 10 mg (0.60 m), indiplon 15 mg (0.57 m), and placebo (0.59 m). Driving variability was significantly greater for zopiclone (0.63 m) compared to placebo (0.59;  $p=0.03$ ). The mean observed speed (in km/h), and deviation from the posted speed limit, respectively, were similar for indiplon 10 mg (128.3; -4.9), indiplon 15 mg (128.8; -5.6), zopiclone (128.4; -5.7), and placebo (128.6; -6.9).

**Conclusion :** Nighttime treatment with indiplon 10 mg and 15 mg produced no significant next-day driving impairment in this driving simulation study. Treatment with zopiclone 7.5 mg impaired simulated driving compared to placebo as measured by the primary endpoint (standard deviation of deviation from the ideal route).

**Support (optional):** Neurocrine Biosciences, Inc, and Pfizer Inc.

### 0134

#### DOSE RESPONSE RELATIONSHIP OF INDIPLON FOR SLEEP ONSET

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**Introduction :** Indiplon is a selective GABA-A receptor potentiator under development for the treatment of insomnia. The effect of indiplon on subjective and objective measures of sleep initiation was characterized as a function of dose.

**Methods :** Data from multiple studies were pooled with 773 insomnia patients included in the analysis of PSG-derived latency to persistent sleep (LPS; 5938 observations) and 2491 patients included in the analysis of subjectively assessed latency to sleep onset (LSO; 110,111 observations). Data were analyzed with nonlinear mixed effects using a sur-

vival analysis model. Covariates such as baseline, and patient demographics were examined as potential determinants of response.

**Results :** Indiplon demonstrated a baseline dependent reduction in LPS with a maximal reduction of 72% (Emax), with half that value achieved with a dose of 7.7 mg (ED50). The maximal reduction in LPS increased with age, being 65% for a 40 year old, 68% for a 50 year old, and 72% for a 66 year old. Similarly, indiplon demonstrated a baseline dependent reduction in LSO with a similar Emax (72%) and ED50 of 4.68 mg. The maximal reduction in LSO increased with age, being 62% for a 40 year old, 67% for a 50 year old, and 72% for a 66 year old.

**Conclusion :** The dose response for measures of sleep initiation shows a decrease in LPS and LSO at doses up to 10 mg, followed by a plateau in response. Drug response is driven to a large extent by baseline sleep parameters. Elderly differ in both disease severity and sensitivity, and potentially less drug may be required in this population.

**Support (optional):** Research funded by Pfizer Inc and Neurocrine Biosciences.

### 0135

#### EFFECTS OF FEXOFENADINE (120 MG) AND CHLORPHENIRAMINE (6MG): A STUDY IN JAPANESE VOLUNTEERS

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**Introduction :** Antihistamines may be associated with sedation and cognitive impairment, but more recently introduced compounds, such as fexofenadine, have been found to be free of impaired performance. However, there is some evidence that fexofenadine possesses stimulant activity. This could limit the usefulness of the drug for nocturnal ingestion.

**Methods :** The effects of chlorpheniramine (6mg), fexofenadine (120mg) and placebo were studied in 18 healthy (male and female) Japanese (20-55) years. The 3 treatments were administered at 23.00h. Overnight sleep was measured from 23.00h to 07.00h using polysomnography. Residual effects were studied at 07.00h and 9.00h the next day, and the latency to sleep (Sleep Latency Test) measured at 09.30h the next morning.

**Results :** Compared with placebo, chlorpheniramine increased the latency to sleep onset ( $P < 0.05$ ), but this was not observed with fexofenadine, though both drugs increased the duration of stage 2 sleep ( $P < 0.01$ ). Chlorpheniramine also increased the latency ( $P < 0.05$ ) and reduced the duration of REM sleep ( $P < 0.01$  respectively). As far as residual effects the next morning were concerned there were decrements in performance with chlorpheniramine, but not with fexofenadine. With chlorpheniramine divided attention ( $P < 0.001$ ), vigilance ( $P < 0.05$ ), working memory ( $P < 0.001$ ) and sensori-motor performance ( $P < 0.01$ ) were impaired, and the latency to daytime sleep was reduced ( $P < 0.001$ ). With fexofenadine the daytime latency to sleep was increased ( $P < 0.05$ ).

**Conclusion :** These studies show that the over night ingestion of chlorpheniramine (6mg) may be associated with difficulty in falling asleep, REM suppression and impaired performance and vigilance up to 10 hours after ingestion. No such effects exist with fexofenadine (120mg), and so the current findings suggest that any existing evidence for increased arousal is unlikely to adversely affect sleep and that fexofenadine is an appropriate anti-histamine for overnight use.

**Support (optional):** This study was supported by the Osaka Foundation for the Prevention of Cancer and Cardiovascular Diseases, Osaka, Japan.

### 0136

#### R228060/YKP10A IS A POTENT NEW WAKE-PROMOTING DRUG

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**Introduction :** We tested the wake-promoting efficacy of the phenylalanine derivate R228060/YKP10A in three strains of mice [AKR/J (AK), C57BL/6J (B6), DBA/2J (D2)]. The effects of R228060/YKP10A were compared to those of d-amphetamine.

**Methods :** Both drugs and saline controls were administered intraperitoneally and effects on sleep-onset and the amount and intensity (i.e. EEG delta power) of recovery sleep were assessed. First, a sleep-onset dose-response relationship was established for R228060/YKP10A ( $n=28$  B6 mice; 25-50-100-150-200mg/kg). Second, a strain comparison of the effects of the maximal effective dose (150mg/kg;  $n=8$ /strain) was performed. Third, an amphetamine dose yielding a similar period of wakefulness was determined ( $n=10$  B6 mice; 1-2-4-5-8mg/kg). Fourth, drug efficacy of R228060/YKP10A (150mg/kg) and amphetamine (5mg/kg) were compared among strains ( $n=7$ /strain).

**Results :** Up to 150mg/kg, R228060/YKP10A dose-dependently induced up 5h of continuous wakefulness during which no abnormal behaviour or EEG activity was observed although theta (5-10Hz) was decreased and beta/gamma (20-55Hz) activity increased. The drug-induced NREMS loss was not compensated during the light period and EEG delta power did not increase. Sleep-onset latency was unaffected by strain and the lack of a NREMS rebound in the light period was confirmed in all strains. During the dark period, D2 mice completely compensated for the lost NREMS, while AK did not, and B6 did partly. Moreover, only in AK mice did delta power significantly increase. REMS rebounds were observed in all strains. Sleep-onset after 5mg/kg amphetamine was shorter in AK mice compared to B6 and D2 and, unlike R228060/YKP10A, amphetamine-induced sleep loss was fully compensated in AK mice.

**Conclusion :** R228060/YKP10A is a potent wake-promoting drug that, in contrast to d-amphetamine, is not immediately followed by hypersomnolence. The interactions between drug and genotype re-emphasizes that taking genetic background into account is crucial when evaluating new drugs. R228060/YKP10A's effects on the waking EEG necessitate further evaluation of cognitive performance.

**Support (optional):** This study was supported by Johnson & Johnson Pharmaceutical Research & Development

### 0137

#### CAFFEINE INTAKE IS INDEPENDENTLY ASSOCIATED WITH NEUROPSYCHOLOGICAL PERFORMANCE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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**Introduction :** We previously reported that patients with obstructive sleep apnea (OSA) consume nearly triple the amount of caffeine as non-apneics, possibly to deal with daytime sleepiness. It is also widely reported that OSA patients experience cognitive deficits. There is an extensive literature on the positive effects of caffeine on cognitive performance. We wondered if greater caffeine intake would similarly be associated with improved neuropsychological performance in patients with OSA.

## Category C—Clinical Pharmacology

**Methods :** 42 untreated OSA patients (AHI=63±31) were administered a standard neuropsychological assessment battery which included tests of: speed of information processing, executive functioning, learning, and attention and working memory domains. A norm-based system was used to generate T-scores for each individual test. Then, these scores were aggregated into a global deficit score (GDS); a GDS score  $\geq 0.5$  is considered impaired. Because of concerns about Type I error, we limited our analyses to this aggregate measure of neuropsychological functioning. Average daily caffeine intake was assessed via a detailed instrument for assessing 24-hour recall of caffeine intake, which has been shown to characterize usual caffeine consumption. Data were analyzed using partial correlation analysis and analysis of covariance, controlling for body mass index (BMI) and apnea hypopnea index (AHI).

**Results :** A significant inverse association was found between caffeine intake and the global deficit score, when one controlled for BMI and AHI ( $r=-0.376$ ,  $p=0.024$ ). Analysis of covariance comparing impaired versus non-impaired groups revealed a significant difference in daily caffeine intake (30mg versus 180mg, respectively;  $p=0.012$ ).

**Conclusion :** Greater caffeine intake is linked with better cognitive functioning in patients with OSA. Patients with impaired cognitive performance ingest one-sixth the caffeine as those with normal cognitive performance. We previously speculated that OSA patients may 'self-medicate' with caffeine to deal with daytime sleepiness. These findings suggest cognitive benefits, as well.

**Support (optional):**

### 0138

#### NOVEL H1 INVERSE AGONISTS FOR THE TREATMENT OF SLEEP MAINTENANCE INSOMNIA

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**Introduction :** Sleep maintenance insomnia, characterized by inappropriate awakening and long latency to return to sleep, particularly in the latter third of the night, represents approximately 60% of all insomniacs, yet adequate treatments are lacking. Using neurobiologically-driven target rationale and a predictive preclinical platform technology (SCORE-2004™), we have developed and characterized a unique series of H1 histamine receptor inverse agonists specifically designed to promote and maintain natural sleep while avoiding numerous limitations intrinsic to contemporary insomnia medications.

**Methods :** Preclinical sleep studies were performed in adult male Wistar rats ( $N>8$  per group) instrumented for recording EEG, EMG, body temperature, locomotor, feeding and drinking behavior for at least 30h before and 30h after acute treatment at CT-18 (6 h after lights-off) with compound HY10275 (1, 3, & 10 mg/kg PO) or 0.25% methylcellulose vehicle. Wake, NREM, and REM stages were scored in 10-s epochs. Group mean±SE post-treatment effects were computed in 5-minute and hourly bins, expressed relative to pre-treatment baseline, and contrasted with vehicle using a mixed model for repeated measures analysis.

**Results :** HY10275 is orally bioavailable, brain penetrant, and significantly increased NREM sleep time (+25±7, +44±11, 48±5 minutes,  $P<0.01$ ) and sleep maintenance (sleep bout duration: +6.0±2.3, 18.8±3.0, 17.2±3.5 minutes,  $P<0.01$ ), but did not produce rebound insomnia, inhibit REM sleep, or impair motor function. HY10275 has nM affinity at H1 and lacks affinity for 62 other off-target receptors and ion channels. Preclinical safety studies in rat, dog and primate, the lack of significant oxidative metabolites or interaction with CYPs, and other pharmacokinetic and safety assessments indicate that this compound is well optimized for the sleep maintenance indication, and the compound has completed Phase I clinical trials.

**Conclusion :** HY10275 represents a novel chemical series with potent

sleep maintenance efficacy while lacking undesirable side-effects and off-target pharmacological properties of currently used sedative hypnotics.

**Support (optional):**

### 0139

#### DAYTIME PHARMACOKINETIC (PK) AND PHARMACODYNAMIC (PD) EVALUATION OF LOW-DOSE TRANSMUCOSAL ZOLPIDEM (TMZ)

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**Introduction :** Currently no medications are available to be used on a prn basis for patients who have middle of the night (MOTN) awakening and who have difficulty falling back asleep. An appropriate therapeutic agent for such insomnia would enable patients to return to sleep rapidly and wake up in the morning without residual effects. TMZ was developed for such treatment by enhancing rapid systemic delivery without affecting other PK parameters. This study evaluated the daytime dose-dependent pharmacokinetic and pharmacodynamics of TMZ.

**Methods :** Healthy adults ( $N=24$ , 15 females, mean age=37.6 yrs) participated in this double-blind, placebo-controlled 4-way crossover study of 2 consecutive days of AM dosing with placebo, 1, 1.75 or 3.5 mg TMZ. After morning dosing, on Day 1 of each period, PD endpoints (DSST, PVT, VAS-sedation, SCT and Buschke) were evaluated at pre-dose, and at 20 minutes 1, 1.5, 2, 3, 4 and 5 hours post-dose. On Day 2, repeated blood samples for PK assessment were drawn over 12 hours.

**Results :** Baseline DSST scores ( $\pm$ SE) were 57.6  $\pm$  2.9, 58.0  $\pm$  3.1, 58.4  $\pm$  2.3, and 56.9  $\pm$  2.7 for the placebo, 1, 1.75, and 3.5-mg. Significant changes in DSST scores were found after 1.75 and 3.5 mg TMZ at beginning of 20 minutes (-6.6;  $p=0.0132$  and -14.8;  $p<0.001$ ) and lasted for 1.5 hours post-dose. Other endpoints showed results similar to DSST. Mean  $T_{max}$  was 36.0, 37.9, and 37.9 minutes for 1.0, 1.75, and 3.5 mg TMZ. Further, the 1.75 and 3.5-mg TMZ reached sedation plasma levels (about 20 ng/ml) within 15 minutes and these levels were maintained for 4-hours or less.

**Conclusion :** Low-dose TMZ has daytime sedative properties at a dose and a  $T_{max}$  of less than half of the approved dose of PO zolpidem (10-mg) in adults and demonstrates potential for shortened sleep onset with MOTN administration.

**Support (optional):**

### 0140

#### RESIDUAL EFFECTS OF A MODERATE DOSE OF ALCOHOL ON SLEEP STAGES OF YOUNG MEN

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**Introduction :** Morning or afternoon alcohol can increase physiological sleepiness or impact nocturnal sleep, even after breath alcohol (BrAC) has reached undetectable levels. We examined such residual effects on sleep following late-evening alcohol administration and extended waking.

**Methods :** Eight healthy adult males (ages 21 to 25, mean=23, SD=1.5 years) kept a fixed 8.5-h or 9-h sleep schedule for two weeks at home, confirmed by actigraphy and diary. Sleep was recorded in the laboratory

for three nights (adaptation, placebo, alcohol); scheduled bedtime on placebo and alcohol nights was 4-h past stabilization bedtime. Double blind placebo and alcohol nights (counterbalanced) were separated by 5-7 stabilization nights at home. The alcohol beverage—vodka (.54 g/kg) mixed with tonic water in a 1:4 ratio—was consumed over 30 minutes on the moderate alcohol night; the same quantity of placebo beverage was given on placebo night. Drinking ended 60 minutes before stabilization bedtime. Various performance tests were administered until bedtime, with BrAC assessed at approximately 20- to 30-min intervals. Sleep stages were scored visually in 30-sec epochs using Rechtschaffen/Kales (1968) criteria for the first 270 min each night.

**Results :** Peak mean BrAC was 0.048 g%, mean BrAC at bedtime was zero. Mean total sleep time was 260 (SD=7) min for alcohol and 259 (SD=7) min for placebo nights, corresponding to sleep efficiencies of 97.4% (SD=3) and 97.3% (SD=2), respectively. No sleep variables (e.g., sleep stages, time awake) showed a significant effect of alcohol.

**Conclusion :** Although a small sample was available for this preliminary analysis, these data indicate a lack of residual effects of nighttime alcohol on late-night sleep. Future planned analyses will expand the sample to include women and individuals with and without a parental history of alcohol abuse/dependence and will also examine spectral EEG characteristics.

**Support (optional):** Research supported by AA13252 (to MAC)

## 0141

### TOPOGRAPHIC PATTERN OF SLOW WAVE ACTIVITY ENHANCEMENT WITH TIAGABINE: PRELIMINARY ANALYSIS

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**Introduction :** Tiagabine, a GABA reuptake inhibitor, increases slow wave sleep (SWS) and slow wave activity (SWA; spectral EEG power in delta frequencies). We examined the topographic pattern of SWA changes with tiagabine 8mg versus placebo.

**Methods :** NREM (stages 2, 3, 4) EEG data from the first 5 hours of a baseline night and a single night with either tiagabine or placebo for 30 healthy adults (tiagabine: 6m, 9f, 27.4 +/- 9.0 years of age; placebo: 7m, 8f, 26.3 +/- 6.7 years of age) were subjected to power spectral analysis. For each night absolute delta power (0.75-4.5 Hz) was calculated for three recording locations (F4/A1, C4/A1, O2/A1).

**Results :** A repeated measures ANOVA for group (2) X night (2) X topographic location (3) revealed a three-way interaction (p=0.05), a night X group interaction (p=0.006), a night X location interaction (p=0.005), a main effect of location (p=0.000), and a main effect of night (p=0.003). There was an increase from baseline in absolute delta power at all locations with tiagabine (p<0.001 for all), but not with placebo. Further, in the tiagabine group the increase in absolute delta power from baseline was greater at more anterior locations (F4>C4>O2; p<0.0375 for all). Delta power at F4 with tiagabine increased 84% over baseline. Moreover, the increase in delta power at F4 was 39% greater than the increase observed at C4 and 208% greater than the increase at O2. The increase at C4 was 121% greater than the increase at O2.

**Conclusion :** The greater increase in delta power with tiagabine in the frontal derivation as compared to more posterior sites is similar to the pattern described during recovery from sleep deprivation. This suggests that the increase in SWS and SWA with tiagabine may be mediated by the same mechanisms as those that homeostatically increase SWS and SWA after sleep loss.

**Support (optional):** supported by Cephalon, Inc.

0142

**DREAM CONTINUITY WITH A CURRENT WAKING CONCERN**

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**Introduction :** The question of whether the images of dreams are continuous with emotionally salient issues or are random until meaning is added in the awakening process, is addressed in this study.

**Methods :** Thirty volunteers all going through a divorce were studied over a five month period. Twenty met major depression criteria on SCID, Hamilton and Beck, and ten were not depressed Controls. A 13 item Current Concern (CC) checklist was administered before each of three nights of REM interruption for recoding recalled mental content. Items were rated as 1=low concern to 5=extreme concern.

**Results :** One or more of the dream reports of fifteen subjects included the ex-spouse as a character (10 of the Depressed and 5 of the Controls). The CC scores of those who included the ex-spouse in dreams was significantly higher on the ex-spouse item than was this score in those who did not. At Month 1 the difference was 4.30 sd 1.25 vs 2.60 sd 1.34  $t=2.92$  df 18  $p=.009$  and at Month 4.4.20 sd 1.54 vs 1.80 sd 1.39  $t=3.63$  df 18  $p=.002$ . Dreams including the ex-spouse were related to remission from depression only if accompanied by appropriate affect and connected to other memory material. Affect in spouse dream of those who did not remit was Absent or Neutral and of Remitters and Controls was Unpleasant. Spouse dreams of Remitters were more complex in characters, scene shifts, than those of Non-Remitters.

**Conclusion :** Dreams which include a character who is rated of high waking concern do not necessarily down-regulate disturbed mood unless the dream is accompanied by appropriate affect and connect the image to a network of other memory fragments.

**Support (optional):** NIMH RO1-50471.

0143

**A SYSTEMATIC CHANGE IN DREAMS AFTER 9/11/01**

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**Introduction :** Studies of dreaming after trauma and stress, by our group and others, suggest that dream imagery becomes more intense or powerful after the trauma. ( Though the actual trauma is seldom replayed in dreams except in Ss who develop PTSD.) The research has involved a variety of traumas, however, and it has been difficult to obtain systematic data comparing dreams before and after trauma. The events of 9/11, which produced some signs of trauma or at least emotional distress in everyone in the U.S., allow us to perform a more systematic study.

**Methods :** Subjects were 44 persons living in the U.S. who had been writing down all their dreams for a period of years. Each sent us twenty dreams from their records - the last ten dreams they had recorded before 9/11/01 and the first ten dreams recorded after that date, without any omission or selection. The 884 dreams obtained were assigned random numbers, and scored blindly on established scales for length, dreamlikeness, intensity of the central imagery, emotion pictured, and nightmare-like quality. They were also scored on three ad hoc content scales rating any mention of airplanes, buildings resembling the WTC or the Pentagon, and attacks. Interrater reliability was .75 to .95 on all scales.

**Results :** The one clear change was an increase in "CI intensity," measuring the intensity or power of the central imagery ( $p<.001$ ). The other dream scales showed no significant changes. Dreams post 9/11 were not longer, more dreamlike or more likely to be nightmares. The ad hoc content scales showed no change on airplanes or buildings and only a slight

increase in "attacks" ( $p<.05$ ).

**Conclusion :** Dream imagery became more intense after 9/11, but dreams were not longer, more dreamlike, or more nightmare-like. There was no direct ("replay") incorporation of 9/11 content. Insofar as one can generalize from these dream-recorders to the population, we all had more intense imagery after 9/11. This is consistent with our other studies, and with the "Contemporary Theory of Dreaming" -- dreams are hyperconnective; the connections are not random, but are guided by the dominant emotion of the dreamer; the dream imagery pictures the dominant emotion of the dreamer; and the intensity of the central image is a measure of emotional arousal.

**Support (optional):**

0144

**INTENSIVE LANGUAGE LEARNING AND EPISODIC MEMORY IN DREAMS**

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**Introduction :** Recently, considerable interest has revived for the study of the relationship between learning, memory, sleep and dreams. The observation that very few episodic memories find their way into REM dreams has been of particular interest. We attempted to further explore this phenomenon by looking at dreams during a period of intensive language learning.

**Methods :** Eight participants, enrolled in a six-week intensive French immersion program, maintained a morning dream diary starting one week before until two weeks after the immersion course. In addition, participants slept in a laboratory for four series of four consecutive nights of polysomnography: one before, two during and one after the course. All dreams were coded using a scale measuring the incorporations of elements related to (1) the French language, (2) the immersion program situation, (3) the sleep laboratory, and (4) the city where the program took place (all participants just moved in). Furthermore, the likelihood of an episodic memory being present in each of the four categories of incorporations was evaluated by using a Likert scale ranging from 1, indicating a low probability to 5, indicating a high probability.

**Results :** Of the 255 dreams reported, 105 (41.18%) contained elements related to the four incorporation categories. As expected, very few dream episodic memories were identified. Indeed, a total of only 5 dreams (1.6%), showed elements that were coded as moderately and highly probable episodic memories (Likert 4-5). Furthermore, these few episodic memories did not show any relationship with the learning performance of the participants during the immersion program.

**Conclusion :** These results support previous research showing very few episodic replay of waking events during dreams. These findings also tend to support the notion that dreams themselves seem to have little role in episodic memory consolidation or in language learning.

**Support (optional):**

0145

**CIRCADIAN AND HOMEOSTATIC INFLUENCES ON DREAMING: NREM MENTATION DURING A SHORT DAYTIME NAP**

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**Introduction :** Mentation production increases across the night in both

REM and NREM sleep. Although circadian factors have been hypothesized to account for this effect, a possible influence of homeostatic-based changes across the night has not been adequately addressed. We compared NREM mentation collected from early-afternoon naps to night reports collected from subjects' core body temperature (CBT) nadir and from the late-morning, after subjects' habitual waking time. Hypothesizing that time-of-night mentation effects are primarily driven by a circadian cycle of cortical activation approximating the CBT rhythm, we predicted that more content would be reported from early-afternoon nap awakenings as compared to CBT-nadir and late-morning awakenings. **Methods :** Twenty subjects reported mentation upon awakening from 20 minutes of uninterrupted Stage 2 sleep between 12pm-1pm ( $M = 12:16\text{pm}$ ). These nap reports were compared to previously collected night NREM reports from subjects' estimated CBT nadir ( $M = 4:52\text{am}$ ) and the late morning ( $M = 9:19\text{am}$ ).

**Results :** Contrary to our hypotheses, substantially less mentation was recalled from nap reports than late morning reports ( $t_{38}=2.21$ ,  $p=.03$ ,  $d=.70$ ). This effect could not be accounted for by individual differences in waking report generation. Some qualitative mentation features were also low in nap reports, though Emotional Intensity was comparable in nap as compared to night mentation.

**Conclusion :** The low mentation production in nap subjects may be due to decreased cortical activation induced by a greater homeostatic need for sleep in nap as compared to overnight subjects. However, as the results of previous studies are incompatible with a purely homeostatic explanation, our data are best accounted for by postulating that the effects of increased circadian-driven activation in nap subjects were counteracted by the effects of increased sleep need. It is likely that previously reported time-of-night mentation effects similarly resulted from the combination of circadian and homeostatic influences on the neural substrate for dreaming.

**Support (optional):** This research was supported by PSC-CUNY Grant # 67586-00 36

## 0146

### HOW DO WE MEASURE NIGHTMARE FREQUENCY AND HOW RELIABLE IS THE DATA?

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**Introduction :** Nightmare frequency is often assessed with questionnaire items. Research based on prospective log data has shown that retrospective measures underestimate nightmare frequency. It has been suggested that this underestimation may be due to increased dream recall caused by keeping a daily log. Our first goal was to assess the accuracy of post-log retrospective reports. The second goal was to assess the reliability of retrospective estimates of nightmare frequency across time.

**Methods :** Participants were 69 undergraduate students (59 women, 10 men; mean age =  $23.4 \pm 6.0$  yrs) recruited as non-paid volunteers. They completed a sleep/dream questionnaire and then recorded their dream experiences each morning in a daily log for 4 consecutive weeks. For each dream narrative reported, participants had to note if the dream was a nightmare, a bad dream, a lucid dream, or a flying dream. After handing in their logs, subjects completed the same questionnaire items, including a question on how many nightmares they had experienced in the previous month.

**Results :** Intraclass correlations between the participants' responses to the questionnaire items administered at 1-month interval ranged from .33 (nightmares reported over the past month) to .73 (nightmares reported over the past year). Thirty-one participants (45%) reported one or more nightmares in their logs for a total of 51 nightmares while 57 participants (83%) reported one or more bad dreams for a total of 163 bad dreams. Retrospective questionnaire estimates of nightmare frequency obtained

after the completion of the logs indicated that these values underestimated the actual number of log-based nightmares by 9%. Bad dreams were underestimated by 21%.

**Conclusion :** Even with a relatively short 1-month interval, there exists considerable variability in people's retrospective assessments of nightmare frequency. Moreover, the results indicate that people's retrospective assessments underestimate the number of nightmares and bad dreams actually reported in daily logs.

**Support (optional):** Canadian Institutes of Health Research.

## 0147

### NIGHTMARES: AN ANALYSIS OF SOME EPIDEMIOLOGIC ASPECTS FROM THE NATIONAL AMBULATORY MEDICAL CARE SURVEY (NAMCS) AND NATIONAL HOSPITAL AMBULATORY CARE SURVEY (NHAMCS) REPRESENTING OVER 944,000 PATIENT VISITS FOR NIGHTMARES BETWEEN 1995 TO 2002

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**Introduction :** Nightmares are a frequently encountered complaint in the sleep clinic. There are no large scale studies of the epidemiology of this clinical sleep symptom.

**Methods :** Data from 1995 to 2002, from the NAMCS which collects information from office based physicians; and the NHAMCS, which is a nationally representative sample of visits to hospital outpatient and emergency departments, were studied. The basic sampling unit in both surveys is the patient visit. The dataset included 3 main reasons for visit, for each patient visit. A 'Nightmare' variable was created by grouping the visits where either one of the 3 reasons for visit was documented as 'nightmares'. All analyses were conducted using the Complex Samples module of SPSS version 14 to account for the multistage probability sampling design used. Standard errors (SE) and the findings from the overall sample are presented with the results.

**Results :** The weighted data represented 944,721±132830 patient visits between 1995 and 2002. There were 67.2% (±4.7%) female and 32.8% (±4.7%) male (58.9%±0.2% female and 41.4%±0.2% male visits overall). The mean±SE age was 41.4±2.3 yrs (mean±SE age 41.98±0.22 overall); with the males (mean±SE age: 35.5±4.1 yrs versus 40.48±0.26 overall) significantly ( $p<0.001$ ) younger than females (mean±SE age: 44.3±4.0 yrs versus 43.02±0.22 overall). The frequency of visits by age in decades for the 'Nightmare' group versus all visits was as follows: age 0 to 10 years: 13.4% ±4.5% (vs. 15.0% ±0.3% overall); 11-20 years: 11.9% ±4.6% (vs. 8.8% ±0.1%); 21-30 years: 3.2% ±1.6% (vs. 10.2% ±0.1%); 31-40 years: 20.2% ±3.7% (vs. 13.0% ±0.2%); 41-50 years: 25.8% ±5.2% (vs. 13.8% ±0.1%); 51-60 years: 3.0% ±1.2% (vs. 12.0% ±0.1%); 61-70 years: 4.5% ±3.2% (vs. 10.9% ±0.1%); 71-80 years: 15.7% ±2.6% (vs. 10.8% ±0.2%); 81-90 years: 2.0% ±0.3% (vs. 4.9% ±0.1%); >90 years: 0.3% ±0.3% (vs. 0.5% ±0.0%). The race of the 'Nightmare' sample (versus all visits) was as follows: 83.7% ±5.4% (vs. 84.3% ±0.7%) 'White'; 14.3% ±5.2% (vs. 11.8% ±0.6%) 'Black/African American'; 2.1% ±1.3% (vs. 3.9% ±0.4%) 'Asian/Native Hawaiian/Other Pacific Islander/Other'. The most frequent primary diagnosis representing 31.8% ± 11.9% of the visits was Posttraumatic Stress Disorder (PTSD) (ICD9-CM code 309.81) (vs. 1.2% ±0.2% of visits related to PTSD overall).

**Conclusion :** Over 45% of the nightmare related visits were among the 31 to 50 years age group; the men as a group were younger than the women. There was a high comorbidity of nightmares with PTSD, a disorder which is possibly underrecognized in the sleep clinic.

**Support (optional):** None

0148

**APNEA AND DREAMS: APNEA PATIENTS DREAM LESS, AND HAVE FEWER APNEA-RELATED DREAMS**

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**Introduction :** In the 19th century a prominent theory of dreams suggested that bad dreams and nightmares were produced by the sleeper's getting tangled in the sheets, choking, losing oxygen. On that view apnea sufferers, who are repeatedly being deprived of oxygen should have a great many bad dreams and nightmares. Recent views that dreams picture important threats and concerns would lead to similar predictions, and would suggest that patients might dream of scenes such as choking or drowning.

**Methods :** Subjects were 446 patients at a Sleep Disorders Center, 296 males and 150 females, each of whom had at least one night of polysomnography. Mean age was 49 years. 252 patients received a diagnosis of sleep apnea ( obstructive or mixed) based on a RDI>5.0 . The other 194 had RDI<5, and were called Non-apnea patients. All patients had a one-hour interview with the senior author, which included questions about frequency of dream recall, frequency of nightmare recall. and frequency of any dreams about snoring, choking, drowning or similar subject matter. ("Apnea-related dreams").

**Results :** Compared to non apnea patients, apnea patients did not differ on sleep time, REM time or other PSG measures. Apnea patients reported significantly FEWER apnea-related dreams (p<.05) and a trend towards fewer dreams and fewer nightmares. Within the apnea-diagnosed group there was a negative correlation between RDI and REM-time (<.001) and a trend towards a negative correlation between RDI and apnea-related dreams, all dreams recalled, and nightmares. It was noteworthy that not a single one of the 72 apnea patients with a RDI>30 reported any apnea-related dreams.

**Conclusion :** Surprisingly, sleep apnea does not appear to produce nightmares, nor dreams about snoring, choking or drowning. Apnea patients have fewer dreams and fewer apnea-related dreams than non-apnea patients. And patients with the most apnea have the fewest apnea-related dreams. This could be related to overall sleep disruption, REM-sleep disruption, and memory processing disruption in apnea patients.

**Support (optional):**

0149

**DREAM CONTENT IN DRUG-NAIVE AND MEDICATED SCHIZOPHRENICS: A LABORATORY INVESTIGATION**

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**Introduction :** We previously found impoverished dream content in acute, drug-naive patients with schizophrenia when compared to controls. These differences appeared to diverge from findings on patients treated with classical neuroleptics. We now compare dream reports from drug-naive patients with those from patients treated with atypical neuroleptics.

**Methods :** Seven acute drug-naive patients with schizophrenia (4 women, 3 men; 29.6+/-15.8 years old) and 12 patients with schizophrenia stabilized

with atypical neuroleptics (1 woman, 11 men; 25.1+/-3.5 years) were recorded for up to three nights. Participants were awakened after 10 to 15 minutes of REM sleep and interviewed for dream content. Transcripts were scored blind by two independent judges using standard Hall and Van de Castle (1966) scales, including characters, social interactions, activities, success and failure, misfortune and good fortune, emotions, settings, objects and descriptive elements. Results were compared with Mann-Whitney U-tests. Number of verbal reports was compared with Chi-squares.

**Results :** Drug-naive participants were awakened eight times, 75.0% of which generated a verbal report. Medicated patients were awakened 20 times; 80.0% of which generated a verbal report. There were no significant differences between the two groups in actual dream content as assessed by the H/V scales. Mean number of words per report (drug-naive: 180.7+/-104.0; medicated: 155+/-180.9) and the number of questions asked by the experimenter (drug-naive: 12.4+/-8.0; medicated: 10.1+/-5.0) were also equivalent in both data sets.

**Conclusion :** These results indicate that acute, drug-naive and medicated patients with schizophrenia are capable of reporting dreams following REM sleep awakenings in a laboratory setting. The dream content of schizophrenic patients does not appear to be affected by chronic treatment with atypical neuroleptics in comparison to drug-naive patients. Supported by the Canadian Institutes of Health Research (CIHR).

**Support (optional):**

0150

**DREAM CONTENT IN COMPLICATED GRIEF AND RELATIONSHIPS WITH PSYCHIATRIC DISTRESS**

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**Introduction :** Based on observations that waking-life events, such as trauma exposure and bereavement, may influence dream content, some authors have suggested that dreaming of the life event may facilitate emotional coping. The goals of the present study were 1) to compare dream content in a sample of adults with Complicated Grief (CG) with dream content norms; and 2) to compare levels of psychiatric distress in CG subjects who did and did not report dreams of the deceased.

**Methods :** The sample included 25 men and 103 women who met criteria for CG, scored > 30 on the Inventory of Complicated Grief, and completed the Hamilton Rating Scales for Depression and Anxiety. Subjects provided a written narrative of their most recent dream. Dream emotions, characters, and social interactions were coded using the Hall and Van de Castle system. Subjects were then grouped according the presence or absence of deceased characters in dream reports, in order to explore whether psychiatric distress differed in these 2 groups. Data were analyzed using h-effect size statistics and t-tests.

**Results :** The CG sample reported more familiar characters and fewer emotions and interactions in their dreams relative to normative data. Deceased characters were more prevalent in CG women's dreams. Clinical scores of grief intensity, depression severity, and anxiety severity did not differ between CG patients who reported dreams of deceased and CG patients who did not.

**Conclusion :** Findings support the hypothesis that emotionally significant waking-life events influence dream content. Dreaming of familiar characters may reflect an attempt to compensate for the loss, and perhaps indicate emotional coping. However, there was no support for the hypothesis that dreaming of the deceased reduces psychiatric distress. Longitudinal studies are needed to further characterize the relationships between CG, dream content, and daytime psychiatric distress.

**Support (optional):** This work was supported by NIMH grant MH60783 (PI: K. Shear)



## 0151

## DREAMS AND SLEEP PATTERN IN WOMEN WITH ANOREXIA NERVOSA

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**Introduction :** Few studies have investigated the dream content in eating disorders, mainly in a descriptive fashion. The aim of the present study was to quantitatively assess the dream characteristics and sleep pattern in patients with Anorexia Nervosa compared to healthy control subjects.

**Methods :** Twenty female patients diagnosed with AN according to DSM-IV (mean age: 21.7±7.0 yrs., range: 14-32 yrs) and 20 age and sex-matched control subjects entered the study. Subjects were asked to recall most recent dreams; verbatim dream descriptions were recorded and scored according to the Hall and Van De Castle method (1966). Coded dreams were processed by dreamSAT software and differences in dream categories were evaluated by means of Cohen's "h" statistic. Furthermore, the two groups were asked to fill the Typical Dreams Questionnaire, the Pittsburgh Sleep Quality Index and the Composite Scale of Morningness.

**Results :** A total of 136 and 156 dreams were collected in AN and controls, respectively. AN patients had higher % of "dream with family characters" (37%vs.19%, p<0.0001) and less "dreams with friend characters" (26%vs.46%, p<0.0001) than controls. AN patients had also a higher % of "dream with at least one aggression" (54%vs.37%, p=0.005) and a lower % of "dreams with a friendly interactions" (43%vs.61%, p=0.002). Few AN patients had "dreams with at least one sexuality element" (2%vs.13%, p<0.0001). Eating themes were present in more than one third of AN dreams (34,82%) and only in 6% of controls (p<0.0001). Among typical dreams, "to eat some delicious food" and "to be suffocated or fail to breath" were more frequently reported in AN than controls (p=0.01 and p=0.008). AN group reported a more disturbed sleep (PSQI total score: 7.7±4.5vs.4.4±2.9, p=0.01) with poorer subjective sleep quality (PSQI subscale 1: 1.5±0.9 vs. 0.9±0.6, p=0.03) and more frequent hypnotic use (PSQI subcale 6: 0.9±1.4vs.0.5±0.2, p=0.01) compared to controls. Finally, AN patients were found to be more "morning-type" than controls (35.5±6.0vs.30.6±4.4; p=0.005).

**Conclusion :** Dream content appears to be altered in AN, indicating possible concomitant adjustment problems. Dream characteristics in patients with AN, as well as poor sleep quality and morningness circadian typology, may be related to peculiar psychopathological aspects or to starvation-induced biological changes. Future longitudinal studies will assess the changes in dream contents in relation to therapeutic interventions and/or weight gain.

**Support (optional):**

## 0152

## A CONTENT ANALYSIS OF YOUNG CHILDREN'S DREAMS COLLECTED IN SCHOOL SETTING

Colace C

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**Introduction :** Studies on children's dreams have frequently shown their utility for our understanding of dreaming processes and psychological child development. This paper summarizes certain significant results of a content analysis of young children's dreams.

**Methods :** Were analyzed 64 dream reports of 64 children (30 female, 34 male) 3-7 years old. Each dream report was tape recorded during individual interview in the morning in a school setting. The initial question was "Can you tell me the last dream you've had?". In addition, a series of

questions to elicit additional details on other aspects of dream (e.g. characters, settings, actions) was made. A simplified version of Foulkes and Shepherd's scoring system was applied to dream reports transcription.

**Results :** Dream length. The typical dream report was more brief in the 3- to 5-year old group (median score, 23 words long) than in the 5- to 7-year-old group (46 words long) (Mann-Whitney, p = 003). Dream characters. The most frequent characters were: -family members- (53% of dreams), -animal characters- (36%), -fantastic characters- (i.e., cartoon, famous character, TV, etc.)- (31%) -unknown characters- (14%) and -known characters (11%) (all ages). The differences between age groups (3-5 vs. 5-7 years-old) were not statistically significant. Dream settings. The most frequent settings were: -home setting (33%), -school setting- (8%), -recreational setting- (2%) (all ages). The differences between age groups were not statistically significant. Social interactions. -Social interactions- were scored less frequently in dream reports in the 3- to 5-year old group (10%) than in the 5- to 7-year-old group (35%) ( $\chi^2 = 5.682$ , df = 1, p = .017)

**Conclusion :** These results are mainly congruent with those of previous studies based on school- and-home-collected dreams. Certain features such as, dream length, frequency of -animal characters- and -home setting-, are also consistent compared to the classical description of children's REM dreams.

**Support (optional):**

### 0153

#### INTERMITTENT AND CONTINUOUS BRIGHT BLUE-ENRICHED LIGHT AUGMENTS CIRCADIAN PHASE ADVANCES

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**Introduction :** The human circadian system is maximally sensitive to short wavelength light. These studies were to determine if bright blue-enriched light can produce larger phase advances than bright white light. **Methods :** Two between-subjects designs were used in which light was timed to phase advance circadian rhythms. In study A, on the first of four treatment days, adults (6m, 3f) were exposed to a 2-hour light pulse beginning 8 hours after the dim light melatonin onset (DLMO). In study B, on the first of three treatment days, adults (5m, 6f) were exposed to four 30-minute light pulses, separated by 30 minutes of dim room light, beginning 1 hour before their baseline wake time. In both studies there was a gradually advancing sleep schedule, with waking time and the start of the light pulses advancing 1 hour each day. Although the total photon density delivered by the fluorescent white lamps was more than the blue-enriched lamps (5.1 x 1015 and 4.4 x 1015 photons/cm2/sec, respectively), and the luminance was greater (5020 versus 3450 lux), the blue-enriched lamps delivered more photons in the blue range (400-490nm) than the white (2.1 x 1015 and 1.1 x 1015 photons/cm2/sec, respectively). Phase advances were calculated by comparing the DLMO and dim light melatonin offset (DLMOff) before and after treatment.

**Results :** In study A, mean phase advances ( $\pm$  SD) for blue-enriched versus white light were 112  $\pm$  23 versus 67  $\pm$  39 minutes for the DLMO, and 110  $\pm$  85 versus 47  $\pm$  47 for the DLMOff. In study B, mean advances for blue-enriched versus white light were 89  $\pm$  26 versus 66  $\pm$  33 for the DLMO, and 86  $\pm$  37 versus 43  $\pm$  49 for the DLMOff.

**Conclusion :** These preliminary data suggest that bright blue-enriched light can produce larger phase advances than bright white light.

**Support (optional):** NIH grant R01 NR007677. White light boxes were donated by Enviro-Med, Vancouver, WA. Blue-enriched light boxes donated by Philips Lighting, the Netherlands.

### 0154

#### CUTTING YOUR SLEEP SHORT MAY IMPAIR PHOTIC PHASE SHIFTS

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**Introduction :** Short sleep episodes, which produce short nocturnal dark episodes (short nights) and sleep deprivation, are increasingly common. In hamsters and mice, either short nights or sleep deprivation can reduce phase shifts to light. Here we examined the effect of short and long nights on circadian phase shifts to light in humans.

**Methods :** Young healthy subjects slept in dark bedrooms for two weeks of short nights (6 hours) and two weeks of long nights (9 hours) in counterbalanced order. After the final day in each condition, subjects experienced a phase assessment where saliva samples were collected and later assayed for melatonin. Subjects maintained the short or long nights for 3 further days, and then there was a 3 day phase advancing bright light stimulus (n=8) or a 2 day phase delaying bright light stimulus (n=7). The bright light stimuli consisted of morning or evening intermittent bright light and a gradually shifting sleep episode. This was immediately followed by another phase assessment.

**Results :** The average phase shift of the dim light melatonin onset was

reduced by approximately half in the short nights compared to the long nights; it advanced 1.5 hours less and delayed 1.4 hours less ( $p < 0.05$ ). Similarly, the dim light melatonin offset phase advanced 1.4 hours less and phase delayed 0.7 hours less during the short nights ( $p < 0.05$ ).

**Conclusion :** These results show for the first time that humans may unwittingly reduce their circadian responsiveness to light when they curtail their sleep. Possible mechanisms include sleep deprivation, photoperiodic history, and a reduction in photosensitivity during the short nights due to the increased duration of ambient light. This finding has significant implications for the sleep deprived general population, and for treating circadian rhythm sleep disorders such as jet lag, night work, advanced sleep phase type and delayed sleep phase type.

**Support (optional):** NHLBI RO1 HL072408 and the American Sleep Medicine Foundation, a foundation of the American Academy of Sleep Medicine.

### 0155

#### CIRCADIAN MODULATION OF FUNCTIONAL BRAIN ACTIVATION

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**Introduction :** The circadian system profoundly modulates attention and sleepiness. Positron emission tomography has shown morning to evening differences in activity in thalamic and brainstem areas involved in alertness. In this study, the effect of the circadian alerting signal on functional brain activation was assessed at multiple time points during the biological night.

**Methods :** 12 healthy adults (ages: 22-36, 5 female) participated in repeated sessions of functional magnetic resonance imaging between 10 PM and 8 AM, using a 3 Tesla scanner. Subjects habitually slept from 10-11 Pm to 6-7 AM. A 9.5 minute 2-back verbal working memory task was used. This allowed at least 4 time points of assessment of functional activation, 10 PM-12 midnight, 1-3 AM, 3-5 AM, and 7-8 AM. Image analysis used Brain Voyager QX (motion correction, linear trend removal, spatial smoothing using a 6 mm filter, Talairach space transformation, analysis using the general linear model approach, statistical maps using a False Discovery Rate of  $< 0.05$ ).

**Results :** Individual and group contrast maps showed a major reduction in activation in the executive network, especially the prefrontal cortex, during the 3-5 AM scan (third) period vs. the earlier and later images. This was associated with a significant slowing of performance only during the third period. The fourth period showed an increase in activation that is plausibly temporally linked to the rising phase of the circadian drive.

**Conclusion :** Functional brain activation is profoundly impaired during the circadian nadir. A striking "circadian effect" is seen within 2 hours of this impairment, when the duration of sleep deprivation is actually longer. Functional imaging studies that are performed late in the biological day (such as those following 35-40 hours of sleep deprivation) are possibly assessing predominantly compensatory rather than sleep deprivation effects.

**Support (optional):** NIH/NHLBI K23 HL004457

### 0156

#### MODERATE INTENSITY LIGHT IN COMBINATION WITH SCHEDULED SLEEP FACILITATES ADAPTATION TO NIGHT WORK

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**Introduction :** A large number of studies have shown that appropriately timed bright light in conjunction with a fixed sleep schedule can facilitate adaptation to night work. However, much less is known about the efficacy of light of moderate intensity or its combined effect with a fixed sleep schedule in facilitating adaptation to night work. In this study, we evaluated the effectiveness of timed exposure to moderate intensity light in combination with two different fixed sleep schedules to facilitate circadian adaptation to a night work schedule.

**Methods :** Thirty-six subjects participated in a 10-day simulated shift-work study, which included four day shifts followed by three night shifts. All subjects slept from 2200-0600 and worked under 25  $\mu\text{W}/\text{cm}^2$  of (73 lux) light during the four day shifts. Subjects were divided into four groups on the night shift, defined by one of two sleep schedules and one of two light intensity levels. Subjects either slept before work (Pre-Night Shift Sleep: 1400-2200) or after work (Post-Night Shift Sleep: 0800-1600), and were exposed to four hours of either moderate intensity (128  $\mu\text{W}/\text{cm}^2$ ; 473 lux) or bright (455  $\mu\text{W}/\text{cm}^2$  ; 915 lux) light from ceiling-mounted fluorescent lamps. Light exposures lasted from 0300-0700 for the Pre-Night Sleep groups and from 2300-0300 for the Post-Night Sleep groups, and lighting during the remainder of the night shift was 25  $\mu\text{W}/\text{cm}^2$ .

**Results :** We measured circadian phase using the Dim Light Salivary Melatonin Onset (DLSMO) before the first night shift and following the final night shift. As expected, subjects in the Pre-Night Sleep groups phase advanced and subjects in the Post-Night Shift Sleep groups phase delayed. When the phase shifts between the two light intensity groups was compared, light intensity did not have a significant effect on the magnitude of the phase shifts (Pre-Night Shift Moderate vs. Bright Light: 2.19 + .54h vs. 3.2 + .47h; Post-Night Shift Moderate vs. Bright Light: -5.05 + .67h vs. -4.9 + .52h).

**Conclusion :** The efficacy of appropriately timed bright light for producing phase shifts and/or facilitating adaptation to night work schedules has been demonstrated in many studies. The current data demonstrate that light of more moderate intensity, in combination with scheduled sleep, can be effective in facilitating adaptation to night work. These results have important implications for maintaining effective functioning in environments with routine night work schedules.

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## 0157

### EFFECTS OF STARTING NIGHT SHIFT WORK

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**Introduction :** There is evidence for a disturbing influence of night shift work on sleep and wakefulness. Most former studies focused on subjects with a longterm experience to night shift work. Little is known about young adults starting night shifts work. In this study student nurses were examined prospectively by using actigraphy (ACT), sleep logs and questionnaires. A period of daytime work was compared to a period with starting night shift work.

**Methods :** 30 student nurses, mean $\pm$ SD age 20.2 $\pm$ 2.1 years, underwent two three week periods (P1 and P2) with ACT (ActiTrac monitors, IM Systems Inc.). P1 was a period of daytime work conditions during theoretical education. P2 during hospital work included shift changes and 3-5

consecutive night shifts. For analysis of activity data ActiTrac software was used. Total sleep time per day (TST) and number of sleep episodes per day was calculated from the activity data. The subjects were asked to complete sleep logs and Epworth Sleepiness Scale (ESS). The seven days following night shift (F) were taken as separate scoring periods from P2. F was matched with a seven day reference period (R) from P1.

**Results :** During P2 TST increased significantly from 451 $\pm$ 37 min during P1 to 466 $\pm$ 36 min ( $p<0.01$ ). During night shift TST was short (404 $\pm$ 66 min). During F TST was significantly increased to 470 $\pm$ 52 min vs. 448 $\pm$ 41 min in R ( $p<0.05$ ). Number of sleep episodes per day increased from 1.18 $\pm$ 0.13 in P1 to 1.23 $\pm$ 0.16 episodes per day in P2 ( $p<0.05$ ). ESS did not change significantly from 7.2 $\pm$ 2.6 at the beginning of P1 to 7.6 $\pm$ 3.5 at the end of P2. Other activity parameters showed no significant changes.

**Conclusion :** We found a reduction of TST under night shift conditions. A significant prolongation during subsequent days was observed. Compared to a daytime working period a three week period with first night shift work conditions increased TST and number of sleep episodes. This might be a compensation for sleep loss or a result of poor sleep quality. These changes in sleep duration were not accompanied by significant changes of other activity parameters or sleepiness. Further research in different age groups is needed to understand short and longterm effects of night shift work.

**Support (optional):** Supported by an research grand from Humboldt University

## 0158

### A TOOL TO ANALYZE MELATONIN PHASE AND AMPLITUDE USING A PHYSIOLOGICALLY-BASED MODEL OF MELATONIN

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**Introduction :** Melatonin has emerged as the preferred marker rhythm of circadian phase due to the low variability in phase estimates compared to other marker rhythms. While crossing-of-threshold-based methods exist to estimate circadian phase from melatonin, these estimates can be confounded by the amplitude of the melatonin pulse, missing data and experimental interventions. Here we present results from a user-friendly, graphical-interface program, MelPhase, which implements a physiologically-based model of melatonin [Brown et al., Am. J. Physiol. 1997] to estimate the time of melatonin synthesis onset (synon), offset (synoff) and amplitude (A).

**Methods :** The equations representing the physiological mechanisms by which melatonin is infused into and cleared from the plasma were programmed into Matlab 7.0.1. The maximum-likelihood estimates of 7 parameters, including synon, synoff and A, were found by an unconstrained nonlinear optimization procedure. R2 was calculated to determine goodness of model fit to the data. MelPhase was validated by analyzing 63 melatonin pulses measured during constant routines from 20 blind subjects. Synon and synoff were compared to phase estimates from the frequently used threshold-based measures half-maximum up-cross and down-cross, respectively.

**Results :** The MelPhase inputs are the melatonin data and the user-estimated start and end times of the pulse (for initiation of analysis only). The MelPhase outputs are the 7 parameter estimates, the melatonin data plotted with the model fit, and the R2 value. The average R2 obtained using MelPhase in the 20 blind subjects was 0.93. The synon vs. up-cross correlation was 0.99. The synoff vs. down-cross correlation was 0.95.

**Conclusion :** The synon and synoff calculated by MelPhase show high correlation with melatonin phases estimated from threshold-based meth-

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ods. MelPhase will be tested on datasets with lower melatonin amplitudes and/or after interventions that affect melatonin phase. Under these conditions, the physiologically-based analytic method is expected to be more accurate than threshold-based methods.

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### 0159

#### THE MELATONIN AGONIST VEC-162 IMMEDIATELY PHASE-ADVANCES THE HUMAN CIRCADIAN SYSTEM

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**Introduction :** Melatonin has been reported to phase-shift circadian rhythms and to affect sleep timing. However, the time course of the phase-shifting effect in humans is not confirmed, primarily due to difficulties associated with using melatonin simultaneously as an intervention and a circadian phase marker. We studied the effects of a dual MT1/MT2 melatonin agonist, VEC-162 (Vanda Pharmaceuticals), on human circadian rhythms and sleep.

**Methods :** Thirty-nine subjects (20 females) aged 18-50 years were studied in a randomized, double-blind, placebo-controlled, parallel groups design to assess efficacy and safety of nightly oral doses (10 mg, 20 mg, 50 mg or 100 mg) of VEC-162 compared to placebo (n=7-9/group) administered 30 minutes prior to bedtime. Subjects were healthy and medication-free. Subjects maintained a fixed sleep-wake schedule for at least 2 outpatient weeks. The inpatient study included 3 days baseline with placebo lead-in, 19-hour constant posture protocol for pre-treatment circadian phase assessment, 3 days of a sleep-wake cycle phase advanced by 5 hours treated with VEC-162 or placebo, and a 24-hour constant posture for post-treatment phase assessment. Plasma melatonin was measured by LC/MS. Sleep was polysomnographically recorded and scored.

**Results :** VEC-162, compared with placebo, phase-advanced melatonin onset in a dose-dependent manner on the first administration. VEC-162 improved overall sleep efficiency especially in the middle third of the phase advanced sleep episode, reduced sleep latency, and attenuated the reduction in REM sleep induced by phase-advancing sleep. VEC-162 was well-tolerated at all dose levels.

**Conclusion :** VEC-162 induced phase advances of the melatonin rhythm of up to 5 hours on the night of the first dose. Improved sleep parameters may be due to both the phase-shifting and sleep promoting properties of the compound. VEC-162 may offer therapeutic potential for sleep-wake disorders including individuals who for work or other reasons rapidly shift their circadian phase.

**Support (optional):** Supported by Vanda Pharmaceuticals Inc. and NIH M01-RR-02635 to Brigham and Women's Hospital General Clinical Research Center.

### 0160

#### REST-ACTIVITY RHYTHMS PREDICT RISK OF MORTALITY IN OLDER WOMEN

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**Introduction :** Disrupted rest-activity rhythms (RAR) have been associated with lower survival in demented nursing home residents and cancer patients. However, the relationship of circadian rhythms and risk of mortality in community-dwelling older adults has not been studied. Using data from the multicenter Study of Osteoporotic Fractures (SOF) we tested the relationship of actigraphic rest-activity rhythms and risk of mortality in older women.

**Methods :** During the SOF Exam 8 in 2002-4, RAR were ascertained by wrist actigraphy (SleepWatch-O®, Ambulatory Monitoring, Inc) in 3,027 women aged 80 and older. Data were collected for a mean of 3.6 days (SD=0.8). The cosinor model was used to fit activity data collected in proportional integration mode. Deaths after Exam 8 were confirmed using death certificates. Cox proportional hazards models were used to test the association of RAR and risk of mortality, adjusting for potential confounders (age, race, BMI, medical conditions, smoking, exercise, self-reported health, and impaired activities of daily living). Results are presented as relative hazards (RH) with 95% confidence intervals (CI).

**Results :** 176 women (5.8%) died during the 2-year follow-up. Robustness of RAR (F-statistic) was strongly related to mortality risk: in multivariate models each standard deviation (SD) decrease in robustness increased risk of mortality by 47% (RH=1.47; 95% CI 1.20 - 1.79). Lower amplitudes (height of peak) similarly increased risk of mortality (RH per SD decrease=1.64; 1.37 - 1.96). Exploratory analysis using regression splines revealed a possible U-shaped relationship between acrophase (timing of the peak) and mortality risk, such that both advanced and delayed rhythms (compared to normal) were associated with decreased survival.

**Conclusion :** Older women with disturbed RAR have higher risk of mortality. Circadian rhythms may provide a useful indicator of biological age. Interventions to regulate RAR in older adults (e.g. physical activity; bright light exposure) may enhance survival.

**Support (optional):** The Study of Osteoporotic Fractures is supported by NIH grant numbers AG05407, AR35582, AG05394, AR35584, AR35583, AG08415

### 0161

#### DIURNAL PREFERENCES AND CIRCADIAN PHASE: A META-ANALYSIS

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**Introduction :** Diurnal preferences show a relationship with an advanced or delayed circadian phase. The relative size of this effect has yet to be thoroughly established, however, particularly across diverse samples and assessments methods. Here we report on a meta-analysis conducted to examine the correlation coefficient between morningness-eveningness and circadian phase.

**Methods :** Studies were identified using Medline, Web-of-Science, and PsycINFO, 1980-present, with the following keywords: circadian phase position; circadian rhythms; and eveningness, morningness; evening-type; morning-type; diurnal preferences; chronotype; circadian typology; owl; lark. A cited reference search was performed, and researchers were contacted to seek out fugitive or in-press literature. Selection criteria included use of an adequate measure of diurnal preferences and an objective assessment of circadian phase (using continuous sampling methods, controlled conditions) in healthy adolescents and adults. Twelve studies with non-overlapping datasets met inclusion criteria (n=527). A Fixed Effects Model was used, and the weighted mean of each effect size (ES)

was calculated with a 95% confidence interval. The ES metric analyzed was  $r/Zr$ . Z-test significance testing was performed for 1 grand meta-analysis, and 4 sub-analyses (to evaluate ES by assessment method).

**Results :** All analyses were significant at the  $p < 0.01$  level, including the correlation coefficient between diurnal preferences and: overall circadian phase (CI =  $-.53 \pm .08$ ,  $Z = 13.04$ ), T<sub>min</sub> (CI =  $-.49 \pm .08$ ,  $Z = 10.23$ ), T<sub>max</sub> (CI =  $-.75 \pm .14$ ,  $Z = 5.93$ ), DLMO (CI =  $-.57 \pm .14$ ,  $Z = 6.29$ ), and DLMO<sub>off</sub> (CI =  $-.54 \pm .17$ ,  $Z = 5.20$ ).

**Conclusion :** A medium-large ES between morningness-eveningness and phase was observed. Greater morningness was associated with an earlier circadian phase. DLMO and T<sub>max</sub> circadian phase assessments produced the highest ES. Two outliers emerged in T<sub>max</sub> analyses, which appeared to be associated with problematic methodology and an inflated ES. According to this meta-analysis, diurnal preferences are strong, albeit imperfect indicators of circadian phase.

**Support (optional):**

## 0162

### A CROSS-SECTIONAL STUDY INVESTIGATING EVENINGNESS-MORNINGNESS, DEPRESSIVE SYMPTOMS, AND SLEEP VARIABILITY

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**Introduction :** Several reports indicate that evening types may be more likely to show elevated mood disturbances compared to morning types. Research furthermore suggests that evening types tend to show greater sleep variability relative to other chronotypes. Despite these findings, a study has yet to examine such relationships within a single investigation using prospective assessments of sleep. Here we report on a cross-sectional study investigating the link between diurnal preferences, sleep variability, and depressive symptoms. Greater eveningness was hypothesized to show a connection with increased sleep variability and mood disturbances.

**Methods :** Eighty-two healthy, non-shiftworkers (aged 18-32) were recruited from a university setting. Each participant completed the MEQ and the Beck Depression Inventory (BDI), as well as a 7-day NSF sleep diary. Diaries were used to calculate the variability of sleep onsets and offsets over a week-long time period. To compute total sleep variability, the standard deviation of sleep onsets and offsets was calculated for each participant.

**Results :** Linear regression analyses were performed to test study predictions. Hypotheses were partially supported. MEQ total scores were not significantly associated with BDI total scores; the link instead emerged as a nonsignificant trend in the expected direction ( $r = -.19$ ,  $t = -1.76$ ,  $p = .08$ ). MEQ scores were significantly associated with sleep variability (SV) scores ( $r = -.23$ ,  $t = -2.11$ ,  $p < .05$ ), with greater eveningness predicting increased variability in sleep onsets and offsets. Next, increased sleep variability was positively and significantly associated with depressive symptoms ( $r = 1.02$ ,  $t = 2.39$ ,  $p < .02$ ).

**Conclusion :** Eveningness appears to show some relationship with elevated mood symptoms, which may be explained, in part, by increased sleep variability. Future investigations are warranted to prospectively evaluate whether an association between eveningness and depressive symptoms is perhaps mediated by irregular sleeping behaviors and delayed entrainment patterns.

**Support (optional):**

## 0163

### SHIFT WORKING BUS DRIVERS AND AGEING: A POLYSOMNOGRAPHIC STUDY

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**Introduction :** Although it has been suggested that aging aggravates sleep disturbances due to shift work, polysomnographic studies are scarce. The present study was designed to explore possible influences of age on daytime and nighttime sleep recorded objectively by polysomnographic means

**Methods :** Subjects included 95 younger ( $< 45$  yo) and 49 older ( $\geq 45$  yo) rotating shift work bus drivers with no evidence of sleep apnea (AHI  $< 5$ ). The drivers were invited to come to the Sleep Institute after a trip for a diurnal or nocturnal PSG commencing at their usual bedtime.

**Results :** Data showed that shift workers had shorter ( $335.2 \pm 73$  vs  $387.8 \pm 73$ ,  $F_{time} = 13.1$ ,  $p < 0.05$ ), and lower sleep efficiency ( $78.3 \pm 12.8$  vs  $85.4 \pm 9.2$ ,  $F_{time} = 11.0$ ,  $p < 0.05$ ) during daytime episodes but there were no significant age effects (F<sub>age</sub> = 1.4 and 3.0,  $p < 0.05$ ). The day sleep was also characterized by short REM sleep duration (%), ( $16.8 \pm 7.4$  vs  $23.1 \pm 6.1$ ,  $F_{time} = 28.5$ ,  $p < 0.05$ ), more pronounced among the older group ( $14.5 \pm 7.8$  vs  $18.2 \pm 6.9$ ,  $F_{age} = 7.0$ ,  $p < 0.05$ ). Older shift workers also had increased percentage of Stage 2 ( $52.0 \pm 10.9$  vs  $48.1 \pm 8.6$ ;  $F_{age} = 5.2$ ,  $p < 0.05$ ) and longer latency (min) to REM ( $118 \pm 67$  vs  $92 \pm 49$ ;  $F_{age} = 6.8$ ,  $p < 0.05$ ). There were no differences for % of Stages 3 and 4, arousals per hour and stage shifts.

**Conclusion :** Our results fail to corroborate that daytime sleep of older shift workers is more disturbed as compared to younger. We decided to study workers without evidence of sleep apnea, a condition known to increase with age. Previously reported differences between older and younger shift workers may have been due to an underlying sleep disorder and its associated changes on sleep architecture.

**Support (optional):** AFIP and FAPESP/CEPID (98/14303-3).

## 0164

### SIMULATOR DRIVING PERFORMANCE IN A FAST FORWARD VERSUS A SLOW BACKWARD ROTATING SHIFT SYSTEM

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**Introduction :** A well-established link exists between shift work and psychological and physiological health problems, such as cardiovascular disease, gastrointestinal disorders, and clinical sleep disorders. Yet, few experimental and field studies report on the driving performance of shift workers at the end of their shift, when they often drive home by car themselves. The aims of this study were to examine simulator driving performance following a morning, an afternoon and a night shift; and, secondly, to compare these effects between two shift schedules, a fast forward and a slow backward rotating shift system.

**Methods :** Thirty-six male volunteers working in a chemical plant participated. Half of the subjects were working for at least 3 years in a slow backward rotating system, whereas the other half had started in a fast forward rotating system 8 to 12 months before the study. According to a counterbalanced design, employees performed a 25-minute driving simulator test at 05:30, 21:30 and 13:30, half an hour before finishing their night, afternoon and morning shift respectively.

**Results :** A significant effect of shift type on lane drifting was found [ $F(2,68) = 5.79$ ;  $p < .01$ ]. Post hoc analyses showed that lane drifting was

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higher following the night shift as compared to the afternoon shift ( $p < .01$ ). No overall effect of rotation system [ $F(1,34)=0.81$ ; n.s.], nor a shift type/rotation system interaction [ $F(2, 68)=0.53$ ; n.s.] could be demonstrated.

**Conclusion :** Driving performance significantly deteriorated following the night shift in comparison with the afternoon shift. This highlights a potential safety risk in shift workers driving home by car themselves after a night shift. Although employees reported lower levels of subjective sleepiness in the fast forward rotating shift system, present results could not demonstrate a difference in performance between both shift systems.

**Support (optional):** The study was supported by the research board of the Free University of Brussels and the Catholic University of Leuven.

### 0165

#### SLEEP, AGE AND SLEEPINESS DURING NIGHT SHIFTS

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**Introduction :** Although there are some cross-sectional studies showing that the sleep disturbances due to shift work are exacerbated after the age of 40-50 years, there is no clear evidence that ageing increases sleepiness and/or fatigue during night shifts.

**Methods :** Data on sleep characteristics and sleepiness/fatigue while working night shifts (23:00 - 07:00 h) were gathered through face-to-face interviews with shift workers working at a nuclear power plant as follows: 175 aged > 45 years and 82 aged < 45 years.

**Results :** The mean (SD) sleep length (h) after night shifts were 5.5 (1.7) for the younger and 5.3 (1.9) for the older group ( $t=0.7$ ,  $p>0.05$ ). Older age was associated with a higher rate (often or almost always) of satisfaction with sleep quality (52.4% vs 34.9%;  $Z = 2.7$ ,  $p<0.05$ ) and being rested after night shifts (48.8% vs 28.7%;  $Z = 3.1$ ,  $p<0.05$ ) as well as a lower frequency of naps during night work (47.4%; vs 60.7%  $Z = 2.0$ ,  $p < 0.05$ ). There were no differences between older and younger shift workers ( $p < 0.05$ ) concerning the frequencies of experiencing difficulties (often or almost always) in falling asleep (20.7% vs 18.6%), staying asleep (31.7% vs 31.4%), early awakening (19.8% vs 23.9%), unintentional sleep attacks (4.9% vs 8.9%) and excessive sleepiness (9.8% vs 16.4%).

**Conclusion :** In contrast with previous studies, we found data that older shift workers might tolerate better the night shift. These results raise the possibility that older shift workers may have developed life styles or strategies that allowed them to better cope with the deleterious effects of night shift on sleep.

**Support (optional):** AFIP and FAPESP/CEPID (98/14303-3)

### 0166

#### CIRCADIAN PHASE IN DELAYED SLEEP PHASE SYNDROME: PREDICTORS AND STABILITY ACROSS MULTIPLE ASSESSMENTS

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**Introduction :** Scant data exist that address the pathophysiology of, or the diagnostic certainty for DSPS. Only a week of sleep diary data or actigraphy are required as prospective data to confirm the diagnosis. Obtaining objective confirmation of delayed circadian phase would increase diagnostic certainty and would also permit more precise timing of the administration of bright light or exogenous melatonin administration as treatments.

**Methods :** Temporal stability and predictors of circadian phase were assessed in young participants with delayed sleep phase syndrome

(DSPS;  $n = 8$ ) and age/gender-matched controls ( $n = 8$ ). Circadian phase was assessed in dim light, by salivary dim light melatonin onset (DLMO) during three laboratory visits, two scheduled at end of week (Friday) and one scheduled at end of weekend (Sunday). Light exposure and rest/activity were assessed via continuous wrist actigraphic monitoring. Prospective sleep diaries were also completed.

**Results :** Circadian phase did not change significantly across the three assessments, in either group. Estimations of circadian phase were not significantly different on weekday versus weekend assessments. Predictors of circadian phase included time of morning light exposure ( $r$ -squared = 0.777;  $p < 0.001$ ), recent average wake time ( $r = 0.701$ ,  $p < 0.001$ ), and self-reported chronotype ( $r$ -squared = 0.320,  $p = 0.016$ ). DLMO preceded wake time in both groups by approximately 10.75 hours.

**Conclusion :** Across serial laboratory assessment on an ad lib sleep schedule, DSPS patients appeared more similar to than different from normal sleepers except for a stable delay in circadian phase. Recent wake time and timing of morning light exposure were excellent surrogate markers for DLMO.

**Support (optional):** Supported by: NIH MH065967-A1

### 0167

#### THE IMPACTS OF SHIFT-WORKING SCHEDULE ON SLEEP DEPRIVATION-PRELIMINARY REPORTS FROM AN OCCUPATIONAL SLEEP DISTURBANCE SCREENING RESEARCH

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**Introduction :** A variety of factors may attribute to sleep problems; shift-working schedule is one of them. In this study, we present the impacts of shift working schedule on the sleep deprivation based on the preliminary data obtained from an occupation sleep disturbance screening research.

**Methods :** A total of 980 employees (52 females, 928 males; age  $44.5 \pm 7.7$  years-old, range 21-64) were administered with 2 sleep-specific questionnaires: the Epworth Sleepiness Scale (ESS) and the Pittsburgh Sleep Quality Index (PSQI). The responders worked on 4 different shift-working schedules: day-time work (DAY,  $n=356$ ), shift on an every-3~5 days schedule (3-5 DAY,  $n=439$ ), shift on an every-1 week schedule (WEEK,  $n=116$ ) and shift on an every-2 week schedule (2 WEEK,  $n=69$ ). Survey data were compared using One-Way ANOVA and Post Hoc analysis between groups.

**Results :** Employees working on DAY schedule have less sleep problems (PSQI indices) in general, as compared to others who work on other types of shift schedules; the differences are statistically significant. As can be observed in less day-time sleepiness ( $p=.000$ ), better sleep quality ( $p=.000$ ), more total sleep time ( $p=.000$ ), better sleep efficiency ( $p=.000$ ), less sleep disturbance ( $p=.000$ ), and less daytime dysfunction ( $p=.000$ ). To the contrary, we find employees working on 3-5 DAY schedule have significant poorer sleep quality ( $1.42 \pm 0.69$  vs.  $1.23 \pm 0.69$ ,  $p=.018$ ), less total sleep time ( $1.28 \pm 0.80$  vs.  $1.07 \pm 0.77$ ,  $p=.034$ ), more sleep disturbance ( $7.53 \pm 4.66$  vs.  $6.32 \pm 4.57$ ,  $p=.025$ ) than do those on WEEK schedule.

**Conclusion :** Our preliminary data show that shift workers have more sleep problems, including daytime sleepiness, sleep quality, total sleep time, sleep efficiency, sleep disturbance, and daytime dysfunction than do daytime workers. Moreover, employees who shift on every-3~5 days schedule have even more problems than do those shift on every-one week schedule. We conclude that employers can significantly improve employee sleep health by avoidance of using every 3~5 days shift schedule.

**Support (optional):****0168****THE EFFECT OF “SLEEPING-IN” WEEKEND MORNINGS ON CIRCADIAN RHYTHMS, SLEEP AND DAYTIME SLEEPINESS***Taylor A, Lack LC, Wright HR*

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**Introduction :** Previous research has shown that delaying both bedtime and wake-up time by two hours on weekend nights results in a 32-minute delay in circadian phase and increased sleep latency. Other studies have shown that delaying wake-up time has a greater effect in delaying circadian phase than delaying sleep onset time. Considering that a common practice is to extend sleep length over the weekend mainly by delaying wake-up time, the aim of the present study was to test the circadian effects of sleeping in later on weekend mornings while keeping bedtime the same.

**Methods :** Sixteen participants repeated two conditions in counterbalanced order; one in which habitual weekday wake-up time was maintained over the weekend, and the other in which wake-up time over the weekend was delayed ad lib by an average of 2.5 hours. Bedtimes and sleep onset times were the same in both conditions. Change in circadian phase was measured using half-hourly salivary samples to determine the dim light melatonin onset (DLMO), assessed on Friday night and Sunday night of each experimental weekend. Sleep onset latency on Sunday night, and subjective sleepiness and fatigue on the week following each experimental weekend were assessed using self-report questionnaires.

**Results :** Compared to habitual weekday wake-up time over the weekend, a delay in wake-up times resulted in a 42 minute delay in DLMO by Sunday night. Later weekend wake times were also followed by an 8 minute longer subjective sleep onset latency on Sunday night and increased subjective sleepiness and fatigue on Monday and Tuesday of the following week.

**Conclusion :** Although there might be some appeal to sleeping-in later on the weekend, its costs are circadian rhythm delay and impaired alertness early in the following week.

**Support (optional):****0169****CIRCADIAN RHYTHMICITY OF CORE TEMPERATURE, HEART RATE, AND BACKGROUND EEG FREQUENCIES BETA AND DELTA MAY BE REGULATED BY A COMMON PACEMAKER***Lindsley G,<sup>1</sup> Doherty T,<sup>2</sup> Kolka M,<sup>3</sup> Dowse H,<sup>4</sup> Leammukda M,<sup>3</sup> Donajkowski C,<sup>3</sup> Johnson C,<sup>3</sup> Stephenson L<sup>3</sup>*

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**Introduction :** There are numerous reports of phasic power increases in the delta EEG frequency band during nighttime sleep with increasing sleep deprivation (SD), and in beta power with stimulation. However, there are also some reports of possible intrinsic circadian rhythmicity in these two frequency bands. One possibility is that the known event-induced increases in delta and beta power may be superimposed on an underlying circadian rhythm. Demonstration of common periodicities among core temperature, heart rate and these two EEG frequency bands would further support the possibility of a common regulatory circadian pacemaker for these variables.

**Methods :** EEG (C3-A2), EKG, and core temperature were recorded in five male subjects (ages 18-23) free of medical, psychiatric and sleep dis-

orders during baseline (B) (five 8-hour sleeping periods and 6 days) under entrained conditions; and for three of these subjects during a comparable experimental SD condition (E) (sleep interrupted after four hours).

**Results :** The period across all four variables was  $24.19 \pm 0.16$  ( $p < .001$  Lomb Spectral Analysis) with no significant between subject, condition or variable differences. Acrophases computed using a double harmonic fit assuming a 24h period were as follows: Tc: B-19:15 h; E-19:49 h; HR: B-17:06 h; E-18:31 h; % beta: B-17:24 h; 18:44 h; % delta: B-02:36 h; E-01:34 h.

**Conclusion :** The finding of ~24 hour periods in all four variables independent of condition suggests there may be a common circadian pacemaker regulating these four distinctly different physiological functions. Given the small N it is unclear how to interpret the apparent B to E phase shifts for HR, delta and beta. Thalamocortical networks likely are involved in regulating the degree to which cortical cells are inhibited or disinhibited, and the dynamics of these networks may explain the sustained antiphase relationship between beta and delta. If so, the relevant thalamic nuclei would be the target of output from the SCN.

**Support (optional):****0170****SLEEPING AND LIFE HABITS IN MORNING AND EVENING TYPES OF SLEEP-WAKE RHYTHM***Kato H,<sup>1</sup> Noda A,<sup>1</sup> Miyata S,<sup>1</sup> Morishita Y,<sup>1</sup> Adachi Y,<sup>1</sup> Iwami A,<sup>1</sup> Sukegawa M,<sup>1</sup> Maeno N,<sup>2</sup> Ozaki N,<sup>2</sup> Koike Y<sup>1</sup>*

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**Introduction :** Humans have a circadian rhythm that includes living habits, sleep and wake, internal secretions, and autonomic activity. Severe working condition, such as experienced by shift and night workers, result in an irregular sleep-wake rhythm that not only increases the night type of circadian rhythm but also the prevalence of sleep-wake rhythm disorders. However, the relations between life habits and the sleep-wake rhythm have not been fully investigated.

**Methods :** Fifty-two university students participated in this study. We assessed how the morning and evening types of sleep-wake rhythm are related to sleep and life habits using Horne and Ostberg's Morningness-Eveningness Questionnaire. We extracted items related to the regulation of life habits, such as those of sitting up all night, dozing, having an afternoon nap, and eating breakfast.

**Results :** Morning, intermediate, and evening types were present in 9.6%, 71.2%, and 19.2% of the subjects, respectively. The sleep length did not significantly differ among three types. 40% of evening type exhibited a variance in sleeping hours of more than 2 hours, and 20% of evening type exhibited a variance in the arising time and bedtime of more than 2 hours. 80% of morning type felt pleasantly or fairly pleasantly on arising, in contrast to only 20% of evening type feeling this. Of the evening type, 60% had a habit of dozing and 20% had a habit of an afternoon nap; none of the morning-type subjects exhibited these habits. All of the morning type and 50% of the evening type had breakfast.

**Conclusion :** These results demonstrated that there were differences in the regularity of sleep satisfaction and in the quality of sleep and life habits between morning and evening types. The assessment of sleep-wake rhythm and life habits should therefore be included in health examinations.

**Support (optional):**

0171

**TIME-OF-DAY MODULATIONS OF REGIONAL CEREBRAL BLOOD FLOW RESPONSE IN FUNCTIONAL BRAIN IMAGING STUDIES : A META-ANALYSIS**

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**Introduction :** Circadian variations and homeostatic sleep pressure determine our sleep-wake cycle and affect several neurophysiological and neurobehavioral parameters. In the context of functional brain imaging studies, we aimed to characterize the set of brain areas in which rCBF is modulated by the time of day of scan acquisition.

**Methods :** From 22 PET studies previously conducted in the Cyclotron Research Centre, 309 subjects were included analysis. All PET data were acquired between 9:00 and 18:00 h using the H215O technique. The resulting 3736 scans were obtained in a variety of modalities during a wide range of experimental paradigms. Data were analysed in SPM2 <http://www.fil.ion.ucl.ac.uk/spm> using a general linear model including the clock time of each scan acquisition as covariate of interest, reported on the average adjusted curve of the circadian component of body temperature rhythm.

**Results :** Regional CBF was positively correlated with time of day in a large set of brain areas. Areas in which activity increased in the course of the day were thalamus and hypothalamus including the suprachiasmatic region, limbic regions including the amygdala, hippocampus, parahippocampal and cingulate gyri, the cerebellum, pre- and post-central areas, precuneus, middle, medial and superior frontal gyri, and superior temporal gyrus.

**Conclusion :** Note that a tighter control of circadian and homeostatic processes should be taken into account in further, prospective, studies. Also, it is worth mentioning that this study was not aimed at identifying rCBF variations specifically related to particular aspects of cognition or sensory modalities. Rather, by gathering many different conditions in a single analysis, our results highlight the set of brain areas in which circadian and homeostatic influences might be expressed. Our meta-analysis suggests that time of day exerts its influence on rCBF distribution in a large set of brain areas in the context of daytime functional brain imaging studies.

**Support (optional):** Supported by FNRS, FMRE and PAI P4/05

0172

**DESCRIPTIVE ANALYSIS OF THE RELATION BETWEEN HUMAN ERROR AND THE WORK SCHEDULE OF PILOTS IN A BRAZILIAN AIR COMPANY**

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**Introduction :** Flight safety is one of the most important and debated issues in the aviation environment. The latest investigations into flight accidents have raised questions regarding the organization of the crew work and whether these conditions have contributed to the fatalities. Fatigue has its roots in physiological limitations, and the performance deficits reflect those physiological limits. The general objective of this study was to describe the times at which there is the highest prevalence of

errors of pilots who work at a company of commercial aviation.

**Methods :** The total sample comprised 515 captains and 472 co-pilots. In order to carry out the research, we used a program of flight data analysis called Flight Operational Quality Assurance (FOQA), which is a tool for safe flying. Its technology allows for the systematic analysis of the flights stored by the Digital Flight Data Recorder (DFDR) of the aircraft. The light-dark cycle was divided into four periods: morning, afternoon, evening and early morning.

**Results :** After analyzing the flight schedules of the company, we observed that 35% of the flights took place in the morning, 32% in the afternoon, 26% at night and 7% in the early morning. The analysis of the percentage of errors regarding the four shifts showed that 33,05% of them happened in the morning, 31,46% in the afternoon, 25,82% at night and 9,67% in the early morning.

**Conclusion :** The results showed that the relation between the proportion of errors and the percentage of flights increases according to the sequence of shifts (morning, afternoon, evening, early morning). There seems to be a tendency to an increase in the number of errors in the early morning, which might be associated with the body temperature curve.

**Support (optional):** AFIP, FAPESP (CEPID 98/143033), CEMSA, CEPE, UNIFESP.

0173

**SLEEP ARCHITECTURE IN LOW ENDOGENOUS MELATONIN SECRETORS**

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**Introduction :** The pineal gland hormone melatonin (5-methoxy N-acetyltryptamine) relays temporal queues to various organs. Melatonin secretion is normally synchronized with the habitual hours of sleep, exhibiting a diurnal pattern. The purpose of this study was to investigate the sleep architecture and quality in patients with low endogenous melatonin.

**Methods :** A total of 51 patients (24 females and 27 males, mean age of  $32.4 \pm 16.2$  years) participated in the study. Melatonin profiles were evaluated using Dim Light Melatonin Onset (DLMO) Test. All patients were seated in a dark room ( $< 5$  Lux) from 1900 hours to 0300 and saliva samples were collected hourly. Melatonin concentrations were measured using ELISA. The DLMO was defined as the first 20% increase in melatonin concentration above 4 pg/ml. All patients underwent standard montage polysomnographic testing for two nights which included electroencephalography, electrooculography, electromyography and respiratory monitoring.

**Results :** Based on the melatonin secretion profile, two groups were created. The normal secretors ( $n=24$ ), with 14 females and 10 males (mean age  $31.8 \pm 14.8$  years). The low endogenous secretors ( $n=27$ ) with 10 females and 17 males (mean age  $32.9 \pm 17.6$  years). The mean amount of melatonin secreted at DLMO and at the nine different collection times were significantly higher in the normals ( $38.038 \pm 21.46$  pg/ml) than the in the low secretors ( $5.771 \pm 2.43$ ). The sleep parameters tested were Sleep Onset Latency (first 30-second epoch of stage 2 sleep), Sleep Efficiency, REM Latency, Slow Wave Sleep percentage, REM percentage, and Arousal Index. Only the second night REM latency was significantly higher in the low secretors ( $144.72 \pm 115.46$  min) than in the normals ( $80.67 \pm 26.67$  min).

**Conclusion :** Low endogenous melatonin secretors do not exhibit altered sleep architecture under polysomnographic testing, exemplifying that melatonin may act more as a chronobiotic than a soporific agent.

**Support (optional):**



## 0174

**COMPARISON OF SLEEP COMPLAINTS AMONG BRAZILIAN MALE SHIFT WORKERS AND THE GENERAL POPULATION**

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**Introduction :** Sleep complaints among shift workers are frequently reported. However, comparison between general population (GP) and shift workers (SW) is still scarce.

**Methods :** Male SW from a nuclear power station were invited to answer questionnaires about their sleep. Three hundred and twelve workers, mean age of 38.2 y (SD=8.9), working a schedule of three shifts - morning (07:00-15:00h), night (23:00-07:00h) and evening (15:00-23:00h) agreed to participate. Results from this sample of SW and from a random sample of Brazilian males from adult GP (N=426) were expressed as proportions and of the 95% confidence interval.

**Results :** Difficulties in falling asleep, staying asleep, early awakening and excessive sleepiness (at least 3 times a week) were equally reported in both populations as follows: SW [15.5% (11.8 - 20.1)], [27.1% (22.3 - 32.4)], [7.2% (4.8 - 10.8) and [4.2% (2.4 - 7.2)], respectively; GP 13.1% (11.2 - 15.3); 24.1% (22.0 - 27.4) 11.3% (9.5 - 13.4) and [3.3% (2.4 - 4.6)], respectively. A higher frequency of shift workers [15.2% (11.5 - 19.8)] than adults from general population [6.1% (4.8 - 7.8)] had sought medical help for their sleep problems.

**Conclusion :** The largest difference in the frequency of sleep problems between shift workers and the general population was found in the rate of physician consulting. Since the overall proportion of shift workers complaining about sleep difficulties is similar to the proportion of individuals asking for help, we can infer that shift workers and their physicians are growing aware of the effects of shift work on sleep. Since sleep disorders, particularly sleep apnea, have been repeatedly associated with increase risk of accidents, objective measurements of sleep, such as polysomnographic recordings, should be considered in order to better identify high-risk individuals, offering them adequate medical care and improving working conditions.

**Support (optional):** AFIP and FAPESP/CEPID (98/14303-3).

## 0175

**TIME ESTIMATION DURING A 90-MINUTE DAY STUDY IN OLDER AND YOUNGER ADULTS**

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**Introduction :** Older adults go to bed and wake up earlier than younger adults, which may be related to changes in circadian function. Another possibility is that older and younger adults sense time differently through endogenous circadian signals. This study addressed whether older and younger adults differ in time estimation when removed from time cues during a "90 minute day" study.

**Methods :** Subjects included healthy older adults (n=17, mean age 76 years) and younger adults (n=19, mean age 23 years) evaluated with medical history, physical examination, and laboratory studies. Subjects lived on a 90 minute sleep-wake cycle (60 minutes awake, 30 minutes in bed) for 2.5 days under temporal isolation. They estimated the time of day and certainty of their guess on a 0-100 visual analog scale at eight irregularly spaced points during the study, selected to cover all circadian phases. Outcome measures included difference and absolute difference between estimations and actual times, and certainty scores. Data analyses used repeated measures ANOVA with age group and time as factors.

**Results :** Difference scores showed a significant time effect ( $p=0.003$ ), but no group effect. Absolute difference scores showed significant time ( $p=0.001$ ) and group ( $p=0.004$ ) effects. Certainty scores also showed significant time ( $p=0.002$ ) and group ( $p=0.03$ ) effects. No significant group\*time interaction was noted for any outcome measure, but post-hoc tests showed age group differences only during the second half of the protocol. For each group, the largest time mis-estimation occurred at 02:30, near the core body temperature nadir. Absolute difference and certainty ratings correlated significantly in both groups (Older:  $\rho=0.18$ ,  $p=0.03$ ; Younger:  $\rho=0.33$ ,  $p<0.001$ ).

**Conclusion :** Older adults demonstrated greater time mis-estimation and less certainty than younger adults during time isolation. Both groups showed decreasing certainty and increasing absolute differences across the protocol. Circadian time estimation could plausibly affect sleep timing decisions.

**Support (optional):** Supported by NIH grants AG15138, AG00972, RR00056, MH24652, AG20677

## 0176

**CIRCADIAN RHYTHMS FOUND IN THE NATURALISTIC BEHAVIORAL EXPRESSION OF POSITIVE BUT NOT NEGATIVE MOOD**

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**Introduction :** Previous research has shown that self-reported positive but not negative mood varies according to a diurnal rhythm (paralleling the circadian rhythm of core body temperature). This disparity between the fluctuations in mood states may reflect differences in the underlying physiological systems involved in mood regulation: a motivational approach system that encourages systematic engagement of the environment and a motivational inhibition system concerned with reactive avoidance of aversive stimuli. Our analysis extends this previous work from self-reported to naturalistically sampled behavioral expressions of mood and investigates the extent to which circadian patterns can be found in the behavioral expression of positive but not negative mood.

**Methods :** The data were derived from a larger study that used a new naturalistic observation method, called the Electronically Activated Recorder (EAR), to unobtrusively track participants' real-world social behaviors and interactions. The EAR periodically records snippets of ambient sounds from participants' momentary environments. Eighty-five participants wore the EAR for two consecutive weekdays during their waking hours. For the current analysis, three behaviorally coded indicators of positive affect (laughing, singing, socializing) and two behavioral indicators of negative affect (arguing, sighing) were selected. Cosinor analysis was used to test the circadian rhythmicity of the behavioral indicators.

**Results :** All 3 indicators of positive affect showed diurnal variations that significantly fit a sinusoidal curve with a 24-hour period (laughing:  $r = .74$ ,  $p < .001$ ; singing:  $r = .61$ ,  $p = .001$ ; socializing:  $r = .82$ ,  $p < .001$ ). After controlling for participants' general level of social activity, laughing no longer fit the model, but singing retained a trend towards significant fit ( $r = .38$ ,  $p = .07$ ) suggesting that singing shows circadian fluctuations that are independent of those in socializing. Neither of the two behavioral indicators of negative affect fit the cosinor model.

**Conclusion :** As predicted, behavioral expressions of positive mood show evidence of circadian rhythms in the same manner as do self-reported positive moods.

**Support (optional):**

0177

### THE RELATIVE EFFECTS OF WORK HOURS AND CIRCADIAN FACTORS ON PILOT PERFORMANCE

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**Introduction :** Preliminary data have revealed that time of departure (morning versus evening) significantly affected pilot performance during ultra-long-range flights (> 18 hrs.). However, the relative contribution of circadian factors versus work hours was unclear. Therefore, subsequent analyses were performed to address this issue.

**Methods :** N=17 pilots flew a Boeing 747-400 simulator for 19.5 hrs, with either a morning or evening departure, and completed a psychomotor vigilance task (PVT) and Visual Analog Scale (VAS) alertness rating every 1.5 hrs. To determine the degree to which work hours and circadian time affected performance, mixed-effects ANOVA were performed on five trials that occurred at the same clock times (2130 - 0500 for both groups). During these selected times, both groups had been awake for approximately an equivalent number of hours (12.33-14.75 hrs); however, the morning group had been flying for 10.5 hrs while the evening group had just started the flight.

**Results :** The absence of a departure-time main effect suggests work hours alone did not significantly influence alertness. However, it appears that circadian factors did influence alertness as indicated by significant main effects of time-of-day on PVT transformed lapses ( $F(4, 60) = 23.63$ ,  $p < .001$ ) and VAS alertness ( $F(2.3, 33.7) = 18.21$ ,  $p < .001$ ). Lapses increased linearly from 2130 to 0500 ( $p < .001$ ) while alertness decreased ( $p < .001$ ).

**Conclusion :** These data suggest that at equivalent hours of continuous wakefulness, pilots experienced high levels of sleepiness and decreased performance, which occurred during the early morning hours. However, the actual work hours (i.e., number of hours spent in flight) did not significantly attenuate or exacerbate this effect. Future analyses will investigate the subjective sleepiness ratings as reported by pilots using the Karolinska Sleepiness Scale (KSS).

**Support (optional):** Research supported by NASA's Human Measures and Performance Project of the Airspace Systems Program.

0178

### RETINAL BLOOD FLOW IS ASSOCIATED WITH THE PHASE OF ENDOGENOUS MELATONIN

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**Introduction :** This study tested the hypothesis that reduction in retinal perfusion pressure is associated with phase advances in endogenous melatonin rhythms of older adults.

**Methods :** Eleven volunteers (mean age:  $66.82 \pm 4.21$  years) were interviewed to obtain demographic and health-related data. They wore an actigraph to monitor ambient illumination and sleep. Fractional urine samples ( $n=10$ ) were acquired for melatonin (aMT6s) assays. Cosine analyses yielded the mesor and acrophase for illumination and melatonin data. The Heidelberg Retina Flowmeter was used to obtain data on retinal capillary blood volume. Blood flow and volume at the papilla were derived

employing a method using a 40X40-pixel retinal area showing no eye-motion artifacts or visible blood vessels; a single pixel was manipulated to obtain 1600 data points from which poorly illuminated values (areas of zero flow) were discarded.

**Results :** None of the volunteers received an eye diagnosis, but 28% were visually impaired using standard criteria. The average BMI was  $27.50 \pm 7.90$ kg/m<sup>2</sup>; actigraphic sleep duration averaged  $7.75 \pm 1.80$ hrs. Median illumination and aMT6s excretions were 636lux and 308ng/h, respectively, and the median for acrophases of illumination and aMT6s were 13.02hours and 2.80hours, respectively. We found an inverse correlation of the area of reduced retinal blood flow to the timing of aMT6s ( $rU = -0.65$ ,  $p=0.04$ ) and to daily illumination levels ( $rU = -0.74$ ,  $p=0.01$ ); age effects were adjusted. Further analysis suggests a direct relationship between blood flow volume and both aMT6s mesor ( $rp=0.43$ ) and timing ( $rU = 0.29$ ), but results were not significant. Reduced retinal blood flow was not significantly correlated to aMT6s mesor or illumination timing.

**Conclusion :** Results suggest that age-related ocular pathologies, potentially affecting blood flow to the retina and to the optic nerve head could reduce photic transmission. Peripapillary retinal damage might have independent effects on the circadian rhythm of melatonin, as neither ambient illumination level nor sleep duration affected the relationships.

**Support (optional):** NIA (AG12364-07S1) supported this work.

0179

### PREDICTION OF MOOD FLUCTUATIONS DURING SLEEP DEPRIVATION WITH THE SAFTE MODEL

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**Introduction :** Several models of fatigue and cognitive performance have recently been proposed. The Sleep, Activity, Fatigue, and Task Effectiveness (SAFTE) Model (Hursh et al., 2004) has emerged as one of the most effective models at predicting cognitive performance based on sleep-wake schedules. The SAFTE Model predicts "performance effectiveness" as a function of the duration of wakefulness, recent sleep, circadian rhythms, and sleep inertia. To date, the SAFTE model has been validated against several cognitive tasks such as psychomotor vigilance speed, serial add-subtract, and choice reaction time, but has never been used to predict other important variables known to be affected by sleep loss, such as fluctuations in mood.

**Methods :** Fifty-four volunteers (29 males) were administered the Visual Analog Mood Scales (VAMS) every two hours during 44 hours of total sleep deprivation. The VAMS includes 8 scales measuring the intensity of current moods. The Fatigue Avoidance Scheduling Tool (FAST), a computerized program which implements the SAFTE model, was used to predict "effectiveness" based on a group sleep-wake schedule for the study period and preceding 5 days. VAMS mood scales were entered into separate linear regression analyses to predict SAFTE effectiveness scores. The resulting regression equations were then used to model predicted scores for each mood scale.

**Results :** All 8 VAMS scales were significantly correlated with predicted effectiveness from the SAFTE Model. The strongest correlations were for Tired ( $r=-.95$ ,  $p<.001$ ), Energetic ( $r=.92$ ,  $p<.001$ ), Happy ( $r=.915$ ,  $p<.001$ ), and Tense ( $r=-.89$ ,  $p<.001$ ), followed by Sad ( $r=-.81$ ,  $p<.001$ ), Afraid ( $r=-.72$ ,  $p<.001$ ), Angry ( $r=-.66$ ,  $p=.001$ ), and Confusion ( $r=-.51$ ,  $p=.02$ ).

**Conclusion :** Results suggest that the effectiveness score from the SAFTE Model, as implemented through the FAST computer program, was highly effective at predicting changes in mood associated with sleep deprivation. These findings extend the applicability of the SAFTE Model to include prediction of higher order cognitive-affective processes.

**Support (optional):****0180****TIMING AND PHASE RELATIONSHIP BETWEEN MELATONIN AND SLEEP IN DELAYED SLEEP PHASE**

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**Introduction :** Previous studies of patients with Delayed Sleep Phase (DSP) show a phase delay in melatonin rhythm, as well as alterations in phase relationship between melatonin and sleep. The aim of the current study was to determine the timing of melatonin rhythm and phase relationships between melatonin and sleep in patients with DSP compared to controls.

**Methods :** 9 DSP (mean age 36.5 years) and 4 healthy age and gender-matched controls (mean age 41.7 years) participated in a four-day inpatient study. DSP was diagnosed according to ICSD criteria. Subjects kept habitual sleep-wake schedules, monitored by wrist actigraphy and sleep logs, for 3-5 weeks prior to the study. Average sleep and wake times during this period served as sleep and wake times during the study. Plasma samples were collected q30 or 60 for 24 hours under dim-light conditions (<10 lux) and later assayed for melatonin. Melatonin levels were adjusted to a percentage of maximum (average 3 highest values).

**Results :** DSP showed a significant delay in the timing of sleep and wake and the melatonin rhythm relative to clock time compared to controls; 50% onset (3.72h), midpoint (4.17h) and 50% offset (3.47h). However, the phase relationship between sleep or wake and melatonin (onset and offset) did not differ between DSP and controls, respectively; sleep onset to 50% onset (-0.9h vs. -1.6h), sleep onset to 50% offset (7.23h vs. 6.96h), 50% onset to wake (9.07h vs. 9.61h), 50% offset to wake (0.77h vs. 1.04h).

**Conclusion :** These results confirm previous findings showing a delay in the timing of sleep/wake cycle and circadian melatonin rhythm relative to clock time in DSP. However, when aligned with circadian time, the phase relationship between melatonin and sleep was similar between DSP and controls. Therefore, these results do not support the hypothesis for internal desynchronization of circadian rhythms in DSP.

**Support (optional):** 1R01 HL069988-01A1 and M01 RR-00048

**0181****THE RELATIONSHIP BETWEEN MELATONIN SECRETION DURATION AND RATE OF CIRCADIAN CLOCK RESETTING IN RATS**

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**Introduction :** It is well known that the rate of circadian clock resetting following time zone changes varies greatly among individuals in both experimental animals and in humans. The cause of individual variations, however, is not understood. We have conducted detailed analysis of melatonin profiles in rats before and after shifts of the light and dark (LD) cycle. This study aims to assess how the rate of circadian clock resetting is associated with various circadian parameters.

**Methods :** Male adult rats were housed in a LD 12:12h schedule and implanted with pineal microdialysis probes. Following recovery, rats were connected to dialysis tubing via a swivel. Pineal melatonin from the freely moving rats was sampled every 10 min and analyzed automatically using an on-line HPLC system.

**Results :** Circadian clock adjustment following a 1h delay or advance shift of the LD cycle took between 2 to 11 days. The majority of rats took more than 4 days to re-entrain their clocks to 1h LD shifts in either direc-

tion. Large individual differences in the entrained phase angles of melatonin onset/offset, melatonin secretion durations, and the rate of clock resetting were seen in the rats. There were significant correlations between the phase angles of melatonin onset and melatonin secretion duration with the rate of the circadian clock resetting (R2 of 0.91 to 0.99).

**Conclusion :** The extended periods required for rats to re-entrain following just a 1h time zone change suggest that clock resetting is not as rapid as previously thought. The finding that the rate of clock resetting is correlated with the entrained phase angles of melatonin onset and with melatonin duration points to a new direction for mechanistic understanding of circadian pacemaker re-entrainment. This finding suggests that simple measurement of melatonin duration could be used to identify slow/fast clock resetters in humans.

**Support (optional):**

**0182****INFLUENCE OF VISUAL IMPAIRMENT AND DEPRESSION ON REST-ACTIVITY CYCLES**

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**Introduction :** This study examined the interaction between visual impairment and depression on physical activity among older adults.

**Methods :** Sixty adults (69 ± 6 years) participated in the study; 32 were Black and 27 were White. Women comprised 71% of the sample and men, 29%. Participants provided physical health data (CARE) and mood profile (GDS); sociodemographic information was also recorded. They received eye exams at SUNY Downstate Medical Center. During the following week, they were asked to wear an actigraph (Actiwatch-L) at home for continuous recording of rest-activity cycles. The mesor and the acrophase of rest-activity data were determined using cosine analysis. Sleep time was estimated using software provided by the manufacturer.

**Results :** Altogether, 14% received an eye diagnosis (i.e., glaucoma, cataract, or ocular hypertension). The average BMI and GDS score were 27.68 ± 5.72kg/m<sup>2</sup> and 7.83 ± 4.74, respectively. The average total sleep time, time to bed, and time out of bed were 8.35 ± 3.20; 22.75 ± 1.67; and 6.89 ± 2.49, respectively. Results of the factorial MANOVA revealed that visual impairment had a significant main effect on the level and timing of physical activity [F=5.54, p=0.02; F= 11.86, p=0.01, respectively]. No significant main effect of visual impairment was found on the duration, timing, and quality of sleep. No significant main effect of depression was found on level or timing of activity, duration, timing, or quality of sleep. However, we found a significant interaction between visual impairment and depression on activity timing [F=4.29, p=0.04]. With control for depression, visual impairment and activity timing remain significantly correlated [rp=-0.33, p=0.01], whereas controlling for visual impairment yielded no significant correlation between activity timing and depression [rp=0.20, p=0.13].

**Conclusion :** Visual impairment was a stronger correlate of physical activity than was depression. Moreover, visual impairment mediated the relationships between depression and physical activity.

**Support (optional):** Funding from NIA (AG12364-07S1) supported this work.

0183

MELATONIN ENTRAINS FREE-RUNNING BLIND INDIVIDUALS WITH CIRCADIAN PERIODS LESS THAN 24 HOURS

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**Introduction :** In more than half of those blind individuals without light perception, the lack of photic input to the circadian pacemaker results in rhythms that free-run with a period typically greater than 24 h. Such blind free-runners (BFRs) suffer from recurrent sleep disruption. Administration of exogenous melatonin has been shown to induce corrective phase advances and entrain BFRs with periods greater than 24 h, resulting in objective improvements in sleep quality. Here we show for the first time that melatonin can also entrain BFRs with periods less than 24 h by inducing corrective phase delays.

**Methods :** Subjects were two healthy blind individuals lacking light perception, BL-62 (41 y.o. F, one eye present) and BL-64 (9 y.o. F, no eyes present), who were studied from 4/05 to 12/05 and 5/05 to 12/05, respectively. Saliva samples were collected every 1-2 h for 14-25 h at the Oregon Health & Science University General Clinical Research Center or at home at approximately 2-week intervals. Salivary melatonin concentrations were measured by radioimmunoassay (American Laboratory Products, Windham, N.H.) and the salivary melatonin onset (MO) was assessed using a 3 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. Criteria for entrainment required that the 95% confidence intervals overlap with 24.00 h for a regression line drawn through at least 4 MOs. Melatonin (0.3 mg) was administered at 06:30 h in BL-62 and 20:00 h to 21:00 h in BL-64.

**Results :** Pre-treatment periods ( $\pm$  95% CI) were  $23.66 \pm 0.05$  h and  $23.81 \pm 0.08$  h in BL-62 and BL-64, respectively. Both subjects entrained to 0.3 mg melatonin. Post-entrainment periods were  $23.97 \pm 0.10$  h and  $23.99 \pm 0.20$  h in BL-62 and BL-64, respectively. The average entrained MO occurred at 21:41 h in BL-62 and 14:42 h in BL-64.

**Conclusion :** Melatonin can entrain BFRs with circadian periods less than 24 h by inducing a daily phase delay. In such individuals, morning administration may be preferable to achieve entrainment at the normal phase (MO occurring 2-3 hours before sleep onset). These results have implications for the treatment of other circadian rhythm sleep disorders (such as advanced sleep phase syndrome, adaptation to night shift work and east-to-west jet lag) where phase delays may be required.

**Support (optional):** R01 MH56874, R01 HD42125, R01 AG21826, 5 MO1 RR000334 and K23RR017636-01.

0184

EFFECTS OF BRIGHT LIGHT AND MELATONIN ON ADAPTATION TO NIGHT WORK. A RANDOMIZED PLACEBO-CONTROLLED FIELD STUDY AT AN OIL RIG IN THE NORTH SEA

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**Introduction :** Night workers complain of increased sleepiness and sleep problems. Bright light and melatonin have been suggested as countermeasures. This study evaluated the effects of bright light and melatonin on

adaptation to night work at an oil rig in the North Sea.

**Methods :** Randomized placebo-controlled crossover field study. Work schedule: two weeks on a 12-hour shift, with the first week on night shift (18:30 to 06:30), the second week on day shift (06:30 to 18:30). Seventeen workers completed the study. In a randomized order, the shift-workers received placebo pills, melatonin (3 mg) or bright light (30 minutes, individually scheduled) during the first four days on the night shift and day shift, respectively. Subjective and objective measures of sleepiness (Karolinska Sleepiness Scale (KSS) and Reaction Time test; at multiple time points) and sleep (diary and actigraphy) were recorded.

**Results :** Melatonin significantly reduced sleepiness during the day shift (KSS: 4.3 to 3.9) and increased subjective sleep length (night shift: 386 to 405 min; day shift: 340 to 355 min). During night shift, bright light significantly reduced sleep onset latency (vs placebo) (diary: 14 to 9 min) and increased sleep length to trend level (actigraphy: 403 to 419 min). On most measures, bright light gave values in between melatonin and placebo, but with few significant results. Reaction time was not affected by treatment. Hardly any side-effects were reported.

**Conclusion :** Melatonin and bright light only modestly improved sleep and sleepiness in this field study. This is in contrast to several well-controlled simulated night work studies, where both melatonin and bright light are effective in alleviating sleepiness and sleep problems. In our study, less effect may be due to competing or conflicting factors present in real life, or that the timing of the treatments was not optimal.

**Support (optional):**

0185

BRIGHT LIGHT TREATMENT, FOR NIGHT WORKERS DURING WINTER AND SPRING

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**Introduction :** This study aimed to study the influence of bright light on alertness and sleep in connection to night work and recovery days during winter and during springtime.

**Methods :** Nineteen permanent night workers worked 12-hour shifts (18-06 h) 2-3 days every week. The group worked at a postal service centre sorting packages. The mean age was 51 years (38-63 yrs) and ten were females. They were exposed to either bright light (BL, 1500lux at eye level) during breaks (20 minutes) or normal light exposure for two weeks in a crossover design. During the study period the workers wore actigraphs with light sensors and answered daily questions on sleep, sleepiness (every two hours).

**Results :** The mean level of natural light exposure (>500lux) during workdays reached 26 minutes during winter and 67 minutes during spring. The mean exposure during days of was 35 minutes (winter) and 122 minutes (spring). A 4-way repeated measures anova on sleepiness ratings (KSS) given during the work period (using the factors season, light treatment, night in sequence and time of day) demonstrated that the interaction light and night in sequence became significant ( $F=2.45$ ;  $p<0.05$ ), showing a reduction of sleepiness during the second night shift both in winter and spring during light treatment. Ratings during four recovery days showed a significant interaction light treatment\*day in sequence\*time of day with less sleepiness during the first recovery day in connection to light treatment ( $F=1.97$ ;  $p<0.05$ ). Season had no effect. Sleep actigraphy was not affected

**Conclusion :** Despite large differences in daily exposures to natural day light between the winter and spring the workers reacted rather similarly to night time light treatment in connection to night work. Light treatment reduced sleepiness at work and on the first recovery day.

**Support (optional):****0186****HOME ELECTRIC LIGHTING EFFECTS ON DIM LIGHT MELATONIN ONSET AND SLEEP PATTERNS OF ADOLESCENTS**

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**Introduction :** Artificial light has an influence upon contemporary humans, which can control their light/dark cycle since they are able to produce artificial light equivalent to daytime levels during solar darkness. The aim of this project was to study the effect of home electric lighting on the expression of the circadian rhythmicity in adolescents from a rural area of Parana State, in the South of Brazil.

**Methods :** Nineteen students, aged 11 to 16, were divided into 4 groups: 5 attending morning shift with home electric lighting (G1), 4 attending morning shift (7:30-12:00) without home electric lighting (G2), 6 attending evening shift (19:00-22:30) with home electric lighting (G3) and 4 attending evening shift without home electric lighting (G4). The adolescents completed a sleep log and wore an actimeter on their wrist during 5 consecutive days, including 3 weekdays and the weekend, to record activity levels at 1-min intervals. In the last evening of the study, saliva samples were collected every half hour, from 7pm to 10pm, to assess dim-light melatonin onset (DLMO). Samples were collected in dim light (<10lux) by chewing on polyester swab salivettes devices. Melatonin concentration in the saliva was determined using a direct radioimmunoassay. Sleep onset times and DLMO were then compared by Kruskal-Wallis ANOVA.

**Results :** G1 (Sleep onset: 21:23±0:34; DLMO: 20:07±0:15), G2 (Sleep onset: 21:24±1:24; DLMO: 20:09±0:17), G3 (Sleep onset: 22:56±1:09; DLMO: 20:43±0:15), G4 (Sleep onset: 22:24±1:09; DLMO: 20:22±0:07). G3 showed later DLMO and sleep onset times when compared to G1 and G2 (p<0,05).

**Conclusion :** Home electric lighting had no effect on DLMO and sleep onset of adolescents submitted to morning shifts. Home electric lighting associated to evening shift delayed DLMO and sleep onset. These results support the idea that circadian rhythms are influenced by artificial light in contemporary society.

**Support (optional):** CNPq, CAPES

**0187****EFFECTS OF A GREEN LIGHT MASK WORN AT NIGHT**

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**Introduction :** Bright white light has been used effectively in circadian phase shifting and in treating both seasonal and non-seasonal depression. We studied whether a green light delivered through closed eyelids at night would be well tolerated, minimally intrusive, and safe for subjects, because recent evidence suggests that green light (which may be preferred by melanopsin-producing retinal ganglion cells) just prior to waking (the- orized phase-response-curve peak) might work more efficiently than white light after awakening.

**Methods :** Thirty young men with minimal-mild depression received light via masks in the last 2.5 hours in bed. Fifteen received bright green light (500nm peak, approximately 10,000lux) and 15 received dim red light placebo. Participants kept sleep and compliance diaries, wore wrist actigraphs and completed PSQI, ESS and Horne-Ostberg scales during 2-

night baseline and 12-night treatment period. Side-effects were measured with the SAFTEE symptom inventory.

**Results :** One subject was unable to remain compliant for most of study. Neither the overall SAFTEE nor 16 subscales were different between groups by Bonferroni criteria, but 2 subscales showed nominally more symptoms in the green light group ("Eye" U=57.0, p=0.014 and "Chest" U=67.5, p=0.021). No comparisons were significant at the item level. The MANOVA for sleep diary variables was significant (T2(4,24)=2.989, p=0.039), but post-hoc tests did not distinguish differences between groups on any individual sleep diary items (TST, WASO, Latency, Efficiency). MANOVAs were not significant for PSQI, ESS, and Horne-Ostberg scales together nor for actigraphic sleep variables (TST, WASO, Latency, Efficiency, Awakenings).

**Conclusion :** Nocturnally-administered 10,000 lux, 500nm light via light masks was fairly well tolerated during the night. Light masks slightly worsened subjective sleep overall as measured by sleep diary, but did not affect actigraphic sleep.

**Support (optional):**

**0188****ARMODAFINIL IMPROVES MEMORY AND ATTENTION IN PATIENTS WITH EXCESSIVE SLEEPINESS ASSOCIATED WITH SHIFT WORK SLEEP DISORDER**

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**Introduction :** Nearly 6 million US residents work at night, and night-shift work is often associated with sleep-wake disruptions. Shift work sleep disorder (SWSD) is characterized by excessive sleepiness (ES) and insomnia and is often associated with impairments in alertness, cognition, and performance. Armodafinil, a wake-promoting agent, is the R-enantiomer of racemic modafinil and has a longer half-life than the S-enantiomer. The effects of armodafinil on memory and attention in patients with ES associated with SWSD are reported.

**Methods :** This was a 12-week, multicenter, randomized, double-blind, placebo-controlled study in permanent or rotating night-shift workers with SWSD. Patients were randomized to receive 150 mg armodafinil or placebo 30-60 minutes before each night shift. Memory and attention were assessed by the computerized Cognitive Drug Research (CDR) battery, which was administered at 2-hour intervals from 0030-0830. Composite factors evaluated from the CDR included quality of episodic secondary memory, speed of memory, power of attention, and continuity of attention.

**Results :** 216 patients were evaluable (armodafinil 150 mg, n=112; placebo, n=104). Baseline memory and attention deteriorated over the course of the night. At final visit, patients receiving armodafinil showed significantly greater improvement than those receiving placebo in mean quality of episodic secondary memory (P<.0001), power of attention (P<.01), and continuity of attention (P<.001). Numerical improvement in speed of memory was observed in the armodafinil group, but the difference vs placebo did not achieve statistical significance (P>.0928). Relative to placebo, patients receiving armodafinil showed improvement in quality of episodic secondary memory and power of attention beginning at 0030 and 0230, respectively, and the effects persisted throughout the night (to 0830). Armodafinil significantly reduced the nocturnal decline in performance.

**Conclusion :** Armodafinil significantly improved long-term memory and attention throughout the night among night-shift workers with ES associated with SWSD.

**Support (optional):** Sponsored by Cephalon, Inc.

0189

**ARMODAFINIL IMPROVES SLEEP LATENCY IN PATIENTS WITH SHIFT WORK SLEEP DISORDER**

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**Introduction :** Shift work sleep disorder (SWSD) is characterized by excessive sleepiness (ES) at night and insomnia during the day. Armodafinil, a wake-promoting agent, is the R-enantiomer of modafinil and has a longer half-life than the S-enantiomer. The effect of armodafinil on sleep latency in patients with ES associated with SWSD is reported.

**Methods :** This was a 12-week, multicenter, randomized, double-blind, placebo-controlled study in permanent or rotating night-shift workers with SWSD. Patients were randomized to receive 150 mg armodafinil or placebo 30-60 minutes before each night shift. Sleep latency during laboratory night shifts was assessed using the Multiple Sleep Latency Test (MSLT; five 20-minute tests conducted at 2400, 0200, 0400, 0600, and 0800) at baseline and weeks 4, 8, and 12. The mean sleep latency on the last 4 tests was the prespecified primary efficacy measure.

**Results :** 216 patients were evaluable (armodafinil 150 mg, n=112; placebo, n=104). Armodafinil significantly improved patients' mean sleep latency at final visit compared with placebo (mean±SD change from baseline, 3.1±4.5 minutes vs 0.4±2.9 minutes; P<.0001). At all time points, mean sleep latency was greater for patients receiving armodafinil than for patients receiving placebo. The difference between the 2 groups at final visit was 5.8 minutes at 2400 (P<.05), 4.1 minutes at 0200 (P<.001), 3.3 minutes at 0400 (P<.001), 1.8 minutes at 0600 (P<.01), and 1.5 minutes at 0800 (P=.0786). Improvement in sleep latency began at the first visit at week 4 and was maintained throughout the remainder of the study (P<.0001 vs placebo).

**Conclusion :** Armodafinil significantly maintains wakefulness throughout the night in patients with ES associated with SWSD.

**Support (optional):** Sponsored by Cephalon, Inc.

0190

**INTRINSIC SCALE-INVARIANT PATTERNS OF LOCOMOTOR ACTIVITY: INFLUENCE OF THE CIRCADIAN PACEMAKER ACROSS A WIDE RANGE OF TIME SCALES - SPANNING 4-24 HOURS**

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**Introduction :** Control of activity is influenced by many factors, both extrinsic (reaction to scheduled and unforeseen events) and intrinsic (circadian and ultradian oscillators). We recently discovered that human activity possesses additional intrinsic scale-invariant patterns at time scales from minutes to 4 h, suggesting an activity control system that orchestrates activity in a fractal pattern. We tested whether such scale-invariant patterns in activity; (i) exist across wider time scales, up to 24 h; (ii) exist in a mammalian species that is nocturnally active, i.e., Wistar rats; and (iii) are influenced by the internal circadian pacemaker (SCN).

**Methods :** Activity was recorded in healthy humans using wrist-actigraphy and in Wistar rats using infrared beam crossings within individual cages. Measurements were for 8-10 days in: (a) humans living in constant dim light (< 8 lux); (b) control rats living under constant darkness; and (c) rats with SCN lesions living under constant darkness. Detrended fluctuation analysis was used for assessment of scale-invariant activity patterns.

**Results :** A scale-invariant pattern of activity occurred in both humans and rats with identical properties across a time scale six times wider than previously detected: from minutes up to 24 h. In rats with SCN lesion, the scale-invariant pattern of activity completely broke down at time scales >4 h resulting in activity fluctuations resembling white noise without feedback control.

**Conclusion :** The SCN imparts scale-invariant patterns of activity across a wide range of time scales spanning 4 to 24 h, similarly in rats and humans. A different neuro-anatomical source must be responsible for the scale free behavior from minutes to 4 h. Our findings suggest a common mechanism of scale-free activity control for human and rats and demonstrate a role of the SCN in activity control at multiple time scales rather than solely at a period of ~24 h.

**Support (optional):** NIH RO1 HL076409; K24 HL076446 to SAS; RO1 HL071972; NCRR GCRC M01 RR02635; Pickwick Fellowship to FAJLS

0191

**CHORDC1 MRNA IS COORDINATELY REGULATED IN A DIURNAL RHYTHM IN RODENT BRAIN**

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**Introduction :** The cellular and molecular mechanisms that underlie the integration of sleep and circadian rhythms are not well understood, and the function of sleep is unknown. Sleep/wake regulation includes both circadian and homeostatic components. The suprachiasmatic nucleus (SCN) is entrained by the light/dark cycle, and establishes a circadian rhythm, while sleep/wake behavior is known to be modulated by homeostatic processes influenced by the ventrolateral preoptic area (VLPO) and lateral hypothalamus (LH). In a preliminary screen aimed at characterizing mRNAs similarly altered in a diurnal fashion within hypothalamus, we identified cysteine and histidine-rich domain (CHORD)-containing, zinc-binding protein 1 (Chordc1) to be uniformly regulated in the VLPO, SCN, and LH. The identification of molecules altered similarly in regions responsible for sleep/wake and circadian rhythms may offer insight into the function of these complex behaviors.

**Methods :** Forty-eight male C57BL/6 mice 5 weeks of age were maintained for 5 weeks on a LD12:12 cycle (Lights on ZT0). At ten weeks, animals were sacrificed in a diurnal time-course, N=3 per timepoint. Brains were dissected and sectioned for in situ hybridization, or punched for VLPO, SCN, and LH, and subjected to Northern blot analysis.

**Results :** In situ hybridization revealed diurnal expression of Chordc1 mRNA throughout the forebrain, including cerebral cortex, hippocampus, thalamus, and hypothalamus. Northern blot analysis revealed a statistically significant diurnal regulation in Chordc1 mRNA expression in the VLPO, SCN, and LH (p<0.001; one-way ANOVA). Peak expression levels of Chordc1 mRNA occurred during the dark period (wake phase).

**Conclusion :** Diurnal Chordc1 expression is similarly regulated in brain centers known to be involved in generating circadian and sleep/wake behavior. These novel findings implicate Chordc1 in coordinated molecular signaling pathways throughout the brain, and offer a candidate molecule from which to study the integration of circadian and homeostatic influences on sleep/wake regulation.

**Support (optional):**

0192

**CENTRAL OREXIN LEVELS SHOW CIRCADIAN VARIATION IN NORMAL ELDERLY AND ALZHEIMER DISEASE***Harper DG,<sup>1,2</sup> Kuo-Leblanc V,<sup>3</sup> Stopa EG<sup>3,4</sup>*

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**Introduction :** Several lines of evidence point to the importance of the orexin/hypocretin system in mediating alertness. In human narcolepsy, CSF orexin is depleted and the cell bodies of orexin secreting neurons are destroyed leading to uncontrollable sleep bouts during the day (catalepsy). Orexin/hypocretin cell bodies are localized in mammalian species in the perifornical hypothalamus and make ubiquitous projections throughout the CNS especially the locus coeruleus, raphe nuclei and to other hypothalamic nuclei. Electrical stimulation of this region in rats promotes increased locomotor activity and other behavior. These findings have focused attention on this tightly localized group of cells as major constituents of the system modulating sleep and wakefulness.

**Methods :** All brains were obtained postmortem within 2-24 hr of death. The diagnosis of Alzheimer disease was made in accordance with accepted National Institute of Aging criteria (n=36). Control brains (n=42) were obtained from patients who displayed no pathological evidence of AD or clinical history of neurological disease. All tissue was obtained from the Brain Banks at Rhode Island Hospital, McLean Hospital, UCLA Human Brain Tissue Resource Center and the Kathleen Price Bryan Brain Bank at Duke University. Autopsy samples of snap frozen supramammillary perifornical hypothalamus, sampled by a board-certified neuropathologist were used for the peptide extraction. For determination of orexin A concentration, the Phoenix Pharmaceuticals ELISA protocol was used. Absorbance O.D was read at 450 nm. Final orexin A levels were expressed as a ratio of nanograms orexin A to milligrams total protein concentration.

**Results :** Cases with confirmed Alzheimer's disease were found to have significantly lower levels of orexin than control cases ( $t_{56.9} = -2.78$ ;  $p < 0.01$ ). When orexin levels (ng/mg total protein) were distributed by time of death, cosinor analysis revealed a significant circadian rhythm in the controls ( $F_{41} = 3.71$ ;  $p = 0.03$ ) and a trend for a circadian rhythm in the AD patients ( $F_{35} = 2.49$ ;  $p < 0.1$ ).

**Conclusion :** Overall orexin levels were significantly reduced in the perifornical region of the hypothalamus in Alzheimer disease vs normal control. With time-series analysis, hypothalamic orexin, as a function of time of death, showed a circadian distribution over 24 hours in normal controls and a trend towards a circadian distribution in Alzheimer disease.

**Support (optional):** R01 AG20654

0193

**INFLUENCE OF CIRCADIAN PHASE ON SLEEP INERTIA***Rodgers JJ,<sup>1</sup> Czeisler CA,<sup>2</sup> Wright KP<sup>1</sup>*

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**Introduction :** The influence of circadian phase on sleep inertia has not been previously quantified while controlling for prior wakefulness. The present study was designed to test the hypothesis that the effect of sleep inertia on cognitive performance will be worse when subjects are awakened from sleep near the circadian minimum versus the circadian maximum of the core body temperature (CBT) rhythm.

**Methods :** Six healthy, drug free females and males aged  $31.8 \pm 6.2$

(Mean $\pm$ SD) participated. After three weeks of maintaining a consistent sleep-wake schedule at home participants completed a 55-day long inpatient protocol including a 28 h day (scheduled 18.66 h wakefulness and 9.33 h sleep) forced desynchrony protocol for 12 consecutive days. A computerized mathematical addition task was administered ~1, 21, 41, and 61 min after scheduled awakening. For each participant, core body temperature (CBT), recorded every minute, was averaged into 15° (1 h) bins with the CBT minimum assigned to 0°( $\pm 15^\circ$ ) and the CBT maximum assigned to 180°( $\pm 15^\circ$ ) degrees. If more than one test battery was available within a circadian bin for a participant, the average of those performance scores was used.

**Results :** Sleep stage upon awakening was stage 2 for fourteen awakenings, stage REM for three awakenings and stage 1 for one awakening. The amount of wakefulness in the 10 min prior to scheduled waketime was on average  $0.2 \pm 0.3$  min. Repeated measures ANOVA with Huynh-Feldt correction for sphericity and modified Bonferroni correction for planned comparisons demonstrated that performance on the addition task was significantly worse immediately upon awakening near the CBT minimum than near the CBT maximum ( $P < 0.015$ ). No other test sessions were significantly different between circadian conditions ( $P > 0.015$ ).

**Conclusion :** Circadian phase influenced performance immediately upon awakening from sleep such that performance was worse when subjects were awakened during the biological night near the CBT minimum as compared to being awakened during the biological day near the CBT maximum.

**Support (optional):** Research Supported in part by NASA Cooperative Agreement NCC 9-58 with the National Space Biomedical Research Institute and by the Undergraduate Research Opportunities Program in collaboration with the Biological Sciences Initiative at the University of Colorado—Boulder.

0194

**CIRCADIAN VARIATIONS IN SLEEP AND WAKEFULNESS IN DEVELOPING RATS***Ray B, Gall AJ, Blumberg MS*

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**Introduction :** There are conflicting reports regarding the existence of circadian rhythms in infant rats. Diurnal organization in sleep-wake patterns is reported to be established by postnatal day 20 (P20) based on the presence of EEG slow wave activity, whereas there are studies indicating the presence of circadian variations in metabolic rate, body temperature, and SCN activity as early as P2. Although the neocortical EEG is not a useful indicator of sleep-wake activity during the first 10 postnatal days in rats, changes in nuchal muscle tone can be used reliably to define sleep and wakefulness. Therefore, we assessed the circadian variation of sleep-wake states in infant rats using nuchal EMG.

**Methods :** EMG electrodes were implanted in the nuchal muscle of P2 and P8 rats under isoflurane anesthesia. After surgery, pups were placed inside a humidified testing chamber maintained at thermoneutrality (35°C). At each age, sleep-wake activity of 3 littermates was recorded for 2 hours during the day (1200 - 1400 h), for 2 hours during the night (2400 - 0200 h), and for 2 hours the next day (1200 - 1400 h). During each test, oxygen consumption was continuously monitored; all values are presented as ml O<sub>2</sub>/kg/min.

**Results :** We found a significant decrease in mean sleep and wake bout durations at night, compared to the day, in P2 rats (mean atonia duration:  $20.1 \pm 1.4$  s during day and  $13.7 \pm 0.8$  s at night; mean tone duration:  $10.8 \pm 0.7$  s during the day and  $6.6 \pm 1.4$  s at night). The trend was similar at P8 (mean atonia duration:  $46.4 \pm 4.3$  s during the day and  $32.0 \pm 5.8$  s at night; mean tone duration:  $16.1 \pm 1.7$  s during the day and  $11.2 \pm 0.2$  s at night). Consistent with previous findings, metabolic rate was higher at

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night than during the day at P2 ( $35.9 \pm 1.4$  vs.  $32.5 \pm 0.8$ ) and also at P8 ( $35.1 \pm 1.7$  vs.  $32.4 \pm 0.7$ ).

**Conclusion :** These preliminary results suggest an unexpected circadian variation in the expression of sleep and wakefulness during the first post-natal week. Older subjects are now being tested and we are also beginning to examine the neural mechanisms that mediate these circadian phenomena in early infancy.

**Support (optional):** Supported by National Institute of Mental Health grants MH50701 and MH66424.

### 0195

#### LIGHT BEHAVIOR OF SHIFT WORKERS IN CONNECTION TO DAY SLEEP

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**Introduction :** Light behaviour in connection to night work might have an influence on the adaptation to work as well as for recovery sleep.

**Methods :** Twenty-two permanent night workers were included in a study and they worked 12-hour shifts (18-06 h) 2-3 days every week. They worked at a postal service centre sorting packages. The mean age was 51 years (38-63 yrs) and half of them were females. They were questioned about sleep disturbances, light behaviour and were also followed with diaries, actigraphs with light sensors (n=19), through four weeks in both winter and spring.

**Results :** The questionnaire indicated that 23% of the workers claimed to have an almost dark sleep environment, 36% had a semi-dark surrounding and 40% had enough light to read or full day light during day sleep. Two groups were formed according to the exposure level in connection with sleep. Those stating more disturbed sleep took greater care in blocking out-door light during day sleep (t-test,  $p=0.010$ ) and those that claimed they slept less heavily (t-test,  $p=0.026$ ). It was reported that 58% (range 15-98%) of the outdoor light could be blocked out by shades. Those with less blocking never or seldom woke up repeatedly and had less difficulty to fall asleep again ( $p=0.033$ ). The amount of natural daylight received at daytime during the study weeks in January was in the diary reported to be 65 ( $\pm 19$ ) minutes in connection to night work, mainly obtained after the day sleep period. On free days the level reached 98 ( $\pm 20$ ) minutes (ANOVA,  $F=2.7$ ;  $p=0.017$ ).

**Conclusion :** Workers with day sleep problems make more an effort blocking out light than others.

**Support (optional):**

### 0196

#### THE CIRCADIAN RHYTHM OF ALERTNESS IN DELAYED SLEEP PHASE DISORDER

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**Introduction :** Several possible causes of Delayed Sleep Phase Disorder (DSP) have been suggested; for example an unusually long circadian period or an altered homeostatic drive for sleep. In addition, patients with DSP report increased levels of alertness in the evening making it difficult to fall asleep earlier. The aim of the current study was to determine if there are changes in the timing of objective and subjective alertness over 28 hours of wakefulness between patients with DSP and controls.

**Methods :** 9 DSP (mean age 36.5 yrs), and 5 age and gender matched controls (mean age 38.8 yrs) completed a 4 day inpatient study. DSP patients were screened using questionnaires and actigraphy and diagnosed according to ICSD criteria. Subjects kept a normal habitual sleep-

wake schedule for 3-5 weeks prior to entering the laboratory. In the laboratory subjects kept this habitual schedule and testing was relative to wake-time (Circadian Time (CT) 0). Testing began at CT2 on day 3 and continued at 2 hourly intervals during 28 hours of sustained wakefulness (13 sessions). Testing included a Multiple Sleep Latency Test (MSLT), and Visual Analogue Scales (VAS).

**Results :** When compared relative to circadian time during the 28 hours of wakefulness there was a significant time effect ( $p<0.0001$ ) but no group or interaction effect for both the MSLT and subjective alertness. As expected alertness levels decreased the longer the subjects were awake.

**Conclusion :** When compared at the same circadian time there is no significant difference in objective (MSLT) or subjective (VAS) alertness for patients with DSP compared to controls. These results suggest that there is not an alteration in the homeostatic drive for sleep in DSP. However, if these results were presented on clock time alertness levels would be greater in the evening in the DSP compared to controls, supporting the reported increased evening alertness in DSP.

**Support (optional):** 1R01 HL069988-01A1 and M01 RR-00048

### 0197

#### INTERNAL CONSISTENCY AND CONSTRUCT VALIDITY OF TWO MORNINGNESS/EVENINGNESS QUESTIONNAIRES IN CHILDREN

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**Introduction :** We assessed internal consistency, construct validity, and predictive validity of two morningness/eveningness (M/E) questionnaires in 5th and 6th grade students.

**Methods :** In a classroom setting, students (n=441; 240 boys, 201 girls) ages 10-14 years completed two M/E scales, one created for adults (AS; Smith et al., J. Applied Psychology, 1989) and one for children (CS; Carskadon et al., Sleep, 1993). Students also responded to questions about "usual" sleep schedules on school days and weekends. We assessed reliability with Cronbach's coefficient alpha. We assessed construct validity with Pearson's correlations for composite M/E scores versus weekend midsleep time (rise time - bedtime; c.f., Ronneberg et al., J. Biol. Rhythms, 2003). Morning- and evening-type categories were defined as 2 SDs or more beyond the scale mean. We evaluated predictive validity by comparing weekend midsleep times between extreme groups.

**Results :** Reliability was adequate for both scales (Cronbach's alpha: AS=.77; CS=.76). Two items on the AS, both related to bedtime, showed low homogeneity with remaining scale items (corrected item-total correlation  $<.20$ ). All CS items showed adequate homogeneity ( $>.20$ ). AS and CS scores were positively correlated ( $r=.84$ ,  $p<.001$ ). AS and CS scores were significantly ( $p<.001$ ) correlated with weekend midsleep times ( $r=-.40$  and  $r=-.37$ , respectively). AS evening-types (scores  $< 23$ ; n=12, 4 boys) reported significantly later weekend midsleep times (M=5:37am, SD=79 mins) compared to AS morning-types (scores  $> 49$ ; n=15, 6 boys; M=2:38am, SD=72 mins). CS evening-types (scores  $< 18$ ; n=12, 3 boys) also reported significantly later midsleep times (M=5:45am, SD=79 mins) compared to CS morning-types (scores  $> 40$ ; n=13, 5 boys; M=3:01am, SD=83 mins).

**Conclusion :** Internal consistency is adequate for both scales. Both scales also show modest construct validity. Extreme group comparisons show good predictive validity based on midsleep times. We will further evaluate construct validity using physiological measures, such as DLMO phase.

**Support (optional):** NR08381



0198

**SLEEP AND CIRCADIAN RHYTHM EFFECTS OF STIMULANTS AND DEPRESSANTS AMONG MEN AND WOMEN WITH HIV INFECTION**Gay CL,<sup>1</sup> Davis H,<sup>2</sup> Nelson K,<sup>1</sup> Bruce S,<sup>1</sup> Aouizerat BE,<sup>3</sup> Lee KA<sup>1</sup>

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**Introduction :** Research suggests a relationship between poor circadian rhythms and use of stimulants and depressants. Stimulants may be effective in phase delaying sleep onset, and depressants may induce sleep, but poor sleep is a likely outcome. The purpose of this study is to describe use of stimulants and/or depressants in relation to sleep and circadian rhythms.

**Methods :** As part of a study of sleep in HIV-infected adults, 72 hrs of wrist actigraphy was used to estimate rhythm strength (24-hr autocorrelation), acrophase, total sleep time (TST), and wake after sleep onset (WASO). Participants also completed the Morningness-Eveningness Scale to estimate circadian preference. Urine screens were used to detect prescribed and non-prescribed stimulants and depressants. Chi-square and analysis of variance with Scheffe post-hoc tests were used to identify group differences.

**Results :** Among the 120 HIV-infected adults (70 men, 42 women, 8 transgender) with complete questionnaire and drug screen data, 52 tested negative for stimulants and depressants (non-users), 46 tested positive for depressants, 12 tested positive for stimulants, and 10 tested positive for both. Given the small sample sizes, the latter two groups were combined for analysis. Those using stimulants were more likely to identify as “evening types” and those using depressants were more likely to identify as “morning types” ( $\chi^2=11.2$ ,  $p=.004$ ). Among the 88 with actigraphy data analyzed to date, those using stimulants had weaker rhythms ( $.26 \pm .12$  vs  $.38 \pm .15$ ) than non-users (Scheffe  $p=.015$ ) and later acrophases ( $15:32 \pm 1:59$  vs  $14:14 \pm 1:24$ ) than those using depressants (Scheffe  $p=2.19$ ,  $p=.031$ ). Stimulant and depressant use was unrelated to TST and WASO.

**Conclusion :** These findings suggest no apparent detrimental effect on sleep as a result of drug use in this patient population. They may be self-medicating to keep their circadian rhythm synchronized to a 24-hr day. Further analysis is in progress to examine effects on their daytime functioning.

**Support (optional):** NIH Grant# R01 MH074358, KA Lee, P.I.

0199

**CIRCADIAN EFFECT ON DEGREE OF SLEEP INERTIA PRESENT AFTER AWAKENING**

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**Introduction :** Sleep inertia is the sleepiness or impaired cognitive performance immediately upon awakening, which dissipates asymptotically over a number of hours. We tested whether there exists a circadian rhythm in the degree of sleep inertia by measuring changes in cognitive performance and subjective sleepiness following awakenings at varied circadian phases.

**Methods :** Seven subjects were studied throughout a 10-day protocol performed in dim light, during which subjects slept across all circadian phases, achieved by scheduling a recurring artificial day length of 28 h. Subjects were awoken using a standardized auditory stimulus three times

each sleep period and immediately performed a computerized 2-minute task consisting of rapid serial additions of paired 2-digit numbers. Subjective sleepiness was also reported (Karolinska Sleepiness Scale). Sleep inertia was quantified as the change in number of additions attempted (cognitive performance) and subjective sleepiness when tests were repeated after ~20 min. Data were analyzed only following awakenings from Stage II sleep. Core body temperature was used as a marker of circadian phase, with data binned into 60° circadian bins, normalized to account for differences between subjects (Z-score), and Cosinor analysis was used to assess circadian rhythmicity.

**Results :** Immediately upon awakening, subjects attempted an average of 22 additions, which improved to 26 after 20 minutes. There was a significant circadian rhythm in sleep inertia of cognitive performance ( $P<0.001$ ), with peak improvement during the biological night (circadian phase bin 300°), no improvement during the biological day (180°), and a peak to trough amplitude of ~20% (4 more additions attempted). Analyzing correct additions gave similar results. Average subjective sleepiness was high immediately upon awakening (7.5 on scale of 1-9) and fell by only 1 unit after 20 minutes. There was no significant circadian rhythm in sleep inertia of sleepiness.

**Conclusion :** There is a clear circadian rhythm in the degree of sleep inertia of cognitive performance but no circadian rhythm in the sleep inertia of subjective sleepiness. These findings may have important implications for professions requiring decision making immediately upon awakening, e.g., on-call medical professionals.

**Support (optional):** NIH HL64815; NCRG GCRC M01 RR02635; Pickwick Fellowship in support of FAJLS

0200

**AGE-RELATED DIFFERENCES IN THE EFFECTS OF MELATONIN IN RHESUS MONKEYS**

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**Introduction :** Melatonin treatment has been shown to acutely promote sleep in humans and diurnal macaques. The objective of this study was to evaluate the potential age-related differences in the effects of melatonin on sleep and circadian phase shift in non-human primates, rhesus monkeys (*Macaca mulatta*).

**Methods :** Ten male rhesus monkeys, 6 aged (21-25 years of age) and 4 young (5-7 years of age), were maintained individually, in a 12:12 light:dark cycle. Following baseline evaluation, animals received four oral doses of melatonin (5-20 ug/kg) or placebo, five days each dose, one or two hours before lights off time (ZT10 or 11). Their actigraphically recorded sleep was continuously documented and, in four animals, sleep was assessed using continuous telemetric polysomnography. Melatonin measurements were conducted at daytime and at night, 1 hour or 7 hours after melatonin or placebo treatment.

**Results :** The data collected indicate that melatonin treatment, administered at ZT10 or ZT11 and resulting in physiological or low pharmacological circulating melatonin levels, can produce both homeostatic and circadian effects on sleep in rhesus monkeys maintained in 12:12 hour light-dark cycle. Young rhesus monkeys are equally sensitive to both homeostatic and circadian effects of melatonin. Aged monkeys are significantly more sensitive to homeostatic than circadian effect of melatonin on sleep.

**Conclusion :** Circadian responses to melatonin decline with age in rhesus monkeys, while homeostatic effects appear to be better conserved. Future studies need to address the mechanisms of these differences in responses to the pineal hormone.

**Support (optional):** This work is supported by NIA Grant AG017636.

### 0201

#### CIRCADIAN RHYTHMS IN MICE WITH GENETIC ABLATION OF THE OREXIN NEURONS

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**Introduction :** The suprachiasmatic nucleus (SCN) controls the circadian timing of sleep-wake behavior, but the relevant neural pathways are not fully understood. Circadian signals probably pass from the SCN to the subparaventricular zone, through the dorsomedial nucleus, and then into the lateral hypothalamus, particularly to the region that contains the orexin neurons. Mice lacking the orexin peptides have normal circadian rhythms of sleep and wakefulness in constant darkness, but the orexin neurons produce other signaling molecules such as dynorphin and NARP. Possibly, these cells still relay circadian timing signals even in the absence of orexin. To study the role of orexin-containing neurons in the circuits that time vigilance states, we analyzed the free-running sleep-wake behavior of orexin neuron-deficient mice.

**Methods :** Male, orexin/ataxin-3 transgenic mice and wild type (WT) littermates (15 weeks old, n=7-8 in each group) were equipped with EEG/EMG electrodes and telemetry transmitters. Sleep-wake behavior, body temperature, and locomotor activity were recorded for 48 hours on a 12:12 light-dark schedule (LD), and then after 5 days of constant darkness.

**Results :** Under LD conditions, the total amounts of wake, NREM, and REM sleep did not differ between orexin/ataxin-3 mice and WT littermates, but orexin/ataxin-3 mice had much shorter sleep and wake bouts. Preliminary analysis suggests that orexin/ataxin-3 mice have lower amplitude sleep-wake rhythms when housed in constant darkness. Immunostaining confirmed a >95% loss of the orexin neurons in orexin/ataxin-3 mice.

**Conclusion :** Loss of orexin peptides fragments sleep and wakefulness, and ablation of the orexin neurons appears to reduce the circadian rhythms of wakefulness and sleep. The orexin neurons may be a critical relay in circadian outflow pathways, and disruption of these timing signals may contribute to the fragmented sleep and daytime sleepiness of narcolepsy.

**Support (optional):** Supported by NIH grants MH62589 and HL60292.

### 0202

#### AN ENDOGENOUS CIRCADIAN RHYTHM IN AN INDEX OF CARDIAC VULNERABILITY CONFIRMED WITH A CONSTANT ROUTINE PROTOCOL

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**Introduction :** There is a peak in adverse cardiac events around 10AM. In humans there is a fractal structure in heartbeat fluctuations that changes with cardiovascular pathology. Using a forced desynchrony protocol we recently found that the circadian pacemaker affects the fractal structure of cardiac control. Specifically, the scaling exponent characterizing fractal structures of heartbeat fluctuations increased - bringing it closer to that observed in cardiovascular disease - at the circadian phase corresponding to ~10AM (Hu et al, PNAS, 2004,101:18223-7). Here we test the robustness of this circadian rhythm in heartbeat fluctuations using a different circadian protocol.

**Methods :** 9 healthy adult subjects were studied throughout a 'constant

routine' protocol (38 h wakefulness, with constant posture, room temperature and dim light, and identical snacks every 2 h). Detrended fluctuation analysis of ECG R-R interval data was used for assessment of fractal structures of heartbeat fluctuations in 1 h bins. The resultant scaling exponent data were aligned according to circadian phase (from core body temperature), normalized to account for differences between subjects (z-score), and circadian rhythmicity was assessed (Cosinor analysis).

**Results :** The scaling exponent characterizing fractal structures of heartbeat fluctuations exhibited a significant circadian rhythm in 8/9 subjects, with peak to trough amplitude between 10-20% of the mean. In the group average, the greatest increase in scaling exponent occurred across the circadian phase corresponding to 7-11AM, peaking soon after this circadian time. There was no significant influence of acute sleep deprivation on the group average scaling exponent.

**Conclusion :** These results confirm the significant endogenous circadian rhythm in heartbeat dynamics independent from scheduled behaviors, with a similar phase and amplitude as we previously found in a forced desynchrony study. The scaling exponent increased around the circadian phase coinciding with the period of highest cardiac vulnerability determined from epidemiological studies. We speculate that endogenous circadian-mediated influences on cardiac control may be involved in the day-night pattern of adverse cardiac events in vulnerable individuals.

**Support (optional):** NIH RO1 HL076409; K24 HL076446; RO1 HL071972; NCCR GCRC M01 RR02635

### 0203

#### PHASE PREFERENCE, SLEEP TENDENCY, AND SLEEP RESTRICTION

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**Introduction :** Sleep timing can be influenced by alignment of sleep/wake to circadian rhythms; phase preference can mark differences in alignment. We tested whether sleep restriction may expose different times of the day to increased sleep tendency as a function of phase preference.

**Methods :** Participants were extreme morning type (MT, upper 2 sd) or evening type (ET, lower 2 sd) (Smith et al., 1989). Eight MT (5 girls) and 5 ET (4 girls), ages 10.7 to 17.3 (mean=12.9, sd=1.6) yr kept stabilized sleep schedules of about 10 hr for 2 wk. Multiple sleep latency tests (MSLTs) at 2-hr intervals were given on the day after stabilization (BL), acute sleep restriction (A-SR=single night with 70 percent stabilized sleep), and prolonged sleep restriction (P-SR=7 nights with 70 percent stabilized sleep).

**Results :** Average daily MSLT scores were lower on consecutive conditions. MSLTs at BL showed a group difference at test three (1100/1300): MT mean=14.7 (sd=4.5); ET mean = 7.8 (sd = 6.9). After A-SR, groups differed at test one (0700/0900): MT mean=12.8 (sd=7.7); ET mean=3.3 (sd=2.6.) After P-SR, MT and ET differed at test seven (1900/2100): MT mean=2.9 (sd=2.3); ET mean=7.1 (sd=4.6).

**Conclusion :** These data support predictions that phase preference can help identify vulnerable times of day for adolescents with insufficient sleep. Thus, if ET wake up earlier relative to the circadian sleep tendency maximum than do MT, sleep restriction should affect sleep tendency differently depending on time of day. Increased midday sleepiness on BL in ET is explained because homeostatic sleep pressure increases earlier than clock-dependent alerting occurs. After A-SR, ET are vulnerable in the morning, since sleep loss is undefended at the time of maximal sleep tendency when they awake. Both groups are vulnerable after P-SR, and MT are more vulnerable in the evening, because they have no evening clock-

dependent alerting.

**Support (optional):** NR08381

## 0204

### IN VIVO DIURNAL RHYTHM OF DOPAMINE MEASURED IN THE PUTAMEN OF NON-HUMAN PRIMATES

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**Introduction :** Traditionally the nigrostriatal pathway is credited with modulating voluntary movement and its degeneration (as in Parkinson's disease (PD)) results in impairment of planning, initiation, and execution of movement. In addition, a proportion of PD patients exhibit pathological daytime sleepiness. The collaterals of the nigrostriatal pathway provide dopaminergic innervation to the thalamus, in particular the reticular thalamus and non-specific midline nuclei, suggesting a possible role for midbrain dopamine in regulating arousal. This study seeks to extend support for this role by establishing an in vivo measure of dopamine levels in primates across the 24 hour cycle with simultaneous measures of arousal.

**Methods :** Dialysate samples were collected within the putamen of chair restrained female rhesus monkeys (n=2; 6-8kg) every 10 minutes for 8 hours. Nine 8 hour perfusion periods were staggered around the clock yielding 3 measurements every 10 minutes of the 24hr cycle (12:12 light:dark) in each of the 2 animals. Dialysate samples were analyzed offline via HPLC for the concentration of DA, DOPAC, 5-HIAA, HVA, 3-MT, and 5-HT. Simultaneous polysomnography measurements (EEG, EMG, and EOG) were monitored to assess arousal state.

**Results :** Dopamine levels peaked 6am-8am, preceding and continuing past lights-on at 7am. Levels declined throughout the afternoon reaching nadir at 3pm-7pm. Significant correlations ( $p < 0.0001$ ) exist between time and DA, DOPAC, HVA, or 5-HT, all of which peak between 6am-11am with nadirs ranging 2pm-10pm. No significant correlations were found between dialysate measures and specific arousal states (wake, NREM, REM, or sleep).

**Conclusion :** In vivo fluctuations of extracellular dopamine concentration, within the putamen of non-human primates, are evident across the 24 hour cycle regardless of specific sleep state. Differences in the amplitude and in the phase of the diurnal rhythm may reflect the individual differences in daytime alertness between the animals.

**Support (optional):** USPHS-NS43374 (DBR) and MH064312 (AF)

## 0205

### USING BAYESIAN NETWORKS TO UNDERSTAND INDIVIDUAL DIFFERENCES THAT AFFECT THE USE OF ACTIGRAPHY AS A PREDICTOR OF SLEEP

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**Introduction :** We propose that developing new activity-to-sleep-wake state algorithms begins with quantifying and characterizing the interaction between activity and other measures that are correlated with PSG defined sleep. We present results from the use of Bayesian networks to characterize the relationships among individual differences in activity, wrist determined light exposure, and polysomnographically-defined

(PSG) sleep-wake.

**Methods :** Corresponding activity and light intensity data (Actiwatch-L, Mini Mitter, Portland, Oregon) and sleep-wake data (Vitaport-2/3, TEMEC Instruments) from nine subjects participating in a previously reported inpatient protocol of the effect of exercise on re-entrainment to a shift in scheduled sleep-wake were used. PSG was recorded during the two 48-hr constant routines (enforced semi-recumbent wake in dim like conditions) and scheduled twelve 8-hr sleep episodes. Activity and light levels were continuously recorded. We evaluated the interaction among variables by fitting all 24 Bayesian network models for three variables to each individual data series. To compare models of different complexity, we used both classification accuracy and the Bayesian Information Criterion.

**Results :** The classification accuracy for the best predictive model for all data for each individual averaged 65.7% (51.6%-87.0%). When only the scheduled sleep data were used, the classification accuracy for the best predictive model for each individual averaged 66.8% (55.0%-86.0%). An analysis of the frequency distributions showed that the large sources of predictive error were: discerning between quiet wakefulness and sleep as well as overlapping activity frequency distributions during sleep and wake.

**Conclusion :** Our analyses suggest that there are individual differences in optimal predictive model and that the variable interaction among activity, light and PSG is inherent within the data. These results suggest that the individual activity frequency distribution should be included in algorithms for converting among activity, light and sleep-wake state. In future work, we will include prior information to improve classification accuracy.

**Support (optional):** Supported by US AFOSR F49620-95-1-0388; NASA-NSBRI cooperative agreements NCC9-58 and NCC2-1 and NIH R01NS36590. EBK supported by NIH K02-HD045459

0206

**RESTLESS LEGS SYNDROME: PREVALENCE AND IMPACT IN CHILDREN AND ADOLESCENTS- THE PEDS REST STUDY**

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**Introduction :** Restless legs syndrome (RLS), a common neurological sleep disorder, occurs in 5% to 10% of adults in the United States and Western Europe. Although about 35% of adults with RLS report onset of RLS symptoms prior to age 20, there is very little literature looking directly at the prevalence of RLS in children and adolescents. In this first pediatric population-based study, we examined the prevalence and impact of RLS in two age groups: 8-11 and 12-17 years old.

**Methods :** Initially blinded to survey topic, families were recruited from a large, volunteer research panel in the UK and US. Administration was via the internet and raw data was weighted by income, region, age, and gender to ensure generalizability. NIH pediatric RLS diagnostic criteria (2003) were used and questions were specifically constructed to exclude positional discomfort, leg cramps, arthralgias, and sore muscles being counted as RLS.

**Results :** Data were collected from 10,523 families. Criteria for definite RLS was met by 1.9% of 8-11 year olds and 2.0% of 12-17 year olds. Moderately or severely distressing RLS symptoms were reported to occur two or more times a week in 0.5% and 1.0% respectively. Convincing descriptions of RLS symptoms were provided. No gender differences were found. Sleep disturbance was significantly more common in those with RLS than in controls ( $p<0.001$ ), as was a history of 'growing pains' ( $p<0.001$ ). Various consequences were attributed to RLS, including 49.5% endorsing a "negative effect on mood". In the US, reported medical diagnoses of ADHD (27%), anxiety disorder (11%), and depression (12%) were higher in those with RLS than expected in the general population. Overall, only 11% of those meeting RLS criteria reported a medical diagnosis of RLS.

**Conclusion :** These population-based data suggest that RLS is prevalent and troublesome in children and teens, occurring more commonly than epilepsy or diabetes.

**Support (optional):** Research supported by GlaxoSmithKline R&D

0207

**PERSONALITY AND NEUROPSYCHOLOGICAL CHARACTERISTICS IDENTIFYING CHILDREN WITH OSA IN A PEDIATRIC AD/HD POPULATION**

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**Introduction :** Individuals with pediatric attention deficit/hyperactivity disorder (AD/HD) have been noted to have high frequencies of obstructive sleep apnea (OSA) in previous studies. This study is designed to identify personality and neuropsychological characteristics that differentiate AD/HD patients with OSA from those without OSA.

**Methods :** This study is a retrospective review of a clinical outpatient

pediatric psychiatry clinic population with an AD/HD diagnosis (N=84, Age: mean 11.8, range 6-17). The AD/HD diagnosis for these patients is based on evaluation by a Board Certified Pediatric Psychiatrist and at least one positive psychological test [Coolidge Personality and Neuropsychological Profile for Children (CPNI)]. The obstructive apnea-hypopnea index (oahi) used in this study is derived from full night nocturnal polysomnography (psg). The total group is divided into groups for comparison with oahi < 2.5 (N=29), 2.5-5 (N=26), and > 5.0 (N=33). Responses to CPNI (198 total questions) were analyzed for significant variance between these groups.

**Results :** 1) Personality variables found to be significantly more common in children with oahi > 5.0 included: a) my child has no close friends ( $p<0.01$ ); b) my child shows very little emotion ( $p<0.01$ ); c) my child neither desires nor enjoys close relationships ( $p<0.02$ ); d) my child has trouble waiting his turn ( $p<0.02$ ); and e) my child almost always chooses to do things by himself ( $p<0.05$ ). 2) Neuropsychological variables found to be significantly higher in children with oahi > 5.0 included: a) my child has poor coordination ( $p<0.01$ ); b) my child was potty trained later than usual ( $p<0.01$ ); c) my child learned to walk later than other children ( $p<0.01$ ) and d) my child learned to talk later than other children.

**Conclusion :** AD/HD children with OSA based on full night PSG evaluation (oahi > 5.0) are reported by their parents to have a higher degree of social isolation than those children without OSA (oahi < 2.5). Neuropsychological responses suggest delayed development of coordination, walking, talking and continence in children with OSA. This finding may be secondary to effects of OSA on development, and may be useful in identifying the sub-group of AD/HD children most likely to have OSA.

**Support (optional):**

0208

**ASYMMETRIC DIMETHYLARGININE (ADMA) PLASMA LEVELS IN PEDIATRIC OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS)**

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**Introduction :** OSAS is associated with severity-dependent cardiovascular consequences manifesting as altered autonomic nervous system and baroreflex functions, left ventricular hypertrophy, and hypertension. The synthesis of nitric oxide is inhibited by endogenous arginine analogues such as asymmetric dimethylarginine (ADMA), and plasma elevations in ADMA levels have been implicated in mechanisms underlying vascular pathophysiology.

**Methods :** Consecutive children with polysomnographically-demonstrated OSAS, and age-, gender-, and BMI-matched non-snoring controls with a normal overnight sleep study underwent a blood draw in the morning after their PSG. ADMA levels in plasma samples were assayed using a high sensitivity ELISA assay.

**Results :** Twenty children with OSAS (mean age  $6.7\pm 1.9$  years; 60% males; BMI:  $20.7\pm 2.4$  kg/m<sup>2</sup>) with a mean AHI of  $14.7\pm 3.6$ /hrTST and nadir SaO<sub>2</sub> of  $82.7\pm 3.1\%$ , and 20 matched control children (AHI<1.0/hrTST and nadir SaO<sub>2</sub>>94%) were included. Mean plasma ADMA levels in OSAS were  $0.96 \pm 0.03$   $\mu$ mole/L and  $1.02\pm 0.03$   $\mu$ mole/L in controls (p-not significant).

**Conclusion :** OSAS in children does not appear to modify the endogenous formation of ADMA, nor does it seem to alter the activity of dimethylarginine dimethylaminohydrolase, the enzyme that selectively degrades ADMA in the circulation. Endogenous arginine analogues do not seem to play a role in the cardiovascular morbidity associated with OSAS in children.

**Support (optional):** Study funded by NIH grant HL-65270.

## 0209

**SLEEP SPINDLE DEVELOPMENT AS A MARKER OF BRAIN MATURATION: EFFECTIVE INDICATOR OF PERFORMANCE ON PREFERENCE FOR NOVELTY TASK?**Daley K,<sup>1,2</sup> Gaultney J,<sup>1</sup> Gingras J<sup>3,1</sup>

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**Introduction :** Sleep spindles reach a stabilization point at 23 weeks of age, at which point they are representative of adult sleep spindles in length, frequency, and synchrony. It is possible that this developmental process may be utilized as a marker of brain development, is influenced by teratogen exposure. Additionally, the Fagan Test of Infant Intelligence (FTII) provides an estimate of infant information processing ability, which may additionally be impacted by brain maturity.

**Methods :** Nocturnal polysomnography data from infants at six months of age was observed for the development of sleep spindles. Sleep spindle synchronicity on the six month nocturnal polysomnogram (NPSG) was compared to intellectual functioning, as measured by performance on the FTII.

**Results :** Sleep spindle development was operationalized as both sleep spindle density in NREM sleep and density of synchronous sleep spindles (SSS) as compared to asynchronous spindles (ASS) as a RATIO score. Sleep spindle indices were created for all sleep stages and total sleep and then correlated with teratogen exposure, as measured by mean quantity of exposure to nicotine, alcohol, and cocaine by trimesters and total exposure, performance on the FTII, and demographic information.

**Conclusion :** The RATIO score was significantly negatively correlated with second and third trimester exposure to alcohol and the overall exposure rates for alcohol and total teratogens. Maternal depression, one of the demographic variables assessed during pregnancy and postnatal, was also significantly correlated with sleep spindle densities, and found to be potentially related to higher sleep fragmentation. The removal of the influence of maternal depression increased the relationship between FTII scores and sleep spindle indices within the teratogen exposure groups, and the presence of sleep spindles in slow wave sleep were significantly linked with preference for novelty scores on the FTII.

**Support (optional):**

## 0210

**C REACTIVE PROTEIN (CRP) SERUM LEVELS IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA SYNDROME (OSAS): EFFECT OF ADENOTONSILLECTOMY**

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**Introduction :** OSAS in children is associated with significant elevations in serum CRP levels that exhibit severity-dependent changes. However, it remains unclear whether OSA is mechanistically involved in such elevations of CRP.

**Methods :** Consecutive children with polysomnographically-demonstrated OSAS underwent a blood draw in the morning after their sleep studies on two occasions, namely at diagnosis of OSAS and 10-14 weeks after adenotonsillectomy. High sensitivity CRP serum concentrations were determined within 2-3 hours after collection, using a particle enhanced turbidimetric immunoassay technique.

**Results :** Twenty children with OSAS (mean age 7.3±1.9 years; 55% males; BMI: 20.1±1.9 kg/m<sup>2</sup>) with a mean obstructive apnea/hypopnea index (AHI) at diagnosis of 15.6±2.9/hr TST and nadir SaO<sub>2</sub> of 82.3±2.5% were included. Mean initial CRP levels at OSAS diagnosis

were 0.67 ± 0.21 mg/dl and decreased to 0.23 ± 0.07 mg/dl after adenotonsillectomy (P < 0.05), along with significant decreases in AHI (2.2±0.8/hrTST; p<0.01) and improved oxygenation (mean nadir SaO<sub>2</sub> (88.6±1.9%; p<0.01).

**Conclusion :** OSAS elicits increases in serum CRP levels that are reversible upon treatment. Therefore, OSAS induces a systemic inflammatory response in children, which if left untreated, may potentially lead to cardiovascular morbidity.

**Support (optional):** Study funded by NIH grant HL-65270

## 0211

**REGIONAL ADIPOSITY AND OBSTRUCTIVE SLEEP APNEA IN OBESE ADOLESCENTS**Kalra M,<sup>1</sup> Donnelly L,<sup>4</sup> Fitz K,<sup>1</sup> Daniels S,<sup>2</sup> Inge T,<sup>3</sup> Garcia V,<sup>3</sup> Dardzinski B,<sup>4</sup> O'Brien K,<sup>4</sup> Rajagopal A,<sup>4</sup> Amin R<sup>1</sup>

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**Introduction :** The prevalence of adolescent obesity, a high risk group for obstructive sleep apnea (OSA), has dramatically escalated. Despite the magnitude of this problem, studies have not addressed the pathogenesis of OSA in obese adolescents. The goal of this study is to determine the association between regional adipose tissue deposits and OSA in obese adolescents.

**Methods :** Obese subjects, 13 to 19 yrs of age, referred to the sleep apnea clinic at Cincinnati Children's were recruited for this study. Subjects with craniofacial abnormalities or with body mass index (BMI)>50 were excluded. Overnight polysomnograms to determine OSA status and MRI scans to measure regional adipose tissue were performed. The MRI scan sequence was axial T1 with scan parameters of TR/TE of 500/14 and a 256 x 160 matrix. Waist circumference and adipose tissue volume were measured by validated in-house image processing software. Subjects with OSA (AHI≥5) were compared to age, gender and BMI matched subjects without OSA.

**Results :** Among males (n=16), OSA subjects (n=10) did not differ from those without OSA (n=6) in their age (15.9yrs±1.9 vs 15.0±1.6), BMI (38.4± 4.0 vs 39.8± 4.9), waist circumference (124.8 cm ± 7.7 vs 123.7± 9.7), parapharyngeal adipose tissue (PAT) (1218.6 mm<sup>3</sup> ±278.7 vs 1117±196.9) or total abdominal adipose tissue (TAAT) (7.9 liters±1.4 vs 7.5±1.4). OSA subjects, however, had a significantly greater volume of intra abdominal adipose tissue (IAAT) than BMI matched subjects without OSA (1.9 liters ± 0.4vs1.4±0.5, P=0.03). Among females (n=17), OSA subjects (n=8) did not differ from those without OSA (n=9) in their age (16.1 yrs ±1.0 vs 16.7±1.9), BMI (47.6±5.2 vs 45.4±5.2), waist circumference (133.5 cm ±8.2 vs 128.9±8.6), PAT (1019.7 mm<sup>3</sup>± 501.3 vs 1088.7 ± 282.6), TAAT (9.1 liters ±1.8 vs 8.9±1.8) or IAAT (1.2 liters ±0.5 vs 1.1±0.3).

**Conclusion :** Our data suggests that intra abdominal (visceral) adipose tissue plays a role in the pathogenesis of OSA in obese male adolescents.

**Support (optional):** Dr. Kalra is funded by the AASM/Pfizer Scholars Grant in Sleep Medicine, GCRC M01 RR 08084-13, and Trustee Grant of Cincinnati Children's Research Foundation.

## 0212

**APOLIPOPROTEIN E 4 ALLELE, NEUROCOGNITIVE DYSFUNCTION, AND OBSTRUCTIVE SLEEP APNEA (OSA) IN SCHOOL-AGED CHILDREN**

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## Category F—Pediatrics

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**Introduction :** OSA in children is associated with severity-dependent changes in neurobehavioral and cognitive functioning. However, the severity of OSA as defined by the respiratory disturbance index, degree of sleep fragmentation, and the magnitude of hypoxemia only accounts for 35-40% of the variance in cognitive performance. Thus, we hypothesized that genetic determinants of individual susceptibility may also contribute to the marked variability in CNS morbidity associated with OSA. Based on the unique susceptibility of Apolipoprotein E (ApoE) knock-out mice to a rodent model of OSA, we hypothesized that the presence of the ApoE  $\hat{A}4$  allele may account for increased neurocognitive morbidity in pediatric OSA

**Methods :** Consecutive habitually-snoring and non-snoring children ages 5-7 years were recruited from the community, and underwent overnight polysomnography and neurocognitive testing and blood drawing the next morning. Children were divided into OSA (OAHI>1/hrTST) or no OSA (OAHI< 1/hrTST). OSA children were further subdivided into those with a composite neurocognitive function <85% (i.e., 1 standard deviation below norm) and those with scores >90%. The presence of the ApoE  $\hat{A}4$  allele was determined from the genomic DNA extracted from the blood sample. For ApoE genotyping, DNA was amplified by polymerase chain reaction by using specific primers. The 244-base pair amplicon was restricted with HhaI, and the DNA fragments were separated by 8%-polyacrylamide gel electrophoresis. APOE genotype was determined by comparison with the combination of fragment sizes described by Hixson and Vernier (J Lipid Res 1990;31:545-548).

**Results :** Among snoring and non-snoring children without OSA, the ApoE  $\hat{A}4$  allele was found in 2 of 114 children. Among children with OSA, the ApoE  $\hat{A}4$  allele was found in 12 out 98 children ( $p<0.01$ ). Furthermore, 9 of 47 children with OSA and cognitive scores <85% had the ApoE  $\hat{A}4$  allele compared to 3 of 51 children with OSA whose cognitive scores were >90% ( $p<0.03$ ).

**Conclusion :** ApoE  $\hat{A}4$  is more frequent in children with OSA, especially in those who develop neurocognitive deficits. These findings suggest that the presence of the ApoE  $\hat{A}4$  allele appears to be associated with increased odds of having sleep-disordered breathing, and also that the latter develops among those children with the ApoE  $\hat{A}4$  allele, the risk for neurocognitive dysfunction is enhanced.

**Support (optional):** Study funded by NIH grant HL-65270

### 0213

#### CRANIOFACIAL RISK FACTORS FOR OBSTRUCTIVE SLEEP APNEA IN OBESE ADOLESCENTS

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**Introduction :** Knowledge of predisposing risk factors for obstructive sleep apnea (OSA) in obese children is important for early identification and treatment of OSA in this high risk group. The contribution of craniofacial morphology to OSA associated with obesity has not been examined exclusively in the pediatric age group. The goal of this study is to determine the association between craniofacial risk factors and OSA in obese adolescents.

**Methods :** Obese adolescents referred to the sleep apnea clinic at Cincinnati Children's were recruited for this study. Subjects with genetic syndromes were excluded. Overnight polysomnograms to determine OSA status and MRI scans to measure craniofacial characteristics were performed. The axial T1 MRI scan sequence had parameters of TR/TE of

500/14 and a 256 x 160 matrix. OSA was defined as apnea hypopnea index (AHI)>5 and severe OSA was defined as (AHI>15). Intermandibular rami distance was considered a measure of skull width and distance between the back of teeth and anterior border of spine considered a measure of the anteroposterior skull dimensions. All MRI measurements were obtained by a single individual, blinded to the OSA status, using an image processing software.

**Results :** The prevalence of OSA in this cohort (n=41) was 56% with 10 subjects diagnosed with severe OSA. Among OSA subjects (n=23 with mean BMI 44.9±7.0, range 31.9-55.5), AHI significantly correlated with skull width to antero-posterior dimension ratio ( $r=-0.41$ ,  $p=0.05$ ). The correlation between AHI and inter-mandibular rami distance was -0.36 ( $p=0.08$ ) and that between AHI and BMI was =0.26 ( $p=0.22$ ). Among severe OSA subjects (n=10), the correlation (r) between AHI and inter-mandibular rami distance was -0.55 ( $p=0.09$ ) and that between AHI and BMI was =0.05 ( $p=0.88$ ).

**Conclusion :** In our cohort of obese adolescents with OSA, skull width to antero-posterior dimension ratio is associated with OSA severity.

**Support (optional):** Dr. Kalra's research is funded by AASM/Pfizer Scholars Grant in Sleep Medicine, Trustee Grant of Cincinnati Children's Research Foundation and the General Clinical Research Center at Cincinnati Children's, M01 RR 01084.

### 0214

#### EPILEPTIFORM ACTIVITY IN HEALTHY CHILDREN DURING SLEEP: HOW OFTEN?

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**Introduction :** The term epileptiform discharge typically refers to interictal paroxysmal activity that usually occurs during sleep. This type of paroxysmal activity does not include the EEG activity observed during a seizure. The prevalence of epileptiform activity in the general pediatric population is unknown.

**Methods :** Polysomnographic studies (PSG) were conducted at Kosair Children's Hospital Research Institute sleep laboratory in healthy children recruited from the general population. All sleep studies included an 8 EEG lead montage. All participants had a negative history of previous seizures and no known neurological disorder. PSG were reviewed by 2 independent investigators. Spike and sharp waves, either alone or accompanied by slow waves, occurring singly or in bursts lasting <5 sec seconds were considered as representing epileptiform activity.

**Results :** 750 children underwent overnight PSG. Of these, 6 children presented evidence of epileptiform activity, in the absence of any additional abnormality in the PSG, indicating a prevalence of 6/1000. No electrographic seizures occurred in any of the children. The epileptiform patterns found were either spike or spike and wave. The epileptiform activity was more prominent during NREM sleep, although 2 subjects had spike and wave activity during REM sleep. The distribution of the epileptiform activity included central, temporal, occipital, and frontal regions, with 4 patients presenting spike and spike and wave patterns in centro-temporal regions, 1 patient in fronto-central regions, and another patient in temporo-occipital regions. None of these 6 children had history of febrile seizure, ADHD, or any other neurological disorder. 3 out of the 6 children had a neurocognitive test (DAS, WISC III, NEPSY) and 2 of these 3 children exhibited abnormal findings in the areas of behavior, attention, hyperactivity, and learning.

**Conclusion :** Thus, the prevalence of epileptiform activity in otherwise healthy children from the community is not high (less 1%), and may be associated with suboptimal cognitive and behavioral functions. Increased awareness by sleep professionals and use of a EEG montage that includes temporal leads and >2 standard EEG leads should facilitate the detection

of epileptiform activity in children.

**Support (optional):** National Institutes of Health HL-65270

## 0215

### TODDLER BEHAVIOR AFTER POLYSOMNOGRAPHY: EFFECTS OF UNINTENDED PARTIAL SLEEP DEPRIVATION

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**Introduction :** Childhood sleep disorders are consistently shown to affect behavior and cognition. However, adaptation nights are rare in laboratory research and first-night effects on behavioral and cognitive assessments are generally unknown. Thus, we sought to examine whether sleep patterns in the laboratory and home differed in healthy toddlers, and how this influenced an assessment of development and behavior.

**Methods :** Twenty-one healthy 14-month-olds wore an actigraph during nighttime sleep at home for five nights preceding and during standard overnight polysomnography (PSG). Efforts were made to follow the home sleep and waking schedules. The Bayley Scales of Infant Development (BSID) and Behavior Record were administered the morning following laboratory PSG.

**Results :** All subjects had normal PSG. Sleep start and end times during PSG did not differ from those at home. Compared to home actigraphic recordings, duration of total sleep time and sleep efficiency were reduced ( $F=7.2, p=.01; F=11.3, p=.003$ ), and there were longer mean wake bouts ( $F=12.5, p=.002$ ), fewer total and percent minutes of immobility ( $F=6.3, p=.02; F=11.3, p=.003$ ), greater total and average activity during sleep ( $F=18.2, p<.001; F=31.5, p<.001$ ), and higher degree of sleep fragmentation ( $F=4.8, p=.04$ ) during the PSG night. BSID did not differ as a function of differences in home versus PSG sleep. However, there were significant correlations on the Behavior Record between Emotional Regulation and difference scores for both percent minutes of immobility ( $r=-.49, p=.02$ ) and fragmentation index ( $r=-.50, p=.02$ ).

**Conclusion :** Although bed and rise times were preserved in the laboratory night, less sleep duration and more fragmented sleep occurred in a laboratory setting compared to home. These differences did not affect next-morning standardized development scores. However, the differences between home and laboratory sleep were associated with greater difficulty with emotional regulation. Therefore, the effects of unintended partial sleep deprivation and fragmentation during a first night laboratory-based PSG should be considered in studies aiming to examine behavioral differences among young children, particularly those vulnerable to changes in emotional regulation.

**Support (optional):** Study funded by NIH grants F32HL074591 (HM-D) and R01HL-65270 (DG).

## 0216

### SLEEP POSITION AND RESPIRATORY DISTURBANCE IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA (OSA)

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**Introduction :** In adults with OSA, the supine position is consistently associated with increased severity of the respiratory disturbance during sleep. However, conflicting findings have emerged regarding children with OSA, and are most likely explained by the relatively small number of patients thus far assessed.

**Methods :** Consecutive children referred for evaluation of snoring in the

absence of craniofacial or genetic abnormalities and with polysomnographically-demonstrated OSAS were identified in the database. Demographic and polysomnographic data were extracted and analyzed using descriptive statistics and unpaired t tests.

**Results :** 408 children with OSA were identified (61.3% male; 54.6% Caucasian and 37% African American). Their mean age was  $6.5\pm 0.2$  years, their BMI was  $22.5\pm 0.5$  kg/m<sup>2</sup>, and their mean tonsillar size (0-4 scale) was  $2.4\pm 0.1$ . Mean total sleep time was  $455\pm 13$  min with  $42.5\pm 1.4\%$  spent in the supine position,  $41.7\pm 1.5\%$  in the side position, and  $15.7\pm 14\%$  in the prone position. Mean obstructive apnea-hypopnea index (OAH) was  $10.5\pm 0.5$ /hrTST and mean obstructive apnea index(OAI) was  $3.7\pm 0.3$ /hrTST. There were no significant differences in OAH among the 3 sleep-related positions. However, OAI<sub>supine</sub> was significantly greater ( $4.6\pm 0.7$ /hrTST) when compared to either OAI<sub>side</sub> ( $2.7\pm 0.3$ /hrTST;  $p<0.001$ ) or OAI<sub>prone</sub> ( $3.3\pm 0.5$ /hrTST;  $p<0.01$ ). Tonsillar size did not appear to be a contributing factor to positional differences in AI or OAH. In contrast, obese children (relative BMI>95%) displayed increased OAH<sub>supine</sub> and AI<sub>supine</sub> compared to non-obese children despite similar total OAH and OAI. Conversely, non-obese patients showed increases in OAH<sub>side</sub> and OAH<sub>prone</sub> compared to OAH<sub>supine</sub> ( $p<0.01$ ), with no significant differences in position-dependent OAI.

**Conclusion :** Our findings support the notion that in otherwise normal children with OSA, the supine position adversely affects the frequency of complete upper airway obstructions, but does not appear to modify the overall magnitude of the respiratory disturbance when OSA is present. Furthermore, while tonsillar size is not associated with positional differences in breathing disturbance, the presence or absence of obesity markedly modifies the frequency of sleep position-related upper airway obstructive events.

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## 0217

### THE NOCTURNAL FLIP-FLOP DURING SLEEP: IS IT DIFFERENT IN PEDIATRIC SLEEP APNEA?

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**Introduction :** In adults with OSA, the supine position is consistently associated with increased severity of the respiratory disturbance during sleep. Although data on this issue in children are currently conflictive, preferential selection of body positions during sleep that reduce the risk for upper airway obstruction could skew polysomnographic findings

**Methods :** Consecutive children referred for evaluation of snoring in the absence of craniofacial or genetic abnormalities and with polysomnographically-demonstrated OSAS were identified in the database, and the sleep time spent in the supine, prone, and side position was extracted, and compared to the sleep position characteristics of healthy children.

**Results :** 430 children with OSA (40.3% female; 56% Caucasian and 37% African American), with a mean age of  $6.5\pm 0.2$  years were included. In addition, 185 age-, gender-, and ethnically-matched children were also studied (CO). For OSA children, mean total sleep time was  $453.7\pm 66.4$  min and  $465.2\pm 43.3$  min in CO (p-NS). OSA children spent more time in the supine position ( $42.0\pm 39.0\%$ TST) vs.  $33.4\pm 25.6\%$ TST in CO ( $p<0.01$ ). In contrast, OSA patients sleep less on their side ( $53.1\pm 24.4\%$ TST vs.  $42.5\pm 35.4\%$ TST;  $P<0.005$ ), with no differences in the percentage of time spent in the prone position. Interestingly, obese children with OSA were more likely to adopt the prone position ( $20.4\pm 29.1\%$ TST) compared to non-obese children with OSA

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(10.9±53.5%TST; p<0.05).

**Conclusion :** Children with OSA appear to spend increasing proportions of their sleep in the supine position and less time in the side position compared to healthy children. While substantial variability was evident in our cohorts, obese children with OSA were more likely to adopt the prone position, suggesting that this position may promote upper airway patency in the presence of obesity.

**Support (optional):** Study funded by NIH grant HL-65270

### 0218

#### SLEEP DISORDERED BREATHING (SDB) AND METABOLIC DYSFUNCTION IN CHILDREN: A PRE- VS. POST-ADENOTONSILLECTOMY STUDY

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**Introduction :** SDB has been associated with a higher prevalence and severity of the metabolic syndrome in adult patients, even after controlling for obesity. In contrast, while obese children are at risk for metabolic dysfunction, SDB in children does not appear to correlate with the magnitude of such metabolic derangements.

**Methods :** To further establish the potential mechanistic role of SDB in metabolic regulation, a prospective study of children with SDB was conducted. Children with polysomnographically-demonstrated SDB underwent a blood draw after an overnight fast in the morning after their sleep studies, i.e., at the time of diagnosis and 4-15 months after adenotonsillectomy (T&A). Glucose (Glu), insulin (Ins), and serum lipid concentrations were determined within 2-3 hours after collection using standard techniques.

**Results :** Nineteen children with SDB (mean age 9.0±2.8 years; M/F: 10/9) with a mean obstructive apnea/hypopnea index (AHI) of 18.0±6.3/hr TST and nadir SaO<sub>2</sub> of 83.0±2.5% at diagnosis were included. After T&A, significant improvements in AHI and sleep fragmentation occurred. Mean initial Glu and Ins levels at SDB diagnosis were 91.0 ± 1.5 mg/dl and 14.1±2.1 mIU/ml, respectively. Glu did not change after T&A (90.6 ± 1.5 mg/dl; P-NS). However, Ins levels were higher after T&A (20.3±2.5mIU/ml; P<0.02). Both total cholesterol and LDL significantly decreased after surgery, but no changes in triglycerides or HDL emerged.

**Conclusion :** SDB does not appear to induce insulin resistance in pediatric patients. However, the significant reductions in LDL cholesterol following T&A suggest a pathogenetic role for SDB in lipid homeostasis.

**Support (optional):** Study funded by NIH grant HL-65270

### 0219

#### SECULAR TRENDS IN OBESITY AND PARENTALLY-REPORTED DAYTIME SLEEPINESS AMONG CHILDREN REFERRED TO A PEDIATRIC SLEEP CENTER FOR SNORING AND SUSPECTED SLEEP-DISORDERED BREATHING (SDB)

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**Introduction :** Obesity is increasingly prevalent among children in the US population and is clearly implicated as a risk factor for obstructive sleep apnea in adults. In the latter, excessive daytime sleepiness (EDS) is extremely frequent. In contrast, EDS is reported in only 7-13% of children with SDB. The aims of the present study were to assess the changes

in the prevalence of obesity and EDS among children being referred to a pediatric sleep center for evaluation of symptomatic habitual snoring.

**Methods :** All records of children ages 2-12 years referred for evaluation of habitual snoring to Kosair Children's Hospital and Tulane University Sleep Centers from July 1996 till July 2005 were reviewed for the presence of obesity (defined as relative body mass index >95% adjusted for age and gender), symptoms of EDS (indexed as a score of >3 in a modified parental questionnaire), and the presence of asthma and/or allergic rhinitis (both as reported by parents).

**Results :** The overall percentage of obese children referred for habitual snoring increased over time (from 26% in 1996 to 49% in 2005) in spite of the overall annual number of patients being also increased (from 456 to 1986/year). Conversely, the presence of failure to thrive decreased from 14% to 3.7%. There was a small trend towards increases in the prevalence of asthma (8.7% to 11.5%) and allergic rhinitis (11.2% to 17%) in the study period. Parallel and proportionate to the increases in obesity trends, increases in the parental reporting of EDS were also apparent (11.4 to 28.4%). Of note, the percentage of children with obesity, EDS, allergy, and asthma were further increased among those snoring children who had OAHl>1/hrTST in their diagnostic sleep study.

**Conclusion :** An increasing proportion of children with symptomatic habitual snoring is obese, sleepy, and displays associated co-morbidities such as asthma and/or allergic rhinitis. These factors will need to be incorporated into future algorithms aiming at development of diagnostic and management approaches for OSA in children.

**Support (optional):** Supported by NIH grant HL-65270

### 0220

#### SLEEP PROBLEMS OF DEVELOPMENTALLY REGRESSED VS NONREGRESSED AUTISTIC CHILDREN

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**Introduction :** Autism is a long-term neurodevelopmental disorders. Developmental regression occurs in about one third of autistic children and sleep problems were commonly reported in such population. In a previous study we found that sleep difficulties seem to start during the second year of life, as does regression, and tend to persist. This would support the hypothesis stating the existence in autistic children of a developmentally critical phase. Results of different studies showed that EEG abnormalities and epilepsy were significantly common in regressed children. Aim of this study was to assess differences in sleep patterns of regressed versus nonregressed children, and their relationship between EEG abnormalities and epilepsy

**Methods :** We examined 68 autistic children, (87% males), aged 2.1-8.2. To assess sleep problems, parents completed Children's Sleep Habits Questionnaire (CSHQ). Previous and current child's sleep was investigated. All children underwent waking and sleeping EEG recordings. Epileptic disorders were assessed following the criteria of the ILAE. Sleep patterns, EEG abnormalities and epilepsy in regressed were compared with those of nonregressed children.

**Results :** As expected, CSHQ score (41 or above) confirmed a prevalence of 95% of sleep problems. Developmental regression was found in 36% of children. A significant prevalence of sleep problems was found in regressed children (100% vs 92%.p<.001), particularly they used to sleep less than one hour (p<.001), have a later bedtime (p<.001), to have sleep onset delay (p<.01), sleep anxiety (p<.01) and more sleep irregularity than nonregressed group (. Moreover, they showed an higher incidence of epilepsy (p<.001) and EEG abnormalities (p<.001).

**Conclusion :** Consistent with other studies our children exhibit sleep problems. Unlike their nonregressed peers, regressed children showed



more disrupted sleep, more EEG abnormalities and epilepsy. Although the biological basis and possible casual relationships of these associations remain to be explained, they may point to different subgroups of patients with autism.

**Support (optional):**

## 0221

### TIME OF DAY AFFECTS PERFORMANCE OF SIMPLE ARITHMETIC SKILLS OF MIDDLE SCHOOL STUDENTS

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**Introduction :** Teens have a circadian tendency to fall asleep at a later time and to wake up at a later time. Although both teens and adults may be sleep deprived, many teens are especially sleepy in the morning due to a delayed circadian rhythm tendency. Because sleepiness may affect learning, several high schools have changed their school times in response to this problem. The primary purpose of this project was to see how the time of day may affect simple arithmetic skills of teenagers.

**Methods :** Eighth grade students and (adult) teachers from a Philadelphia school were recruited. Participants were asked to complete a questionnaire and to take a timed two minute, simple arithmetic test during first period and in the afternoon. Tests were taken in either order to minimize an experience or learning effect.

**Results :** 23 eighth graders (14 males, age 13.7 +/-0.4 years) completed testing. 10 adults (7 males, age 36.7 +/-14.1 years) completed testing. Both teens and adults appeared sleep deprived. Teens slept an average of 8.0 +/- 0.9 hours; adults slept an average of 6.9 +/-1.4 hours. Both teens and adults felt more alert in the afternoon. Teens rated alertness as 5.4 (0:sleepy-10:alert) in the AM compared to 6.7 for afternoon (p=0.0487). Adults rated alertness as 5.5 in the AM and 6.5 for afternoon (p=0.2031). Both teens and adults had more correct answers on the afternoon test. Teens had 10.8 correct afternoon answers compared to 9.5 AM answers (p=0.0374); adults had 12.8 correct afternoon answers and 10.9 correct AM answers (p=0.0098). Teens had more incorrect answers on AM testing (1.7) compared to afternoon testing (1.0) (p=0.0242). Time of day did not affect incorrect answers for adults who had 1.5 incorrect answers for both AM and afternoon testing (p=1.00).

**Conclusion :** Both teens and adults were sleep deprived. Both teens and adults felt more alert in the afternoon. There was no correlation with subjective alertness and the amount of previous sleep. Both teens and adults got more correct answers on afternoon testing. Only teens had more incorrect answers on morning testing. Time of day does affect testing results on a simple two minute arithmetic test. If correct answers show the degree of alertness and incorrect answers shows the degree of inattentiveness, then teens are both less alert and more inattentive in the morning. This may have implications on learning and safety (driving to school) in the morning for teens.

**Support (optional):**

## 0222

### GENDER DIFFERENCES IN TOTAL SLEEP TIME AND ITS DETERMINANTS IN BOYS AND GIRLS

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**Introduction :** The present study uses data collected in a survey of sleeping and other life style habits of high school students conducted in 2000 by the Board of Education of Akita Prefecture in Japan to examine gender differences in total sleep time (TST) and determinants of insufficient sleep.

**Methods :** The analysis is based on 10,469 questionnaires completed by students of consenting parents. The variables analyzed were: TST on school night (hours), TST on holidays (hours), time spent commuting to school (minutes), time spent exercising (minutes), frequency of having breakfast, and regularity of bed time. In addition students were asked if they get enough sleep and to reasons for perceived sleep deficit.

**Results :** TST was 7.0 (SD±1.1) hrs on school nights and 8.4 (SD±1.6) on holiday nights. Although girls reported sleeping slightly more (0.1 hrs) than boys on school night (p<0.001), the significantly more girls (13.7%) than boys (8.2%) reported sleeping less than 6 hours on school nights (p<0.0001). Overall, more girls 84.5% than boys (79.9%) thought they obtained insufficient sleep on school nights (p<0.0001). There was no gender difference in the proportion of girls and boys who stated difficulty sleeping as a reason for insufficient sleep (20.9%). However, more girls than boys endorsed studying (35.4% vs. 26.5%) and talking on the phone (13.9% vs. 9.6%) as reasons for insufficient sleep and more boys than girls endorsed use of media (TV and radio, 46.0% vs. 37.5%) and use of computer (25.6% vs. 6.3%). Regression analyses revealed that irregular bedtime and time spent commuting where the only significant predictors of TST on school nights (p<0.0001).

**Conclusion :** There are significant gender differences in prevalence of and reasons for insufficient sleep, suggesting that future effort to increase TST in teens will need to target different factors for boys and girls.

**Support (optional):**

## 0223

### EARLY SLEEP REGULATION IN HIGH-RISK INFANTS: MEDICAL AND CONTEXTUAL FACTORS

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**Introduction :** Sleep patterns in young infants are influenced by both medical/biologic and contextual factors with distinct differences across development and sleep parameters. For example, night waking in newborn infants is considered a biologic function, whereas night waking after 4 months of age is often attributed to contextual factors. Infants experiencing medical or contextual risks may be particularly sensitive to sleep pattern disruption which may contribute to other developmental or regulatory difficulties. Following an ecological perspective, this study assessed both medical/biologic and contextual factors in early sleep development in high-risk infants.

**Methods :** This study presents preliminary data from a larger study focusing on regulation development in high-risk infants. Ninety four preterm/low birthweight infants were followed from hospital discharge to 4-months postterm. Information was collected on 4-month infant sleep patterns, medical history prior to hospital discharge, family socioeconomic factors, and breastfeeding. Infant sleep parameters were collected via maternal report and included daytime sleep, night waking, nighttime sleep, sleep per 24-hour cycle, and diurnal sleep consolidation.

**Results :** Bivariate correlations and multiple regression were used to test the associations between each sleep parameter and infant medical/biologic factors, family socioeconomic variables, and breastfeeding. As expected, breastfeeding was the most robust predictor of night waking. For bottle fed infants (N = 73), higher maternal education and Respiratory Distress Syndrome (RDS) were associated with more night waking. Total

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nighttime sleep related to both breastfeeding and RDS, and diurnal sleep consolidation related to birthweight. Infants with higher birthweights had better diurnal sleep consolidation.

**Conclusion :** In this high-risk sample, both medical/biologic (e.g., birthweight) and contextual factors (e.g., breastfeeding) related to infant sleep behaviors, with distinct differences across parameters. Birthweight and RDS were the most influential medical/biologic factors and, consistent with previous research, breastfeeding was the most influential contextual factor.

**Support (optional):**

### 0224

#### COSLEEPERS VERSUS SOLITARY SLEEPERS IN CHILDHOOD BEHAVIORAL INSOMNIA

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**Introduction :** Aim of this study was to investigate sleep characteristics, behavioral and emotional problems, parental relationship and psychological distress of cosleepers versus solitary sleepers in childhood behavioral insomnia.

**Methods :** A sample of 148 children, with behavioral insomnia was selected. Fortyfour regular cosleepers (mean age 9.2 years) were compared with 104 solitary sleepers (mean age 9.0 yr). Sleep was assessed through Children Sleep Habits Questionnaire (CSHQ) and sleep diary. Emotional adjustment was evaluated through Child Behavior Checklist (CBCL) and parental distress and psychological assessment through Dyadic Adjustment Scale (DAS) and Symptom Checklist-90 (SCL-90).

**Results :** Cosleepers scored significantly higher on CSHQ total than solitary sleepers (60 vs 55;  $p < .001$ ). Particularly, cosleepers showed significantly higher scores on bedtime resistance (16 vs 8;  $p < .001$ ), night-wakings (7 vs 6;  $p < .01$ ) and sleep anxiety (11 vs 7;  $p < .001$ ) CSHQ subdomains. Cosleepers showed significant later bedtime (11.45 vs 11 pm;  $p < .01$ ) and shorter nighttime sleep duration (400 mins vs 480 mins;  $p < .001$ ). Moreover, cosleepers had more emotional problems (CBCL total score 71 vs 67;  $p < .001$ ). Parents of cosleepers showed a significant higher level of psychological and couple distress. Independent risk factors for cosleeping, as determined from the multiple logistic regression analysis, are couple distress (OR 2.34; CI 1.11-4.9), child emotional problems (OR 0.91 CI 0.83 -0.99) and, among sleep variables, later bedtime (OR 1.77; 1.06-2.94), bedtime resistance (OR 1.61; 1.02-2.56) and sleep anxiety (OR 3.72 ;1.57-8.82).

**Conclusion :** Results of our study pointed out that best predictors of current cosleeping were sleep onset difficulties and mainly high level of sleep anxiety. Additionally, our study suggested that an overall higher level of marital maladjustment and parental psychological distress, as well as more children's emotional maladjustment, might contribute to the choice of this sleep practice in children with behavioral insomnia. Thus, when cosleeping is present child's emotional adjustment, family relationships and parental psychological problems should be investigated

**Support (optional):**

### 0225

#### PRELIMINARY DATA REGARDING CHILDHOOD SLEEP FROM THE AVON LONGITUDINAL STUDY OF PARENTS AND CHILDREN (ALSPAC)

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**Introduction :** The aim of this study was to provide normative data regarding childhood sleep and parasomnias.

**Methods :** In 1991-92, 14,541 pregnant women were recruited into ALSPAC, and their children have been followed with regular questionnaires and clinic assessments to the present (age 13-14y). We present preliminary analyses of parent-reported sleep data from repeated questionnaires collected between 6 and 81mths and potential factors associated with sleep duration at age 81mths (using linear/logistic regression as appropriate).

**Results :** We found differences in reported sleep duration between boys and girls at all ages studied with girls sleeping longer. Sleep durations at different ages were correlated. A greater percentage of boys were reported to take daytime naps particularly at ages of 30 (boys: 61.1%; girls: 55.1%) and 42mths (boys: 23.8%; girls: 20.5%). Napping decreased dramatically in both sexes from nearly all children at 18mths to only 1.2% at 81mths. At 81mths, a child from the cohort was more likely to sleep longer if their mother was younger (, coefficient = -0.023 hours of sleep/maternal age years;  $p < .001$ ), did not drink alcohol during the 2nd trimester (<1glass/week Vs >1 glass/week, , = -0.128;  $p < .001$ ), and if the child watched less television (hours/week) at 38mths (Vs <7 hours; 7-8 hours: , = -0.014; >9 hours: , = -0.095;  $p < .001$ ) and spent more time outdoors (hours/week) at 38mths (Vs < 7 hours; 7-13 hours: , = -0.038; 14-20 hours: , = -0.025;  $p < .001$ ). Up to 70% of children were still reported to wake up in the night at age 81months. There was no sex difference in the parent-reported frequency of nightmares, which increased from approximately 10% at age 18mths to about 50% at 81mths. No sex difference in reported snoring was observed but over 60% of the cohort were reported to snore at 81mths. Bedwetting was reported in 32.3% of boys Vs 22.4% of girls ( $p < .001$ ; t-test) at age 81mths.

**Conclusion :** We report differences in sleep duration between boys and girls from 6-81mths (ranging from 7-15 minutes) in a population-based cohort of children. Sex differences were also found in bedwetting, but not other parasomnias. Sleep durations at each of the ages examined were significantly correlated suggesting that sleep patterns track over time. Snoring is reported to occur in a significant number 6-7y olds. Longer sleep duration at 81mths is negatively associated with TV viewing supporting previous studies reporting sleep loss with TV viewing.

**Support (optional):**

### 0226

#### A LONG-TERM FOLLOW-UP STUDY OF PERIODIC LIMB MOVEMENT DISORDERS IN CHILDREN AFTER IRON THERAPY

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**Introduction :** We previously showed that children with periodic limb movement disorders (PLMD) have low levels of serum iron and ferritin. In addition, these children favorably responded to a 3-month course of iron therapy with improvement in clinical symptoms and a decrease in PLM index. However, there is no information available on the long-term follow-up of this population. We therefore conducted a prospective follow-up study in children with PLMD who received iron therapy.

**Methods :** Previously diagnosed children with PLMD who received iron therapy were identified and invited for follow-up assessments. Most of

these children had been maintained on multi-vitamin with iron. A sleep study, serum iron and serum ferritin were obtained from these children before treatment (Pre), upon completion of iron therapy (post-1) and 1-2 years after iron therapy (post-2). Any child with incomplete follow-up data or with known hematological or neurological disorders was excluded from the study.

**Results :** Eleven children met the criteria for entry into the study. Mean age was  $7.1 \pm 0.9$  [SE] years, with 7 being male. Mean PLM index was  $30.3 \pm 5.0$ /hr, and all children had serum ferritin levels  $< 50$   $\mu\text{g/l}$ . After completion of iron therapy, there was a significant decrease in PLM index ( $10.3 \pm 1.9$ /hr in post-1;  $P < 0.05$ ) along with a significant increase in serum ferritin levels ( $63.4 \pm 4.1$  [post-1] vs  $29.2 \pm 6.1$   $\mu\text{g/l}$  [pre];  $P < 0.05$ ) and serum iron ( $63.4 \pm 4.0$  [post-1] vs  $55.0 \pm 6.6$  mg/dl [pre];  $P < 0.05$ ). At 1-2 years after this therapeutic intervention, there was a persistent decrease in PLM index ( $4.6 \pm 0.7$ /hr [post-2],  $P < 0.05$ ), a sustained increase in serum ferritin ( $80.0 \pm 7.7$   $\mu\text{g/dl}$  [post-2];  $P < 0.05$ ) and serum iron ( $81.7 \pm 2.9$  mg/dl [post-2];  $P < 0.05$ ). All children remained asymptomatic at 1-2 years after treatment.

**Conclusion :** We conclude that children with PLMD demonstrate sustained improvements in their PLMD 1-2 years after iron therapy, with serum iron and ferritin remaining at adequate levels after treatment. Thus, iron replacement therapy appears to lead to long-lasting resolution of PLMD.

**Support (optional):** Constance Kaufman Fund and General Clinical Research Center, Tulane University Health Science Center

## 0227

### NEW REFERENCE VALUES FOR INFANT AND TODDLER SLEEP DURATION AND DISTRIBUTION

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**Introduction :** The amount and distribution of children's sleep is a frequent parental concern. As part of a larger study on the incidence of sleep-disordered breathing symptoms, relevant information was collected on the distribution of diurnal and nocturnal sleep and developmental changes across the first two years of life.

**Methods :** Surveys were filled out by parents of children ages two weeks through two years who were either attending well-baby checkups at one of five multiple-provider pediatric practices, or were born at one of six local hospitals. Questions included the child's current bedtime, risetime, and usual number and duration of naps. Daily sleep was calculated as the time from bedtime to risetime plus the number of daytime naps multiplied by the usual length of naps.

**Results :** There were 1,038 respondents distributed over 10 age groups corresponding to standard checkup time points. No age effects for reported daily sleep were found. From two weeks through two years, children were reported to sleep an average of 12.8 hours. The proportion of daily sleep accounted for by daytime naps decreased across ages ( $F = 12.5, p < 0.001$ ), as did the number of reported nocturnal awakenings ( $F = 16.1, p < 0.001$ ). One or more nocturnal awakenings were reported by parents of 49.4% of 12-month olds and 45.9% of 24-month-olds. There was large variance on each measure.

**Conclusion :** These daily sleep durations for infants and young toddlers are shorter than the values commonly recommended by healthcare professionals. Since there is no conclusive evidence indicating that sleep duration below a certain threshold in this age range is less than optimal or that it imposes particular morbidities, justification of current recommendations for 16 hours/day sleep appears somewhat arbitrary. Furthermore, such a priori excessive expectations could lead parents to manage their child's sleep routines inappropriately, and potentially lead to the erro-

neous belief that their child suffers from a sleep disorder.

**Support (optional):** Study funded by NIH grants F32HL074591 (HM-D) and R01HL-65270 (DG).

## 0228

### OCCULT SLEEP DISTURBANCES IN PRESUMABLY NORMAL KINDERGARTEN CHILDREN PREDICT LEARNING FAILURE IN FIRST GRADE

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**Introduction :** We have recently shown that kindergarten children who fail to qualify to first grade had worst sleep than controls. In the current study we followed-up for one year on the control group of presumably normal children who progressed to first grade. We hypothesized that even in this group, those who sleep better will demonstrate better achievements at the end of first grade.

**Methods :** The study group consisted of 98 presumably normal kindergarten pupils. All children/parents filled a sleep questionnaire and underwent an ambulatory one-week of actigraphic sleep/wake study toward the end of kindergarten. Achievement evaluations in reading, writing and arithmetic were administered to the children at the end of first-grade. Correlations between sleep variables and scholastic achievements were assessed.

**Results :** Children's sleep latency (SL), sleep efficiency (SE) and total sleep time in kindergarten were  $23 \pm 15$ min,  $93 \pm 3\%$  and  $534 \pm 24$ min, respectively. Of the 98 pupils, 6 failed the end of first-grade's achievement tests. When looking at their sleep patterns a year earlier, they had significantly longer SL ( $41 \pm 31$  vs  $22 \pm 12$ min,  $p < 0.05$ ), increased arousals from sleep ( $4.2 \pm 0.9$  vs  $1.8 \pm 1.0$ ,  $p < 0.01$ ), and decreased SE ( $90.5 \pm 1.1$  vs  $94.3 \pm 2.8\%$ ,  $p < 0.05$ ) than pupils who passed the tests. Actigraphic parameters at the end of kindergarten significantly correlated with achievements at the end of first grade (e.g.  $r = 0.57$  between SE and reading achievements,  $r = -0.73$  between arousals and mathematics, and  $r = -0.58$  between arousals and writing,  $p < 0.05$  for all). Stepwise multiple regression analysis showed that sleep variables can explain 39% of the variability in first graders' achievements!

**Conclusion :** Our data show strong correlations between sleep patterns in kindergarten and scholastic achievements at the end of first grade, with considerable ability to predict failures just by evaluation of sleep. We believe these findings suggest that sleep should be routinely evaluated in kindergarten pupils, and perhaps earlier.

**Support (optional):**

## 0229

### SLEEP AND NEUROBEHAVIORAL FUNCTIONING IN CHILDREN WITH ADHD CHARACTERIZED AS POOR OR GOOD SLEEPERS

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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 contribute to these symptoms. In our previous study, no relationship was observed between sleep and neurobe-

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behavioral functioning in children with ADHD. Here, we compared the neuropsychological functions of ADHD children who were good sleepers versus poor sleepers.

**Methods :** The study population consisted of 46 children (7.4 to 12 years old) diagnosed with ADHD (DSM-IV; DISC diagnosis confirmed by multidisciplinary consensus). Twenty-two of these children were defined as “poor sleepers,” meeting one or both of the following criteria while on placebo: (1) an average of at least three awakenings per night; or (2) a sleep duration < 85% of total bedtime. Nightly sleep actigraphic recordings were taken during a double-blind, placebo-controlled crossover clinical study (1 week of 0.5 mg/kg MPH; 1 week of placebo). On the 3rd day of each condition, neuropsychological functioning was assessed. Sleep was monitored using actigraphy. In addition, parents were asked to complete nightly sleep logs and a sleep questionnaire. The Conners Continuous Performance (CPT) Test was used to assess neuropsychological functioning.

**Results :** Sleep deteriorated following the administration of MPH only in the group of the good sleepers. Poor sleepers performed less well on CPT measures associated with sustained attention and response inhibition during the placebo week, while no differences were found between poor and normal sleepers when study participants received medication.

**Conclusion :** Among unmedicated children with ADHD, good sleepers perform better than poor sleepers on measures of sustained attention and response inhibition. These results may suggest that sleep intervention could improve functioning in non-medicated children with ADHD and poor sleep patterns.

**Support (optional):**

### 0230

#### CHEYNE STOKES RESPIRATION IS ABSENT IN CHILDREN WITH CONGESTIVE HEART FAILURE

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**Introduction :** Up to 50% of adults with congestive heart failure (CHF) demonstrate Cheyne Stokes Respiration (CSR), which has not been reported in children. Potential CSR mechanisms are prolonged circulation time, dynamic upper airway instability and increased chemosensitivity. Thus, we sought to study the prevalence of CSR in children with low and high output CHF, hypothesizing that existence of CSR only in children with low output CHF would support the circulatory delay mechanism.

**Methods :** Ten children with CHF (5m/5f) participated, each on 2-3 medications (i.e. Furosemide, Digoxin, Captopril, Spironolactone). Seven of them had high-output CHF and three had cardiomyopathy with low output CHF. They all underwent a careful cardiac evaluation and in-lab polysomnography.

**Results :** Children's average age ( $\pm$ SEM) was  $3.2\pm 2.1$  years. The average ejection fraction of the three children with low-output CHF was  $22\pm 6\%$ . The remaining seven had normal-high cardiac output. They were all tachypneic ( $56\pm 7$  breaths/min) and tachycardic ( $128\pm 9$  BPM) during stable sleep. Their sleep time was  $202\pm 51$  min, with a low sleep efficiency of  $66\pm 6\%$ . All had occasional (sporadic, not periodic) hypoxemic and hyper/hypocapnic events, yet none of them had a pattern of CSR at any time during the studies.

**Conclusion :** The complete absence of CSR in our small sample of 10 children with CHF suggests that CSR may be an age-dependent phenomenon. None of our patients had CSR, despite potential stimuli such as low output cardiac failure, pulmonary congestion, hypoxic events, arousals

from sleep and hypocapnia. Thus, we speculate that regardless of the exact mechanisms that cause CSR, age is an over-riding factor.

**Support (optional):**

### 0231

#### MID-SLEEP TIME AND SCHOOL READINESS IN BLACK AND WHITE PRESCHOOL CHILDREN

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**Introduction :** As in adolescents and adults, mid-sleep time (MST; midpoint between bedtime and wake time) on “free” days in children may be a marker of chronotype (Morningness-Eveningness). Chronotype-related differences in daytime functioning (e.g., academic performance) have been identified in adolescents and adults. The present study examined the association between weekend MST and school readiness in preschool children. Prior studies have shown racial differences in both weekend MST (see Jacobs et al. abstract) and school readiness; thus, we also investigated whether racial differences in school readiness might be mediated by differences in weekend MST.

**Methods :** Data were collected from a representative community sample of 77 children (62% White-non Hispanic; 48% male) aged 3- to 5-years from southern Mississippi. Caretakers reported their child's typical weekday and weekend bedtime and rise time. Children were administered the Bracken Basic Concept Scale - Revised.

**Results :** Weekend MST yielded the highest correlation with school readiness ( $r = -.49$ ) of the sleep variables examined (bedtimes, wake times, time in bed, MSTs for both weekdays and weekends). Late weekend MSTs were associated with low school readiness scores on the Bracken. Criteria were met for a mediated regression analysis. Race was associated with school readiness before (mean difference = .7 SD;  $p < .001$ ), but not after, adding weekend MST as a mediator variable to the model. Parametric and nonparametric analyses of the indirect effect yielded significance ( $p < .01$ ).

**Conclusion :** Chronotype variability may be importantly related to daytime functioning in preschool children and may contribute to racial differences in academic readiness. Weekend, relative to weekday, MST may better reflect chronotype-related preference as weekend sleep may be less influenced by social demands on the child and caretakers.

**Support (optional):**

### 0232

#### BRUXISM IN CHILDREN: EFFECT ON SLEEP ARCHITECTURE AND DAYTIME COGNITIVE PERFORMANCE AND BEHAVIOR

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**Introduction :** Sleep bruxism is an involuntary mandibular movement with tooth-grinding or clenching occurring during sleep. The prevalence of sleep bruxism in children is high and may lead to frequent arousals with altered daytime functioning. We investigated the sleep architecture, the incidence of gastro-esophageal reflux and the daytime cognitive-behavioral functioning in a group of children with sleep bruxism.

**Methods :** This prospective study included 10 children (5-15 years).

Polysomnographic data with pH probe analysis was compared with 10 age/matched controls. Each patient completed a dental evaluation, a night-time polysomnography and cognitive-behavioral tests (Kaufman Brief Intelligence Test and Achenbach Child Behavior Checklist (CBCL)). **Results :** Eight of 10 children had clinically significant bruxism and the two remaining patients had recent teeth exfoliation making assessment difficult. There was no difference on sleep architecture between patients and controls, except for a higher arousal index for the bruxism group (36.7 vs. 20.7,  $p < 0.007$ ). Sleep bruxism occurred more frequently in stage 2 and REM sleep with associated arousals in 66% of the cases. There was no relationship of bruxism to gastro-esophageal reflux or intelligence (KBIT). However, forty percent of the patients had elevated scores on the CBCL indicating parental reports of significant attention and behavioral problems, and there were moderate correlations between the arousal index (number of arousals per hour) and several of the behavioral problem scales from the CBCL (0.5 to 0.6).

**Conclusion :** The data suggest that children with bruxism have a higher arousal index, which may be associated with an increased incidence of attentional and behavior problems. Future studies investigating pediatric sleep bruxism will need to focus on behavioral issues that may be prevalent in this population.

**Support (optional):**

### 0233

#### OBSTRUCTIVE SLEEP APNEA AND INSULIN RESISTANCE IN OBESE CHILDREN

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**Introduction :** Previous evidence has demonstrated the association between obstructive sleep apnea (OSA) and obesity in adults. It has been suggested that OSA may increase the risk of developing cardiovascular disease independent of obesity. However, these associations have yet to be fully evaluated in children.

**Methods :** We studied 26 (12 M, 14 F) obese children (mean BMI 36 +/- 8.7) with a mean age of 12.6 +/- 3.9 years old (range 5 - 18.5 years old), who were referred for polysomnography because of sleep related complaints. Height and weight measurements, polysomnography studies, as well as an OGTT and fasting lipid panel were obtained. The homeostasis model of insulin resistance index (HOMA-IR) was calculated as a marker of insulin resistance.

**Results :** Among the 26 obese children, the prevalence of OSA (defined as an apnea/hypopnea index  $> 1.5$  and a minimum oxygen saturation of  $< 92\%$ ) was 81%. Both the HOMA-IR and triglyceride levels were significantly higher in the subgroup of children with OSA than in those without ( $p < .05$ ). We then grouped the children according to quartile of BMI z score (or standard deviation score), and compared the polysomnogram results. No significant differences were found between subjects with the highest BMI z scores and subjects with the lowest BMI z scores.

**Conclusion :** Our results suggest that, even in the pediatric population, markers of insulin resistance and the metabolic syndrome are associated with obstructive sleep apnea. Obesity does not seem to be a confounding factor. Further studies in a larger population sample are warranted.

**Support (optional):**

### 0234

#### NURSE-REPORTED SLEEP IN HOSPITALIZED CHILDREN

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**Introduction :** Past research into the sleep of hospitalized children has focused on disrupted sleep in the pediatric intensive care unit. However, no specific analyses of in-hospital sleep disturbance as experienced by different sub-types of pediatric inpatients have been reported. The primary goal of this study was to determine if illness type [acute life threatening (ALT; i.e., traumatic brain injury), acute non-life threatening (ANLT; i.e., appendicitis), chronic life threatening (CLT; i.e., neoplasms), or chronic non-life threatening (CNLT; i.e., diabetes)] was related to the likelihood of in-hospital sleep disruption.

**Methods :** Nurses of 621 hospitalized children and adolescents, ages infancy through 19 years, completed the Pediatric Inpatient Behavior Scale (324 females; 292 males). Mean age of the sample was  $12.27 \pm 3.9$  years. Three specific items were analyzed regarding enuresis, poor sleep, and nightmares.

**Results :** ANOVA analysis indicated a significant difference between groups in the category of poor sleep ( $F = 3.35$ ;  $p = .019$ ). There were no differences between groups on reported enuresis ( $F = 1.90$ ;  $p = .129$ ) or nightmares ( $F = 1.02$ ;  $p = .382$ ). Post-hoc analyses revealed that the CLT group showed significantly poorer sleep than the CNLT group ( $p = .002$ ).

**Conclusion :** According to nurse reports, children with chronic life threatening illnesses suffer from poorer sleep than any other hospitalized children, specifically those with chronic non-life threatening illnesses. As children with chronic non-life threatening illnesses also experience repeated hospitalizations, the poor sleep in these patients could be due to the stress and nature of the life threatening illnesses as opposed to specifically in-hospital sleep disruption. These findings may be useful for further exploration of sleep problems in hospitalized children with chronic illnesses.

**Support (optional):** NIH HL65270, The Children's Foundation Endowment for Sleep Research, and Norton Healthcare Community Trust

### 0235

#### OCURANCE OF OBSTRUCTIVE SLEEP APNEA IN CHILDREN WITH SICKLE CELL DISEASE

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**Introduction :** Emerging data suggest that Obstructive Sleep Apnea Syndrome (OSAS) is common among patients with sickle cell disease (SCD). However, previous studies have relied on nocturnal oxygen saturation monitoring to assess the co-morbidity of these two conditions. The objective of this study was to evaluate with polysomnography (PSG), a group of children with SCD who had symptoms suggestive of OSAS.

**Methods :** PSGs of patients with SCD with snoring and irregular nighttime breathing referred to our sleep laboratory between 2004 and 2005 were reviewed.

**Results :** Nineteen patients (13 boys, ages 2.8-19.3 years; mean: 10.5 years) underwent PSGs. Mean BMI was 19.6 (range: 13 - 37). Mean REM and slow wave sleep percentages were 17.6% (range: 0 - 30%) and 21.6% (range: 11 - 33%). Mean arousal index was 30/hr (range: 12-60/hr). Lowest oxygen saturation mean was 82.5%, (range: 61 - 97%). Peak end tidal CO<sub>2</sub> mean was 55 mm Hg (range: 40 - 68 mm Hg). Mean Apnea/hypopnea index (AHI) was 4.2/hr (range: 0 - 22/hr). 78% of patients had  $> 50\%$  of their episodes during REM sleep, and 40% had  $> 50\%$  of their episodes in supine position. Mean snoring percentage was 61.5%, (range: 0 - 100%). Mean duration of desaturation  $< 92\%$  was 26 minutes (range: 0 - 139 minutes) which was 8.1% of total sleep time. Overall, 15 patients (79%) were diagnosed with OSAS and upper airway resistance syndrome. A total of 5 patients with OSAS subsequently had adenotonsillectomy. A follow-up PSG performed on one of these patients

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showed improvement from moderate OSAS to habitual snoring.

**Conclusion :** OSAS appears to be a common co-morbid condition in children with SCD. As such, physicians treating patients with SCD should screen for OSAS in this population, since treatment of OSAS will improve the overall medical and neuro-cognitive outcome of these children.

**Support (optional):** Pennsylvania Department of Health Impact Grant

### 0236

#### LONGITUDINAL DOCUMENTATION OF NREM DELTA EEG DECLINE IN EARLY ADOLESCENCE

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**Introduction :** Cross sectional studies suggest that NREM delta (SWS) declines from age 5 through 20, with the decline being steepest from age 10 through 20. We have hypothesized that this decrease reflects brain maturational processes that include synaptic pruning and decreased cerebral metabolism. We present here data from an ongoing longitudinal study of sleep EEG and related measures in two age cohorts: C9, initially age 9, and C12, initially age 12.

**Methods :** Data are from the first 4 semiannual recordings of sleep EEG in C9 (n=31, 16 female) and C12 (n=38, 19 female). All subjects were studied in their own homes on their habitual sleep schedules with ambulatory recorders. EEG power density (power/min) in the 0.3-3 Hz (delta) band was calculated using PASSPLUS for all artifact free epochs in the first 5 hours of NREM sleep.

**Results :** In C9 NREM delta power density did not change significantly ( $F_{3,87}=0.32$ ,  $p=0.8$ ) across 9.3 - 11.9 years, and there was no effect of sex. In C12 delta power density decreased by about 25% over the ages 12.3-13.9 years ( $F_{3,108}=40.3$ ,  $p<0.0001$ ). Power density was lower in girls than boys ( $F_{1,36}=13.1$ ,  $p=0.0009$ ), but their declines were parallel. While we present only data for delta, in C12 subjects power density also changed in other frequencies.

**Conclusion :** The stable delta power density in C9 contradicts the cross-sectional data and suggests that the brain maturational processes reflected in the delta decline have not fully begun until after age 11. The C12 data indicate that these maturational processes occur at about the same rate in boys and girls. However, the girls appear to have initiated their adolescent brain maturation earlier since their absolute delta levels are lower.

**Support (optional):** NIH grant RO1MH62521 supported this work.

### 0237

#### FIRST LONGITUDINAL EVIDENCE SHOWING THAT THE DELTA DECLINE IN ADOLESCENCE IS INDEPENDENT OF SEXUAL MATURATION (TANNER STAGE) AND SOMATIC GROWTH

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**Introduction :** The decline in NREM delta EEG across adolescence is one of the most dramatic manifestations of late brain maturation. Longitudinal studies are required to determine whether this decline is linked to concomitant physical growth and sexual maturation.

**Methods :** Four consecutive nights of sleep EEG are being obtained with home (ambulatory) recordings at 6 month intervals in two cohorts: C9, initially age 9 yrs (n = 31, 16 girls), and C12, initially age 12 yrs (n=38, 19 girls). Height and weight were obtained on the study week. One physician judges Tanner stage by direct physical observation on all subjects. Four semiannual recordings have been completed and analyzed in this ongoing study. Delta (0.3-3 Hz) EEG was analyzed with FFT by PASS-

PLUS. Delta power/min was calculated for the first 5 hrs of NREM sleep.

**Results :** There were no significant changes in C9 in either delta power density or Tanner stage between 9.3-11.9 yrs. In C12 delta power decreased and Tanner stage, height and weight increased significantly between 12.3-13.9 yrs. A mixed effect analysis revealed that age was significantly related to the delta decline with Tanner controlled, but Tanner stage, height, weight and BMI were not significantly related to delta power with age controlled. This result also held for boys and girls separately.

**Conclusion :** The physical manifestations of sexual maturation (Tanner stages) and somatic growth are unrelated to the delta decline, supporting our view that this decline is fundamentally related to changes in brain structure and physiology. Nevertheless, it remains possible that reactivation of hypothalamic GnRH secretion (which drives sexual maturation) interacts with other hypothalamic/brain systems to trigger or otherwise participate in regulating the brain changes of adolescence. Measurement of sleep EEG may provide an inexpensive, non-invasive, precisely measurable index of adolescent brain reorganization.

**Support (optional):** NIH grant RO1MH62521 supported this work.

### 0238

#### SLEEP PROBLEMS IN AUSTRALIAN INDIGENOUS CHILDREN

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**Introduction :** Up to 40% of primary school children in Australian communities report significant sleep problems but their frequency more specifically in indigenous Australian children, of Aboriginal or Torres Strait Islander ancestry, has not been studied. The aim was to assess sleep problems in Australian indigenous children and compare them to a group of matched non-indigenous children.

**Methods :** Children from years 1-6 in seven urban schools in Darwin Australia were invited to participate in the study. Parents completed the well-validated Sleep Disorders Scale for Children (SDSC), which generates six T-scores [mean=50 (SD = 10)] for several types of sleep problems and a total sleep problem score.

**Results :** Results From a total sample of 136 children, 25 indigenous subjects were matched for age (mean years (SD) 9.05 (1.47), range 7.01 - 12.10), year at school, and gender with 25 controls from the same schools. Mean (SD) differences in sleep problems T-scores between Indigenous and Non-Indigenous were as follows ; behavioural sleep problems 57.6 (14.4) vs 62.4 (13.1) ; sleep disordered breathing 49.4 (12.3) vs 51.0 (9.4), arousal disorders 58.1 (18.1) vs 54.0 (10.7), sleep wake transition disorders 57.7 (17.3) vs 56.8 (14.1), excessive daytime sleepiness 52.2 (10.5 vs 59.1 (14.1), and total sleep problems 57.0 ( 15.2) vs 60.4 ( 13.2). ANOVA revealed only one trend towards significance for excessive daytime sleepiness ( $p = 0.06$ ).

**Conclusion :** Conclusion: These findings suggest that childhood sleep problems are similarly frequent in children from indigenous families despite potential differences in cultural traditions and genetic heritage. Children from non-indigenous backgrounds, in comparison to those from indigenous families, may have more difficulty with excessive daytime sleepiness.

**Support (optional):**

## 0239

## THE RELATIONSHIP BETWEEN SLEEP AND BODY MASS INDEX (BMI) IN AUSTRALIAN CHILDREN

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**Introduction :** Reduced sleep duration in adults may contribute to risk for overweight and obesity. We therefore aimed to study the relationship between sleep and BMI in Australian school children.**Methods :** Parents of children at 7 urban primary schools in Darwin, Australia completed the well-validated Sleep Disorders Scale for Children (SDSC). Children completed a sleep diary. The SDSC generates T-scores [mean=50 (SD = 10)] for total sleep problems and more specifically for behavioural problems with sleep initiation or maintenance; sleep-disordered breathing; arousal disorders; sleep-wake transition disorders; excessive daytime sleepiness and hyperhydrosis.**Results :** Questionnaires were completed by 136 children (79 girls) with mean age (SD) 9.2 (1.5) years, range 6.1-12.1. Participants resembled non-participants in age and ethnicity, but girls were over-represented ( $p < 0.05$ ). BMI was not available for 24 children. Of the remaining children, 22 (19.6%) were overweight and 9 (8.0%) were obese based on published standards (Cole et al, 2000). Among the 6 children who slept 7 hours or less each night, 2 did not report BMI, 1 had a normal BMI (17.7), and the remaining 3 were either obese (BMI=22.0) or overweight (18.7, 20.5). Correlations between BMI and each SDSC score showed moderate associations between BMI and excessive daytime sleepiness ( $r = 0.24$ ,  $p < 0.05$ ), and between BMI and total sleep problems ( $r = 0.27$ ,  $p < 0.01$ ). No other significant relationships were found.**Conclusion :** In this initial sample of schoolchildren, higher BMI was associated with overall reports of sleep problems, and with daytime sleepiness in particular, though not with reduced sleep time or symptoms of sleep-disordered breathing. These findings raise the possibility that impaired sleep in children could contribute to overweight.**Support (optional):**

## 0240

## PLAYING AS AN INSTRUMENT OF COPING WITH STRESS IN SLEEP DISORDERS

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**Introduction :** In response to all kinds of stressful stimuli, the Hypothalamic-Pituitary Adrenal axis is requested to perform the "fight and run" reaction, releasing pituitary adrenocorticotrophic hormone which on its turn facilitates the release of glucocorticoid hormones. Sleep disorders may act as hidden stressful factors in children. This study investigated if playing is a good instrument of coping with stress in children with sleep breathing disorders (SBD)**Methods :** 190 children ranging from ages 4 to 14.91 years were examined for plasma cortisol levels (PCL) from March to September, 2005. Caretakers answered a sleep questionnaire to establish which children presented SBD according to Bruni's criteria. The children were offered to play in a toy library in alternating weeks, and came to the laboratory for regular blood tests. The blood samples were collected at 8 a.m.**Results :** The sample consisted of 96 boys (mean age 8.86  $\pm$  2.8) and 94 girls (mean age 8.92  $\pm$  2.86) divided in 2 groups: control (CG - didn'tplay) with 90 children and experimental group (EG - played) with 100 children, and a sub group with children who refused to play in the EG (ERP, n=46). 69 children (36.3%) had SBD, with mean PCL (MPCL) of 12.39  $\mu$ g/dl  $\pm$  5.15. Children with SBD in the CG showed MPCL of 13.40  $\mu$ g/dl  $\pm$  5.20 and those in the EG had MPCL of 10.01  $\mu$ g/dl  $\pm$  3.70 ( $p \leq 0.009$ ). Comparing the EG and ERP (MPCL = 13.29  $\mu$ g/dl  $\pm$  5.64) groups with SBD,  $p$  was  $\leq 0.05$ .**Conclusion :** Plasma Cortisol Levels were lower among SDB children who played compared to those that did not, suggesting that playing seems to be a good tool of coping with stress in children with SBD.**Support (optional):**

## 0241

## WHY ARE TEENS SO SLEEPY?

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**Introduction :** Adolescent sleepiness is well-documented; however, factors which affect sleepiness are not widely understood. The aim of this study was to examine the effects of subject characteristics and sleep time on sleepiness in adolescents who are participating in the Cleveland Children's Sleep and Health Study, a community-based cohort of 13-16 year-old adolescents.**Methods :** Data on sleep time were gathered from 3-7 day wrist actigraphy (Ambulatory Monitoring Inc., Ardsley, NY) and from adolescent reported sleepiness via the Epworth Sleepiness Scale (ESS). Linear regression was used to assess the association between subject characteristics including gender, age, ethnicity, pubertal status, preterm status, body mass index (BMI), and attention deficit hyperactivity disorder (ADHD), as well as average total sleep time, with sleepiness.**Results :** Participants (n=208) had a mean age of 13.6 (+0.4), were 53.4% male, 51.9% ethnic minorities, 55.8% preterm, and had a mean sleep time of 7.9 (+0.94) hours. The mean ESS score was 8 (+4.5) with 26.6% of the sample reporting clinically significant sleepiness (ESS score > 10). In multivariable models, minority status was significantly associated with sleepiness when controlling for socioeconomic variables and vacation status; minority teens reported being sleepier than non-minority teens (9.04 vs. 6.90;  $p < .005$ ). Conversely, teens born prematurely reported being less sleepy than term-born teens (7.37 vs. 8.80;  $p < .05$ ). Associations with other subject characteristics were not found. Average total sleep time was also inversely associated with level of sleepiness ( $p < .05$ ). In addition, the inclusion of sleep time did not explain the association of sleepiness and minority ethnicity.**Conclusion :** Analysis of the association of subject characteristics and sleep time with sleepiness showed that minority teens, those born full-term, and those with the least mean sleep time reported being the sleepiest. Interventions to reduce teen sleepiness should address sleep time as well as target vulnerable groups such as minority teens.**Support (optional):**

## 0242

## DEMOGRAPHIC INFLUENCES ON SLEEP DURATION AND NIGHT-TO-NIGHT SLEEP VARIABILITY IN AN URBAN COMMUNITY SAMPLE OF ADOLESCENTS

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## Category F—Pediatrics

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**Introduction :** Adolescents experience normative biopsychosocial changes which may contribute to insufficient as well as irregular sleep. The aim of this study was to describe the association between gender, ethnicity, parent income, and parent education with sleep time and variability of sleep time in a cohort of 13-16 year-old adolescents who are participating in the community-based Cleveland Children's Sleep and Health Study.

**Methods :** Outcome variables were estimated from 3-7 day wrist actigraphy (Ambulatory Monitoring; Ardsley, NY). The association of gender, ethnicity, parent income, and parent education with mean total sleep time and mean night-to-night variation was evaluated using linear regression; analyses were adjusted for potential confounders (e.g., age, preterm status, BMI, attention deficit hyperactivity disorder (ADHD), and vacation status (on vacation or usual school schedule during actigraphy).

**Results :** The sample consisted of 213 adolescents (54% males; 52% ethnic minorities) with a mean age of 13.59 +0.64 yrs. Mean sleep time was 7.91 (+0.94) hours, and the average coefficient of variation (a measure of night-to-night variation in sleep time), was 16% (+8%). Gender and minority status were found to be associated with total sleep time, with boys averaging less sleep than girls (7.70 vs. 8.11 hours;  $p<.005$ ) and minorities averaging less than non-minorities (7.71 vs. 8.10 hours;  $p<.01$ ). Minorities also demonstrated more night-to-night variation than non-minorities ( $p<.005$ ).

**Conclusion :** Analysis of the associations of gender, ethnicity, parent income, and parent education with total sleep time and night-to-night variability indicate that shorter sleep duration is associated with male gender and minority status, and that more variability is associated with minority status. In contrast, adjusted models indicated that sleep time and variability was unassociated with parent income or education. Findings suggest the potential utility of targeting boys and minority children for interventions aimed at improving sleep habits.

**Support (optional):**

### 0244

#### HEART RATE VARIABILITY DURING SLEEP IN CHILDREN WITH MILD SLEEP-DISORDERED BREATHING

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**Introduction :** Changes in autonomic system have been described in adults with SDB. The author's hypothesis is that mild SDB in children can present abnormal autonomic activity during sleep. The aim of this study was to investigate the heart rate variability during sleep in children with mild SDB.

**Methods :** 10 children and adolescents with mild SDB, and 10 controls matched for age, gender and Tanner stage were studied. All subjects underwent clinical evaluation and polysomnography. HRV was performed in each sleep stage. The Standard Time and Frequency Domains were calculated for each 5-minute period.

**Results :** All patients were chronic heavy snorers. They presented an AI=0, HI= 0.8, RDI=10.2/h and with a lowest SaO<sub>2</sub>Hb = 96.1±2.4%. The total power of HRV was decreased in all stages but it was significant during slow wave sleep (SWS) (U test;  $p=0.04$ ). There was also a decrease in NN50 during all sleep stages compared to healthy controls: in stage 2 [14

(75) vs 120 (75)]; in slow wave sleep [17 (15) vs 115 (84)]; and in REM sleep [14 (15) vs 99 (63)], respectively (U test;  $p<0.01$ , all).

**Conclusion :** Reduction in HRV, associated to possible predominant reduction in parasympathetic tone may represent an autonomic impairment during sleep in children with mild SDB.

**Support (optional):**

### 0245

#### POLYSSOMNOGRAPHIC EVALUATION OF THE AIRWAY LIMITATION IN PATIENTS WITH CLASS II, DIVISION 1 MALOCCLUSION AND MANDIBULAR RETROGNATHISM TREATED WITH THE HERBST APPLIANCE

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**Introduction :** The objective of this investigation was to examine the sleep pattern in adolescents (maximum peak of puberty development) with Class II, division 1 malocclusion and mandibular retrognathism treated with the Herbst appliance.

**Methods :** Polysomnographic recordings were obtained from 16 adolescents with Class II, division 1 malocclusion and mandibular retrognathism pre-treatment, 5 months after initiated treatment and post-treatment with the Herbst appliance. All patients had permanent denture and were either at stage 3 or 4 of skeletal maturation, according to the technique described by Helm et al. (1971).

**Results :** After a year of treatment with the Herbst appliance, we verified a statistically significant reduction in the number of events of upper airway limitations ( $p<0.001$ ) detected by the nasal canula, that is, there was a reduction in resistance of the upper airways.

**Conclusion :** Our results suggest that precocious treatment of Class II, division 1 malocclusion and mandibular retrognathism promotes reduction in the resistance of the upper airways manifested by a significant reduction in the number of air flow limitations detected by the nasal canula. Thus, the precocious treatment of mandibular retrognathism may diminish the risk of obstructive sleep apnea-hypopnea syndrome at older ages when there occurs greater muscular flaccidity, once this bone anomaly is described in the literature as a risk factor for this syndrome.

**Support (optional):** AFIP, FAPESP, CEPID

### 0246

#### ASSESSMENT OF THE VOLUME OF THE UPPER AIRWAYS IN ADOLESCENTS TREATED WITH THE HERBST APPLIANCE

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**Introduction :** The objective of this investigation was to evaluate the volume in the upper airways of adolescents with Class II, division 1 malocclusion and who were treated with the Herbst appliance.

**Methods :** Magnetic resonance graphs were obtained from 16 adolescents with Class II, division 1 malocclusion and mandibular retrognathism, pre and post treatment with the Herbst appliance. All patients had permanent dentures and were at stage 3 or 4 of skeletal maturation, that is, at the maximum peak of pubertal growth. The upper airway was divided into three distinct segments and assessed so. The overall volume of the upper airway was also assessed.

**Results :** The portions that were evaluated were the nasopharynx, oropharynx and the hypopharynx. A statistically significant ( $p<0.001$ ,  $p<0.01$  and  $p<0.001$ , respectively) volumetric increase was observed as a consequence of growth stimuli imposed to the mandible by treatment with the Herbst. When the upper airways were evaluated as a whole, the



increase in volume was also statistically significant ( $p < 0.001$ ) in relation to the volume verified at the beginning of the treatment of Class II, division 1 malocclusion and mandibular retrognathism.

**Conclusion :** Our results suggest that the precocious treatment of Class II, division 1 malocclusion and mandibular retrognathism provides an augmentation of volume in all of the three portions that were evaluated as well as in the overall volume of the upper airway. We thus raised the hypothesis that precocious treatment of mandibular retrognathism may diminish the risk of developing obstructive sleep apnea-hypopnea syndrome, once this bone abnormality is described in the literature as a risk factor for this syndrome.

**Support (optional):** AFIP, FAPESP, CEPID

## 0247

### SLEEP CYCLIC ALTERNATING PATTERN AS A MARKER OF CHRONIC PAIN AND SLEEP LOSS AS A MARKER OF INFLAMMATORY PROCESS IN CHILDREN

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**Introduction :** Pain has a strong influence in the quality of life with daily fluctuations in wellbeing in adults and children. Changes in EEG sleep patterns are expressed as sleep fragmentation. Sleep loss has been described as contributor to inflammation in adults. The aim of this study was prospectively to investigate the sleep disturbances in an inflammatory chronic syndrome, juvenile idiopathic arthritis (JIA). It was performed in order to correlate the sleep fragmentation parameters with clinical manifestations of disease.

**Methods :** 12 young individuals between the ages of 9 and 17 years with JIA were compared to controls matched for age, Tanner stage and gender. All subjects underwent polysomnography after one night of habituation to the sleep laboratory. The recordings were analyzed blindly for staging scoring, ASDA arousal, and visual cyclic alternating pattern (CAP) scoring.

**Results :** JIA patients showed an increase in nocturnal disrupted sleep compared to controls as indicated by ASDA arousal scorings and mostly by CAP analyses. The overall CAP rate was significantly higher in children with chronic pain than in controls ( $p < 0.01$ ). A positive correlation was found between the time awake after sleep onset (WASO) and the index of phase A2 subtype during slow wave sleep (SWS) ( $rS = 0.62$ ;  $p < 0.01$ ). The number of joints with impairment and painful process was positively correlated with CAP rate ( $rS = 0.24$ ;  $p < 0.01$ ) and ASDA arousal index ( $rS = 0.29$ ;  $p < 0.01$ ). Finally, the erythrocyte sedimentation rate was strongly correlated with WASO in minutes ( $rS = 0.76$ ;  $p < 0.01$ ) but negatively correlated with CAP rate ( $rS = -0.48$ ;  $p < 0.01$ ).

**Conclusion :** CAP analysis is an important tool to investigate children with chronic pain during sleep and sleep loss can be a marker of inflammatory process in children with JIA. Further studies in other inflammatory diseases are needed.

**Support (optional):** Dr. MC Lopes was supported by FAPESP-CEPID (98/14303-3), FAPESP (2003/12208-3), and AFIP, FCT-BSAB (373).

## 0248

### OBSTRUCTIVE SLEEP APNEA SYNDROME IS HIGHLY PREVALENT IN CHILDREN 4-10 Y.O. WITH TONSILLAR HYPERTROPHY

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**Introduction :** Tonsillar hypertrophy is a recognized risk factor for obstructive sleep apnea syndrome (OSAS) in childhood. Conversely, it is known that a large proportion of children with tonsillar hypertrophy do not have obstructive sleep apnea. The purpose of this study was to determine the degree to which tonsillar hypertrophy increases the risk for OSAS as well as to assess the sensitivity and specificity of a history of snoring in this high risk group.

**Methods :** 226 children ages 4-10 y.o. were enrolled from 2 private pediatric practices at the time of the child's yearly well child evaluation. The subjects' parents completed a short questionnaire including 7 breathing and snoring related questions from the Pediatric Sleep Questionnaire (PSQ). The pediatrician completed a brief form grading tonsil size from 0 to 6 using sample pictures. Children with tonsils graded as  $\geq 3$  (taking up 51-75% of the lateral diameter of the posterior pharynx) were recruited to undergo polysomnography.

**Results :** 59 children were identified with tonsillar hypertrophy. Of those, 22 underwent polysomnography. 41% (9/22) were found to have obstructive sleep apnea as defined by an apnea-hypopnea index of  $\geq 5$  events/hour. History of symptoms suggestive of OSAS were not predictive of positive polysomnography. A history of snoring  $\frac{1}{2}$  the time had a sensitivity=55% and a specificity=69%; history of loud snoring had a sensitivity=67%, specificity=85%; and history of heavy breathing during sleep had a sensitivity=78%, specificity=54%.

**Conclusion :** Children with tonsillar hypertrophy have a high prevalence of OSAS. Historical information regarding symptoms of sleep disordered breathing is neither sensitive nor specific for the presence of polysomnographically identifiable obstructive sleep apnea in these high risk individuals. These children may require routine screening polysomnograms given the poor predictive value of parentally reported symptoms.

**Support (optional):**

## 0249

### RISK FACTORS FOR SYMPTOMS OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN CHILDREN AGES 4-10 Y.O. WITHOUT TONSILLAR HYPERTROPHY

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**Introduction :** Tonsillar hypertrophy has long been recognized as a risk factor for obstructive sleep apnea syndrome in childhood. However, some children without tonsillar hypertrophy also have obstructive sleep apnea. The purpose of this study was to determine risk factors for obstructive sleep apnea syndrome in children without tonsillar hypertrophy.

**Methods :** 226 children were enrolled from 2 private pediatric practices at the time of the child's yearly well child evaluation. The subjects' parents completed a short questionnaire that included 7 breathing and snoring related questions from the Pediatric Sleep Questionnaire (PSQ). The pediatrician then completed a brief form grading tonsil size from 0 to 6 using sample pictures of each size. Tonsils graded as 3 (taking up 51-75% of the lateral diameter of the posterior pharynx) or higher were considered "large". The parent's responses on the 7 PSQ questions were summed (sum-PSQ), and a score of 3 or higher was utilized to define a group with symptoms strongly suggestive of obstructive sleep apnea. We then analyzed which factors were associated with sum-PSQ  $> 3$  in those without tonsillar hypertrophy.

**Results :** The factor most associated with a sum-PSQ  $\geq 3$  was tonsil size of 3 or higher (18/59, 31%). The frequency of sum-PSQ  $\geq 3$  in those with-

## Category F—Pediatrics

out tonsillar hypertrophy was only 8% (13/167). History of allergies (6/13) and parentally reported mouth breathing (5/13) were identified as statistically significant ( $p < 0.005$ ) associated risk factors for  $\text{sum-PSQ} \geq 3$  in children without tonsillar hypertrophy.

**Conclusion :** The most significant risk factor for symptoms of obstructive sleep apnea syndrome is tonsillar hypertrophy. In children without tonsillar hypertrophy, both a history of allergies or a history of mouth breathing were significantly associated with symptoms of obstructive sleep apnea.

**Support (optional):**

### 0250

#### OBJECTIVE QUANTIFICATION OF SHORT SLEEP DURATION IN OBESE CHILDREN

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**Introduction :** Shorter sleep duration has been linked to an increased prevalence of obesity in children and adults. However, this relationship was established through questionnaires to subjectively estimate sleep duration.

**Methods :** 34 children were recruited through primary care clinics and the school system. Each group had anthropometric measurements (height, weight, BMI) and wore an actigraph for 24 hours over 7 days.

**Results :** The obese group (Ob) of 21 children was significantly older (Mean age =  $10.4 \pm 1.9$  years) than the normal weight (NI) group of 13 children (Mean age =  $8.0 \pm 1.0$  years;  $t = 4.23$ ,  $p < .001$ ). Ob had significantly more African American children (86%) than did NI (8%;  $\chi^2 = 15.7$ ,  $p < .001$ ). Mean BMI of Ob was  $30.39 \pm 5.5$  ( $z = 2.28 \pm .31$ ) and of NI was  $15.89 \pm 2.0$  ( $z = -.09 \pm 1.05$ ). Females were overrepresented (62%), but there were no gender differences between groups. Analysis of covariance and partial correlations were obtained using age, gender, and race as covariates. Ob obtained significantly less sleep each night (Mean = 495.2 minutes) than NI (Mean = 566.7 minutes;  $F = 7.3$ ,  $p < .001$ ). Ob had a significantly later mean sleep onset time (11:26 p.m.) than NI (10:37 p.m.;  $F = 4.3$ ,  $p < .01$ ). BMI z-scores were significantly correlated with mean total sleep time (partial  $r = -.43$ ,  $p = .018$ ). Using multiple linear regression, mean total sleep time, mean sleep onset time, and mean wake time significantly predicted BMI z-scores ( $R^2 = .43$ ,  $p = .001$ ).

**Conclusion :** Using actigraphic recordings, obese children slept 71.5 minutes less each night than their normal weight peers, even while controlling for race, gender, and age. This is most likely due to their later bedtimes (49 minutes later than NI). These findings may be useful in understanding mechanisms underlying pediatric obesity.

**Support (optional):** NIH Grant # RO1 HL 070911-01 and University of Louisville School of Medicine Grant-in-Aid

### 0251

#### ORAL APPLIANCES AND FUNCTIONAL ORTHOPEDIC APPLIANCES FOR SLEEP OBSTRUCTIVE APNEA IN CHILDREN - COCHRANE SYSTEMATIC REVIEW

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**Introduction :** The most common treatment for obstructive sleep apnea syndrome (OSAS) in childhood is adenotonsillectomy. This approach is limited by its surgical risks and in some patients, by recurrence that can be associated with craniofacial problems. Functional Orthopedic Appliances (FOA) have been used for patients who have OSAS and craniofacial anomalies because they change the mandible posture forwards and potentially enlarge upper airway and increase upper airway, improving the respiratory function. Objective: To assess the effectiveness of Oral Appliances (OA) and/or FOA for OSAS in children.

**Methods :** Search strategy: Types of studies: A sensitivity search was realized for randomized or quasi-randomized controlled trials (RCT) on Cochrane library, Pubmed, Embase, Lilacs, Scielo, and Brazilian Odontology Bibliographic, without restriction of language or source of information using MeSH and free terms. References from original papers and review articles were cross-checked to identify additional trials. Types of participants: Children and adolescents, in which over 80% of included participants are 15 years or younger, receiving OA/FOA to treat obstructive sleep apnea. Trials including patients with cleft lip and/or palate were excluded. There was no gender restriction. Types of intervention: All types of OA/FOA used to treat OSAS were compared to placebo or no treatment. Types of outcome measures: Primary outcome: Reduction to less than one episode of apnea. Secondary outcomes: dental and skeletal relationship, improvement sleep parameters, cognitive and phonological function, behavioral problems, drop outs and withdrawals, quality of life, side effects (tolerability), economic evaluation.

**Results :** 384 articles were met, but only 1 of them was included, but without all outcomes searched. This paper treating SDB (Sleep Disordered Breathing) with oral appliance reported lower apnea hypopnea index after treatment.

**Conclusion :** There is a lack of RCT in children addressing the treatment of SDB with OA/FOA. We suggest these clinical trials on SDB should include craniofacial, respiratory sleep variables, phonological and cognitive outcomes.

**Support (optional):**

### 0252

#### SLEEP AND NAP TIMES IN PRESCHOOL CHILDREN ATTENDING CHILD CARE CENTERS

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**Introduction :** Preschool children are confronted with multiple challenges, such as transition to child care, development of emotional regulation, social competence, peer relationships, and longer periods of parent-child separation that influence their daily routine and sleep schedule. This study describes night sleep and nap times in boys and girls attending child care.

**Methods :** Data were collected from 53 children in two full-day university-affiliated child care centers. Ankle actigraphy was used continuously to estimate night sleep and nap times on 3 consecutive weekdays (Tuesday-Thursday). Children were also simultaneously observed during naps. Parents used a sleep diary to record their child's sleep at home.

**Results :** Parents were partnered and had moderate to high income. Children were 43% White, 32% multi-ethnic, 15% Chinese, 4% Black, 4% Hispanic, 2% Korean, and 2% Native American. They ranged in age from 27 to 59 (46.4+7.9) months; 57% were male and 43% were female. At night, children slept 551+49.8 minutes. There was no significant difference in total sleep time (TST) between boys and girls. Mean TST was

549+52.5 minutes for boys and 553+43.3 minutes for girls. Average nap time was 62.3+31.7 minutes by actigraphy and 61.6+32.9 minutes by observation. Actigraphy and observation measures of nap times were not significantly different and were correlated ( $r>.88$ ) on day 2 and day 3. There was no significant difference in nap time between boys and girls. Five of the 53 children did not nap. Mean actigraphy nap time for boys was 63.5+30.8 minutes and mean actigraphy nap time for girls was 60.1+35.5 minutes.

**Conclusion :** Given that 25% of preschool children experience sleep disturbances, and over 80% attend childcare outside their home environment, results from this study may further our understanding of expectations for children's napping behavior during childcare and effects of poor sleep on their health and wellbeing

**Support (optional):** NIH Grant,T32NR07088 KA Lee, P.I.

## 0253

### FAMILY INVENTORY OF SLEEP HABITS: RELIABILITY AND APPLICATION TO CHILDREN WITH AUTISM SPECTRUM DISORDERS

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**Introduction :** Sleep hygiene plays a pivotal role in initiating and maintaining sleep. We developed and piloted the Family Inventory of Sleep Habits (FISH) to quantify sleep hygiene in children with autism spectrum disorders (ASD) as a tool to identify and treat causes of insomnia in this population. The FISH is an 11-item scale that assesses sleep habits, such as whether the child engages in stimulating activities (e.g. video games) before bed and presence of a bedtime routine.

**Methods :** Participants with ASD were 4-10 years old, had normal cognitive function and were free of psychotropic medications and seizures; age-matched typically developing (TD) children were also included. Parents completed the FISH, the Child Sleep Health Questionnaire (CSHQ; Owens, 2000), and the Parental Concerns Questionnaire (PCQ, McGrew et al., unpublished), which quantifies parental concerns about children's functioning, including sleep.

**Results :** The sample included 28 children with ASD, 14 with no or mild parental sleep concerns (ASD good sleepers) and 14 with moderate to severe sleep concerns (ASD poor sleepers), and 20 children with TD, all with no or mild sleep concerns. Age did not differ among the groups (5.9 ± 1.6 years; mean ± standard deviation). Internal consistency for the FISH was 0.71 combined and 0.73 in the ASD group, and test-retest reliability was 0.82 combined and 0.87 in the ASD group. FISH score in the ASD poor sleepers was lower (i.e., less optimal) compared to ASD good sleepers and to TD children ( $p = 0.01$ ). Total FISH score was correlated with a modified CSHQ total score (that includes bedtime resistance, sleep duration, sleep onset delay, sleep anxiety, and night wakings;  $r = -0.52$ ;  $p < 0.0001$ ).

**Conclusion :** The FISH appears to be a reliable measure in children with ASD and may be a useful tool in assessing sleep hygiene in this population.

**Support (optional):** Vanderbilt University Interdisciplinary Discovery Grant Vanderbilt University General Clinical Research Center MO1 RR00095 Vanderbilt Kennedy Center for Research in Human Development National Alliance for Autism Research

## 0254

### CEPHALOMETRIC EVALUATION OF PHARYNGEAL AIRWAY IN CHILDREN ANGLE CLASS I, ANGLE CLASS II,1 AND ANGLE CLASS III

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**Introduction :** Angle's classification define anterior-posterior relationship between maxilla and mandible: Class I, normal anterior-posterior relationship; Class II.1, mandible is distal in relation to maxilla; Class III, mandible is mesial to maxilla. Our objective was to investigate if different relationship between maxilla and mandible reflect different pharyngeal spaces.

**Methods :** A cross-sectional study was conducted with lateral cephalograms of 90 children aged from 6 years and 4 months to 11 years and 9 months (45 boys, 45 girls); 30 in each Angle group (class I, II.1, III). The following dates were measured: PAS (pharyngeal airway space); SPAS (superior pharyngeal airway space); IPAS (inferior pharyngeal airway space) and two age groups were considered: age group 1 (6-9 years) and age group 2 (10-12 years). The Multiple Linear Regression, Kruskal Wallis K Test and Mann-Whitney U Test were used to compare the groups. The significance level was 0,05.

**Results :** Mean IPAS - there was no difference among groups; mean SPAS - in group class II.1 mean was larger than in group class III ( $p<0.05$ ) and not differing to group class I; mean PAS - in group class II.1 mean was smaller than in group class I and in group class III ( $p<0.01$ ). In Multiple Linear Regression, mean SPAS in female was larger than mean in male( $p<0.05$ ); mean PAS and mean IPAS in age group 2 were larger than in age group 1 ( $p<0.05$ ), and IPAS mean in group class II was smaller than in group 1 and 3 together ( $P<0.05$ ).

**Conclusion :** This cross-sectional study showed that children class II.1 present smaller pharyngeal airway space (PAS) than children class I or children class III and larger superior pharyngeal airway space (SPAS) when compared with children class III.

**Support (optional):**

## 0255

### AGE AND RACIAL DIFFERENCES IN THE SLEEP DISTRIBUTION OF 2- TO 12-YEAR-OLD CHILDREN

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**Introduction :** In adolescents and adults, functioning while awake is related to how sleep is distributed. This is especially true when wake/sleep patterns conflict with academic and work-related demands. In childhood, sleep distribution varies widely across individuals and groups (see Crosby et al., 2005), but relatively little is known about the significance of this variation. This report describes age and racial group differences in children's sleep distribution. Of interest were differences in napping, weekday vs. weekend sleep duration, and sleep phase (as indexed by mid-sleep time) that may have psychosocial significance.

**Methods :** Caretakers of 715 (66% White, non-Hispanic) 2- to 12-year-old children representative of a tri-county area in southern Mississippi provided demographic information and data on their child's sleep including napping behavior and weekend/weekday bedtimes and wake times.

**Results :** Although nearly all White children stopped napping by age 6 (school age), 64% of 6- to 12-year-old Black children continued to nap at least once per week. Beginning at school age in White children, weekend time in bed was 20-30 minutes longer than weekday time in bed. In Black children, this difference emerged at the age of 3. A progressive delay in mid-sleep time (MST; midpoint between bedtime and wake time) began at about the age of 8 for both groups. A later MST was seen in Black chil-

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dren relative to White children of all ages, especially on weekends (30-40 minute difference).

**Conclusion :** Differences in weekday/weekend time in bed suggest children may not be getting enough sleep on weekdays. The racial differences in nap tendency and sleep phase may be important to understanding racial differences in school readiness and academic performance.

**Support (optional):**

### 0256

#### A RETROSPECTIVE EXAMINATION OF BODY MASS INDEX AND POLYSOMNOGRAPHIC MEASURES OF SLEEP IN ADOLESCENTS

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**Introduction :** Studies have shown that total sleep is inversely associated with body mass index (BMI), an observation not well characterized in adolescents. The purpose of the study was to explore associations among polysomnographic (PSG) sleep measures and BMI (kg/m<sup>2</sup>).

**Methods :** A retrospective chart review was conducted of 52 adolescents ages 12 to 18 years evaluated with a laboratory-based polysomnogram at a university-affiliated sleep center. Height and weight were obtained via parental report. Exclusion criteria included diagnosis of narcolepsy, severe medical or psychological disease, and taking stimulant medications. The sample included 34 males (65.4%) and 18 females (34.6%); 51.9% were Caucasian, 38.5% were African American, and 7.8% were Hispanic. Subjects were categorized into three weight groups (normal weight, at risk for overweight, and overweight) based on CDC BMI-for-age and gender specific graphs. Nonparametric procedures were used for data analysis ( $\alpha = .05$ ).

**Results :** Mean BMI and age for the total group was  $30.27 \pm 11.61$  and  $14.32 \pm 1.82$  years, respectively. Of the total group 11.5% were at risk for overweight and 53.9% were overweight. The overweight group was significantly older than the normal weight group ( $z = -2.58$ ,  $p = .01$ ) indicating that the prevalence of obesity may increase with age. Mean TST for the entire sample was  $310.48 \pm 63.82$  minutes. There were no significant differences between the three groups in TST, % Stage 2, 3, or 4, obstructive apneas and limb movements. Significantly more % Stage 1 ( $z = -3.01$ ,  $p = .003$ ) and greater number of hypopneas ( $z = -2.29$ ,  $p = .022$ ) were noted in the overweight versus normal group and overweight versus at risk for overweight groups ( $z = -2.59$ ,  $p = .013$ ).

**Conclusion :** These findings suggest that sleep problems are associated with obesity and age. Further evaluation of this population may offer insights into the mechanisms underlying the relationship between sleep and obesity.

**Support (optional):**

### 0257

#### SLEEP AND PHYSICAL STRESS IN PEDIATRIC RESIDENTS: A PROSPECTIVE OBSERVATIONAL STUDY

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**Introduction :** Acute and chronic sleep deprivation and fatigue in physicians are associated with reduced performance, medical error and motor vehicle crashes. Duty-hour regulations were introduced to protect residents from causing or suffering harm. The Professional Association of Interns and Residents of Ontario (PAIRO) regulations limit the number of on-call days (maximum of 7) and stipulate 2 weekends without duty in any 28 consecutive day periods. They also ensure relief from duty by

noon of the post-call day. The goal of this prospective observational study was to describe walking distance, physical stress and sleep patterns during an on-call period in pediatric residents working within the PAIRO regulations.

**Methods :** Consenting senior and junior pediatric residents working within PAIRO regulations wore Actigraph wrist watches for their 4-week general pediatric rotation. Complete 24 hour blocks (8am-8am) of Actigraph data were identified and classified according to specified time-periods (on-call, post-call, working weekday, or weekend off). Total sleep duration was determined using Actigraph 4 software. The daily average sleep duration was calculated according to the standardized roster time-periods (7 on-call, 7 post-call, 10 weekday, 4 weekend days off). The physical burden of call was assessed in 62 additional on-call period periods by measuring total distance walked, post-call urinary specific gravity and post-call frequency of ketonuria.

**Results :** There were 407 usable 24-hour blocks [101 call, 83 post-call, 172 weekday & 51 weekend] from 26 residents (range 4-28 blocks each) over the 16 weeks studied (55% of all days). The mean sleep duration for residents during the 28-day study period was 7.3 hours/day. The hours slept for each 24-hour block were: 4.6hrs [call period], 9.5hrs [post-call], 7.2hrs [week day] and 8.7hrs [weekend]. Residents slept less than 4 hours in 49 (49%) shifts. In the 62 shifts with additional data, ketonuria occurred after 12(19%) shifts, the median distance walked was 5.5 km (3.1-7.2); median post-call urine SG was 10.25.

**Conclusion :** Acute sleep deprivation (<4h) still occurs during half of the on-call periods monitored, and post-call catch up sleep >9h hours on post-call days. Ketonuria and urine concentration, surrogate measures of dehydration, were present in a number of shifts Current PAIRO regulations, while a step in the right direction, still expose residents to acute sleep deprivation and physical stress on-call.

**Support (optional):**

### 0258

#### PARENT-REPORTED SHORTENED SLEEP DURATION IN OBESE SNORING CHILDREN

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**Introduction :** Shorter sleep duration has been linked to an increased prevalence of obesity in children and adults. However, this relationship has not been analyzed in the context of polysomnographically-documented sleep variables.

**Methods :** A previously validated sleep questionnaire was administered to parents of 5- 8- year-old children enrolled in the Jefferson County, Kentucky school system. A subset of 171 snoring children were selected to have nocturnal polysomnographic recording and anthropometric measurements (height, weight, BMI). Children were subdivided into two groups: obese (Ob) with BMI < 95th percentile for gender and age ( $n = 51$ ) and normal weight (NI) with BMI < 95th percentile for gender and age ( $n = 120$ ). Parentally-reported typical sleep duration, bedtime, and rise time were analyzed.

**Results :** Mean age was  $6.9 \pm 0.6$  years; 54% male; 59% Caucasian. There were no age, gender, or racial differences between groups. Mean BMI of Ob was  $22.5 \pm 4.3$  kg/m<sup>2</sup> and of NI was  $15.78 \pm 4.5$  kg/m<sup>2</sup>. Ob had significantly higher apnea-hypopnea indices (AHI); Mean =  $3.95 \pm 8.4$ /hr TST) than NI (Mean =  $1.6 \pm 3.8$ /hr TST;  $t = 2.5$ ,  $p = .013$ ). There were no respiratory arousal differences between groups. Analyses of covariance were obtained using race and AHI as covariates. Ob had later parent-reported bedtimes than NI ( $F = 4.27$ ,  $p = 0.006$ ) with similar rise times ( $F = 1.38$ ,  $p = 0.25$ ), resulting in significantly shorter parent-reported sleep duration ( $F = 10.94$ ,  $p < 0.001$ ), independent of race and AHI.

**Conclusion :** According to parental reports, obese snoring children have significantly later bedtimes than normal weight snoring children, regardless of race or apnea-hypopnea index. These findings may be useful in understanding mechanisms underlying pediatric obesity.

**Support (optional):** Supported by: NIH Grant HL 65270

## 0259

### NEW APPROACHES TO THE STUDY OF LEG MOVEMENTS DURING SLEEP IN ADHD CHILDREN

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**Introduction :** Children with attention-deficit hyperactivity disorder (ADHD) have been reported to have a high prevalence of Periodic Limb Movements during Sleep (PLMS) at a rate of >5 per hour of sleep, compared to control children. PLMS, in these patients, have been thought to have direct correlations with the symptoms of ADHD through the mechanism of sleep disruption or through a genetic link, underlying a hypothetical common dopaminergic deficit. However, this association was only analyzed by using the simple PLMS index; the aim of our study was to evaluate the lower limb motor pattern during sleep in children with ADHD by means of newly proposed tools of analysis, able to detect periodicity and distribution of intervals between LMs in a more refined way.

**Methods :** A group of 10 school-age children with ADHD underwent standard polysomnography. PLMS were detected following standard criteria and the PLMS index calculated. Subsequently, all EMG bursts were detected with a duration between 0.5 and 15 s; the threshold used was 10  $\dot{I}V$  (with resting EMG tracings consistently below 2  $\dot{I}V$ ) from both anterior tibialis muscles. Events were considered as separate when an interval of at least 0.5 s was found between them. The same interval was used for the definition of monolateral or bilateral LMs. For each LM, the interval from the preceding LM (onset-to-onset), duration and area under the curve ( $\dot{I}V/s$ ) were measured.

**Results :** All children with ADHD had a "classical" PLMS index >5 (range 5.34-22.24); however, the application of the new analysis methods disclosed that the distribution of their inter-LM intervals showed only a main peak at 2-4 s which decreased progressively throughout the time window used (up to 100 s) but never reaching values close to 0, in the same time window. The so-called "periodicity index" (PI = number of sequences of 3 intervals  $\geq 10 \leq 90$  s / total number of intervals) showed relatively low values (0.211-0.587); most LMs showed a duration between 0.5 and 7 s and a small area under the curve.

**Conclusion :** Despite the apparent similarity between the PLMS index found in ADHD children with that of patients with RLS/PLMS, the analysis of the inter-LM interval distribution and of the PI seems to indicate that the structure of mechanism generating LMs during sleep in ADHD is different from that observed in RLS/PLMS. In fact, in ADHD low levels of periodicity characterize LMs during sleep which cannot be described by the simple calculation of the PLMS index.

**Support (optional):**

## 0260

### LONGITUDINAL CHANGES IN SLEEP IN ADOLESCENTS

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**Introduction :** There is considerable interest in age-related changes in sleep architecture throughout the life cycle, but particularly in develop-

mental influences on sleep. Adolescence is associated with substantial changes in the timing and the amount of sleep. However, most of the current data are based on cross-sectional studies and do not include longitudinal assessments of sleep changes within individuals. The present study examined longitudinal changes in sleep architecture and slow-wave activity in adolescents 10-17 years of age.

**Methods :** Seven girls and two boys participated in the study. Each participant followed a regularized home schedule for 5 days prior to study, followed by two consecutive weekend nights in the lab. The same procedure was followed 2-5 years later. Standard visual stage scoring quantified sleep architecture and power spectral analysis was used to quantify delta activity (0.5 - 4 Hz). Slow-wave activity (SWA) was derived from average delta power in NREM sleep (Stages 2, 3 & 4). Within-subject ANOVA and intra-class correlations compared changes in sleep within individuals.

**Results :** None of the sleep measures showed significant changes from the first to second recording period. In fact, group means were very similar across the sleep studies. Intra-class correlations indicated that several measures were extremely stable across time within individuals, including: sleep latency ( $r=0.82$ ,  $p<.01$ ), sleep efficiency ( $r=0.72$ ,  $p<.03$ ) and SWA power in the first NREM period ( $r=0.78$ ,  $p<.02$ ). REM latency, % Stage 1, % Stage 2 and the total sleep period were not strongly correlated with individuals with a range of intra-class correlations from -0.06 - 0.29.

**Conclusion :** This preliminary study suggests that sleep latency, sleep efficiency and SWA measures are remarkably stable over 2-5 years within adolescents. Other sleep measures, most notably those in REM, are more labile.

**Support (optional):**

## 0261

### THE EFFECT OF INTRANASAL BUDESONIDE THERAPY IN CHILDREN WITH MILD SLEEP DISORDERED BREATHING (SDB): A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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**Introduction :** Adenoids and tonsils, particularly those of patients with SDB, express high levels of glucocorticoid receptors, suggesting a potential therapeutic role for topical corticosteroids. In the last few years, 3 separate studies have shown significant improvements in moderate to severe SDB after intranasal corticosteroid therapy. However, the role of topical corticosteroid therapy in mild SDB remains undefined.

**Methods :** Children with polysomnographically-demonstrated mild SDB ( $1 < \text{AHI} < 5$  /hr TST and/or Respiratory Arousal Index (RAI)  $> 2$  /hr TST) were prospectively recruited and randomly assigned to receive either 6 weeks of intranasal budesonide (Rhinocort Aqua ©, Aztra Zeneca; 32  $\dot{I}g$ /spray, 1 spray in each nostril at bedtime) or placebo. At the end of the treatment period, a second overnight sleep study was performed.

**Results :** Twenty-six children with mild SDB (mean age  $8.4 \pm 0.4$  years [SEM]; 54% females; BMI:  $18.8 \pm 1.2$  kg/m<sup>2</sup>), with a mean AHI at diagnosis of  $2.7 \pm 0.5$  /hr TST, mean RAI of  $2.4 \pm 0.4$  /hr TST, and nadir SaO<sub>2</sub> of  $91.2 \pm 0.7$  %, were included. Treatment with intranasal budesonide for 6 weeks resulted in significant improvements in AHI ( $1.0 \pm 0.1$  /hr TST;  $p < 0.002$ ), as well as in total arousal index (from  $10.4 \pm 1.0$  /hr TST to  $7.0 \pm 0.8$  /hr TST;  $p < 0.02$ ), and in RAI ( $1.3 \pm 0.2$  /hr TST;  $p < 0.01$ ). However, no significant changes in nadir SaO<sub>2</sub> occurred ( $91.9 \pm 0.7$  %;  $p$ -ns).

**Conclusion :** Intranasal budesonide therapy for 6 weeks is associated with objective ameliorations in sleep fragmentation and respiratory disturbance in children with mild SDB whom otherwise would not be candidates for surgical removal of tonsils and adenoids. We speculate that tar-

geted improvements in nasopharyngeal resistance constitute an important aspect of the clinical management of snoring children.

**Support (optional):** Study funded by an investigator initiated grant from Astra Zeneca Ltd.

## 0262

### HEART RATE VARIABILITY IN OBESE CHILDREN WITH SYMPTOMS OF OBSTRUCTIVE SLEEP APNEA SYNDROME

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**Introduction :** Frequency power domain of heart rate variability (HRV) describes cardiac autonomic balance. Parasympathetic control is reflected in high frequency power (HFP), while low frequency power (LFP) reflects sympathetic and parasympathetic input to the sino-atrial node. Controversy exists as to whether decreased HRV in obese subjects results from co-morbid OSAS or is a direct result of obesity. We examined HRV during nocturnal polysomnography (NPSG) obtained in children referred with symptoms of OSAS.

**Methods :** HRV data was available from 54 children (32 males)  $\leq 18$  yrs evaluated from September 2000 through October 2004. Subjects with craniofacial syndromes, neuromuscular disease or significant developmental disorders were excluded. Subjects were stratified by BMI%ile. HRV analysis was performed on 5 minute epochs of EKG data obtained during NPSG. Studies were scored by a registered technician using standard pediatric criteria and reviewed by a certified pediatric sleep specialist.

**Results :** Twenty-four subjects were of normal BMI%ile (BMI<85%ile); 10 were at risk for overweight (85%ile $\leq$ BMI $\leq$ 95%ile) and 20 were overweight (BMI>95%ile). Average age was 9.2 $\pm$ 4.1 years. Mean apnea-hypopnea index (AHI) was 12.6 $\pm$ 18.8 events/hr with half of the subjects classified as having obstructive sleep apnea syndrome (AHI $\geq$  5). BMI%ile correlated positively with LFP/HFP ratio ( $p<0.05$ ). LFP/HFP ratio was increased ( $p<0.05$ ) in obese compared to at risk and normal weight children. Normalized LFP (LFPnu) was decreased ( $p<0.05$ ) and normalized HFP (HFPnu) was increased ( $p<0.05$ ) in obese compared to at risk and normal weight children. No significant correlation was found between LFP/HFP ratio, LFPnu or HFPnu and AHI.

**Conclusion :** Decreased heart rate variability occurs in obese children. As approximately 30% of obese children have OSAS, it is unclear whether this sympathetic over-drive results from obesity or is due to commonly comorbid OSAS. We have demonstrated that decreased heart rate variability consistent with sympathetic over-drive is related more to the degree of obesity than the presence of OSAS.

**Support (optional):**

## 0263

### SLEEP, PAIN AND MOOD IN CHILDREN WITH JUVENILE RHEUMATOID ARTHRITIS

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**Introduction :** Juvenile rheumatoid arthritis (JRA) is associated with disturbed sleep that could be related to pain and mood. The purpose of this study was to describe sleep and examine contributions of pain and mood to nighttime awakenings in children with JRA.

**Methods :** Thirty-two children (n=26 female, age 8.84  $\pm$  1.97 years) with JRA had their sleep patterns inventoried with the Children's Sleep Habits Questionnaire (CSHQ). Disease severity was measured by physician

global assessments (PGA, 0 to 10, active disease < 1). Children maintained a daily symptom diary and evening pain and number of nighttime awakenings were averaged across the week. Child Behavior Check List (CBCL, parent report) subscales for depression and the Revised Children's Manifest Anxiety Scale (RCMAS) were used to assess mood state. Sleep patterns were characterized with descriptive statistics; stepwise linear regression was used to evaluate the impact of disease severity, depression, anxiety, evening pain, and age on mean number of self-reported nighttime awakenings. The P-value for inclusion in the regression model was set at .05.

**Results :** Children with active (n = 17) did not differ significantly on self-reported sleep from those with quiescent (n = 15) JRA. Forty-five percent (n=14) of all children reported trouble sleeping and 61% (n=19) reported waking at night when their parents thought they were asleep. Self reports of pain 'sometimes or usually' waking them at night were reported by 54.8 % (n = 17), but there were no differences between children with active or quiescent JRA. Stepwise regression revealed that mean evening pain was a significant predictor of mean number of nighttime awakenings R<sup>2</sup> of 0.53 (P < .001).

**Conclusion :** Children with JRA report disturbed sleep and nighttime pain but may be underreporting these symptoms to their parents. Levels of evening pain may be a useful predictor of nighttime awakenings.

**Support (optional):** NINR,CWHGR NR04011, NR08136

## 0264

### NORMATIVE PEDIATRIC HEART RATE DATA DURING SLEEP FROM ETHNICALLY DIVERSE COHORTS

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**Introduction :** Published normative pediatric heart rate data are based on electrocardiograms (ECGs) collected during wakefulness in a large sample of French-Canadian children. There is a paucity of comparable heart rate data collected during sleep across the ages from which lower and upper limits of normal might be extrapolated. Valid threshold criteria for heart rate abnormalities during sleep require comparison to the range of normative data acquired during sleep.

**Methods :** We abstracted ECG-derived heart rates collected during overnight sleep studies from two large, ethnically diverse community based pediatric cohorts [Cleveland Children's Sleep and Health Study (CCSHS) and TuCASA in Tucson, Arizona]. All children were without major co-morbidities and had respiratory disturbance indices < 5. Data were summarized and compared using least square means from analysis of variance models, controlling for other covariates (age, gender, ethnicity) and BMI.

**Results :** The TuCASA sample consisted of 487 children (50.5% female, 41% Hispanic, 49% Caucasian; aged 6 to 12 years). The CCSHS sample consisted of 770 children (48.7% female, 34.7% African-American, 60.8% Caucasian, 1.6% Hispanic; aged 8 to 11 years). In both samples, adjusted heart rates were between 4 and 5 beats per minute (bpm) higher in girls compared with boys ( $p<0.0001$ ). In the CCSHS sample, adjusted heart rates in African-American children were almost 3 bpm higher compared with Caucasian children ( $p=0.0012$ ). In contrast, heart rates in Caucasian and Hispanic children were not different in the TuCASA sample. Heart rates were highest in the youngest children, then decreased 0.5 to 2 bpm per year with increasing age up through age 11 years. For the entire CCSHS sample, two standard deviations below and above the mean yielded sleeping heart rate values of 53 bpm and 92 bpm, respectively.

**Conclusion :** Mean heart rates during sleep are almost 20% lower than

published awake resting heart rates in the same aged samples and vary with age, gender, and ethnicity in school-aged children.

**Support (optional):** R01HL60957, R01HL062373, K23HL04426, M01RR00080, all from NIH

## 0265

### CARDIO-RESPIRATORY ABNORMALITIES IN INFANTS WITH APPARENT LIFE THREATENING EVENT (ALTE)

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**Introduction :** Apparent life threatening event (ALTE) is a unifying diagnosis of diverse etiologies with constellation of symptoms that include apnea, color change and changes in muscle tone. A sub group of infants with ALTE can have evidence of sleep-disordered breathing with abnormal polygraphic variables that are suggestive of cardio-respiratory control dysfunction. The purpose of the present study is to describe the cardiorespiratory abnormalities in a series of infants hospitalized with ALTE.

**Methods :** We reviewed the PSG studies from a consecutive series of infants who were younger than 12 months and admitted with a diagnosis of ALTE to a tertiary care academic medical center between 2000 to 2005. The infants were referred for overnight PSG studies at the discretion of primary physician. The recording included EEGs (C3/A2, C4/A1) right and left electrooculograms, chin EMG, oronasal airflow, thoracic and abdominal efforts, O2 saturation, EKG and end tidal (Et)CO2 monitoring. All recordings were scored using established international criteria and cardio respiratory abnormalities were classified as central, obstructive, mixed apneas, hypopneas, desaturations, hypoventilation and abnormal cardiac rate and rhythm based on breathing patterns, oxygen saturation and EtCO2 monitoring, heart rate and EKG.

**Results :** A total of 28 infants underwent PSG evaluation during the study period. Mean age was 5 months. Cardiorespiratory abnormalities were found in 13 (46%) infants. The most common abnormality included central hypopneas (6 infants/26%). Other observed abnormal events include central hypopneas (3 infants), obstructive apneas (2 infants), hypoventilation (4 infants) and desaturations (8 infants). No abnormal cardiac events were observed. These abnormalities led to a specific diagnosis in five infants.

**Conclusion :** In a select population of hospitalized infants with ALTE, cardiorespiratory abnormalities were found in a significant proportion of infants suggesting the possibility of sleep related impairment of respiratory control.

**Support (optional):**

## 0266

### DOES A PERIODIC LIMB MOVEMENT INDEX (PLMI) > 5 UNIQUELY DEFINE PERIODIC LIMB MOVEMENT DISORDER (PLMD) IN CHILDREN?

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**Introduction :** Previous literature defined a PLMD group as having PLMI 5 or greater on polysomnography (PSG). Here we demonstrate that a PLMI > 5 by itself may be insufficient to identify un-confounded groups of children with PLMD due to its association with other sleep disturbances.

**Methods :** Information on 422 children referred to a private sleep medicine practice over 2 years was extracted from parent-completed questionnaires, chart review, and PSG. 39% were diagnosed with PLMD, some

with co-morbid conditions. A diagnosis of PLMD was assigned when the patient had a clinical sleep disturbance and PLMs were present on PSG. Three main groups were identified for study: 75 with PLMD only, 179 with Sleep Disordered Breathing (SDB) only, and 43 with co-morbid PLMD and SDB (PLMD/SDB). Children in each of the 3 groups were categorized as having a PLMI < 5 or > 5. Mean PLMI was calculated for each group, and the frequency distribution of PLMI category examined.

**Results :** Predictably, the PLMD group had the highest average PLMI (18.22) and the greatest percentage of PLMIs > 5 (93%). Children in the co-morbid group had an intermediate PLMI (14.27), with 84% > 5. Children with SDB had the lowest average PLMI (7.17); however 48% had a PLMI > 5.

**Conclusion :** In this cohort about half the children with un-confounded SDB had a PLMI > 5 with no clinical sleep disruption. Therefore, we conclude that a diagnosis of PLMD based on a PLMI > 5 may, by itself, be insufficient to define a PLMD group for research purposes. The existing literature on PLMD in children may be subject to increased Type I and Type II errors due to this confounding.

**Support (optional):** Study sponsored in-part by an unrestricted, research grant by GlaxoSmithKline, Inc. and internal support, United Sleep Medicine Centers

## 0267

### PHARYNGEAL COLLAPSIBILITY IN CHILDREN WITH SLEEP DISORDERED BREATHING IN THE TUCSON CHILDREN'S ASSESSMENT OF SLEEP APNEA STUDY (TUCASA)

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**Introduction :** Neuromuscular abnormalities and a collapsible pharynx contribute to sleep disordered breathing (SDB) in children. Children with severe obstructive sleep apnea (OSA) have a more collapsible pharynx than those with primary snoring, but there are little data concerning children with mild SDB. We tested the hypothesis that the pharynx of children with mild SDB primarily manifested as hypopnea, is more collapsible than the pharynx of those without significant SDB.

**Methods :** 17 subjects were recruited, 10 control subjects 3M/7F, age 9.4 + 0.5 years with a hypopnea index (HI) 1.9 + 0.2 and 7 subjects with mild SDB 4M/3F age 10.6 + 0.5 years with HI 11.5 + 0.1. None had enlarged tonsils or adenoids, nor did they undergo previous tonsillectomy or adenoidectomy. Airway collapsibility was measured during non-rapid eye movement (NREM) sleep, by brief (2 breath duration) and sudden reductions in pharyngeal pressure produced by applying negative pressure to the breathing mask. Flow-pressure curves were constructed for each subject, and the critical collapsing pressure of the upper airway was measured as the pressure at the x-intercept (Pcrit).

**Results :** Pcrit was significantly higher in children with mild SDB than in the controls (-4.4 + 4.80 vs. -17.5 + 2.50 cmH2O, P < 0.05). AHI and Pcrit were significantly correlated (P = 0.0317, r2 = 0.329) as were the hypopnea index and Pcrit (P = 0.0122, r2 = 0.419).

**Conclusion :** Children with mild SDB have more collapsible upper airways than age and BMI-matched children during NREM sleep. Our observations suggest that children with mild SDB and relatively positive Pcrit values should be thoroughly evaluated, as they may be predisposed to more severe pharyngeal collapse later in life.

**Support (optional):** Supported by HL 62373 and HL 56876 with equipment support from Respironics

0268

**CLINICAL PRESENTATION, DAYTIME SEQUELAE AMONG CHILDREN WITH PERIODIC LIMB MOVEMENT DISORDER AND SLEEP DISTURBED BREATHING: A COMPARATIVE STUDY**

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**Introduction :** Periodic Limb Movement Disorder (PLMD) may be under-recognized in the pediatric population. We report the prevalence of PLMD (39%) from a two-year retrospective evaluation of children seen at a private practice of sleep medicine. Several presenting characteristics distinctive to PLMD were identified, that can be used to distinguish PLMD from Sleep Disordered Breathing (SDB), a more common disorder in children.

**Methods :** Information from 442 children was extracted from parent-completed questionnaires, chart review, and polysomnography. Children were classified into 3 groups for analysis: 104 with PLMD with or without occasional symptoms of restless legs, (PLMD+/-RLSx group; PLMI=20.5), 179 with SDB only (SDB group; PLMI=7.17), and 60 with co-morbid PLMD and SDB with or without RLSx (Comorbid group; PLMI=13.38). Ninety-nine children were excluded from analysis because they lacked one of the three disorders of interest or had confounding comorbidity and/or missing data. ANOVA and Fisher's Least Significant Differences were used to determine statistical significance.

**Results :** Data from 343 children (60% male, 70% Caucasian, 27% African American; mean age=8.12) were analyzed. Predictably, the PLMD+/-RLSx group had greater pain/sensations in legs than children with SDB, who had more disturbed breathing during sleep. Children with PLMD+/-RLSx and the comorbid group were more likely to have bedtime-resistant behaviors, difficulty initiating and maintaining sleep, parasomnias and woke up more irritable than the SDB group. Hyperactivity, aggression, temper, and anxiety were also significantly higher among the PLMD+/- RLSx and comorbid groups. Depression was more characteristic of children in just the PLMD+/-RLSx group than those in the other two groups. Reported group differences were significant at the .05 level.

**Conclusion :** 1. PLMD is prevalent in this cohort. 2. Children with PLMD have distinctive presenting and daytime behavioral characteristics. 3. PLMD should be considered in children who have sleep initiation and maintenance difficulties, and daytime mood/behavioral problems.

**Support (optional):** Study sponsored in-part by an unrestricted, research grant by GlaxoSmithKline, Inc. and internal support, United Sleep Medicine Centers

0269

**UMBILICAL CORD LEVELS OF NUCLEATED RED BLOOD CELLS IN SNORING WOMEN**

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**Introduction :** Previous reports have shown that pregnancy is associated with new onset sleep-disordered breathing (SDB) concomitant with increased fetal risk. One of the consequences of intrauterine hypoxia is increased fetal erythropoiesis and elevation of nucleated red blood cells (nRBCs) at birth. Indeed conditions such as intrauterine growth restriction, maternal hypertension, maternal diabetes mellitus or smoking are associated with elevated nRBCs count at birth. We hypothesized that snoring in pregnant women will result in increased numbers of nRBCs in

cord blood at birth.

**Methods :** Parturients with a singleton, full-term uncomplicated pregnancy were recruited during labor at the delivery room. All participants completed together with their sleep partner a questionnaire on snoring, sleep pauses and sleepiness (ESS) during the current pregnancy. Cord blood was obtained immediately following delivery and differential cell counts were manually performed. Nucleated RBC were counted per 100 white blood cells and expressed as an absolute number.

**Results :** 36 women were recruited. The mean age and BMI were 29.0±4.8 y and 26.8±2.6 kg/m<sup>2</sup>, respectively. Participants were divided into 3 groups: women who snored before and during pregnancy (SDB, n=7), women who began to snore during the current pregnancy (pregnancy-induced snoring, n=15) and women without snoring (controls, n=14). Significant increase in cord absolute nRBCs count was found in the pregnancy-induced snoring group (1066.1±1060 x 10<sup>6</sup>/L) compared to the SDB group (341.6±159.0 x 10<sup>6</sup>/L) and the control group (542.1±281.9 x 10<sup>6</sup>/L) (p<0.05). No significant differences in BMI, weight gain during pregnancy and smoking rates were found between the 3 groups. No significant differences in ESS score were found.

**Conclusion :** New onset of snoring during pregnancy is associated with enhanced erythropoiesis resulting in increased cord blood counts of nRBCs. We suggest that the relatively short period of time in pregnancy-induced snoring does not allow maternal adaptive mechanisms already existing in chronic SDB.

**Support (optional):**

0270

**SDB IN CHILDREN: PRELIMINARY FINDINGS FROM A POPULATION SAMPLE**

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**Introduction :** The epidemiology of sleep disordered breathing (SDB) in adults has been extensively studied. However, the epidemiology of SDB in children, especially in the general population, has received much less attention.

**Methods :** The overall objective of this two-phase protocol was to establish the prevalence of various types of SDB in children in a random sample of the general population. The first phase obtained general information by questionnaire from the parent about every child in a selected elementary school (K through 5), with a response rate of 80%. The second phase evaluated a subsample for a single-night with polysomnographic, psychometric, ENT & pulmonary examinations, with a response rate of 70%. Data currently reported were collected mainly in the second phase.

**Results :** This analysis is based on 442 children who completed the second phase of this study. We observed a prevalence of 0.7% with an apnea/hypopnea index (A/HI)≥5, 1.1% with an A/HI≥4 and 3.4% with an A/HI≥3. A prevalence of 2.7% was observed with obstructive apnea index >1 and snoring was observed in 23.5%. Using logistic regression SDB was independently predicted by systolic blood pressure (BP) (p=0.01) and parental report of frequent coughing (p=0.02), but not by age, gender, body mass index (BMI), waist/hip ratio, tonsil size, mouth breathing, wheezing or chronic sinusitis. Attention deficit hyperactivity disorder (ADHD) was independently predicted by parental reports of difficulty falling asleep (p=0.002), restless during sleep (p=0.04), male



( $p=0.002$ ) and BMI ( $p=0.01$ ), but not SDB. Using multivariate regression diastolic BP was independently predicted by BMI ( $p=0.003$ ), while systolic BP was predicted by BMI ( $p<0.001$ ), age ( $p=0.001$ ) and SDB ( $p=0.01$ ).

**Conclusion :** This preliminary evaluation raises a question whether tonsil size is the primary mechanism for SDB. Further, SDB did not appear to be associated with ADHD, but it was associated with systolic BP independent of BMI.

**Support (optional):** R01 HL 63772, M01 RR010732, C06 RR016499

## 0271

### PHONOAUDIOLOGICAL TREATMENT FOR CHILDREN WITH OSAS (OBSTRUCTIVE SLEEP APNEA SYNDROME), AFTER PALATINE AND FARINGEAL TONSILECTOMY

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**Introduction :** Children with OSAS (Obstructive Sleep Apnea Syndrome), who had their diagnostic throat polysomnogram and fiberoptic nasopharyngolaryngoscopy, were submitted to surgical removal of palatine and faringeal tonsils. After surgery (about 6 weeks), the patients were submitted to another polysomnogram.

**Methods :** The patients with persistence of AHI were divided into 2 groups. One group (8 patients) was submitted to myofunctional therapies for 16 weeks, with exercises to elevate the palatus, lowering the tongue, stomatognathic functions and breathing. The control group (7 patients) was followed clinically, without exercises.

**Results :** After the phonoaudiological treatment (16 weeks) the patients of the two groups were submitted to another polysomnogram. The patients who were submitted to phonoaudiological treatment presented improvement in AHI, better sleep, social behavior and cognitive functions when compared to the control group.

**Conclusion :** We concluded that the phonoaudiological treatment improved the surgical outcome of children with OSAS who presented persistence of symptoms after surgery.

**Support (optional):**

## 0272

### EPIDEMIOLOGY OF ADOLESCENT INSOMNIA, PSYCHOLOGICAL DISORDERS, AND SUICIDE

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**Introduction :** Approximately 17% of children and adolescents suffer from insomnia. Adult studies show insomnia is a risk factor for the development of depression, anxiety, other psychological disorders, alcohol and drug abuse or dependence, and suicide. The current study examined if adolescent insomnia was a risk factor for psychological disorders and suicide in young adulthood.

**Methods :** This study was a reanalysis of data from a national longitudinal study, which evaluated health behaviors in 4712 adolescents (mean age 14.9 years [SD 1.7]). Reevaluation occurred 7-8 years later in young adulthood. Participants completed in-school and in-home questionnaires during adolescence, and in-home questionnaires as young adults. Insomnia was operationally defined as a report of insomnia "Almost everyday" or "Everyday" during the past year at the adolescent interview. Participants were excluded if no ethnicity, gender, or insomnia data were given.

**Results :** Using our definition, 10.5% of the adolescents reported insomnia (52% females). Adolescent insomnia was a significant risk factor for

the development of depression ( $p < .001$ ), suicidal thoughts ( $p < .001$ ), and the use of prescription medications for depression and stress ( $p < .001$ ) in young adults. Adolescent insomnia was not a risk factor for suicide attempts or alcohol, substance, and tobacco abuse/use.

**Conclusion :** Preliminary results indicate that adolescent insomnia is a risk factor for depression, suicidal thoughts, and prescription medication use for depression and stress in young adulthood. Epidemiological data alone cannot determine causality. However, the current study identifies insomnia as a precursor to the above disorders, which argues for the exploration of preventative treatments in adolescents with insomnia. Further analyses will control for other sources of variance (e.g. gender, baseline depression), and complete analyses will be presented at APSS.

**Support (optional):**

## 0273

### USEFULNESS OF POLYSOMNOGRAPHY IN CHILDREN WITH UNEXPLAINED BEHAVIORAL PROBLEMS

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**Introduction :** Most polysomnographic (PSG) studies in children with behavioral problems have focused on sleep apnea. In this population, sleep architecture can be affected not only by the underlying medical illness but also by medications used in their treatment. Identifying treatable causes may provide yet another therapeutic avenue in the management of this difficult problem.

**Methods :** We retrospectively reviewed chart data on 36 serial patients who underwent polysomnography at our Pediatric Sleep Center over the last year. Patients had been referred for unexplained behavioral problems by both pediatricians and also subspecialists (pediatric pulmonology, ENT and neurology services). No child had clearly defined daytime sleepiness or obvious sleep apnea. All patients underwent standard digital video polysomnography with extended seizure montage and also end tidal CO<sub>2</sub> recordings. All studies were scored by registered sleep technologists and interpreted by board certified physicians.

**Results :** The most common PSG abnormality was reduced sleep efficiency (66.9% mean) due to increased sleep onset latencies and also multiple unexplained awakenings. Slow wave sleep was not affected (mean 223.36%) but REM sleep was reduced at 12.7%. In 10 patients (27.7%) a new diagnosis was suggested by the study. Obstructive sleep apnea was seen in 4 patients (11%), interictal epileptiform activity in 2 (5.5%) and periodic limb movements were seen in 4 (11.1%).

**Conclusion :** Polysomnography in children with unexplained behavioral problems may help identify potentially treatable sleep and neurological disorders. Reduced sleep efficiency and REM sleep were most common on polysomnography. As many children were below 6 years of age, we could not perform multiple sleep latency testing (MSLT). It is possible that MSLTs at least in the older children would have helped identify narcolepsy which is another cause of behavioral problems in this age group.

**Support (optional):**

## 0274

### SLEEP TERRORS IN CHILDREN: A PROSPECTIVE STUDY ON TWINS

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**Introduction :** There is growing evidence that genetic factors are involved in the occurrence of sleep terrors. Twin studies provide invaluable information regarding genetic and environmental factors that can affect the manifestation of the disease. Previous twin studies on sleep terrors have been done retrospectively. This project is the first prospective longitudinal study using a cohort of twins to clarify the genetic and environmental contributions to sleep terrors in childhood.

**Methods :** Subjects are monozygotic and dizygotic twins recruited at birth (between November 1995 and July 1998) for a longitudinal study (Quebec Newborn Twin Study-Canada). Questions about the frequency of night terrors at 18 and 30 months of age (never, sometimes, often and always) were asked to the biologic mother. Zygosity was determined by blood typing.

**Results :** Analyses were based on results obtained from 161 pairs of monozygotic and 229 pairs of dizygotic twins at 18 months of age, and 140 pairs of monozygotic and 207 pairs of dizygotic twins at 30 months of age. The prevalence of sleep terrors (at least occasionally) was 36.9% at 18 months and 19.7% at 30 months. At 18 months, the polychoric correlation was 0,63 for the monozygotic and 0,36 for the dizygotic twins (heritability = 0,54) and was 0,68 for the monozygotic and 0,24 for the dizygotic twins at 30 months (heritability = 0,88). A model fitting analysis showed that sleep terrors are explained by a two-component model at 18 months (43.7% genetic and 56.3% non-shared environment) and also at 30 months (41.5% genetic and 58.5% non-shared environment).

**Conclusion :** These results in monozygotic and dizygotic twins strongly support the heritability of sleep terrors. The genetic predisposing factor seems to be associated with the persistence of sleep terrors symptoms (to at least the age of 30 months).

**Support (optional):**

### 0275

#### POLYSOMNOGRAPHIC FINDINGS IN PATIENTS WITH APPARENT LIFE THREATENING EVENTS (ALTEs)

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**Introduction :** Polysomnographic (PSG) studies investigating infants who have had an ALTE have described several abnormalities including impairment in sleep architecture and cardiorespiratory defects. However, no definitive conclusions have been reached as to which, if any, physiological features are abnormal in infants who suffer an ALTE. Our aim in this study is to describe PSG findings in patients following ALTEs and to compare those patients who had a normal PSG (NLPSG) to those with an abnormal study (ABNLPSG).

**Methods :** All patients less than six months of age admitted to the Children's Hospital of Wisconsin with an ALTE and who underwent a PSG between January 1, 2000 and December 1, 2005 were included. Medical and PSG records were reviewed and are summarized below.

**Results :** Twenty eight patients (12 females) had an ALTE and underwent PSG. Six of the patients were premature (all 32-37 weeks). Eleven of the PSG were interpreted as abnormal (39%) and 17 were normal (61%). The mean age at the time of the ALTE was slightly higher in the ABNLPSG (1.35 vs. 0.98 months, NS) although the mean age when the PSG was done was higher in the NLPSG group (2.83 vs. 2.11 months, NS). A significant difference was found between the two groups in the mean delay from ALTE diagnosis to PSG completion (0.77 month in ABNLPSG vs. 1.85 month in NLPSG,  $p=0.007$ ). The major PSG abnormalities included defects in respiration, ventilation and oxygenation. Infants with an ABNLPSG had a significantly higher apnea-hypopnea index of 15 vs. 1 ( $p=0.005$ ) and a higher max EtCO<sub>2</sub> of 59.8 vs. 48.5 ( $p=0.002$ ), and tend-

ed to have more time with SpO<sub>2</sub> < 90%, 5.0% vs. 0.9% ( $p=0.17$ ). Of the 11 abnormal PSG, 5 patients had obstructive apnea, 3 had central apnea, and 1 of each had hypoventilation, desaturation episodes, and significant periodic breathing. There were no differences in sleep architecture between the two groups in regards to the total, active or quiet sleep times, and there were no documented arrhythmias or seizures. pH studies were done in 19 patients and were abnormal in 4 of the 7 ABNLPSG and in 3 of the 12 NLPSG (NS).

**Conclusion :** Polysomnography can be helpful in elucidating the respiratory-associated abnormalities in patients with ALTEs. These data also suggest that PSG studies may be more helpful when done soon after the ALTE and when done in conjunction with pH studies.

**Support (optional):**

### 0276

#### AGE AND SEX MODERATE THE RELATIONSHIP BETWEEN SLEEP PATHOLOGY AND BEHAVIORAL FUNCTIONING AMONG OBESE CHILDREN

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**Introduction :** Sleep is known to relate to daytime behaviors in children, but few have examined whether there are differential relationships across ages and sexes. Sleep problems are common in obese children. This study examined the relationships between sleep pathology and parent-reported behaviors among obese children.

**Methods :** We reviewed charts from 162 children aged 5-16 who were involved in a hospital-based pediatric weight management program. All exceeded the 95th percentile for body mass index for their age and sex. Children with a history of neurological illness or who used psychotropic medication were excluded. Children were divided into four groups ( $n=31-47$ ) by sex and age (5-9 vs. 10-16 yrs). Parents completed a validated behavior questionnaire (Behavior Assessment System for Children) and reported on academic grades. Parents also reported weeknight and weekend sleep duration and several sleep concerns, grouped here into symptoms of sleep-disordered breathing (SDB: snoring, breathing pauses) and non-SDB sleep complaints (difficulties awakening or falling asleep, frequent awakenings, restless sleep).

**Results :** The four groups did not differ on race, SDB symptoms, or non-SDB sleep complaints. Older children received less weeknight sleep than younger children, and girls received more weekend sleep than boys. Hyperactivity was associated with SDB among young boys, with older boys showing a smaller association and neither group of girls showing an effect. Aggression was associated with SDB among boys, but not girls, in both age groups. Symptoms of depression were associated with non-SDB sleep problems in all groups except young boys, in whom they instead were related to SDB. Poor academic grades were associated with short sleep in older boys, but not the other groups.

**Conclusion :** Among obese children, the relationships between sleep and daytime behaviors vary by age and sex. SDB appears to be a particular risk factor for daytime emotional and behavior problems in young boys.

**Support (optional):** Cincinnati Children's Hospital Medical Center Trustee Grant, American Sleep Medicine Foundation (#22-YI-03), National Institutes of Health/NHLBI (K23 HL075369)

**0277****A PRELIMINARY REPORT OF SLEEP DISTURBANCES IN CHILDREN WITH WILLIAMS SYNDROME***O'Brien LM,<sup>1</sup> Mervis CB<sup>2</sup>*

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**Introduction :** Williams syndrome (WS) is a neurodevelopmental disorder caused by deletion of about 25 genes on chromosome 7q11.23. Parents often report significant sleep problems although these are not well defined. Children with WS have high rates of behavioral disturbances, particularly attention deficit/hyperactivity disorder (ADHD). We aimed to describe sleep patterns of children with WS with and without co-morbid ADHD relative to their siblings'.

**Methods :** As part of a larger ongoing study, parents completed a pediatric sleep questionnaire (PSQ) for their child with WS aged 2-18 years and the sibling (if any aged 2-18) closest in age. The diagnosis of WS was confirmed by FISH.

**Results :** Questionnaires have been completed for 18 children with WS and 9 siblings thus far. Children with WS were more likely to wake more than two times per night (23.5% vs. 0%), have trouble going back to sleep (23.5% vs. 0%), wake early (28% vs. 0%), and feel sleepy (28% vs. 0%). Twenty-nine percent of teachers reported that WS children are sleepy at school compared to 0% for siblings. Eight children with WS had co-morbid ADHD (WS-ADHD). Parents of WS-ADHD tended to report more growing pains than parents of WS only (62.5% vs. 0%), more leg jerks (25% vs. 0%), and more night sweats (43% vs. 0%). WS-ADHD were also more likely to be hard to wake up (50% vs. 20%), feel sleepy in the day (37.5% vs. 0%), and have teacher-reported sleepiness (37.5% vs. 0%).

**Conclusion :** Children with WS appear more likely than their typically-developing siblings to have altered sleep/wake behavior. Moreover, WS-ADHD appear more likely to have disrupted sleep than those with WS alone. These data suggest that co-morbid ADHD may contribute to reported sleep disruption in children with WS.

**Support (optional):** NINDS grant# R01 NS35102 (CB Mervis, PI), NICHD grant# R37 HD29957 (CB Mervis, PI)

**0278****DO PEDIATRICIANS SCREEN INDIVIDUALS WITH DOWN SYNDROME FOR SLEEP DISORDERS? - A PILOT STUDY***Kiel M,<sup>1</sup> Rotenberg J<sup>2</sup>*

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**Introduction :** With a high prevalence of sleep disorders in individuals with Down Syndrome (DS), the American Academy of Pediatrics published consensus recommendations (2001). The Academy recommends screening all individuals with DS annually beginning at 12 months for obstructive sleep apnea (OSA). This study investigated clinical patterns of screening individuals with DS for disordered sleep since these recommendations were published.

**Methods :** We retrospectively analyzed a random sample of outpatient charts of individuals 12 months of age and older with DS seen in general and specialty pediatrics clinic from March 2001 to October 2005. At this institution, all pediatric encounters by trainees are reviewed by attending physicians. We compared the frequency of clinical screening for sleep disorders to other chronic health problems in DS, generalists' to specialists' patterns and the rate of referral for polysomnogram and consultation.

**Results :** A total of 91 outpatient appointment records were reviewed. Pediatricians asked about sleep less often than thyroid status ( $p<0.019$ ).

Of the total appointments, 21 (23.1%) addressed sleep in some way by asking about sleep symptoms. In comparison, 37 (40.7%) addressed thyroid issues by noting recent thyroid function values or ordering labs. At well child exams, pediatricians addressed sleep half as often as thyroid function ( $p<0.01$ ). At appointments in which there was a concern for disordered sleep, 20% had further diagnostic evaluation requested by sleep study or ENT referral. General pediatricians asked about sleep less often than specialists (Developmentalist and Geneticist), (22.8% versus 66.7%,  $p<0.1$ ).

**Conclusion :** This pilot study suggests that at this tertiary care center, general pediatricians infrequently screen for sleep disorders in DS patients, despite the high prevalence of disease (e.g. OSA 50-75%). Thyroid disorders, however, are often screened for although the risk in DS is lower (15%). Further evaluation regarding clinical practices in chronically ill children is warranted.

**Support (optional):**

**0279****WHAT TEMPERAMENT, TENSION AND TIME HAVE TO DO WITH PEDIATRIC SLEEPLESSNESS: SCIENCE TO SCENARIOS***Wills LM,<sup>1</sup> Kurcinka MS<sup>2</sup>*

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**Introduction :** Pediatric sleep onset and sleep maintenance insomnia is multi-factorial in its etiology. (Or, in plain English, there are many reasons why children aren't sleeping.) Integrating research on child temperament, arousal systems and stress with our knowledge about sleep can help pediatric practitioners more effectively identify these factors and select strategies to help families get the sleep they need. Information presented is drawn from the work of John Bates, PhD, Ronald Dahl, MD, Megan Gunnar, PhD, Sara Harkness, PhD, Jerome Kagan, PhD, Steven Porges, PhD, and others. Insight into individual differences can help us and our patients understand the link between daytime behavior and sleep deprivation and also why some children react very differently from others to similar routines and interventions. How to translate this information into an accessible form for the general public will be discussed. Special emphasis on effective methods for working with more challenging families will be included in this clinically oriented presentation.

**Methods :** A specialized parent education curriculum, based on a thorough review of the research on temperament, stress and sleep, was developed which treated sleep issues, focusing on the entire family system. Information was collected from families participating in the Minnesota state-wide "Early Childhood Family Education" Program, which serves families with children, ages birth to five, from individuals attending parent education workshops conducted across North America, and from families in a sleep clinic setting.

**Results :** Through self reports, participant parents have demonstrated an increased awareness of temperamental differences that affect sleep, and the importance of sleep in helping their children regulate emotions and behavior and consequently have described ability to employ strategies that successfully improved quality of sleep for the entire family.

**Conclusion :** It is important for pediatric sleep practitioners to treat pediatric sleep problems in a family context. Education can change parent-child interaction patterns. By gaining an understanding of the nature of sleep, child temperament, tension and time factors, parents can learn to establish a sleep routine that "fits" their child and family. Incorporating these principles into patient education in clinical settings, as well as consideration of alternative parent education approaches can be effective therapeutic strategies. Further systematic evaluative research is needed.

**Support (optional):**

**0280**

**CRANIOFACIAL MORPHOLOGY OF ORAL BREATHING GIRLS RELATES TO OBSTRUCTIVE SLEEP APNEA CEPHALOMETRIC PATTERN EARLIER THAN ORAL BREATHING BOYS**

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**Introduction :** Many studies have shown a connection between craniofacial morphology and Obstructive Sleep Apnea Syndrome (OSAS). Furthermore there is a correlation of oral breathing and alterations of maxillo-mandibular growth and development. We are questioning if there are differences of craniofacial growth when we compare boys and girls. Objective: to analyze cephalometric measures between oral and nasal breather (OB and NB) boys and girls and also to compare the craniofacial pattern similarities of OB children with that of apnea patients.

**Methods :** The study analyzed the standing lateral skull radiograph of 142 children (85 boys, 52 OB; 57 girls, 25 OB) aged 7 to 14 years to determinate angular and linear craniofacial measures and upper airway dimensions. We compared the cephalometric pattern of these children with those of OSAS patients in the literature, measured by the following parameters: SNA, SNB, ANB, NSPIO, NSGoGn, I.NA, I-NA, I.NB, I-NB, UPAS, PAS, MP-H and C3H. Statistical analysis was based on t-Test and Chi-square.

**Results :** The OB boys and girls presented abnormal cephalometric values with reduced Upper Pharyngeal Airway Space (<8mm) compared to literature ( $p<0.001$ ), the same measures of OSAS patients. OB girls had craniofacial morphology alterations earlier than boys and the measures showed mandible retropositioned, the occlusal and mandibular plane angles enlarged, the incisors proclined. The measures showed differences between OB and NB children and they were the same when we compared the apnea cephalometric pattern: SNB, NSGoGn, NSPIO, UPAS and PAS ( $p<0,01$ ).

**Conclusion :** The measures showed evident differences between OB and NB children when we compared with the apnea cephalometric pattern. The girls grow up quicker than boys' do and they show alteration of craniofacial morphology earlier than boys.

**Support (optional):**

**0281**

**IMPACT OF THE AMERICAN ACADEMY OF PEDIATRICS CLINICAL PRACTICE GUIDELINE ON REFERRALS FOR PEDIATRIC SLEEP EVALUATIONS**

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**Introduction :** In April of 2002, the American Academy of Pediatrics (AAP) published a clinical practice guideline for the diagnosis and treatment of childhood obstructive sleep apnea syndrome (OSAS). The purpose of the guideline was to increase the recognition of OSAS by pediatricians, thereby decreasing diagnostic delay and preventing the subsequent development of significant sequelae of OSAS. The aim of our study was to evaluate the impact of the AAP guideline on the clinical practice patterns of pediatricians. Specifically, we sought to determine the impact of the guideline on referrals to a specialist in managing sleep-disordered breathing in children.

**Methods :** A retrospective chart review of 300 pediatric sleep patients referred to the Center for Pediatric Sleep Disorders between April 1, 2000 and December 31, 2004 was conducted. Three groups of patients were identified: Group 1 consisted of referrals from 4/1/00-12/31/00 (pre-guideline); Group 2 consisted of referrals from 4/1/02-12/31/02 (immediately post-guideline); while Group 3 consisted of referrals from 4/1/04-12/31/04 (recent). Sibling referrals were excluded. Seven referral sources were identified: self-referral, pediatrician, otolaryngologist, neurologist, pulmonologist, or endocrinologist. Data from the first one hundred referrals within each time period was analyzed.

**Results :** A total of 257 patient charts had complete data and were available for analysis. Patient numbers in each of the three groups analyzed were similar. Only 26% of referrals for sleep evaluations in Group 1 were from the child's pediatrician, with the highest percentage of referrals in Group 1 being self-referrals (32%). Immediately following the AAP guideline (Group 2), referrals from pediatricians increased to 40%, while our most recent data (Group 3) show a referral rate of 55% from pediatricians. Self-referrals in Group 3 declined to 14%, and additional sources of referrals included geneticists and child psychologists, albeit in small numbers (2% and 1%, respectively).

**Conclusion :** We conclude that the 2002 AAP clinical practice guideline for the diagnosis and management of childhood OSAS has had a significant impact on the referrals for pediatric sleep evaluations. Specifically, pediatricians are now the most common referral source for sleep evaluations. Our data suggests that pediatricians are screening for snoring at increased rates. Educational efforts to heighten the recognition of childhood OSAS in the primary care setting are succeeding.

**Support (optional):**

**0282**

**SLEEP AND REM DENSITY IN CHILDREN WITH PARTIAL CEREBELLAR RESECTIONS**

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**Introduction :** Because of its roles in motor coordination and autonomic system integration, the cerebellum has been postulated to have a role in respiratory control, particularly during sleep. Children with a history of partial cerebellar resections have clinical apnea, but the extent of breathing abnormalities during sleep is unknown. We postulated that children who have undergone resections of cerebellar lesions would have sleep disordered breathing.

**Methods :** Subjects with histories of midline cerebellar lesion resections due to neoplasms without brainstem involvement underwent overnight polysomnography in a pediatric sleep laboratory after normal lung function was documented by pulmonary function tests. Studies were scored by 2 investigators, including individual eye movements in REM sleep.

**Results :** Seven subjects (3 female; age  $9.0 \pm 5.4$  years, BMI  $19.5 \pm 4.2$ ) underwent PSG. Sleep architecture was similar compared to published pediatric normative values: sleep efficiency ( $89 \pm 6.2\%$ ); sleep latency ( $7.7 \pm 9.4$  minutes); stage I ( $6.9 \pm 4.8\%$ ); stage 2 ( $38.9 \pm 7.1\%$ ); delta sleep ( $30.3 \pm 5.3\%$ ); REM sleep ( $23.8 \pm 5.5\%$ ). When compared to our laboratory's normative standards, apnea-hypopnea index was higher ( $2.7 \pm 2.6$ ), nadir oxygen saturation was lower ( $86 \pm 13.1\%$ ), and peak end-tidal CO<sub>2</sub> was higher ( $49.0 \pm 2.7$  torr) than expected. Interestingly, REM density (number of eye movements per minute of REM sleep) were decreased compared to published pediatric control values ( $3.0 \pm 3.9$  vs.  $11.7 \pm 4.0$ ;  $p=0.0006$ ).

**Conclusion :** Children with partial cerebellar resections appear to have the presence of mild sleep-disordered breathing. In addition, they have a decrease in REM density. We speculate that this may be due to the cerebellum's role of motor coordination both for maintaining upper airway patency as well as coordinating extraocular movements during sleep.

**Support (optional):** ML Chen was supported by the CHLA Saban Research Institute Research Career Development Fellowship.

## 0283

### NAP PREVALENCE, FREQUENCY, AND DURATION DURING THE FIRST 7 YEARS: A DATA BASED ANALYSIS OF THE EXISTING LITERATURE

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**Introduction :** Numerous school districts have eliminated napping from early childhood programs. The implications of these policies are unknown as there are currently no data based guidelines for daytime sleep need or its importance in behavior regulation. This literature search and analysis of published results attempted to estimate normative daytime sleep habits of children aged 6 months to 7 years.

**Methods :** A literature search of PubMed identified 95 articles; a subgroup of 15 (n=8132) met selection criteria that included, children (0-80 months) and reports of percentage napping, nap duration, or frequency. A linear regression model related age to each napping variable in order to estimate norms for napping across development.

**Results :** Strong and significant negative associations with age were found for all three variables. R squares and fitted estimates for each age, 12, 24, 36, 48, 60, 72 months, are presented below. For percent napping, (R squared=0.77) estimates by age are: 100%, 85.76%, 68.24%, 50.70%, 33.17%, 15.64%. For naps per week, (R squared=0.78) estimates by age are: 10.42, 8.45, 6.49, 4.52, 2.55, 0.59. The minutes napped per day (R squared= 0.68) estimates by age are: 158.08, 135.74, 113.39, 91.04, 68.68, 46.33.

**Conclusion :** As predicted, percentage, duration, and frequency of napping decreased with age. It is notable that half of 4 year olds, a third of 5 year olds, and 15% of 6 year olds nap. This study has direct implications for educational policy given increasing numbers of children entering pre-school programs at earlier ages and rising numbers of early childhood programs in public schools. In spite of serious methodological issues with self reported data and discrepancies in methods of collecting napping data, these results indicate the strong need for standardized normative data on napping patterns across development. It is also critical to assess the impact of the elimination of naps in early childhood programs.

**Support (optional):**

## 0284

### RELATIONSHIP BETWEEN CHILD SLEEP DISTURBANCES AND MATERNAL SLEEP, MOOD, AND STRESS

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**Introduction :** Although it has clearly been established that poor quality sleep is related to negative mood and poor functioning in adults, little is known about the relationship between child and maternal sleep patterns. This study examined the relationship between child sleep pattern, maternal sleep patterns, and maternal daytime mood, stress, and functioning.

**Methods :** 47 mothers completed measures of parent and child sleep (two-week sleep diary, Children's Sleep Habits Questionnaire), depres-

sion (Center for Epidemiological Studies - Depression Scale), parenting stress (measures of overload and maternal distress), and daytime functioning (Iowa Fatigue Scale, Stanford Sleepiness Scale). Mothers were 98% Caucasian, ages 30-50 years (mean=38.4), with 72% working outside the home. Children ages 3-14 years (mean=7.4), 64% male, and 79% had their own bedroom.

**Results :** Using the clinical cutoff on the Children's Sleep Habits Questionnaire, significant differences in maternal mood and stress were found between mothers of children with and without significant sleep disturbances. Multiple regression analyses found the quality of the child sleep disruptions significantly predicted maternal sleep quality,  $F(1,42)=8.66$ ,  $p=0.005$ , accounting for 15% of the variance. Maternal sleep quality was a significant predictor of overload,  $F(1,42)=14.37$ ,  $p<0.001$ , (15% of the variance), depression,  $F(1,42)=7.35$ ,  $p=0.01$ , (24% of the variance), parental distress,  $F(2,41)=7.20$ ,  $p=0.002$ , (controlling for employment status, 22% of the variance), fatigue,  $F(1,42)=15.91$ ,  $p<0.001$ , (26% of the variance), and sleepiness,  $F(1,42)=6.09$ ,  $p=0.01$ , (11% of the variance).

**Conclusion :** Together these results suggest that the quality of children's sleep has a significant impact on maternal sleep quality, and in turn, maternal mood, stress, and functioning during the day. Results from this study highlight the importance of screening for and treating pediatric sleep disruptions, as these problems may impact not only the child's functioning, but the entire family's.

**Support (optional):** This study was funded by the National Sleep Foundation's Pickwick Postdoctoral Fellowship in Sleep Medicine.

## 0285

### SLEEP DISTURBANCES IN CHILDREN HOSPITALIZED IN PEDIATRIC INTENSIVE CARE UNIT.

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**Introduction :** Sleep is of great importance to hospitalized patients. Sleep improves mental, physical functions (e.g. the immune system), and facilitates recovery. Intensive Care Units (ICU) are characterized by intense activity; the work of the nursing staff involves noise and requires light day and night. There is hardly any difference between day and night activities, which might result in unnecessary sleep disturbances. The purpose of this study was to characterize and quantify sleep disturbances in the PICU.

**Methods :** Sleep patterns of convenient sample of 30 children were monitored by Actigraphy and Manual sound level meter starting on second night of admission. The record period lasted for 12 hours, from 7pm till 7am the next morning. Factors that may interrupt sleep (e.g. noise levels, light intensity and invasive and non-invasive instrumentation) were monitored. In addition, the principal investigator observed and recorded "blindly" the activities of the nursing staff. Data analysis: Sleep characteristics were correlated with a number of variables which past research found to have an adverse effect on sleep.

**Results :** Thirty children (19M/11F) were observed. All were fully conscious, not treated by any hypnotics or sedatives and no history of sleep disorders. Their mean age was  $6\pm 4$  years. Average total sleep time was  $4\pm 2$  hours, with a sleep efficiency of  $40\pm 21\%$ . A significant negative correlation existed between sleep efficiency and the nursing staff activity level ( $r= -0.53$ ,  $p<0.05$ ), total general activities ( $r= -0.51$ ,  $p<0.05$ ), light above the patient ( $r= -0.73$ ,  $p<0.001$ ), the number of patients in the PICU ( $r= -0.48$ ,  $p<0.01$ ), the instrumentation level ( $r= -0.56$ ,  $p<0.001$ ) and the average noise level ( $r= -0.74$ ,  $p<0.001$ ). Similarly, total sleep time correlated negatively with these factors ( $r= -0.49$ ,  $-0.39$ ,  $-0.48$  and  $-0.62$ ,

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$p < 0.05$  for all).

**Conclusion :** Children's sleep pattern in the PICU is severely disturbed, and their sleep disturbances are correlated with preventable factors such as increased noise levels or activities which can take place during day-time. Nursing staff is unaware of the importance of efficient sleep, which facilitates recovery. Future studies should focus on the outcome effects of modifying these preventable adverse factors.

**Support (optional):**

### 0286

#### THE USE OF PHARMACOTHERAPY TO TREAT PEDIATRIC INSOMNIA IN HOSPITALIZED PATIENTS

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**Introduction :** Although hypnotic use has been recommended for pediatric insomnia in response to medical illness and related issues (e.g., pain, hospitalization), little is known about the medications prescribed for sleep in hospitalized children. The aims of this study are (1) to determine the percentage of hospitalized children who receive medication for sleep disturbances, (2) to determine what medications are prescribed for sleep difficulties, and (3) to examine medical and demographic variables related to medications used for sleep difficulties in pediatric hospitals.

**Methods :** This study utilizes a chart review methodology for all inpatients at three pediatric hospitals from 26 randomly selected days between January 1 and December 31, 2004. Demographic, medical, and medication data will be collected on over 20,000 patients.

**Results :** Preliminary results ( $n=3544$ ) indicate that 5.4% of hospitalized children are prescribed medications for sleep, with antihistamines the most frequently prescribed medication (36%), followed by benzodiazepines (31%). Other common medications included anticonvulsants (10%), alpha agonists (7%) and hypnotics (6%). Children who were prescribed medications for sleep were significantly older than the average age of all hospitalized children (9.9 vs. 6.3 years),  $F(1,3642)=51.2$ ,  $p < 0.001$ , had longer hospitalizations (28.3 vs. 22.9 days),  $F(1,3642)=3.09$ ,  $p=0.08$ , were more likely to be Caucasian,  $\chi^2(3)=11.3$ ,  $p=0.01$ , and on a critical care service,  $\chi^2(3)=72.8$ ,  $p < 0.001$ .

**Conclusion :** This study is the first to examine the use of pharmacotherapy for sleep problems in hospitalized children. While non-pharmacological interventions for pediatric sleep disturbances are effective, they may not be appropriate for hospitalized children with sleep problems due to the length of time needed before behavioral treatments can be effective. While these results indicate variability in the types of medications prescribed, antihistamines and benzodiazepines are the most common ones currently used for hospitalized pediatric patients. The results of this study suggest the need for further examination of and physician training focusing on sleep problems and potential interventions for hospitalized children.

**Support (optional):** This study was funded by Sepracor.

### 0287

#### CIRCULATING CYSTEINYL LT 1 RECEPTOR IN CHILDREN WITH MILD SLEEP DISORDERED BREATHING

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**Introduction :** We have shown that Cysteinyl leukotriene 1 receptor (LT-

1 R) is abundantly expressed in tonsils and adenoids of children with SDB, and how therapy with a LT-1 R antagonist is associated with significant clinical improvements in children with mild SDB. We hypothesized that the LT-1 R is over-expressed in circulating white blood cells of children with mild SDB in comparison to children with Apnea Hypopnea Index (AHI)  $< 1$ .

**Methods :** Twenty children underwent polysomnographic evaluations. Samples for plasma CRP level were drawn the next morning. White blood cells (WBC's) were separated from blood samples with dextran sedimentation, and extracted proteins were assessed for the presence of LT-1 R with western blots

**Results :** 11 boys and 9 girls aged  $5.3 \pm 3.1$  years, BMI of  $19.1 \pm 0.34$  kg/m<sup>2</sup>, were studied. 10 children with mild Sleep Disordered Breathing (SDB) (AHI=  $5.1 \pm 2.4$ ), and 10 with out SDB (AHI=  $0.67 \pm 0.13$ ). CRP was not different among the 2 groups ( $0.065 \pm 0.012$  vs  $0.071 \pm 0.013$  mg/dl,  $p=0.68$ ). In contrast LT-1 R/ Beta Actin expression was significantly higher in the mild SDB group ( $1.38 \pm 0.34$  vs  $0.66 \pm 0.27$ ,  $p < 0.01$ )

**Conclusion :** LT-1R is expressed in circulating WBC's of children with mild SDB at the presence of normal CRP. LT-1R may serve as a circulating marker for a selective inflammatory pathway, in contrast to crude known markers such as CRP in children with mild SDB. The effects of anti inflammatory therapy on such a marker need to be determined.

**Support (optional):**

### 0288

#### EXCESSIVE DAYTIME SLEEPINESS IN TEENS TREATED FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD)

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**Introduction :** Healthy children appear behaviorally inattentive when sleep restricted, raising questions about sleepiness in children diagnosed with ADHD. Since adolescence is marked by increased risk for inadequate sleep patterns and increasing prominence of inattentive symptoms in the diagnosis of ADHD, we examined daytime sleepiness in teens medicated for ADHD.

**Methods :** Teens diagnosed with ADHD and treated with a stimulant medication were enrolled. Participants were recorded with daytime MSLT on one, two, or three weekends during the school year. Participants followed normal sleep and medication routines at home prior to each MSLT recording, but were told not to take medication on the day of testing. Sleep and wake patterns at home were monitored with actigraphy, and medication use was monitored with electronic pill-bottle. A clinical MSLT protocol was used at the first laboratory visit, allowing sleep to continue for 15 minutes at each nap opportunity. Remaining visits used a research MSLT protocol, ending naps as soon as sleep occurred. Results are mean latency from the first four naps each day, scheduled for 0900, 1100, 1300, and 1500.

**Results :** Thirty-two adolescents (20 boys), 12 to 17 yrs ( $M=15$ ), were tested. Twelve were tested on more than one weekend. Mean latencies from clinical MSLT ranged from 1 to 19 minutes ( $n=28$ ;  $M=11$  min.,  $SD=5$ ), while mean latencies with the research MSLT ranged from 1 to 20 minutes ( $n=20$ ;  $M=8$  min.,  $SD=6$ ). Eleven participants (34%) had mean latency of 6 minutes or less for at least one visit.

**Conclusion :** Excessive sleepiness in one-third of teens medicated for ADHD, while not surprising, is cause for concern. Behavioral manifestations of excessive sleepiness could overlap with the clinical symptoms that justify continued diagnosis and treatment in these students. Excessive

sleepiness could also interfere with any therapeutic action of medication treatment.

**Support (optional):** MH63199

## 0289

### ADENOTONSILLECTOMY AND MAXILLARY DISTRACTION IN SNORING CHILDREN

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**Introduction :** Children with sleep disordered breathing have been improved with adenotonsillectomy and maxillary distraction. But maxillary distraction was performed on subjects that previously had had adenotonsillectomy. The possibility that one treatment is sufficient has never been explored.

**Methods :** 32 successively seen children, mean age 6.9 SD:1.6) years, with clinical symptoms (parasomnia, daytime fatigue, hyperactivity, inattention, school or behavioral problems and regular snoring) and AHI>1 at polysomnography with nasal cannula-pressure transducer, presenting with tonsils graded 2 or 3 and narrow maxilla were randomized to have treatment started either by surgical removal of adenotonsils (n=17) or by maxillary distraction (n=15). Parents were told that both treatments were thought to be needed in view of the anatomic findings, but second phase would not be performed if results were sufficient as indicated by clinical re-evaluation and mid-point polysomnography. All children had standardized treatment performed by the same 2 trained surgeons and orthodontists. Radio-frequency of turbinates was performed at time of adenotonsillectomy if needed. Polysomnography was performed 3 months after end of each phase of total treatment with possibility to stop further therapy at that time.

**Results :** Independently of initial treatment, all children had to undergo the second treatment phase, as residual events were seen at PSG. And 9 of the 32 children presented residual flow limitation and low AHI after completion of both treatments, despite disappearance of major complaints. The persistence of abnormal AHI was related to the limited gain obtainable with orthodontic treatment when mandibular and maxillary narrowing are both present, or an associated antero-posterior skeletal growth problem is present.

**Conclusion :** adenotonsillectomy and orthodontic treatment are both needed if narrow maxilla is present, and residual AHI may be seen despite combine treatment approach due to skeletal built-up.

**Support (optional):**

## 0290

### PERFORMANCE ON A COMPUTERIZED VIGILANCE TASK CORRELATES WITH ACTIGRAPHY-DEFINED SLEEP DISRUPTION, BUT NOT PSG INDEXES OF SLEEP DISRUPTION OR HYPOXIA, IN OBESE ADOLESCENTS

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**Introduction :** Sleep disordered breathing is known to affect attention in

children and adults. However, only weak and inconsistent correlations have been found between measures of vigilance and polysomnography (PSG)-defined indexes of sleep disturbance or hypoxia. This study examined the relative ability of indexes derived from PSG and actigraphy to predict obese adolescents' performance on a computerized vigilance task.

**Methods :** Obese individuals aged 10-16 from a hospital-based pediatric weight management program (n = 73) or sleep clinic (n = 16) underwent single-night PSG and office-based attention testing. All exceeded the 95th percentile of body mass index for their age and sex. Of these, 68 also wore an actigraph, scored using a validated algorithm, for at least 5 nights. Vigilance was assessed with the Gordon Diagnostic System (GDS), which yields indexes of sustained attention (total correct) and impulsivity (commission errors). Spearman correlations examined the associations between these tests and measures of hypoxia (PSG nadir oxygenation) and sleep disruption (PSG sleep efficiency post-onset, arousal index, apnea + hypopnea index; Actigraph-defined sleep efficiency post-onset, arousals, and arousals longer than 5 minutes).

**Results :** The sample was 64% female; 42% Caucasian; 56% African-American; and generally quite obese (mean BMI=38.8, 99th %ile). No PSG index even approached a significant correlation with GDS scores ( $|r| < .15$ ,  $ps > .15$ ). In contrast, actigraphically-defined sleep efficiency post-onset correlated with sustained attention ( $r = .29$ ,  $p = .019$ ) and impulsivity ( $r = .42$ ,  $p < .001$ ), arousals correlated with impulsivity ( $r = .34$ ,  $p = .005$ ), and arousals longer than 5 minutes correlated with impulsivity ( $r = .49$ ,  $p < .001$ ).

**Conclusion :** Poor sleep quality, as indexed by actigraphy-detected movement patterns, predicted poor vigilance and impulsivity on a computerized test. In contrast, and consistent with much of the literature, PSG indexes were poor predictors of vigilance and impulsivity.

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## 0291

### FAMILIAL STUDY OF SLEEP PATTERNS AND SLEEP PROBLEMS IN ADOLESCENTS

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**Introduction :** Sleep changes in adolescence have been demonstrated to be related to biological changes associated with the onset of puberty and psychosocial factors. Adolescent sleep patterns or disturbances may also be determined by genetic and family environmental factors. This report is aimed to examine whether adolescent sleep patterns or disturbances are associated with parent sleep behavior.

**Methods :** This report represents part of an ongoing longitudinal study on sleep and adolescent health in 4 middle schools and 3 high schools in Jinan city of Shandong Province, China. A total of 1,066 adolescents completed the first wave survey, including 625 boys and 441 girls, 557 middle school students (mean age = 13.5 years, SD = 0.6) and 509 high school students (mean age = 16.4 years, SD = 0.7). Adolescents and parents reported their own sleep patterns and sleep problems, respectively, via self-administered questionnaires.

**Results :** Adolescent sleep patterns differed between weekdays and weekends: average bedtime, 22:12 vs. 22:21; morning rising time, 05:55 vs. 08:17; sleep duration, 7.5 h vs. 9.4 h. Of adolescents, 16.1% had insomnia symptoms and 13.0% felt very sleepy during daytime at least 3 times a week, 13.3% reported nightmares and loud snoring at least once a week. Significant correlations were observed between adolescents and parents for bedtime ( $r = .27$  with both parents) and sleep duration ( $r = .17$  with mothers,  $r = .19$  with fathers) at weekdays, and for bedtime ( $r = .34$  with mothers,  $r = .44$  with fathers) and morning rising time ( $r = .21$  with moth-

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ers,  $r = .25$  with fathers) at weekends. Self reported sleep latency, sleep quality, and sleep need were also significantly correlated between adolescents and mothers and fathers, with an average correlation  $r = .20$ . History of chronic insomnia in parents were significantly associated with increased risk for difficulty initiating sleep in adolescents (OR = 4.0 for mothers and OR = 7.0 for fathers). History of chronic insomnia in fathers was also associated with adolescent difficulty returning to sleep once awaking (OR = 8.0) and early morning awaking (OR = 4.8).

**Conclusion :** Adolescents and parents have low to moderate correlations in sleep patterns, sleep latency, and reported sleep quality. History of chronic insomnia in mothers and fathers is a significant predictor of adolescent insomnia symptoms. Further studies are required to examine the effects of genetic and environmental interaction on adolescent sleep changes and disturbances.

**Support (optional):**

### 0292

#### ANALYSIS OF ADOLESCENT SLEEP BY GRADE AND INSOMNIA TENDENCY DURING SCHOOL AND VACATION

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**Introduction :** Teenagers are known to limit their sleep during the school week; sleeping about nine hours ad lib but only 7 - 7.5 hours during the school week. Our aim was threefold: 1) examine sleep patterns during transitions from a school week to vacation 2) assess differences in sleep patterns from 9th to 12th grade and 3) compare adolescents who report poor sleep with those reporting good sleep.

**Methods :** Subjects were randomly selected from a high school in suburban New York. Sixty-four adolescents, grades 9-12 (41 females, 23 males, mean 16.0 years) completed sleep logs during a consecutive 3 week period in which there were vacation days sandwiched between school days (start time:7:30 AM). Dependent variables included total sleep time (TST), bedtime (BT), arise time, and sleep latency. Poor (n=21) and good sleepers (n=17) were identified by a questionnaire.

**Results :** Mean TST for school nights (6.5 hours) differed from vacation nights (8.2 hours) ( $p < .01$ ). Subjects delayed bedtime on vacation (12:31 AM) but school night bedtimes were also late (11:26 PM). Mean arise times for school mornings was 6:15 AM and 9:28 AM on vacation. There were no differences in sleep latency. Comparisons by grade yielded a progressive reduction in TST on school (9th-7.2h, 10th-6.9h, 11th-6.4h, 12th-6.25h) and vacation nights (9th-10h, 10th-8.7h, 11th-8h, 12th-7.6h) ( $p < .01$ ), a progressive delay in bedtime by grade but no differences in arise time. TST also differed for a subset of "poor sleepers" on school nights (6.4h) and vacation nights (8.0h) when compared to "good sleepers" (n=17) (school-7.3h, vacation-8.5h) ( $p < .01$ ). "Poor sleepers" also went to bed later, had longer sleep latencies and more awakenings than "good sleepers" on both school and vacation nights.

**Conclusion :** Our results support the view that adolescent sleep is constrained by school schedules and circadian tendencies and that this trend worsens progressively with age. The findings in the "poor sleepers" is quite provocative and suggests that adolescents at risk for developing insomnia may be identified in their teens.

**Support (optional):**

### 0293

#### THE ASSOCIATION OF THE PEDIATRIC DAYTIME SLEEPINESS SCALE (PDSS) WITH MEAN SLEEP LATENCY TEST (MSLT) AND POLYSOMNOGRAM (PSG) RESULTS IN CHILDREN AND ADOLESCENTS

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**Introduction :** The PDSS is a validated questionnaire to subjectively quantify sleepiness in children aged 11-15 years. The MSLT is an objective physiological measure of daytime sleepiness. The purpose of this study is to determine if an association exists between the level of sleepiness as measured by the PDSS score and the level of sleepiness as measured by MSLT. The association between the PDSS score and the diagnosis of apnea was also evaluated.

**Methods :** A retrospective review of all children <18 years who had a completed PDSS and MSLT between 9/1/2003 -10/31/2005 was performed. The mean sleep latency (MSL) from the MSLT, the AHI and mean sleep latency from a recent PSG were collected. The MSL of all children and a subset aged 11-15y were analyzed. MSL was collapsed into 3 levels: Normal (>10), Mild/Moderate (<5-10) and Severe (<5). Pearson Correlation Coefficients were used to assess the association between two continuous measures. ANOVA was performed to assess associations between categorical and continuous measures.

**Results :** A total of 30 children (age 6-16y) were included in this analysis. PDSS was not found to be associated with PSG sleep latency ( $r=0.19, p=0.31$ ), MSL in the overall sample ( $r=0.16, p=.41$ ) or MSL in a subset of children aged 11-15y ( $r=0.13, p=0.63$ ). PDSS was not found to be associated with MSL severity in the overall sample ( $p=0.52$ ), MSL severity in a subset of children aged 11-15 y ( $p=0.74$ ), or with PSG diagnosis of apnea ( $p=0.32$ ).

**Conclusion :** The PDSS was not found to have a significant association with MSL or PSG measures (MSL, PSG AHI & sleep latency). Study limitations include small sample size and possible bias concerning whether the patient or parent filled out the PDSS. Further studies with a greater sample size are needed.

**Support (optional):**

### 0294

#### ADENOTONSILLECTOMY IMPROVES ENURESIS IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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**Introduction :** To evaluate the prevalence of nocturnal enuresis in children diagnosed with obstructive sleep apnea syndrome and the effect of tonsillectomy and adenoidectomy on enuresis.

**Methods :** All children 4-18 years of age who underwent polysomnography (PSG) between January 2003 and May 2004 were included (n=161). The evaluation was based on a retrospective review of a standard sleep questionnaire and a full overnight PSG, followed by an additional structured telephone questionnaire performed 9 months after T&A (range 5-14).

**Results :** We identified 144 (89%) children with an apnea hypopnea index >1. Of these 144 children, 42 [29.2% (95% CI, 21.8 - 36.6)] reported to have enuresis. Among the 27 children who had undergone adenotonsillectomy, 74.1% had frequent enuresis before the procedure compared to 37% one month after [n=27 ( $\chi^2=5.56, P=0.018$ )]. Of the 27 children who



underwent adenotonsillectomy, a decrease in enuresis severity was reported by 70.4% (95% CI 53.2-87.62), while in 56% (95% CI 41.96-70.06) the improvement had occurred within one month following surgery. In 11/27 children (41%), enuresis disappeared within one month, while in 3/27 (11%) enuresis disappeared throughout the remaining time of follow-up.

**Conclusion :** Obstructive sleep apnea in children is frequently associated with nocturnal enuresis. Adenotonsillectomy has a favorable therapeutic effect on enuresis in children with obstructive sleep apnea presenting this symptom.

**Support (optional):**

## 0295

### SLEEP DISTURBANCES ASSOCIATED WITH DEPRESSIVE PHENOMENOLOGY AND COMORBIDITY IN CHILD AND ADOLESCENT DEPRESSION

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**Introduction :** Sleep disturbances in children with depression are very prevalent. However, whether children with and without sleep disturbances or with different types of sleep problems manifest different clinical characteristics remains unexplored. The purpose of this study is to examine the clinical profiles of depressive symptoms and comorbid disorders in depressed children with different types of sleep disturbances.

**Methods :** Subjects included 553 children with major depressive disorder (MDD), recruited for an ongoing study from 22 mental health facilities in Hungary between April 2000 and December 2004. Of the sample, 55% were boys, mean age was 11.7 years (SD = 2.0, range = 7.3-14.9), 94% were Caucasian. MDD and comorbid disorders were diagnosed according to DSM-IV criteria, based on standardized clinical evaluations via the Interview Schedule for Children and Adolescents-Diagnostic Version (ISCA-D) and consensus best-estimate diagnoses.

**Results :** Based on the ISCA-D clinicians' symptom ratings, 72.7% of the sample had sleep disturbance, including insomnia (53.5%), hypersomnia (9.0%), and both (10.1%). No age and sex differences in the prevalence rates of insomnia, hypersomnia, and both were detected (for all  $p > .05$ ). Compared with children without sleep disturbance, insomniac children demonstrated more frequent depressed mood (OR = 2.2), worse mood in the morning (OR = 1.6), and distinct sadness (OR = 1.9); hypersomniac children showed more frequent weight loss (OR = 2.4), weight gain (OR = 2.2) and distinct sadness (OR = 2.6), but less frequent worthlessness (OR = 0.35); children with both sleep disturbances evidenced more frequent loss of interest (OR = 3.3), weight loss (OR = 2.5), psychomotor agitation (OR = 2.1), retardation (OR = 2.2), distinct sadness (OR = 3.5), and inappropriate guilt (OR = 2.5) after controlling for other depressive symptoms. Rates of comorbid anxiety and attention-deficit/hyperactivity disorder (ADHD) did not significantly differ across groups.

**Conclusion :** Close to 73% of depressed children evidence sleep disturbance, with the majority having insomnia. Children with insomnia, hypersomnia, and both types of sleep problems demonstrate different depressive profiles. Differentiating sleep disturbances may contribute to a better understanding of the etiology of child depression and may lead to improved clinical classification and treatment.

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## 0296

### SLEEP NASOPHARYNGOSCOPY IN THE MANAGEMENT OF PEDIATRIC SLEEP DISORDERED BREATHING

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**Introduction :** While endoscopy for airway conditions constitutes a cornerstone for management, sleep nasopharyngoscopy (SNP) is not routinely used for pediatric sleep disordered breathing (SDB) in healthy children. Our aim is to demonstrate the spectrum of endoscopic findings associated with SDB, and assess the diagnostic value of a structured scoring scheme based on SNP.

**Methods :** A retrospective case series of children presenting to a tertiary pediatric otolaryngology practice with persistent SDB and requiring treatment. All endoscopies were performed under Propofol/Remifentanyl infusion or boluses. The endoscopic findings at all levels were systematically reported and digitized. Demographics, diagnoses and co-morbidities, surgeries, techniques, complications and sleep studies data were collected. A binary score for SNP findings deemed equivalent to  $<$  or  $>$  1 Apnea-Hypopnea/hr index (AHI) was devised. A record of the "awake" tonsillar size was transformed into a binary score. Statistical analysis included descriptive data, kappa analysis ( $k$ ), and sensitivity and specificity analysis with reference to AHI.

**Results :** Over 2 years, 148 children underwent SNP (82 boys; mean:6.5years (range: 7mths-16.5years). 14 patients were syndromic. 24 children obstructed at one level, 93 at two, and 31 at three. 73 had dynamic pharyngeal obstructions. 22 had laryngeal obstruction. 12 had obstruction at tongue base. While 63 children had visible obstructive tonsils in the clinic (Brodsky classification), 93 had hypopharyngeal tonsillar extension on SNP. 31 patients had Polysomnography based on American Thoracic Society criteria, the remainder had pulse oximetry.  $k=0$  for agreement between the SNP and clinic findings for non-obstructive tonsils.  $k=0.66$  (good agreement) between the AHI defined SDB and SNP findings. SNP sensitivity was 0.96, specificity 0.60 (PPV 0.92 & NPV 0.75).

**Conclusion :** SNP has good diagnostic value and our data shows that anaesthetic-induced sleep does not impact negatively on demonstration of pathology. We speculate that SNP represents a readily available, minimally invasive diagnostic information which may help avoid unnecessary surgery and supplement polysomnography in pediatric SDB.

**Support (optional):**

## 0297

### THE EFFECTS OF AN INTEGRATIVE BEHAVIORAL SLEEP MEDICINE INTERVENTION ON TRAUMATIC STRESS SYMPTOMS IN ADOLESCENTS RECENTLY TREATED FOR SUBSTANCE ABUSE

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**Introduction :** Insomnia and psychiatric symptoms are independent predictors of substance abuse in adolescents. Of the internalizing psychiatric symptom clusters, posttraumatic stress disorder is one of the most predictive of later substance use. The purpose of this study was to test whether improvement in sleep by an integrative, behavioral sleep treatment would

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reduce traumatic stress (TS) symptoms in a sample of adolescents recently treated for substance abuse. Interventions focusing on insomnia and TS may be particularly useful in preventing substance abuse relapse.

**Methods :** Participants were 20 adolescents who completed a 6-week integrative, behavioral sleep intervention and at least 4 weeks of sleep diaries. Upon enrollment into the study, all adolescents had disturbances in sleep or daytime sleepiness and had recently completed treatment for substance abuse at outpatient community centers. Traumatic stress symptoms were assessed by the Traumatic Stress Index (TSI) of the Global Appraisal of Individual Needs assessment at baseline, post-treatment, 3-months post-treatment, and 12-months post-treatment.

**Results :** Sleep diary index intercepts and slopes were computed and each was separately entered as the independent variable in a series of mixed model analyses estimating growth trajectories for TSI scores. From this, a statistically significant Intercept x Time interaction emerged for Time in Bed,  $\Delta 11 = -.01$ ,  $p = .02$ , and an interaction trend emerged for the Total Sleep Time (TST) intercept,  $\Delta 11 = -.009$ ,  $p = .06$ . Individuals with more TIB and TST at the beginning of treatment had more improvement in TS trajectories across treatment and the 12-month follow-up period. Interaction trends also emerged for the sleep onset latency (SOL) slope,  $\Delta 11 = .24$ ,  $p = .09$  and the lights-out time slope,  $\Delta 11 = -.0008$ ,  $p = .08$ . Adolescents who had a decrease in SOL and a tendency to turn off their light later throughout treatment had greater improvements in TSI over time.

**Conclusion :** Results from this study suggest that higher levels of TST and TIB may decrease TS symptoms in adolescents with a history of substance abuse. Moreover, a decrease in the latency to sleep onset, potentially due to a delayed lights-out time, may facilitate improvement in TS symptoms. Overall, these results indicate that stimulus control, a therapy that encourages patients to attempt sleep only when they are sleepy, may be particularly helpful for adolescents with trauma and substance abuse histories.

**Support (optional):** This study was supported by contract from the Office of National Drug Control Policy. The views expressed in this article are those of the authors and do not necessarily reflect those of the funding agency.

### 0298

#### THE EFFECTS OF SLEEP RESTRICTION ON PERFORMANCE TESTING ON CHILDREN WITH OBSTRUCTIVE SLEEP APNEA (OSA) AND A HEALTHY COMPARISON GROUP

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**Introduction :** OSA has a negative impact children's neurocognitive functioning although the specific mechanisms of the effects of OSA are not yet fully understood. In this study we used two computerized-based measures of attention to investigate the impact of OSA and acute sleep restriction on children aged 6 to 10.

**Methods :** A total of 76 children aged 6 to 10 were recruited for this study. The participants included 59 otherwise healthy OSA participants (54.2% female, mean age= 7.9±1.4 years) and 17 healthy children not diagnosed with OSA (58.8% female, mean age=8.4±1.4 years). Participants completed a baseline neurocognitive assessment and then returned within two weeks and were re-tested immediately following a night of sleep restriction (sleep period: 4-8am). The battery of tests included a large number of neurocognitive measures, two of which, Test of Variables of Attention (TOVA) and the Attentional Networks Test (ANT) are reported on here.

**Results :** The groups were comparable with respect to age, gender and race. During baseline polysomnography the OSA group when compared to the comparison group had a significantly higher arousal index (mean

=15.4±12.9 vs. 82.+2.0 ) and RDI (mean= 8.7±13.1 vs. 0.1±.1),  $p's < .05$ . Two x 2 repeated measures ANOVAs compared baseline and between group differences. Significant group and time main effects, but no interaction effects were observed for increased response time and decrements in performance following the night of sleep restriction  $p < .05$ .

**Conclusion :** Acute sleep restriction had a significant impact on the performance of both groups of participants resulting in longer response times, more errors of omission and poorer signal detection. Significant group differences were also observed in performance with the OSA group performing significantly worse. The acute sleep restriction challenge did not have a more negative impact on the OSA group who have chronic sleep and sleep related respiratory disturbance.

**Support (optional):** National Institute of Mental Health K01001958

### 0299

#### THE TIMING OF CARDIOPULMONARY ARRESTS IN HOSPITALIZED PEDIATRIC PATIENTS

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**Introduction :** Previous studies in adults in outpatient and inpatient settings have examined the timing of cardiopulmonary arrests in a 24-hour period. These studies found a bimodal distribution with increased rates of cardiopulmonary arrests between 10:00 a.m.-12:00 p.m. and between 4:00-8:00 p.m. Our aim was to evaluate whether a similar pattern of cardiopulmonary arrests was present in children.

**Methods :** 1077 pulseless cardiopulmonary arrests in hospital settings in subjects age 18 years old and younger from January 2000 through December 2003 were evaluated in this population based retrospective study. Data was obtained from the National Registry of Cardiopulmonary Arrests (NRCPR), maintained through the American Heart Association. Three age groups, < 1 year, 1-10 years, and 10-18 years, were analyzed. Further analysis in < 1 month and < 3 months subsets, with overlapping subjects, was performed. Density plots, vonmises distributions and histogram plots in one hour increments were analyzed by likelihood ratios and Watson tests. The results were compared for differences in sex, location in the hospital and presenting rhythm by the Watson two sample test for circular data. Inter-group differences were evaluated by Pearson's Chi-squared tests.

**Results :** Three peaks of cardiopulmonary arrest were demonstrated. For the combined age group, vonmises distribution peaks occurred at 9:18 a.m., 4:11 p.m. and 1:42 a.m. All methods of analysis and age group divisions demonstrated a similar pattern of distribution.

**Conclusion :** Unlike adult patients in whom a bimodal distribution has been reported, three peaks of cardiopulmonary arrests were seen in pediatric patients. The unique peak occurred between 1:00-2:00 a.m. Other peaks occurred in a similar distribution to those described in adult studies (9:00-10:00 a.m. and 4:00-5:00 p.m.). Whether intrinsic (circadian rhythm) or extrinsic (staffing, admission trends) influences were the etiology for this pattern requires further investigation.

**Support (optional):**

**0300****A NEW EVOKED POTENTIAL COMPONENT DURING SLEEP IN CHILDREN***Colrain IM*

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**Introduction :** It has been known for nearly 70 years that K-complexes (KC) and vertex sharp waves (VSW) can be elicited by stimuli presented during NREM sleep in adults. We sought to determine the impact of Tanner stage on phasic events elicited during stage 2 sleep in children.

**Methods :** Data were collected from 12 pairs of same sex twins and one singleton subject aged between 8 and 17 years. One twin from each pair was selected for the present analysis. Sufficient responses were obtained from 12 subjects (6 boys), with 4 in T1, 3 in T2, and 5 in T3 or T4, which were combined for analysis. 64 channel EEG data were collected from a single night can using Neuroscan Synamp2 hardware and Scan 4.3 software. Responses were collected to auditory (80db 50 ms) tones presented binaurally via inert earphones. Data were scored for sleep stage and then for the type of phasic event produced by each stimulus within stage 2 sleep.

**Results :** Traditional KC responses were elicited to  $48 \pm 12\%$  of stimuli. In addition however, a previously undescribed evoked response was elicited to  $16 \pm 8\%$  of stimuli. It consisted of a positive-negative-positive complex, with a very large negative component ( $-200 \pm 26$   $\mu$ V in T1,  $-139 \pm 24$   $\mu$ V in T2 and  $-126 \pm 37$   $\mu$ V in T3/4) at approximately 350 ms. The complex lasted approximately 700 ms. The negative component displayed significant site ( $p < .001$ ) and site by Tanner stage interaction ( $p < .001$ ), being largest at Cz, but having a broader scalp topography in T1 and T2 than T3/4.

**Conclusion :** Children can readily elicit K-complexes, but also produce an additional delta frequency response with a vertex maximum and a much shorter latency. This component would appear to have features of both a VSW (scalp distribution and latency) and a KC (period reflecting delta generation).

**Support (optional):** HL058585

**0301****INCREASING TANNER STAGE LEADS TO "FRONTALIZATION" OF N550 SCALP TOPOGRAPHY***Colrain IM,<sup>1,2</sup> Baker FC,<sup>1,4</sup> Sullivan S,<sup>1</sup> Marcus CL<sup>3</sup>*

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**Introduction :** Adolescence is associated with a dramatic reduction in delta EEG activity during sleep. Both SWS% and slow wave activity measured by period amplitude analysis have been shown to decrease as a function of sexual development indexed by Tanner (T) stage. These changes are thought to reflect underlying changes in brain development, especially dendritic pruning. K-complexes are also delta EEG events and thus should also show Tanner stage-related changes reflective of dendritic pruning. We hypothesized that the scalp topography of evoked K-complexes should start as being broadly distributed and then become more frontally focused with increasing Tanner stage.

**Methods :** Data were collected from 12 pairs of same sex twins and one singleton subject aged between 8 and 17 years. One twin from each pair was selected for the present analysis. Sufficient responses were obtained from 12 subjects (6 boys), with 4 in T1, 3 in T2, 2 in T3 and 3 in T4. T3 and T4 were combined for analysis. 64 channel EEG data were collected from a single night can using Neuroscan Synamp2 hardware and Scan 4.3 software. Responses were collected to auditory (80db 50 ms) tones pre-

sented binaurally via inert earphones. Data were scored for sleep stage and then for the type of phasic event produced by each stimulus within stage 2 sleep. K-complexes were averaged and the N550 component measured at 8 midline sites ranging from FPz to Oz.

**Results :** KC+ N550 amplitude displayed a significant effect of site ( $p < .001$ ) with larger values over frontal sites generally. There was no main effect of Tanner stage, but there was a significant Tanner stage x site interaction ( $p < .05$ ), with substantially broader scalp distributions in the Tanner 1 and 2 children than seen in the Tanner 3/4 children. There was no effect of Tanner stage on KC elicitation.

**Conclusion :** K-complexes are readily elicited in stage 2 sleep in children. The scalp distribution of the N550 component shows evidence of "frontalization" with increasing sexual development and thus is a putative index of dendritic pruning in the developing brain.

**Support (optional):** HL058585

**0302****BEHAVIOR PROBLEMS IN CHILDREN AND ADOLESCENTS WITH PERIODIC LIMB MOVEMENT DISORDER (PLMD) AND RESTLESS LEGS SYNDROME (RLS)***Haak J, Huntley E, Lewin DS*

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**Introduction :** PLMD and RLS have been associated with sleep disturbance, behavior problems, and attention deficit hyperactivity disorder (ADHD) in children. The pathophysiology and the mechanisms of the neurobehavioral effects of RLS/PLMD in children have only been addressed in a few studies. This descriptive study evaluated the prevalence of behavior problems in a well characterized sample of children with RLS/PLMD

**Methods :** A retrospective chart review of 4-18 year old RLS/PLMD patients (N=22, 46% female, mean age= 9.0+4.5 years) presenting to a pediatric sleep program was conducted. Data summarized for this review included PSG results, serum ferritin levels, clinic interviews, and the Child Behavior Checklist (CBCL). Children with mild, obstructive sleep apnea were included in the study, but only if they met specific criteria (e.g. an RDI<5 or if the PLMI  $\geq$  RDIx2).

**Results :** The mean PLMI was  $13.2 \pm 8.9$  and the RDI was  $1.3 \pm 1.5$ . The mean CBCL, Total, Internalizing, Somatic, Withdrawn/Depressed, Affective and ADHD subscales were in the borderline or clinically significantly range. One-sample t tests indicated that there were significant differences between the Total, Internalizing and Externalizing CBCL scales and normative CBCL values. Serum ferritin levels (Mean 30.3mcg/ml) were available in a subgroup of 6 patients all of whom had at least borderline scores on the Total Problems scale. While not significant there was a positive correlation between CBCL scale scores and the PLMI ( $r = .22$ ). There was no association between the RDI or serum ferritin levels and CBCL scales.

**Conclusion :** This study found that pediatric patients referred to a sleep program and diagnosed with RLS/PLMD have an increased prevalence of neurobehavioral problems. While mild OSA may have accounted for some of the PLMI and behavior problems, this study demonstrates the need for further studies assessing the efficacy of iron supplementation as well as other treatment strategies to address RLS/PLMD and associated neurobehavioral problems.

**Support (optional):** 5R01NS040829

0303

**SLEEP HYGIENE PRACTICES IN TWO COMMUNITY DWELLING SAMPLES OF OLDER ADULTS**

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**Introduction :** Most cognitive-behavioral treatments for insomnia are not currently in widespread use. Sleep hygiene is the notable exception. Research in younger adults suggests insomniacs engage in poorer sleep hygiene than normal sleepers. Whether this is also the case for older insomniacs is unclear. This study examines common sleep hygiene practices in two community-based samples of older adults to determine which practices differentiate individuals with and without insomnia.

**Methods :** Sample 1-310 older adults (65+), Memphis, TN metropolitan area. Sample 2-103 older adults, Gainesville, FL area. Two weeks of sleep diaries and sleep hygiene practice measures (caffeine, nicotine, and alcohol usage; daytime napping; bed/wake time variability) were collected. Recruitment involved random digit dialing (sample 1) and advertisements (sample 2). Individuals with primary sleep disorders were excluded (apnea, PLMS).

**Results :** With the exception of nap frequency, insomniacs and subjective insomniacs did not engage in poorer sleep hygiene practices than individuals without insomnia. For sample 1 only, older insomniacs and subjective insomniacs reported napping 1.5 more days per week than older individuals without insomnia. Basal rates for the other sleep hygiene practices were generally low.

**Conclusion :** Overall, sleep hygiene behaviors did not differentiate individuals with and without insomnia. Thus, the efficacy of sleep hygiene as a therapy for late-life insomnia remains questionable. Although insomniacs and subjective insomniacs napped more frequently than individuals without insomnia in sample 1, the implications of this finding are unclear, because: 1) this result did not replicate in sample 2, and 2) research on the impact of daytime napping on nighttime sleep has been equivocal. Inconsistencies of the present research with research in younger adults support concerns regarding the generalizability of findings based on younger samples to older populations. Future research specifically targeting older individuals' sleep hygiene practices, in general, and napping, in particular, is warranted.

**Support (optional):** Sample 1 - National Institute on Aging, AG12136 & AG14738, Kenneth Lichstein

0304

**AROUSAL NORMS BY AGE**

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**Introduction :** Brief arousals have been systematically scored during sleep for over 20 years. Despite significant knowledge concerning the importance of arousals for the sleep process in normals and patients, comprehensive norms have never been published. These norms are now available.

**Methods :** Seventy-six normals (40 male) without sleep apnea or PLMS, ages 18-70, slept in the sleep laboratory for one or more nights. Sleep and arousal data were scored by the same scorer for the first night (compara-

ble to clinical polysomnograms) and summarized by decade.

**Results :** There were no statistically significant differences for sex or interaction of sex by age ( $p > .5$  for both). Mean arousal index (AI) by decade with standard deviation was: Age 18-20: AI=10.6 (6.2); 21-30: AI=10.8 (6.4); 31-40: AI=16.8 (6.4); 41-50: AI=16.5 (6.3); 51-60: AI=21.9 (6.4); 61-70: AI=21.9 (6.4). Newman-Keuls comparisons (.05) showed arousals in the 18-20 and 21-30 groups to be significantly less than arousals in the other four age groups. Arousals in the 31-40 age group were less than in the 61-70 age group. AI was significantly negatively correlated with total sleep time and all sleep stages (positive correlation with stage 1 and wake). AI was also significantly correlated with age, weight (positive), and sex (more in males). The level of correlation of AI with other sleep events like TST ( $r = -.67$ ) and SWS ( $r = -.45$ ) was similar to sleep stage intercorrelations (TST x SWS  $r = .49$ ) and remained significant even when age was partialled out (AIxTST.age  $r = -.47$ ).

**Conclusion :** Brief arousals are an integral component of the sleep process. They increase with other EEG markers as a function of age. They are highly correlated with traditional sleep stage amounts and are related to major demographic variables. Age-related norms may make identification of pathological arousal easier.

**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.

0305

**CHANGES IN THE SLEEP, CIRCADIAN RHYTHMS AND DAYTIME ALERTNESS OF HEALTHY SENIORS AS INDUCED BY A 2H CHANGE IN BEDTIME**

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**Introduction :** The sleep of seniors is impaired relative to that of younger adults. Some of this impairment can be attributed to a circadian pacemaker whose timing is not appropriate for (i.e., has the wrong phase angle to) the chosen bedtime. Rather than change the timing of the pacemaker (e.g., with bright lights), we instead sought to change the timing of the sleep period, to improve sleep quality.

**Methods :** A within-subject design was used with each subject attending for three 5-day/night (~120h) sessions. Nights #1 and #2 always had bedtime and wake-time at the subject's habitual (2-week diary). Nights #3 through #5 had bedtime specified but wake-time was totally at the subject's discretion under complete temporal isolation. Under the 'control' condition (always first condition experienced), these three bedtimes were at the subject's habitual, under the 'advance' condition they were 2h before it, under the 'delay' condition they were 2h after it (order counter-balanced). Rectal temperatures were recorded continuously and all sleeps polysomnographically recorded. Assessments (4/d) were made of alertness, mood and performance. Reported are data from eight seniors (7f, 1m, 70y-82y).

**Results :** There were statistically reliable differences in circadian temperature phase (Tmin) in the final three circadian cycles from each segment ('advance' 02:06, 'control' 02:51, 'delay' 03:56;  $p < 0.03$ ), but no differences in amplitude. Significantly more sleep was obtained under 'advance' than under 'delay' (6.2h versus 5.3h,  $p < 0.01$ ), with 'control' intermediate (5.9h). This increase in sleep was accompanied by a decrease in sleep efficiency ('advance' 75.1% 'delay' 82.4%,  $p < 0.01$ ), with 'control' again intermediate (79.6%). Alertness in the days following bedtime 'advance' was greater than that following 'delay' (77.5 vs. 73.7,  $p < 0.02$ ), with 'control' again intermediate (74.9).

**Conclusion :** A 2h earlier bedtime led to more sleep being obtained and to greater daytime alertness, despite a drop in sleep efficiency.

**Support (optional):** Supported by AG13396, AG020677, NNJ04HF76G,

RR00056.

**0306****PSYCHOSOCIAL INFLUENCES ON THE COURSE OF LATE-LIFE INSOMNIA***Ellis JG, Hampson SE, Cropley M*

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**Introduction :** A plethora of research has charted the psychological and behavioral factors relating to late-life insomnia. However, very little research has focused on the circumstances which relate to insomnia within specific subgroups. The aim of the present study was to examine the psychosocial and behavioural factors involved in the development of acute insomnia, in the natural remission from insomnia and insomnia characterized by depression, within older adults.

**Methods :** From an ongoing longitudinal study of late-life insomnia, three subgroups were examined for risk factors relating to changes in reported insomnia status. Normal sleepers who developed insomnia over the course of a year ( $n = 13$ ) and Chronic Insomniacs who reported a natural remission over the course of a year ( $n = 10$ ). Additionally, a matched pairs design was employed to examine differences between a group of late-life insomniacs with depression ( $n = 25$ ) against those without depression ( $n = 25$ ). Participants were administered a battery of questionnaires examining psychological and physiological health, stress, depression and anxiety, quality of life, coping styles, sleep-related dysfunctional beliefs, lifestyle behaviors and sleep functioning at baseline and a year later.

**Results :** Use of worry as a cognitive coping strategy, high sleep-related dysfunctional beliefs and high anxiety levels were related to the development of insomnia within a year. However, there were no significant differences in psychosocial factors between time points for those who reported spontaneous remission. Depressed insomniacs reported poorer psychological and physical health, poorer social relationships, higher levels of anxiety and considerably longer durations of insomnia, compared to their non-depressed counterparts.

**Conclusion :** The results provide a tentative insight into the psychological and bio-behavioural factors involved in the development and course of late-life insomnia. However, it is important to note that as there were no factors highlighted as predictors of natural remission, it is likely that these individuals are vulnerable to relapse. The results are also discussed in terms of the possible progression from chronic insomnia to insomnia comorbid with depression.

**Support (optional):****0307****INSOMNIA AND PAIN IN OLDER ADULTS***Payne KL,<sup>1</sup> Lichstein KL,<sup>1</sup> Durrence H,<sup>2</sup> Riedel BW,<sup>3</sup> Taylor DJ,<sup>4</sup> Bush AJ<sup>5</sup>*

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**Introduction :** Chronic pain is a common problem for older adults. The present study is aimed at investigating the differences between sleep variables for older adults who report pain and those who do not.

**Methods :** Random-digit dialing was used to recruit 772 participants, ages 20-98 in the Shelby County, TN area. Participants completed sleep diaries and questionnaires on general health, mood, and sleep-related variables. A subset of these participants aged 60 or older ( $n=322$ ) were used in the following analyses. There were 131 participants from this subset who reported pain (41%).

**Results :** A series of seven t-tests were conducted to examine the differ-

ence in sleep variables among those older adults who do and those who do not report pain. Specifically, older adults with pain reported worse sleep as evidenced by: higher mean sleep latencies,  $t(215.4) = 4.43$ ,  $p < .001$ ; a higher number of awakenings,  $t(320) = 2.5$ ,  $p < .05$ ; more awake time,  $t(320) = 2.65$ ,  $p < .01$ ; worse sleep efficiency,  $t(263.8) = -4.16$ ,  $p < .001$ ; and lower quality of sleep,  $t(320) = -1.98$ ,  $p < .05$ . There were no significant differences between groups on the number of naps or total sleep time. The number of years of pain was significantly correlated with sleep latency,  $r = .24$ ,  $p < .01$ , but none of the other six sleep variables. Among those reporting pain, a series of seven t-tests were conducted to assess the difference in sleep among those taking pain medications and those who were not. All of these tests were non-significant.

**Conclusion :** Self-reported sleep is worse in older adults with pain as compared to those reporting no pain. Older adults who are experiencing pain and present for treatment should be questioned about their sleep and targeted for insomnia treatment.

**Support (optional):** Research supported by National Institute on Aging grants AG12136 and AG14738.

**0308****LONG-TERM CPAP MAY IMPROVE COGNITION, SLEEP, AND MOOD IN PATIENTS WITH ALZHEIMER'S DISEASE AND SDB***Cooke JR,<sup>1,3</sup> Amador X,<sup>2,3</sup> Lawton S,<sup>2,3</sup> Greenfield D,<sup>2,3</sup> Liu L,<sup>2,3</sup> Marler M,<sup>2,3</sup> Palmer B,<sup>2,3</sup> Ancoli-Israel S<sup>2,3</sup>*

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**Introduction :** Our 6-week continuous positive airway pressure (CPAP) treatment of sleep disordered breathing (SDB) in mild Alzheimer's disease (AD) patients showed differences in cognitive deterioration. Patients who did or did not purchase CPAP machines upon completing the protocol were re-tested at 6-months to evaluate CPAP's long-term effects on cognition and sleep.

**Methods :** Ten participants ( $f=3$ , mean age=76,  $SD=6$ ), 5 continuing CPAP (CPAP+) matched by time of completion of initial study with 5 discontinuing CPAP (CPAP-) with mild AD (mean MMSE=24,  $SD=4$ ) were re-studied. Each completed a neuropsychological test battery and sleep/mood questionnaires. Mean change scores between the final initial study visit and the 6-month follow-up visit were compared, but due to the small sample size, p-values were not computed.

**Results :** Compared to the CPAP- group, the CPAP+ group had less cognitive deterioration (Dementia Rating Scale where lower scores imply more dementia: CPAP+=-0.8,  $SD=23.8$ ; CPAP=-5.0,  $SD=12.0$ ; Trails B [assesses mental flexibility and psychomotor speed]: CPAP+=-8.95 seconds,  $SD=53.5$ ; CPAP=-+1.8 seconds,  $SD=88.0$ ; Stroop Color-Word Score [assesses response inhibition and processing speed], where higher scores imply less interference: CPAP+=+10.8,  $SD=11.7$ ; CPAP=-2.5,  $SD=12.4$ ; FAS Total Letter Score [assesses efficiency of lexicon search and processing speed], where higher scores represent better functioning: CPAP+=+0.8,  $SD=21.9$ ; CPAP=-6.6,  $SD=13.4$ ). The CPAP+ group also had less depression (Cornell Scale for Depression where higher scores suggest more depression: CPAP+=+1.8,  $SD=2.5$ ; CPAP=-+5.6,  $SD=2.4$ ), less daytime somnolence (Epworth Sleepiness Scale: CPAP+=+2.6,  $SD=5.1$ ; CPAP=-+5.6,  $SD=4.4$ ), and better subjective sleep quality (Pittsburgh Sleep Quality Index where lower scores reflect better sleep quality: CPAP+=-0.8,  $SD=2.7$ ; CPAP=-+2.4,  $SD=3.1$ ).

**Conclusion :** Results suggest that those who continued CPAP have less cognitive deterioration, less depression, less daytime somnolence, and better subjective sleep quality than those who discontinued CPAP. These results are encouraging and suggest that CPAP treatment should be considered for AD patients with SDB.

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### 0309

#### THE WAKE-PROMOTING EFFECTS OF HYPOCRETIN-1 ARE BLUNTED IN AGED RATS

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**Introduction :** We hypothesize that age-related sleep disruption may be in part related to dysfunction of the Hcrt system. In support of this hypothesis, we have previously shown that mRNA for the HcrtR2 is significantly reduced in the pons, medulla, thalamus and hippocampus of aged mice (Terao et al., 2002). The current study investigates the effects of Hcrt infusion into the lateral ventricle of both young and old Wistar rats.

**Methods :** Thirteen aged (24 mos) and 7 young (3 mos) male Wistar rats were surgically implanted for sleep recordings and with an infusion cannula into the lateral ventricle. Employing a counterbalanced repeated measures design, either 10 or 30 µg/kg of Hcrt-1 or saline was infused ICV at the beginning of the light period (ZT0). EEG and EMG signals were scored for W, REM sleep, or NR sleep in 10 s epochs by standard criteria.

**Results :** In the young group, both the 10 and 30 µg Hcrt-1 treatments produced a significant increase in the initial period of continuous wakefulness (148 + 25.4 and 150 + 36.5 min respectively) compared to saline (34.9 + 4.6 min). In the aged rats, the 30 µg dose produced a significantly longer latency to sleep (82.6 + 12.9 min) compared to saline (40.6 + 3.9 min) but the 10 µg dose did not. The overall effects of Hcrt-1 on arousal states were also more robust in young rats compared to old rats. Hcrt-1 infusion produced significant increases in W and decreases in NREMS in young rats that lasted for 5 h post-infusion. However, in the aged group, only the 30 µg dose of Hcrt-1 produced increased W, which was significant during h 2-3 post-infusion. Hcrt-1 had a suppressive effect on REM sleep in young rats but not in old rats.

**Conclusion :** The current findings demonstrate an age-related reduction in the wake-promoting response to Hcrt-1. Although our data confirm previous reports that ICV administration of Hcrt-1 in young rats produces increased waking and decreased NR and REM sleep (Vogel et al., 2002; Smith et al., 2003; Piper et al., 2000), these effects are significantly blunted in aged Wistar rats. References Piper DC, Upton N, Smith MI, Hunter AJ. *Eur J Neurosci.* 2000 Feb;12(2):726-30. Smith MI, Piper DC, Duxon MS, Upton N. *Neurosci Lett.* 2003 May 8;341(3):256-8. Terao A, Apte-Deshpande A, Morairty S, Freund YR, Kilduff TS. *Neurosci Lett.* 2002 Nov 8;332(3):190-4. Vogel V, Sanchez C, Jennum P. *J Neurosci Methods.* 2002 Jul 30;118(1):89-96.

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### 0310

#### SLEEP DISORDERED BREATHING INCREASES THE RISK OF FALLS IN OLDER MEN

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**Introduction :** Poor sleep quality has been associated with increased risk of falls, but no study has investigated the relationship of sleep disordered

breathing (SDB) and risk of falls. Therefore, using data from the multicenter study, Outcomes of Sleep Disorders in Older Men (MrOS Sleep Study), we tested the relationship of SDB and incident falls.

**Methods :** 2,865 men aged 67 and older underwent actigraphy and in-home polysomnography (Safiro, Compumedics). Incident falls were ascertained tri-annually by self-report. 'Fallers' were defined as those reporting 2+ falls during the year after the sleep exam. 1,354 men with at least a year of follow-up since the sleep exam were included in this preliminary analysis. Using logistic regression, we tested the association between indices of SDB and short-term risk of falling. We further tested if these relationships were independent of potential confounders, including age, race, BMI, medical conditions, medication use and a variety of other factors. Results are presented as odds ratios (OR) with 95% confidence intervals (CI).

**Results :** 286 men (21.2%) were classified as fallers. The mean apnea-hypopnea index (AHI) was 17.0 (SD=15.7). In fully adjusted models, each standard deviation (SD) increase in AHI was associated with a 16% increase in risk of falling (OR=1.16; 95% CI 1.02-1.33). Each SD increase in the % sleep time < 90% oxygen saturation (SaO<sub>2</sub>) increased risk of falls by 27% (OR=1.27; 1.13 - 1.43). Among the 10% of men with any sleep time spent in < 80% SaO<sub>2</sub>, the risk of falls was more than double (OR= 2.14; 1.40, 3.26) compared to men with no such episodes.

**Conclusion :** Older men with SDB are at significantly greater risk of falling as compared to those with more normal sleep patterns. Further analyses are underway to determine possible mechanisms for this association. Interventions to reduce risk of SDB may reduce risk of falls in older men.

**Support (optional):** The Osteoporotic Fractures in Men (MrOS) parent study is funded by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute on Aging (NIA), and the National Cancer Institute (NCI), under the following grant numbers: U01 AR45580, U01 AR45614, U01 AR45632, U01 AR45647, U01 AR45654, U01 AR45583, U01 AG18197 and M01 RR000334. The MrOS Sleep Study is supported by the National Heart, Lung, and Blood Institute (NHLBI) under the following grant numbers: R01 HL071194, R01 HL070838, R01 HL070839, R01 HL070848, R01 HL070847, R01 HL070842, R01 HL070841, R01 HL070837

### 0311

#### EFFECTS OF AGE AND GENDER ON AUTONOMIC CARDIAC MODULATION DURING SLEEP

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**Introduction :** Both age and gender are known to affect both sleep and autonomic cardiovascular modulation. The aim of this study was to assess the effect of age and gender and their interaction on the cardiac autonomic regulation during NREM and REM sleep in healthy individuals.

**Methods :** We studied 2 groups of 16 subjects (each including 8 F and 8 M) aged respectively between 20 to 30 years and 50 to 60 years. All females in both groups were under hormonal treatment (estrogen and progesterone). One night of polysomnographic recording was used to assess RR variability during NREM (stage 2) and REM sleep. Time and frequency domain analysis were done on consecutive 5-minute segments selected across sleep during stable conditions: no arrhythmia, stable breathing pattern, apart from sleep stages changes and arousals. The following variables were calculated and averaged for each sleep stage: mean

RR, standard deviation of RR (sdRR), low frequency and high frequency in normalized units (LFnu and HFnu) and LF/HF ratio.

**Results :** In comparison to younger subjects, older subjects had lower sdRR with higher LFnu and LF/HF ratio during both NREM and REM sleep. Older individuals also had a greater NREM-to-REM related LF/HF increase (interaction age by sleep stage  $p=0.05$ ). Females (of all ages) had lower RR and lower sdRR than males across sleep stages (both  $p<0.05$ ). Females showed a slight HFnu predominance ( $p=NS$ ) during NREM sleep but a more marked increase in LFnu and LF/HF ratio from NREM-to-REM compared to males (interaction gender by sleep stage  $p<0.05$ ). No gender by age by sleep stage interaction was observed.

**Conclusion :** Both age and gender influence sleep related cardiac autonomic response. Aging and female gender are both associated with an enhanced REM-related sympathetic response suggesting that older females might be more vulnerable to cardiovascular events during REM sleep. These findings remain to be confirmed in postmenopausal women without hormone replacement therapy.

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### 0312

#### EFFECTS OF THE CHRONIC SLEEP RESTRICTION IN THE OLD RATS

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**Introduction :** Age-related impairments occurring in the sleep-wake cycle are not well documented in animals. Few studies have focus on the effects of the aging over the wake-sleep cycle on the quality of the sleep. The purpose this work was evaluates the effects of the chronic sleep restriction in old rats.

**Methods :** 12 male old Wistar rats (22 months) were implanted with electrodes to record electrocorticogram/eletromyogram signals. For control group (CG) were register 5 animals, and for sleep restriction group (SRG) 7 animals. The single platform technique was used for deprivation of the sleep. The sleep restriction procedure (11 days) based in submitting the rats of the platform during 18h (4h pm - 10h am), and allows the rats sleep during 6 h (10h am - 4h pm) when the sleep was recorded.

**Results :** The results showed that there was no difference between the groups of the 2-11 days in the sleep efficiency (SE), except for D1 and increased of SE in the SRG. There was a decrease of the SE in the 8-11 days when compared to baseline sleep. There was an increased in the D4 and D6 in the paradoxical sleep (PS) of the SRG when compared baseline and between groups (only D6). There was not difference between groups in the slow wave sleep (SWS), but there was a decrease of the SWS when compared the baseline sleep in the SRG. The sleep latency increased gradually throughout of the recorder to SRG.

**Conclusion :** The old rats showed less ability to recovery sleep during the period of the rest, as measured by decreased of the SE and by increased of the latency of the sleep. In addition, the recovery of the PS was more pronounced only in the sixth day in SRG rats.

**Support (optional):** AFIP, FAPESP and CEPID

### 0313

#### SLEEP DISTURBANCES IN AN ELDERLY POPULATION: AN EPIDEMIOLOGICAL SURVEY

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**Introduction :** Sleep in elderly population shows progressive changes caused by general aging processes, neurological and medical conditions. The aim of our study was to characterize and to evaluate sleep disturbances, in particular insomnia, in a population of elderly people of a rural Italian community.

**Methods :** Between April and October 2001, we surveyed the inhabitants aged 65 years or more living in the municipality of Vecchiano, Pisa. This elderly population consisted in 2366 subjects. All subjects underwent a complete medical evaluation, a questionnaire to assess sleep disturbances, Mini Mental State Examination (MMSE) and the cognitive and self-contained part of Cambridge Examination for Mental Disorders of the Elderly (CAMCOG), to assess cognitive impairment, and Geriatric Depression Scale (GDS) to evaluate depression. According to the responses to the sleep-related questions, subjects were classified into three categories: (1) no insomnia (2) level 1 insomnia with absence of day-time dysfunction and (3) level 2 insomnia with presence of day-time dysfunction.

**Results :** Complete informations were available for 1596 subjects (642 M, mean age  $74,59 \pm 10,31$  yrs; 954 F, mean age  $75,65 \pm 7,56$  yrs, range 65-105 years). Insomnia was reported by 65,8% of all interviewed patients, with 22,4% classified as level 1 and 43,4% as level 2. Early morning awakening was reported in 78%, while early morning awakenings (53%), difficulty falling asleep (52%) and non-refreshing sleep (38%) were less frequent. Depression (odds ratio, 1.82; CI, 1.37-2.43), hypertension (odds ratio, 1.28; CI, 1.01-1.61), cognitive impairment (odds ratio, 1.24; CI, 1.08-1.57) were associated with insomnia. The analysis of total sample showed a correlation between insomnia severity and MMSE ( $p<0.05$ ), age ( $p<0.05$ ), GDS ( $p<0.01$ ), CAMCOG ( $p<0.05$ ).

**Conclusion :** Collected data in our sample showed a high prevalence of insomnia symptoms among elderly and their correlation with depression, hypertension, cognitive impairment and age.

**Support (optional):**

### 0314

#### HOMEOSTATIC SLEEP REGULATION UNDER LOW SLEEP PRESSURE: ARE THERE AGE EFFECTS?

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**Introduction :** We have recently found an attenuated frontal predominance in EEG delta activity in response to high sleep pressure (40h of sleep deprivation) in older volunteers (1). Here, we quantified age-related changes in homeostatic sleep regulation in response to low sleep pressure conditions (a 40-h multiple nap protocol).

**Methods :** After an 8-h baseline sleep episode at habitual bedtimes, 16 healthy young (20-31y; 8F) and 16 healthy older volunteers (57-74y; 8F) underwent 10 cycles of 150-min scheduled wakefulness and of 75-min scheduled sleep under constant posture conditions (in bed, light levels  $<8$  lux). An 8-h recovery sleep episode followed the 40-h nap paradigm. EEGs were continuously recorded throughout the entire study and subjected to spectral analysis (FFT).

**Results :** Total sleep time and sleep efficiency averaged over the ten 75-min naps did not significantly differ between the age groups ( $p>0.1$ ). Moreover, in both age groups relative EEG delta activity (0.5 -1.25 Hz) decreased in response to sleep satiation (multiple naps) during the first non-rapid eye movement sleep (NREMS) episode in recovery sleep. However, the response to sleep satiation lasted significantly longer in the young (across the first two NREMS episodes) than in the older participants (only the first NREMS episode;  $p<0.05$ ; Duncan's multiple range test).

**Conclusion :** Our results show age-related differences in the time course of EEG delta power during a recovery night under low sleep pressure conditions. To further elucidate whether this shorter lived EEG delta response in the elderly is related to deterioration in homeostatic sleep regulation, the EEG during scheduled wake episodes will be analysed. Reference: 1. Münch, M. et al., *Eur J Neurosci* 20, 1402-1410 (2004).

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### 0315

#### TOLERANCE OF MODERATE SLEEP RESTRICTION IN OLDER SELF-REPORTED LONG SLEEPERS

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**Introduction :** Epidemiologic studies have consistently shown that long self-reported sleep duration ( $\geq 8$  hr) is associated with increased mortality. Conceivably, sleep restriction might prolong life, but preliminary studies are needed before exploration of this hypothesis can be justified. The aim of this ongoing study is to examine whether older self-reported long sleepers can tolerate moderate sleep restriction without negative consequences.

**Methods :** We examined 32 older adults (50-70 yr) who reported sleeping  $\geq 8.5$  hr per night. Following screening (e.g. for apnea) and a 2-week baseline, participants were randomly assigned to two 8-week treatment group. (1) A sleep restriction group was asked to spend 90 min less time-in-bed (TIB) compared with baseline while following a fixed sleep-wake schedule. (2) A control group followed a fixed sleep-wake schedule with TIB equivalent to average baseline TIB. Glucose tolerance was assessed before and after the study. Sleep/wake was assessed continuously via wrist actigraphy. Sleepiness was assessed thrice daily with the Stanford Sleepiness Scale. Following baseline and every two weeks thereafter, participants completed the following: Epworth Sleepiness Scale, Geriatric Depression Scale, SF-36 health-related quality of life, and the Functional Outcomes of Sleepiness scale (FOSQ). Following baseline and three times thereafter, a neurobehavioral performance battery was given (PVT, memory, vigilance). These preliminary data were analyzed by treatment by time repeated measures ANOVA.

**Results :** Median restriction of TIB has been 93 min (range 50-130 min) and 11 min (range 9 min increase to 26 min decrease) in the sleep restriction and control groups, respectively. A small, but significant decrease in the FOSQ vigor subscale was found following sleep restriction vs. control, e.g.  $3.3 \pm 0.6$  at week 10 vs.  $3.5 \pm 0.5$  at baseline. No other significant treatment, time or treatment by time interaction was found for the other dependent variables: glucose tolerance, sleepiness, depressed mood, quality of life, or neurobehavioral performance. In follow-up time periods up to 1 yr, many participant report continued sleep restriction with positive consequences.

**Conclusion :** The data suggest that older self-reported long sleepers can tolerate moderate sleep restriction without negative consequences. Older long sleepers might be spending too much time in bed and might benefit from moderate sleep restriction.

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### 0316

#### EFFECT OF CPAP ON COGNITION IN ALZHEIMER'S PATIENTS WITH APNEA

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**Introduction :** Patients with obstructive sleep apnea (OSA) often experience cognitive problems. CPAP treatment of OSA alleviates cognitive symptoms. Patients with Alzheimer's disease (AD) often have OSA. This study examined whether treating OSA in AD would improve cognition.

**Methods :** 47 AD patients (mean age = 77.9, SD=7.3; mean MMSE=25.0, SD=3.1) were randomly assigned to 6-weeks of therapeutic CPAP (n=22) or 3-weeks of shamCPAP followed by 3-weeks of therapeutic CPAP (n=25). A neuropsychological test battery was administered before, after 3 and after 6-weeks of CPAP. Each test score was transformed to a normalized z-scale, with z-scores across tests computed for each patient as a composite measure of cognitive functioning. Analyses included: a paired t-test on the change in standardized score following 3-weeks of therapeutic treatment (CPAP and shamCPAP groups combined); correlation between change in standard score and CPAP adherence (mean nightly usage); ANCOVA comparing change across the first three weeks of the study (therapeutic CPAP vs. shamCPAP with hours of use as covariate).

**Results :** There was statistically significant improvement in the composite score after 3-weeks of therapeutic CPAP ( $t=2.593, df=38, p=0.013$ ) for the combined groups. The therapeutic CPAP group showed improvement after 3-weeks with no continued improvement after a second 3-weeks and the shamCPAP group showed a non-significant decline in the first 3-weeks (indicating lack of placebo effect), followed by significant improvement after 3-weeks of therapeutic CPAP. Improvement was unrelated to hours of CPAP compliance ( $r = 0.036$ ).

**Conclusion :** These results suggest CPAP might improve some aspects of cognition in AD with OSA. While we would not assert that OSA is the primary cause of cognitive deficits in AD, it may exacerbate those deficits. Treatment of OSA in AD patients should be considered as a component of clinical care for patients with AD.

**Support (optional):** NIA AG08415, NIH M01 RR00827, NIA P50 AG05131, VASDHS Research Service.

### 0317

#### INTERACTION OF POLYSOMNOGRAPHY AND PHYSIOLOGY OF ALZHEIMER'S DISEASE

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**Introduction :** The primary objective of this study is to characterize the disruption of sleep and circadian rhythmicity in patients with Alzheimer's disease (AD). We hypothesize that AD patients with delayed core-body temperature (CBT) rhythms will show disturbed sleep characterized by increased sleep latency and a delayed phase of REM sleep.

**Methods :** We conducted a 72-hour recording of activity and CBT during a 40-hour simplified constant routine protocol. Additionally a 24-hour polysomnographic recording was taken if possible. We also collected



urine samples to characterize the melatonin rhythm. To date, we have complete data on 5 AD subjects and activity and CBT data on 8 normal controls. All MMSE scores are 0 in AD subjects. Activity and CBT data were assessed by two harmonic Cosinor analysis.

**Results :** We found the CBT nadir time in AD is delayed compare to controls. Mean AD Nadir time was 520 141 min past from midnight (from 24:00, SD), and mean control nadir was 237 59 min ( $p=0.001$ , t-test). We also found significant difference between CBT Mesor, AD 37.41 0.19 Co, control 36.69 0.72 Co, ( $p=0.01$ , t-test). Sleep structure of 5 AD subjects were assessed, Mean duration within 24hours was WAKE; 17h05min, STAGE1; 5h28min, STAGE2; 38min, STAGE3; 10min, STAGE4;0min, REM; 40m. Melatonin data and polysomnographic data collection were not successful in some cases due to abnormal activities.

**Conclusion :** As in previous studies, the nadir of CBT in AD was delayed compared to control. We also observed patterns of sleep onset and REM appearance that in some subject were coordinated with CBT rhythm, however other subjects showed dysregulation of the coordination between sleep onset, REM timing and CBT. (Data collection is kept under operation.)

**Support (optional):** ROI-AG20654, P130 AG13846 and The Dept. of Veterans Affairs

### 0318

#### RELATIONSHIP BETWEEN CAREGIVER REPORT OF NIGHTTIME AGITATED BEHAVIORS AND SLEEP IN PEOPLE WITH DEMENTIA

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**Introduction :** Sleep disruption and nighttime agitated behaviors in people with dementia (PWD) are predictive of institutionalization. Caring for PWD can be taxing at night because their sleep is often disrupted and agitated behaviors occur more frequently at night. This study describes the relationship between nighttime agitated behaviors (biting, pacing, screaming) and sleep in community living PWD.

**Methods :** This cross-sectional study used de-identified secondary data from a multivariate cross-sectional descriptive study. Participant selection criteria included DSM-IV diagnosis of dementia, living with a caregiver, ambulatory, and medically stable. Caregivers of participants completed the 36-item Cohen-Mansfield Agitation Inventory for Community (CMAI-C). Nighttime agitated behaviors were rated on a seven point scale for frequency over the past two weeks. The CMAI-C measures four factors of agitation: verbally nonaggressive (VNA), verbally aggressive (VA), physically nonaggressive (PNA), and physically aggressive (PA). For analysis purposes, it is not useful to calculate a total score by adding all the factors. We obtained two nights of attended polysomnography on 42 PWD in their homes.

**Results :** Participants' mean age was 79.8 (sd = 6.5), mean Mini Mental State Examination score 20.5 (sd = 6.8). Mean sleep efficiency was 66.6 (sd =19.6), total sleep time was 334.0 (sd =116.9) minutes, and mean number of awakenings was 35.3 (sd = 13.4), indicating fragmented sleep of short duration. Mean scores for VNA, VA, PNA, and PA were 18.6, 9.4, 15.2, and 21.3 respectively, indicating caregiver report of verbal and physical behaviors. Correlations between VNA and sleep efficiency ( $r = -.40$ ;  $p=.00$ ) were significant. Correlations between VA and sleep efficiency tended toward significance ( $r = -.28$ ;  $p=.08$ ).

**Conclusion :** In this sample, decreased sleep efficiency was associated

with agitation characterized by verbal but not physical behaviors. Further study is indicated to understand differences in the relationship between physical and verbal agitated behaviors and sleep.

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### 0319

#### APNEA-HYPOPNEA INDEX IS ASSOCIATED WITH ELEVATED WAKING CORTISOL LEVELS AS A FUNCTION OF APOE GENOTYPE

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**Introduction :** Obstructive Sleep Apnea/Hypopnea (OSAH) is associated with cognitive impairment, and has been suggested to activate the hypothalamic-pituitary-adrenal (HPA) axis resulting in higher cortisol levels. Presence of the Apolipoprotein E (APOE)  $\epsilon 4$  allele is a genetic risk factor for both the development of cognitive decline as well as for the development of OSAH; it has also been linked to hypercortisolemia in cognitive decline and Alzheimer's disease. This raises the question of whether APOE may moderate a possible association between OSAH and elevated cortisol levels in non-demented older adults.

**Methods :** Fifty-seven community-dwelling non-demented participants, 21 with and 36 without the  $\epsilon 4$  allele, were assessed for level of OSAH and waking cortisol levels (20 men, 37 women; age  $71.2 \pm 8.7$ ; BMI  $25.7 \pm 4.1$ ). The Apnea-Hypopnea Index (AHI) was assessed using unattended in-home ventilatory polygraphy (EdenTrace<sup>©</sup> Model II) using standard definitions. Salivary cortisol levels were obtained at home during two consecutive days and averaged for this study.

**Results :** The AHI was found to be overall significantly associated with waking cortisol levels ( $r=.335$ ,  $p=.013$ ). However, carriers of the APOE  $\epsilon 4$  allele show a stronger correlation between higher levels of OSAH and increased waking cortisol levels ( $r=.435$ ) than non- $\epsilon 4$  carriers ( $r=.221$ ). No significant differences were observed between the  $\epsilon 4$  and non- $\epsilon 4$  group with respect to demographic, respiratory and cognitive variables.

**Conclusion :** This study provides preliminary evidence for a positive association between levels of OSAH and waking cortisol levels as a function of APOE genotype. It remains to be elucidated in a longitudinal study how OSAH and APOE genotype may interact to increase HPA axis activity. This interaction may have significant implications for targeting treatment of OSAH in older adults, as hypercortisolemia in this age group has been associated with the development of insomnia and late-life depression, as well as the metabolic syndrome.

**Support (optional):** Research supported by NIA funding (AG 18784).

### 0320

#### THE RELATIONSHIP BETWEEN SLEEP QUALITY AND PAIN AMONG PERIMENOPAUSAL WOMEN

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**Introduction :** In a prior investigation that examined sleep quality, quality of life, and somatic symptoms among perimenopausal women, elevated levels of bodily pain reports were observed. Perimenopausal women often report somatic symptoms such as hot flashes, headaches, muscle tension, and aching and sore joints. One might consider increased pain reports as yet another manifestation of the somatic complaints initiated by the hormonal changes or ageing processes. However, given the well-documented, albeit complex, relationship between sleep quality and pain, we

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hypothesized that their elevated pain may represent a different mechanism than the coinciding somatic complaints, and that sleep quality may be one mechanism that explains these elevations. In the current study, we examined the degree to which sleep quality, relative to somatic complaints themselves, was associated with SF-36 pain reports.

**Methods :** The data used in this study was part of a larger community sample (N = 168) that evaluated sleep quality in perimenopausal women. Several questionnaires were administered to the women and we used the following in our assessment: Pittsburgh Sleep Quality Index, SF-36 - Bodily Pain subscale, and Women's Health Questionnaire - Somatic subscale.

**Results :** We found that sleep quality and somatic complaints contributed to approximately 29% of the variance in reporting pain ( $r^2 = .29$ ,  $F(2,127) = 26.02$ ,  $p < .001$ ). However, the sleep quality co-efficient was a significant factor ( $t = -5.38$ ;  $p < .001$ ) whereas the somatic complaints co-efficient was not significant ( $t = 1.89$ ;  $p > .05$ ).

**Conclusion :** Our findings suggest, that in perimenopausal women, sleep quality plays a unique role in the reporting of pain. As pain is known to affect sleep in other populations, it is important to understand the role it plays in perimenopausal women.

**Support (optional):**

### 0321

#### SLEEP AND AGING IN AN ENVIRONMENT WITHOUT ELECTRICITY

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**Introduction :** Little is known about sleep characteristics in non-industrialized populations nor is it known whether age-related changes in sleep observed in industrialized countries also occur in these regions. This study examined sleep duration and quality in adults from a rural area of Haiti without electricity (Fondwa), as compared to Haitians who have been living in the U.S. for at least one year (mean residency  $23.1 \pm 12.6$  years).

**Methods :** Subjects wore wrist actigraphy monitors for three consecutive days and kept sleep logs. Estimates of time in bed, sleep duration, sleep latency, and sleep efficiency (percent of time in bed spent sleeping) were derived from the actigraphy data.

**Results :** Fifty-eight Haitians (50% female) aged 18-88 years from Fondwa, Haiti and 20 Haitians (50% female) aged 20-83 years living in Chicago participated. Mean time in bed was 9.3 hours for Fondwa residents and 7.8 hours for Chicago residents ( $p < 0.01$ ). Mean sleep duration was 7.0 hours for Fondwa residents and 5.9 hours for Chicago residents ( $p < 0.01$ ). Mean sleep latency (43 minutes for Fondwa residents and 32 minutes for Chicago residents) and mean sleep efficiency (76% for both) did not differ significantly between groups. Regression analyses that included age and sex indicated that US residents had shorter sleep duration and time in bed than Fondwa residents ( $p < 0.05$ ). Time in bed and sleep duration increased with age ( $p < 0.05$ ). Age did not impact sleep latency or efficiency. No gender differences were observed in any of the sleep variables.

**Conclusion :** Time allotted for sleep appears curtailed when individuals from a rural non-industrialized community move to the US. The age-related declines in sleep duration and quality typical of adults in industrialized countries were not observed in Haitians living in Fondwa or the US, suggesting that the etiological factors associated with these age-related declines are not universal.

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### 0322

#### PERCEPTION OF SLEEP QUALITY IN AN ELDERLY POPULATION : RELATIONSHIP TO PSYCHOLOGICAL DISTRESS

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**Introduction :** Sleep disorders and mental health problems co-occur frequently in the elderly population (Morgan, 2000; Roberts et al., 2000; Xavier et al., 2002; Giron, 2002;). The goal of this research was to explore this phenomenon in a context where the term "psychological distress" is used to describe anxiety and/or depression symptoms, whether or not diagnostic criteria of the DSMIV (1994) are met.

**Methods :** Participants were 296 adults (M age=74.2, SD=7.1 years; 39.8 % men, 60.2% women) selected from a probabilistic sample composed individuals living at home in three different areas of the province of Québec. The inclusion criterias were : being older than 65 years old, understanding and speaking French and having no diagnostic of cognitive disorders. The interview was held at the residence of the participants. The DIS (Diagnostic Interview Schedule) was used to evaluate the presence of depression or anxiety symptoms in the last 12 months, whereas the PSQI was used to measure sleep quality (Buysse, 1989).

**Results :** The DIS revealed that 24.5% of the participants had at least 1 diagnostic of mental health problem. For subject scoring more than 5 on the PSQI there was a significant difference between participants who had no diagnostic (17%), compared to those having at least one diagnostic (29.7%) ( $p < .05$ ). A sleep efficiency lower than 75% was found in 28.7% of individuals without a diagnostic compared to 44.7% for those with at least one diagnostic ( $p < .01$ ). Hypnotic were used by 16.5% of individuals without a diagnostic and 24.6% for those with at least one diagnostic.

**Conclusion :** Since psychological distress leads to an increased use of psychotropic drugs (Watson et al., 1989; Préville et al., 2002), its relationship with sleep is important and could benefit from further exploration.

**Support (optional):** Research supported by the Canadian Institute of Health Research.

### 0323

#### THE EFFECTS OF WORKERS AGE ON SELF-REPORTED ADAPTATION TO SHIFT WORK AND OTHER SLEEP PROBLEMS AT AN OIL RIG IN THE NORTH SEA

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**Introduction :** The workforce is getting older and studies show that age results in an increasing frequency of sleep disturbances and difficulties coping with shift work. The goal of this study was to examine the effects of worker's age on self-reported adaptation to shift work and other sleep problems at an oil rig in the North Sea.

**Methods :** All subjects (n=109) working nights at an oil platform in the North Sea completed a questionnaire about possible sleep complaints in relation to shift work. The workers had a schedule of two weeks on a 12-hour shift, with the first week on night shift (18:30 to 06:30) and the second week on day shift (06:30 to 18:30). Subjects completed a modified version of Karolinska sleep/wake questionnaire. They were divided into groups according to age, "under 30 years", "30-39 years", "40-49 years" and "50 years and above".

**Results :** The oldest age group tended to have more subjective sleep problems than younger workers (2.8 CI 2.2-3.4 vs 2.1 CI 1.6-2.6; scale 1-5,  $p < 0.1$ ). There were significant differences in sleep variables between the

age groups in other parameters, such as snoring, sleep apnoea, sleep latency, whether they were tired at work or at home, and whether or not they had tried melatonin treatment (all parameters,  $p < 0.05$ ). There was a tendency for self-reported sleep need to gradually decrease with age (461 min to 421 min). For many other self-reported sleep variables, no significant differences between the age groups were found. In general, many of the offshore workers seemed to handle the shift schedule without major difficulties.

**Conclusion :** We found that some subjective sleep complaints increased with increasing age in our sample of offshore North Sea workers. Surprisingly, many of the workers were not complaining of sleep problems, even in the oldest age group.

**Support (optional):**

### 0324

#### ASSOCIATIONS OF RACE AND SOCIOECONOMIC STATUS WITH SLEEP QUALITY AND DURATION: RESULTS FROM THE SWAN SLEEP STUDY

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**Introduction :** Lack of adequate sleep and associated daytime dysfunction are important public health problems. Whether being a minority and having a low socioeconomic status are associated with poor sleep quality is the subject of a growing epidemiologic literature. In general, nonCaucasians and lower income participants report sleeping fewer hours than Caucasian and higher income participants; blacks have less stage 3-4 sleep than do others. We report the associations of race and income with sleep quality and duration in the SWAN Sleep Study.

**Methods :** 345 women (mean age 50.7, range 48-57 years) were enrolled in Chicago, Detroit, Oakland CA, and Pittsburgh. Women self-identified as African American, Caucasian, or Chinese. Three nights of in-home polysomnography were conducted. Total sleep time, wake time after sleep onset (WASO), and sleep stage percentages were averaged across nights 2 and 3. The Pittsburgh Sleep Quality Index measured subjective sleep quality. Regression analyses were conducted to examine race and income effects on sleep.

**Results :** Independent of income, African American women had worse sleep than Chinese and Caucasian women, with shorter sleep duration (360 vs. 389 and 393 minutes), higher WASO (63 vs. 43 and 47 minutes), less stage 3-4 sleep (2.5% vs 3.2% and 4.5%), and poorer subjective sleep quality (7.4 vs 6.2 and 6.0), all  $p$ -values  $< .001$ . Independent of race, income was associated with short sleep duration,  $p = .03$ . Multivariate models adjusting for age, site, menopausal status, body mass index, depression, and anti-hypertensive or diabetes medications showed similar race effects, but income was no longer associated with sleep duration.

**Conclusion :** Independent of income, mid-life African American women experience worse sleep than Chinese and Caucasian women as indicated by both objective and subjective measures. Poor sleep may increase the risk for health problems associated with poor sleep among African American women.

**Support (optional):** The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institutes of Health, DHHS, through the National Institute on Aging, the National Institute of Nursing Research and the NIH Office of Research on Women's Health (Grants NR004061; AG012505, AG012535, AG012531, AG012539, AG012546, AG012553, AG012554, AG012495, AG019360, AG0019361, AG019362, AG019363, IR01-AG19361; NIH/NCRR/GCRC Grant MO1-RR000056).

### 0325

#### EFFECTS OF REGULAR AEROBIC EXERCISE ON SLEEP QUALITY IN OLDER ADULTS WITH CHRONIC INSOMNIA

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**Introduction :** Although previous studies show regular exercise improves sleep in older adults, less is known regarding exercise as a treatment for insomnia in this population. The aim of this study is to determine the effects of an aerobic exercise intervention on sleep and performance in older adults with chronic insomnia.

**Methods :** Sedentary older adults (age 55 and up) with primary chronic insomnia were randomized to either an aerobic exercise intervention (3-5x/wk, 30-40 min) and sleep hygiene education or a non-physical activity program of similar frequency and duration and sleep hygiene education. Patients with other sleep disorders, unstable medical conditions and major psychiatric disorders were excluded. Baseline and post-tx evaluation included cardiopulmonary testing, sleep and quality of life questionnaires, one week of actigraphy, and three nights of polysomnographic sleep recording. During the entire intervention all participants continuously wore an Actiwatch and maintained sleep/activity diaries.

**Results :** To date, 15 subjects have enrolled; of these, eight (5 exercise, 3 control) have completed all phases of the study. One participant was withdrawn due to inability to maintain adequate logs. Preliminary results from the exercise group show improvement in subjective sleep quality (PSQI pre:11.0 post:5.5), decreased sleepiness (ESS: pre:8.4 post:4.0) along with improved mood (CES-D: pre:11.2 post:1.4) and quality of life (FOSQ: pre:93.8 post:111.2; SF-36 vitality: pre:13.6 post:21.4). Similar improvements were not seen in the 3 control subjects. In addition, PSG measures from the 4 subjects in the exercise group showed a decrease in latency to persistent sleep (pre:9.0 min post:2.5 min) and a small decrease in WASO (15 min).

**Conclusion :** These preliminary results support the potential use of a structured aerobic exercise program for the treatment of chronic insomnia in older adults.

**Support (optional):** Research was supported by National Institutes of Health grant number P01 AG 114 12 and, in part, by M01 RR-00048 from the National Center for Research Resources

### 0326

#### THE IMPACT OF AGE UPON CONTINUOUS POSITIVE AIRWAY PRESSURE COMPLIANCE IN OLDER ADULTS

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**Introduction :** Obstructive sleep apnea (OSA) is a prevalent and serious medical issue exacerbating many health problems in older adults. Treatment compliance with continuous positive airway pressure (CPAP) in this population is an important issue meriting the study of the effects of age upon CPAP compliance.

**Methods :** Data was collected retrospectively from the charts of 100 patients age 55 and older found to have moderate to severe OSA (AHI 37.5±31.0) during a split night study, reached an optimal pressure, and had not received previous treatment. Patients were categorized by age: 55-59(35%),60-69(12%),70-74(11%),and 75 & older(13%). CPAP compliance was assessed by subjective report of use. In a subset of 12 patients, objective data was obtained from a card installed in the CPAP machine. Each patient's subjective report of nightly CPAP use was obtained by a registered nurse during a follow up clinic visit or phone call. Compliance was defined as  $> 4$  hrs of nightly use per CPAP data card or patient self report of good tolerance and nightly use. Data was analyzed using means

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and all values were expressed as mean  $\pm$  SD.

**Results :** Our sample (n=100) was comprised of subjects with OSA (54 males) age  $63.7\pm 7.5$ . Baseline AHI varied slightly between the groups:  $41.0\pm 40.1$ ,  $31.3\pm 19.4$ ,  $41.8\pm 25.2$ ,  $24.3\pm 20.1$ ,  $49.0\pm 34.2$ . Generally, the percentage of subjects returning equipment within 6 months increased with age: 8.5%, 13.8%, 0%, 27.3%, 30.1% while the number of subjects refusing treatment setup AMA decreased with age: 5.7%, 3.4%, 0%, 0%, and 0%. The percentage of patients accepting of CPAP and using it regularly declined with increasing age 71.4%, 68.9%, 66.6%, 63.6%, and 61.5%. Residual AHI was similar in each group at  $1.9\pm 2.3$ ,  $1.8\pm 2.2$ ,  $2.3\pm 2.4$ ,  $2.1\pm 2.9$ , and  $1.8\pm 2.1$ . Optimal CPAP pressures were also comparable at  $9.9\pm 3.0$ ,  $9.8\pm 2.9$ ,  $9.3\pm 2.2$ ,  $7.5\pm 1.9$ , and  $8.5\pm 2.0$ .

**Conclusion :** CPAP compliance is negatively correlated with increasing age. The age of subjects over 55 years is a significant factor influencing CPAP compliance.

**Support (optional):**

### 0327

#### FEASIBILITY STUDY: TONE INDUCED SLEEP FRAGMENTATION METHOD IN PEOPLE WITH ALZHEIMER'S DISEASE

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**Introduction :** Studies have described sleep fragmentation in people with Alzheimer's disease (PWAD) but we do not know how or if sleep fragmentation impacts attention, the first non-memory domain affected in AD. To separate the effects of sleep fragmentation and AD on attention, we adapted a method used to separate the effects of sleep fragmentation and hypoxemia in obstructive sleep apnea (Bonnet, 1985). The purpose of this study was to explore the feasibility of a tone induced sleep fragmentation (TISF) method in PWAD.

**Methods :** Five people with mild AD experienced one undisturbed and one fragmented night of sleep monitored with attended polysomnography in the General Clinical Research Center (GCRC). GCRC nurses monitored daytime sleep and dietary intake. We measured attention each AM at 10 with the Psychomotor Vigilance Task (PVT). Inclusion criteria were consensus diagnosis mild AD, apnea-hypopnea index < 10, periodic limb movement index with awakenings < 15, adequate hearing, not receiving or on a consistent dose of a cholinesterase inhibitor for 7 days, and availability of family member to stay with participant in the GCRC. After 10 minutes of EEG scored sleep I presented audiometer tones via earphone. If no awakening was scored, tones increased by five decibels until wake was scored. If 85 decibels was reached tones ended and I entered the participant's room to awaken the participant.

**Results :** Four participants completed two nights of PSG and tolerated the earphone (50% of tones produced awakenings). In participants with mild AD we were able to score awakenings ( $X=31.4$ ,  $sd=10.3$  on the undisturbed night and  $X=41.5$ ,  $sd=8.2$  on the TISF night), arousals and NREM stages. Due to equipment failure we collected PVT data on three participants. The last participant to complete the protocol had the greatest increase in awakenings ( $\uparrow 51.6\%$ ) and reaction times ( $\uparrow 54.6$  millisecond).

**Conclusion :** Based on these results we believe this method is feasible in people with mild Alzheimer's disease to explore the effect of sleep fragmentation on attention.

**Support (optional):** John A. Hartford Foundation Building Academic

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### 0328

#### FIRST VOID 6-SULFATOXYMELATONIN AS A MEASURE OF MELATONIN PRODUCTION IN ELDERLY MEN

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**Introduction :** Melatonin production decreases with advancing age and may be associated with a variety of diseases including neoplasms and sleep disorders. Measurement of the melatonin metabolite 6-sulfatoxymelatonin (aMT6S) in a 24-hour urine collection provides a measure of total daily melatonin production. However, 24-h urine collections are difficult to obtain. Previous studies have demonstrated that first void urine aMT6S, corrected for creatinine concentration, provides a reliable estimate of 24-h melatonin production in women and healthy young men. We hypothesized that despite more frequent nighttime voids among older men, first void aMT6S would still provide a useful estimate of 24-hour aMT6S in this population.

**Methods :** Participants were 100 men ages 69-94 (mean: 77) years randomly selected from 273 men enrolled in the Portland Oregon cohort of the Outcomes of Sleep Disorders in Older Men (MrOS Sleep Study). First void urine aMT6S, measured by Buhlmann ELISA, was divided by urine creatinine to correct for urine concentration. Corrected first void aMT6S was compared to 24-h urine aMT6S collected a week prior, using a Pearson's correlation coefficient. 24-h urine aMT6S values > 50,000 ng were excluded (n=4).

**Results :** Mean (sd) 24-h urine aMT6S for the 96 samples was 8.9 (7.0) ug and mean creatinine corrected first void aMT6S was 16.7 (15.0) ng/dL. The correlation of the log-transformed values for the two measures was  $r = 0.83$  ( $p < 0.0001$ ). Categorization into tertiles had a concordance of 75%.

**Conclusion :** Measures of creatinine corrected first void and 24-h urine aMT6S are highly correlated. Although categorization into tertiles resulted in some misclassification, we conclude that first void urine aMT6S permits a useful approximation of 24-hour melatonin production in older men. This may be particularly useful in large-scale studies investigating the association of melatonin production with a variety of diseases.

**Support (optional):** The Osteoporotic Fractures in Men (MrOS) Study is supported by National Institutes of Health funding. The following institutes provide support: The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute on Aging (NIA), and the National Cancer Institute (NCI), under the following grant numbers: U01 AR45580, U01 AR45614, U01 AR45632, U01 AR45647, U01 AR45654, U01 AR45583, U01 AG18197, and M01 RR000334.

0329

**RELATIONSHIP BETWEEN NIGHTTIME SLEEP AND BEHAVIORAL SYMPTOMS IN PERSONS WITH DEMENTIA***Glover JU,<sup>1,2</sup> Richards K,<sup>1,3</sup> Cole CS,<sup>1</sup> Lambert C,<sup>3</sup> Luchsinger MS,<sup>3</sup> Williams JS,<sup>4</sup> Shue VM<sup>5</sup>*

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**Introduction :** Nighttime sleep of persons with dementia is often disrupted by frequent awakenings. When persons with dementia wake up during the night, they often exhibit behavioral symptoms such as pacing, screaming, and falling. The specific aims of this study were to: 1) describe the sleep patterns of persons with dementia; and 2) explain the relationship between nighttime behavioral symptoms and total sleep time, sleep efficiency, and total nighttime awakenings.

**Methods :** This was a secondary analysis of data from a multivariate cross-sectional descriptive study, which included persons who were 65 years and over, had dementia, and had caregivers who reported at least five nighttime behaviors at least three times a week. Sleep technicians collected two nights of attended polysomnography in participants' homes (n = 42) and observed nighttime behaviors using the Cohen-Mansfield Agitation Inventory every 5 minutes from bedtime to rise time. Inter-rater reliability was 0.90 among observers. Descriptive statistics were used to describe participants' sleep patterns. The Pearson Correlation statistic was used to determine the relationship between the variables of interest.

**Results :** Participants' mean age was 79.8 (sd = 6.5); sleep efficiency was 66.1% (sd 19.55%); minutes slept was 334.05 (sd 116.92); number of awakenings was 34.37 (sd 13.44); and average number of behaviors was 8.2 (sd 4.97). Nighttime behavioral symptoms were highly correlated with sleep efficiency ( $r = -.560$ ;  $p < .001$ ), moderately correlated with total sleep time ( $r = -.397$ ;  $p = .014$ ), and not significantly correlated with total number of nighttime awakenings.

**Conclusion :** Findings suggest a relationship between nighttime behavioral symptoms and decreased total sleep time and lower sleep efficiency.

**Support (optional):** Veterans Affairs H VA NRI 01-077-1 Medical University Of South Carolina Institute of Minority for Research and Minority Training IT32 AG021794-02.

0330

**RELATIONSHIP BETWEEN NIGHTTIME SLEEP AND CAREGIVER BURDEN IN PERSONS WITH DEMENTIA***Glover JU,<sup>1,2</sup> Richards K,<sup>1,3</sup> Cole CS,<sup>1</sup> Lambert C,<sup>3</sup> Luchsinger M,<sup>3</sup> Williams JS,<sup>4</sup> Shue VM<sup>5</sup>*

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**Introduction :** Nighttime sleep disturbances of persons with dementia can be burdensome for family caregivers who often awaken when the person with dementia does. Caregivers often experience sleep loss, become burdened, and, as a result, decide to institutionalize the person with dementia. The specific aims of this study were to: 1) describe the sleep patterns of persons with dementia; and 2) explain the relationship between caregiver burden and total nighttime awakenings, total sleep time, and sleep efficiency in persons with dementia.

**Methods :** This was a secondary analysis of the data from a multivariate cross-sectional descriptive study, which included persons with dementia 65 years and over and their caregivers (n=42) who reported five or more nighttime behaviors at least three times a week. Sleep technicians collected two nights of attended polysomnography data in participants' homes. Caregivers completed a 21-item Caregiver Burden Scale. Descriptive statistics were used to describe sleep patterns of persons with dementia. The Pearson Correlation statistic was used to determine the relationship between the variables of interest.

**Results :** Persons with dementia had an average sleep latency of 27 minutes (sd 25.8) and a sleep efficiency of 66% (sd 19%). They slept 334 (sd 116.2) minutes, were awake 153.22 (sd 75.81) minutes, and awoke 35.26 (sd 12.16) times. The average caregiver burden score was 28.3 (sd 14.42) indicating low burden. Scores ranged from 2 to 60. Caregiver burden was not significantly correlated with the sleep variables of interest.

**Conclusion :** These findings suggest that self-report caregiver burden scales may be inadequate to measure caregiver problems associated with assisting persons who have dementia and sleep disturbances during the night. Future research should include polysomnography studies of family caregivers to determine insomnia, which can have negative health outcomes for family caregivers and may contribute to their decision to institutionalize persons with dementia.

**Support (optional):** Veterans Affairs H VA NRI 01-077-1 Medical University Of South Carolina Institute of Minority for Research and Minority Training IT32 AG021794-02.

0331

**MORE DAYTIME SLEEPING AMONG OLDER PEOPLE UNDERGOING POST-ACUTE REHABILITATION PREDICTS WORSE FUNCTIONAL RECOVERY***Alessi CA,<sup>1,2</sup> Martin JL,<sup>1,2</sup> Webber AP,<sup>2</sup> Alam T,<sup>1,2</sup> Josephson KR,<sup>1</sup> Harker JO<sup>1</sup>*

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**Introduction :** Many factors predict functional recovery among older people undergoing rehabilitation, but there has been little study of the effects of sleep. This study tested whether sleep disturbance among older people in post-acute rehabilitation predicts immediate and long-term functional recovery.

**Methods :** This prospective, descriptive study enrolled adults (aged > or = 65 years) on admission to two post-acute rehabilitation sites (one VA, one community). During the rehabilitation stay sleep was assessed subjectively (Pittsburgh Sleep Quality Index, PSQI) and objectively (7-day wrist actigraphy and 2-daytime observations of sleep/wake). Edentrace II recordings were used to screen for sleep-disordered breathing (SDB). Functional status was assessed by the Functional Independence Measure motor component (mFIM) on admission, discharge and 2, 6, and 9 months after enrollment.

**Results :** We enrolled 245 participants (mean age 80.6 years, 38% female, 80% non-Hispanic white, average length of stay in rehabilitation 21.0 days). PSQI scores were worse in rehabilitation than pre-morbid sleep (total score and subscales, all  $P < .008$ ). Actigraphy demonstrated partici-

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pants slept 16% of daytime hours (08:00-20:00) and only 52% of nighttime hours (22:00-06:00). There was good agreement between actigraphy and observed daytime sleep. Using regression models, more daytime sleeping (but not nighttime sleep) during the rehabilitation stay was associated with less mFIM improvement. SDB variables did not correlate with PSQI, actigraphy or functional recovery. More daytime sleeping predicted fewer hours of rehabilitation therapy received ( $t=-3.66$ ,  $p<.0005$ ). Even after adjusting for other significant predictors of mFIM change (e.g., hours of rehabilitation therapy received, mental status, re-hospitalization), less daytime sleeping during post-acute rehabilitation predicted greater functional recovery (mFIM improvement) between admission and discharge ( $p=.005$ ), and 2-month ( $p=.004$ ) and 6-month ( $p=.004$ ) follow-up (adjusted R-square .234,  $p < .0001$ ). By 9 months, the adjusted analysis was no longer statistically significant.

**Conclusion :** Abnormal sleep/wake patterns are common among older people during post-acute rehabilitation, and more daytime sleeping during rehabilitation predicts worse functional recovery up to 6 months after admission.

**Support (optional):** Veterans Administration HSR&D (IIR-01-053-1; AIA-03-047) and VA Greater Los Angeles Healthcare System Geriatric Research, Education and Clinical Center (GRECC)

### 0332

#### AMBIENT LIGHT, NOCTURNAL SLEEP, PSYCHOLOGICAL ADJUSTMENT, AND NAPPING IN COMMUNITY DWELLING OLDER ADULTS

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**Introduction :** Light is the major zeitgeber for the sleep/wake cycle. Because older adults often experience phase advanced sleep/wake cycles (early evening sleepiness/early morning awakenings), the ambient light/nocturnal sleep relationship in older adults is of particular interest. We examined the relationship between daytime ambient light exposure (lux and duration), subjective/objective nocturnal sleep, psychological adjustment, and napping in community dwelling older adults.

**Methods :** 103 community-dwelling older adults ( $M=72.81$  yrs,  $SD=7.12$ ) were recruited from North Central Florida. Participants completed daily sleep diaries and wore an Actiwatch-L® (24 hours/day) for 14 days. Ambient light variables: maximum illumination (MAX-lux)-average peaks of light received, and average total illuminance exposure (TOTEX)-average lux per minute received. Subjective/objective nocturnal sleep variables: wake time after sleep onset (WASO), sleep onset latency (SOL), sleep efficiency (SE). Other measures: total nap time (NAP-from sleep diary), Beck Depression Inventory-Second Edition (BDI-II), State-Trait Anxiety Inventory (STAI). Results are based on the 12 days for which we had ambient light data for a full 24hr period.

**Results :** For subjective sleep, correlations revealed MAX-lux was negatively correlated with NAP ( $r=-.26$ ,  $p<.01$ ), WASO ( $r=-.29$ ,  $p<.01$ ), and SOL ( $r=-.21$ ,  $p<.05$ ) and positively correlated with SE ( $r=.24$ ,  $p=.015$ ). For objective sleep, MAX-lux was positively correlated with SE ( $r=.24$ ,  $p<.05$ ) and negatively with WASO ( $r=-.24$ ,  $p<.05$ ). For subjective sleep, correlations revealed TOTEX was negatively correlated with WASO ( $r=-.24$ ,  $p<.05$ ), and NAP ( $r=-.23$ ,  $p<.05$ ). For objective sleep, TOTEX was positively correlated with SE ( $r=.20$ ,  $p<.05$ ) and negatively with WASO ( $r=-.21$ ,  $p<.05$ ). A t-test comparing participants with high ( $>3000$ ) and low ( $<1000$ ) MAX-lux revealed a significant difference in WASO [ $t(88)=2.80$ ,  $p<.05$ ]. Participants exposed to low levels of illumination had approximately 34 more minutes of unwanted nightly awake time than those exposed to high levels of illumination.

**Conclusion :** Greater ambient illumination and exposure were associated with better nighttime sleep. Further exploration of ambient light as an

intervention for late-life insomnia is warranted.

**Support (optional):**

### 0333

#### ASSESSING TIME OF DAY OF NAPPING BEHAVIOR IN OLDER ADULTS: IMPLICATIONS FOR NOCTURNAL SLEEP

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**Introduction :** Daytime napping is a factor that has been studied in relation to impaired sleep in older adults. Various aspects of napping behavior have been observed including the frequency of naps, duration of naps, and time of day of naps. Previous research regarding the most effective method for assessing the time of day that naps occur is mixed. We examined the relationship between categorical and continuous measures of time of day of napping (TOD-Nap) and objectively and subjectively measured nocturnal sleep.

**Methods :** 103 community-dwelling older adults ( $M$  age=72.81,  $SD=7.12$ ) completed daily sleep diaries and wore an Actiwatch-L® (24 hours/day) for 14 days.

**Results :** The peak nap time for the sample occurred at 9:30 p.m. MANOVAs were performed to compare individuals who napped during the day to individuals who engaged in both daytime evening and naps across objective and subjective sleep variables. Main effect of TOD-Nap was significant for actigraphy sleep variables (Wilks'  $L=0.81$ ,  $F(4,77)=4.82$ ,  $p<.01$ ,  $\eta^2 = 0.19$ ) and non-significant for sleep diary sleep variables. Univariate tests revealed significant differences for sleep onset latency ( $F(1,80)=4.37$ ,  $p<.05$ ), wake time after sleep onset ( $F(1,80)=14.27$ ,  $p<.001$ ), and sleep efficiency ( $F(1,80)=12.01$ ,  $p <.01$ ). Individuals who napped in the evening and during the day had significantly less WASO (7 minutes) and less SOL (21 minutes) compared to those who only napped during the day. Also, individuals who napped both during the day and evening had significantly higher sleep efficiency (5%) overall.

**Conclusion :** Although the combination of day and evening naps was associated with better nighttime sleep in this study, we hesitate to conclude that napping throughout the day and evening should be recommended for older individuals. Further exploration of other aspects of napping behavior (duration, frequency) and other age-related factors (health, medication usage) is needed to clarify the relationship between timing of napping and nocturnal sleep in older adults.

**Support (optional):**

### 0334

#### DOES SLEEP AFFECT PHYSICAL FUNCTION? THE OUTCOMES OF SLEEP DISORDER IN OLDER MEN (MROS SLEEP STUDY)

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**Introduction :** Sleep related problems affect many older adults. Physical function is an important predictor of disability and frailty. Little is known about the impact of sleep on physical function.

**Methods :** During 2003-2005, 2911 men from the multi-center Osteoporotic Fractures in Men (MrOS) Study participated in the MrOS Sleep Study, which involved overnight in-home polysomnography (PSG), at least three days of actigraphy and measures of physical performance. Sleep duration, %REM sleep and apnea-hypopnea index (AHI) were

measured from PSG; awakening after sleep onset (WASO) was measured from actigraphy. Linear and logistic models were used and included age, BMI, clinic, smoking, antidepressant use, medical conditions, hypertension, and physical activity.

**Results :** The mean ( $\pm$  SD) age of these men was 76.4 (+ 5.5) years, and 91% were Caucasian. The means for sleep duration was 355.5 (+69.4) minutes, WASO 78.3 (+44.2) minutes, % REM sleep 19.3% (+6.6) and AHI with 3% desaturation 17.1 (+15.1). The means for the physical performance measures were: grip strength 37.9 (+8.2) kg, walking speed 1.14 (+0.23) m/s and narrow walk pace 1.13 (+0.26) m/s; 5% were unable to perform the chair stand. In unadjusted models, all sleep measures were significantly related with physical functioning ( $p < .05$ ). For each 30-minute increase in WASO, the adjusted risk of being unable to perform the chair stand increased 19% (95% confidence interval (CI) 1.08, 1.31), grip strength decreased 0.33 kg (95% CI -0.52, -0.14), walking speed decreased 0.012 m/s (95% CI -0.017, -0.007), and narrow walk pace decreased 0.009 m/s (95% CI -0.016, -0.002). For each SD decrease in % REM sleep, grip strength decreased 0.45 kg (95% CI -0.73, -0.17), walking speed decreased 0.010 m/s (95% CI = -0.018, -0.003), and narrow walk pace decreased 0.009 m/s (95% CI -0.019, 0.001).

**Conclusion :** Our findings show that higher WASO and decreased % REM sleep adversely affect physical performance.

**Support (optional):**

### 0335

#### THE INTERACTION OF APOE ALLELE STATUS AND SLEEP DISORDERED BREATHING ON COGNITIVE FUNCTION

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**Introduction :** Sleep disordered breathing (SDB), ApoE genotype, and cognitive function overlap in many arenas. Their exact interactions have not been explained. ApoE4 allele status is associated with about a two-fold increased risk for sleep disordered breathing in the general population. ApoE4 is also associated with altered cognitive and as well as mental stress testing results at various stages in life, including in early life. Sleep disordered breathing is associated with impaired cognitive performance. Many studies on ApoE and cognition do not account for SDB effects, which are likely high in this population. One human study found that a greater number of respiratory events in older adults had a negative impact on memory function in ApoE4 carriers only. In mice, ApoE4 status predicted cognitive impairment following challenges that mimic SDB. **Methods :** Subjects of a general population cohort have already undergone a full nocturnal polysomnography evaluation, ApoE genotyping, as well as a battery of cognitive testing. This study evaluates only those with an apnea-hypnea index between 15 and 30 events per hour to compare those with a similar level of sleep disordered breathing but different ApoE4 status. These subjects (n=55) were separated into those with a positive ApoE4 allele and a negative ApoE4 allele status, and then compared on cognitive parameters (n=25 and 30 respectively). Cognitive testing included the RAVLT (Reys Auditory and Visual Learning Test) for immediate and delayed recall, trial making test A and B, and digit cancellation test.

**Results :** Preliminary evidence suggests those with a positive ApoE4 allele status demonstrated poorer results on the RAVLT. Further findings will be discussed.

**Conclusion :** ApoE4 allele status puts a person at a higher vulnerability to the cognitive impacts of sleep disordered breathing. This may be due to a decreased ability for neuronal recovery to the insults of apneas than peo-

ple who do not have this ApoE4 vulnerability.

**Support (optional):**

### 0336

#### INTRAINDIVIDUAL VARIABILITY IN DAILY OBJECTIVE AND SUBJECTIVE SLEEP PATTERNS AND AFFECT IN COMMUNITY DWELLING OLDER ADULTS

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**Introduction :** Variability is an important, but often neglected factor in sleep research. Daily sleep data is typically averaged over multiple nights to reduce night-to-night fluctuations. Interestingly, research from other areas of biology and psychology suggests such fluctuations, or intraindividual variability (IIV), may provide unique information. Both sleep and affect are subject to variability and are fundamental to older adults' well-being. We examined IIV in objective/subjective sleep and its relationship to daily fluctuations in affect in a community-based sample of older adults.

**Methods :** 103 community-dwelling older adults (M=72.81yrs, SD=7.12) from North Central Florida. completed daily sleep diaries, the Positive and Negative Affect Scale(PANAS), and wore an Actiwatch-L® (24 hours/day) for 14 days. Subjective/objective sleep variables examined included: sleep onset latency(SOL), total sleep time(TST), total wake time(TWT), and sleep efficiency(SE).

**Results :** Linear mixed effects modeling analyses were performed for both positive and negative affect and: 1-subjective sleep quality, 2-subjective SOL, TST, TWT, SE, 3-objective SOL, TST, TWT, SE. As subjective sleep quality increased, both positive [Estimate=1.07,t(1314.34)=7.86,p<.001] and negative [Estimate=-0.62,t(1311.72)=-6.66,p<.001] mood significantly increased. As subjective SOL increased, positive mood significantly decreased [Estimate=-.02,t(1292.78)=-3.01,p<.01] and negative mood significantly increased [Estimate=0.01,t(1289.76)=2.05,p<.05]. As subjective SE increased, negative mood significantly decreased [Estimate=-0.10,t(1303.63)=-2.66,p<.05]. As objective SOL decreased, positive mood increased [Estimate=-0.01,t(1310.27)=-2.08,p<.05]. Additionally, as objective SOL and TWT increased, negative mood increased [Estimate=0.01,t(1308.07)=3.61,p<.001; Estimate=-0.01,t(1306.63)=-2.32,p<.05, respectively].

**Conclusion :** As subjective sleep quality improves, individuals may experience emotions more fully; perhaps as a consequence of increased cognitive resources. Several sleep variables seemed to have a stronger impact on negative mood. Potential reasons are: 1)negative mood may be better reflected in the PANAS, or 2)negative mood may be influenced more by a single night's sleep. SOL predicted mood, suggesting longer SOL leads to feelings of frustration while shorter SOL leads to positive feelings. These findings highlight the importance of IIV in sleep research.

**Support (optional):**

### 0337

#### STRESS AND DEPRESSIVE SYMPTOMATOLOGY ARE CORRELATES OF DISTURBED SLEEP IN MID-LIFE WOMEN

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**Introduction :** The frequency of sleep complaints increases dramatically in mid-life women and this increase is not fully explained by age and

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changes in sex steroids associated with the menopause. Symptoms of depression and stress, which have been associated with sleep complaints in other populations, may be important correlates of sleep in mid-life women. We evaluated cross-sectional associations among depressive symptomatology, stress, and sleep in a multi-ethnic sample of mid-life women.

**Methods :** Participants were 338 women (mean age: 51.7 + 2.2 years; 122 African-American, 163 Caucasian, 53 Chinese) enrolled in the multi-site SWAN Sleep Study (Chicago, Detroit area, Oakland CA, Pittsburgh). The majority of participants were peri-menopausal cycling women whose sleep studies were conducted during the early follicular stage of the menstrual cycle. Exclusion criteria included hormone use, shift work, current alcohol abuse, and chemotherapy/oral corticosteroid use. Questionnaires included the Inventory of Depressive Symptomatology, the Impact of Event Scale (stress-related intrusive thoughts and avoidance behaviors) and the Pittsburgh Sleep Quality Index. Night 2 summary sleep measures, collected via in-home polysomnography, focused on indices of sleep continuity and architecture.

**Results :** There were significant associations between depressive symptomatology, stress and indices of sleep continuity and quality. Higher symptoms of depression and stress-related intrusive thoughts and avoidance behaviors were associated with lower sleep maintenance, greater WASO, and poorer sleep quality ( $p < .01$ ). After adjusting for age and race in multivariate analyses, higher depressive symptoms were inversely related to sleep quality ( $p < .001$ ) while stress-related intrusive thoughts and avoidance behaviors were associated with lower sleep maintenance and greater WASO ( $p < .01$ ).

**Conclusion :** Stress and mood are significant correlates of sleep in mid-life women, even considering age and race. These psychological factors may represent an important target of opportunity for addressing sleep disturbances and disorders that emerge during mid-life.

**Support (optional):** Supported by AG019360, AG019361, AG019362, AG019363, RR00056.



## 0338

## A DIARY BASED EXAMINATION OF NURSE SLEEP PATTERNS AND PATIENT SAFETY

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**Introduction :** The hazards associated with long shifts and sleep deprivation among resident physicians have been recognized for many years. It is not known however, if the extended shifts worked by the majority of nurses in the United States are coupled with inadequate sleep, and if so, what effect this has on patient safety. The goal of this study was to examine the sleep patterns of hospital staff nurses, and to determine if shorter sleep durations among hospital staff nurses were associated with an increase in self-reported errors and difficulties remaining awake on duty.

**Methods :** Two samples of full time hospital staff nurses (ANA sample =393 participants, AACN sample=502 participants) completed a demographic questionnaire and logbooks with daily information about sleep, alertness on duty, work hours, and errors for 28 days. Generalized Estimating Equation Logistic regression modeling was used to examine the relationship between nursing errors and sleep durations, and difficulties remaining awake on duty.

**Results :** Shift durations ranged from 0.5-23.7 hrs, and sleep durations on workdays ranged from 0-18 hours. On average, participants in the ANA sample obtained  $6.8 \pm 1.7$  hrs on workdays, and participants from the AACN Sample (all critical care nurses) obtained  $6.64 \pm 1.8$  hrs sleep. Nurses reporting errors obtained significantly less sleep, The risks of making an error were 1.17 (95% CI: 1.06-1.28,  $p < 0.001$ ) and 1.08 (95% CI: 1.101-1.15,  $p = 0.032$ ) times more likely with one hour less sleep in the ANA and AACN samples respectively. Struggling to stay awake was common and not confined to night shift: approximately 2/3 of the participants reported struggling to stay awake on duty at least once during the 28-day data gathering period. Nurses reported fighting sleep about once every five shifts (2258/11,218 shifts), and those who obtained approximately 6.2-6.3 hours of sleep were significantly more likely to report struggling to stay awake than nurses who obtained more sleep. For every hour decrease in sleep time, nurses were 10% ( $p < 0.001$ , ANA Sample) and 18% ( $p < 0.001$ , AACN Sample) more likely to have difficulties remaining awake on duty.

**Conclusion :** Patient safety is adversely affected when hospital nurses do not obtain enough sleep. Nurses with shorter sleep durations are more likely to report errors and to struggle to stay awake on duty.

**Support (optional):** Financial support for this study provided by the Agency for Healthcare Research and Quality (R01 HS11963-01) and an American Nurses Foundation Grant (Scott)

## 0338

## A DIARY BASED EXAMINATION OF NURSE SLEEP PATTERNS: FACTORS EFFECTING SLEEP DURATION

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**Introduction :** Recent studies have shown that hospital staff nurses often obtain less than optimal amounts of sleep, frequently struggle to remain

awake on duty, and that shorter sleep durations are associated with higher risks of making a medical error. The goal of this study was to determine what factors predicted short sleep durations among a large sample of full-time hospital staff nurses.

**Methods :** Two samples of full-time nurses (393 and 502 participants for the ANA and AACN samples respectively) completed a demographic questionnaire and logbooks with daily information about sleep, alertness on duty, work hours, and errors for 28 days. Participants in the ANA sample worked on a variety of different hospital units, while members of the AACN sample were all critical care nurses. Generalized Estimating Equation Logistic regression modeling was used to examine the relationship between sleep duration and biologic, lifestyle, and work-related factors.

**Results :** Shorter sleep durations on workdays were associated with increased age, higher caffeine intakes, complaints of difficulty sleeping, longer commutes, longer work shifts and in the AACN sample only, working on a coronary care unit. Although childcare or eldercare responsibilities did not influence sleep duration on workdays, they did have an adverse effect on sleep duration on non-work days. Other factors that were associated with shorter sleep durations on non-work days included older age and high caffeine intakes (AACN sample only), and complaints of difficulty sleeping. Sleep durations were not influenced by gender, ethnicity, marital status, years experience as a RN, shift type (night shift versus non-night shifts), or moonlighting.

**Conclusion :** Predictors of shorter sleep durations among hospital staff nurses included several biologic, lifestyle and work-related factors. These findings can be used as a foundation for improving sleep patterns, implementing fatigue countermeasures, and increasing the alertness of hospital staff nurses.

**Support (optional):** Financial support for this study provided by the Agency for Healthcare Research and Quality (R01 HS11963-01) and an American Nurses Foundation Grant (Scott)

## 0339

## RISK FACTORS FOR SLEEP-RELATED CRASHES IN KOREAN PROFESSIONAL TRUCK DRIVERS

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**Introduction :** Drowsy drivers have long been acknowledged to constitute a potential hazard for automobile accident. Drowsiness of heavy truck drivers could result in life-threatening critical accident. Commercial vehicle operators (especially long range truck drivers) are at more increased risk for drowsy driving and sleep-related crash due to such factors as extended driving times, irregular work and sleep schedules, higher frequency of nighttime driving, and inadequate sleep. However in Korea, there were very little concern about this serious risk factors.

**Methods :** We developed questionnaire composed of 43 questions investigating personal information, working condition, sleep and drowsiness related factors. The questionnaire also includes sleep diary and Epworth sleepiness scale. We distributed 1100 questionnaires and 315 Commercial truck drivers who drives heavy truck (at least 5 tons or more) or container trailers responded. (the response rate was 28.63%) Among 315 respondent, we excluded 42 because they did not completed requested ESS or Sleep diary. We divided respondents into 2 groups; the first group(N=183) is "No or minor crash group" which consisted of drivers with no sleep-related accident or only minor collision without injuring any persons, the second group(N=86) is "Serious crash group" which consisted of drivers with more serious sleep-related crashes involving human injury. Then we compared two groups by statistical method.

**Results :** All participant of this study was male, and their mean age range was  $41.87 \pm 7.88$  years. Statistically significant difference between two

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groups (Group 1 vs Group 2) were identified in following factors: the percentage of driving time after sunset per day ( $54.8 \pm 24.3$  vs  $64.2 \pm 23.1$ ,  $P=0.003$ ), mean daily sleep hours ( $5.24 \pm 1.95$  vs  $4.85 \pm 1.20$ ,  $P=0.048$ ), nights of sleeping in their trucks per month ( $13.12 \pm 9.31$  vs  $16.83 \pm 8.56$ ,  $P=0.002$ ).

**Conclusion :** The Korean professional truck drivers have been driving more than half of their work hours after sunset. They usually have been slept in their own truck more than 15 nights per month. These were significant risk factors of more serious sleep-related human-injuring crashes. In addition, their insufficient sleeping time per each day was one of another risk factor.

**Support (optional):**

### 0340

#### SLEEP PATTERNS OF CADETS AT THE UNITED STATES MILITARY ACADEMY: INTERIM FINDINGS OF A FOUR-YEAR LONGITUDINAL STUDY

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**Introduction :** In 2003, the authors began a four-year longitudinal study on sleep patterns of Cadets at the U.S. Military Academy (USMA). This presentation reports findings from the first two years of the study. Carskadon & Davis (1989) studied incoming Brown University students during the Spring semester of their senior year in high school and again during the Fall semester of their freshman year at Brown. During Spring of the senior year in high school, students reported receiving an average of 6.98 h of sleep on weeknights and 8.75 h on weekends. As freshmen at Brown, they reported receiving 6.67 h of sleep on weeknights and 8.15 h on weekends. At the 2004 APSS Annual Meeting, we reported our findings on the sleep patterns of Cadets during their initial summer training and the 30 day period prior to their arrival at USMA. This report presents nighttime contiguous sleep and napping data on the same 80 Cadets for the first four academic semesters and compares with the study conducted at Brown.

**Methods :** Actigraphy data were collected on 80 members of the USMA Class of 2007 from Fall 2003 through Spring 2005. In addition, self-reported napping data were collected on the same Cadets during the Spring 2005 semester.

**Results :** Earlier findings showed Cadets received a mean of 8.39 h of sleep ( $SD = 1.62$ ) for the month prior to reporting to USMA. During the first four semesters, their average contiguous nighttime sleep on weeknights was 4.88 hrs. (Fall 2003), 5.06 hrs. (Spring 2004), 5.28 h (Fall 2004), and 5.23 h (Spring 2005). On weekends, contiguous nighttime sleep was 6.87 h (Fall 2003), 6.48 h (Spring 2004), 7.04 h (Fall 2004), and 6.31 h (Spring 2005). Self-reported napping data during the Spring 2005 semester indicate a bimodal distribution with most of the naps occurring in the late morning and early afternoon. Cadets napped an average of once every 3.08 days. Average length of Cadets' naps was 1 h 29 m.

**Conclusion :** This study continues to chronicle sleep habits of Cadets at USMA. Compared to their sleep habits prior to arriving at the Academy, Cadets received approximately three hours less sleep after their arrival at USMA. Overall, Cadets received two hours less sleep per night compared to students at Brown. Benefits of the study include identification of Cadets with sleep disorders; access to the Academy's senior leadership with empirical findings which has led to policy changes; and, education of Cadets, staff and faculty with respect to the benefits of good sleep hygiene.

**Support (optional):**

### 0341

#### THE INFLUENCE OF INSUFFICIENT SLEEP ON CEREBRAL BLOOD VOLUME

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**Introduction :** Insufficient sleep is related to the quality of life and health-related variables. The insufficiency of sleep increases the risk of errors and accidents because of cognitive disturbance. Near-infrared spectroscopy (NIRS) enables the noninvasive observation of brain functions by measuring hemoglobin concentrations and cerebral blood volume. Thus, this study was carried out to elucidate the influence of insufficient sleep on cerebral blood volume change during cognitive activation in healthy adults.

**Methods :** Fifteen healthy adults who showed a normal sleep pattern on polysomnography (PSG) (11 males, 4 females; age  $31.1 \pm 8.2$  years, mean  $\pm$  SD) were enrolled in this study after giving consent. All participants slept for  $\geq 6$  hours (sufficient sleep) with PSG monitoring, and were then limited in their total sleep time to  $< 4$  hours (insufficient sleep). The oxyhemoglobin (oxyHb) level was measured on the mornings following the sufficient- and insufficient-sleep periods. The relative concentrations of oxyHb were measured with frontal probes every 0.1 sec during a word-fluency task with a 24-channel NIRS recorder (Hitachi ETG-100, Hitachi Medical, Tokyo, Japan). We measured the peak oxyHb level, time from the start of the task to the peak oxyHb level, and the time for the oxyHb level to recover from the peak to the baseline level.

**Results :** The peak oxyHb level was significantly lower after insufficient sleep than after sufficient sleep ( $0.21 \pm 0.12$  vs  $0.74 \pm 0.33$  mmol,  $p < 0.05$ ). The oxyHb recovery time tended to be shorter after insufficient sleep than after sufficient sleep. The time between the start of task and the peak oxyHb level did not differ significantly between insufficient sleep and sufficient sleep.

**Conclusion :** Insufficient sleep might adversely affect the cerebral blood volume during the daytime. NIRS can be a useful tool for understanding the interrelation between insufficient sleep and psychiatric symptoms.

**Support (optional):**

### 0342

#### ACCUMULATION OF RAPID EYE MOVEMENT SLEEP PROPENSITY IN THE RAT: A ROLE FOR WAKEFULNESS

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**Introduction :** Hypothesis concerning the origination of REM-sleep homeostatic need are contradictory. The waking-related model of REM-sleep regulation predicts that REM-sleep propensity/pressure accumulates during waking. According to the nonREM-sleep related model, REM-sleep occurs in response to prior nonREM-sleep expression. We recently showed that during acute REM-sleep restriction, rats exhibit different degrees of REM-sleep homeostatic pressure defined by the number of attempts to enter into REM sleep while exhibiting similar amounts of nonREM-sleep. The present study examines the relation between the degree of REM-sleep pressure and concurrent waking experience in

REM-sleep restricted rats.

**Methods :** Ten Sprague-Dawley rats were REM-sleep restricted for 2 hours during the light period; they were subjected to gentle arousing stimuli after the first 20-25 sec. of each REM-sleep episode. Rats were divided into groups with high (n=5) and comparatively low (n=5) REM-sleep pressure defined by the number of attempts to enter into REM-sleep during the restriction period (58±3.1 and 27±2.9 attempts, respectively). Percentage time and the pattern of nonREM-sleep and waking during the restriction period were compared between the rats with high and low REM-sleep pressure. Differences in percentage time spent in nonREM-sleep and waking, the frequency and mean duration of nonREM-sleep and waking episodes between the two groups of animals were assessed with an unpaired t-test.

**Results :** High REM-sleep pressure rats exhibited a lower percentage of waking (20.3 ±0.1% versus 29.4±0.2%, p=0.009) and a lower number of spontaneous awakenings (12.4 ±0.8 versus 20.8±2.8, p=0.021) during the REM-sleep restriction period compared to low REM-sleep pressure animals. Percentage time spent in nonREM-sleep did not differ between the two groups, while mean duration of nonREM-sleep bouts was reduced in low REM-sleep pressure rats.

**Conclusion :** Findings of this study are consistent with the hypothesis that REM sleep is functionally and homeostatically related to nonREM-sleep rather than to waking.

**Support (optional):** Supported by the Department of Veterans Affairs and MH 63323

### 0343

#### LIFE AFTER LAPSES: USING DISTRIBUTION PLOTS TO CHARACTERIZE PERFORMANCE CHANGE ACROSS SLEEP DEPRIVATION

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**Introduction :** The psychomotor vigilance task (PVT) is a measure of neurobehavioral performance that is sensitive to sleep loss. 'Minor lapses', (reaction time responses >500ms) have become accepted as a particularly sensitive PVT measure. In total sleep deprivation (TSD) studies, however, significant proportions of data accumulate in the >500ms response range. The aim of the present study was to explore alternative characterizations of PVT data to determine whether greater resolution of the changes occurring during TSD might be achieved

**Methods :** Data was used from 18 subjects (14M, 4F; age±SD=25.8±4.3y), with habitually low caffeine usage (<300mg/d), who participated in a protocol that included an 8-hr sleep period (2300-0700h) followed by 77h of TSD. Most data was collected during two-hourly blocks from 0100 to 0900h, which were preceded by baseline performance tests and either caffeinated (200mg) or placebo chewing gum (Stay Alert®, Amurol Confectioners).

**Results :** The first finding was that the signal-to-noise ratio of the traditional PVT test mean was very low. This was largely due to the wide range of response times measured, which were from approximately 200ms to over 40 seconds. This was resolved by using all responses for every test in order to create a distribution of responses instead of a single mean per test. The second finding was that because of individual variability in baseline PVT performance, the aggregate distributions across all subjects still had relatively low signal-to-noise ratios. This was resolved by using relative scores instead of absolute ones. Standard statistical comparisons using group means, variance, and area under the curve were all successfully applied to the distributions

**Conclusion :** For studies involving long periods of TSD, distributions of relative PVT measures provide considerably higher resolution of per-

formance than lapse counts. This is true for performance changes occurring over time as well as those associated with experimental interventions

**Support (optional):**

### 0344

#### NO EVIDENCE OF A POST-CAFFEINE PERFORMANCE 'CRASH' DURING 77 HOURS OF SLEEP DEPRIVATION

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**Introduction :** Caffeine enhances cognitive performance in well-rested and sleep deprived individuals. However, it is not known whether individuals who are periodically administered caffeine show any measurable negative rebound, or 'crash', between doses.

**Methods :** Thirty subjects (23M, 7F; age±SD=25.3±4.1y), with habitually low caffeine usage (<300mg/d), participated in a protocol that included an 8-hr sleep period (2300-0700h) followed by 77h of sleep deprivation. Most performance measures were administered bi-hourly, between 0100-0900h, and were preceded by administration of caffeine (200mg) or placebo chewing gum (Stay Alert®, Amurol Confectioners, Yorkville, IL). Due to hardware failure and subject drop out, 23 full data sets (12 caffeine, 11 placebo) were analyzed. Evidence for caffeine-related 'crash' was determined using PVT tests carried out before daily caffeine administration began at 0100h as baseline (i.e., when caffeine blood levels would be expected to be minimal). Post-hoc t-tests (for group level differences) and mixed-effect ANOVA (for individual level differences) were performed.

**Results :** Post-hoc t-tests failed to show any significant differences in any measures (PVT RT, speed, lapses[>5s, >3s, >1s, total], anticipations, false starts). Using the mixed-model approach, a single covariate (PVT baseline speed) showed moderate, systematic variability at the individual level in a single measure (PVT speed). Other covariates considered in the mixed-model were age, body mass index, and habitual caffeine use. Other measures assessed were PVT mean RT, median RT, speed, and lapses (>5s, >3s, >1s).

**Conclusion :** The finding from the mixed-effects model that systematic individual variability was negligible was predicted since strict inclusion/exclusion criteria ensured that the subject group was homogeneous. Of greater interest was the failure to find differences in subsequent daytime performance between the caffeine and placebo groups. Although further analyses and studies are planned, these initial findings suggest that there is no performance crash between doses of caffeine across 77 hrs of sleep deprivation.

**Support (optional):**

### 0345

#### ABILITY OF CAFFEINE TO MAINTAIN NIGHT-TIME PERFORMANCE DURING THREE CONSECUTIVE NIGHTS WITHOUT SLEEP

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**Introduction :** Previous research has demonstrated the efficacy of caffeine to maintain alertness during a night without sleep, but few studies have evaluated its repeated use on consecutive nights without sleep. This study examined the affects of caffeine on performance of a monotonous simple reaction time task (PVT), during three nights without sleep.

**Methods :** Thirty healthy, non-smoking males (N=23) and females who habitually consumed less than 300 mg of caffeine per day volunteered for this study. Groups of four were randomly assigned to receive caffeine

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(CAF) or placebo (PLA). After completing an eight hr sleep period (2300-0700) subjects were kept awake for 77 hr. There were four two hr test blocks (0100-0300, 0300-0500, 0500-0700, 0700-0900) each night. At the beginning of each block, subjects chewed two pieces of Stay Alert® gum (100 mg caffeine/piece) or a placebo for five min. Each two hr block consisted of nine 5-min PVTs and a single Tower of Hanoi (TOH) and grooved peg board (GPB).

**Results :** Data were analyzed using two-way mixed ANOVAs, with corrections for repeated measures. Post hoc comparisons were done when appropriate. Sessions were collapsed into the 2-hour blocks during which the drug administration took place. The most significant effect on PVT was the Group x Block interaction where significant differences ( $p < 0.000$ ) were found for Speed, and Lapses  $> 1, 3$  and  $5$  seconds ( $p < 0.000$ ). Speed on TOH was slower ( $P < 0.004$ ) and Time for GP was longer ( $p < 0.001$ ) in PLA vs CAF.

**Conclusion :** The administration of caffeine during 3 nights without sleep had a significant positive affect on alertness, cognitive function, and manual dexterity. Caffeine maintained alertness at baseline for the first 36 hrs while placebo declined by 35%. Performance in both groups declined between 36-68 hrs but the caffeine group had half as many major lapses during that period

**Support (optional):**

### 0346

#### RISK TOLERANCE AND DECISION MAKING DURING TOTAL SLEEP DEPRIVATION

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**Introduction :** Sleep deprivation appears to impair decision making. However, many studies have used complex multimodal decision tasks. Thus, they cannot identify which aspect(s) of decision making is impaired. We examined the effects of one night sleep deprivation on risk tolerance in decision making.

**Methods :** Subjects ( $n=20$ , 7F, age= $23.1 \pm 4.6$  edu= $14.9 \pm 1.7$ ) performed a lottery choice task both well-rested (WR) and after 22-23 hours total sleep deprivation (TSD). Subjects made a series of choices, each one between a safer and a riskier gamble involving either gains or losses of money (but never both) with known probabilities. At the end of the study, gambles were randomly played out and subjects were paid based on the outcomes. We analyzed the proportion of risky choices across the four conditions.

**Results :** The proportion of riskier choices made (i.e., preference for risk) was: WR gains =.25, TSD gains =.41, WR losses =.81, TSD losses =.70. The 2x2 ANOVA (night vs gain/loss) showed a significant interaction [ $F(1,19)=9.35$ ,  $p=.006$ ]. Risk tolerance for gains increased with TSD, while risk tolerance for losses decreased.

**Conclusion :** WR subjects responded as predicted by Prospect Theory. For gambles with known odds, they showed risk aversion for gains and risk seeking for losses. Following TSD, subjects became less risk averse for gains and less risk seeking for losses. These data suggest that, overall, individuals become less sensitive to risk with TSD. With TSD, subjects moved towards a risk-neutral position, meaning that risk may have played a smaller role in their decisions. Relative to their risk preferences when well-rested, during TSD, individuals become less conservative (take greater risk) when they stand to gain, but more conservative (take less risk) if they stand to lose. These data hold major implications for settings

where safety and lives are at stake, as well as for fiscal settings.

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### 0347

#### SUBJECTIVE SLEEPINESS DURING PARTIAL SLEEP LOSS DEPENDS ON THE CONTEXT

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**Introduction :** Subjective ratings of sleepiness are often made without lack of control for preceding activity. The present study sought to compare ratings during 5 days of 4h sleeps after different types of activities.

**Methods :** 9 subjects were exposed to 5 days of 4h sleep (PSD) with a 3-day baseline and a 7-day follow-up. Here sleepiness ratings using the Karolinska Sleepiness Scale (KSS, scale 1-9 very alert to “very sleepy, fighting sleep, an effort to remain awake”) are presented. Ratings were obtained after 5 minutes with open + closed eyes, a 20min driving simulator test, and a 6 minute reaction time test (3 minutes between tests).

**Results :** A repeated measures ANOVA across phase was highly significant ( $F(2,14)=38.7$ ,  $p < .001$  after Huyn-Feldt correction) as was the effect of activity ( $F(2,14)=17.8$ ,  $p < .001$ ), but the interaction was not ( $F(4,28)=1.3$ , ns). The eyes closed activity showed KSS varying from  $5.8 \pm 4$  at baseline to  $7.9 \pm 3$  on the 5th day of sleep reduction to  $5.6 \pm 4$  on the 3rd day of recovery. For the driving simulator test the values were  $4.7 \pm 3$ ,  $7.7 \pm 3$ , and  $4.7 \pm 2$ , and for reaction time  $4.9 \pm 3$ ,  $7.6 \pm 3$ ,  $5.9 \pm 2$ . Ratings immediately before and 20 min after the test (under conditions of interaction) showed strongly reduced sleepiness.

**Conclusion :** Subjective sleepiness during partial sleep loss will depend on the preceding activity. Not controlling for activity may result in erroneous conclusions.

**Support (optional):** Bank of Sweden tercentenary fund. Research Council for Working Life and Social Sciences

### 0348

#### READING DECREMENTS IN A PROOFREADING TASK AFTER A NIGHT OF SLEEP LOSS

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**Introduction :** Previous research has shown that sleep deprivation may be associated with certain dysfunctions in language although its effects on reading are unclear. The present study evaluated proofreading ability during 36 hr sleep deprivation.

**Methods :** Twenty-seven volunteers were divided into sleep-deprived (SD,  $n = 14$ ) and non-SD (NSD,  $n = 13$ ) groups. Testing occurred at 2030 h on Day 1 after approximately 12 hr wakefulness, and at 0830 h and 2030 h on Day 2. NSD participants obtained approximately 8 hours of sleep between Days 1 and 2. Following a practice session, participants proofread a short story and circled embedded homophone, pseudohomophone, semantically related- and unrelated word-type errors. Three equivalent error versions were counterbalanced across participants and sessions. Following final testing, a homophone check confirmed understanding of those words.

**Results :** A 2(group) x 3(time) mixed factor analysis of covariance (reading ability adjusted) was conducted for each dependent variable. Significant interactions indicated that at 0830 h Day 2 the SD group declined in their ability to detect homophones [ $F(2, 48) = 4.9$ ,  $p = .01$ ],

and semantically related word-type errors [ $F(2, 48) = 6.6, p < .01$ ]. However, by 2030 h Day 2 they recovered these error detection abilities. A significant group main effect indicated, following sleep deprivation, the SD group had difficulty detecting the semantically unrelated word-type errors in comparison to the NSD group [ $F(1, 24) = 6.2, p = .02$ ; post hoc  $p < .05$  for 0830 h Day 2 only]. SD did not affect pseudohomophone error detection.

**Conclusion :** Results demonstrate that sleep deprivation had a stronger influence on performance near the circadian dip, concurrent with the morning testing session, but apparently had little effect on performance near the circadian peak, concurrent with the evening testing session. In this study significant decrement occurred in proofreading ability during sleep deprivation.

**Support (optional):**

### 0349

#### REDUCED SLEEP IS A RISK FACTOR FOR WEIGHT GAIN

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**Introduction :** Recent physiologic research suggests sleep restriction has important metabolic effects that may predispose to weight gain. We sought to investigate the association between self-reported usual sleep duration and subsequent weight gain.

**Methods :** Women in the Nurses Health Study who responded to a question about habitual sleep duration in 1986 were followed for the subsequent 16 years. Information regarding weight and important covariates were obtained via questionnaire every 2 years. Multivariate linear regression and Cox proportional hazards models were used to assess sleep duration as a predictor of weight gain.

**Results :** Data from 68,183 women were analyzed. In analyses adjusted for age and baseline body mass index (BMI), women sleeping 5 hours or less per night gained 1.04 kg (95% CI [0.39-1.69]) more than those sleeping 7 hours over 16 years and women sleeping 6 hours gained 0.68 kg (95% CI [0.39-0.97]) more. The relative risks of a 15 kg or more weight gain were 1.32 (95% CI [1.19-1.47]) and 1.12 (95% CI [1.06-1.19]) for those sleeping 5 and 6 hours respectively. The relative risks for development of obesity (BMI > 30 kg/m<sup>2</sup>) were 1.15 (95% CI [1.04-1.26]) and 1.06 (95% CI [1.01-1.11]). These associations remained significant after inclusion of important covariates and were not affected by adjustment for physical activity or dietary consumption.

**Conclusion :** Short sleep duration is an independent predictor of future weight gain and incident obesity. Further research is needed to understand the mechanisms by which sleep duration may affect weight.

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### 0350

#### EFFECTS OF SLEEP DEPRIVATION DURING THE 80-HOUR WORK WEEK

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**Introduction :** Sleep deprivation in residents adversely affects cognitive and behavioral function and quality of life.

**Methods :** We created a questionnaire regarding residents' "most difficult rotation". Included were the Epworth sleepiness scale (ESS), a graded opinion scale, and questions about medical problems. We compared our data with data from the pre 80-hour workweek (PRE80). Statistical analyses were done using descriptive statistics, Chi square and Pearson corre-

lation

**Results :** 52 of 150 residents responded (51% women). Sleep was 2.2 hours per night on call and 6.8 off. There was a significant correlation between hours of sleep and ESS score ( $r = -0.3009, p = 0.035$ ). Mean ESS was 12.9, with no intergender difference or correlation with age or residency type. This was slightly better than one PRE80 report where mean ESS was 14.6. Our ESS score falls in a risk range for accidents, errors, personal conflicts, use of stimulants and alcohol, and weight change. (Note: ESS for obstructive apnea is 11.7). Residents' level of sleep deprivation compromised patient care (61.5%); learning (82.7%); ability to exercise (78.9%); mental health (65.4%); medical health (69.2%); interpersonal relationships (71.2%); overall quality of life (82.7%). 69% used caffeine/stimulants to stay awake, and 26.9% admitted to using sleeping aids including alcohol. The above data are consistent with reports PRE80, except that 25% reported falling asleep behind the wheel, which is less than 44% PRE80. Unique is our observation that 55.5% of 81 chronic illnesses exacerbated and 51.6% of 64 acute illnesses developed.

**Conclusion :** Our study raises concern that problems related to sleep deprivation still exist for residents. However, additional investigation with a larger number of respondents would be more definitive in assessing the effects of 80-hour workweek.

**Support (optional):**

### 0351

#### SLEEP DEPRIVATION AND BRAIN CONNECTIVITY: THE IMPACT OF SLEEP DEPRIVATION AND TASK DIFFICULTY ON NETWORKS OF FMRI BRAIN RESPONSE

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**Introduction :** Previous research has found both increased & decreased regional brain responses after total sleep deprivation (TSD) and that task difficulty influences these changes. An alternative strategy is to consider not just discrete regional changes with TSD, but changes in how brain regions interact with one another. Here, we apply structural equation modeling (SEM) to functional MRI (fMRI) data in order to examine differences in networks of brain response during verbal encoding in sleep deprived and well-rested (WR) individuals.

**Methods :** Normal controls ( $n = 23, 10F, \text{age} = 24.0 \pm 4.8\text{yrs}$ ) memorized words either easy or hard to recall during fMRI after being well rested (WR) and after 36 hours without sleep (TSD). Based upon our previous work, regions of interest were defined prior to data analyses: left and right inferior frontal gyrus (LIFG & RIFG) left inferior parietal lobe (LIPL) and left superior parietal lobe (LSPL). Using SEM, we evaluated two a priori models specifying different patterns of interactions among these regions. Model 1 specified a strong interaction between LIFG and the two parietal regions while Model 2 specified strong RIFG to parietal interactions

**Results :** Task difficulty, not TSD, determined which model fit the data. For easy words, Model 1 produced excellent fits both nights, while Model 2 best fit hard words. TSD, however, produced significant changes in the interactions among brain regions. For both easy and hard words, TSD reduced the strength of LIFG-RIFG and IFG-LIPL interactions and increased the strength of the LIPL-LSPL interaction. For hard words only, the RIFG-LSPL interaction became stronger with TSD.

**Conclusion :** While TSD did not affect which model best fit the data, it did strikingly alter the patterns of interaction among brain regions during

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task performance: interhemispheric prefrontal interactions were diminished and intrahemispheric parietal interactions increased. These results demonstrate that examining the interactions among brain regions can reveal new findings and a more detailed picture of the effects of TSD on brain function.

**Support (optional):** Mental Illness Research, Education, and Clinical Centers (MIRECC) Postdoctoral Fellowship in Advanced Psychology US Army DAMD17-02-1-0201

### 0352

#### BRAIN ACTIVATION WHILE WELL-RESTED PREDICTS PERFORMANCE DURING TOTAL SLEEP DEPRIVATION

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**Introduction :** While total sleep deprivation (TSD) impairs cognitive performance and attention on a variety of tasks, the susceptibility of this impairment is not constant across individuals. Recent research has found brain activation while well-rested (WR) predicts performance on working memory during TSD. Here, we examined whether WR activation can also predict TSD performance on a psychomotor vigilance task (PVT) and a verbal learning task (VL).

**Methods :** Subjects performed the cognitive tasks during functional MRI (fMRI) both while WR and after 36 hours TSD. 20 subjects (age=27.4 ± 6.7yrs; 8F) performed PVT, and 32 subjects (age=27.6 ± 6.6yrs; 14F) performed VL. Activation within clusters related to WR performance or to increased activation with TSD was correlated with TSD performance.

**Results :** Greater activation in medial BA9, right BA46, left BA10/32, and right putamen during optimal PVT performance while WR predicted a smaller reaction time standard deviation during TSD; Right BA46, left BA10/32, and left putamen/globus pallidus predicted fewer lapses. For VL Hard words, baseline activation within left BA45, BA10, BA32, BA8, and BA7 predicted increased delayed free recall during TSD. Bilateral BA32 and left BA8 predicted maintenance of free recall scores during TSD. These correlations ranged from .36-.64 (p<.05). No correlations were found with VL Easy words.

**Conclusion :** Overall, individuals showing greater activation in task-related brain areas during PVT and VL while WR, also showed better TSD performance on these tasks. Specifically, greater engagement of sustained attention regions during WR PVT performance predicted more consistent reaction times and fewer lapses during TSD. Similarly, those who did not need to inhibit task irrelevant regions performed better during TSD. These data are consistent with prior research on working memory suggesting that baseline fMRI activation predicts differential vulnerability to the effects of TSD. Thus, fMRI may prove a useful tool in the search for trait factors that underlie this differential vulnerability.

**Support (optional):** American Sleep Medicine Foundation 01-01-01 Cephalon, Inc. UCSD GCRC M01 RR00827

### 0353

#### EFFECTS OF EARLY LIFE EVENTS ON BEHAVIOURAL RESPONSE OF FEMALE RATS TO CHRONIC ADMINISTRATION OF ETHANOL AND THE INFLUENCE OF SLEEP DEPRIVATION

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**Introduction :** Prolonged separations from the mother (3 to 24h - mater-

nal separation [MS]) lead to altered hormonal (HPA axis) and behavioural response to stress in adult animals, whereas short-term separations (3-20 min - early handling [EH]) result in attenuated stress response and lower spontaneous ethanol intake.

**Methods :** Whole litters (5 males and 5 females) were submitted to EH (15 min) or MS (360 min) from days 2 to 14 of life. At 75 days of age, female rats were injected i.p. with saline (SAL) or ethanol (EtOH, 2.0 g/kg, 20% w/v) for 15 days and locomotor activity was evaluated on the first and last days of treatment. After six days of withdrawal, rats were stressed by 24h of sleep deprivation in the modified multiple platform technique. At the end of the deprivation period, rats were challenged with EtOH and their locomotor activity, assessed again. Ten min later, trunk blood was collected, centrifuged and the plasma was assayed for ACTH levels.

**Results :** MS females ambulated less than EH rats on both testing days (p = 0.008). Acute ethanol administration reduced locomotor (EtOH=63.7; SAL=113.1 squares; p=0.0002) and rearing activities (SAL=26.3; EtOH=2.6; p=0.0002) in both groups. MS ethanol challenged rats ambulated less (MS=44.8; EH=83.4; p=0.004) and reared less (MS=1.7;EH=5.5; p=0.02) than EH animals, regardless of whether they were sleep deprived. Chronic ethanol treatment resulted in lower ACTH levels (SAL=465.7 pg/ml; EtOH=317.2 pg/ml; p=0.04) and MS sleep-deprived rats exhibited lower ACTH levels than control rats (PSP=309.5 pg/ml; CTL=577.1 pg/ml; p=0.03).

**Conclusion :** Both EH and MS groups developed behavioural tolerance to ethanol. The smaller ACTH response to sleep deprivation in MS EtOH-treated rats suggests an adaptation of the HPA axis to ethanol. Sleep deprivation did not influence the response of females to ethanol

**Support (optional):** Associação Fundo de Incentivo à Psicofarmacologia and Conselho Nacional de Desenvolvimento Científico e Tecnológico

### 0354

#### INCREASED EXPRESSION OF PARADOXICAL SLEEP IN RATS SUBMITTED TO CHRONIC FOOTSHOCK DURING PARADOXICAL SLEEP DEPRIVATION

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**Introduction :** Studies have suggested that the stress associated to the flower-pot technique could affect the expression of rebound sleep during the recovery period. The purpose of the present study was to examine how the exposure to a mixed psychological/physical stressor could alter the sleep rebound of rats submitted to paradoxical sleep (PS) deprivation.

**Methods :** Males Wistar rats were implanted with electrodes for recording of sleep-wake cycle and heart rate during the entire experimental period (96h of PS deprivation followed by 72h of recovery). Control non-deprived (CTL) and PS deprived groups were distributed in 1) Acute footshock (AF - 40 min; 2mA; 0.1s; 5-7 shocks/min) at the end of PS deprivation; 2) Chronic footshock (CF - same characteristics, applied twice/day, at 7:00h and 19:00h + 1 session at the end of PS deprivation); 3) No-footshock (NF). ACTH levels were determined in each group.

**Results :** The sleep of CTL rats was not altered by either AF or CF. AF suppressed low amplitude slow wave sleep in PS-deprived rats. PS-deprived rats exposed to chronic footshock exhibited increased expression of PS during the recovery period, compared to PS-deprived+NF rats (176%), CTL+CF (361%) and PS-deprived+AF rats (219%). This increase was due to augmented length of PS episodes. Heart rate was augmented in PS-deprived rats irrespective of whether they were stressed or not, and remained so elevated during the 72h recovery period. ACTH levels were increased in CTL+AF, being further elevated by CF. IN PS-deprived rats, footshock cause a slight elevation of ACTH. Levels were back to basal after sleep recovery.

**Conclusion :** Chronic footshock indeed alters the sleep rebound of PS-deprived rats, and this alteration is directed towards increased expression of paradoxical sleep.

**Support (optional):** Associação Fundo de Incentivo à Psicofarmacologia, Fundação de Amparo à Pesquisa de São Paulo (CEPID Grant 98/14303-3) and Conselho Nacional de Desenvolvimento Científico e Tecnológico.

### 0355

#### CONSEQUENCES OF INTERMITTENT HYPOXIA AND PARADOXICAL SLEEP DEPRIVATION ASSOCIATION ON CARDIOVASCULAR RISK FACTORS IN RATS

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**Introduction :** Several studies have proposed that hypoxia and sleep fragmentation as a consequence of obstructive sleep apnea are implicated in cardiovascular risk. The objective of this investigation was to evaluate the effects of paradoxical sleep deprivation, intermittent hypoxia, and their combination on cardiovascular risk factors in rats.

**Methods :** Rats (n=10 per group) were randomly distributed into four treatment groups: 1) control, 2) intermittent hypoxia for 4 days during the light period (cycles with 2 min room air - 2 min 10 percent O<sub>2</sub>), 3) paradoxical sleep deprivation for 4 days, 4) 4 days of paradoxical sleep deprivation combined with intermittent hypoxia.

**Results :** The effects of intermittent hypoxia on pH, pO<sub>2</sub>, and pCO<sub>2</sub> of arterial blood samples were evaluated at the end of the first cycle of hypoxia showed an increase pH and pCO<sub>2</sub> compared to pre-hypoxia concentrations. At the same time pO<sub>2</sub> was reduced. Similar alterations were seen in blood collected at the end of the 5th, 10th, and 20th cycle of hypoxia. Paradoxical sleep deprivation reduced total homocysteine, triglycerides and very low-density lipoprotein (VLDL) cholesterol concentrations, whereas increased total cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol. Intermittent hypoxia did not alter any of these parameters. However, the combination of paradoxical sleep deprivation with intermittent hypoxia did not modify the values of total cholesterol, HDL, and LDL compared to control group. Concentration of cysteine, folate, and vitamins B6 and B12 did not change.

**Conclusion :** These results suggest that paradoxical sleep deprivation induced a marked impairment in the biochemical parameters associated to cardiovascular risk. When paradoxical sleep deprivation is associated with intermittent hypoxia some of the biochemical parameters evaluated are comparable to control values.

**Support (optional):** AFIP, CNPq, FAPESP and CEPID

### 0356

#### INFLUENCE OF ACUTE AND CHRONIC EXPOSURE TO INTERMITTENT HYPOXIA AND PARADOXICAL SLEEP DEPRIVATION IN BIOCHEMICAL BLOOD FACTORS IN RATS

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**Introduction :** Since studies suggest that both hypoxia and sleep fragmentation are related to cardiovascular alterations induced by obstructive sleep apnea the present study was designed to determine the effects of acute and chronic exposure to intermittent hypoxia (IH) and paradoxical sleep deprivation (PSD) in the biochemical blood factors that are associ-

ated to cardiovascular risk.

**Methods :** Wistar rats (n=9 per group) were randomly distributed into four treatment groups: 1) control, 2) IH, 3) PSD, and 4) PSD combined with IH. In the acute experiment IH rats were exposed to cycles with 2 min room air - 2 min 10% O<sub>2</sub> during the light period and/or PSD for 3 days. Consequences of chronic IH exposure were examined after 21 consecutive days of IH protocol from 1000-1600 pm followed by a PSD period of 18 h.

**Results :** During acute exposure the rats belonging to the PSD and HI+PSD groups presented a reduction of plasma homocysteine, triglycerides and VLDL concentrations but no alteration in total cholesterol, HDL, cysteine and B6 e B12 folate. In the chronic experiment, the animals exposed to IH displayed a reduction of vitamin B6 and an increase of triglycerides and VLDL. Rats of the PSD and HI+PSD groups presented a diminished concentration of triglycerides, VLDL and an increase of vitamin B12. The animals under PSD for 21 days showed a reduction in the concentration of homocysteine but the animals of the HI+PSD did not display any alterations in this parameter. In this latter group still, an augmentation of cysteine concentration was observed. No alterations were perceived in total cholesterol, HDL and folate among groups.

**Conclusion :** Acute alterations in the biochemical factors related to cardiovascular risk were associated to PSD. Chronic PSD and HI modified blood parameters in distinct ways.

**Support (optional):** AFIP, CNPq, FAPESP and CEPID

### 0357

#### EFFECTS OF SLEEP DEPRIVATION ON THE DEVELOPMENT OF AUTOIMMUNE DISEASE IN AN EXPERIMENTAL MODEL

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**Introduction :** Sleep is hypothesized to have a restorative function on immune system. In turn, disordered sleep is thought to impair host defense mechanisms and chronic sleep deprivation is health risk factor that appears to compound disease process. The (NZB/W)F1 mice develop autoimmune disease that strongly resembles Systemic Lupus Erythematosus in humans. The mice develop a high titer of antinuclear antibodies associated with development of rapidly progressive and lethal glomerulonephritis. This research has examined the onset and development of lupus when these mice are submitted to sleep deprivation.

**Methods :** At the age of ten weeks, the female mice (n=28) were deprived of sleep in two phases of 96h using the platform method. Animals in the cage control group (n=22) remained in their home cages in the same room where sleep deprivation procedure took place. Blood samples were collected fortnightly, to evaluate seric antinuclear antibodies and anti-double-stranded DNA which are important sorologic parameters of disease evolution. Proteinuria, longevity and body weight also were measured.

**Results :** The mice submitted to sleep deprivation exhibited an earlier onset of the disease in comparison with the control group. This was shown by the positivity and high titer of seric antinuclear antibodies measured in the first week after sleep deprivation. However, no statistical difference was found in another parameters analyzed.

**Conclusion :** Sleep deprivation was considered a risk factor for the onset of disease but do not for changing its severity. Sleep deprivation is a stimuli able to accelerate the onset of murine lupus. These results suggest that sleep as behavior may be a useful model for elucidating further the interaction between the central nervous and immune system.

**Support (optional):** FAPESP/CEPID and AFIP.

0358

**EFFECTS OF SLEEP DEPRIVATION ON BINDING TO PROSTAGLANDIN E2 RECEPTORS IN RAT BRAIN**

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**Introduction :** A characteristic functional effect of sleep deprivation (SD) are changes in thermoregulatory capacity, an effect that in turn may induce a number of other functional consequences, and may be a factor in the lethality of prolonged SD. We have found that the hyperthermia induced by 96 h of SD can be blocked by sodium diclofenac, a potent inhibitor of prostaglandin synthesis. We hypothesize that temperature changes after SD may be mediated by PGE2 receptors. To address this issue we propose to examine the effects of SD on the density of PGE2 binding sites in the rat brain using in vitro autoradiography.

**Methods :** Male Wistar rats were deprived using the platform technique. Rats in the cage control group were kept in groups of 5 in wire mesh cages. Colonic temperature was measured with a thermocouple. The thermistor probe was introduced into the rectum to a depth of 5 cm and temperature was taken at 9 AM during 7 days (habituation) and 4 days of the SD procedure. In a separate group, after 96 hr of SD rats were sacrificed by decapitation, brains were rapidly removed and frozen over dry ice. Sections were incubated in buffer containing 20 nM [3H]PGE2 and in the presence of 100 fM PGE2 for determination of nonspecific binding. Densitometric analyses were performed using M2 MCID system.

**Results :** The temperature of sleep-deprived rats increased from the first to the fourth day of deprivation compared to basal and with respective control group. However, the results indicated that [3H]PGE2 binding was not significantly altered by SD in any of hypothalamic areas examined.

**Conclusion :** These data suggest the hyperthermia induced by SD is not related to changes in PGE2 receptors binding in modulating the increase in temperature during SD. The possibility remains that other prostaglandin receptor subtypes are significantly altered by SD.

**Support (optional):** AFIP, FAPESP(CEPID) and CNPq.

0359

**THE EFFECTS OF PARADOXICAL SLEEP DEPRIVATION ON ESTROUS CYCLES OF THE FEMALE RATS**

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**Introduction :** Although a significant body of literature describes the effect of sleep deprivation on males, little attention has been given to the female's response. Several observations indicate that sleep is differentially regulated between males and females, suggesting that distinct effects may modulate their sleep pattern and different behavior consequences could be expected. Thus, the present purpose was to examine how paradoxical sleep deprivation (PSD) affects the estrous cycle of the female rat.

**Methods :** Forty-four PSD and 44 CTRL female rats were distributed into 4 subgroups of 11 animals each according to the phase of estrous cycle and were subjected to sleep deprivation for 96h by the multiple platform technique. After PSD period, vaginal estrous cycles were taken for an additional 9 days.

**Results :** Animals that were submitted to PSD in diestrous phase had their estrous cycles disrupted during the recovery period by showing a constant diestrus during the first week. As for hormone alterations, progesterone concentrations were statistically higher in PSD-diestrus compared to respective phase control. In addition, PSD-diestrous phase exhibited higher concentrations of corticosterone and lower estrogen than the respective

control rats.

**Conclusion :** These data indicate that PSD may modulate the ovarian hormone release through alterations in hormonal-neurochemical mechanisms.

**Support (optional):** AFIP, FAPESP, CEPID

0360

**EFFECTS OF SLEEP DEPRIVATION ON BLOOD PARAMETERS ASSOCIATED WITH CARDIOVASCULAR RISK IN OVARIECTOMIZED RATS**

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**Introduction :** It is widely documented that premenopausal women have a lower risk for coronary heart disease (CHD) than men. Since several studies have related the risk of developing a heart condition increases after menopause, the purpose of this study was to investigate the effects of paradoxical sleep deprivation (PSD) in blood circulating lipoproteins (total cholesterol, HDL, LDL and triglycerides) in males, intact and ovariectomized (OVX) female rats.

**Methods :** Three groups of animals (male, intact and OVX female rats) were submitted to PSD or maintained in home-cages as control. The OVX was performed in female rats at 3 months of age and they were submitted to PSD 4 months later. The intact females were submitted to PSD according to the phase of the estrous cycle.

**Results :** The results indicate that PSD significantly reduced cholesterol in intact females compared to OVX and male rats; it reduced triglycerides in all groups and increased HDL levels in male rats compared with the respective controls. PSD also increased LDL levels in male and OVX when compared to intact females.

**Conclusion :** All these results suggest that the cardiovascular response is differentially regulated in males, intact and OVX female rats, especially when submitted to PSD. This study can contribute to understanding the mechanisms involved in the protection of the CHD during the reproductive female life and worse of the cardiovascular risk factors after menopause in women or OVX in rats.

**Support (optional):** AFIP, FAPESP, CEPID

0361

**SLEEP QUANTITY AND QUALITY DURING PREGNANCY IS ASSOCIATED WITH CHANGES IN IN VITRO CYTOKINE PRODUCTION**

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**Introduction :** Sleep loss has been shown to increase pro-inflammatory cytokines levels. Women who experience pregnancy complications have higher levels of the same pro-inflammatory cytokines. Although women commonly report their sleep to be disrupted during pregnancy, the effects of sleep disruption on maternal immunity or pregnancy outcomes have not been studied.

**Methods :** Participants were 37 highly educated, primarily Caucasian women in their late 3rd trimester of pregnancy. Cross-sectional data included venous blood draws, the PSQI and a 2-week sleep diary. Microarray assays were used to quantify secreted cytokines (IL-1, IL-6, IL-10 and TNF-) from stimulated lymphocytes (Novagen, USA).

**Results :** Diary-based ratings of sleep quantity and quality were significantly associated with IL-6 levels whereas habitual sleep quality, as measured by the PSQI, was not. Diary-based ratings of sleep latency and WASO were used to categorize participants into two groups; women



reporting difficulty initiating or maintaining sleep exhibited higher secretion of IL-6 ( $t = -2.2, p = .05$ ). Similarly, shorter sleep duration was linearly associated with an increase in IL-6 levels ( $r = -.92, p = .012$ ). Averaged daily sleep quality ratings (1=best, 10= worst) were linearly associated with IL-6 ( $r = 1.3, p = .03$ ). Women reporting worse sleep had higher levels of IL-6.

**Conclusion :** Sleep duration and sleep quality measured by the 2-week sleep diary were significant correlates of IL-6. Pregnant women with longer periods of WASO, and shorter sleep duration had higher IL-6 levels. Similarly, those who complained of poor sleep quality had higher secreted levels of IL-6. These data are consistent with reports of increases in IL-6 secretion in relation to disturbed sleep in a variety of populations including healthy men and patients with primary sleep disorders (Irwin et al, 2004, Vgontzas et al., 2004). Research that considers the relationship between sleep and immune function in pregnancy may be important to understanding pregnancy outcomes.

**Support (optional):**

### 0362

#### DAYTIME SLEEP REDUCES RISK OF CESAREAN DELIVERY AMONG SHORT SLEEPERS

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**Introduction :** Although adequate sleep during pregnancy is important, it is a common time for sleep disturbance. Our previous research indicates that women who sleep less than 6 hours per night during their last month of pregnancy are at higher risk for cesarean deliveries and longer labors than women who sleep more than 6 hours. This study further explores this relationship by determining the effect of daytime sleep.

**Methods :** As part of a larger randomized clinical trial, data were collected among a sample of 131 women expecting their first child. Their sleep was assessed with 48 hours of wrist actigraphy (Ambulatory Monitoring Inc.) and a 2 day Sleep Log at an average of  $26.6 \pm 10.0$  days before delivery. The sample was grouped based on both their day sleep (0900-2100) and their night sleep by actigraphy (<6 h, 6-6.9 h, 7+ h).

**Results :** The sample was ethnically diverse, educated, and had moderate to high incomes. Among the total sample, daytime sleep was unrelated to delivery type after controlling for infant birth weight. Daytime sleep was associated with work status: working women slept less during the day than non working women, but work status was unrelated to delivery type. Among the 19 women who slept < 6 hours per night, those who napped > 60 minutes had a significantly lower rate of cesarean delivery (1/10) than those who had < 60 minutes of daytime sleep (6/9). Whereas women who slept < 6 hours per night had longer labors, adding a daytime nap of 60+ minutes, did not change their labor duration.

**Conclusion :** These findings suggest that women who have trouble sleeping at least 6 hours per night during their third trimester may be able to reduce their risk of cesarean delivery by napping for at least 60 minutes during the day.

**Support (optional):** NIH Grant# RO1 NR005345, K.A. Lee, PI

### 0363

#### FORMULA-FEEDING DOES NOT HELP NEW PARENTS GET MORE SLEEP

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**Introduction :** Current literature shows conflicting results about type of infant feeding in relation to parental sleep patterns. This study describes

sleep quantity and quality of parents who supplement their infant with formula, either before bedtime or during the night, compared to exclusively breastfeeding mothers and their partners.

**Methods :** The study is part of a randomized clinical trial with 152 couples expecting their first child. Wrist actigraphy estimated total sleep time (TST) during the past two nights, and the Lee General Sleep Disturbance Scale (GSDS) estimated perceived sleep disturbance during the past week. Feeding type (exclusive breastmilk or formula) was determined from infant feeding diaries for two time periods: 18:00-23:59 (evening) and 24:00-06:00 (night). Independent sample t-tests ( $p < .05$ ) were used to test for differences in TST and GSDS of mothers and partners who used formula during the evenings or nights compared to exclusive breastfeeding mothers and partners at 3 months postpartum.

**Results :** During the evening, breastfeeding mothers slept  $38 \pm 16$  minutes more than mothers who gave their infant formula. Similarly, their partners slept an average of  $42 \pm 17$  minutes more than partners of formula feeding infants. During the night, breastfeeding mothers slept  $45 \pm 20$  minutes more than mothers who gave formula. In contrast, there was no significant difference in TST during the night between partners of breastfeeding and partners of formula feeding mothers. There were no significant differences in GSDS between breastfeeding and formula-feeding parents.

**Conclusion :** Contrary to popular belief, formula feeding (either evening or during the night) did not help new parents get more sleep. Parents who use formula slept less than breastfeeding mothers and their partners, when sampled between 9 and 15 weeks postpartum. Parents should be encouraged to continue breastfeeding because 30 minutes sleep loss every night would affect daytime functioning, especially for working parents.

**Support (optional):** NIH Grant# R01 NR05345, KA Lee, P.I.

### 0364

#### SEARCHING FOR A MARKER OF REM PROPENSITY IN HUMANS

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**Introduction :** Delta activity during sleep and Theta activity while awake increase proportionately with the homeostatic drive for sleep, and are understood to be markers for sleep propensity. There is no accepted EEG marker for REM propensity in humans, although REM Theta has been correlated with REM density (REMd) in animals. Alpha is thought to be negatively correlated with REM measures. Here we examined whether Power Spectral Analysis (PSA) of the EEG during REM could clarify whether Theta can serve as a marker of REM propensity or intensity.

**Methods :** 30 subjects (age= $24.3 \pm 4.7$ , 15F) participated in a 6 consecutive night study in the sleep lab: Screen (SCR), Baseline (BL), TSD (DEP1 & DEP2), and Recovery (REC1 & REC2). PSA and hierarchical regression were used to examine the relationship between relative power in three frequency bins [Theta (4-7.5Hz), Delta (.5-4Hz), and Alpha (7.5-10Hz)] during REM and two measures of REM propensity (REM% and REMd).

**Results :** Theta accounted for a significant amount of the variance in REM% during BL, REC1 and REC2 ( $p < .002$ ). While Alpha contributed to variance explained during REC1 ( $p < .01$ ), Delta did not add to variance accounted for on any night. Spectral power in all 3 bands was much less related to REMd, with the only significant relationships being Theta for

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REC1 ( $p < .004$ ) and Alpha for BL ( $p < .04$ ). Alpha was not negatively correlated with REM measures.

**Conclusion :** Theta power appears more related to REM% than to REMd. While Theta seems to be a reliable marker for the amount of REM sleep on a given night, it only accounted for about 34% of the variance. Furthermore, it did not index REMd well, nor the changes in REMd seen with TSD and Recovery. Theta power did not seem to be as good a marker for REM sleep as Delta power is for SWS.

**Support (optional):** UCSD GCRC M01RR00827 US Army DAMD17-02-1-02-01

### 0365

#### SLEEP DEPRIVATION UNDER SUSTAINED HYPOXIA INCREASES GLUTATHIONE LEVELS IN SEVERAL RAT BRAIN REGIONS

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**Introduction :** We showed that sustained hypoxia (SH, 10% O<sub>2</sub>) increased thiobarbituric acid reactive substance (TBARS) levels and glutathione reductase (GR) activity in the rat cerebellum and pons. Also, that 6 hours of total sleep deprivation (SD) increased superoxide dismutase (SOD) and glutathione peroxidase (GPx) activities in the rat hypothalamus, cerebellum and brainstem. In this study we show that 6 hours of total sleep deprivation under sustained hypoxia (SDSH) increases glutathione levels in the rat brainstem, hypothalamus, cortex and hippocampus.

**Methods :** Twelve male Sprague Dawley rats (400-500g) were handled daily for 1 week under normoxic condition (21% O<sub>2</sub>) to habituate them to the handling stimulus. On the day of the experiment, the O<sub>2</sub> level was changed from 21% to 10% and the rats were subjected to 6 hours of total sleep deprivation beginning at lights on (8AM). Sleep deprived animals (SDSH) were kept awake, by handling or with novel objects, each time they showed physical signs of sleepiness, while yoked control animals (YCSH) were stimulated simultaneously regardless of their sleep-wake state. All animals remained under 10% O<sub>2</sub> for 6 hours. Rats were sacrificed by decapitation after halothane anesthesia, and total glutathione levels (GSHt) were measured in various brain regions. The paired student's t-test was used to determine statistical significance.

**Results :** SDSH animals had significantly higher GSHt levels in the brainstem (14%,  $t = -6.2$ ,  $df = 5$ ,  $p = 0.002$ ), hypothalamus (22%,  $t = -2.9$ ,  $df = 5$ ,  $p = 0.04$ ), cortex (20%,  $t = -2.5$ ,  $p = 0.05$ ) and hippocampus (15%,  $t = -2.5$ ,  $df = 5$ ,  $p = 0.05$ ) compared to YCSH animals. No significant differences in GSHt levels were seen in the cerebellum ( $t = -2.2$ ,  $df = 5$ ,  $p = 0.08$ ) or basal forebrain ( $t = -2.2$ ,  $df = 5$ ,  $p = 0.08$ ) of SDSH animals compared to YCSH animals.

**Conclusion :** We conclude that sustained hypoxia, sleep deprivation and sleep deprivation under sustained hypoxia induce different antioxidant response mechanisms and that these changes are manifested in different brain regions.

**Support (optional):** Research supported by HL41370, 1P50, HL060296 and the VA Medical Research Service.

### 0366

#### A REASSESSMENT OF THE HYPERPHAGIA/WEIGHT LOSS PARADOX DURING SLEEP DEPRIVATION

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**Introduction :** Previous studies have shown that during sleep deprivation

rats are hyperphagic but, paradoxically, lose body weight. However most previous studies failed to account for food spillage, which may be considerable during sleep deprivation. Therefore, in the present study we revisited the issue of feeding changes in sleep-deprived rats and introduced different procedures to allow accurate estimation of food spillage prior to, during, and after sleep deprivation.

**Methods :** Nine male Wistar rats were housed individually for 4 days with sawdust as bedding material on a solid floor. For the next 4 days, a second metal floor was introduced, above the original floor, with 1/4 of its area consisting of a wire mesh grid positioned under the feeder, which allowed spillage to be collected on paper towels underneath. For the next four days, the container was filled with water to a height below that of the second floor, and spillage was allowed to fall in the water, as occurs during sleep deprivation. For the next 5 days, the second floor was removed and animals were sleep-deprived on a single narrow platform. This was followed by 4 days of sleep recovery on the metal floor. Finally, for the last 4 days the metal floor was replaced by sawdust as in the original baseline phase. Food removed from feeders and body weights were recorded daily. Food spillage recovered was dehydrated and mathematically treated before used to determine the food intake.

**Results :** The main finding was that once corrected for spillage, food intake was not significantly altered during sleep deprivation. Increases in food removed from feeders were accompanied by proportional increases in food spillage.

**Conclusion :** While there was no evidence of hyperphagia, body weight declined continually over the five days of deprivation, in agreement with other evidence of increased metabolic activity during sleep deprivation.

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### 0367

#### ACUTE AND LONG TERM ADAPTATION OF THYROTROPIN AND PROLACTIN TO RESTRICTED SLEEP AND RECOVERY

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**Introduction :** The main aim was to evaluate how the regulation of human thyrotropin (thyroid stimulating hormone=TSH) and prolactin adapts to restricted sleep and subsequent recovery.

**Methods :** Nine subjects participated in a strict 6-week sleep protocol, in which subjects slept in the sleep laboratory for 12 days, one habituation day (sleep 23-07h), two baseline days (23-07h), five days with restricted sleep (03-07h) and four recovery days (23-07h). For 9 of those days, blood was drawn every hour 23-08h and every 3rd hour 08-23h.

**Results :** Both mean TSH and prolactin varied significantly across days ( $p < .0001$ ), across time within days ( $p < .0001$ ), and showed a significant interaction between days and time ( $p < .001$ ). Contrasts ( $p < .05$ ) showed: 1) an acute increase of TSH during restricted sleep between 23-03 (when subjects normally slept); 2) a gradual decrease across days with restricted sleep; 3) a strong further reduction during the first recovery day; 4) an increase with a return to normal on the second recovery day; and 5) a continued increase the 3rd recovery day. The effects of restricted sleep on prolactin showed the reversed pattern with: 1) an acute decrease the first nycthemeron; 2) a continued decrease the second day; 3) normal levels after 5 days with PSD; 4) an increase the first day with recovery; 5) continued high levels during recovery days 2 and 3; and 6) normal levels were reached after 7 recovery days.

**Conclusion :** There were strong acute effects on TSH and prolactin regulation by sleep restriction (4h) and of recovery sleep (8h). However, the

strong acute effects were followed by a gradual adaptation to the new sleep pattern with levels returning to baseline. The adaptation seemed to be somewhat faster for TSH than prolactin.

**Support (optional):**

### 0368

#### DIFFERENCES IN FEEDING BEHAVIOR DETERMINE THE METABOLITES AND HORMONE RESPONSES OF SLEEP DEPRIVED RATS

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**Introduction :** Epidemiological studies have shown a negative relationship between daily sleep hours and body mass index. However, rats differ from humans, since their weight does not increase with sleep deprivation (SD). Our objective was to study the body weight homeostatic control of rats, assessing its feeding behavior, hormonal and metabolites response to sleep deprivation.

**Methods :** Male rats, living under controlled conditions, were housed individually for each experiment and signed as control (CTR, n=10), sleep deprived for 96h by the platform technique (SD-96h, n=10) and rats SD-96h recovered for 24h (REB, n=10) groups. In the first experiment animals were fed with chow pellets (fCP), while in the second they were fed with a liquid diet (fLD) seven days before and during SD procedure

**Results :** After correcting by food spillage, food intake was reduced in fCP rats, which lead to larger body weight (BW) decrease. In addition, we found lower stomach weight, liver glycogen (LGly) and triacylglycerol, while ketones bodies and LDL cholesterol showed higher levels in SD-96h. Body weight, stomach weight and ketones bodies were not recovered in REB group. On the other hand, fLD rats have shown food intake increase during SD, which was followed by soft BW reduction. Further, we found a reduction in LGly, HDL cholesterol and triacylglycerol, while LDL cholesterol increased. Only HDL cholesterol was not recovered in REB group. Reinforcing the evidences that fCP rats have exacerbated metabolic changes, we found diminished insulin, leptin and increased glucagon, ghrelin and corticosterone in SD-96h group, while only a decreased leptin and higher corticosterone levels were found in fLD rats.

**Conclusion :** The fCP rats are unable to have all food that they seek, which exacerbate the negative energy balance induced by SD. In addition, LGly was the major factor related to increases in food intake in fLD rats sleep deprived.

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### 0369

#### METABOLIC STATUS DETERMINE CHANGES IN THE ANTIOXIDANT SYSTEM AND LIPOPEROXIDATION IN SLEEP DEPRIVED RATS

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**Introduction :** Many studies have related sleep disturbances to medical conditions by resulting from pro-oxidative process. However, although previous studies using animal models of sleep deprivation have shown a reduction in antioxidant defense they fail to evidence oxidative damage. We verified the effects of sleep deprivation on blood and liver oxidative status of rats.

**Methods :** Thirty male rats, living under light:dark cycle 12h:12h and

room temperature of 22±1°C, were housed individually and signed as control (CTR), sleep deprived for 96h by the platform technique (SD-96h) and SD-96h recovered for 24h (REB) groups. Chow pellets and water were ad libitum. Immediately after sleep deprivation we examined the oxidative damage accessed by lipid peroxidation potential measurement and the antioxidant defense changes in blood and liver samples. Cu/Zn superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), total glutathione (tGSH) content and malondialdehyde production (accessed as TBARS) were measured.

**Results :** Body weight (BW) was strictly reduced in SD-96h (-6.23±2.58%) and REB (-7.10±2.31%) groups compared to CTR (+1.08±1.54%). Blood parameters showed reduced erythrocyte tGSH in SD-96h and REB compared to CTR. Meanwhile, liver oxidative stress markers showed reductions in SD-96h and REB groups on tGSH, CAT and TBARS. A correlation analysis showed a relationship between BW changes and erythrocyte tGSH (r=0.65), liver tGSH (r=0.54), liver CAT (r=0.73) and liver TBARS (r=0.49).

**Conclusion :** Although reductions in erythrocyte and liver tGSH and liver CAT could suggest an oxidative stress sleep deprivation-induced, it was not confirmed by blood and liver TBARS either. In addition, the correlation between all oxidative stress parameters modified by sleep deprivation and BW changes are in accordance to the proposal that the metabolic status modify the free radical-scavenging system, and therefore it will be important to differentiate between changes due to the decrease in BW and those due to the sleep disturbance itself.

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### 0370

#### INFLUENCE OF CHRONIC COCAINE TREATMENT AND SLEEP DEPRIVATION ON SEXUAL BEHAVIOR AND NEUROGENESIS OF THE MALE RAT

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**Introduction :** The present study investigated the influence of chronic cocaine treatment of genital reflexes associated to paradoxical sleep deprivation (PSD), anxiety-like behaviors and possible alterations in hippocampus neurogenesis of the male rat.

**Methods :** At 21 days of age, the animals were distributed into two groups: (1) saline injection or (2) cocaine injection (7mg/kg, i.p, 3x/week). Following the chronic treatment, the two groups were subdivided into three sets of 9-11 animals: a) Experiment 1: Genital reflexes evaluation; b) Experiment 2: Anxiety-like behaviors, c) Experiment 3: Neurogenesis quantification.

**Results :** The results showed that chronic cocaine treatment in control rats challenged with saline induced penile erection (PE) in 40% of the animals; however, an acute injection of cocaine in rats after long-term saline treatment reduced this proportion significantly. Concerning the effect of sleep deprivation, the current findings indicate that the genital reflexes of PSD rats treated with cocaine and challenged with saline did not differ from that of their respective control group. As demonstrated previously, the association of PSD and cocaine potentiates genital reflexes when compared to what was observed in PSD+saline (saline challenged) treated rats. In fact, such effects disappeared in the long-term cocaine treated rats. Chronic cocaine treatment challenged with cocaine increased exploratory activity and did not modified anxiety-like behaviors when compared to the saline challenged groups. In addition, the bromod-

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eoxyuridine (BrdU) approach indicated that there was a reduction in BrdU-positive cells in the adult hippocampus after chronic cocaine treatment.

**Conclusion :** These findings indicate that chronic cocaine administration from the period of brain development to adulthood had a marked effect on genital events and possibly on neurocognitive deficit in adulthood.

**Support (optional):** AFIP, FAPESP, CEPID

### 0371

#### EFFECTS OF PROGESTERONE BLOCKADE OVER COCAINE-INDUCED GENITAL REFLEXES OF PARADOXICAL SLEEP DEPRIVED MALE RATS

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**Introduction :** Paradoxical sleep deprivation (PSD) enhances cocaine-induced genital reflexes (penile erection [PE] and ejaculation [EJ]) in male rats and induces a significant increase in progesterone concentration. As progesterone treatment facilitates PE in PSD castrated rats, we may speculate that progesterone appears to be a relevant hormonal factor eliciting genital reflexes in PSD males.

**Methods :** different doses of antiprogesterin mifepristone (vehicle, 2.5, 5, 10 and 20mg/kg, s.c.) were administered to PSD rats at the end of a four-day period of PSD one hour prior to cocaine administration (7mg/kg, i.p.) and placed in observation cages for the evaluation of genital reflexes.

**Results :** Pretreatment with vehicle induced PE in all rats and this effect was significantly reduced by mifepristone at 5 to 20 mg/kg doses that lowered the proportion to 40% of the rats. The frequency of PE was also significantly reduced for all doses used. There were no significant differences between vehicle and mifepristone in EJ behavior. As for hormone concentrations, mifepristone reduced progesterone concentrations at the 5-20 mg/kg doses compared to vehicle group. At 20 mg/kg it also elevated testosterone concentrations. In addition, mifepristone administration induced a significant decrease in the duration of PS episodes at all doses.

**Conclusion :** These data suggest that progesterone exerts an essential role in erectile response induced by cocaine in PSD male rats.

**Support (optional):** AFIP, FAPESP, CEPID

### 0372

#### THE EFFECTS OF SHIP MOTION ON THE SLEEPING PATTERNS OF CREWMEMBERS ABOARD A HIGH SPEED NAVAL VESSEL

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**Introduction :** Sleep of crewmembers aboard high speed Naval vessels may be disrupted by the unusual conditions caused by ship motion. The sleep debt that accumulates in such conditions has major implications for the safety and performance of the crew. The current study was conducted on the HSV-2 SWIFT to determine what factors contribute to sleep quality of its crew. The relationship between sleep and motion was of particular interest.

**Methods :** Data were collected over a 14-day Atlantic transit including a 7-day sea-keeping trial. A questionnaire was administered to 19 participants (48% of the crewmembers) at the beginning and ending of each watch rotation. The questionnaire included questions about motion sickness, sleep quantity, subjective sleepiness, and light exposure. Sleep amount and quality, and overall activity were evaluated by actigraphs and self-reported sleep log.

**Results :** Sleep deficit (more than 1 hour on average per day) was evident

in more than 25% of the participants. The cumulative deficit was increasing by time although ship's schedule was relatively decreased workload. Factors significantly interfering in crew's sleep, was a) noise originating from other crew members in the compartment or from outside, b) the need to use the restroom, c) ship's motion. Sleep fragmentation and disruption were significantly correlated to ship's motion and increased during rough weather or when the ship was travelling at high speeds. Fatigue Avoidance Scheduling Tool predicted performance decreased faster over the initial seven-day period than the increase during the following six-day decreased workload period. Wakefulness periods were significantly extended (42% larger than 16 hours and 8% larger than 20 hours).

**Conclusion :** Over the study period, sleep debt continued to accrue in the crewmembers. It was evident that ship motion due to high speed and sea state significantly influenced sleep quality. However, other factors that almost certainly affect sleep quality in the ship berthing spaces remain to be explored. The decline in predicted effectiveness of crewmembers coupled with an increased workload caused by reductions in crew size raises the question of safety and acceptable performance during periods of extended operations.

**Support (optional):**

### 0373

#### MEMORY FOR COGNITIVE AND AFFECTIVE STATE DURING A SINGLE NIGHT OF TOTAL SLEEP DEPRIVATION: HOW BAD WAS IT?

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**Introduction :** A single night of total sleep deprivation (SN-TSD) is typically remembered as being a highly aversive state. Much research, however, has indicated that memory for visceral states, for example, is particularly poor. Do memories for SN-TSD accurately reflect experiences of sleep deprivation? Our study examined memory for affective, physical, and cognitive states one month after a SN-TSD.

**Methods :** 20 participants completed measures of cognitive, physical, and affective state at four times during a SN-TSD. One month later, we asked them to remember how they felt during the SN-TSD and to complete the mood questionnaires twice more, to reflect how they remembered feeling at the "worst" and at the "best" points of the night. We then compared the real-time and retrospective profiles; one-way ANOVAs were calculated for each of the 6 sub-scales during the night and for retrospective ratings. Total word counts for open-ended questions were transformed into standardized percent scores to compare across participants and across time of night.

**Results :** We compared retrospective with real-time profiles for POMS subscales (Anger, Depression, Tension, Fatigue, Vigor, and Confusion). Retrospective ratings for "worst time of the night" were statistically significantly worse compared to real time ratings in all cases, especially for Anger (overall  $F = 9.47$ ,  $p < .0001$ ), Tension (overall  $F = 14.72$ ,  $p < .0001$ ) and Depression (overall  $F = 12.03$ ,  $p < .0001$ ); posthoc comparisons were significant at .05. Analysis of word counts revealed no differences across time of night.

**Conclusion :** Participant retrospective ratings of affective and cognitive states were not consistent with real-time ratings. Data reveal a pattern of either minimizing during real-time experience, or exaggerating during retrospective reporting. Another possibility is that participants are unable to accurately report emotional state in conditions of sleep deprivation. These data may represent methodological dilemmas for researchers who rely on self-report of affective or cognitive state during or after sleep deprivation protocols.

**Support (optional):**

## 0374

## EFFECTS OF SLEEP DEPRIVATION ON DECISION MAKING AND REWARD PROCESSING STUDIED USING FMRI

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**Introduction :** Behavioral studies have shown that sleep deprivation (SD) impairs decision making, leading to reduced choice acuity in tasks involving risk. In this study, the effects of sleep deprivation on decision making and subsequent reward processing were investigated using a gambling task that involved varying levels of risk.

**Methods :** Twenty-six participants were tested following a night of normal sleep (RW) as well as after 24 hours of SD. The sessions were counterbalanced across participants. There were three basic gamble types: certain (C), positive-risk (PR) and negative-risk (NR), which varied parametrically on the level of potential loss associated, with C being the least risky choice and NR the most risky. These gambles were presented in two possible pairs, C-PR and PR-NR, and participants had to choose between the gambles with the objective of maximizing their winnings. The winnings from each gamble were revealed after a variable anticipation phase. Subjects were paid a percentage of winnings from each trial.

**Results :** Subjects took longer to make decisions following SD but there was no difference in risk preferences for both C-PR and PR-NR pairs between the two states. Decision making and anticipation was associated with reduced activation in the posterior parietal regions following SD. Risk taking (choosing the riskier option) activated the bilateral nucleus accumbens (NAcc) to a greater extent after SD relative to RW. After SD, negative rewards were associated with reduced activation of the left insula and lateral orbitofrontal cortex.

**Conclusion :** As NAcc activation is known to correlate with anticipation of higher reward, the relatively greater activation of this area following SD suggests that SD may result in higher expectations in risky gambles. Together with the reduced activation for loss in insula and orbitofrontal cortex, this suggests that the SD participants were less concerned with negative consequences when presented with a potentially high reward.

**Support (optional):** DMERI, SingHealth Foundation, Shaw Foundation

## 0375

## RIGHT VENTROLATERAL PREFRONTAL CORTEX ACTIVATION AND INHIBITORY EFFICIENCY AFTER 24 HOURS OF TOTAL SLEEP DEPRIVATION

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**Introduction :** Executive control of behavior is known to be impaired following short-term total sleep deprivation (SD). Event-related fMRI was used to elucidate the neural correlates of inhibitory efficiency in this context.

**Methods :** Twenty-seven participants performed a Go/No-Go Task following a night of normal sleep (RW) as well as after 24 hours of SD (SD24). Stimulus presentation was individually titrated at RW to produce an approximately equal number of stops (appropriate No-go) and errors ('Go' response when no response was appropriate). Test sessions were a week apart and their order counterbalanced across participants. For each state, the functional imaging data was analyzed using the general linear model with one block predictor (Task; representing the predominant go responses) and two event-related predictors (Stops, Errors) using mixed-effects analysis. Behavioral performance was indexed by the intra-individual coefficient-of-variation of RT for the Go trials.

**Results :** There was greater tonic task-related bilateral activation in the ventrolateral PFC (BA10/46, R>L) and right anterior insula at RW compared to SD. The contrast between RW and SD24 for Stops and Errors

indicated no significant differences in any regions. Functional ROI analysis was performed in regions significantly activated during Stops and Errors at RW. Participants were divided into tertiles based on their change in performance from RW to SD24. Repeated-measures ANOVA showed significant interaction of State and Group for the right ventrolateral PFC (BA10/46) for Stops. Those who maintained inhibitory efficiency following SD showed increased activation of these regions relative to RW whereas those whose inhibitory efficiency declined showed a drop in activation.

**Conclusion :** The data suggest that there is inter-individual variability in inhibitory efficiency following SD. Tonic activation in the ventrolateral PFC (corresponding to the task block dominated by go responses) consistently decreased with SD and may correspond to decline in general task monitoring/sustained attention. The ventrolateral PFC has also been associated with the suppression of irrelevant responses. Individuals able to maintain inhibitory efficiency following SD have a more efficient (requiring less activation) engagement of the ventrolateral PFC during RW. This in turn may allow them to adaptively recruit this region to maintain inhibitory efficiency during SD.

**Support (optional):** DMERI, SingHealth Foundation, The Shaw Foundation

## 0376

## A WORKING WEEK WITH SLEEP RESTRICTION: EFFECTS ON CYTOKINES AND SELF-RATED HEALTH

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**Introduction :** Acute sleep restriction has strong effects on human homeostasis, but there is little understanding of how our biological systems react if sleep restriction is continued. The aim of the present study was to study how a working week (five days) with sleep restriction affects immune responses and self-rated health (among other variables). Self-rated health was chosen as it is a powerful predictor of future morbidity and mortality.

**Methods :** Nine subjects participated in a strict 6-week sleep protocol, in which subjects slept in the sleep laboratory for 12 days, one habituation day (sleep 23-07h), two baseline days (23-07h), five days with restricted sleep (03-07h) and four recovery days (23-07h). For 9 of those days, blood was drawn every hour 23-08h and every 3rd hour 08-23h. Selected blood samples were stimulated in vitro with phytohemagglutinin, incubated for 48 hours, frozen, and later analysed with respect to cytokines. Levels of circulating cytokines are presently being analysed.

**Results :** As a result of sleep restriction, self-rated health decreased gradually ( $p < .0001$ ) and had returned to baseline levels only after three days of recovery. Besides a strong diurnal pattern, the immune responses to phytohemagglutinin were increased after 5 days of sleep restriction. TNF- and MCP-1 (monocyte chemoattractant protein-1) increased during late evening and early night hours as compared to baseline values ( $p < .01$ ). Similar tendencies were observed for IL-1, and IL-2 ( $p < .10$ ).

**Conclusion :** An ecologically valid model (one working week) of restricted sleep had strong effects on self-rated health. In contradiction with the hypothesis, five days with sleep restriction did not reduce the immune response to phytohemagglutinin. Instead there was an increased response in the late evening. The relationship between the cytokine response of restricted sleep and health perception will be further explored.

**Support (optional):**

0377

**IDENTIFICATION OF A BIOMARKER FOR SLEEP DRIVE IN FLIES AND HUMANS**

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**Introduction :** There is no simple quantifiable marker that can detect an individual who is excessively sleepy before adverse outcomes become evident. Using the power of *Drosophila* genetics we have identified a biomarker, Amylase, that is highly correlated with sleep drive. Importantly salivary amylase activity is also responsive to extended sleep deprivation in humans.

**Methods :** Sleep was evaluated in flies according to standard procedures. Homeostatic mechanisms were differentially activated using genetic and pharmacological manipulations that produce periods of waking that are not compensated by a homeostatic response and compared with waking conditions that are associated with sleep homeostasis. Amylase mRNA extracted from whole heads was evaluated using real-time quantitative PCR. Salivary amylase activity was evaluated in 9 healthy human adult volunteers after a full nights sleep or after 28 h of waking. Normal sleep architecture was confirmed by polysomnography. Saliva was collected from salivettes and rapidly frozen until assayed.

**Results :** Amylase mRNA was dramatically elevated following manipulations that result in a homeostatic response indicating that it is responsive to increasing levels of sleep debt. In contrast, manipulations that produce waking periods that are not compensated by a homeostatic response do not induce Amylase mRNA. Thus Amylase is not simply a marker for waking but for conditions where sleep drive is elevated. Amylase activity is increased in both humans and flies following 28 h of sustained waking compared to untreated circadian-matched controls ( $p < .05$ ). In flies, paraquat did not alter amylase activity suggesting these changes were not due to stress.

**Conclusion :** A major question about *Drosophila* sleep research is whether it has relevance for human sleep studies. We demonstrate here that 28 h of waking in human subjects significantly increased amylase activity compared to untreated circadian-matched controls. Thus, a marker originally identified in flies is also modified by extended episodes of waking in humans.

**Support (optional):**

0378

**SLEEP DISTURBANCE AND NATURAL KILLER CELL ACTIVITY IN CAREGIVERS**

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**Introduction :** A growing literature has linked sleep to immunocompetence, although results vary widely across studies. Few of these studies have evaluated risk factors for disturbed sleep, which might clarify the significance and direction of sleep-immune relationships. In the present study, we used caregiving as a model of chronic stress. We hypothesized that caregiving would potentiate the relationship between sleep and immunocompetence, as measured by natural killer cell activity (NKCA).

**Methods :** The study sample included 10 family caregivers and 12 age- and sex-matched non-caregiver controls. Sleep was assessed by polysomnography (PSG) over 3 consecutive nights. PSG measures of interest were sleep latency, wakefulness after sleep onset (WASO) and percent delta sleep, each of which has been associated with stress in previous studies. NKCA was measured at a follow up assessment, approximately 3 months later. General linear models were used to evaluate the

impact of group on the sleep-immune relationship. When interactions were significant, Spearman rank order correlations were used to characterize relationships between sleep and immune function, by group.

**Results :** Significant group x sleep interactions were found for two of the three sleep measures: WASO and percent delta sleep. Spearman correlations revealed significant sleep-immune relationships among caregivers only. Among caregivers, lower NKCA was associated with greater WASO ( $\rho = -.68$ ,  $p = .02$ ) and decreased percent delta sleep ( $\rho = .55$ ,  $p = .05$ ). The group x sleep latency interaction was not significant.

**Conclusion :** As hypothesized, PSG assessed sleep disturbances in caregivers were associated with impaired immune function. PSG assessed WASO and percent delta sleep were predictors of subsequent NKCA in caregivers suggesting that caregiving is an appropriate model for stress to use in a study of sleep and immunity. The extent to which disturbed sleep contributes to the adverse health effects seen in caregiving remains to be evaluated.

**Support (optional):** NIMH grant MH01554

0379

**SLEEP FRAGMENTATION DECREASES ANXIETY RELATED BEHAVIOR WHILE INCREASING CORTICOSTERONE IN RATS**

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**Introduction :** Sleep disruption has been shown to alter stress, mood, and anxiety. The effect of sleep fragmentation on stress and anxiety was studied in rats.

**Methods :** Forced locomotion on a treadmill was used to awaken male Fischer-Norway rats every 2 min using a schedule of 30s on: 90s off. An exercise control (EC) used a forced locomotion schedule of 10min on: 30min off. Observation of behavior in an open field and an open field test of anxiety were used. In the anxiety test, rats were placed into a start box of the open field. A door separating the start box from the open field arena was remotely opened after a 60s acclimation period, allowing free access to the entire apparatus for 5min. After the same SI or control treatment, another group of rats was rapidly decapitated and trunk blood collected.

**Results :** Observation of SI rats suggested that 24h of SI increased activity (exploration, rearing, locomotion, & escape attempts) as well as aggressive behaviors (nipping, struggling, & defensive behaviors). Subsequent formal use of the open field in a neophobic test of anxiety revealed that 24h of SI ( $n=7$ ) decreased anxiety-related behavior (increased entries, time spent in the open field, and decreased latency to enter the open field) compared to naïve control ( $n=7$ ) and EC ( $n=8$ ) rats. 24h of SI ( $n=6$ ) and EC ( $n=6$ ) both resulted in an increase in plasma CORT levels compared to naïve control ( $n=7$ ) rats.

**Conclusion :** When rats were tested immediately after 24h of SI they exhibited behavioral measures associated with a decrease in anxiety. The CORT data indicate that stress/CORT and anxiety measures vary independently. The findings suggest an SI-induced change in emotional valence that does not resemble somnolence or sedation.

**Support (optional):** VA and NIH

## 0380

## EVIDENCE OF INHIBITORY DEFICITS FOLLOWING TOTAL SLEEP DEPRIVATION AS REVEALED BY EVENT-RELATED POTENTIAL CHANGES ELICITED DURING A GO/NOGO TASK

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**Introduction :** While some evidence suggests that the prefrontal cortex (PFC) is particularly vulnerable to sleep deprivation (SD), results vary widely with task difficulty. The present study was designed to disentangle the effects of frontal engagement and task complexity that have confounded previous SD studies by using a simple cognitive task. The PFC regulates the inhibition of prepotent but irrelevant responses but is much less involved in target detection, which is regulated by the parietal cortex. In a Go/NoGo task, the detection of rare targets elicits an event-related potential, the Go P3, which maximizes over posterior regions of the scalp, while response inhibition elicits an anteriorly distributed P3, the No Go P3. We hypothesized that SD would have a larger impact on inhibitory processes, regulated by the PFC, resulting in a smaller NoGo P3 in anterior during SD compared to the Go P3, with a return to baseline levels after recovery sleep (RS).

**Methods :** A Go/NoGo task was administered to 11 participants at six different times during 37 h of SD and once again one hour after waking up from 10 h of RS. EEG was recorded from Fz, Cz and Pz.

**Results :** While Go P3 declined as a function of practice, NoGo P3 declined as a function of SD. Following RS, only NoGo P3 was larger at Cz when compared to 19 h, 25 h and 37 h of SD. In addition, the smaller NoGo P3 in anterior was correlated with increases in false detection. NoGo P3 was sensitive to practice and to time-of-day, but in much lesser extent than Go P3 was.

**Conclusion :** The present results support the notion that SD impairs inhibitory processes involving the PFC in a task that makes minimal cognitive demands on the part of the sleep-deprived participant, and that NoGo P3 is a neurophysiological marker of this phenomenon.

**Support (optional):** This research was supported by the Canadian Institute of Health Research (CIHR)

## 0381

## REM DEPRIVATION EFFECTS ON PHYSIOLOGIC SLEEPINESS, PERFORMANCE, AND MOOD

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**Introduction :** Studies of REM versus NREM deprivation have no differential performance effects, equivocal differential effects on physiological sleepiness, and no differences in mood effects. However, none of these studies contained sleep deprivation controls. This study included a 6-hr sleep deprivation to further investigate sleepiness, performance, and mood following REM deprivation.

**Methods :** Six healthy adults, 18-35 yrs, with normal sleep and daytime alertness, participated. Each underwent four sessions of 2 nights and days: 8 hrs uninterrupted TIB (T8), 2 hrs uninterrupted TIB (T2), 9.5 hrs TIB with REM deprivation (RD), and 9.5 hrs TIB with NREM awakenings (NR). On RD nights subjects were awoken each time they went into REM sleep and remained awake for 15 min before going back to bed and on NR nights they awakened at corresponding times during NREM. MSLT (1000, 1200, 1400, 1600, 1800 hrs), PVT (0930, 1130, 1330, 1530, 1730 hrs), and POMS (0945, 1145, 1345, 1545, 1745 hrs) assessments were conducted the following day.

**Results :** Sleep time for RD (5.3 hrs) and NR (5.2 hrs) conditions did not differ, but both differed from T8 (6.7 hrs). Minutes of REM sleep in RD (12.2 min) was reduced relative to NR (49 min,  $p<.015$ ), and NR also differed from T8 (88.3 min,  $p<.003$ ). RD average daily sleep latency (MSLT) was longer than NR and T2 ( $p<.001$ ) and similar to T8. PVT showed a significant linear slowing ( $p<.05$ ) in reaction time (fastest 10%) across T8, RD, NR, and T2 conditions, respectively. Differential RD vs NR effects on POMS were absent; RD increased fatigue and reduced vigor vs T8 ( $p<.016$ ) and was similar to NR.

**Conclusion :** REM deprivation did not enhance sleep drive relative to NREM awakening and 6 hrs sleep deprivation, but produced similar effects on ratings of fatigue and vigor, and intermediate effects on performance.

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

## 0382

## TRAIT ANGER PREDICTS RESISTANCE TO SLEEP LOSS

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**Introduction :** Although there are individual differences in the ability to resist the adverse effects of sleep loss on vigilance performance, the basis for these differences remains relatively unexplored. Prolonged wakefulness reduces metabolic activity within the prefrontal cortex, but there are also individual differences in global brain activity that may be related to emotional and personality traits. Individuals high in trait anger, particularly those who express anger via verbal or physical aggression, show greater activity within the left prefrontal cortex. Therefore, we hypothesized that individuals high in trait-anger would be more likely to maintain tonic activation of the left prefrontal cortex, and therefore, be less susceptible to the adverse effects of sleep deprivation.

**Methods :** Twenty-three healthy volunteers (19 men) participated. Volunteers were given 8 hours time in bed, followed by 77 hours of continuous wakefulness. The State-Trait Anxiety Inventory (STAXI-2) was administered at rested baseline at 1500. For the next three nights, participants completed psychomotor vigilance testing (PVT) at 10 minute intervals from 0015 to 0845. Speed ( $1/\text{Reaction Time} \times 100$ ) was calculated for each PVT and converted to percent of baseline performance (PVT%). We correlated scores on the STAXI-2 scales with PVT% scores.

**Results :** Two trait-anger scales correlated with better PVT% performance: Trait Anger Expression-Out (AX-O;  $r=.49$ ,  $p=.009$ ) and Trait Angry Temperament ( $r=.43$ ,  $p=.019$ ). In contrast, two state-anger scales were negatively correlated with PVT%: State Anger (S-Ang;  $r=-.40$ ,  $p=.03$ ), Feeling Angry (S-Ang/F) ( $r=-.51$ ,  $p=.007$ ). Neither state nor trait anger was predictive of PVT% for the second or third nights.

**Conclusion :** Trait anger and the frequency of outward anger expression were significantly predictive of sustained overnight performance on the PVT, consistent with evidence suggesting that trait anger is associated with increased prefrontal activation. Interestingly, state anger was inversely related to performance, suggesting that trait-, but not state-anger confers some resistance to sleep loss.

**Support (optional):**

## 0383

## THE INTERACTION OF COPING SKILLS AND STIMULANTS ON SUSTAINING VIGILANCE: POOR COPING MAY KEEP YOU UP AT NIGHT

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## Category H—Sleep Deprivation

**Introduction :** Individuals appear to differ in their ability to resist the detrimental effects of sleep deprivation on performance, and these decrements are highly reproducible within a given individual, suggesting that there may be trait differences in the resilience to sleep loss. We investigated the relationship between the personality trait of constructive thinking and the ability to sustain psychomotor vigilance across 61 hrs of sleep deprivation.

**Methods :** Individuals appear to differ in their ability to resist the detrimental effects of sleep deprivation on performance, and these decrements are highly reproducible within a given individual, suggesting that there may be trait differences in the resilience to sleep loss. We investigated the relationship between the personality trait of constructive thinking and the ability to sustain psychomotor vigilance across 61 hrs of sleep deprivation.

**Results :** In the caffeine group, the ability to sustain PVT performance on Night 1 was predicted by a combination of lower scores on Behavioral Coping ( $r = -.90$ ), Personal Superstitious Thinking ( $r = -.48$ ) and Esoteric Thinking ( $r = -.47$ ). On night 2, only low scores on Behavioral Coping ( $r = -.61$ ) predicted better vigilance performance. By Night 3, better performance was predicted by a combination of low Behavioral Coping ( $r = -1.07$ ) and high Emotional Coping ( $r = .62$ ). In contrast, personality traits had no predictive value in the placebo group until night 3, where again, low scores on Behavioral Coping predicted better performance ( $r = -.64$ ,  $p = .04$ ).

**Conclusion :** Individuals with poorer coping skills were generally most resistant to sleep deprivation, an effect exacerbated by caffeine. Individuals with poor coping skills may find the combination of sleep deprivation and repeated vigilance testing more distressing, leading to greater frustration and autonomic arousal. Such emotional arousal may actually yield greater alertness and sustained vigilance performance during prolonged periods of wakefulness.

**Support (optional):**

### 0384

#### 56 HOURS OF WAKEFULNESS IS ASSOCIATED WITH A SUBCLINICAL INCREASE IN SYMPTOMS OF PSYCHOPATHOLOGY

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**Introduction :** Sleep loss leads to temporary changes in mood and cognition. However, it is not clear to what degree self-reported clinical symptoms of psychopathology are affected by sleep deprivation in healthy individuals. Therefore, we administered a well-validated measure of psychopathology to participants undergoing chronic sleep deprivation.

**Methods :** Twenty-five healthy adults (20 male), ranging in age from 20 to 35 years, were given a full night of sleep (8 hours time in bed), followed by 77 hours of continuous wakefulness. Participants completed the Personality Assessment Inventory (PAI) at rested baseline and again following 56 hours of continuous wakefulness. Half of the sample ( $n=11$ ) received caffeine gum (200mg) every two hours from midnight to 0845 as part of a larger study of the effects of caffeine on vigilance performance. We compared scores on the PAI between the two testing sessions and across drug groups.

**Results :** There was no significant main effect or interaction between caffeine and PAI scale (all  $ps > .05$ ). There was, however, a significant main effect of testing day ( $p = .002$ ), suggesting that several global indices of psychopathology increased significantly from baseline to sleep deprived sessions. Bonferroni corrected post-hoc comparisons across testing days for each of the scales revealed significant increases in somatic complaints

( $p = .029$ ), anxiety ( $p = .02$ ), depression ( $p = .006$ ), paranoia ( $p < .001$ ), and borderline features ( $p = .048$ ), but no significant increase in anxiety related disorders, mania, schizophrenic or antisocial features, alcohol or drug problems, aggression, suicidal ideation, perception of stress, perceived social support, treatment rejection, dominance, or warmth. These increased levels of symptoms, while statistically significant, were still within normal limits for the population.

**Conclusion :** Prolonged wakefulness of 56 hours was associated with a statistically significant, though not clinically pathological increase in self-reported symptoms of psychopathology. The greater affective dysregulation may be the result of the reduced prefrontal metabolic activity associated with sleep deprivation.

**Support (optional):**

### 0385

#### TIRED AND FRUSTRATED: USING A PROJECTIVE TECHNIQUE FOR ASSESSING RESPONSES TO STRESS DURING SLEEP DEPRIVATION

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**Introduction :** Sleep deprivation produces negative effects on mood and cognitive function. Changes in mood resulting from sleep loss may affect how individuals respond to the stresses imposed by mildly frustrating situations. Previous studies have almost exclusively utilized objective rating scales, which do not permit evaluation of idiosyncratic and unstructured responses. In this study, the Rosenzweig Picture-Frustration (P-F) Study, a projective technique, was used to assess unstructured narrative responses to frustrating circumstances following 55.5 hours of continuous wakefulness.

**Methods :** Twenty-six healthy volunteers (21 men) remained awake continuously for 77 hours. Participants completed the P-F on the baseline day and then again at the same time of day (1430) following 55.5 hours of wakefulness. In the P-F, subjects provided written verbal responses for an ambiguous character confronted with various frustrating scenarios. Following published guidelines, each response was coded according to the "type" and "direction" of aggression (e.g., directed towards others or towards the self).

**Results :** A repeated measures analysis of covariance, with gender as a covariate, indicated that sleep-deprived individuals provided more uncommon types of responses in reaction to a frustrating situation in comparison to baseline ( $p = .015$ ). Furthermore, when sleep deprived, individuals responded with greater blame and increased hostility towards others ( $p = .029$ ). In addition, individuals higher in assertiveness were less likely to accept blame ( $p = .014$ ) and more likely to insistently point out their frustration ( $p = .036$ ) when they were sleep deprived relative to when they were fully rested.

**Conclusion :** Sleep deprivation affects the ways individuals direct their aggression in response to a frustrating situation. Specifically, sleep deprived individuals were more likely to react to frustration in a hostile manner and blame others rather than accepting the blame themselves. Personality characteristics, such as assertiveness, also appear to exacerbate the tendency to blame others and overtly express frustration when sleep deprived.

**Support (optional):**



0386

**RECOVERY OF BEHAVIORAL PERFORMANCE FOLLOWING 64 HOURS OF TOTAL SLEEP DEPRIVATION***Salamat JS,<sup>1</sup> Chen T,<sup>1</sup> McKenna BS,<sup>1,2</sup> Orff HJ,<sup>1,2</sup> Drummond S<sup>3,4</sup>*

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**Introduction :** Individuals typically show some behavioral impairment during total sleep deprivation (TSD). Less clear is how long it takes to recover behavioral performance after a given length of TSD. We examined the effects of 64 continuous hours of TSD and recovery sleep on performance on three tasks.

**Methods :** Forty healthy subjects (22M, age=24.0 ± 4.9yrs., edu=15.3 ± 1.7yrs) were studied for five days in the lab and underwent five conditions: baseline sleep (BSL), two days and nights TSD (TSD1, TSD2), and two full nights of recovery sleep (REC1, REC2). An arithmetic working memory (Math) task, verbal learning task (VL), and the PVT were administered the same times each day at two (AM) and twelve (PM) hours post BSL wake-up time

**Results :** Performance showed a main effect of condition on all tasks (all  $p < .001$ ), deteriorating steadily from BSL through TSD. Only VL showed an interaction between time of day and condition, with impairment (words recalled) being greater for AM than PM testing during TSD. Performance on both Math (accuracy) and VL PM (but not AM) recovered to BSL levels during REC1 ( $p > .09$ ). Both VL AM and PM recovered, and actually showed improvements over BSL, by REC2. In contrast, PVT performance (lapses and speed of slowest 10% responses) did not recover to BSL after either REC1 or REC2 (all  $p < .05$ ).

**Conclusion :** Time of day only affected VL performance, with AM testing showing more deterioration and slower recovery than PM testing. While complete recovery to BSL performance levels was seen on Math (after REC1) and VL (after REC2), PVT performance never returned to BSL, even after two full nights of recovery sleep. These results suggest performance on tasks measuring different cognitive domains recovers at significantly different rates following 64 hours TSD.

**Support (optional):** 1. US Army DAMD17-02-1-0201 2. UCSD GCRC M01 RR00827

0387

**EMOTIONAL INTELLIGENCE SCORES DECLINE DURING SLEEP DEPRIVATION***Lipizzi EL, Killgore DB, Kahn-Green ET, Kamimori GH, Killgore WD*

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**Introduction :** Sleep deprivation has been found to reduce metabolic activity in ventral regions of the prefrontal cortex. According to the somatic marker hypothesis, this region of the brain is where a linkage is established between environmental stimuli and corresponding emotional states. It is at this connection - between emotion and cognition - where emotional intelligence is believed to emerge. Given the reduction in brain activity within the ventromedial prefrontal cortex associated with sleep loss, we predicted that sleep deprivation would decrease the ability to use emotion to guide cognition (i.e., a reduction in emotional intelligence scores).

**Methods :** Twenty-six healthy volunteers (5 women and 21 men; Age Range = 20 to 35 years) were kept awake for 77 hours, followed by 8 hours of recovery sleep. Emotional intelligence was measured at baseline and again when after 58 hours of wakefulness using the BarOn Emotional

Quotient Inventory (EQ-i), a self report assessment consisting of 5 subscales (Interpersonal; Intrapersonal; Adaptability; Stress Management; General Mood).

**Results :** A repeated measures analysis of covariance, with age as a covariate, confirmed a significant decline ( $p = 0.012$ ) in overall emotional intelligence scores following sleep deprivation. In particular, subjects demonstrated a significant decline in Intrapersonal ( $p = 0.040$ ), Interpersonal ( $p = 0.026$ ) and Stress Management ( $p = 0.010$ ) scores. There was no difference, however, in subjects' Adaptability or General Mood scale scores. Furthermore, the magnitude of change in emotional intelligence was correlated with age ( $r = .421$ ,  $p = 0.032$ ) with younger subjects showing the greatest declines in emotional intelligence following sleep loss.

**Conclusion :** Consistent with previous reports of decreased ventromedial prefrontal metabolism during sleep loss, measured emotional intelligence scores significantly declined after 58 hours of sleep deprivation. This change was most apparent in intrapersonal and interpersonal skills and functioning, as well as stress management abilities, which were particularly vulnerable with increasing age.

**Support (optional):**

0388

**DECISION MAKING CAPABILITIES DECLINE WITH INCREASING DURATION OF WAKEFULNESS***Lipizzi EL, Leavitt BP, Killgore DB, Kamimori GH, Killgore WD*

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**Introduction :** In a previous report from our laboratory, we found that 49 hours of sleep loss significantly impaired decision-making performance on the Iowa Gambling Task (IGT) - a test used to measure complex cognitive functions, such as judgment and decision making, which are believed to be mediated by the ventromedial prefrontal cortex. In the current study, performance on the IGT was evaluated over three days of sleep deprivation in order to assess this impairment and its progression.

**Methods :** Twenty-six healthy volunteers (5 women and 21 men; Age Range = 20 to 35 years) were kept awake for 77 hours, followed by 8 hours of recovery sleep. After a full night of sleep, subjects completed a baseline administration of the IGT. Alternate versions of the IGT were later given to subjects on Day 3 (after 55 hours of wakefulness) and on Day 4 (after 75 hours of wakefulness). In each session, the ratio of risky versus advantageous deck selections was calculated for each 20-card block, resulting in 5 Net Scores per session.

**Results :** A repeated measures analysis of variance revealed an interaction between session and block ( $p = 0.017$ ). Post hoc comparisons showed a significant difference between subjects' performance at baseline and both sleep deprived trials (at 55 and at 75 hours of sleep deprivation) during the final 20-card block ( $p = 0.011$  and  $p = 0.028$ , respectively). Furthermore, the decline in decision-making performance showed a trend toward worsening performance with increasing hours awake.

**Conclusion :** Sleep deprivation significantly impaired decision making capabilities mediated by the ventromedial prefrontal cortex, as evidenced by degraded performance on the IGT. The ability to make advantageous decisions declined with increasing duration of wakefulness. These data replicate our previous findings and further suggest that the magnitude of decision-making impairment was dose-dependent according to the duration of sleep deprivation.

**Support (optional):**

0389

### IMPACT OF AN OBESIGENIC ENVIRONMENT ON HUMAN BODY WEIGHT IN THE PRESENCE OR ABSENCE OF SLEEP LOSS

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**Introduction :** Sleep loss due to voluntary bedtime curtailment is an increasingly common aspect of the “western lifestyle”, characterized by lack of physical activity and overeating. Epidemiological data reveal an association between short sleep duration and increased BMI, however sleep deprivation in rodents results in increased energy expenditure and weight loss despite marked hyperphagia. To address this controversy, we examined the changes in human energy metabolism and body weight in the setting of physical inactivity and unlimited access to palatable food with or without sleep restriction.

**Methods :** Four men and 2 women, ages 36 to 49 years with BMI between 25 and 29 kg/m<sup>2</sup>, completed 2 studies in a random, cross-over design at least 3 months apart. Each study combined 2 weeks of sedentary indoor activity with ad libitum food intake and bedtimes restricted to either 8.5 or 5.5 hours/night. We monitored daily calorie intake, energy expenditure (doubly labeled water), and sleep duration (polysomnography). Weight and body composition (DEXA) were measured at the beginning and end of each treatment.

**Results :** Sleep durations were 435 ± 13 and 312 ± 3 minutes during the 8.5 and 5.5-hour bedtime conditions (mean ± SE; p<0.01; n=6; repeated measures ANOVA). Caloric intake was 3906 ± 497 kcal/day with extended and 4020 ± 417 kcal/day with restricted sleep (p=0.53; n=5), which exceeded corresponding energy expenditure levels (2687 ± 112 vs. 2721 ± 173 kcal/day; p=0.84). Both treatments were accompanied by comparable amounts of weight gain: 2.5 ± 1.0 kg during bedtime extension, and 2.1 ± 0.6 kg during bedtime restriction (p=0.58; n=6). Analysis of additional data is in progress.

**Conclusion :** In contrast to predictions from rodent studies, partial sleep curtailment in humans does not result in a negative energy balance. Sleep loss does not alter human energy expenditure under sedentary inpatient conditions.

**Support (optional):** NIH grants PO1-AG11412 and MO1-RR00055

0390

### EFFECTS OF CHRONIC SLEEP LOSS AND SLEEP EXTENSION ON VIGILANCE PERFORMANCE

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**Introduction :** Nearly one-third of Americans between the ages of 18 and 65, approximately 57 million people, are estimated to sleep < 6.5-h per night. This amount of sleep is considered inadequate to maintain optimal daytime alertness, cognitive and neurobehavioral function. It has been reported that extending sleep opportunities from 7/8-h up to 10-h per night improves alertness and neurobehavioral function. Therefore, we hypothesized that extending the sleep opportunity of subjects who habitually sleep < 6.5-h by ~2-h per night for 2 weeks would improve neurobehavioral function.

**Methods :** Twenty-six healthy subjects (11 women and 15 men), aged 22.4 ± 4.0 (±SD), who reported habitual sleep schedules of < 6.5-h during the work/school week completed a month long protocol. Habitual

wakefulness-sleep schedules were first monitored for 2 weeks at home using wrist actigraphy, diaries, and call-ins to a time-stamped recorder. Subjects lived in the laboratory for ~24-h during which baseline performance and sleep EEG measures were recorded. Following this lab visit, wakefulness-sleep schedules were again monitored for 2 more weeks. Twelve subjects were randomized to a sleep maintenance condition and were asked to maintain their habitual wakefulness-sleep schedules. Fourteen subjects were randomized to the sleep extension condition which required subjects to increase their time in bed by ~2-h per night. Performance and sleep were then assessed during a second ~24-h lab visit. Vigilance performance (visual Psychomotor Vigilance Test [PVT] lapses and median reaction time[MedRT]), assessed at scheduled awakening and every 2-h thereafter, was analyzed with repeated measures ANOVA.

**Results :** Subjects who maintained their habitual sleep schedule across the study (n=12) spent on average 6.0 ± 0.6-h (±SD) and 6.1 ± 0.5-h per night in bed during the first two and second two weeks of the protocol, respectively. Subjects in the sleep extension condition (n=14) spent on average 6.0 ± 0.6-h and 8.2 ± 0.7-h per night in bed during the first two and second two weeks, respectively. We observed a significant reduction in the number of PVT lapses and faster MedRT performance for the sleep extension compared to sleep maintenance condition (all P<0.05).

**Conclusion :** Extending the sleep opportunity of subjects who chronically obtain inadequate sleep to the recommended ~“8-h” of sleep per night improves neurobehavioral performance.

**Support (optional):** Research Supported by the American Sleep Medicine Foundation

0391

### THE EFFECT OF 44 HOURS OF SLEEP DEPRIVATION ON MOOD USING THE VISUAL ANALOG MOOD SCALES

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**Introduction :** Studies of total sleep deprivation consistently demonstrate that global mood ratings decline with duration of wakefulness. Mood is a complex phenomenon, however, and little is known about the specific dimensions that are most affected by sleep loss and how they are related to circadian rhythms. To more precisely measure changes in mood across multiple dimensions, we administered the Stern Visual Analog Mood Scales (VAMS), every two hours over the course of 44 hours of sleep deprivation.

**Methods :** Fifty-four volunteers (29 males) were administered the VAMS and the Stanford Sleepiness Scale (SSS) every two hours in order to track their subjective mood and sleepiness ratings during 44 hours of total sleep deprivation. The VAMS is a well-validated and reliable measure that includes 8 scales measuring the mood states of “afraid,” “angry,” “confused,” “energetic,” “happy,” “sad,” “tense,” and “tired.” Each scale is rated along a 100 mm line anchored by an emotional cartoon face at one end and a neutral face at the other.

**Results :** All eight VAMS were significantly correlated with sleepiness ratings (all ps<.01). Specifically, with ratings of greater subjective sleepiness, energy and happiness ratings declined while negative mood dimensions increased. A repeated measures ANOVA revealed a significant interaction between testing session and mood scale (p<.0001) and a significant main effect of sleep deprivation on six of the eight VAMS (p=.03). Linear and polynomial trends indicated significant worsening of moods with greater wakefulness, with ratings of happiness showing the greatest susceptibility to sleep loss and rhythmic variability.

**Conclusion :** Continuous wakefulness of up to 44 hours significantly worsened several dimensions of mood. Interestingly, the major change in

mood due to sleep loss appears to be produced by a decline in happiness and energy ratings rather than an elevation of negative mood states such as sadness, fear or anger.

**Support (optional):**

### 0392

#### MOOD AND WELL BEING PATTERNS DURING SLEEP DEPRIVATION BASED ON FACTOR ANALYSIS

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**Introduction :** Sleep deprivation has been reported to negatively impact mood and well being. The aim of this study was to assess the relationship between multiple measures of subjective mood and well being during one night of total sleep deprivation to determine whether or not a global pattern in mood and well-being occurs in response to sleep loss.

**Methods :** Forty healthy subjects (26 men, 14 women), aged 30.7±8.6 (Mean±SD), participated. Participants were scheduled to sleep 8-h per night for 3 baseline weeks at home, verified by sleep diaries, call-ins to a time stamped recorder, and by actigraphy for at least one week. Subjects lived in the laboratory for three to six days with 8-h scheduled sleep episodes each night at their habitual times. This was followed by 40-h of total sleep deprivation under constant routine conditions. Mood and well being were assessed every 2-h during scheduled wakefulness using visual analog scales. Scales include measures of: tranquil, competent, friendly, sociable, content, stress, sadness, relaxed, physically exhausted, strong, sick, fresh as a daisy, clearheaded, alert, energetic, quickwitted, sharp, attentive, interested, well-coordinated, and motivated. Factor analysis (varimax rotation, normalized) was performed on data from hours awake 25-40.

**Results :** Exploratory factor analysis reduced the 21 mood and well-being measures to four factors with eigenvalues > 1.0. These four factors explained over 80% of the variance during sleep deprivation. Factors loadings were representative of amiableness, negative emotion/fatigue, mental sharpness, and health/motivation. Sleep deprivation had a negative impact on all these factors.

**Conclusion :** One night of sleep deprivation negatively impacted the mood and well-being of otherwise healthy men and women. However, the mood structure observed is not explained by one global factor and thus mood structure during sleep deprivation appears complex.

**Support (optional):** Research Supported in part by NASA Cooperative Agreement NCC 9-58 with the National Space Biomedical Research Institute and by NIH MH45130.

### 0393

#### SHORTER HABITUAL SLEEP DURATION IS ASSOCIATED WITH HIGHER INCREASE IN SUBJECTIVE ESTIMATION OF PAIN IN RESPONSE TO A TOTAL SLEEP DEPRIVATION (TSD) CHALLENGE

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**Introduction :** Epidemiological evidence suggests that shorter habitual sleep durations are associated with increased risk for inflammatory-related diseases. Experimental models of sleep loss, both chronic partial deprivation as well as acute total sleep deprivation lead to increased inflammatory mediators in circulation. We correlated habitual sleep duration with changes in subjective pain in response to a total sleep deprivation (TSD) challenge to test the relationship between habitual sleep duration

and vulnerability to sleep loss.

**Methods :** Healthy participants (N=17, 25-55 years, habitual sleep durations between 6.5 and 8.5 hrs) underwent 88 hours of TSD after two baseline days with a sleep opportunity of 8 hrs. Habitual sleep duration was assessed by a 2-week sleep log period prior to study start. During the 7 day in-hospital stay, computerized visual analog scales (VAS) were presented every 2 hours during the waking periods to assess emotional and physical well-being. Intensity of headache, backache, generalized body pain, muscle, joint, and stomach pain were compiled to create global pain variable.

**Results :** Ratings of subjective pain increased linearly throughout TSD ( $p<.001$ ); with no daytime vs. nighttime difference in pain estimations (7am-23pm vs. 23-7am). Subjective pain started to increase by 3.9±1.0% on the first day of TSD ( $p<.002$ ) and reached a 9.2±2.6% increase above baseline on the 3rd day of TSD ( $p<.002$ ). In parallel, leukocyte counts increased linearly throughout TSD from 6.0±0.3 to 6.5±0.4 K/ul ( $p<0.05$ ). Habitual sleep duration predicted the increase in pain ratings in response to TSD ( $r=-.52$ ,  $p<0.05$ ), indicating that short habitual sleep duration is associated with a higher pain response to a TSD challenge. Habitual sleep duration did not predict increase in fatigue ( $r=-.34$ , n.s.). Furthermore, subjects with short habitual sleep duration tended to have a higher monocyte increase in response to a TSD challenge than those with longer sleep duration ( $r= 0.46$ ,  $p<0.07$ ).

**Conclusion :** In pain-free, healthy subjects, prolonged TSD led to a 9%-increase of subjective pain. Increase in pain was more pronounced in subjects with shorter habitual sleep durations, suggesting that habitual sleep duration may contribute to interindividual variability in the pain response to TSD.

**Support (optional):** National Institutes of Health (HL075501, GCRC grant RR01032).

### 0394

#### THE MAJORITY OF NURSES REPORT DIFFICULTIES WITH DROWSINESS DRIVING HOME AFTER WORK

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**Introduction :** According to the National Highway Transportation Safety Association, working long hours and/or rotating shifts increases the risk of falling asleep while driving home after work. Since hospital staff nurses often work ≥ 12 consecutive hours, rotate shifts or work nights, they are at high risk for experiencing difficulties remaining alert driving home from work. The goal of this study was to determine how often nurses have difficulty remaining awake driving home and what factors are associated with drowsy driving.

**Methods :** Two random samples of full time hospital staff nurses from the American Nurses Association (ANA sample = 393 participants) and the American Association of Critical Care Nurses (AACN sample = 502 participants) completed a demographic questionnaire and logbooks with daily information about sleep, alertness on duty, work hours, and errors for 28 days. Summary statistics and parametric tests were used to examine the data.

**Results :** Two-thirds of the participants reported difficulty remaining awake driving home at least once during the 28-day data-gathering period. On average, nurses struggled to remain alert on their drive home approximately once every four shifts they worked (2920/11,167 shifts). Although 80% of the nurses who worked exclusively night shift reported

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at least one episode of drowsy driving, over half (58.5%) of the nurses working exclusively day shifts also reported at least one episode of drowsy driving. Drowsy driving was more common when nurses left work between 2400 and 0800 than when nurses left work between 0800 and 1600 or between 1600 and 2400 (46% of the shifts compared to 29% and 18%, respectively). Nurses who reported drowsy driving had significantly longer commutes ( $32.2 \pm 19.5$  minutes compared to  $25.3 \pm 15.9$  minutes,  $p < 0.001$ ), and obtained on average 30 minutes less sleep than those who were able to remain alert driving home from work ( $6.33 \pm 3.1$  hours versus  $6.83 \pm 1.64$  hours,  $p < 0.001$ ).

**Conclusion :** Although we expected night shift nurses to report occasional difficulties with drowsy driving, we did not expect that the majority of nurses would report difficulties driving home during the 28-day period. The high number of drowsy driving episodes reported between 0800 and 2400 parallels the findings from a 2003 NHTSA report.

**Support (optional):** Financial support for this study was provided by the Agency for Healthcare Research and Quality (R01 HS11963-01) and an American Nurses Foundation Grant (Scott).

### 0395

#### TIME ON TASK EFFECT OF CHRONIC SLEEP RESTRICTION

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**Introduction :** Chronic sleep restriction is common in real-world operational environments. Laboratory studies have shown that sleep restriction degrades sustained attention performance in a dose-dependent manner. We hypothesized that this sleep dose-dependent performance degradation involves intensification of the time on task (ToT) effect.

**Methods :**  $n=66$  healthy volunteers (age range: 24-55; m/f: 50/16) were studied in a chronic sleep restriction paradigm while in residence in a sleep research laboratory. The paradigm included 3 baseline days with 8h time in bed (TIB), 7 days with sleep restriction or augmentation at 3h, 5h, 7h or 9h TIB ( $n=18, 16, 16, 16$ ), and 3 recovery days with 8h TIB. Throughout the study, subjects were tested on a 10min psychomotor vigilance task (PVT) at 09:30, 12:30, 15:30, and 21:30. The magnitude of the ToT effects in this task was operationally defined as the linear change in reaction time (RT) across the 10min task duration. Changes in the ToT effect among experimental conditions and across days in the study (starting with the third baseline day) were analyzed by means of mixed-effects ANOVA.

**Results :** The main ToT effect was statistically significant ( $F=315.9$ ,  $P < 0.001$ ). The ToT effect interacted significantly with experimental condition ( $F=69.3$ ,  $P < 0.001$ ) and days in the study ( $F=4.53$ ;  $P < 0.001$ ). Moreover, there was a significant three-way ToT by condition by day interaction ( $F=3.14$ ,  $P < 0.001$ ). The ToT effect varied among conditions in a dose-dependent manner—shorter sleep durations corresponded with greater ToT effects. In the sleep restriction conditions, the ToT effect increased considerably across restriction days, and reduced again during recovery days.

**Conclusion :** The sleep dose-dependent degradation of PVT performance across days of chronic sleep restriction was associated with intensification of the ToT effect. This finding suggests that in operational environments requiring sustained attention the risk of performance failure due to chronic sleep restriction may increase progressively with ToT.

**Support (optional):** U.S. Army Medical Research and Materiel Command; Federal Motor Carrier Safety Administration

### 0396

#### SLEEP PROBLEMS AND HEALTH: THE LONGITUDINAL EMERGENCY MEDICAL TECHNICIAN ATTRIBUTES & DEMOGRAPHICS STUDY (LEADS)

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**Introduction :** Emergency medical technicians (EMTs) commonly report sleep “problems” (EMT-Basics 29.9% EMT-Paramedics 19.8%). EMT’s work requires optimum performance (high speed driving, time sensitive decision making, and initiation of life saving interventions). Using the LEADS 2005 project survey, we assessed self reported snoring (Sn), sleep disordered breathing (SDB), sleep apnea (SA), hypersomnia, and insomnia (Insom) on health perception, drowsy driving, and time off from work related accidents.

**Methods :** A validated 30-item Sleep Survey measuring indicators of sleeping problems along with both occupational and non-work habits were included in the 2005 LEADS Project survey (a panel survey of nearly 2,000 nationally registered EMTs sampled from the National Registry of US Emergency Medical Technicians’ database, which consists of approximately 185,000 EMTs). Random disproportionate sampling (EMT-Paramedic vs. EMT-Basic; white vs. non-white; newly registered vs. registered for more than one year) was performed. Means analysis to compare groups and general linear regression analysis (SURVEYREG, American Institutes for Research, Palo Alto, CA) to adjust for age, gender, race, and education level were used.

**Results :** In EMT’s, habitual snoring (8.8%), SDB (9.0%), SA (4.8%), hypersomnia (45.2%), sleep onset and sleep maintenance insomnia (45.1 and 57.1% respectively) were common. Risk of reported poor general health, decreased physical activity, and days missed on job accidents was higher for all sleep problems. Sleep problems continued to predict poorer general health, impaired physical activity, drowsiness driving short distances, and drowsiness driving long distances after adjustment. Insomnia groups also demonstrated more days missed from work.

**Conclusion :** Sleep disorders including sleep disordered breathing, insomnia and hypersomnia are common in EMT personnel. These disorders are independently associated measures of poorer general health, drowsy driving, and missed work days.

**Support (optional):**

### 0397

#### FIVE DAYS WITH PARTIAL SLEEP DEPRIVATION AND THE EFFECTS ON PERFORMANCE, SLEEPINESS AND EFFORT

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**Introduction :** The aim of the present study was to evaluate performance and subjective ratings during 5 days of partial sleep deprivation (PSD) and during recovery.

**Methods :** Nine subjects slept in the laboratory for 12 days, which included 5 days with PSD (03-07h) and 4 recovery days (23-07h). Every day at 08.30h, 14.00h and 20.30h subjects performed a 6-min reaction time (RT) test that was followed by subjective ratings of sleepiness (Karolinska Sleepiness Scale, KSS) and effort.

**Results :** RT (median) deteriorated across PSD days and the highest value was found the 5th PSD day ( $342 \pm 41$  ms,  $p < 0.05$ ). The values for the second baseline day was  $284 \pm 19$  ms. RT was also elevated for the first recov-

ery day ( $319 \pm 26$  ms) but declined across recovery days. Lapses ( $\geq 500$  ms) showed a similar pattern, but the highest number of lapses was observed on the 7th recovery day (8 vs. 3 for the 1st baseline day). KSS showed an increase across PSD days, but the recovery was more immediate and no elevated levels were observed during the 7th recovery day. The mean KSS was  $5.0 \pm 0.2$  for the 1st baseline day,  $7.6 \pm 0.2$  for the 5th PSD day, and  $5.5 \pm 0.3$  for the 1st recovery day. The rating “tried to do my best” (0 not at all–6 almost all the time) showed a different pattern ( $p < 0.05$ ). It decreased across days, and the lowest value was observed for the 2nd recovery day ( $3.1 \pm 0.3$  vs.  $4.2 \pm 0.2$  for the 1st baseline day).

**Conclusion :** Reaction times and subjective sleepiness increased across days with PSD. The recovery of reaction time was, however, slower compared to subjective sleepiness, and lapses occurred frequently during the 7th recovery day. The decline in “tried to do my best” across days might contribute to the elevated reaction time levels during the recovery days.

**Support (optional):**

### 0398

#### EMOTIONAL INTELLIGENCE MODERATES THE EFFECT OF SLEEP DEPRIVATION ON MORAL REASONING

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**Introduction :** Sleep deprivation reduces glucose metabolism within the ventromedial prefrontal cortex. This region is also critical for emotional decision-making, especially in situations involving moral judgment. Functional neuroimaging studies show that moral situations that are personally relevant and highly emotional (Moral-Personal, MP) activate this region more than judgments that are impersonal and less emotionally engaging (Moral-Impersonal, MI) or which do not involve moral judgment (Non-Moral, NM). We investigated whether sleep loss would differentially affect the types of judgments that volunteers (classified as high or low in emotional intelligence) would make to these types of moral dilemmas.

**Methods :** Twenty-six healthy volunteers (21 men) were administered the Bar-On Emotion Quotient Inventory (EQ-i) at baseline. Participants were classified as normal or high EQ based on a median split of the sample ( $EQ = 111$ ). Following a full night of bed rest (8 hours), volunteers remained awake for 77 hours. Two versions of the Moral Reasoning Test were administered in counterbalanced order at baseline and again after 53.5 hours of sleep deprivation. Volunteers made judgments as to the “appropriateness” of various courses of action for three types of moral dilemmas (MP, MI, NM).

**Results :** A repeated measures ANOVA revealed a significant interaction between test session and EQ level for responses to MP scenarios ( $p = 0.047$ ), indicating that volunteers with normal EQ showed altered moral reasoning with sleep loss, whereas high EQ individuals were unaffected.

**Conclusion :** Sleep loss leads to a greater propensity to judge controversial solutions to moral dilemmas as “appropriate,” but this effect appears to be mitigated by premorbid emotional intelligence. Individuals with normal levels of EQ were susceptible to an alteration in moral reasoning due to sleep loss, whereas high EQ volunteers remained stable. Findings support the theory that prefrontal regions of the cortex are particularly vulnerable to the detrimental effects of sleep loss.

**Support (optional):**

### 0399

#### SLEEPY PEOPLE SMELL WORSE: OLFACTORY DECREMENTS AS A FUNCTION OF SLEEP DEPRIVATION

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**Introduction :** Functional neuroimaging studies have demonstrated that extended periods of wakefulness produce a significant reduction in prefrontal lobe activity, particularly within ventromedial and orbitofrontal regions. These same brain regions also receive extensive afferent neural connections from the olfactory system, and some evidence suggests that ability to detect odors is a reliable indicator of the functional integrity of the orbitofrontal cortex. Along these lines, an earlier study in our laboratory investigated whether olfactory discrimination was influenced by sleep loss. In that study we found that odor identification accuracy decreased significantly after 24 hours awake. The present study attempted to replicate the earlier findings and further investigated whether a deficit would be greater if time awake was extended to 52 ½ hours.

**Methods :** Twenty four healthy volunteers (19 males) were tested when fully rested (baseline) and again after 52 ½ hours awake using the University of Pennsylvania Smell Identification Test (UPSIT). The UPSIT is a commercially available, self-administered test that consists of 4 booklets, each containing ten “scratch & sniff” odorants. Two booklets were administered at baseline. Volunteers remained awake and were administered 2 additional booklets when sleep deprived. Booklet order was counterbalanced across sessions.

**Results :** Odor identification accuracy decreased significantly ( $p = .02$ ) after 52 ½ hours awake. Sleep deprived performance scores declined 5.7% compared to baseline scores. However, the present decrement was not significantly different than the decrement observed in our previous study following 24 hours awake (6.3% decline).

**Conclusion :** These data replicate our earlier findings showing that sleep loss significantly affects the ability to accurately identify odors. However, it appears that extending time awake from 24 to over 52 hours does not increase the degree of olfactory deficit. The decline in olfactory performance is consistent with expectations based on evidence showing decreased prefrontal metabolism during continuous sleep deprivation.

**Support (optional):**

### 0400

#### EFFECT OF COGNITIVE WORKLOAD ON DELTA POWER IN THE NREM EEG OF RECOVERY SLEEP FOLLOWING ACUTE SLEEP DEPRIVATION

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**Introduction :** This study investigated the effect of cognitive workload during total sleep deprivation (TSD) on slow-wave activity (SWA) in the NREM sleep EEG.

**Methods :** 21 healthy subjects (age  $28.5 \pm 5.5$ ; 11 females) spent eleven consecutive days in the laboratory. They underwent three 36h TSD periods. The first TSD was preceded by two baseline nights (12h TIB), and all TSDs were followed by two recovery nights (12h TIB). Every 2h during TSD, subjects completed a moderate (0.5h) workload or high (1.0h) workload neurobehavioral test battery. Moderate cognitive workload testing occurred during two TSDs, and high cognitive workload testing during the third TSD, in randomized, counterbalanced order. Sleep periods

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were recorded polysomnographically. For the present analysis, 16 subjects each contributed four records: the second baseline night, two recovery nights after moderate workload, and one recovery night following high workload (six records were missing). For every record, SWA (0.75-4.5Hz) in the NREM sleep EEG (Fz, C3, C4, Oz vs. Ax) was assessed. Recovery sleeps following moderate vs. high workload were compared using mixed-effects ANOVA, controlling for baseline, systematic individual differences, order effects, and multiple comparisons.

**Results :** A significant effect of workload on SWA in the NREM sleep EEG was found for the Oz derivation ( $t_{23}=2.76$ ,  $P=0.011$ ). In recovery sleep following TSD with high workload, compared to moderate workload, SWA increased by  $201\pm 73(\mu V)/2/Hz$  (mean $\pm$ SE). Significant effects were not found for the other EEG derivations.

**Conclusion :** Higher cognitive workload during TSD resulted in increased NREM sleep SWA on the occipital EEG derivation during subsequent recovery sleep. Since SWA is considered a marker of sleep homeostasis, this preliminary result indicates that waking cognitive activity (in addition to wake duration) may affect sleep homeostatic regulation. This finding correlates with recent reports suggesting that sleep regulation may be use-dependent. Why the present workload effect was observed only occipitally remains to be investigated.

**Support (optional):** Supported by NIH grants HL70154 and RR00040.

### 0401

#### CAFFEINE ADMINISTERED TO MAINTAIN OVERNIGHT ALERTNESS DOES NOT DISRUPT PERFORMANCE DURING THE DAYTIME WITHDRAWAL PERIOD

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**Introduction :** Numerous studies have demonstrated that caffeine maintains performance on complex cognitive tasks following extended wakefulness. However, the degree to which performance is affected in the hours after administration has ceased and caffeine is clearing from the system is unknown. In this study, participants were administered repeated doses of caffeine bi-hourly throughout the night. We evaluated the effects of caffeine withdrawal on complex cognitive task performance during the 18 hours between caffeine administrations.

**Methods :** Twenty six volunteers (21 males) were repeatedly administered a computerized version of the Tower of Hanoi (TOH) test, which served as a complex over-learned cognitive-psychomotor task. Individuals were trained to asymptote on the task, given 8 hours in bed, then administered the task every 2 hours during 72 hours of continuous wakefulness. In a double-blind design, 12 volunteers received caffeine, 200 mg, 4 times per night (0100, 0300, 0500 and 0700). Average time per move and number of moves made was collected. A speed x accuracy score (throughput) was calculated as a measure of efficiency. Performance during the intervening 18 hours between caffeine administrations was evaluated.

**Results :** Over the course of testing, individuals in the caffeine group were significantly more efficient at completing the task than the placebo group ( $p<.004$ ). Post hoc comparisons indicated that the caffeine group remained significantly better than the placebo group across the 18 hour post drug delivery period.

**Conclusion :** Nighttime administration of caffeine did not disrupt TOH performance during the 18 hour withdrawal period between drug administrations. In fact, those who received repeated nightly administration of caffeine were able to maintain efficient performance on the TOH task for up to 18 hours after caffeine delivery. Findings suggest that repeated caffeine administration during the night does not lead to significant withdrawal effects on an over-learned complex cognitive task the following day.

**Support (optional):**

### 0402

#### THE PERCEPTION OF FACIAL EMOTION IS ENHANCED BY PSYCHOSTIMULANTS FOLLOWING TWO NIGHTS OF SLEEP DEPRIVATION

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**Introduction :** Sleep deprivation produces deficits in simple cognitive abilities such as alertness and vigilance, but its effects on higher order capacities such as judgment and facial perception are not well understood. Stimulant medications are often used to temporarily counteract the detrimental effects of sleep deprivation on cognition, although their effects on higher cognitive processes are largely unexplored. We examined the effects of three commonly used psychostimulants (caffeine 600 mg, modafinil 400 mg, and dextroamphetamine 20 mg) on the ability of sleep deprived individuals to accurately label the emotion expressed on faces.

**Methods :** Fifty-four healthy volunteers (29 males) participated. Two tasks were used, the Ekman 60 face test (simple emotion labeling) and the Emotion Hexagon (labeling complex blends of emotions), which were administered at rested baseline, following drug administration at 47 hours of sleep deprivation, and again after recovery sleep. Scores were compared across drug groups and test session.

**Results :** Overall, for simple emotion labeling, accurate assessment of facial emotions was not significantly enhanced by any of the stimulants relative to placebo. In contrast, for complex emotion blends, all three stimulants were superior to placebo for the total score, and for the perception of blended expressions including happiness or sadness (all  $p's<.05$ ), and none of the stimulants differed significantly from one another.

**Conclusion :** The use of psychostimulants during sleep deprivation significantly improved the ability to identify subtle emotional differences on a task involving complex but not simple emotional face perception. Because all three stimulants were equally effective at enhancing performance, it suggests that the improvement is likely due to a general alerting effect, rather than from activation of specific neural sites that are differentially acted upon by the three drugs. These findings extend the usefulness of stimulant medications beyond simple vigilance to include higher order cognitive and emotional functions.

**Support (optional):**

### 0403

#### SLEEP DEPRIVATION DIMINISHES CONSTRUCTIVE THINKING

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**Introduction :** Recent research suggests that the prefrontal cortex is particularly vulnerable to the detrimental effects of sleep loss, and that as little as 24 hours of wakefulness is associated with significant declines in glucose metabolism within the prefrontal regions. The ventromedial region of the prefrontal cortex is important for the control of complex behavior, motivation, and inhibition, and is believed to be the seat of personality functioning. We hypothesized that two days of sleep loss would lead to alterations in personality functioning typically associated with flexible and constructive thinking.

**Methods :** Twenty-one males and five females were deprived of sleep for 77 hours following a full night of sleep (8 hours time in bed). The Constructive Thinking Inventory (CTI), a self-report measure of flexible and constructive responses to circumstances, was administered at rested baseline and again following 55.5 hours of wakefulness. The CTI includes

a general “Global Constructive Thinking” scale, and six subscales, including Emotional Coping, Behavioral Coping, Personal Superstitious Behavior, Categorical Thinking, Esoteric Thinking, and Naïve Optimism. **Results :** A repeated measures ANOVA yielded a significant interaction between testing session and the CTI scale ( $p=0.037$ ). Specifically, sleep loss was associated with a significant decline in Behavioral Coping ( $p=0.007$ ) and a significant increase in Esoteric Thinking ( $p=0.04$ ). Despite significant changes due to sleep loss, these scores remained within the normal (i.e., non-clinical) range. Other CTI scales were unaffected by sleep loss.

**Conclusion :** Sleep loss was associated with a significant decline in the tendency of participants to think in ways that facilitate effective behavioral action (e.g., appropriate optimism, action orientation, conscientiousness), and a significant increase in reported esoteric beliefs (e.g., magical thinking; superstitious/paranormal beliefs). Findings are consistent with a growing body of research indicating that the cognitive processes mediated by the prefrontal cortex are adversely affected by prolonged sleep loss. **Support (optional):**

#### 0404

##### INTROVERSIVE PERSONALITIES ARE MORE RESILIENT AGAINST SLEEP LOSS

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**Introduction :** According to Eysenck’s (1990) theory of Introversion-Extroversion (I-E Theory), introverts possess higher levels of basal activity within the cortico-reticular loop, leading them toward chronically higher levels of cortical arousal than extraverts, who are described conversely as chronically under-aroused and easily bored. Based on I-E Theory, we hypothesized that individuals high in the trait of Extraversion (i.e., low in cortical-reticular activity) would be more susceptible to the detrimental effects of sleep loss than more Introverted individuals.

**Methods :** Twenty-three healthy volunteers participated (19 men;  $M$  age=25.3,  $SD=4.1$ ). Following arrival on Day 0, volunteers completed the Revised NEO Personality Inventory (NEO PI-R) and obtained a full night of sleep (8 hours time in bed). After awakening at 0700 on Day 1, volunteers remained awake continuously for 77 hours. For the next three nights, participants completed psychomotor vigilance testing (PVT) at 10 minute intervals from 0015 to 0845. Half of the sample ( $n=12$ ) received caffeine gum (200mg) every two hours. Speed ( $1/Reaction\ Time \times 100$ ) was calculated for each PVT and converted to percent of baseline performance (PVT%) for each subject. We correlated scores on the 5 NEO Factors with PVT% scores.

**Results :** For Night 1, Extraversion was the only NEO factor to correlate with PVT% scores ( $r=-.38$ ,  $p=.037$ ). When the night was divided into thirds, Extraversion predicted PVT% in the early ( $r=-.52$ ) but not middle or latest third of the night. Higher Extraversion was associated with greater decline in PVT% only during Night 1. Gregariousness and Activity sub-factors of Extraversion were most predictive of PVT% decline. When caffeine and placebo groups were examined separately, caffeine enhanced these relationships relative to the placebo group.

**Conclusion :** Consistent with Eysenck’s cortico-reticular activation theory of Introversion-Extroversion, individual differences in the trait of Extraversion predicted resilience to sleep loss and these differences were enhanced by caffeine.

**Support (optional):**

#### 0405

##### MORAL REASONING IS AFFECTED BY SLEEP DEPRIVATION

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**Introduction :** Recent neuroimaging studies of rested volunteers demonstrate that emotionally charged moral judgments (Moral Personal; MP) significantly activate the ventromedial prefrontal cortex relative to moral judgments involving low emotional arousal (Moral Impersonal; MI) or Non-Moral judgments (NM). Because sleep deprivation is associated with decreased activity within the prefrontal cortex, especially the ventromedial regions associated with emotional decision-making, we predicted that sleep loss would lead to alterations in moral judgments specifically involving highly emotionally charged decisions.

**Methods :** Twenty-six healthy volunteers participated (21 men;  $M$  age=25.3,  $SD=4.1$ ). Following arrival on Day 0, volunteers obtained a full night of sleep (8 hours time in bed). Volunteers awakened at 0700 on Day 1 and remained awake continuously for 77 hours. Participants completed a moral reasoning test on the baseline day and again at the same time of day (1230) following 53.5 hours of wakefulness, counterbalanced across subjects. Three types of moral dilemmas were presented: MP, MI, and NM. Responses were scored for reaction time (RT) and the percent of moral response options endorsed as “appropriate.”

**Results :** Analysis of variance of RT scores revealed a significant three-way interaction ( $p=.04$ ) among day (baseline vs sleep deprived), type of question (MP, MI, NM), and response type (“appropriate” vs. “inappropriate” endorsement). Relative to baseline, sleep deprived participants showed a significant increase in RT for judging MP dilemmas as “appropriate” versus “inappropriate” ( $p=.005$ ). Furthermore, volunteers were more likely to endorse the same MP dilemma responses as “appropriate” when sleep deprived than at baseline ( $p=.037$ ). MI and NM judgments, in contrast, were unaffected by sleep loss.

**Conclusion :** Sleep deprivation selectively affected judgments of highly emotionally charged moral dilemmas, but did not affect judgments about similar dilemmas with low or no emotional involvement, consistent with recent suggestions that the ventromedial prefrontal cortex is particularly vulnerable to the detrimental effects of sleep loss.

**Support (optional):**

#### 0406

##### THE RELATION BETWEEN SUBJECTIVE SLEEPINESS AND REACTION TIME PERFORMANCE: AN INTRA-INDIVIDUAL APPROACH

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**Introduction :** It has been claimed that subjective ratings of sleepiness dissociate from performance on many tasks. The aim of this study was to describe the intra-individual correlations between simple reaction time and subjective ratings of sleepiness and effort in a partial sleep deprivation (PSD) protocol.

**Methods :** Nine subjects slept in the laboratory for 12 days (3 baseline days including habituation, 5 days with PSD, and 4 recovery days). Every day at 08.30h, 14.00h and 20.30h subjects performed a 6-min reaction time (RT) test that was followed by subjective ratings of sleepiness (Karolinska Sleepiness Scale, KSS) and effort. The statistical analysis was based on pooled data and used a multiple regression analysis, with subjects as forced dummy variables (omitting one subject).

**Results :** All variables showed a significant variation across days. The

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following ratings showed significant correlations with median RT: “had to fight sleep during the test” ( $r=0.35$ ,  $p<0.001$ ), KSS ( $r=0.34$ ,  $p<0.001$ ), mental effort ( $r=0.32$ ,  $p<0.001$ ), “dozed off during the test” ( $r=0.30$ ,  $p<0.01$ ), and “mental exhaustion” ( $r=0.28$ ,  $p<0.01$ ). A negative correlation was observed for “it was fun to do the test” ( $r=-0.22$ ,  $p<0.05$ ). Thus, longer RT values were associated with high levels of fighting sleep and high KSS, increased mental effort and mental exhaustion, and low levels of “it was fun to do the test”. If one controls for KSS, the remaining correlations became non-significant. More or less the same pattern was observed for lapses, albeit the correlation coefficients became slightly weaker.

**Conclusion :** In conclusion, a moderately strong covariation was observed between subjective ratings of sleepiness, effort and reaction times. However, the covariation with increased boredom (as indicated by the negative correlation with the rating “it was fun to do the test”) suggests that psychological processes also might have some association with reaction time performance.

**Support (optional):**

### 0407

#### ACTIGRAPHIC ASSESSMENT OF SLEEP IN US AIR FORCE ACADEMY CADETS

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**Introduction :** Sleep is fundamental part of managing the details of everyday functioning during undergraduate training. In fact, sleep quantity has been shown to be the best predictor of performance in college settings. Studies have also shown that sleep loss may affect not only performance in school but also cooperativeness among students, mood changes, and aggressive behavior in students. These factors are critical to all college students but especially U.S. Air Force Academy Cadets who, in addition to studying for their Bachelor of Science degree, are training to become military officers. This project examines sleep in a military academy using actigraphy across the Spring '04 semester comparing freshmen and seniors. We hypothesized that freshmen will sleep less than seniors across the semester. We also hypothesized that as the semester progresses, the subjects' sleep quantity will decrease due to seasonal changes of light and dark. Finally, we expect that napping will be more frequent in freshmen than seniors.

**Methods :** We examined the temporal relationship of sleep with seasonal fluctuation by measuring 20 volunteers (10 freshmen, 10 seniors) via actigraph early in the academic semester (Feb) and again late in the semester (May). Therefore, each volunteer wore the actigraph on two separate one-week periods.

**Results :** We found that USAFA Cadets are sleeping less than 6 hours during the weekday and well over 8 hours on weekends. Freshmen are napping significantly more than seniors and report lower levels of post-sleep refreshment. We found no significant differences of total sleep time as the semester progressed.

**Conclusion :** This study is the first objective sleep analysis at USAFA and lays the foundation for future projects in sleep and circadian rhythms. More research on sleep at the Academy is forthcoming.

**Support (optional):** This project was supported by a small grant from the United States Air Force Academy.

### 0408

#### FUNCTIONAL IMAGING OF WORKING MEMORY FOLLOWING NORMAL SLEEP AND AFTER 24 AND 35 HOURS OF SLEEP DEPRIVATION: CORRELATIONS OF FRONTO-PARIETAL ACTIVATION WITH PERFORMANCE

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**Introduction :** Working memory was evaluated after normal sleep, and at 24 and 35 hours of sleep deprivation (SD) in 26 healthy young adults to examine the neural correlates of inter-individual differences in vulnerability to SD. Recent work (Mu 2005) suggested that WM related cortical activation at RW might be useful in predicting performance decline following SD. We tested the reproducibility of this finding using a different working memory task. As different imaging studies have evaluated volunteers at 24, 33, 35 and 48 hours of SD, we also wished to determine if scanning at SD24 and SD35 would give significantly different results that might account for the variations in findings reported in existing imaging studies involving SD.

**Methods :** Twenty-six young, healthy adults whose sleep history was verified by wrist actigraphy participated in a block-design fMRI experiment. Three tasks were engaged to identify a common network of regions involved in verbal working memory. RW scans took place between 0900 and 1030. In the SD session, participants were observed in the laboratory from 1900h onwards and were scanned on the next day between 0600h and 0800 (SD24) and 1800h and 1900h (SD35). The RW and SD sessions were a week apart and their order counterbalanced across participants. Voxel based and region-of-interest based analyses were performed on the imaging data.

**Results :** The extent of performance decline was not significantly different between the two SD test periods although there was greater variability in performance at SD35. In both SD sessions, there was reduced task-related activation (relative to normal sleep) in both superior parietal regions and the left thalamus. Activation of the left parietal and left frontal regions after normal sleep was negatively correlated with performance accuracy decline from normal sleep to SD24 thus differentiating persons who maintained working memory performance following SD from those who were vulnerable to its effects.

**Conclusion :** Cortical activation during the engagement of verbal working memory at RW appears to predict the magnitude of working memory performance decline at SD24 corroborating earlier work using a Sternberg-type test. Evaluating working memory at SD24 and SD35 yields imaging results that do not differ significantly.

**Support (optional):** NMRC (Singapore), SingHealth Foundation

### 0409

#### SLEEP BEHAVIOR OF US AIR FORCE ACADEMY CADETS AROUND AND DURING SPRING BREAK

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**Introduction :** The sleeping habits of college students is generally accepted as less than perfect, and most traditional college students receive far less than the 9+ hour per night ideal. This often causes students to “make up” for lack of sleep using irregular sleeping behaviors at times of vacation. United States Air Force Academy cadets face similar difficulties, but because of the added military pressures and time constraints created by the institution, their sleep deprivation and compensation patterns



may be even more extreme. In this study, 13 USAFA cadets (6 seniors, 7 freshmen) wore actigraph activity monitors to measure their sleep patterns for 19 days surrounding Spring Break. We hypothesized that freshmen would sleep more while on vacation than seniors and that seniors would report less fatigue and less sleep than freshmen. We also hypothesized mood levels would be lowest upon return from Spring Break for both classes.

**Methods :** Participants wore an actigraph for 4 days before, 10 days during, and 5 days after Spring Break vacation. Participants also filled out daily sleep journals that questioned them about their napping behavior, caffeine intake, dreams, and their mood and level of rejuvenation after waking, among other inquiries. We compared freshman and senior sleeping behaviors, as well as the variation of sleep patterns between the three periods of interest.

**Results :** Results indicate freshmen were sleeping significantly less than seniors before and after Spring Break with no differences during Break. Freshmen volunteers slept under 5 hours during the school week while seniors slept over an hour longer. Levels of feeling refreshed were not different between classes. Napping behavior was significantly increased for freshmen during the school weeks examined. Finally, mood levels were lowest for seniors before break with freshmen significantly lower after Break.

**Conclusion :** In sum, all USAFA Cadets in our sample are sleeping far below the recommended levels of 9 hours during the work week with freshmen sleeping less than seniors. Future analyses will attempt to assess the circadian patterns of Cadets in a larger scale project examining how performance might also be impacted.

**Support (optional):** This project was supported by a small grant through the United States Air Force Academy.

## 0410

### INTERNAL MEDICINE RESIDENTS' SLEEPINESS DURING DIFFERENT CALL CONDITIONS

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**Introduction :** Taking call has a significant effect on sleep debt and circadian rhythm of an on call resident. Recently published research has demonstrated the impact of long work hours and extended call (> 24 hours) on the risk of motor vehicle crashes among medical interns and medical errors. This pilot study is one of the first to explore internal medicine residents' experiences during night float call (12 hours) and extended call (>24 hours) using the modified Epworth Sleepiness Scale (ESS-M) and Multiple Sleep Latency Testing (MSLT).

**Methods :** An observational prospective cohort design was used with repeated measures under changing call conditions. Residents were identified and recruited from the Internal Medicine Program at Summa Health System. During call, residents completed the ESS-M at predetermined intervals. Post-call, residents completed a questionnaire about the call and the MSLT in a sleep lab.

**Results :** A total of 16 residents were recruited and completed night float (n=10), first extended call (n=16), and last extended call (n=13). At the end of last call, 31% of the residents responded they did not feel able to perform the duties of a physician well. Yet, only one resident felt unable to drive home safely. Chance of dozing during shift tasks (measured by the ESS-M) increased significantly over the course of all shift types with the greatest increase from shift start reported by residents in the last extended call around 4am (11.3 mean change,  $p < .001$ ). However, no significant differences in sleepiness were found between call types. Significant correlations were found between ESS-M scores and post-call sleepiness measured through MSLT trials for night float ( $r = -.58, p = .04$ ), first call ( $r = -.71, p = .001$ ), and last call ( $r = -.51, p = .04$ ). Mean MSLT

scores were similar for all call types at set intervals.

**Conclusion :** The ESS-M can be considered as an option to evaluate resident sleepiness when MSLT is unavailable. Night float shifts when compared with extended call reveal less resident sleepiness during overnight hours and could result in improved resident performance. The results from this pilot study are being used to design a follow up study to assess sleep patterns in the recently redesigned residency training program schedule with reduced hours for call.

**Support (optional):**

## 0411

### CEREBRAL ACTIVATION DURING 60 HOURS TOTAL SLEEP DEPRIVATION: COMPENSATORY FAILURE ON THE SECOND NIGHT

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**Introduction :** We have previously reported 36 hours total sleep deprivation (TSD) increases brain activation as measured with functional MRI (fMRI) during a verbal learning task. It remains unclear, though, for how many hours of TSD the brain can continue to compensate. Here, we examine this question by measuring brain activation with fMRI throughout 60 hours TSD. We hypothesized the brain would show compensatory recruitment during the first TSD night, but be unable to compensate for a second night of TSD, thus showing decreased activation relative to baseline.

**Methods :** 26 subjects (13F, age=26.6 ±5.4; edu=15.2 ±1.7) participated in a 6 night/day protocol, including two consecutive nights each of the following: baseline sleep, TSD, and recovery sleep. These analyses focus on a verbal learning task performed during fMRI 12 hours after waking from normal sleep (NORM), and at the same time of day after each TSD night (TSD1: 36hrs, TSD2: 60hrs). Due to our specific hypothesis, we analyzed the data for a negative quadratic trend: increased activation from NORM to TSD1 and decreased activation from TSD1 to TSD2. Whole brain alpha = .05.

**Results :** Several brain regions showed the expected negative quadratic change across days, including: bilateral inferior frontal gyrus (left BA45/47, right BA44/45), left inferior (BA40/2) and superior (BA7) parietal lobes, bilateral temporal lobes (left BA39/22, right BA21, right BA22), and several motor-related regions.

**Conclusion :** While the brain can recruit additional resources during task performance after one night TSD, a second TSD night appears to overwhelm the brain's capacity to compensate. These data show there is a failure of the compensatory recruitment response during TSD2 in the same regions previously reported to show increased activation after one night TSD. These findings suggest a functional limit to the brain's ability to compensate for TSD and hold implications for operational settings where TSD extends beyond 36 hours.

**Support (optional):** US Army DAMD17-02-1-0201 UCSD GCRC M01 RR00827

## 0412

### THE ASSOCIATION BETWEEN ASSAYS OF SLEEP DRIVE AND OBJECTIVE VERSUS SUBJECTIVE SLEEPINESS

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## Category H—Sleep Deprivation

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**Introduction :** There is significant variability in self-reported sleep durations amongst the general population, even in the absence of reported daytime sleepiness. We evaluated several assays of “intensity of sleep drive” {total sleep time[TST] and sleep efficiency [SE]} by polysomnography [PSG], time in bed [TIB] as reported by a two-week sleep diary, and difference in weekday and weekend TIB [WE-WD-DIFF] in relation to objective measures of sleepiness versus subjective measures of sleepiness.

**Methods :** A population-based sample of 566 subjects were assessed using an 8.5 hours PSG followed by a daytime multiple sleep latency test (MSLT). A two week sleep diary was obtained prior to the subjects coming into the laboratory. MSLT and Epworth Sleepiness Scale (ESS) scores were grouped into quartiles as objective and subjective assays of sleepiness respectively. These groups were then compared using a one-way ANOVA for TIB, TST, SE, and WE-WD-DIFF.

**Results :** Mean MSLT latency was inversely related to habitual TIB ( $p<.005$ ). On PSG, higher SE and higher TST were associated with lower mean MSLT latencies ( $p<.001$ ). There was an inverse linear dose-response relationship between objective sleepiness and WE-WD-DIFF ( $p<.001$ ). In contrast, there were no robust ( $r<.09$  for all) correlations between any assay of sleep drive and subjective sleepiness as quantified by the ESS.

**Conclusion :** Objective sleepiness had a significant relationship with all assays of sleep drive versus subjective sleepiness which had little correlation with these measures. Clearly, subjective estimates of sleepiness have little relation to the degree of accumulating sleep drive in the general population.

**Support (optional):** MH59338 and MH068372 to Dr Roth and Dr Drake

### 0412

#### EFFECT OF WORK-HOUR REDUCTION ON SLEEPINESS AND WELL-BEING OF RESIDENT PHYSICIANS AND FELLOWS IN THE INTENSIVE CARE UNIT

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**Introduction :** Reducing work-hours for interns in an intensive care unit (ICU) can decrease medical errors, but a systematic assessment of the effects of work-hour reduction on physicians' quality of life and medical errors of other ICU housestaff - residents and fellows - has not been performed. We set out to determine the effect of work-hour reduction on quality of life of ICU housestaff. A secondary objective was to determine the effect of work-hour reduction on patient and physician safety: errors in order entry and sleepy driving in physicians.

**Methods :** We studied 34 residents and 10 fellows from a single center, before-and-after the Accreditation Council of Graduate Medical Education (ACGME) mandated work-hour limitation in July 2003. We collected information regarding quality of life (SF-36), subjective and objective sleepiness (Epworth scores, daily morning Likert sleepiness scores, and multiple sleep latency test), errors in medical orders (chart review), and self-reported sleepy driving.

**Results :** After work-hour reduction, residents reported better quality of life in the vitality, social functioning, and general health domains ( $p<0.05$ ); and errors in orders written by residents and fellows combined, decreased from  $7.5 + 3.4$  to  $2.1 + 0.9$  per 100 patient-days ( $p=0.01$ ). In a multiple regression model, only longest continuous work-hours explained

variance in commission of medical errors ( $r^2=0.18$ ;  $p<0.01$ ). In residents, sleepiness while driving decreased by 48% ( $p=0.02$ ). Despite work-hour reductions, 58% of housestaff were objectively sleepy (mean sleep latency  $< 10$  minutes) before beginning extended-work hour period. After work-hour reduction, 18% of ICU housestaff developed rapid eye movement sleep within 15 minutes of sleep onset.

**Conclusion :** Benefits to quality of life of physicians, physician and patient safety were realized by work-hour reductions that may be due to ACGME-mandated work-hour limitations, but significant levels of sleepiness and errors in order entry remain.

**Support (optional):** American Lung Association of Metropolitan Chicago

### 0413

#### SLEEP DEPRIVATION-INDUCED INCREASES IN ADENOSINE A1 RECEPTOR MRNA AND PROTEIN IN RODENT CHOLINERGIC BASAL FOREBRAIN: A RESETTING OF THE SLEEP HOMEOSTATIC SET POINT

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**Introduction :** In cholinergic basal forebrain (CBF) levels of extracellular adenosine (AD) increase with increasing duration of sleep deprivation (SD), thus increasing inhibition, and promoting sleep, effects mediated by the AD A1 receptor (A1R). A1R activation triggers a sequence of intracellular events leading to the activation of transcription factor NF- $\kappa$ B and increased expression of A1R mRNA. To determine if membrane A1R receptor density changes occurred, we used 6, 12 and 24h of SD.

**Methods :** Male Sprague Dawley rats (250g) were sleep deprived by gentle handling for 6, 12 or 24 h starting from 7AM (lights on 7:00AM; off 7:00PM). Total A1R changes were examined by western blots of whole tissue homogenates using A1R rabbit antibody (1:1000 AbCam, Cambridge, MA) and HRP conjugated anti-rabbit secondary antibody. To detect the membrane receptor density the rat brains were frozen and 30  $\mu$ m thick sections were subjected to receptor autoradiography using 3H-DPCPX.

**Results :** The total (membrane+cytoplasmic stores) A1R protein levels first decreased (-29%,  $p<0.05$ ; N=6) following 6h SD. They increased to control levels following 12 h SD. Of note, membrane receptor density showed a trend-level increase following 12h SD & a more profound and statistically significant increase after 24h SD (fmol/mg protein, SD  $2563+90$  vs controls  $2239+75$ ;  $p<0.04$ , N=6). All experiments showed no cingulate cortex changes.

**Conclusion :** Initially, an increase in extracellular adenosine may result in extensive receptor internalization and subsequent degradation, with immediate replacement of the membrane receptors from the cytoplasmic reserves. This maintains the membrane receptor density but decreases the total A1R protein following 6h SD. The increase in mRNA results in increased A1R translation and production of receptor protein by 12 and 24h SD. This A1R up-regulation will increase the sensitivity of neurons to extracellular adenosine, and hence increasing inhibition and sleep propensity for a given extracellular AD level, a resetting of the homeostatic set point.

**Support (optional):** VA Merit Award (RB) and MH39683(RWM)

## 0414

**SLEEP DEPRIVATION IN THE PIGEON USING THE CONVEYOR-OVER-WATER METHOD**

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**Introduction :** We previously performed prolonged sleep deprivation in pigeons using the disk-over-water method (DOW), which we found less effective in pigeons than in rats. We have developed a new apparatus, termed the conveyor-over-water (COW) to produce more effective sleep deprivation in the pigeon.

**Methods :** The COW operates similarly to the original DOW, with one deprived bird and its yoked control receiving the same stimulation. Fifteen birds were instrumented for recording EEG and EMG. Weight, food, water consumption and subcutaneous temperature were recorded daily. Birds were totally sleep deprived for seven days, allowed to recover for seven days, then deprived for up to 21 days and again allowed to recover.

**Results :** Total sleep time on the first day of deprivation was reduced to an average of 12% of baseline amounts; this was a greater amount of deprivation than achieved using the DOW with pigeons (average of 38% of baseline). REM sleep was almost completely eliminated. Recovery sleep showed increases in REM sleep exceeding 200% of baseline. Energy expenditure and temperature showed trends to increase and decrease, respectively, and to a greater extent in deprived birds compared to controls.

**Conclusion :** The COW is much more effective than the DOW in achieving total sleep deprivation in the pigeon. Pigeons show a pattern of physiological changes similar to those seen in rats, but with less separation between Deprived and Control animals. This may be due to pigeons' ability to change behavioral state quickly; they fall asleep almost instantly when the belt stops. Thus, stimulation rates are high, increasing the control birds' level of deprivation. Our data suggest that birds may be less vulnerable to sleep deprivation and/or the methods used to achieve it in comparison to rats. Alternatively, due to their rapid behavioral state transitions, birds may be better able to acquire enough sleep to avoid the deprivation syndrome seen in rats.

**Support (optional):**

## 0415

**CALORIC INTAKE DURING SLEEP DEPRIVATION WITH OR WITHOUT CIRCADIAN MISALIGNMENT**

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**Introduction :** Sleep loss has been associated with increased appetite. Epidemiological studies have shown that shift workers, who are chronically sleep deprived, have an increased risk of developing obesity. It is not known whether circadian misalignment (sleeping during the daytime) impacts food intake independently of sleep loss.

**Methods :** 18 healthy males (age  $24 \pm 1$  y, BMI  $23.1 \pm 0.5$  kg/m<sup>2</sup>) participated in one of two protocols: extended wakefulness (EW) or extended wakefulness with displaced sleep (EWD). Following 3 baseline nights with 10-h bedtimes, the subjects had 8 days with 5-h bedtimes, either from 0030 to 0530 every night (EW protocol), or with daytime sleep (0900-1400) on the 2nd, 3rd, 5th and 6th nights (EWD protocol). The recovery period (two 12h nights and one 10h night) were identical for both protocols. Food was given as meals (breakfast, lunch and dinner) and the subjects also had free access to various snack items. In the EWD protocol, a midnight meal was served when sleep was displaced.

**Results :** Total sleep time over the 8 days of sleep restriction was similar

in both protocols. Daily energy intake was  $26\% \pm 6\%$  higher during sleep deprivation than during recovery for both protocols ( $p < 0.05$ ). Energy intake during breakfast and lunch was the same for both protocols whereas dinner intake was higher in EW subjects ( $p < 0.05$ ). Energy derived from snacks was higher in EWD subjects ( $p < 0.05$ ), especially during days of daytime sleep. The snacks had higher carbohydrate and lower protein content than the meals ( $p < 0.05$ ).

**Conclusion :** Recurrent partial sleep deprivation resulted in increased total energy intake, with no additional effect of circadian misalignment. However, circadian misalignment was associated with a higher proportion of energy intake from snacks relative to meals. Because snacks are usually of poorer nutritional value, circadian misalignment may aggravate the consequences of the increased appetite due to sleep deprivation.

**Support (optional):** Supported by NIH grant HL-72694 and the National Sleep Foundation (Pickwick Award, Ulf Holmback)

## 0416

**VARIABLES PREDICTING SLEEPING AT THE WHEEL AMONG LONG-HAUL TRUCKERS**

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**Introduction :** Long-haul truckers who fall asleep at the wheel pose a threat to themselves and others who share the highways with them. Motor vehicle crashes are the cause of most occupational deaths among truck drivers. An expected 20% job growth in the U.S. trucking industry between the years 2000-2010 makes this an especially timely issue in occupational safety and health. Predictor variable identification may lead to the design and implementation of meaningful sleep-related motor vehicle crash prevention strategies.

**Methods :** Data were collected in this cross-sectional study from a convenience sample of long-haul truckers (N = 843) at truck shows across the U.S. and truck stops in Kentucky. Binary logistic regression analysis using backward stepwise likelihood ratio methods was used to determine whether the initial eight independent variables predicted the probability of falling asleep at the wheel at either 30 days or 12 months.

**Results :** Statistically significant predictive models were derived for falling asleep at the wheel within 30 days (chi square = 35.32,  $p < .001$ ) and 12 months (chi square = 43.08,  $p < .001$ ). Five predictor variables were retained in the final models: Epworth Sleepiness Scale score  $> 10$ ; driving more than six hours at night; sleeping less than six hours per night and the use of medication to stay awake. Overall rates of correct classification for the final models were 94.6% for sleeping at the wheel within 30 days and 91.3% for sleeping at the wheel within 12 months. Hosmer and Lemeshow Goodness-of-Fit testing indicated a good fit of the models to the data.

**Conclusion :** Findings from this study indicate focus areas for assessment of sleep-related motor vehicle crash risk. Focal points for sleep hygiene education; work redesign strategies and policy changes may be drawn from the study.

**Support (optional):** National Institute of Occupational Safety and Health. 1R01OH07931 (Debra G. Anderson PhD, Principal Investigator)

0417

**THE INABILITY TO FORM NEW HUMAN EPISODIC MEMORIES WITHOUT SLEEP**

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**Introduction :** Although sleep has been implicated in post-training memory consolidation, few studies have investigated the requirement of adequate pre-training sleep for initial memory encoding/formation. Here we investigate the impact of sleep deprivation on human episodic memory formation of emotional and non-emotional material.

**Methods :** Subjects (n=20) were either sleep deprived for 38hr or allowed to sleep normally before performing an incidental encoding session containing positive, negative, and neutral stimuli. Following two subsequent nights of recovery sleep, subjects returned for an unexpected recognition task to evaluate encoding.

**Results :** Overall, subjects in the sleep-deprived condition exhibited a 40% impairment in memory retention relative to subjects who slept normally ( $p < 0.01$ ). When these data were separated into the three emotional categories, the encoding deficit remained, although the magnitude was different. There was a severe disruption of encoding for neutral and especially positive emotional memory in the sleep-deprived group, exhibited a 59% retention deficit relative to the sleep-control condition ( $p < 0.01$ ). Most interesting, however, was the resistance of negative emotional memory to sleep deprivation, showing a markedly smaller (19%) and non-significant encoding impairment.

**Conclusion :** These findings indicate that a single night of sleep deprivation profoundly disrupts the ability to form new human episodic memories, resulting in significantly worse retention two days later. Although the detrimental effects of sleep deprivation were directionally consistent across memory types, the most pronounced impact was on the formation of emotionally positive, and to a lesser degree, neutral memories, while the formation of negative memories appears more resistant to the effects of prior sleep deprivation. Most recently we have begun replicating this paradigm using event-related fMRI. Early pilot data suggesting these memory encoding deficits are associated with dramatic impairments in hippocampal function under conditions of sleep deprivation, despite overcompensatory activation in dorsolateral prefrontal regions.

**Support (optional):** NIH; NIMH NIDA

0418

**NEUROGENESIS AND SLEEP DEPRIVATION: POSSIBLE ROLE OF GROWTH HORMONE**

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**Introduction :** Sleep deprivation induces a decline in neurogenesis in the dentate gyrus (DG) of the hippocampus, which, in turn, is associated with an impair in hippocampal-dependent learning. We tested whether the deleterious effects of sleep restriction on neurogenesis in the hippocampus of the rat is prevented by growth hormone (GH) administration, which is required for normal development of the mammalian body and reported recently, for the brain. GH is also a sleep factor related to slow wave sleep induction.

**Methods :** In order to evaluate the neurogenesis, Wistar male rats (250-300 g) were injected with BrdU (50 mg/Kg/day for 7 days, i.p.). Simultaneously, one group of animals were injected with two different doses of GH (5 ng/ml or 10 ng/ml) or vehicle, while a third animal group

was additionally sleep deprived (SD) per 96 h (day 4 to day 7). After this experimental protocol, brain slices were obtained and processed for detection of new born neurons using a Kit I for BrdU staining. Double labeling (NeuN) was used by identify neuronal phenotype. Brain samples were analyzed by Confocal microscopy and the number of the new neurons were counted using a digital analyzer.

**Results :** Low doses of GH (5ng) induced an increase in BrdU/NeuN positive cells in DG (+56% vs. control). In contrast, the administration of high doses (10ng/ml) had the opposite effect on the number of BrdU/NeuN positive cells. SD reduced the number of BrdU/NeuN positive cells (-35% vs. control). Interestingly, the reduction of the new neurons induced by SD was prevented by GH administration (5 ng/ml) but not per high doses of GH.

**Conclusion :** These findings suggest that GH induce neurogenesis in the DG of the adult rat. In addition, GH prevents the deleterious effect that the SD has on the neurogenesis, suggesting a protective role of GH.

**Support (optional):** This work was supported by PROMEP grant No. UVER-PTC-118

0419

**IMPACT OF ONE WEEK OF PARTIAL SLEEP DEPRIVATION WITH OR WITHOUT CIRCADIAN MISALIGNMENT ON THE PLASMA LEVELS OF C-REACTIVE PROTEIN**

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**Introduction :** Both acute and partial sleep deprivation increases C-reactive-protein (CRP), an inflammatory marker known to be a predictor of cardiovascular risk. Since shift workers have an increased risk of developing cardiovascular disease, we sought to determine if circadian misalignment (occasional shift of the sleep period to daytime) has intrinsic effects on CRP concentrations that exceed those of sleep loss alone.

**Methods :** 18 healthy males (aged  $24 \pm 1$  yrs, BMI  $23.1 \pm 0.5$  kg/m<sup>2</sup>) participated in one of 2 protocols. After 3 nights of 10 hours in bed (rested condition, bedtimes: 2200 to 0800), the subjects were submitted to 8 nights of 5 hours in bed (sleep restriction), either with the sleep period always centered at 3 am (bedtimes: 0030 to 0530, n=10) or with the sleep period shifted to 0900 to 1400 on 4 days (short sleep days 2,3,5,6; n=8). The two protocols were designed such that the subjects lost the same amount of sleep. CRP levels were measured every 4 hours for 24 hours at the end of the rested condition and at the end of sleep restriction.

**Results :** CRP levels increased significantly from the rested condition to the sleep restriction condition in both protocols (by nearly 70% in the protocol without sleep displacement,  $p = 0.0085$  and by nearly 150% in the protocol with sleep displacement,  $p = 0.0052$ ). The difference between the two protocols was close to statistical significance ( $p=0.065$ ).

**Conclusion :** One week of sleep restriction to 5 hours of sleep per day is associated with a marked increase in CRP levels, irrespective of the timing of the sleep period. It is possible that circadian misalignment may exacerbate the increase in CRP caused by sleep loss alone.

**Support (optional):** Supported by NIH grant HL-72694 and the National Sleep Foundation (Pickwick Award, Ulf Holmback).

## 0420

## OBJECTIVE AND SUBJECTIVE SLEEPINESS ON LATE NIGHTS WITH AND WITHOUT ALCOHOL

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**Introduction :** We examined effects of late nights with and without alcohol on objective and subjective sleepiness. We hypothesized all measures would show an increase with time awake and with alcohol, but that levels of subjective sleepiness would not predict objective sleepiness.

**Methods :** Twenty-nine adults (males=9) ages 21 to 25 years (M=22.6, SD=1.2) spent one week on an at-home schedule (of 8.5 or 9 hours) followed by 3 in-lab nights: Adaptation, Placebo, and Alcohol (non-consecutive, separated by 5 to 7 nights on stabilized schedule). Alcohol (vodka; .54 g/kg for men; .49 g/kg for women) was consumed over 30 minutes ending 1 hour before stabilized bedtime; the same quantity of placebo beverage was given identically on Placebo night. Sleep Latency Tests (SLTs) occurred 30, 120, and 210 minutes after alcohol/placebo ingestion (15, 16.5, and 18 hours after waking). Stanford Sleepiness Scales (SSS) and Visual Analog (VAS) Sleepiness scales were completed before each SLT.

**Results :** Mean Breath Alcohol Concentration for consecutive Sessions on the Alcohol night were .041 (SD=.013), .033 (SD=.009), and .012 (SD=.009) grams %. Analyses for the SLT, SSS (scale 1 to 7), and VAS (scale 1 to 100) showed participants became significantly sleepier on each variable across Sessions (time awake). Mean values for consecutive Sessions were: SLT = 6.5, 3.5, 3.2 minutes, SSS = 4.3, 5.0, 5.7, and VAS = 60, 74, 82. Only the SSS showed higher levels of sleepiness with alcohol (Placebo M = 3.9, 4.9, 5.6; Alcohol M = 4.6, 5.5, 5.7). No interactions were significant. Correlations between subjective sleepiness measures were significant (SSS versus VAS, Placebo  $r = 0.67$ , .52, .66; Alcohol  $r = .75$ , .69, .52); subjective sleepiness was not significantly correlated with SLTs.

**Conclusion :** As predicted, all sleepiness measures increased with time awake and subjective sleepiness was not predictive of objective sleepiness. Only SSS increased with Alcohol.

**Support (optional):** Research supported by AA 13252

## 0421

## SLEEPINESS IN ACADEMIC AND PRIVATE PRACTICE PHYSICIANS

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**Introduction :** Restricted sleep in residents due to prolonged work hours leads to increased medical errors, motor vehicle crashes, and depression. Here, we determine prevalence of sleepiness in attending physicians, average hours worked per week, and hours slept when “on call” or “not on call.”

**Methods :** We queried physicians’ opinions on prolonged work hours by asking them to complete an anonymous survey that included the Epworth Sleepiness Scale (ESS) and an 18-item semi-quantitative questionnaire measuring the effects of sleepiness on learning and cognition, job performance, and personal life.

**Results :** To date, 108 physicians responded (42 academicians and 66 private practitioners). Respondents were primarily white (88%) and male

(74%). Forty-two percent were (46-55 years and 37% had practiced 11-20 years. Mean score for the ESS was 7.7 (+/- 3.9) with 31% having excessive sleepiness (ESS>10). Mean duration of hours worked per week was similar in academicians (56.9 hours) and private practitioners (57.3 hours). Overall, 13% reported > 80-hour workweek. Mean sleep durations “not on call” (7.05 hours) and “on call” (5.45 hours) were similar between academicians and private practitioners. A majority of physicians (72%) believed work hour limitations would be “beneficial to the quality of life of practicing physicians”. A majority of physicians (61%) believed work hour limitations would be “beneficial to the quality of patient care provided by practicing physicians.” Few physicians (7%) would consider a stimulant agent e.g. Modafinil/Provigil or Methylphenidate/Ritalin to aid wakefulness during work.

**Conclusion :** Excessive sleepiness (ESS score >10) was prevalent (31%) in these attending physicians and 13% exceeded recommended 80-hour workweek restrictions for resident physicians. However, attending physicians appeared to recognize the possible effects of heavy work hours on physician quality of life and quality of patient care. Further research should evaluate specific effects of sleepiness and long work hours in attending physicians.

**Support (optional):** Division of Sleep Medicine and Department of Internal Medicine, Eastern Virginia Medical School

## 0422

## INCREASED INDUCIBLE HEAT SHOCK PROTEIN-32 MARKS OXIDATIVE STRESS INDUCED BY SLEEP DEPRIVATION

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**Introduction :** Sleep deprivation (SD) is widely believed to produce adverse health effects. Specific sites or mechanisms affected by SD have not been identified, nor specific biomarkers discovered. Our recent studies have shown that SD results in oxidative stress in the liver and the heart in association with cell injury of an unspecified origin. Further, recovery sleep increases enzymatic antioxidant activities in both the liver and the heart, and normalizes antioxidant content in liver. The purpose of the present study was to build on these findings by measuring heat shock protein-32 (hsp32) in the liver, the main detoxifying organ. Hsp32, also known as inducible heme oxygenase, is a biomarker of cellular stress associated with metabolism of heme proteins that can be toxic to cells.

**Methods :** SD was produced in rats by the Rechtschaffen-Bergmann method for 5 or 10 days, which was tolerated and produced hypercatabolism and hyperphagia. Arousal conditions entailed an ambulatory requirement of 6 sec upon sleep onset. Comparisons included yoked (Y) rats with disrupted sleep due to the same locomotor condition, and undisturbed baseline control (BC) rats. Other 10-day SD and Y rats were studied after 2 days of recovery sleep. Subjects numbered 6-8 per group. Hsp32 detection by Western blot chemiluminescence was quantified by densitometry, indexed to standards, and tested for group differences by planned comparisons and  $P = 0.016$ .

**Results :** Liver hsp32 detection was 40% greater in 10-day SD rats than in BC and 10-day Y rats (index of 53% of standard vs. 37 and 38%, respectively; each  $P < 0.016$ ). This same increase (i.e., 55% of standard) also was present in SD rats allowed recovery sleep. SD and Y rat values of liver hsp32 at 5 days were not statistically different and are considered intermediate, indexed at 43-46%. Y rats during the recovery phase also tended to have intermediate values, but these were not statistically different from those of other groups.

**Conclusion :** Hsp32 is a biomarker of cellular oxidative stress, and its induction indicates potential cell injury and activation of antioxidant

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mechanisms by sleep deprivation. These findings provide evidence that sleep deprivation effects may be localized and observed at the level of cell function by biochemical changes associated with prooxidant-antioxidant pathways and detoxifying activities. A high level of induced liver hsp32 during the recovery phase suggests that either recovery was incomplete or recuperation induced new oxidative burdens.

**Support (optional):**

**0423**

### ATTENTION TO DRIVING ACROSS A NIGHT OF SLEEP DEPRIVATION

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**Introduction :** Although it is known that driving while fatigued contributes to traffic accidents, few studies in the literature have examined driving skills across repeated testing sessions under sleep deprivation conditions. The purpose of the current study was to document the effects of 26 hours of sleep deprivation on performance in a driving simulator across 5 separate testing sessions.

**Methods :** Twenty-three volunteers (mean age:  $20.4 \pm 2.18$ ) were sleep deprived for 26 hours. During the last 17 hours of sleep deprivation, the volunteers completed a 20 minute driving task 5 times, once per testing session (8 - 10:30PM, 10:45 - 1:15AM, 1:45 - 4:15AM, 4:30 - 7:00AM, and 7:30 - 10AM). The driving task took place in a high-fidelity driving simulator. Lane keeping ability, speed keeping ability, and the position of the accelerator pedal were monitored during a straight portion of the track about 8 minutes into the drive. Other tasks were also completed in each testing session. All tasks were counter-balanced.

**Results :** Repeated-measures ANOVAs were completed on the data. The participants showed a significant increase in variability in changes in lane position across the 5 testing periods ( $p=.000$ ). The participants also showed a significant increase in mean velocity across the 5 testing periods ( $p=.000$ ) with a corresponding significant increase in the mean accelerator pedal position (i.e., progressively closer to the floorboard).

**Conclusion :** The results indicated that as participants became more sleep deprived they had increasing difficulty maintaining the correct lane position and increased their driving speed. These data show that attention to driving decreases significantly across several testing sessions in a single night of sleep deprivation. The compounded effect of increasing speed while gradually drifting out of the driving lane, increases the safety risk involved when driving while fatigued.

**Support (optional):** This research was funded by the Department of Defense through the Center for Advanced Study of Language, University of Maryland.

**0424**

### THE DIFFERENTIAL EFFECTS OF SLEEP DEPRIVATION AND RECOVERY ON BEHAVIORAL PERFORMANCE IN THE YOUNG AND ELDERLY

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**Introduction :** While evidence has shown that deficits in cognitive performance associated with sleep deprivation subside with one night of recovery sleep in the young, the response in the elderly has yet to be defined. Age related changes in recovery from sleep deprivation were examined using tasks of response inhibition (RI) and psychomotor vigilance (PVT).

**Methods :** Young ( $25.6 \pm 3.7$  yo,  $n = 8$ ) and elderly ( $67.8 \pm 5.7$ ,  $n = 9$ )

subjects were given a baseline night of 9 hours time in bed (TIB) followed by a 38 hour sleep deprivation (SD) period and 10 hours TIB recovery sleep. Performance was assessed every two hours (8:30, 10:30, 12:30, 14:30) in baseline, SD, and recovery conditions. These 4 timepoints were averaged for performance in each condition. PVT lapses > 500ms.

**Results :** The elderly responded slower than the young on both tasks, and both groups exhibited significantly slowed reaction times (RT) in the SD as compared to the baseline and recovery conditions (For “condition”  $p<0.005$ , “age”  $p<0.01$  rm-ANOVA). RT variability in the young increased to a greater extent than in the elderly during SD (“sleep\*age”  $p<0.01$  rm-ANOVA). PVT lapses were more prevalent in the elderly ( $p<0.001$ ), and the elderly tended to have a greater increase in lapses in the SD condition. For the RI task, inappropriate responses increased in both groups in the SD condition (“condition”  $p<0.005$ ), and the elderly did not return to baseline levels after recovery.

**Conclusion :** These data suggest that the elderly are more prone to lapses in SD and slower to recover inhibitory control than the young. While 10 hours TIB is sufficient to return both groups to baseline performance levels on the PVT, it may be insufficient to return elderly inhibitory control to baseline levels. Thus, the extent of performance recovery differs with age and task.

**Support (optional):** Supported by P01 AG11412, NCR-00048, R01 HL67604, AG13854, F31 MH074291

**0425**

### EFFECTS OF CHRONIC SLEEP RESTRICTION ON INTERLEUKIN-1BETA AND TUMOR NECROSIS FACTOR-ALPHA IN THE RAT BRAIN

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**Introduction :** Chronic sleep restriction (CSR) increases inflammatory cytokines such as tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and interleukin-6 in human blood. However, it is unclear whether brain cytokines are altered by CSR. Therefore, we determined levels of interleukin-1beta (IL-1 $\beta$ ) and TNF- $\alpha$ , two best-characterized cytokines in sleep regulation, in different brain regions after CSR in rats.

**Methods :** Twenty male Sprague-Dawley rats were implanted with EEG and EMG electrodes, and maintained on 12:12 hour light-dark cycles. EEG and EMG were recorded continuously for 7 days. The first day served as the baseline. In the following 6 days, CSR was performed with disc treadmill method. The sleep onset (detected by the predetermined EEG and EMG thresholds) triggered brief rotations of the cage bottom, which woke up the animals. Within each 120-min block during CSR, the CSR animal was allowed to sleep for 60% and 20% of time during the daytime and nighttime, respectively. Each CSR animal was matched with a control animal, which received the same amounts of physical stimuli applied in the last 12 min in each 120-min block. At the end of CSR, the animals were sacrificed by decapitation. IL-1 $\beta$ , and TNF- $\alpha$  levels were measured by ELISA method in the brain samples from different regions.

**Results :** After CSR, IL-1 $\beta$  levels were increased in the frontal cortex ( $+13.29 \pm 2.69$ ,  $p<0.001$ ), occipital cortex ( $+7.89 \pm 2.26$ ,  $p<0.01$ ) and brainstem ( $+11.15 \pm 2.27$ ,  $p<0.0005$ ), decreased in the parietal cortex ( $-15.55 \pm 3.18$ ,  $p<0.001$ ) and temporal cortex ( $-17.05 \pm 5.52$ ,  $p<0.02$ ), and not altered in the hypothalamus. After CSR, TNF- $\alpha$  levels were significantly increased in the frontal cortex ( $+18.37 \pm 7.15$ ,  $p<0.04$ ), occipital cortex ( $+29.32 \pm 6.49$ ,  $p<0.002$ ), hippocampus ( $18.79 \pm 7.17$ ,  $p<0.03$ ) and brainstem ( $+53.04 \pm 19.78$ ,  $p<0.03$ ), decreased in the parietal cortex ( $-26.84 \pm 7.22$ ,  $p<0.005$ ), temporal cortex ( $-34.09 \pm 6.72$ ,  $p<0.001$ ) and hypothalamus ( $-35.59 \pm 6.37$ ,  $p<0.0004$ ).

**Conclusion :** Our results indicate that CSR influences brain IL-1 $\beta$  and

TNF- levels in a region-specific manner.

**Support (optional):**

**0426**

**COMPARISON BETWEEN AUDITORY AND VISUAL PSYCHOMOTOR VIGILANCE TASK PERFORMANCE DURING SLEEP DEPRIVATION**

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**Introduction :** It has been reported that optimum response times (10% fastest reaction times) are faster for auditory reaction time versus visual reaction time performance during sleep deprivation. The aim of the current study was to compare metrics of auditory and visual versions of the psychomotor vigilance task (PVT) at baseline and in sleep deprived subjects.

**Methods :** Forty-one healthy participants (27 men and 14 women), aged  $30.8 \pm 8.6$  (Mean  $\pm$  SD), were scheduled to sleep 8-h per night for 3 baseline weeks at home. Sleep times were verified by sleep diaries, call-ins to a time stamped recorder and by actigraphy for at least one week prior to entry into the laboratory. Baseline PVT performance metrics were assessed across 3-6 baseline days during which subjects were scheduled to sleep for 8 h per night at their habitual time. This was followed by 40-h of sleep deprivation. Subjects performed 10 min auditory (N=21) or visual (N=20) versions of the PVT every 2-h during scheduled wakefulness. Subjects responded to over 3000 reaction time stimuli on average during baseline days. Lapses were calculated based upon the standard 500 msec cutoff and also based on individually defined lapse cutoffs calculated as two standard deviations more than the individual subjects' mean at baseline. The sleep deprivation analysis compared auditory (aPVT) and visual (vPVT) performance at 2-4 versus 26-28 hours awake, thus controlling for circadian phase.

**Results :** Individually defined lapse cutoffs were on average  $\sim 100$  msec faster for aPVT compared to vPVT performance during baseline days. Repeated measures ANOVA showed that the number of lapses and median reaction time performance for aPVT and vPVT significantly worsened during sleep deprivation ( $P < 0.05$ ). There were no significant differences using a standard 500 msec ( $P = 0.17$ ) or individually determined lapse cutoff ( $P = 0.47$ ) for the number of lapses on aPVT versus vPVT during sleep deprivation. There was however a significant difference in the standard deviation of reaction time performance with aPVT being smaller than that for vPVT during sleep deprivation ( $P < 0.05$ ). Lastly, there was a non-significant trend for faster median reaction times on average for aPVT versus vPVT during sleep deprivation ( $P = 0.08$ ).

**Conclusion :** These preliminary analyses show that auditory and visual versions of the PVT are sensitive to the effects of one night of sleep deprivation and that auditory performance is less variable than visual performance.

**Support (optional):** Research Supported by the University of Colorado.

**0427**

**EXPERIMENTAL SUPPRESSION OF SLOW WAVE SLEEP WITHOUT CHANGE IN TOTAL SLEEP TIME IS ASSOCIATED WITH DECREASED INSULIN SENSITIVITY AND INCREASED DAYTIME SYMPATHETIC ACTIVITY**

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**Introduction :** Sleep disordered breathing (SDB) is characterized by frequent microarousals and reductions in slow wave sleep (SWS). Abnormal sympathetic output has been proposed as the mediating mechanism in the link between SDB and insulin resistance. Previously, we have shown that

experimental suppression of SWS without change in total sleep time is associated with decreased insulin sensitivity in healthy young adults. We investigated the role of sympathovagal balance in the decreased insulin sensitivity in these healthy young adults.

**Methods :** Nine healthy lean adults (mean age:  $24 \pm 1$  years; 4 women) were studied under two conditions (baseline, SWS suppression) in a randomized order. Subjects had no sleep complaints. Sleep disorders were ruled out by polysomnography. Undisturbed sleep was recorded on two consecutive baseline nights (B1, B2). Sleep was continuously monitored and acoustic stimuli (1000-2000Hz, 40-110dB) were administered during NREM sleep to induce microarousals and suppress SWS for three consecutive nights (S1, S2, S3). At the end of each condition, daytime continuous resting electrocardiography was recorded. Spectral analysis of heart rate variability was computed (PRANA software, Phitools) by fast Fourier transform for cardiac sympathetic modulation i.e. low frequency (LF) and parasympathetic modulation i.e. high frequency (HF) bands using a 5-min segment that was free of ectopy and artifacts. Normalized high (HF<sub>n</sub>) and low (LF<sub>n</sub>) frequency components were calculated using the percentage of each band power to their sum.

**Results :** Sleep fragmentation decreased the amount of SWS (min;  $71.8 \pm 5.1$  on baseline vs  $6.5 \pm 2.0$  on S1,  $9.8 \pm 3.0$  on S2,  $10.6 \pm 1.7$  on S3;  $p = 0.0002$ ) despite no differences in total sleep time between study conditions (min;  $466.8 \pm 6.5$  on baseline vs  $458.1 \pm 4.2$  on S1,  $467.0 \pm 2.0$  on S2,  $455.9 \pm 3.1$  on S3;  $p = 0.20$ ). HF<sub>n</sub> was decreased ( $39.3 \pm 3.7$  vs  $32.1 \pm 4.3$ ,  $p = 0.038$ ), LF<sub>n</sub> was increased ( $60.7 \pm 3.7$  vs  $67.9 \pm 4.3$ ,  $p = 0.038$ ) and sympathovagal balance (LF/HF) was increased ( $1.8 \pm 0.3$  vs  $2.6 \pm 0.5$ ,  $p = 0.02$ ) with SWS suppression compared to baseline. Respiratory rate and heart rate were not different between study conditions.

**Conclusion :** The current findings provide the first evidence that, in healthy young adults, disruption of sleep quality with reductions of SWS that are typical of normal ageing and SDB is associated with increased daytime sympathetic activity.

**Support (optional):**

**0428**

**MOTIVATION AND ENJOYMENT FOLLOWING TASK PERFORMANCE DURING A NIGHT OF SLEEP DEPRIVATION**

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**Introduction :** Although the effects of short term sleep deprivation on performance on cognitive and vigilance tasks have been researched, little is known about the effect of sleep deprivation on subjective measures. The purpose of this study was to determine the relationship between motivation and enjoyment following a cognitive and vigilance task under sleep deprivation conditions.

**Methods :** Twenty-six participants (mean age:  $20.3 \pm 2.09$ ) were paid to remain awake for one night. The automated performance test system (APTS) consisted of four portions: math processing, code substitution, grammatical reasoning and memory search. The psychomotor vigilance task (PVT) consisted of pushing a button as soon as numbers flashed on a digital display located on the handheld device. After completing each task, participants were asked to complete a visual analog scale (VAS) for the previous task, measuring various subjective variables such as perceived alertness, motivation, enjoyment, and interest. The participants completed both tasks five times during the night (8 - 10:30PM, 10:45 - 1:15AM, 1:45 - 4:15AM, 4:30 - 7:00AM, and 7:30 - 10AM). All tasks were counter-balanced.

**Results :** Repeated-measures ANOVAs were completed on the APTS, PVT, and VAS scores. While performance remained stable on the APTS across the testing sessions, performance on the PVT decreased significantly ( $p = .000$ ). In contrast, the average VAS score for motivation and

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enjoyment decreased significantly following both the APTS and PVT tasks across the night ( $p=.000$  for all comparisons).

**Conclusion :** The current data indicate that regardless of task complexity, motivation and enjoyment are negatively affected by one night of sleep deprivation. However, despite a decrease in motivation and enjoyment, participants remained capable of completing the APTS task but were not able to maintain performance levels on the PVT across the testing sessions, indicating that the type of task may be a better indicator of performance than motivation or enjoyment.

**Support (optional):** This research was funded by the Department of Defense through the Center for Advanced Study of Language, University of Maryland.

### 0429

#### EFFECTS OF SLEEP DEPRIVATION ON ESTIMATED PERFORMANCE AND MOTIVATION FOLLOWING LANGUAGE TASKS

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**Introduction :** Few studies have examined the effects of stressors such as sleep deprivation on language performance and subjective estimates related to performance. The purpose of the current study was to examine subjective measures related to language performance across a night of sleep deprivation.

**Methods :** Twenty-six participants (mean age =  $20.3 \pm 2.09$ ) were paid to remain awake for 28-hours. Participants completed 3 language tasks as part of a battery of tasks five times during the night (8 - 10:30PM, 10:45 - 1:15AM, 1:45 - 4:15AM, 4:30 - 7:00AM, 7:30 - 10AM). All tasks were counter-balanced. The verbal portion of the SAT provided reading comprehension, grammar, and analogies problems. The Rapid Automatized Naming (RAN) task presented 245 pictures (from a set of 25) for participants to name. The Speech Perception in Noise (SPIN) task was an auditory task which required participants to write down the last word for each of 50 sentences. After each task administration, participants completed Visual Analogue Scales (VAS) focused on a variety of subjective measures, including motivation and performance.

**Results :** Repeated-measures ANOVAs were completed on the performance and subjective data. Performance on the SAT decreased significantly across the night ( $p=.000$ ) whereas performance remained stable for both RAN and SPIN. In contrast, subjective motivation decreased significantly across the night for the SAT, RAN, and SPIN ( $p=.000$  for each). Estimated performance also decreased significantly for the SAT ( $p=.000$ ), RAN ( $p=.001$ ), and SPIN ( $p=.000$ ).

**Conclusion :** Although participants felt that their performance decreased on each of the tasks, their performance only decreased on the SAT. Thus, due to the similar decreases in subjective ratings of motivation and estimated performance across the night, it appears that participants' estimated performance may reflect processes that are independent of actual performance on some types of task.

**Support (optional):** This research was funded by the Department of Defense through the Center for Advanced Study of Language, University of Maryland.

### 0430

#### SLEEPINESS AFFECTS ATTENDING PHYSICIANS BOTH PROFESSIONALLY AND PERSONALLY

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**Introduction :** Negligible data exists concerning the effects of limited sleep on attending physicians' ability to function. We hypothesized that practicing physicians would note work errors, driving concerns and negative effects on personal life secondary to rigorous work hours and reduced sleep.

**Methods :** We administered an anonymous / validated survey to Eastern Virginia Medical School academicians and area private practitioners. The survey incorporated demographic and opinion questions, the Epworth Sleep Scale (ESS) and an 18-item questionnaire querying effects of sleep loss at work, while driving and at home.

**Results :** To date, 108 physicians (42 academic physicians and 66 private practitioners) have responded. Respondents were primarily white (88%), male (74%), 46 to 55 in age (42%), and had practiced 11-20 years (37%). The 24.1% who admitted to making errors at work because of sleep loss/fatigue had a higher mean ESS (9.0 vs. 7.3,  $p=0.05$ ). Thirty-three percent admitted writing an incorrect order secondary to sleepiness and 3.9% stated they might fall asleep while examining a patient. Seventy-four percent heard of their colleagues making mistakes due to sleep loss and fatigue, and 73.1% agreed that their thinking was affected by sleep loss. The 47% who worried about driving post-call had significantly higher ESS scores (9.3 vs. 6.3,  $p=.0002$ ). Only 58.8% could recognize being too tired to drive home. Fifty-five percent agreed that sleep loss/fatigue had a major effect on their life. Women were more apt to acknowledge such consequences. Only 60.8% believed their family understood their demanding job and sleep needs.

**Conclusion :** Similar to resident physicians, data indicate that long work hours and reduced sleep compromise attending and private practice physicians' performance. Academicians and private practitioners also acknowledge potential deleterious effects of sleep loss and fatigue in their practices and home lives. Whether work hour limitations are a practical and effective intervention will require investigation.

**Support (optional):** Division of Sleep Medicine and the Department of Internal Medicine, Eastern Virginia Medical School

### 0431

#### GABAERGIC AND GLUTAMATERGIC NEURONS IN THE PERIFORNICAL LATERAL HYPOTHALAMIC AREA EXHIBIT DIFFERENTIAL FOS-EXPRESSION AFTER SLEEP DEPRIVATION VS. RECOVERY SLEEP

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**Introduction :** The perifornical-lateral hypothalamic area (PF-LHA) is involved in the regulation of behavioral arousal. It contains various cell types including neurons containing hypocretin, melanin-concentrating hormone, GABA, and glutamate. We hypothesized that increased glutamatergic tone within PF-LHA contributes to the activation of PF-LHA neurons during waking whereas increased GABAergic tone within PF-LHA contributes to the suppression of PF-LHA neurons during sleep.

**Methods :** Experiments were conducted on 10 male Sprague-Dawley rats. In one group ( $n=5$ ) rats were allowed to sleep normally (13.30 - 15.30 hr) after six hrs of sleep deprivation (7.30 - 13.30 hr, lights-on at 7.00 hr). A second group of 5 rats was kept awake for 2 hrs (13.30 - 15.30 hr). At the end of the experiments rats were immediately sacrificed and the brain tissues were processed for Fos-protein immunoreactivity (Fos-IR), and markers for GABAergic and glutamatergic neurons.

**Results :** The number of Fos-IR neurons in PF-LHA and dorsal posterior



hypothalamic area (DPHA) was higher in sleep-deprived rats as compared to rats that were allowed to sleep after sleep-deprivation. The percentage of Fos-IR in GABAergic neurons as compared to total Fos-IR neurons was higher in rats following recovery sleep as compared to sleep-deprived rats (PF-LHA:  $55.0 \pm 3.5\%$  vs.  $21.4 \pm 4.3\%$ ,  $P = 0.0069$ ; DPHA:  $42.8 \pm 2.6\%$  vs.  $16.4 \pm 3.3\%$ ,  $P = 0.0059$ ). The percentage of Fos-IR in glutamatergic neurons was higher in awake rats as compared to sleeping rats (PF-LHA:  $56.4 \pm 1.1\%$  vs.  $36.8 \pm 1.8\%$ ,  $P = 0.0001$ ; DPHA:  $46.7 \pm 3.0\%$  vs.  $26.3 \pm 2.6\%$ ,  $P = 0.0007$ ).

**Conclusion :** These results indicate that in PF-LHA and DPHA a significantly higher number of glutamatergic neurons are active during waking versus sleep while a significantly higher number of GABAergic neurons are active during sleep versus waking.

**Support (optional):** NS-050939, MH-47480, HL-60296, and MH-63323.

## 0432

### THE EFFECTS OF SHORT-DURATION REM DEPRIVATION ON ACQUISITION AND REVERSAL OF A SPATIAL LEARNING TASK

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**Introduction :** Studies have indicated that rapid eye movement sleep deprivation (RD) impairs acquisition of spatial memory tasks. However, many of these studies suffer from potential confounds, including testing or training animals while sleep deprived or using extended periods of RD which may impair performance by increasing stress. The present study was designed to determine the influence of short-term RD on the acquisition and reversal of a spatial learning task while controlling for these types of confounds.

**Methods :** Sixteen rats were trained in the Morris water maze, in which they were required to learn the location of a submerged, hidden platform in a large tank of water. For each training trial, rats were placed into the tank of water at varying locations and the latency to locate the submerged platform was recorded. Rats were given 4 training trials per day for 3 days. Eight rats were subjected to 6 hours of RD (accomplished by the flowerpot method) immediately after the completion of each training day. The remaining eight rats were exposed to a control condition in which they were placed on a larger platform, thereby allowing for normal REM. After completion of the training phase, the location of the platform in the tank was reversed and rats were given 4 reversal trials per day for 3 days to learn the platform in its new location. There was at least a 48 hour interval between all sessions to insure that animals were not tested while sleep deprived.

**Results :** All animals demonstrated a reduction in latency to locate the platform as training progressed, but REM-deprived and control animals did not differ. There was a transient increase in latency to locate the platform after reversal but latencies quickly decreased. Again, REM-deprived and control rats showed no differences in latency to locate the platform.

**Conclusion :** There are several potential reasons for the discrepancy between these results and those that have been observed previously. First, it is possible that the consolidation of this spatial learning task is unaffected by short-term RD. Second, this difference may be due to procedural factors, such as the duration and timing of RD. Further research will be necessary to determine the possible reasons for this discrepancy.

**Support (optional):**

## 0433

### SUPPRESSION OF PARADOXICAL SLEEP MEDIATED BY ALCOHOL IN MALE RATS

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**Introduction :** Sleep disorders are among the host of consequences of alcohol abuse and is observed in human beings as well as in rats. The specific central mechanisms involved in the effects of alcohol over the sleep pattern have not yet been elucidated. The purpose of this study was to investigate the effects of several doses of alcohol in the sleep of rats, and examine the participation of the cholinergic system in the alteration of the sleep pattern when associated to alcohol.

**Methods :** After basal (48h) electrocorticalgraphic recording of 48 rats, these subjects were administered either vehicle orally or 0.5; 1.0; 2.0; 3.0 e 4.0 g/kg of alcohol orally. Pilocarpine and atropine (2,5; 5,0 and 10mg/kg) were administered subcutaneously prior to the administration of alcohol. Immediately after the administration of alcohol, the animals were submitted to electrocorticalgraphic recording for 48 hours.

**Results :** An acute dose of 4 g/kg of alcohol induced the suppression of paradoxical sleep in relation to the vehicle group and baseline recording. The concomitant administration of different doses of pilocarpine (a cholinergic antagonist) associated to alcohol sustained the inhibition of paradoxical sleep. In contrast, atropine (a cholinergic antagonist) when associated to alcohol increased paradoxical sleep during the first 3h of recording.

**Conclusion :** Results demonstrate that alcohol causes alteration in the sleep pattern of rats, notably, the suppression of paradoxical sleep, most likely due to the participation of the cholinergic system.

**Support (optional):** AFIP, FAPESP, CEPID

## 0434

### TOTAL SLEEP TIME AFFECTS SEIZURE FREQUENCY IN PATIENTS WITH REFRACTORY EPILEPSY

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**Introduction :** Despite numerous reports of the activating effect of sleep deprivation on epilepsy over several decades, virtually no studies have investigated the role of chronic partial sleep deprivation in this vulnerable population. The purpose of this study is to correlate self-reported total sleep duration (TSD) with seizure frequency in refractory epilepsy patients.

**Methods :** Fifty two patients with refractory epilepsy completed a sleep questionnaire addressing the relationship between seizures and the sleep/wake cycle, sleep habits, seizure frequency and the presence of sleep disorder symptoms among other variables. Subjects were stratified into three groups based on TSD as follows: Group 1 (n=12):  $\leq 6$  hrs; Group 2 (n=12):  $> 6$  and  $< 8$  hrs; Group 3 (n=28):  $\geq 8$  hrs. The unpaired t-test and Mann Whitney test were used for statistical evaluation of normalized and non-normalized data respectively. We correlated TSD with average monthly frequency of complex partial seizures (CPS), generalized tonic clonic seizures (GTC) and total seizures.

**Results :** For the entire group, mean TSD was 7.59 hrs (4.5-10 hrs). The overall mean monthly seizure frequency was 12.9 (0-120) for CPS and 1.54 (0-30) for GTC. Mean monthly total seizure frequency (CPS + GTC) was 14.4 (1-125). As compared with Group 3, Group 1 had a greater mean monthly CPS frequency ( $25.5 \pm 35.7$  versus  $9.4 \pm 11.2$ , respectively,  $P=0.03$ ) and mean total seizure frequency ( $26.3 \pm 36.7$  versus  $11.8 \pm 11.8$  respectively,  $P=0.08$ ). There was no significant difference in mean seizure frequency of CPS, GTC or total seizures between groups 1 and 2 or 2 and 3.

## Category H—Sleep Deprivation

**Conclusion :** There is an inverse relationship between TSD and seizure frequency, particularly for CPS, in patients with refractory epilepsy suggesting an adverse effect of chronic partial sleep deprivation on seizure control. Further studies investigating this relationship are warranted.

**Support (optional):**

### 0435

#### SLEEP PATTERN IN RATS UNDER DIFFERENT STRESS MODALITIES

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**Introduction :** The present study was designed to evaluate the sleep pattern of rats submitted to chronic stressors (restraint, electrical footshock, swimming and cold) applied to male rats.

**Methods :** After 48 h-baseline recording, rats were submitted to 4 days of chronic stress, and electrocorticogram recordings were carried out continuously. The stressors (footshock, swimming and cold) were applied twice a day for periods of 1 h at 9:00 and 16:00 h. Restrained animals were maintained in plastic cylinders for 22 h/day.

**Results :** The findings indicated that sleep efficiency, slow wave sleep (SWS) and paradoxical sleep (PS) were decreased on the third and fourth days of unpredictable shocks compared to baseline while immobilization and swimming presented reduced sleep efficiency in all 4-day recordings. Swimming led to decreased SWS, whereas augmented PS was observed on the first day compared to baseline. Immobilization produced drastic alterations in sleep patterns since it reduced SWS during the 4 days and PS at days 1 to 4 in relation to baseline. Of all stressors, cold was the only one that did not result in any statistical differences in sleep pattern during the light periods. Regarding the effect of stress compared to baseline on the dark recordings, PS was higher during cold stress periods, whereas footshock increased PS on days 2 to 4 and swimming only on day 2. Immobilization decreased PS throughout the 4 days of the stress sessions.

**Conclusion :** Thus, the data suggest that different stress modalities result in distinct sleep responses, with immobilization producing the most dramatic alterations.

**Support (optional):** AFIP, FAPESP, CEPID

### 0436

#### SLEEP RESPONSE TO CHRONIC PARTIAL SLEEP DEPRIVATION IN YOUNG RATS

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**Introduction :** In this study, we examined sleep patterns in rats during and after chronic partial sleep deprivation at different times of the day.

**Methods :** Young male F344 rats (N=8) underwent 20hr of sleep deprivation (SD) and 4hrs of sleep restriction (SR) per day for 5 days, followed by 5 days of sleep recovery (R). Sleep deprivation using the slowly rotating wheel was performed at two different times of the day, restricting sleep either at the beginning of the 12-hr light (Light Onset group) or the 12-hr dark phase (Dark Onset group).

**Results :** In the Light Onset group, animals lost most of their sleep during the 20hr sleep deprivation procedure. During all five 4-hr SR periods they did not show any significant NREM rebound, whereas they exhibited a REM sleep rebound compared to the baseline. Overall, animals lost 35 hours of sleep during the five SD days and recovered only 2.6 extra hours during the first 3 recovery days. NREM delta power was not increased, compared to baseline values, during any SD and SR periods except SR1. However, significantly higher wake delta power values were observed during SD2, 3 and 5. On sleep recovery days, animals exhibited

a NREM rebound only during the dark phase on R1 and 2, associated with a negative NREM delta power rebound for about 48hrs. In contrast, there was a significant REM rebound during the first 24hrs of SR. The Dark Onset group showed similar homeostatic sleep responses to those found in the Light Onset group. Between the two groups, however, there were differences in the magnitude of the sleep responses relative to their own baseline, which were probably due to the different times of sleep restriction.

**Conclusion :** These data suggest that under chronic partial sleep deprivation conditions, rats recover their sleep partly by increasing delta power during wake and partly by adapting their sleep homeostasis to a new condition.

**Support (optional):** This research was supported by NIH (AG-18200 and AG-11412) and NSBRI (NCC9-58-174 / HPF 00206 #8).

### 0437

#### POWER SPECTRAL PROFILES OF SLEEP FOLLOWING 64-HOUR TSD

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**Introduction :** Total sleep deprivation (TSD) alters the macroarchitecture of sleep during recovery. Compared to baseline, sleep is more consolidated and homeostatic competition between slow wave and REM sleep results in significant changes in relative sleep stage distribution during recovery. Here we examined changes in sleep microarchitecture by comparing the spectral components of sleep on baseline and for two consecutive nights of recovery sleep following 64-hours of TSD.

**Methods :** 30 subjects (24.3±/4.7 yo, 15F) participated in this study. The protocol involved one night baseline sleep, 64hrs TSD and 2 nights recovery sleep (REC1, REC2). 14 spectral windows were evaluated: 0-.3hz, .3-.5hz, .5-2hz, 2-4hz, 4-7.5hz, 7.5-10hz, 10-12hz, 12-14hz, 14-16hz, 16-25hz, 25-35hz, 35-45hz, 45-100hz, 100+hz. Relative power for whole night NREM and REM sleep was calculated. Data analyses utilized repeated measures ANOVAs with planned contrasts.

**Results :** For NREM sleep, significant main effects of power across nights ( $p<.05$ ) were observed in all frequencies (0-25hz) with the exception of the 0-.3hz. Power in .3-.5hz was observed to decrease across the nights. Power in the .5-4hz range increased on REC1 and decreased in REC2. Power in the 4-25hz range decreased on REC1 and returned to baseline levels on REC2. No significant main effects were noted in frequencies >25hz. For REM sleep, significant main effects of night ( $p<.05$ ) were noted for all frequencies except .3-.5hz, 12-14hz, and >45hz. In the slower frequencies (<7.5hz) power increased on REC1 and decreased on REC2, with the opposite pattern observed for frequencies between 7.5-45hz.

**Conclusion :** These data provide information on changes in sleep microarchitecture that are associated with TSD. Delta changes in NREM sleep paralleled slow wave sleep changes previously reported during recovery sleep. Interestingly, theta changes in REM did not parallel REM% changes previously reported, although most high frequencies did. This suggests that REM rebound may be characterized by higher frequency activity than normal REM sleep.

**Support (optional):** UCSD GCRC M01 RR00827 US Army DAMD17-02-1-0201

0438

**DISTORTION IN MENTAL PRODUCTION OF SHORT-DURATION INTERVALS DURING SLEEP DEPRIVATION***Brown FM,<sup>1</sup> LaJambe CM,<sup>2</sup> Santamaria JP,<sup>1</sup> Reichardt RM<sup>3</sup>*

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**Introduction :** Mental production of less than 60-sec durations are involved in driving, military maneuvers, and sequential athletic, musical, and work performance. Circadian influences on time production are well established, but effects from homeostatic sleep processes remain equivocal. These were further investigated by including a control group and multiple time intervals.

**Methods :** Intermediate circadian chronotypes with similar sleep-wake schedules constituted a non-sleep deprived (NSD, n=13) and a 36-hr sleep deprived (SD, n=15) group. They produced randomized computer-generated time durations (11, 18, 32 secs), measured to 0.001 sec, with immediate knowledge of results. Following approximately 12 hr wakefulness, beginning with session 1 (1830h), 3 productions of each duration were recorded. The SD group produced 13 more duration sets at 2-hr intervals, from session 2 (2030h) day 1 until session 14 (2030h) on day 2. The NSD group slept after session 2, and resumed 2-hr testing on day 2 (0830h) until 2030h. Percent-of-baseline (baseline=sessions 1-2 combined) was calculated for sessions 3-14 for SD and 8-14 for NSD to facilitate direct comparison of changes in the 3 production durations.

**Results :** Repeated-measures Time(7) x Group(2) ANOVA indicated mean overestimation by SD for 11 sec across day 2 (group effect:  $F(1,26)=5.4, p<.028$ ) but slight underestimation with longer productions (although  $p > .05$ ). Standard deviation variability increased for SD across day 2 sessions for 18-sec (group effect:  $F(1,26)=14.7, p=.001$ ) and 32-sec (group effect:  $F(1,26)=16.7, p<.001$ ) productions. All NSD production means remained near baseline across all sessions as did their standard deviations, indicating absence of a learning effect. Across 12 sessions SD progressively underestimated 32-sec production ( $F(11,143)=2.3, p=.027$ , Huynh-Feldt (HF) correction), and increased in standard deviation variability for 18-sec ( $F(11,143)=2.1, p=.037$ , (HF)) and 32-sec productions ( $F(11,143)=2.8, p=.024$ , (HF)).

**Conclusion :** Homeostatic sleep processes have differential effects on mental production depending upon length of short time intervals.

**Support (optional):**

0439

**IMPACT OF THE ACCREDITATION COUNCIL FOR GRADUATE MEDICAL EDUCATION DUTY HOUR STANDARDS ON RESIDENT SLEEP, EDUCATION, AND SAFETY: A MULTICENTER STUDY***Landrigan CP,<sup>1,2</sup> Fahrenkopf AM,<sup>2</sup> Lewin D,<sup>3</sup> Sharek P,<sup>4</sup> Barger L,<sup>1</sup> Eisner M,<sup>3</sup> Edwards S,<sup>1,2</sup> Wiedermann BL,<sup>3</sup> Sectish TC<sup>4</sup>*

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**Introduction :** Sleep deprivation substantially increases the risk of physicians-in-training (residents) making serious medical errors and suffering motor vehicle crashes. The ACGME introduced duty hour standards in 2003 for all residents, in an effort to mitigate these risks. The success of the standards in effecting work hour reductions, improving sleep, and improving residency experience has not been adequately assessed.

**Methods :** Our specific aims were to determine whether residents' mean

nightly sleep duration, work hours, motor vehicle crashes, medication error rates, and self-ratings of work, educational experiences, and mental health changed following implementation of the ACGME standards. Data were collected at three major pediatric residency programs in the spring of 2003 and 2004, pre- and post-implementation of the standards. Participating residents logged work and sleep daily using a previously validated logbook, and completed surveys regarding motor vehicle crashes, self-reported medical errors, mood, health, and residency experience.

**Results :** 144 resident subjects participated in 2003, and 124 participated in 2004. Subjects' mean nightly sleep duration, mean weekly work hours, and number of extended shifts were no different following implementation of the standards. In addition, rates of motor vehicle accidents, needle-stick injuries, and self-reported medical errors were unchanged, as were overall ratings of work and educational experiences and rates of screening positive for depression (HANDS scale). The mean length of extended duration (on-call) shifts decreased 0.8 hours to 28.5 hours ( $p<0.005$ ), and fewer residents were burnt out (Maslach burnout inventory) following implementation of the standards (57.0% vs.75.4%,  $p=0.007$ ).

**Conclusion :** Fewer pediatric residents experienced burnout in the year after implementation of the ACGME duty hour standards, but the standards have had little impact on work and sleep durations, educational experience, or rates of depression, motor vehicle crashes, or self-reported medical errors. Further reductions in work hour limits may be needed to improve residents' sleep and safety.

**Support (optional):** This work was supported by the Agency for Healthcare Research and Quality (K08 HS13333), the Brigham and Women's Hospital, the Lucile Packard Children's Hospital Department of Pediatrics, the Children's National Medical Center Department of Pediatrics, and the Children's Hospital Boston Department of Medicine.

0439

**PSYCHOMOTOR VIGILANCE TESTING(PVT) IN A VA COHORT OF PATIENTS AT HIGH RISK FOR OBSTRUCTIVE SLEEP APNEA(OSA)***Roehrs JD*

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**Introduction :** Fatigue and excessive daytime sleepiness are hallmarks of OSA. Objective measures to document treatment effect are poorly defined. Belenky et al. have used PVT to document the effects of sleep deprivation and demonstrated efficacy in the method in sleep deprived patients..

**Methods :** In patients with OSA we tested them before and after therapy using PVT to document a change in their reaction time. We measured the Epworth Sleepiness scale and FOSQ. Each patient was given the same number of practice opportunities prior to final testing. Twenty patients were studied. Ten control staff subjects were given the same protocol

**Results :** There was a trend toward improvement of the PVT after therapy in those patients with Sleep Apnea who were documented to have used the therapy prescribed for the sleep apnea

**Conclusion :** PVT testing showed improvement after therapy and mirrored the subjective improvement of patient's who used the prescribed therapy.

**Support (optional):**

0440

**HABITUAL SLEEP DURATION PREDICTS HEART RATE RECOVERY FOLLOWING EXERCISE IN MEN***Meier-Ewert HK,<sup>2</sup> Seo JY,<sup>1</sup> Haack M,<sup>1</sup> Hyppolite G,<sup>1</sup> Gervino E,<sup>1</sup> Mullington JM<sup>1</sup>*

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## Category H—Sleep Deprivation

**Introduction :** Both heart rate recovery and habitual sleep durations of <7 hours have been associated with increased risk of cardiovascular disease. We examined heart rate recovery following exercise and its relationship to habitual sleep duration in healthy adults.

**Methods :** Subjects were 76 healthy volunteers between the ages of 21-55 years with BMI<40 and habitual sleep durations between 6-9.5 hours. All subjects were non-smokers with no past or current history of sleep, cardiovascular, psychiatric or other medical disorders. Subjects filled out a sleep diary twice daily for 2 weeks (upon waking up in the morning and prior to going to sleep at night). Exercise Stress Test: Subjects ran on a treadmill in three minute stages of increasing workload via increasing speed and incline (standard Bruce Protocol). Heart rate, and blood pressure were recorded every minute. Exercise was discontinued when the subjects felt fatigued. Heart rate and blood pressure were recorded at one, two, three, four, five, seven, and ten minutes after cessation of exercise. Heart rate recovery was defined as the decrease in heart rate from the peak heart rate at each minute after cessation of exercise. Lesser heart rate recovery is associated with increased cardiovascular events.

**Results :** There were no significant sex differences in age, BMI, and habitual sleep duration in this sample. Heart rate recovery was positively correlated with habitual sleep duration in males but not in females. Heart rate recovery for males after one, two, and five minutes was significantly correlated with habitual sleep duration ( $p<0.05$ ). This effect was no longer present seven and ten minutes post exercise.

**Conclusion :** Heart rate recovery is a measure of vagal tone, and reflects the reactivation of the parasympathetic system following sympathetic activation. More rapid return to baseline following peak exercise is associated with lowered cardiovascular risk status. Heart rate recovery is correlated with habitual sleep duration in healthy males, but not in females.

**Support (optional):** Research supported by NIH Grants HL75501, MH60641, RR01032

### 0441

#### MODULATION OF SLEEP HOMEOSTASIS VIA SLEEP DEPRIVATION LEADS TO REDUCTIONS IN GLUCOSE METABOLISM IN THE CEREBRAL CORTEX DURING RECOVERY SLEEP IN HUMANS: A REPEATED MEASURES PET FDG STUDY

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**Introduction :** Sleep is homeostatically regulated, whereby sleep restores a sleep debt that is built during waking. Functional neuroimaging studies in humans have shown that NREM sleep is associated with declines in activity in broad cortical areas in relation to waking and that sleep deprivation leads to reductions in cortical activity during waking. While extensive quantitative EEG sleep studies have documented increased slow wave activity (SWA) in recovery sleep as a correlate of sleep drive, no functional neuroimaging studies have assessed the cerebral metabolic correlates of sleep drive in humans.

**Methods :** Homeostatic sleep drive was modulated in a within-subjects design via sleep deprivation. Four young adult healthy male subjects (mean age + s.d. = 24.9 ± 1.2 years) received [<sup>18</sup>F] fluoro-2-deoxy-D-glucose positron emission tomography ([<sup>18</sup>F]-FDG PET) assessments during NREM sleep after a normal night of sleep and again after 36 hours of sleep deprivation. Absolute and relative regional cerebral glucose metabolic data were obtained and analyzed.

**Results :** In relation to baseline NREM sleep, subjects' recovery NREM sleep was associated with 1) increased SWA; 2) global reductions in whole brain metabolism; and 3) relative reductions in glucose metabolism

in broad regions of frontal, parietal and temporal cortex.

**Conclusion :** This represents the first functional neuroimaging study in humans in which cerebral glucose metabolism was assessed in recovery NREM sleep in relation to rested NREM sleep. The results demonstrate that the homeostatic recovery function of sleep is associated with global reductions in whole brain metabolism as well as greater relative reductions in broad regions of frontal, parietal and temporal cortex. Neurobiological models of sleep homeostasis, therefore, need to account for the inverse relationship between SWA and cerebral glucose utilization and suggest that the increased SWA associated with sleep deprivation is a marker for an increased need for cerebral metabolic restoration.

**Support (optional):** This research was supported in part by MH61566, MH66227, MH01414, MH30915, RR00056, and MH24652

### 0442

#### EFFECTS OF PARTIAL SLEEP DEPRIVATION ON PAIN INHIBITION IN HEALTHY WOMEN

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**Introduction :** While several largely uncontrolled studies suggest that sleep deprivation (SD) may increase pain sensitivity, the effects of SD on central pain-inhibition (an important mechanism in chronic pain models) have not been investigated. Consequently, we evaluated whether partial sleep loss altered endogenous pain-inhibition [Diffuse Noxious Inhibitory Controls (DNIC)].

**Methods :** 32 healthy, pain-free, medication-free females (age, 25±5) were polysomnographically studied for 7 nights. On Nights 1-2 (Baseline), subjects slept undisturbed for eight hours. After Night 2, subjects were randomized to: Control (N=12), Forced Awakening [FA, N=10] and Restricted Sleep Opportunity [RSO, N=10] conditions. Controls slept undisturbed for 8 hours every night. FA underwent 8 forced awakenings (one per hour of sleep opportunity) on Nights 3-5. RSO subjects were yoked to FA on total sleep time (TST), but received partial SD by delaying bedtime. On Night 6, both FA & RSO underwent 36 hours total sleep deprivation (TSD), followed by 11-hour recovery sleep (Night7). Subjects completed standardized pain testing procedures twice per day. Testing included assessment of Pressure Pain Threshold (PPT<sub>h</sub>) and DNIC, operationalized as percent change in PPT<sub>h</sub> during a cold pressor task (Increased PPT<sub>h</sub> during cold pressor reflects pain inhibition).

**Results :** FA and RSO demonstrated 50% reductions in TST during partial SD. FA showed reduced NREM S3+S4 and increased NREM S1. Both FA & RSO demonstrated approximately 50% reductions in REM, but NREM S3+S4 was spared in RSO. Mixed model ANOVAS revealed no significant effects of deprivation on PPT<sub>h</sub>. For DNIC, a significant Group by Time interaction [ $F(10,130)=2.9, p<.01$ ] indicated that following partial SD, FA showed reduced DNIC scores (i.e., failure of PPT<sub>h</sub> to increase during cold pressor) compared to RSO and Controls ( $p<.05$ ).

**Conclusion :** These data suggest that sleep continuity disturbance, but not simple sleep restriction, impairs endogenous pain-inhibitory function, supporting a pathophysiologic role of sleep disturbance in chronic pain.

**Support (optional):** This research was supported by NIH grants: 1R21 NSO 51770-02 (MTS), 1K23 NSO 47168-02 (MTS), and General Clinical Research Center M01-RR-02719

## 0443

## EFFECTS OF ESTRADIOL ADMINISTRATION ON SLEEP DEPRIVATION-INDUCED C-FOS IMMUNOREACTIVITY IN OREXIN (HYPOCRETIN) NEURONS OF OVARIECTOMIZED RATS

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**Introduction :** The extent to which the ovarian hormone estrogen influences sleep-wake cycles and sleep homeostasis is poorly understood. We investigated whether administration of estradiol modulates the activation of wake-promoting hypothalamic orexin neurons in response to sleep deprivation (by gentle handling for 6 h) in ovariectomized rats, using c-Fos and Egr-1 immunoreactivity (ir) as markers of neuronal activation.

**Methods :** Adult female Wistar rats were ovariectomized and implanted subcutaneously with silastic capsules containing oil vehicle or 17, -estradiol (E, 10.5 µg) to mimic diestrus levels of E (Low E). After 2 weeks, animals with E capsules received a subcutaneous injection of either oil, or E (10 µg/kg) to achieve proestrus E levels (High E). Twenty-four h later, animals were either left undisturbed or sleep-deprived (SD) for 6 h starting 1 h after lights-on. Behavioural states were assessed during the last 2 h. Rats were perfused at the end of the deprivation period and brains processed for dual immunostaining for orexin B and c-Fos or Egr-1.

**Results :** Non-SD rats in both Low and High E groups showed similar non-significant increases in percentages of lateral hypothalamic orexin neurons expressing c-Fos (5-7%) compared with non-SD vehicle group (0.3%). Regardless of hormonal condition, non-SD animals slept 66-74% of the 2 h preceding perfusion. Sleep deprivation increased the proportions of c-Fos-ir orexin neurons to 26-28% irrespective of hormone condition. The percent increase over baseline, however, was significantly lower in both E groups than in controls, with no difference between Low and High E groups. Few orexin neurons expressed Egr-1 under any sleep or E conditions. Serum E assay is in progress.

**Conclusion :** Physiological doses of E slightly but non-significantly increased c-Fos-ir in lateral hypothalamic orexin neurons in basal conditions, but reduced the relative increase from baseline following 6 h sleep deprivation, without affecting the total number of immunoreactive cells. These results suggest that estrogen treatment may reduce the impact of sleep deprivation on the activity of orexin neurons. Analyses of gene expression changes in neurons of other sleep/wake-promoting regions are underway.

**Support (optional):** CIHR

## 0444

## ADULT HIPPOCAMPAL NEUROGENESIS IS REDUCED BY SLEEP FRAGMENTATION IN THE ADULT RAT

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**Introduction :** The adult hippocampal dentate gyrus is a site of continuing neurogenesis; adult born neurons play a critical role in explicit memory function. We have previously shown that total sleep deprivation reduces adult neurogenesis in rats. In humans, sleep fragmentation is a more common sleep condition than total sleep deprivation. Sleep frag-

mentation (SF) characterizes obstructive sleep apnea as well as other sleep disorders, but has been little studied in experimental animals. In this study, we assessed a hypothesis that sleep fragmentation would suppress adult neurogenesis.

**Methods :** Male albino rats were implanted for polysomnographic recording. An intermittent treadmill system was used for SF. SF was achieved by 3 sec treadmill movement every 30 sec (SF). For sleep fragmentation control (SFC), the treadmill moved 15 min every 150 min. SF was conducted for 3 durations: 1 day, 4 days and 7 days (n = 6 per group). The thymidine analog BrdU was injected two hours prior to the end of each experimental condition. Cell proliferation was detected by immunohistochemical procedures and assessed using stereologically-guided counting.

**Results :** SFC rats continued to have substantial amounts of NREM sleep whereas the SF animals exhibited discontinuous episodes of NREM. The number of BrdU positive cells was reduced by 70.08 and 70.14 % (p < 0.05 t test) in the SF groups after 4 and 7 days of experimental conditions whereas no differences were observed after 1 day. In a second experiment, the percentage of cells expressing a neuronal phenotype was higher in the SFC in comparison with the SF groups for all 3 durations of SF.

**Conclusion :** The results show that sustained SF induced marked reduction in hippocampal neurogenesis. Interestingly suppression of neurogenesis by SF was greater than that produced by total SD after 4 days. Suppression of neurogenesis could account for explicit memory deficits associated with SF in humans.

**Support (optional):** This was made possible by a grant from the American Sleep Medicine Foundation, a foundation of the American Academy of Sleep Medicine and by the US Department of Veterans Affairs Medical Research service, NIH grants 47480 and HL 60296

## 0444

## SLEEP COMPLAINTS BY HOSPITAL STAFF NURSES

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**Introduction :** The 2005 National Sleep Foundation survey found that 54% of respondents reported experiencing at least one symptom of insomnia at least a few nights a week. Hospital staff nurses often work >12 hour shifts or work nights that may result in increased risk for sleep complaints. This study sought to determine the prevalence and factors associated with sleep complaints in nurses.

**Methods :** A demographic questionnaire and logbooks with daily information about sleep, alertness on duty, work hours, and errors for 28 days were completed by two samples of full time hospital staff nurses: 393 nurses randomly selected members from the American Nurses Association (ANA) and 502 nurses randomly selected from the American Association of Critical Care Nurses (AACN). Generalized Estimating Equation Logistic regression modeling was used to examine the relationship between sleep complaints and factors that influenced sleep problems.

**Results :** There were no significant differences in the frequencies of sleep complaints between the samples. Nearly all participants, N=849 (95%), reported at least one symptom suggestive of insomnia. Seventy-nine percent of participants reported trouble falling asleep, 88% had trouble staying asleep and 83% reported waking up too early. While there were no differences in sleep complaints, there were differences in the factors associated with sleep complaints by sample. On work days, caffeine intake (ANA sample) and caring for elderly (AACN) predicted sleep complaints.

## Category H—Sleep Deprivation

Female gender (ANA sample) predicted sleep complaints on non-work days. Factors that made sleep complaints less likely on work days included being married (ANA), duration of commute (ANA), years of RN experience (ANA) and type of unit assignment-pediatrics + other (AACN sample). On non-work days, being married (ANA) and number of children (AACN) were factors that made sleep complaints less likely.

**Conclusion :** Results suggest that the number of sleep complaints of full-time hospital staff nurses working exceed the number of sleep complaints reported by population-based surveys of adults in the United States. Identified factors that influenced sleep complaints may be used to plan strategies to improve sleep quality in hospital staff nurses.

**Support (optional):** Financial support for this study was provided by the Agency for Healthcare Research and Quality (R01 HS11963-01) and an American Nurses Foundation Grant (Scott).

### 0445

#### SLEEP FRAGMENTATION AND REM SLEEP IN MORBIDLY OBESE ADULTS WITHOUT SIGNIFICANT OBSTRUCTIVE SLEEP APNEA

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**Introduction :** Sleepiness and fatigue are frequent complaints of obese subjects even in the absence of obstructive sleep apnea (OSA), yet little is known about sleep in morbid obesity. This study compares sleep in morbidly obese subjects without significant OSA as compared to age- and gender-matched lean controls.

**Methods :** Thirty-five volunteers had an overnight laboratory polysomnography. The obese group (n=17, 16 women) aged 35±10 yrs (mean ± SD), had an average body mass index (BMI) of 53±9 kg/m<sup>2</sup> (range: 40-80 kg/m<sup>2</sup>), and an AHI of 4.2±4.0 (all <15). The lean group (n=16, 14 women) aged 34±11 years, had a BMI of 23±2 kg/m<sup>2</sup> (range: 20-26 kg/m<sup>2</sup>) and an AHI of 0.9±1.3 (p<0.01 as compared to obese subjects). The subjects were not taking any medication known to affect sleep and/or breathing.

**Results :** In the morbidly obese, sleep latency to stage 1 tended to be shorter (p=0.07) and wake after sleep onset longer (WASO; 34±4 min versus 22±5 min) after controlling for AHI and age (p<0.05). Morbidly obese subjects tended to have an increased number of microarousals (p=0.07). Two controls and two patients had a total number of microarousals > 250. When these subjects were excluded from the analysis, the morbidly obese had a higher number of microarousals, independent of AHI (120±18 versus 74±19, p<0.005 by ANOVA). Sleep stage distribution was similar in both groups. In morbidly obese subjects, the amount of REM was inversely related to BMI (r=0.511, p=0.036). In contrast, there was no relationship between amount of REM and AHI or age. There was also no association between AHI and BMI.

**Conclusion :** Morbidly obese subjects without significant SDB have more fragmented sleep than lean controls. High BMI appears to impact REM regulation.

**Support (optional):**

### 0446

#### THE EFFECTS OF MODERATE SLEEP DEPRIVATION AND LOW DOSES OF ALCOHOL ON DRIVER PERCEPTION OF DROWSINESS AND DRIVING PERFORMANCE DURING A 70 MINUTE SIMULATED DRIVE

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**Introduction :** We previously showed that sleep restricted young drivers had impaired driving simulator performance at 0100 hours, (speed deviation, steering deviation and number of crashes) following low dose alcohol, without significant changes in perception of sleepiness and driving performance. The present study investigated the effects of combining sleep restriction and alcohol on subjective sleepiness and perception of driving performance at 1400 hours, using a similar experimental protocol with two low doses of alcohol.

**Methods :** The study was a repeated measures design with four experimental conditions. Normal sleep with no alcohol (Control), Sleep Restriction (SR) alone and SR plus two low dose blood alcohol concentrations (SR+A1~0.025 and SR+A2~0.035 g/dL). 19 healthy male volunteers (age 22.3±3.7 yrs, BMI 25.2±6.8) rated their perception of sleepiness and driving performance throughout a 70 minute simulated driving task under each condition.

**Results :** Blood alcohol concentration was 0.0 g/dL during the Control and SR conditions. Prior to the driving task during SR+A1 and SR+A2 conditions mean BAC was 0.025±0.008 and 0.033±0.009g/dL respectively. After the drive the corresponding BACs were 0.014±0.008 and 0.024±0.005g/dL. There were significant condition (p<0.01), time (p<0.01) and condition/time (p<0.01) effects on drowsiness and subjective driving performance ratings, with progressively poorer ratings in SR, SR+A1 and SR+A2 conditions as time on the task had increased, which appeared to partially recover after 40 minutes on task in SR, and SR+A1 conditions but not SR+A2. Compared with SR, the SR+A2 condition showed no increase in sleepiness or perceived driving impairment early in the drive (when BAC relatively high) but marked increase late in the drive (BAC low).

**Conclusion :** These data suggest that the combination of sleep restriction and low-dose alcohol has a delayed dose-dependent effect on perception of sleepiness and driving performance during afternoon driving.

**Support (optional):** The study was supported by the Australian Brewer's Foundation.

### 0447

#### SLEEP QUALITY, SCHOOL PERFORMANCES AND DRIVING HABITS IN ADOLESCENTS

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**Introduction :** We studied subjective sleep quality and its related factors, including driving habits and car accidents, in a population of adolescents.

**Methods :** Data were collected by self administered questionnaire (School Sleep Habits Survey by M.Carskadon, translated by Giannotti F. and Cortesi F) supplemented with some questions exploring driving style for students with driving license. Questionnaires were submitted to seven high schools. The final cleaned sample population was 1505 (383 had already passed their driving test), mean age 17.8 yrs, range 17-21 yrs. Frequency distributions, statistical indicators of location and dispersion, t-tests and Kolmogorov-Smirnov tests were calculated

**Results :** One hundred fourteen subjects (7.57 %) complained of insufficient sleep (INS) often or always, 151 subjects (10.04%) referred excessive daytime sleepiness (EDS), as moderate or severe problem, often or

always. Stochastic ordering and association tests demonstrated that INS subjects referred a worse school achievement and more attention problems than normal subjects; subjects with EDS referred more attention problems, like INS, but no worsening in school achievement. Among 383 subjects with driving license, one hundred forty seven subjects (38%) declared they are sleepy when driving sometimes or often, and, when it happens, 80.8% of them keep on driving. Furthermore, 87 students (23%) had had one or more car crashes and 27 subjects (7%) declared they had risked crashes because of sleepiness. Sleepiness was reported as the main cause of accident in 17% of crashes, speed in 40% and alcohol assumption in 18%. Students who had had at least one crash go to bed later ( $p < 0.0005$ ), wake up later ( $p < 0.0005$ ) and with difficulty ( $p < 0.0005$ ), and judge the quality of their sleep worse ( $p = 0.015$ ).

**Conclusion :** Our results emphasize the role of sleep education in improvement of school achievement and in preventing car accidents in young people

**Support (optional):** Research supported by Italian Ministry of Health

## 0448

### PSYCHOMOTOR VIGILANCE TASK-RELATED PUPIL DILATION RESPONSES DURING SLEEP DEPRIVED AND NORMAL SLEEP CONDITIONS

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**Introduction :** Sleep deprivation (SD) is consistently associated with performance decrements on the Psychomotor Vigilance Task (PVT). We compared a physiological measure of cognitive processing—task-related pupil dilation (larger dilation indicates greater processing)—during sleep deprived and normal sleep (NS) conditions.

**Methods :** Healthy young adults were randomized to a night of total SD ( $n=8$ ) or NS ( $n=10$ ). The next afternoon, a standard 10-minute PVT (3-10 s inter-stimulus interval with reaction time (RT) feedback) was administered during continuous pupil diameter recording. NS versus SD group pupil dilation waveform averages for lapse (RT  $>500$  ms) and non-lapse trials were computed controlling for RT.

**Results :** In non-lapse trials, the initial peak dilation response to targets (2 s post-RT) was significantly larger in SD compared to NS,  $t(16)=-2.49$ ,  $p=0.02$ . By the fifth second, pupil size returned to baseline. The pupil remained at baseline in the NS group, but fell significantly below baseline in the SD group,  $t(16)=3.81$ ,  $p=0.00$ . For lapses, the initial peak dilation response was larger in both groups ( $F(1,9)=5.07$ ,  $p=0.05$  and  $F(1,7)=7.15$ ,  $p=0.03$ , for NS and SD respectively), with a trend toward larger responses in SD compared to NS,  $t(16)=-2.03$ ,  $p=0.06$ . For NS participants, the pupil response then fell significantly below baseline in lapse versus non-lapse trials ( $F(1,9)=8.50$ ,  $p=0.02$ ), appearing similar in overall shape and magnitude to non-lapse trials during SD.

**Conclusion :** Initial pupil dilation responses during the PVT were larger in SD versus NS, and in lapse versus non-lapse trials regardless of the experimental manipulation. This may reflect greater compensatory effort required to make a target response when sleep deprived or during times of low vigilance in NS conditions. The RT feedback that is provided might also influence pupil dilation responses. Following a heightened pupil dilation response (non-lapse SD and lapse NS trials), the ensuing pupillary constriction response suggests that vigilance quickly dissipates after responding.

**Support (optional):** Supported in part from MH16804, MH30915, RR00056, MH24652, and AG00972

## 0449

### NREMS CONTINUITY AND EEG SLOW-WAVE ACTIVITY AFTER SLEEP DEPRIVATION IN RATS

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**Introduction :** After sleep loss, compensatory increases in NREMS amounts and increases in the slow-wave activity (SWA) of the EEG during NREMS occur. Commonly, SWA is regarded as a measure of NREMS intensity. Other measures of NREMS, e.g., the number and the average duration of NREMS episodes, are also elevated after sleep deprivation. The aim of the resent experiments was to determine if there is a correlation between sleep deprivation-induced increases in episode numbers and average episode durations and the power of various frequency ranges of the EEG during rebound sleep.

**Methods :** Male rats ( $n = 11$ ) were implanted with EEG and EMG electrodes and kept on a 12:12 h dark-light cycle at 24 C. After a baseline day, the animals were sleep deprived by gentle handling for the last 6 h of the light period and then recovery sleep was recorded. FFT analysis of the EEG was performed on 0.5 Hz bands in the 0.5-20 Hz frequency range separately for W, NREMS and REMS episodes.

**Results :** Sleep deprivation induced well-known increases in NREMS amounts as well as in episode numbers and average episode durations. The time course of the changes in episode durations showed a biphasic pattern: an initial increase was followed by a decrease ~12 h after sleep deprivation. These changes were mirrored by and significantly correlated with biphasic changes in the power of the low frequency range of the EEG, especially in the 0.5-3 Hz spectrum.

**Conclusion :** Our results confirm prior findings that there is a strong correlation between NREMS continuity and SWA. It is known that SWA gradually increases within a NREMS episode in rats. Therefore, it is possible that increases in NREMS episode length play a simple permissive role, allowing for the gradually increasing SWA within the episode to reach higher intensities during sleep deprivation-induced rebounds.

**Support (optional):**

## 0450

### MEASURING THE IMPACT OF SLEEP DEPRIVATION ON SLEEPINESS AND AFFECT REACTIVITY WITH PUPILLOGRAPHY

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**Introduction :** Sleep deprivation (SD) impacts mood, however, evidence using objective measures is scarce. Pupilligraphy is an ideal method to objectively measure affect reactivity, sleepiness, and their interaction. A physiological consequence of sleepiness, slow pupillary oscillations can be reliably quantified with the Pupillary Unrest Index (PUI). The pupil can also index of cognitive and affective processing by measuring task-related dilation responses to stimuli.

**Methods :** Nine healthy young adults underwent a night of total SD. Sleepiness (PUI) and affect reactivity were assessed the next afternoon while continuously recording pupil diameter; testing was repeated 1-2 weeks later under normal sleep (NS) conditions. PUI was quantified during an 11-minute fixation period in the dark. The affect task consisted of viewing 3 blocks of positive, negative, and neutral pictures; each block contained 5 same-valenced pictures. The paradigm consisted of a 2 s pre-stimulus onset visual warning, 6 s picture presentation, followed by a 6 s equilluminant screen.

**Results :** Only during negative picture presentation was there a signifi-

## Category H—Sleep Deprivation

cant difference between SD and NS pupil dilation waveforms ( $F(1,8)=16.95, p<0.01$ ). Notably, this effect was significant both during pre-stimulus and during-stimulus periods. Average pupil size during the significant pre-stimulus (NEG-PRE) and during-stimulus (NEG-ON) periods were calculated and correlated with participants' PUI scores. In both groups, increased sleepiness (PUI) predicted greater reactivity (increased pupil dilation) to negative pictures: NEG-PRE  $r^2=.28$  and  $.11$ , NEG-ON  $r^2=.45$  and  $.35$ , for SD and NS respectively.

**Conclusion :** SD was associated with greater affect reactivity as evident by enhanced pupil dilation during the pre-stimulus warning, which due to the block design reflects anticipatory processing, and negative picture presentation periods. Sleepiness, as measured with an objective pupil-based measure, was associated with increased affect reactivity during both SD and NS conditions. Pupil dilation is a novel indicator of sleep-related alterations in affect, and deserves further study.

**Support (optional):** Supported in part from MH16804, MH30915, RR00056, MH24652, and AG00972

### 0451

#### INCREASED SPECTRAL POWER IN THE WAKING EEG AFTER TOTAL SLEEP DEPRIVATION IS A DIRECT EFFECT AND NOT DUE TO INCREASED SAMPLING IN DROWSINESS

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**Introduction :** Increased spectral power in EEG bands with TSD (Borbely 1981, Broughton et al. 1998) could represent inclusion of more mini-époques with drowsiness. This confusion arose in epileptology where an activating effect on EEG discharges after 1 night of TSD was shown later to reflect increased amounts of mild drowsiness that causes discharge activation.

**Methods :** 10 normal males, 2 females, aged  $54.6 \pm 6.5$  were studied rested and after 1-night TST. All had history, physical, screening PSG, study PSG and next day MSLT with 20-min naps at 1000, 1200, 1400 and 1600h. Artefact free 5-sec mini-époques were selected just prior to MSLT naps. All 19 standard electrodes (10/20 system) were referred to linked mastoids (10kohm resistor separating). EOG was bilateral supraorbital-to-infraorbital and submental. EMG was standard with electrode impedances  $<5000$  ohms. EEG was digitalized at 200 Hz (flat response 0.2-30.0 Hz) and stored on CDs. qEEG topography used a 8-electrode sub-montage. Statistics included ANOVA, multiple regression analyses with Bonferroni-Holm corrections.

**Results :** qEEG analysis showed a significant increase after TSD in spectral power at all electrode sites for delta, theta and alpha bands. Increased theta-1 and theta-2 band power was the most sensitive, and was greatest and symmetrical frontally. MSLT showed significant shortening of mean-SL and no SOREMPs. Analysis of SEMs during the sampled mini-époques for both conditions showed no significant difference.

**Conclusion :** Increased spectral power in various frequency bands, especially theta, in the waking EEG after TSD is a direct effect, and a measure, of prior SD and is not due to selecting more mini-époques during lower vigilance.

**Support (optional):**



## 0452

**A NATIONAL SURVEY OF THE EFFECT OF SLEEP MEDICINE SPECIALISTS AND AMERICAN ACADEMY OF SLEEP MEDICINE ACCREDITATION ON MANAGEMENT OF OBSTRUCTIVE SLEEP APNEA**

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**Introduction :** A systematic assessment of the effect of American Academy of Sleep Medicine (AASM) accreditation and sleep medicine certification of physicians on clinical outcomes in patients with obstructive sleep apnea syndrome (OSAS) has not been performed and is direly needed. We set out to study the effect of AASM accreditation of centers and certification of physicians on outcomes in patients with OSAS.

**Methods :** A national, cross-sectional, web-based survey of 632 patients with OSAS. Self-reported data on details of whether patients with OSA were using positive airway pressure (PAP) devices, the timeliness of institution of PAP therapy, and overall satisfaction of care received from physicians and centers were collected.

**Results :** Of the 842 'hits' to the website, 632 responded. Thirty-five percent of the patients (51 + 10 years; body mass index of 35.7 + 8.9 Kg/m<sup>2</sup>) were women. Average self-reported PAP level was 11.5 + 3.6 cm H<sub>2</sub>O. After adjusting for covariates, lack of accreditation-certification status of providers was independently associated with discontinuation of PAP therapy (OR 1.9, 95%CI, 1.1-3.2; P=0.03) and low self-reported hours of PAP device usage (P<0.05). Patient education leading to perception of risk associated with OSA (OR 0.5, 95%CI, 0.2-0.9) 'protected' against discontinuation of PAP therapy. Certified physicians and accredited centers were more likely to educate their patients and received greater satisfaction ratings than non-certified physicians and non-accredited centers (P<0.05). Time delays in instituting PAP therapy was not influenced by accreditation-certification status, but such delays unfavorably impacted patient satisfaction.

**Conclusion :** In this web-based survey, accreditation-certification status of sleep centers and physicians was associated with better indexes of clinical management in patients with OSA. Better patient education that fostered risk perception may have been partly responsible for such an association. Prospective studies designed to collect objective data regarding the effect of accreditation-certification status on outcomes in patients with OSAS are still needed.

**Support (optional):** SAVAHCS Research Award and American Sleep Medicine Foundation of the American Academy of Sleep Medicine

## 0453

**COGNITIVE IMPROVEMENT (BY DIGIT SYMBOL SUBSTITUTION CHANGE SCORE) MAY EXPLAIN ONE-MONTH COMPLIANCE WITH CONTINUOUS POSITIVE PRESSURE AMONG OBSTRUCTIVE SLEEP APNEA PATIENTS**

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**Introduction :** Recent research has attempted to determine predictors of patient compliance with continuous positive airway pressure (CPAP) for obstructive sleep apnea syndrome (OSAS). One consistent predictor for continued CPAP use is severity of self-reported daytime sleepiness. We examined additional measures to identify potentially non-compliant patients.

**Methods :** From August 2003 to June 2005, 452 adult patients with pri-

mary complaints of excessive daytime sleepiness or sleep disordered breathing participated in a randomized clinical trial of various CPAP units. After informed consent and prior to diagnostic nocturnal polysomnography, subjects completed the Epworth Sleepiness Scale (ESS) and a 2-minute Digit Symbol Substitution Test (DSST). One of our clinicians graded the severity of OSAS symptoms using a 5-point Clinical Global Impression (CGI). Symptomatic change was assessed by repeat ESS, CGI, and DSST during scheduled follow-up at 4-6 weeks (1-month), 6 months, and 1 year. Compliance data was downloaded at each visit.

**Results :** 435 subjects underwent polysomnography, and 226 were prescribed CPAP. Sixty-four percent (n = 145) returned for 1-month follow-up. Linear regression revealed a predictive relationship between one-month CPAP use and a multi-factor aggregate including (initial CPAP pressure; baseline apnea/hypopnea index (AHI) and nocturnal oxygen desaturation; proportion of deep sleep and REM; change scores on ESS, CGI and DSST) [adjusted R square = 0.396]. DSST change score [p = .014] and AHI [p = .037] emerged as the best correlates of short-term CPAP compliance.

**Conclusion :** Objectively measured cognitive improvement (DSST) correlated with CPAP use more than changes in either ESS or clinical impression. Three-month CPAP use is strongly predictive of long-term compliance. Improved cognition may partly explain short-term, hence long-term, compliance.

**Support (optional):** This research was partly supported by a grant from the ResMed Corporation.

## 0454

**MORPHOLOGICAL ANALYSES OF POSITIONAL DEPENDENCE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME**

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**Introduction :** In patients with obstructive sleep apnea hypopnea syndrome (OSAHS), respiratory events during sleep are reduced when they lie on their side than when they lie on their back. Positional OSAHS is defined as a syndrome in patients in whom the apnea hypopnea index (AHI) is at least twice as high in the supine position as in the lateral position. OSAHS in patients in whom the AHI in the supine position is less than twice that in the lateral position is called nonpositional OSAHS. Positional dependence during sleep has the tendency to be associated with mild and moderate OSAHS rather than severe OSAHS. However, not all mild and moderate patients are positional OSAHS. One of the major factors contributing to this positional dependence is thought to be anatomical factors in the upper airway; however, studies on the correlation between craniofacial and upper airway morphologies and positional dependence in OSAHS patients have not yet been reported. The purpose of this study is to clarify the anatomical risk factors in patients with positional OSAHS.

**Methods :** Positional and nonpositional OSAHSs were diagnosed by overnight polysomnography (PSG). Lateral cephalometric radiographs and upper airway magnetic resonance imaging were performed on the OSAHS patients. Using three-dimensional (3D) imaging software V-works (Cybermed Inc., Seoul, Korea), 3D structures of the upper airway were obtained for both groups.

**Results :** The comparisons of the craniofacial morphologies using cephalometric radiographs revealed that there were no significant difference between the two groups in the upper airway volume, facial axis, SNA, SNB, ANB, MP-H, PNS-P, and IAS. However, the patients with positional OSAHS had a significantly wider ANB (p= 0.025).

## Category I—Sleep Disorders-Breathing

**Conclusion :** The relative positional relationship between the mandible and maxilla might explain the possible important role of positional dependence in OSAHS patients.

**Support (optional):** This work was supported by Research Grant No. 17591802 to M. S. from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

### 0455

#### SNORING AND RISK OF BENIGN PROSTATIC HYPERPLASIA. A POPULATION BASED STUDY

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**Introduction :** Objective of this study was to evaluate the association between the snoring severity and the subjective and objective measures of benign prostatic hyperplasia.

**Methods :** A cross-sectional study with administration of urologic and sleep questionnaires to a random sample of 1017 community dwelling males. Randomly selected subset of 417 males also underwent measurement of the prostate volume, prostate-specific antigen and urinary peak flow rate.

**Results :** Median age was 65 years (range 51-92). Based on the sleep questionnaire the 1017 subjects were divided into categories of heavy (n = 123), moderate (n = 705) and no (n = 189) snoring. There was a significant difference in the lower urinary tract symptoms across the snoring categories (p < 0.05). The age-adjusted odds of having moderate to severe symptoms was 1.8 (95% CI 1.1, 2.9) for the heavy snoring group compared to the non-snorers. The objective urologic measurements were assessed in the population subset of 417 patients. There was no association of the urinary peak flow with snoring. There was a non-significant trend towards a smaller median prostate volume in patients with heavy snoring. The age-adjusted odds of having a prostate volume > 30ml in the heavy snoring group compared with the non-snoring group was 0.3 (95% CI 0.1, 0.7).

**Conclusion :** There is a direct association between the lower urinary tract symptoms and snoring severity. The inverse relationship between the prostatic volume and the snoring severity, however, deserves further study.

**Support (optional):**

### 0456

#### THE DIFFERENTIAL EFFECT OF MODERATE AND SEVERE CHRONIC INTERMITTENT HYPOXIA (CIH) ON LIPID METABOLISM

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**Introduction :** Obstructive sleep apnea (OSA) is associated with multiple metabolic abnormalities, including hyperlipidemia, atherosclerosis, insulin resistance, and fatty liver disease. CIH, a key feature of OSA, has been implicated in metabolic complications of this disease. We have previously demonstrated in a murine model that severe acute intermittent hypoxia (IH) increases serum and liver lipid levels. The goal of the present study was to determine whether the metabolic dysregulation associated with CIH is dependent on the severity of the hypoxic stimulus.

**Methods :** Lean C57BL/6J mice on a regular chow diet were exposed to CIH for 4 wks with a nadir of FiO<sub>2</sub> nadir of either 10% (n = 8, moderate CIH) or 5% (n = 8, severe CIH). Liver lipid peroxidation (malondialdehyde assay, MDA), fasting serum lipid, glucose, insulin, and corticosterone levels were compared to control mice (n = 8).

**Results :** Both severe and moderate CIH led to significant increases in

lipid peroxidation in the liver (94.4±5.4 nmol MDA/mg and 65.5±4.5 nmol/mg vs. 53.1±6.2 nmol/mg in control mice, p < 0.001), but oxidative stress was greater in severe CIH (p = 0.002 vs. moderate CIH). Severe CIH also resulted in significant increases in serum levels of total cholesterol (129.1±2.8 mg/dl vs. 118.1±4.1 mg/dl in the control group, p = 0.05), LDL cholesterol (85.7±8.5 mg/dl vs. 61.3± 3.0 mg/dl respectively, p < 0.05), and HDL cholesterol (102.5±6.0 vs. 73.2±3.1 mg/dl respectively, p < 0.001). Moderate CIH did not cause any changes in serum lipid levels. Neither severe nor moderate CIH affected fasting serum free fatty acids, glucose, insulin, or corticosterone levels.

**Conclusion :** Our data imply that (1) metabolic abnormalities in CIH depend on the severity of the hypoxic insult; (2) only severe CIH leads to hypercholesterolemia in lean mice; (3) even mild to moderate CIH causes oxidative stress and increases lipid peroxidation in the liver.

**Support (optional):** HL68715, HL80105, HL79554

### 0457

#### STUDY OF EFFICACY AND ADVERSE EFFECTS OF ANTI-SNORING NASAL SOLUTION (XANTHANE NASAL SOLUTION) IN TREATMENT OF PRIMARY SNORING

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**Introduction :** To study efficacy and adverse effects of Xanthane nasal solution in treatment of primary snoring.

**Methods :** Prospective, randomized, double-blinded, placebo-controlled, cross-over study was done. Patients diagnosed as primary snoring by polysomnography (AHI not more than 5) were included. Acute intercurrent illness or surgery within the past 4 weeks, severe deviated nasal septum, any abnormal obstructive mass in upper aerodigestive tract, obese patients (BMI > 30 kg/m<sup>2</sup>), patients who received any surgery for sleep-disordered breathing within 3 months or had any rhinopharyngeal infection during the study were excluded. Fifty nine primary snoring patients were recruited between Jan2003 and May2004. Each patient was randomized into two groups. In phase one, all subjects in group1 used Xanthane and group2 used placebo for 1 week. The following week was wash-out period. In phase two, all subjects in group1 used placebo and group2 used Xanthane for 1 week. Loudness of snoring was assessed by their regular bed partner using visual analog scales (0-10). Adverse effects were graded (0-4). ANOVA for cross-over design and Friedman test were used for statistical analysis.

**Results :** Fifty one patients were able to follow the protocol until the end of the study. There was no significant difference (p= 0.06; 95% CI= -0.06 to 0.13) in loudness of snoring between Xanthane nasal solution and placebo. Nevertheless, adverse effects were not different between two groups.

**Conclusion :** This study showed no beneficial effects of Xanthane nasal solution in primary snoring patients, but no adverse reactions.

**Support (optional):** This study was sponsored by Anben Pharma, 14, Avenue Mendes France, 67300 SCHILTIGHEIM (France).

### 0458

#### EFFECTIVE DIAGNOSTIC AND THERAPEUTIC POLYSOMNOGRAPHY IN PATIENTS WITH CENTRAL SLEEP APNEA SYNDROME

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**Introduction :** Suspicion of central sleep apnea (CSA) prior to the sleep study, effectiveness of positive airway pressure therapy (PAP), and

requirements of the patients' insurers influence the diagnostic and therapeutic approach to patients with CSA. We aimed to analyze the testing patterns and modes of therapy used during diagnostic and therapeutic polysomnograms (PSGs) in patients with CSA.

**Methods :** We retrospectively analyzed clinical data of consecutive patients who were evaluated between 2/1/2004 and 5/31/2005. We included patients with diagnostic polysomnograms showing: (1) central sleep apnea index (CSAI) $>5$ , (2) CSAI higher than the combined obstructive and mixed apnea index (OSAI + MSAI), and (3) CSA as a predominant condition identified in the clinical interpretation of the PSG. We considered apnea-hypopnea index (AHI) $<10$  during therapeutic trial as successful.

**Results :** Twenty-seven patients (21M, 6F) aged 68.0 (52.5-74.0) years (median, IQR) with CSA were identified with AHI of 44.0 (28.5 - 65.0). Split-night studies had a diagnostic portion of 134.0 (125.0-163.7) minutes and a median of 2 (range 0-5) therapeutic portions of 127.0 (51.7-205.2) minutes over 1-2 nights. Eight patients (29.6%) required two nights to undergo full evaluation; in 6/8 of these patients (75%), the diagnosis of CSA was not suspected prior to the sleep study. In 12 (44.4%) patients treated with continuous PAP (CPAP), oxygen (O<sub>2</sub>), CPAP+O<sub>2</sub>, bi-level spontaneous-timed PAP (BIPAP-ST), or BIPAP-ST + O<sub>2</sub>, evaluation resulted in therapeutic success. In 6/8 patients application of BIPAP-ST (5 patients) or O<sub>2</sub> (1 patient) on the second night resulted in a therapeutic success.

**Conclusion :** When ordering a split-night study, anticipating CSA or specifying therapies that should be tried if CPAP fails for CSA may allow completing the evaluation in one night. Our results suggest that BIPAP-ST or O<sub>2</sub> therapy should be tried as a third portion of a split night study in patients with CSA.

**Support (optional):**

#### 0459

##### COMPARISON OF SLEEP AROUSALS BEFORE AND AFTER CPAP TITRATION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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**Introduction :** Obstructive sleep apnea syndrome (OSA) causes sleep fragmentation and arousals during sleep which leads to excessive daytime sleepiness. Although CPAP improves sleep architecture, its effect on sleep arousals is unclear.

**Methods :** A retrospective analysis was done on 84 patients with OSA who underwent baseline polysomnography and subsequent CPAP titration. Apnea/Hypopnea index (A/H) was used to divide patients into two groups of mild OSA (N=19, A/H: 5-15) and moderate-severe OSA (N=65, A/H $>15$ ). Spontaneous arousals per hour (SA) and arousals with limb movements per hour (PLMAI) were compared in both groups before and after CPAP.

**Results :** In mild OSA group spontaneous arousals and arousals with limb movements decreased slightly post CPAP but the difference was not statistically significant (SA:  $t = 0.23$ ,  $p = 0.81$ ; PLMAI:  $t = 1.26$ ,  $p = 0.22$ ). In moderate-severe OSA group there was no significant difference in spontaneous arousals ( $t = -0.97$ ,  $p = 0.33$ ) but PLMAI's significantly increased ( $t = -3.7$ ,  $p < 0.001$ ).

**Conclusion :** The increase in arousals associated with limb movements after CPAP titration in patients with moderate-severe OSA but not in patients with mild OSA would support the concept that subtle hypopneas may remain uncorrected with CPAP in severe OSA. PLMAI may serve as an indicator for CPAP titration in patients with OSA.

**Support (optional):**

#### 0460

##### CORRELATION BETWEEN DAYTIME FUNCTIONING SCORE AND SEVERITY OF OBSTRUCTIVE SLEEP APNEA (OSA)

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**Introduction :** Obstructive sleep apnea results in significant daytime functional impairment such as sleepiness, cognitive dysfunction and poor quality of life. We have developed a disease-specific quality of life questionnaire consisting of 15 yes/ no questions about daytime fatigue, sleepiness, irritability, concentration, attention, motivation, loss of interest in pleasurable activities and sleepiness while driving. The primary purpose of this study was to test the hypothesis that patient responses to questions directed at identifying impairment in daytime functioning correlate with the severity of OSA as reflected by the AHI and nocturnal hypoxemia.

**Methods :** We retrospectively reviewed 100 consecutive adult patients diagnosed with OSA by standard polysomnography who also had MSLT. All patients answered a comprehensive sleep questionnaire prior to their tests. Data included age, gender, BMI, Apnea-hypopnea index (AHI), mean oxygen desaturation (SpO<sub>2</sub>), MSLT and daytime functioning score. Statistical analysis was performed using SPSS 11.0 software

**Results :** Age ranged from 18 to 79 with a mean of 45.7 + 13.9. There were 60 men and 40 women. The mean AHI was 39.4 + 28. Average mean SpO<sub>2</sub> was 90.2% + 5.2%. The MSLT ranged between 1.5 to 20 minutes with a mean of 9.9 + 5.2. The daytime functioning score ranged from 0 to 14 with a mean of 7.7 + 7.9. There was no correlation between the daytime functioning score and the AHI ( $r = -0.29$ ,  $p = 0.77$ ) nor SpO<sub>2</sub> ( $r = -0.59$ ,  $p = 0.58$ ). There was a weak negative correlation between the daytime functioning score and the MSLT ( $r = -0.228$ ,  $p = 0.02$ ) even after controlling for age, BMI and AHI

**Conclusion :** The patient's own perception of daytime functioning impairment does not correlate with the severity of OSA as reflected by the AHI or the severity of oxygen desaturation. It correlates weakly with the objectively measured MSLT.

**Support (optional):**

#### 0461

##### COMORBID DIABETES MELLITUS IS ASSOCIATED WITH SLEEP DISORDERED BREATHING IN PATIENTS WITH STABLE HEART FAILURE

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**Introduction :** Diabetes (DM) is a common comorbid condition among persons with cardiovascular disease, including heart failure (HF). Both HF and DM appear to be associated with prevalent sleep disordered breathing. The purpose of this study was to examine the extent to which DM was associated with sleep disordered breathing in a sample of stable HF outpatients recruited from HF/Heart transplant centers.

**Methods :** We recruited a sample of 95 patients who had stable NYHA Class II-IV HF (M age = 58.08, SD = 16.38 years; 68/72% men, 27/28% women; M ejection fraction (EF) = 29.74, SD = 13.89. Home polysomnographic studies were conducted with the Safiro (Compumedics, Inc.) sleep recorder. EEG, chin EMG, EOG, ECG, respiratory effort, nasal airflow and nasal cannula were obtained and scored using Rechtschaffen and Kales and AASM criteria. The Pittsburgh Sleep Quality Index, Epworth Sleepiness Scale, SF36 Bodily Pain Scale, and the Centers for the Epidemiological Studies of Depression Scale were administered.

## Category I—Sleep Disorders-Breathing

Diagnosis of DM and other clinical data were obtained by medical record review.

**Results :** Thirty two percent of the sample (n = 30) had DM. Patients with DM were older (55.11, SD = 17.33 vs. 64.53, SD = 12.03 years p = 0.008). Twenty four (35%) of the males vs. 6 (22%) of the females had DM. HF patients with comorbid DM had significantly more obstructive (OSA index M = 7.82, SD = 10.72 vs. 2.29, SD = 4.52 p < .001) and central (CSA index M = 7.2, SD = 14.10 vs. 3.15, SD = 8.6, p = 0.09) apnea. Regression analysis demonstrated that DM explained 5% of the variance in apnea index (AI), independent of the effects of age, BMI, gender, NY Class and EF. Comorbid DM was not associated with self-reported sleep quality, arousal index, sleepiness, BMI, or NY Class. Diabetic HF patients had more self-reported bodily pain and a higher percentage of wake after sleep onset.

**Conclusion :** DM appears to contribute to higher levels of central and obstructive apnea among stable HF outpatients. DM may contribute to respiratory instability in these patients. Therefore, HF patients with comorbid DM may be at higher risk for sleep disordered breathing. Further study is needed of the mechanisms underlying this relationship.

**Support (optional):** 5 R01 NR08022

### 0462

#### OUTCOMES OF HOME DIAGNOSIS AND TREATMENT OF OBSTRUCTIVE SLEEP APNEA - RESULTS OF A RANDOMISED TRIAL

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**Introduction :** Obstructive Sleep Apnea (OSA) is typically diagnosed during in-lab supervised overnight polysomnography (PSG). The access to PSG testing is often limited. Whether OSA can be diagnosed and treated at home using level III monitoring (HM) and auto-CPAP is not clear. We have performed a randomised trial of home monitoring followed by auto-CPAP vs. routine care (PSG with CPAP titration). We have assessed outcomes such as subjective sleepiness (Epworth Sleepiness Scale), sleep quality, CPAP compliance and blood pressure after four weeks of CPAP treatment.

**Methods :** We have randomly assigned 53 consecutive subjects (28 males; age: 46.6 +/- 10.8 years; BMI: 32.8 +/- 6.8; ESS: 12.2 +/- 4.5; baseline BP: systolic 131 +/- 14 mmHg, diastolic 86 +/- 8 mmHg) presenting with symptoms of OSA to undergo either unattended HM (Embletta) and auto-CPAP (one week) followed by therapy with fixed CPAP pressure based on the 95% pressure from auto-CPAP or to PSG with CPAP titration. Groups were similar in age, ESS and arterial blood pressure at baseline. Diagnosis of OSA was made if RDI > 5 (HM) or AHI > 5 (PSG). The primary outcome was daytime sleepiness (Epworth Sleepiness Scale, ESS) after four weeks of CPAP. Secondary outcomes included sleep quality (Pittsburgh Sleep Quality Index, PSQI), CPAP compliance and arterial blood pressure. Unpaired t-tests were used for comparison between groups, paired t-tests for within group comparison before and after CPAP. P values of 0.05 or less were considered statistically significant.

**Results :** Thirty-seven subjects have completed four weeks of CPAP therapy (21 - PSG, 16 - HM). Mean AHI was 26.3 +/- 24.2. There was significant improvement in ESS in both groups (PSG group before: 12.6 +/- 5.9 vs. after CPAP: 6.3 +/- 4.0, p < 0.001; HM group 12.6 +/- 2.9 vs. 5.7 +/- 2.0; p < 0.001) and PSQI (PSG before: 8.2 +/- 2.8 vs. after CPAP 6.1 +/- 2.9, p = 0.09; HM: 10.0 +/- 3.9 vs. 6.4 +/- 3.6, p < 0.001). At four weeks there were no differences in ESS, PSQI, arterial BP and CPAP compliance between groups.

**Conclusion :** At four weeks of CPAP therapy subjects who were diagnosed with OSA at home using level III monitoring and who received

fixed CPAP therapy based on the 95% pressure of the Auto-CPAP had similar improvements in sleepiness, sleep quality and arterial blood pressure to subjects who were diagnosed with OSA in the sleep laboratory and treated with fixed CPAP. These preliminary results suggest that some patients with suspected OSA may be diagnosed and treated outside of the sleep laboratory.

**Support (optional):** Authors wish to thank Kelsey-Trail Health Region and Saskatoon Health Region for support.

### 0463

#### SLEEP OF MARRIED COUPLES BEFORE AND AFTER TREATMENT OF THE HUSBAND'S OBSTRUCTIVE SLEEP APNEA

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**Introduction :** It is well established that snoring/sleep apnea rates are higher in males than in females and that females have more trouble falling asleep, maintaining sleep and more daytime sleepiness than males. Many wives of OSA patients sleep separately or complain of sleep disruption secondary to the husband's noisy breathing. A single split night study of 10 married patients sleeping together showed the partners' sleep efficiency improved from 74% to 87% and Arousal Index dropped from 21 to 12 when the patient was treated with CPAP the second half of the night.

**Methods :** Ten married couples with the husband diagnosed as OSA were recruited to sleep together in the laboratory on two occasions, one immediately following the diagnostic night before starting CPAP treatment and again after two weeks of home treatment. Both complete the ESS, Marital Satisfaction Index-R, Calgary SAQLI before and after the two weeks of treatment. Each also completes home sleep logs noting compliance with CPAP, and whether sleeping together. PSGs are scored for both partners' sleep stages, sleep efficiency, A+HI, number of snores, number of arousals and whether these are initiated by the partners' respiratory events or their arousal.

**Results :** This study is in process and will be completed April 2006. First results show dramatic improvement in the SE of both partners, before CPAP husband 54.4% wife 73.2% with CPAP husband 68.2% wife 82%. Husband snore Index 75.2 with CPAP 5.1. ESS Before CPAP husband 14 wife 12, after CPAP husband 3 wife 6. Quality of their relationship improved for husband from 1.8 to 6.3 on a 7 point scale and wife from 2.9 to 5.8.

**Conclusion :** Sleep efficiency, daytime sleepiness, satisfaction in the relationship all benefit both partners when husband's OSA is treated with CPAP

**Support (optional):**

### 0464

#### PREDICTORS OF QUALITY OF LIFE IN CHINESE PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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**Introduction :** Obstructive sleep apnea (OSA) has been linked to quality of life (QoL) impairment, excessive daytime sleepiness (EDS), and mood disturbance. Identification of factors related to QoL can assist in targeting supportive interventions to improve QoL in this population. The purpose of this study is to determine the predictors of the QoL in patients with OSA, and to better understand the relationship between QoL and objective severity of OSA, EDS, and mood in the Chinese population.

**Methods :** A total of 108 patients (87 men and 21 women) with newly diagnosed OSA were assessed for QoL using the disease-specific measure, the Calgary Sleep Apnea Quality of Life Index (SAQLI), for EDS using the Epworth sleepiness scale (ESS). Mood was assessed using the Zung self-rating depression scale (SDS) and the Zung self-rating anxiety scale (SAS). The severity of OSA was measured by Polysomnographic (PSG) variables including the apnea-hypopnea index (AHI), and the mean and minimum oxygen saturation. The associations between each domain and the total score on the SAQLI and the PSG variables, ESS score, SDS score and SAS score were examined by Pearson linear correlation. Stepwise multiple regression analyses controlling for age, body mass index, gender, and hypertension medication were performed with the total score and each SAQLI domain as the dependent variable.

**Results :** Age, BMI, and AHI of this sample were  $47.6 \pm 10.8$  years,  $27.3 \pm 3.3$  kg/m<sup>2</sup>, and  $38.7 \pm 25.1$ , respectively. Fifty-nine patients (54.6%) were hypersomnolent (ESS score >10). Forty-five patients (41.7%) self-rated for a depressed mood (SDS score >50) and 21 patients (19.4%) recorded an anxious mood (SAS score >50). Significant correlations were observed between SDS score and ESS score ( $r = .210$ ,  $p < .05$ ), and between SAS score and ESS score ( $r = .220$ ,  $p < .05$ ). Stepwise multiple regression analysis identified the SAS score (partial  $R^2 = .376$ ) and the ESS score (partial  $R^2 = .136$ ) as independent factors for predicting the total score on SAQLI. The two variables accounted for 43.4% of the total variance in the total SAQLI score ( $R^2 = .434$ ,  $p < .001$ ). None of the PSG variables were significant predictors of any domain or total score of SAQLI.

**Conclusion :** QoL in the patients with OSA is not strongly related to objective severity, but instead may be caused by mood disturbance and perception of sleepiness. A careful evaluation and intervention for symptoms of anxiety are highly important for improving QoL in patients with OSA.

**Support (optional):**

## 0465

### CHARACTERISTICS OF PATIENTS WITH RAPID EYE MOVEMENT RELATED OBSTRUCTIVE SLEEP APNEA

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**Introduction :** Several demographic and clinical features have been shown to be helpful in assessing the likelihood of obstructive sleep apnea (OSA). Some authors have suggested that rapid eye movement (REM) related OSA affects a different patient population, but there has been conflicting data. In previous reviews, the occurrence in female subjects has ranged from 29-63%. We conducted a retrospective review to determine the gender distribution and OSA severity in patients with REM-related OSA.

**Methods :** We reviewed the charts of adult patients who had undergone nocturnal polysomnography at our institution between 2000 and 2005. REM-related OSA was defined as an apnea hypopnea index (AHI) in REM that was two times the overall AHI (REM plus non-REM). OSA was scored as mild (AHI 5-15 events per hour), moderate (16-30) and severe (>30).

**Results :** A total of 3000 charts were reviewed, and 87 patients met our definition of REM-related OSA. Seventy percent of our patients were female. While the median overall AHI was 11.3 (range 1.5- 40.5), the median REM AHI was much higher at 36.3 events per hour (range 9.8-84.7). Eleven patients did not meet criteria for OSA (AHI < 5) but did have mild (10 patients) or moderate (1 patient) disease during REM sleep. Of the 55 patients with mild OSA, 34 (62%) were found to be severe in

REM. Snoring was the most common presenting symptom (62 patients), and excessive daytime somnolence was found in 50 patients.

**Conclusion :** This review of patients with REM-related OSA at our institution reveals a predominance of female patients. We also found that while the majority of these patients had a total AHI <15, a large number had severe OSA during REM sleep. Further studies may be warranted to better assess risk factors, presenting symptoms, and comorbidities associated with REM-related OSA.

**Support (optional):**

## 0466

### SLEEP SPECTROGRAMS AND CENTRAL SLEEP-DISORDERED BREATHING IN THE SLEEP HEART HEALTH STUDY

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**Introduction :** Central sleep apnea and periodic breathing are characterized by relatively precise timing of respiratory events and recovery (nearly identical event-to-event timing), while obstructive sleep apnea demonstrates variable event-to-event timing as the upper airway structures do not oscillate with the same fundamental frequency.

**Methods :** The SHHS-II raw data (approximately 3000) was obtained in edf format. Sleep spectrograms were generated from the ECG in 2800 subjects, using the previously described cardiopulmonary coupling technique (Sleep 2005;28:1151-61). This method generates high frequency coupling (HFC) during stable NREM sleep, and low frequency coupling (LFC) during unstable NREM or disrupted REM sleep. In "central" disease, LFC demonstrates a narrow spectrum/band characteristic (NBLFC, where there is one dominant oscillating frequency). Obstructive disease is characterized by a broad band/spectrum (BBLFC). Events that seems mixed or obstructive by standard polysomnographic features may occur within the narrow band spectrum; the reverse (standard central disease with a BBLFC feature) is extremely rare. NBLFC and BBLFC % of total sleep time were computed, tabulated and analyzed in relation to clinical and polysomnographic co-variables from the SHHS data set.

**Results :** Spectrographic displays of cardiopulmonary coupling can clearly identify periods of central-like disease not constrained by visual scoring. 918/2800 (33%) subjects had at least 5 minutes of NBLFC, while 15% spent at least 5% of TST in NBLFC. As a group, these patients (relative to those with BBLFC) had an increased arousal index ( $16.2 \pm 8$  vs.  $21.9 \pm 12.5$ ,  $p < 0.001$ ) and AHI ( $7 \pm 8.3$  vs.  $18 \pm 17.9$ ,  $p < 0.001$ ). The odds ratio using logistic regression for prevalent hypertension using % time in NBLFC / TST as the independent variable was 7.2 (95% CI: 2.6-20.5), while that using the AHI (apneas + desaturating hypopneas) was 1.02 (95% CI: 1.01-1.03), in this data set. More detailed analysis will be available at the time of presentation.

**Conclusion :** Sleep spectrograms provide dynamic assays of interactions between upper airway obstruction and respiratory control dysfunction in the genesis of sleep-disordered breathing. The prevalence of a significant component of control dysfunction is at least 15% in the SHHS-II population. Strong correlations with prevalent hypertension raises the possibility that carotid chemoreflexes may be central to both phenomena (hypertension, respiratory dyscontrol).

**Support (optional):** NIH / NHLBI R21HL079248 to RJT

## 0467

### CHANGES IN CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) DURING THE FIRST SIX MONTHS FOLLOWING BARIATRIC SURGERY

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**Introduction :** Obstructive sleep apnea (OSA) is common in the morbidly obese. Bariatric surgery results in dramatic weight loss and attenuates OSA severity, but is not curative in all cases. Intervention with self-adjusting CPAP compensates for pressure changes that are likely to occur during weight loss. The following study examined the change in CPAP pressure requirements during the first six months following bariatric surgery.

**Methods :** Eight bariatric surgery patients (mean BMI  $57.5 \pm 12$  kg/m<sup>2</sup>) diagnosed with OSA via laboratory polysomnography were placed on self-adjusting CPAP (Autoset Spirit™) before surgery and were seen at 2-weeks, 3-months and 6-months after surgery. Compliance and pressure data were obtained at each time point and weight was recorded.

**Results :** Data were analyzed with repeated measures ANOVA using weight loss as a covariate and Tukey's HSD for post hoc comparisons. Weight loss averaged 9 kg (4.1-15.5) at 2-weeks, 23 kg (14.5-33.2) at 3-months and 39.4 kg (29.4-48.2) at 6-months. A main effect for the 95th pressure centile (P95) and median pressure (PMed) were observed. The mean P95 decreased from 11.7 cm H<sub>2</sub>O pre-operatively to 9.6 cm H<sub>2</sub>O 2-weeks after surgery (95% CI 0.3-3.9). The PMed decreased from 9.5 cm H<sub>2</sub>O pre-operatively to 7.2 cm H<sub>2</sub>O 2-weeks after surgery (95% CI 0.4-4.1) and to 6.0 cm H<sub>2</sub>O at 3-months (95% CI 0.3-6.7). The maximum pressure did not change over time. A main effect for weight loss was not observed.

**Conclusion :** Reduction in optimal CPAP pressure (P95) was observed 2 weeks after surgery and remained stable at 3-months and 6-months. The PMed was significantly lower at 2-weeks and 3-months, whereas no change in PMax was observed. Pressure changes were independent of weight loss. Rapid weight loss and changes in hormonal regulation of weight and metabolism may be responsible for the pressure reductions.

**Support (optional):**

### 0468

#### TREATMENT FOR OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH PERSISTENT ASTHMA IMPROVES QUALITY OF LIFE- A RANDOMIZED-CONTROLLED STUDY

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**Introduction :** Obstructive sleep apnea (OSA) is common among asthmatics, but the impact of comorbid OSA on asthma-specific or generic quality of life has not been studied.

**Methods :** After a 4-week run-in phase with completion of an asthma diary, ten asthmatics with persistent asthma symptoms (NAEPP steps 2-4 despite optimal therapy) and OSA (apnea/hypopnea index [AHI]>5) were enrolled in an 8-week randomized controlled study of continuous positive airway pressure (CPAP) therapy (n=4) vs. no intervention (n=6). The validated Asthma Quality of Life Questionnaire (AQLQ), SF-36, and spirometry were completed at baseline and 8 weeks. An asthma symptom-free day was defined by absence of daytime or nighttime symptoms, and no rescue bronchodilator use. One-sided Wilcoxon two-sample exact tests were used to compare the two groups.

**Results :** At baseline, mean age ( $\pm$ standard deviation) was  $54 \pm 8$  years; 6 subjects were women; BMI was  $36.3 \pm 9$ ; forced expiratory volume in one second as percent of predicted value (FEV1%) was  $81.9 \pm 14.39$ ; one subject was in asthma severity step 2, seven in step 3 and two in step 4 (CPAP vs. control groups,  $p > 0.10$  for each variable). Mean AHI was  $21.1 \pm 7$  ( $26.9 \pm 1.8$  vs.  $17.1 \pm 5.5$ ,  $p = 0.009$ ); mean minimum oxygen saturation during sleep was  $78.8 \pm 6.2$  ( $p = 0.16$ ). CPAP use was  $4.5 \pm 2.2$  hours/night in treated subjects. At 8-weeks, the AQLQ improved significantly more from

baseline in CPAP vs. control subjects (mean score change  $0.82$  vs  $-0.56$ ,  $p = 0.009$ ), with significant improvements in the activities ( $p = 0.005$ ) and symptoms ( $p = 0.03$ ) domains. On the SF-36, greater improvements in physical functioning ( $p = 0.01$ ), energy-vitality ( $p = 0.02$ ), and "health change from the year before" ( $p = 0.03$ ) were seen in the CPAP group than in the control group. Baseline AHI did not predict changes in the AQLQ or specific SF-36 domain scores (linear regression models, all  $p > 0.10$ ). There was a trend toward a higher percentage of symptom-free days in CPAP vs. control subjects ( $p = 0.09$ ). Changes from baseline in FEV1% did not differ between groups ( $p = 0.47$ ).

**Conclusion :** Initial results from this randomized controlled trial suggest that treatment of comorbid OSA in persistent asthmatics improves quality of life in meaningful ways, perhaps in part because asthma symptoms are reduced.

**Support (optional):** M01-RR00042, 5T32NS007222 (MT)

### 0469

#### DETERMINANTS OF HEART RATE ACCELERATIONS IN RESPONSE TO SLEEP-DISORDERED BREATHING AMONG CARDIAC PATIENTS

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**Introduction :** Repeated HR arousals with return to baseline are seen in association with obstructive apnea (OA) and hypopnea (H) during sleep, occurring at the termination of each event. We explored factors influencing the magnitude of HR accelerations (HRA) during these arousals.

**Methods :** N=123 patients with known cardiac disease (age  $58 \pm 10$  yrs, 76M, 47F, 55% post-MI, 55% on  $\beta$ -blockers) were recruited for a study of depression and sleep apnea. Subjects underwent 2 nights of polysomnography. ECGs from the 2nd night were extracted and scanned on a Holter analyzer that generated HR tachograms of normal-to-normal interbeat intervals. Tachograms were integrated with sleep stage and respiratory event type using MatLab, and the HRA associated with each event (OA=4582, H=7548) was calculated. Multivariable regression analysis identified the determinants of HRA including: event type (OA, H), sleep stage (REM, non-REM), age group (<60,  $\geq 60$  yrs), gender, BMI (<25, 25-30, >30), Hx of MI, depression and  $\beta$ -blocker use

**Results :** HR change during REM was  $15 \pm 10$  bpm (range 0-62 bpm) and  $14 \pm 8$  bpm (range 0-64) during non-REM. HRA was  $0.9 \pm 1.1$  bpm/sec (range 0-5.8) during REM and  $0.8 \pm 0.8$  bpm/sec (range 0-13.7) during non-REM. HRA was positively related to OA, REM sleep and younger age. Event type and sleep stage modified the effect of BMI, and sleep stage modified the effect of gender. There was no effect of Hx of MI, depression or  $\beta$ -blocker use. The  $\uparrow$ HRA in OA occurred both during REM and non-REM, but was greater during REM (OA:  $0.98 \pm 0.05$  vs. H:  $0.64 \pm 0.04$ ). HRA was  $\downarrow$  for H in REM compared with H in non-REM. The  $\uparrow$ HRA for patients <60 was more exaggerated in REM and during OA (REM <60:  $0.96 \pm 0.06$  vs.  $\geq 60$ :  $0.66 \pm 0.06$ ; OA <60:  $1.08 \pm 0.06$ ; OA  $\geq 60$ :  $0.77 \pm 0.06$ ). HRA was greater among overweight patients (BMI 25-30), although obese patients had >HRA than normal weight patient. Also, females had  $\uparrow$ HRA during OA in non-REM and  $\downarrow$ HRA in REM, with no difference in H events.

**Conclusion :** Rapid HR accelerations occur, especially in association with OA during REM sleep, suggesting dramatic and possibly dangerous changes in autonomic tone. Magnitude was not affected by  $\beta$ -blockade. Lesser accelerations seen in older patients suggest a loss of autonomic

sensitivity with aging or a possible habituation to sleep apnea.

**Support (optional):**

#### 0470

##### DRUG-INDUCED SLEEP ENDOSCOPY FOR EVALUATION IN OBSTRUCTIVE SLEEP APNEA SURGERY

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**Introduction :** Airway obstruction in obstructive sleep apnea can occur at many levels, including the palate and hypopharynx. The goal of surgical evaluation is to identify the site(s) of airway obstruction to produce tailored, effective surgical treatment. Drug-induced sleep endoscopy (DISE) requires the pharmacologic induction of sleep and fiberoptic endoscopy to characterize the location and configuration of upper airway collapse. As opposed to other evaluation tools, DISE uniquely provides a dynamic assessment of the breathing, sleeping patient. The objective of this study was to compare DISE findings with other methods commonly used in the evaluation of obstructive sleep apnea surgical patients.

**Methods :** Patients with moderate or severe obstructive sleep apnea underwent DISE using Propofol prior to surgical treatment. Mueller maneuver, Friedman Stage evaluation, and lateral cephalometry were also performed. DISE assessment included the overall pattern of obstruction (palate and/or hypopharynx) and whether specific structures (palate/tonsils, lateral pharyngeal walls, tongue base, and epiglottis) contributed to airway obstruction. Cohen's kappa statistic and chi-squared testing were used to test the agreement between the global assessment of DISE and other evaluation techniques. Chi-squared testing determined the association between contributions of individual structures to airway obstruction on DISE and specific findings of other methods.

**Results :** Fifty patients underwent DISE. Mean age was  $44.5 \pm 10.6$  years, and mean apnea-hypopnea index was  $48.8 \pm 31.1$ . Comparing the global pattern of obstruction during DISE to other evaluation techniques, Cohen's kappa statistic varied from 0.65 (substantial agreement) for the Friedman Stage to 0.03 (slight agreement) for the Mueller Maneuver. No findings from other evaluation techniques were strongly associated with the contribution of specific structures to airway collapse on DISE.

**Conclusion :** DISE provides a unique and distinct assessment of obstructive sleep apnea patients considering surgery. Other evaluation techniques can provide similar global evaluations, but DISE may better identify specific structures involved in airway obstruction. Future research will address the association between DISE findings and surgical outcomes.

**Support (optional):**

#### 0471

##### SLEEP DISORDERED BREATHING AND SLEEPINESS, SLEEP QUALITY, AND SLEEP-RELATED QUALITY OF LIFE IN OLDER MEN: A PROSPECTIVE STUDY WITH OBJECTIVE MEASURES OF SLEEP

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**Introduction :** Previous studies have demonstrated an association between obstructive sleep apnea and daytime sleepiness, sleep quality, and sleep-related quality of life among middle-aged adults; however, the evidence concerning these relationships in older adults is mixed. This study is the first to combine objective measures of sleep time and sleep-

disordered breathing (SDB) to examine their relationship to daytime sleepiness, sleep quality, and sleep-related quality of life in a large cohort of primarily non-institutionalized older men.

**Methods :** Subjects are participants in the Osteoporotic Fractures in Men (MrOS) Study, a multicenter, longitudinal study of 5,995 men aged 65 or older that began in 2000. A sample of 2,911 older men underwent in-home overnight polysomnography and wrist actigraphy in the Outcomes of Sleep Disorders in Older Men (MrOS Sleep Study). Outcomes of interest were daytime sleepiness (using the Epworth Sleepiness Scale), sleep quality (Pittsburgh Sleep Quality Index), and sleep-related quality of life (Functional Outcomes of Sleep Questionnaire). Analysis of variance (ANOVA) and multiple regression analyses examined the association between SDB severity, as measured by apnea-hypopnea index and percentage of sleep time with oxygen saturation below 90%, and these outcome measures. Regression models were adjusted for age, body mass index, and medical comorbidity index. We further explored whether these associations were mediated by sleep deprivation by adjusting models for total sleep time.

**Results :** Mean age was 73.0 years, and mean body mass index was  $27.4 \pm 3.7$  kg/m<sup>2</sup>. Mean apnea-hypopnea index was  $17.1 \pm 15.1$ . SDB severity was modestly associated with Epworth Sleepiness Scale and Functional Outcomes of Sleep Questionnaire scores on ANOVA and regression analyses; this relationship was somewhat attenuated by adjustment for total sleep time. Before adjustment for total sleep time, a 15-point increase in apnea-hypopnea was associated with a 0.25 (95%CI 0.11,0.38) increase in Epworth Sleepiness Scale score and a 0.09 (95%CI 0.03,0.15) decrease in Functional Outcomes of Sleep Questionnaire score. Pittsburgh Sleep Quality Index scores were associated with total sleep time but not SDB severity.

**Conclusion :** SDB severity in community-dwelling older men is modestly associated with daytime sleepiness and sleep-related quality of life but is not associated with poor sleep quality.

**Support (optional):** The National Heart, Lung, and Blood Institute (NHLBI) provides funding for the MrOS Sleep ancillary study, "Outcomes of Sleep Disorders in Older Men," under the following grant numbers: R01 HL071194, R01 HL070848, R01 HL070847, R01 HL070842, R01 HL070841, HL070837, HL070838, and HL070839.

#### 0472

##### STAGE-SPECIFIC SLEEP-DISORDERED BREATHING AND SUBJECTIVE EXCESSIVE DAYTIME SLEEPINESS

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**Introduction :** It has been reported that in patients with apnea-hypopnea index (AHI)<10, REM sleep specific AHI (AHIREM)>15 is associated with excessive daytime sleepiness (EDS). This, however, has not been confirmed by subsequent studies. We hypothesized that an elevated AHI in other sleep stages may have a better relation to subjective measures of sleepiness than AHIREM.

**Methods :** We reviewed polysomnographies (PSG) of 347 patients, 180 males, aged (mean±SD)  $40 \pm 13$  years, with AHI<10AH/h, mean AHI  $4 \pm 2$  AH/h. Sleepiness was assessed by the Epworth sleepiness scale (ESS). Apneas and hypopneas occurring in each sleep stage were quantified by indices calculated for the amount of the sleep stage.

**Results :** Mean ESS was  $9 \pm 5$ , range 0 to 23. Comparing AHI in Stage 1 (AHI1), AHI in Stage 2 (AHI2), and AHIREM, the total AHI and arousal index (AI), we found that AHI2 presents the strongest correlation with ESS (Spearman's rho= 0.216, p= 0.000). Of the 347 studied patients with total AHI<10, 140 (40%) had an AHIREM>10, 87 (25%) an AHI1>10, and 16 (5%) an AHI2>10. Area under the ROC curve for detecting

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ESS>10 was significant only for AHI2 (Area= 0.6,  $p= 0.006$ ); the best accuracy being obtained when AHI2 is considered positive if  $> 2.5\text{AH/h}$  (sensitivity= .54, specificity= .57). Using ESS as dependent variable in stepwise multiple regression analysis AHI2 was the only variable entered in the model ( $r= 0.251$ ,  $p= 0.035$ ) when controlling for AHI1, AHI2, AHIREM, age, sex, body mass index (BMI), cervical circumference, smoking, and depression. AHIREM>15 did not show significant association with ESS>10 ( $p= 0.48$ ). Body mass index correlated significantly with ESS ( $\rho=0.176$ ,  $p=0.001$ ).

**Conclusion :** In this sample of patients with borderline AHI, clinically significant subjective EDS, as indicated by an ESS score>10, is not be associated with REM-specific SDB. Stage 2-specific SDB may deserve investigation as a possible predictor of EDS.

**Support (optional):**

### 0473

#### EXPLORING POTENTIAL ASSOCIATIONS OF C-REACTIVE PROTEIN (CRP) WITH SLEEP DURATION AND SLEEP-DISORDERED BREATHING

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**Introduction :** Increasing evidence suggests that alterations in sleep duration are associated with obesity, insulin resistance, and cardiovascular disease (CVD). Additionally, sleep disordered breathing (SDB), which is associated with disturbed nighttime sleep and hypoxemia, may be an independent risk factor for CVD. C-reactive protein (CRP) is an inflammatory marker that is an important predictor of CVD. We investigated potential associations between circulating CRP, and sleep duration and SDB in 907 men and women from the Wisconsin Sleep Cohort Study (WCS).

**Methods :** SDB and other sleep parameters were evaluated by overnight polysomnography. Body habitus measures and a health questionnaire were completed in the evening; a fasting blood sample was obtained in the morning. CRP was measured in duplicate by a highly sensitive enzyme-linked immunoassay. The relationships between CRP, SDB, and sleep parameters were evaluated using multiple linear regression with and without control for age, sex, and BMI.

**Results :** As previously reported, sex and body mass index (BMI) were strongly associated with CRP. CRP showed a significant positive association with smoking, self-reported exercise, the metabolic syndrome, waist-hip ratio (WHR), body fat, LDL, triglycerides, leptin, insulin, and homeostatic model assessment (HOMA), independent of age, sex and body mass index (BMI). Significant independent negative associations were observed with HDL, quantitative insulin sensitivity check index (QUICKI), and hours of exercise. CRP levels showed significant associations with the apnea-hypopnea index (AHI) and snoring. These associations were not significant after adjustment for age, sex and BMI. No significant association between CRP levels and measures of sleep duration (polysomnographic and self-reported) were found.

**Conclusion :** There was no significant association between CRP levels and SDB after correction for age, sex and BMI. There was no significant association between CRP levels and measures of sleep duration. Previously reported relationships between SDB and CRP are likely to be mostly driven by its primary association with excess body weight, and in particular, visceral obesity.

**Support (optional):** National Institutes of Health grants MH-073435 and HL-62252 (E.Mignot) and HL62252, AG14124, and RR03186 (T. Young). Howard Hughes Medical Institute: S. Taheri (former research

associate) and EM (investigator).

### 0474

#### SEASONAL AFFECT ON APNEA-HYPOPNEA INDEX AND CONTINUOUS POSITIVE AIRWAY PRESSURE LEVEL

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**Introduction :** Studies have suggested seasonal allergies, nasal congestion, and asthma affect airway tone, cause airway narrowing, or worsen snoring with rhinitis an independent risk factor for increased apnea hypopnea index (AHI). These factors vary seasonally, in some geographic areas. This study investigated whether the season in which a patient underwent polysomnography influenced AHI or optimal CPAP settings.

**Methods :** A total of 639 patients (ages 6.8-92.0,  $X=51.7$ ,  $Sd=14.8$ ; 358 male, 281 female) undergoing polysomnographic studies in the Martha Jefferson Sleep Medicine Center from September 22, 2004-September 21, 2005 were included for review. Patients were divided into 4 groups based upon the season of their study: autumn (September 22, 2004-December 20, 2004), winter (December 21, 2004-March 19, 2005). Spring (March 20, 2005-June 20, 2005), and summer (June 21, 2005-September 21, 2005). Patient age, gender, AHI and optimal CPAP pressures were analyzed and average AHI and CPAP titration pressure was calculated for each season.

**Results :** Average age of patients as well as male to female percentage did not differ significantly between seasonal groups. Optimal CPAP settings did not differ significantly between seasons, although optimal summer pressures showed a slight trend towards being higher (autumn  $X=10.6$  cmH<sub>2</sub>O, winter  $X=10.5$  cmH<sub>2</sub>O, spring  $X=10.4$  cmH<sub>2</sub>O, summer  $X=11.4$  cmH<sub>2</sub>O). Average AHI tended to be highest in the autumn, but patient number was inadequate to confirm significance (autumn  $X= 32.8$  events/hour, winter  $X=28.8$  events/hour, spring  $X=27.7$  events/hour, summer  $X=29.2$  events/hour).

**Conclusion :** These results demonstrate that based upon this collection of patients, the season in which a CPAP titration occurs does not appear to strongly influence AHI or optimal CPAP titration pressures. One limitation of this protocol is the lack of detailed temperature measurements, pollen, mold and other environmental allergen measurements, etc. for the individual sleep study dates. Studies with higher patient numbers may be needed to determine exact seasonal effect.

**Support (optional):**

### 0475

#### THE BERLIN QUESTIONNAIRE FOR SLEEP APNEA IN A SLEEP CLINIC POPULATION: RELATIONSHIP TO POLYSOMNOGRAPHIC MEASUREMENT OF RESPIRATORY DISTURBANCE

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**Introduction :** The Berlin Questionnaire (BQ) has been shown to perform with relatively high sensitivity and specificity in identifying patients at high risk for having sleep apnea in primary care and atrial fibrillation patients. The BQ may be a useful adjunct in sleep medicine and research but it has never been validated in a sleep clinic population. The aim of the study is to determine the specificity and sensitivity of the BQ as compared to the gold standard, the respiratory disturbance index (RDI), in a sleep clinic population.

**Methods :** This is a retrospective chart review study of 130 sleep clinic patients who were referred for sleep assessment. Patients' demographics,



BQ scores and RDI measurements were extracted from the patients' charts. All patients were administered the BQ and underwent 2 overnight polysomnographic studies in the sleep laboratory. The RDI values were obtained from averaging the measurements from the two nights of recordings.

**Results :** Of the 130 charts reviewed, the BQ identified 75 (58%) as being at high-risk for sleep apnea but overnight polysomnography found only 30 of the 130 patients (23%) had an RDI>10. The BQ performed with 0.60 sensitivity and 0.43 specificity at the RDI>10 level and resulted in 40% false negatives and 57% false positives. At the RDI>5 level the BQ performed with 0.67 sensitivity and 0.48 specificity and resulted in 33% false negatives and 52% false positives. The BQ score correlated poorly with the RDI obtained from the first ( $r=0.152$ ) or second ( $r=0.201$ ) night of polysomnographic recording.

**Conclusion :** Due to the low sensitivity and specificity as well as the large number of false negatives and positives, the Berlin Questionnaire is not an appropriate instrument for identifying patients with sleep apnea in a sleep clinic population.

**Support (optional):** University of Toronto, Institute of Medical Sciences Summer Studentship

## 0476

### ARE RESPIRATORY DISTURBANCE INDICES CORRELATED WITH SLEEP ARCHITECTURE IN PATIENTS WITH SLEEP APNEA SYNDROME?

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**Introduction :** Patients with sleep apnea syndrome (SAS) often experience nonrestorative sleep and poor sleep quality. The objective of this study was to determine the relationship between respiratory disturbance indices (RDI) and sleep architecture in patients with sleep apnea syndrome.

**Methods :** The study included 86 (63 males and 23 females) untreated SAS subjects with a wide range in severity (RDI: 10-101.1). Two consecutive overnight polysomnographic recordings for each subject were carried out. These subjects were free of psychotropic medications at the time and two weeks prior to the sleep studies. In order to avoid first night effect, only second night sleep study was analyzed. Pearson correlation analysis was used in the statistical analysis. RDI measurements included RDI in total sleep time (RDI TST), RDI in non-REM sleep (RDI NREM) and RDI in REM sleep (RDI REM). Sleep architecture measurements included the percentages of stage 1-4 sleep, slow wave sleep (SWS), REM sleep (REM) and wakefulness.

**Results :** The values of correlation coefficient ( $r$ ) were 0.317 ( $p=0.003$ ) between RDI TST and stage 1 sleep (%), -0.218 ( $p=0.044$ ) between RDI TST and stage 4 sleep (%) and -0.235 ( $p=0.029$ ) between RDI TST and SWS (%). The  $r$  values were 0.358 ( $p=0.001$ ) between RDI NREM and stage 1 sleep (%), -0.253 ( $p=0.019$ ) between RDI NREM and stage 3 sleep (%), -0.239 ( $p=0.027$ ) between RDI NREM and stage 4 sleep, -0.279 ( $p=0.009$ ) between RDI NREM and SWS (%). There was no correlation between RDI REM and sleep architecture.

**Conclusion :** The results indicated that in this group of SAS patients, respiratory disturbance indices correlated significantly with multiple polysomnographic measurements. RDI TST had a positive correlation with stage 1 sleep and a negative correlation with stage 4 and slow wave sleep. RDI NREM sleep had a positive correlation with stage 1 sleep and a negative correlation with stage 3, stage 4, and slow wave sleep. Sleep apnea alters quality of sleep with resulting in deep sleep and more light sleep.

**Support (optional):**

## 0477

### A NOVEL CPAP DEVICE: POLYSOMNOGRAPHIC COMPARISON WITH STANDARD CPAP THERAPY IN OBSTRUCTIVE SLEEP APNEA PATIENTS ON CPAP

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**Introduction :** Compliance with CPAP is suboptimal and in part related to sensations of dyspnea, discomfort and anxiety. Traditional CPAP devices use variable speed blowers to generate flow, resulting in temporary increases in expiratory pressure. A novel CPAP device, the PolarisEX (Invacare, Elyria, OH), uses a fixed speed blower with a variable resistance valve controlled by SoftX™ technology to reduce the duration of the expiratory pressure rise. This pilot study evaluates the effectiveness and acceptability of this novel CPAP device versus conventional CPAP.

**Methods :** Subjects with mild to severe OSA (AHI 5-60 events/hr) compliant with CPAP (> 3 hrs/night) were eligible. Participants underwent 2 polysomnograms (PSGs), one on the novel CPAP and one on their home CPAP, in random order and separated by 1 week. The Stanford Sleepiness Scale (SSS) and Treatment Satisfaction Questionnaire were completed following each PSG. One RPSGT, blinded to the treatment, scored all PSGs. Data were analyzed in SPSS as follows: normally distributed continuous variables by paired t-test, nonparametric continuous variables by Wilcoxon signed rank.

**Results :** Ten subjects were studied. Demographics: 50% male, mean age 46 years, mean BMI 36.7 kg/m<sup>2</sup>, mean baseline AHI 31.6 (range 6-58), mean CPAP setting 10.4 cm H<sub>2</sub>O (range 6-14). There was no sequence effect to the treatment order. No significant differences were found in any PSG parameter (AHI, lowest oxygen saturation, time < 90%, arousal index, and sleep efficiency), the SSS or in treatment satisfaction between the novel CPAP device and conventional CPAP.

**Conclusion :** The novel CPAP device appears equivalent to conventional CPAP for controlling a broad spectrum of OSA in patients currently compliant with CPAP therapy. Despite patients being exposed to the novel CPAP for the first time on the night of their study PSG, they tolerated the therapy as well as their usual CPAP device.

**Support (optional):** Support provided by Invacare Corporation, Elyria, OH and by General Clinical Research Center grant # MO1 RR00080

## 0478

### THE CLINICAL EFFICACY AND COMFORT OF EXPIRATORY PRESSURE RELIEF (EPR) COMPARED WITH FIXED CONTINUOUS POSITIVE AIRWAYS PRESSURE (CPAP)

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**Introduction :** CPAP with EPR provides decreased pressure during exhalation. This may increase patient comfort but may also cause break through residual respiratory events. A study was conducted at the Sleep & Chest Disorders Centre in Sydney, Australia, to investigate the clinical efficacy and subjective comparison of comfort and satisfaction of EPR compared to CPAP.

**Methods :** Subjects diagnosed with obstructive sleep apnoea, established on CPAP therapy, were recruited to this randomized single blinded study. Subjects gave written informed consent. Subjects were previously using a range of CPAP devices and all were using ResMed masks. Subjects trialed the S8 AutoSet (ResMed Ltd) set in CPAP mode with varying levels of EPR in a randomized order, for at least 3 nights in each mode, in their

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own home. The modes trialed were CPAP, EPR of 1cmH<sub>2</sub>O, 2cmH<sub>2</sub>O and 3cmH<sub>2</sub>O. Subjects returned to the sleep center for each mode change and at that time: (1) had the S8 AutoSet downloaded [Apnoea-Hypopnoea Index (AHI), Apnoea Index (AI), Hypopnoea Index (HI), Leak, Pressures and Usage data] (2) completed subjective questionnaires relating to comfort and satisfaction for that mode. Statistical analysis was performed using a 2-sided paired T-test,  $p < 0.05$  CPAP v's EPR.

**Results :** 19 subjects completed the study [12male:7female, mean age: 52(28-71), mean Body Mass Index: 33.5(20.9-49.6), mean initial Respiratory Disturbance Index:47.3(7.1-111.4), mean therapy pressure:10cmH<sub>2</sub>O]. There was no difference between EPR and CPAP with respect to Average Usage, AHI, AI, HI and Maximum Leak for all 3 EPR modes. 79% of subjects preferred one of the 3 levels of EPR over CPAP, with an EPR of 3cmH<sub>2</sub>O the most popular. The majority of subjects rated EPR to be as, or more, comfortable and satisfying than CPAP.

**Conclusion :** EPR was equivalent to CPAP in the efficacy of treatment. The majority of subjects preferred EPR over CPAP.

**Support (optional):** Study sponsored by ResMed Ltd.

### 0479

#### CHRONIC RECURRENT APNEA INDUCED NEURONAL DEGENERATION AND APOPTOSIS IN THE GUINEA PIG FOREBRAIN: A LIGHT AND ELECTRON MICROSCOPIC STUDY

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**Introduction :** Obstructive sleep apnea (OSA) and sleep-disordered breathing (SDB) can result in impaired cognition, degradation in mental acuity, the generation of mood disorders, including depression, etc., which occur principally as a consequence of damage to neurons in the hippocampus and related brain regions (Gozal et al., *J Neurosci*. 21:2442-50, 2001). However, the mechanisms of neuronal damage, i.e., apoptosis and/or necrosis, have not been elucidated. Accordingly, using immunohistochemical and microscopic techniques, we examined the morphological effects of chronic recurrent apnea on neurons in the hippocampus and related forebrain sites.

**Methods :** Adult guinea pigs were exposed to six hours of recurrent apnea; control animals were normally respired. For immunohistochemical analyses, sections from the hippocampus, amygdala, and cingulate, insular and prefrontal cortices were obtained and stained with antibodies against activated caspase-3 and single-stranded DNA (ssDNA); the sections were then examined under light microscopy. For electron microscopic analysis, sections were processed as previously described (Zhang et al., *Brain Res*. 797:333-338, 1998).

**Results :** Neurons labeled by anti-caspase-3 or anti-ssDNA antibody were present in the hippocampus, amygdala, and cingulate, insular and prefrontal cortices in conjunction with periods of recurrent apnea; electron microscopic examination revealed necrotic and apoptotic damage to these neurons. Necrotic changes included early organelle swelling (mitochondria, rough endoplasmic reticulum and Golgi apparatus), intracytoplasmic vacuoles as well as lethal changes such as increased mitochondrial flocculent densities and discontinuous cell and nuclear membranes. Apoptotic damage consisted of cellular shrinkage, cytoplasmic condensation and chromatin condensation. Degenerated dendrites containing large vacuoles and demyelinated axons were also observed in the hippocampus and related sites. The preceding changes were not present in control animals.

**Conclusion :** The present data indicate that recurrent apnea results in cell

death in the hippocampus and related forebrain regions via mechanisms of necrosis and apoptosis.

**Support (optional):** This research was supported by grants MH 69372 and HL 60296.

### 0480

#### ONE-YEAR TREATMENT WITH A HERBEST MANDIBULAR ADVANCEMENT SPLINT IMPROVES OBSTRUCTIVE SLEEP APNEA AND ENDOTHELIAL FUNCTION

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**Introduction :** Obstructive sleep apnea (OSA) is associated with endothelial dysfunction (ED). The Herbest mandibular advancement splint (MAS) offers an alternative treatment to CPAP. In the current study we assessed the effect of long-term Herbest MAS treatment on OSA and on endothelial function (EF). We hypothesized that both will improve with treatment, correlated with each other

**Methods :** 16 subjects participated (11m/5f). Mean age and BMI were 54.0±8.3/y and 28.0±3.1 kg/m<sup>2</sup>, respectively. EF was measured in the morning using the Endo-PAT 2000 (Itamar Medical, Caesaria, Israel), based on the reactive hyperemic response of the finger's arterioles to five minutes of arterial obstruction. Apnea severity and EF were assessed after 3 months and 1 year on treatment

**Results :** Mean baseline (pre-treatment) AHI and ODI were 29.7±18.5/hr and 14.9±17.7/hr, respectively. Mean BMI and cardiovascular co-morbidities did not change during the study. AHI has decreased significantly with treatment during the 3 months and 1-year assessments to 17.7±11.1/hr and 19.6±11.5/hr, respectively ( $p < 0.005$  for both). ODI decreased significantly at these time points to 6.6±7.6 and 6.2±10.0 ( $p < 0.05$ , for both). Epworth Sleepiness Score decreased significantly from a baseline level of 12.4±6.0 to 10.2±6.6 (3 months) and 7.8±3.8 (1 year) ( $p < 0.001$ , for both). The index of EF increased significantly from a baseline level of 1.77±0.4 to 2.1±0.4 (3 months,  $p < 0.05$ ) and 2.0±0.3 (1 year), ( $p = 0.055$ ). There was a significant correlation between the improvement in AHI and in EF ( $r = 0.55$ ,  $p = 0.05$ )

**Conclusion :** The Herbest MAS is an effective treatment in patients with OSA, at least for 1 year, improving both breathing and EF. The correlation between the improvement in apnea indices and EF suggest that the respiratory abnormality causes the vascular abnormality. The improvement in EF to control levels without a complete elimination of apneic events suggests that there is a threshold effect of OSA on EF

**Support (optional):**

### 0481

#### ENDOTHELIAL FUNCTION OF PATIENTS WITH OBSTRUCTIVE SLEEP APNEA IMPROVES FOLLOWING 3 MONTHS ON CPAP

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**Introduction :** We have recently shown that Obstructive sleep apnea (OSA) is associated with endothelial dysfunction (ED), as assessed by the non-invasive technique of peripheral arterial tone response to reactive hyperemia (RH-PAT)<sup>1</sup>. This novel technique allows assessing endothelial functioning immediately after waking up from sleep in an automatic manner. Such post awakening measurements in sleep apnea patients may be of great clinical importance as ED is the first sub-clinical sign of atherosclerosis and is prognostic for future cardiovascular events. In the current study we sought to extend our study and examine whether this technique can demonstrate improvement in endothelial function of patients with OSA on CPAP.

**Methods :** 8 subjects participated (6m/2f). Their mean age BMI and AHI were  $50.8 \pm 13.1/y$ ,  $31.7 \pm 5.3 \text{ kg/m}^2$  and  $47.0 \pm 1.5/hr$ , respectively. Five of them had hypertension. Seven had severe OSA. Endothelial function was measured by the Endo-PAT 2000 device (Itamar Medical, Caesaria, Israel). It was quantified in the morning after waking-up from sleep at baseline (prior to treatment) and after 3 months on CPAP treatment.

**Results :** AHI on CPAP (after 3 months of usage) was significantly reduced to  $4.6 \pm 2.3/hr$  ( $p < 0.001$ ). Likewise, minimum oxygen saturation improved from  $76.0 \pm 15.0\%$  to  $92.7 \pm 1.5\%$  ( $p = 0.03$ ). BMI and blood pressure did not change during the study period. The index of endothelial functioning as determined by the Endo-PAT 2000 increased significantly from a baseline level of  $1.67 \pm 0.25$  to  $2.1 \pm 0.18$  on treatment ( $p = 0.01$ ).

**Conclusion :** Our results show that the non-invasive peripheral arterial tone response to reactive hyperemia (RH-PAT) is a sensitive technique, demonstrating improved endothelial function following 3 months of CPAP treatment in obese patients with severe OSA. Post awakening measurements of endothelial functioning in sleep apnea patients may provide important information about the risk of cardiovascular morbidity in these patients and on treatment efficacy. Reference: 1. Itzhaki S, Lavie L, Pillar G, Tal G, Lavie P. Morning-evening variation of Endothelial Function in Obstructive Sleep Apnea. SLEEP 28: 594-600, 2005.

**Support (optional):**

## 0482

### HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME AND COPD (OVERLAP SYNDROME)

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**Introduction :** Obstructive sleep apnea syndrome (OSAS) and Chronic Obstructive Pulmonary Disease (COPD) are both prevalent health problems with well-defined effects on health-related quality of life. The simultaneous occurrence of OSAS and COPD, known as overlap syndrome (OVS), is not rare because both are common diseases. Our primary aim was to determine the possible impact of sleep related breathing disorders in the quality of life in patients with OVS.

**Methods :** The St. George's Respiratory Questionnaire was used in order to assess the quality of life in 15 COPD patients with unsuspected OSAS (Epworth Sleepiness Scale  $< 10$ ). A control group consisting of 10 age matched COPD patients with comparable BMI, pulmonary function testing and arterial blood gases was used for statistical evaluation.

**Results :** The OVS group showed a reduction in REM sleep, increased arousal index and significant oxygen desaturation during sleep. The mean AHI of the above OVS group was  $12.9 \pm 17.8$ . A statistically significant increase in all 3 components of the St. George's Respiratory Questionnaire (symptoms, activities and impact) was observed in patients with OVS compared to the control group. The symptom, activity and impact components were  $53.7 \pm 20.9$  versus  $32.6 \pm 18.03$  ( $p = 0.003$ ),  $62.1 \pm 17.4$  versus  $42.09 \pm 10.8$  ( $p = 0.004$ ) and  $38.4 \pm 27.5$  versus  $19.3 \pm 6.4$  ( $p = 0.045$ ) respectively (Range in all components 0-100).

**Conclusion :** OSAS can significantly impair the quality of life in patients with OVS even in the absence of sleep related daytime complaints. Management of underlying sleeping disorders in such patients could be effective in decreasing morbidity and improving quality of life.

**Support (optional):**

## 0483

### EVENING-MORNING DIFFERENCES IN BLOOD PRESSURE IN SLEEP APNEA SYNDROME: GENDER RELATED DIFFERENCES

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**Introduction :** Obstructive sleep apnea (OSA) is associated with hypertension. Increased morning versus evening blood pressure (BP) may be associated with OSA and with increased cardiovascular risk. In the current study we sought to determine if the morning-evening differences in BP would correlate with the severity of OSA, and if there are gender-related differences, as men are at higher risk for both OSA and cardiovascular diseases.

**Methods :** The study consisted of 2009 patients referred to the sleep lab with suspected OSA: 870 non-hypertensive men (non-HT), 696 hypertensive (HT) men, 258 non-HT women, and 185 HT women. All underwent a full night PSG, and 4 BP measurements; two measurements (5 minutes apart) in the evening, and 2 in the morning. The average of the two measurements was calculated. The relationship between evening and morning difference in BP and Apnea-Hypopnea Index (AHI) was analyzed separately for HT and non-HT men and women.

**Results :** In men, increase in AHI was associated with increase in morning BP, and the evening-morning difference in BP became negative. These trends were found significant by linear regression analyses both for HT (for systolic BP  $r = 0.75$ , for diastolic BP  $r = 0.96$ ) and non-HT patients (for systolic BP  $r = 0.93$ , for diastolic BP  $r = 0.94$ ,  $p < 0.05$  for all). Unlike men, in women increasing AHI was not associated with increase in the evening-morning BP differences. None of the regression lines fitted to the data was significant.

**Conclusion :** In men, the evening-morning difference in BP is linearly related to the severity of OSA, in both HT and non-HT patients. These results may have practical relevance in screening for patients with OSA and may have prognostic clinical value in predicting cardiovascular events. We speculate that the lack of these relationships in women may result from the recently reported better and deeper sleep of women with OSA vs men with OSA.

**Support (optional):**

## 0484

### COMPARISON OF SLEEP PARAMETERS ON TITRATION NIGHT BETWEEN PRECEDED AND INITIAL CONTINUOUS POSITIVE AIRWAY PRESSURE TREATMENTS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME

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**Introduction :** Obstructive sleep apnea hypopnea syndrome (OSAHS) patients usually touch continuous positive airway pressure (CPAP) machines for the first time on titration night, and then the effect of overnight CPAP treatment is estimated immediately. In contrast, autoadjusted CPAP or formula-calculated fixed CPAP treatment is sometimes preceded before titration night to allow patients to come familiar with CPAP machines or to prevent cardiovascular or cerebrovascular attack. To compare the effects of preceded and initial CPAP treatment on sleep parameters on titration night, we performed a prospective randomized controlled parallel study.

**Methods :** One hundred forty patients who had been diagnosed with OSAHS by baseline polysomnography were divided into two groups ran-

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domly. Seventy OSAHS patients received auto-CPAP treatment for two months and then received the standard manual titration (CPAP preceded group). The other seventy did not receive any treatment before receiving the standard manual titration (initial CPAP group).

**Results :** There were no significant differences in age, body mass index, or baseline PSG parameters between the two groups. The CPAP preceded group had a significantly improved sleep efficiency compared with the initial CPAP group. In contrast, there were no significant differences between the two groups for changes in %REM, %stage 1, %stage 2, %slow wave, sleep latency, REM sleep latency. There was a significant difference for changes in arousal index in non-REM sleep, however, no significant differences were recognized for changes in the arousal index in REM sleep, spontaneous arousal index in either non-REM or REM sleep, respiratory arousal index in either non-REM or REM sleep between the two groups.

**Conclusion :** Although preceding CPAP treatment could be of benefit in the case in which sleep efficiency is low, the initial CPAP trial caused little influences on sleep parameters on titration night, when sufficient intervention for CPAP treatment was performed on OSAHS patients.

**Support (optional):** This work was supported by Research Grant No. 17591802 to M. S. from the Ministry of Education, Culture, Sports, Science and Technology, Japan.

### 0485

#### RESPIRATORY GRAPHIC ANALYSIS ON BILEVEL TITRATION FOR SLEEP APNEA

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**Introduction :** Graphic display of respiratory mechanics of pressure (cm/H<sub>2</sub>O), flow (leak/sec), and volume are currently used to optimize ventilatory setting in ICU and to avoid catastrophe. We, therefore, used the same principle for optimal bilevel titration in the sleep laboratory during a full night PSG study.

**Methods :** All patients in the study were failure to CPAP up to max tolerated pressure and none have history of pulmonary process and with normal SpO<sub>2</sub> at rest. This was a retrospective study of 17 patients with the average age of 36 all with severe obstructive sleep apnea with a mean index of 58 and mean lowest SpO<sub>2</sub> of 70%. In all patients, VPAP was used and titrated according to STD protocol provided by the manufacturer. The PV and volume scalar were displayed on PSG for analysis for patients-ventilatory desynchrony.

**Results :** In all patients, some sort of desynchrony was observed and these were consistent with inspiratory asynchrony/triggering, expiratory asynchrony/triggering, "air hunger", lack of triggering, especially in REM (presence of flow with lack of pressure signal), auto cycling, prolonged TI, excessive effort to cut inspiration off, prolonged TE, periodic breathing. Improvement of triggering was seen in most but not all patients with adjustment of the flow variable (rise time, IPAP max and IPAP min).

**Conclusion :** Limitation of current bilevel used in the sleep laboratory is the lack of "on live" monitoring of the P/flow/volume. In addition the evaluation of ventilatory asynchrony is very difficulty, if not impossible, in the presence of mask ventilation due to excessive leak. Optimal setting of nasal CPAP could be achieved if additional consideration is given to ventilatory wave form scalar.

**Support (optional):**

### 0486

#### SELF-EFFICACY AND CPAP SIDE EFFECTS

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**Introduction :** The purpose of this secondary analysis of data collected in a study of CPAP adherence was to determine if exposure to CPAP treatment or experiencing CPAP side effects influenced self efficacy with regards to CPAP treatment. Self-efficacy is the individual's perception of ability to engage in health promoting behaviors. The components of self-efficacy are: perception of the risk of having the illness, evaluation of the benefit of treatment, and confidence in the ability to engage in the task.

**Methods :** 185 participants (47.2% male, mean age 48.7, mean BMI 38.7, AHI > 5) completed the sleep diaries and self efficacy tools. Self efficacy was measured with the Perceived Self-Efficacy Questionnaire for Sleep Apnea, which has subscales measuring each dimension. Participants filled out this instrument at baseline and following one week of CPAP use. CPAP usage was measured as the mean mask on time at prescribed pressure/24 hours. Participants completed a daily diary that included a checklist of CPAP side effects, ranging from "never" to "serious problem." An index of CPAP side effects was calculated using the number and levels of side effects.

**Results :** CPAP use was 3.94 ± 2.53 hours/day. Mean self efficacy for CPAP use at baseline was 2.97±0.75, and 3.07±0.60 at the end of a week (N.S.). Baseline evaluation of benefit of using CPAP did not correlate significantly with subsequent CPAP use. Mean CPAP use correlated significantly with the changes in confidence in ability to use CPAP (0.16, p < 0.02). Side effects index correlated significantly with the change in perception of the benefit of CPAP treatment (r = -0.28, p < 0.0001).

**Conclusion :** Greater use of CPAP is associated with self evaluation of having greater confidence or self-efficacy in the ability to use CPAP. Those who experienced fewer side effects tend to have higher evaluations of the benefits of doing so. However, the change in self efficacy after one week's exposure to CPAP was not significant. The lack of significant change may be related to the short time period not providing sufficient exposure to the treatment for the individuals to reevaluate their ability to use CPAP.

**Support (optional):**

### 0487

#### INCIDENCE OF COMPLEX SLEEP RELATED BREATHING DISORDER (CSRBD) IN COMMUNITY BASED HOSPITAL

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**Introduction :** CSRBD is a combination of periodic breathing/subtype and sleep apnea/hypopnea/subtype. These types of breathing disorders are seen in patients mostly with underlying cardiac and to a lesser degree in CNS, Mu<sub>2</sub> Receptor Agonist, and or iatrogenic due to nasal positive pressure therapy. The incidence of CSRBD is unknown. We therefore did a respective study of all medical records that were referred for symptoms of snore, unrestful sleep, and daytime sleepiness.

**Methods :** A retrospective study of PSGs within the past one year identified 30 patients or 1.6% meeting the criteria for CSRBD. All patients were monitored in addition to STD PSG monitoring with nasal pressure, flow, CU, TC diaphragmatic EMG, RIP, oral/nasal thermistor, +/- TC02. Of these 30 patients, 12 were cardiac, 7 CNS, 5 CNS + cardiac, and 8 medications.

**Results :** Even though the results do not suggest a substantial amount of

referral to community based hospital (CSRBD) but give an understanding about their existence in all sleep laboratories.

**Conclusion :** The terminology of CSRBD first is used by Dr. Robert Thomas, BIDH Boston, and added more to the understanding of breathing disorders other than apnea/hypopnea during sleep. Careful evaluation of the PSG and low threshold of diagnosis of CSRBD may give more prevalence of this condition in the community hospital. Treatment modalities are different from conventional apnea/hypopnea which is either resistant or even worsened by CPAP or bilevel, S versus ST mode, and this per se is a clue about underlying CSRBD.

**Support (optional):**

## 0488

### RESPIRATORY EFFECT OF MU2 RECEPTOR AND METHADONE DURING FULL NIGHT PSG AND EFFECT ON POSITIVE PRESSURE THERAPY

Sadrnoori B

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**Introduction :** MU2 receptor agonist and methadone are frequently used for pain control. In spite of this, very few publications are available about the effect of these medications on sleep, and especially the effect of positive pressure therapy (CPAP versus bilevel) on sleep related breathing disorders in patients maintained on these medications. We therefore retrospectively reviewed the PSG of patients on maintenance dose of either of these medications and evaluated the effect of positive pressure therapy.

**Methods :** A total of 21 patients with average age of 42 and mean AHI of 43/hr and SpO2 nadir of 81% were enrolled and divided into 2 different groups. Group 1 had a mixture of obstructive and central apnea with Group 2 primarily central sleep apnea. In Group 1, medication doses were smaller and in Group 2, higher doses of medication were used or a mixture of medication (fentanyl and MS and anti-depressant medication and BZ). All patients underwent CPAP and bilevel titration.

**Results :** In Group 1, all responded to CPAP with some residual central apnea but in Group 2 both CPAP and bilevel S mode were effective, with improvement of events on ST mode.

**Conclusion :** The effect of MU2 receptor and methadone depend on several factors, including the mixture of MU2 medication, dose of medication, and mixture of MU2 medication with anti-depressants/BZ. Central apnea persisted in spite of nasal CPAP, or bilevel, in the second group and necessitated ST mode to improve central apnea. This finding may have implications postoperatively in patients with sleep apnea and maintained on their home setting of CPAP and receiving high dose of MU2 receptor.

**Support (optional):**

## 0489

### FACTORS ASSOCIATED WITH INITIAL ADJUSTMENT TO CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)

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**Introduction :** Continuous positive airway pressure (CPAP) has served as the first line treatment for obstructive sleep apnea syndrome over the past 2-3 decades. However, resistance to and intolerance of CPAP continue to pose serious limitations to its use. Previous studies link CPAP intolerance to a variety of factors including mask comfort, various medical symptoms, lack of education, as well as others. Studies investigating the role of psychological factors are limited. The current study sought to develop a

questionnaire to assess for common psychological factors and investigate the role of these factors in initial adjustment to CPAP.

**Methods :** Ninety-two participants diagnosed with moderate to severe obstructive sleep apnea were recruited from a local sleep apnea support group meeting. Participants completed the Kentucky PAP Questionnaire, an instrument developed to assess common factors associated with non-compliance with CPAP therapy. These factors included assessing for common mask problems (i.e. air leaks, skin irritation) and medical symptoms (i.e. dry mouth or throat, nasal congestion). The instrument also assessed various psychological/behavioral factors (i.e. difficulty relaxing, difficulty getting to sleep) and social support/education factors (i.e. supportive family, understanding of sleep apnea).

**Results :** Results of exploratory principal component analyses identified four factors among the questions: Mask Comfort, Medical Symptoms, Psychological Symptoms, and Social Support/Education, all with good internal consistency ( $\alpha = 0.80, 0.75, 0.86,$  and  $0.75$  for the 5, 6, 5, and 6 items scales respectively). Consistent with the findings of previous studies, mask comfort ( $r = .65, p < 0.01$ ) and medical symptoms secondary to CPAP therapy ( $r = .50, p < 0.01$ ) were both significantly associated with patient's initial adjustment to CPAP therapy. Psychological symptoms ( $r = .76, p < 0.01$ ) and social support/education ( $r = .33, p < 0.01$ ) were also significantly associated with adjustment to CPAP.

**Conclusion :** The current study supports previous studies suggesting that mask comfort, management of medical symptoms, and education are important factors related to adjustment to CPAP. In addition, psychological factors appear to be just as important, if not more important. These psychological factors include symptoms of insomnia and anxiety. Identification and management of these symptoms may prove to be crucial when considering ease of initial adjustment and long-term compliance with CPAP.

**Support (optional):**

## 0490

### SLEEP ARCHITECTURE AND SLEEP DISORDERED BREATHING IN 6-11 YEAR OLD HISPANIC AND CAUCASIAN CHILDREN

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**Introduction :** There are relatively few studies of sleep architecture in schoolchildren with sleep disordered breathing (SDB). This report compares polysomnographically measured sleep architecture from a population based sample of Hispanic and Caucasian schoolchildren with and without SDB.

**Methods :** Unattended home polysomnograms (PSG) were obtained on 76 children as part of the larger TuCASA childhood sleep study. PSGs were scored using Rechtschaffen and Kales criteria. SDB was determined to be present if a child had a respiratory disturbance index (RDI) of 2 or more events per hour with an accompanying 3% or greater oxygen desaturation. There were 38 children identified as having SDB who were gender, ethnicity, and age matched to 38 children with an RDI < 0.5 events per hour. Paired t-tests were used to examine differences in sleep architecture between SDB and non-SDB groups.

**Results :** The mean age was 8.42 years. Characteristics of the sleep architecture of the total sample include means (sd) of: total sleep time-484 min (80), sleep efficiency-89% (5.9), sleep latency-19 min (21), REM latency-126 min (42), stage 1-6% (5%), stage 2-50% (7%), stage 3/4-23% (6%), and REM-21% (5%). There were no statistically significant group differences in any sleep architecture variables listed above. Characteristics of Normal vs SDB group include means of: total sleep

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time-495min vs 473 min ( $p<0.16$ ), sleep efficiency-89% vs 88% ( $p<.40$ ), sleep latency-16 min vs 22 min ( $p<.15$ ), REM latency 117 min vs 136 min ( $p<.06$ ), stage 1-7% vs 6% ( $p<.30$ ), stage 2-49% vs 51% ( $p<.20$ ), stage 3/4-22% vs 22% ( $p<.70$ ), REM-22% vs 21% ( $p<.33$ ).

**Conclusion :** In this sample of Hispanic and Caucasian 6-11 year old schoolchildren, there were no differences in the sleep architecture of those children with SDB versus those with no SDB.

**Support (optional):** Supported by HL62373

### 0491

#### COMPARISON OF CIRCULATION TIME IN CENTRAL APNEA, PERIODIC BREATHING AND OBSTRUCTIVE SLEEP APNEA

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**Introduction :** Cheyne-Stokes respiration (CSR), a central apnea characterized by crescendo-decrescendo pattern of ventilation, is noted in some patients with obstructive sleep apnea syndrome (OSAS) suggesting comorbid congestive cardiac failure (CCF). Central sleep apnea (CSA) commonly occurs during NREM sleep in adults with CCF and also in some subjects without CCF. Circulatory delay is known to contribute to CSA including Cheyne-Stokes respiration depending on presence or absence of CCF. In patients with obstructive sleep apnea (OSA), CCF may occur contributing to increased morbidity and mortality.

**Methods :** We performed overnight polysomnography (PSG) in 7 patients with the suspicion of obstructive sleep apnea (OSA). We measured lung to finger circulation time (LFCT) from onset of the first breath after central or obstructive apnea to the subsequent nadir of SaO<sub>2</sub> measured by finger oxymetry. LFCT was measured from cyclic apneas observed in 3 patients with CSR and 4 with OSA and CSA (299 CSR, 41 CSA without CSR and 273 OSA) during NREM sleep. We compared LFCT in CSA with OSA patients.

**Results :** LFCT (mean of 25 seconds in CSR; 26 in CSA without CSR; and 19 in OSA) was significantly longer in CSA with or without CSR compared with OSA. LFCT was longer in the second half of the night in CSA patients with CSR compared with CSA without CSR and OSA.

**Conclusion :** In patients with OSAS presence of CSA or CSR associated with circulatory delay may suggest incipient CCF. Furthermore, progressive lengthening of circulation time may imply concurrent deterioration of cardiac function overnight in such patients. Determination of circulation time from overnight PSG recording is a simple non-invasive technique to predict incipient CCF in OSAS patients. Prompt treatment may improve cardiac function, morbidity and mortality in such patients.

**Support (optional):**

### 0492

#### ORAL GREEN TEA CATECHIN POLYPHENOLS (GTP) ATTENUATE INTERMITTENT HYPOXIA (IH)-INDUCED EXPRESSION OF NADPH OXIDASE AND LIPID PEROXIDATION IN RAT BRAIN

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**Introduction :** Green tea catechin polyphenols (GTP) have emerged as potential neuroprotective agents in the treatment of neurodegenerative disorders due to their anti-oxidant properties. Intermittent Hypoxia (IH), a typical feature of sleep-disordered breathing (SDB), increases the expression of NADPH oxidase (i.e., p47(phox) sub-unit), the major enzyme underlying oxygen radical production, and is also associated with increased oxidative stress, as evidenced by increased malondialdehyde (MDA) tissue concentrations within various brain regions of rodents exposed to IH. We therefore hypothesized that oral GTP administration

may favorably affect oxygen radical load during IH by reducing both NADPH expression and downstream lipid peroxidation.

**Methods :** Male Sprague Dawley rats were exposed to IH for up to 14 days (chamber O<sub>2</sub> levels oscillating between 21% and 10% every 90 seconds during daylight hours). Animals were randomly assigned to either a mixture of green tea polyphenolic compounds, polyphenon-60, ad libitum (GTP) in their drinking water or to water alone (CO). MDA brain tissue levels were measured using a spectrophotometric assay and p47(phox) expression was assessed using RT-PCR.

**Results :** CO-IH rats showed doubling of cortical MDA levels compared to room air (CO-RA), while GTP-IH animals showed approximately 40% reductions in MDA levels upon IH exposure ( $n=4$ /group). Similarly, a 5-6 fold increase in p47Phox NADPH oxidase sub-unit expression occurred in CO-IH vs. CO-RA ( $n=4$ /group). In contrast, GTP-IH animals exhibited only minor increases in p47(phox) expression (around 15% of CO-IH). Of note, animals exposed to GTP-RA also showed similar reductions in MDA levels vs. CO-RA.

**Conclusion :** Oral GTP administration appears to mitigate IH-induced oxidative stress possibly through multiple beneficial effects on the pro- and anti-oxidant enzymatic cascades. Since these oxidative processes underlie components of the neurocognitive deficits associated with IH, the potential therapeutic role of GTP in SDB deserves further exploration.

**Support (optional):** NIH HL69932, P50HL6029, and Swiss National Foundation

### 0493

#### NIGHTLY CPAP ADHERENCE OVER FIRST 14 NIGHTS OF TREATMENT

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**Introduction :** Patient adherence to CPAP therapy is disappointingly low. Examination of the patterns of nightly use may increase our understanding about how those patterns develop. Previous work ( $n=32$ ) found that consistent and inconsistent users could be distinguished as early as the 4th night of use. We performed a similar analysis on a larger clinic sample of CPAP users over their first 14 nights of CPAP use.

**Methods :** 909 patients at a local sleep clinic were diagnosed with OSA and prescribed CPAP over a recent 2.5yr period. This study examined the downloaded CPAP data from patients who returned to clinic for follow-up ( $n=528$ ). CPAP adherence was defined as the number of hours of use at the prescribed pressure. CPAP adherence groups were based on mean adherence level over the mean CPAP treatment period of 5.2 months: 0-2 hours/night (38.3%); 2-4 (22.5%); 4-6 (19.5%) and >6 (19.7%). Mean age was 59 years and mean AHI was 38.8+/-22.5. Mean CPAP adherence for the entire group was 3.1hrs/nt (SD=2.5; range=0.1-9.3).

**Results :** CPAP adherence groups could be distinguished as early as the first night of CPAP use ( $F[3,1]=50.4$ ;  $p<.0001$ ). Random effects modeling showed that the line of best-fit across the first 14 nights of CPAP therapy for the two CPAP adherence groups with at least 4hrs mean nightly use was a flat line, but there was a decline in CPAP use for the two groups with less than 4hrs mean CPAP use.

**Conclusion :** In contrast to previously published analysis of the patterns of CPAP use over the first 2 weeks of therapy, the current analysis suggests that CPAP use patterns are established as early as the first night of therapy. If this is true, then pre-existing differences (i.e., factors present prior to CPAP therapy start) may help to explain CPAP adherence patterns.

**Support (optional):** Department of Veteran Affairs HSRD 02-275;

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**0494**

**BRAIN FUNCTION IN OBSTRUCTIVE SLEEP APNEA: AN ASSOCIATION WITH AGE**

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**Introduction :** We have previously reported that intact verbal learning performance in obstructive sleep apnea (OSA) patients was associated with increased cerebral activation relative to controls. Similar findings have been reported in older adults. These findings in both healthy older adults and OSA patients suggest a compensatory recruitment response to maintain cognitive performance. Here, we examined the interaction between age and OSA and to test whether the combination would lead to a stronger compensatory response or overwhelm the brain's capacity to compensate.

**Methods :** Twelve untreated OSA patients (11 men, age=44.2 ±11.9, range: 27-59 years; BMI=31.3 ±5.9; AHI=35.1 ±21.1) and 12 healthy controls (11 men, age=43 ±9.1, range 25-59 years; BMI=29.2 ±3.5; AHI=1.9 ±1.7) were studied with PSG and functional MRI. Multiple regression analysis was used to test the interaction between Group (OSA/Control) and Age on brain function during a verbal learning task.

**Results :** OSA patients showed increased activation compared to controls, as previously reported. Similarly, increased age was associated with increased brain activation (left inferior parietal lobe, thalamus, caudate, middle temporal gyrus, and fusiform; right anterior cingulate; and bilateral precuneus and cerebellum). However, the interaction between increasing age and OSA was associated with decreased brain activation (right superior temporal gyrus and anterior cingulate; and bilateral parahippocampal gyri, caudate, precuneus, cerebellum, and fusiform gyrus)

**Conclusion :** These data show that the brain is able to recruit additional resources to maintain intact performance, thereby compensating for either OSA or aging individually. However, the combination of both OSA and increasing age lead to decreased activation, suggesting an overwhelming effect on the brain's compensatory mechanism. These findings suggest there are greater deleterious effects of OSA on brain function as we age and may have implications for the importance of early diagnosis and treatment.

**Support (optional):** NIH M01 RR00827, NIMH 5 T32 MH18399, NIA AG08415, NIA AG024506

**0495**

**CARDIORESPIRATORY COUPLING IS INVOLVED IN THE NORMALIZATION OF THE CARDIAC SYMPATHOVAGAL BALANCE DURING SLEEP IN OBSTRUCTIVE SLEEP APNEA PATIENTS UNDER CONTINUOUS POSITIVE AIRWAY PRESSURE TREATMENT**

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**Introduction :** Continuous positive airway pressure (CPAP) is the first choice treatment for obstructive sleep apnea (OSA) patients. Auto-adjusting CPAP (APAP) seems to provide an enhanced patients' compliance. However, we have recently observed that CPAP, but not APAP, treatment

was associated with decrease in arterial pressure and insulin-resistance. CPAP is known to reduce night- as well as day-time sympathetic activation which plays a major role in linking OSA to cardiovascular diseases. Aim of this work was to assess the effects of the two ventilatory treatments on the cardiac sympathovagal balance during sleep.

**Methods :** We applied heart rate variability (HRV) spectral and cross-spectral algorithms to polysomnographic ECG and nasal respiratory signal recordings from OSA patients on CPAP (n=10) or APAP (n=9) and from 7 overweight controls. The three groups were matched for age, sex, BMI, AHI and ODI. HRV was performed considering the typical Wake (W), 2, 3, 4 and REM sleep stages. Variance, LF (low frequency, index of sympathetic modulation), HF (high frequency, index of parasympathetic modulation), the LF/HF ratio and coherence values between HRV and respiration were considered.

**Results :** Compliance to therapy (hours/night) was similar in CPAP and APAP groups. Both treatments were effective in reducing AHI, ODI, and sleepiness symptoms. Heart rate and arterial pressure were similar. During W, no differences in total HRV and LF/HF ratio, index of the sympathovagal balance, were detected between the three groups. During sleep, the LF/HF ratio progressively decreased from W to 4 and went back to W levels during REM, similarly in CPAP and Controls, while in APAP it increased significantly from W to sleep and remained greater in all sleep stages. Coherence levels between HRV and respiration, was highest in CPAP and controls through all sleep stages, while APAP showed coherence values significantly and constantly lower.

**Conclusion :** Our results suggest that, at difference with CPAP, APAP treatment is associated with a greater sympathetic activation during sleep, likely to be due to irregular respiratory efforts interacting with the HRV signal. Thus, a reduction in cardiorespiratory coupling, even in absence of apneas and oxygen desaturations, is able to increase cardiac sympathetic drive during sleep. This finding may have important implications for cardiovascular outcomes in OSA.

**Support (optional):** PRIN 2003 and FIRST 2005 Grants

**0496**

**CROSSOVER TRIAL TO DETERMINE EFFICACY AND PATIENT SATISFACTION WITH AUTOCPAP WITH C-FLEX VERSUS STANDARD CPAP**

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**Introduction :** The RemStar Auto with CFLEXTM(RSAC) combines Auto CPAP technology with a variable comfort level, which reduces delivered pressure during the expiratory phase of breathing. Increased comfort levels associated with C-Flex therapy have potential to improve long-term compliance. The purpose of this study is 1) to confirm treatment efficacy of the RSAC and 2) to determine patient preference when compared to standard CPAP.

**Methods :** 14 patients who had previously undergone formal CPAP titration polysomnography were treated with either the RSAC or conventional CPAP in a crossover trial. Patients were blinded to the treatment modality, which was assigned in random order on consecutive visits to the sleep lab. Patient satisfaction levels were recorded using visual analog scales (VAS) on the morning following testing. Technicians recorded all interventions (e.g mask adjustment) during the study. Analysis was performed using paired t tests.

**Results :** 14 patients have completed the study. Baseline characteristics include; age 50.3±11.9, BMI 36.4±5.6, baseline AHI 53.1±39.9, AHI post CPAP 2.0±2.3, and CPAP Pressure 11±1.8. Outcomes of interest are expressed as RSAC v CPAP and include patient preference (VAS -10 - +10), 3.9 ± 1.5 v -3.9 ± 1.5 (p=0.001) and summated patient VAS score (0-

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10),  $7.9 \pm 0.2$  v  $7.3 \pm 0.2$  ( $p=0.009$ ). Sleep characteristics were similar between groups with a trend to increased slow wave sleep with the RSAC,  $4.1 \pm 1.5\%$  v  $1.6 \pm 0.5\%$  ( $p=0.1$ ). Post treatment AHI was  $3.4 \pm 0.9$  v  $2.4 \pm 0.7$  ( $p=0.4$ ). Required technician interventions was  $1.4 \pm 0.45$  per night v  $2.3 \pm 0.4$  per night ( $p=0.1$ )

**Conclusion :** Both modes of treatment were effective at abolishing sleep-related respiratory events. Patients expressed preference for the RSAC mode of treatment. Pooled VAS scores also indicated a preference for the RSAC. Patient preference may have been influenced by increased comfort levels along with a trend towards an increase in slow-wave sleep.

**Support (optional):** Respironics Inc.

### 0497

#### THE EFFECT OF ABDOMINAL COMPRESSION ON UPPER AIRWAY FUNCTION DURING SLEEP IN HEALTHY WEIGHT MALES

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**Introduction :** Obstructive sleep apnoea (OSA) is a respiratory disease common in obese males. Studies in anaesthetised animals indicate that upper airway (UA) collapsibility increases when tension on the airways is reduced. Subsequently, abdominal compression in centrally obese males may reduce UA tension during sleep due to cranial displacement of the diaphragm and interdependent intrathoracic structures. The importance of this mechanism and the influence of the mechanical effects of central obesity in humans are unknown. The aim of this study was to examine the effects of experimental abdominal compression on UA collapsibility during wakefulness and sleep in healthy weight males.

**Methods :** Eighteen young ( $22.4 \pm 1.4$  years) healthy weight males (BMI  $24.3 \pm 1.6$  kg/m<sup>2</sup>) participated. Changes in gastric pressure (Pga), transdiaphragmatic pressure (Pdi), UA collapsibility (assessed during periods of brief mid-inspiratory negative pressure pulses) and UA airflow resistance were calculated during both wakefulness and sleep with and without abdominal compression via inflation of a pneumatic cuff to a level compatible with sleep.

**Results :** Both UA collapsibility and UA resistance significantly increased from wakefulness to stage II sleep ( $P < 0.007$ ). Pga significantly increased with abdominal compression during wakefulness ( $9.7 \pm 0.9$  versus  $12.4 \pm 1.3$  cmH<sub>2</sub>O) and sleep ( $9.2 \pm 1.3$  versus  $10.6 \pm 1.4$  cmH<sub>2</sub>O,  $P = 0.013$ ). Pdi also increased with cuff inflation during wakefulness ( $2.3 \pm 1.4$  versus  $4.9 \pm 1.3$  cmH<sub>2</sub>O) and sleep ( $4.0 \pm 1.4$  versus  $4.8 \pm 1.2$  cmH<sub>2</sub>O,  $P = 0.012$ ). However, cuff inflation had no effect on UA collapsibility or UA airflow resistance in either wakefulness (collapsibility;  $31.9 \pm 6.7$  versus  $33.9 \pm 7.0\%$ , resistance;  $3.3 \pm 0.5$  versus  $3.3 \pm 0.4$  cmH<sub>2</sub>O/L/s) or sleep (collapsibility;  $61.7 \pm 3.5$  versus  $64.5 \pm 5.3\%$ , resistance;  $11.0 \pm 1.3$  versus  $11.1 \pm 3.3$  cmH<sub>2</sub>O/L/s).

**Conclusion :** Despite clear state-dependent changes in UA collapsibility and resistance, experimental abdominal compression in healthy weight individuals had no measurable effects on UA function in wakefulness or sleep. However, the ~20% increase in Pga tolerated by subjects in this study is substantially less than pressures noted in the majority of obese OSA patients. Consequently, the effects of more substantial abdominal compression on UA function during sleep warrants further investigation.

**Support (optional):**

### 0498

#### OBSTRUCTIVE SLEEP APNEA SYNDROME AND LOWER AIRWAY HYPERRESPONSIVENESS: IS THERE AN ASSOCIATION?

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**Introduction :** Obstructive sleep apnea syndrome (OSAS) is a common and important disorder in children. The link existing between upper and lower respiratory airway has led during the last years to the concept of the "united airway disease". Recently, it has been confirmed in vivo the clinical, functional and immunological unity of the upper and lower respiratory tracts. The aim of this study was to investigate the effect of intranasal corticosteroid therapy on lung function parameters.

**Methods :** Ten consecutive patients (9 males, age 4.6-9.5yr) affected by OSAS and 6 age-matched healthy subjects (3 males, age 5-10yr) were enrolled. All children filled out a form with questions about breath disorders during sleep and underwent lung function tests and nocturnal polysomnography. All patients with OSAS were treated with intranasal corticosteroid for 15 days per month, for 3 months. After treatment, the patients performed again lung functions tests.

**Results :** Intranasal corticosteroid significantly improved nasal obstruction and snoring in all patients. Moreover, the FEV1 values after topic corticosteroid treatment were significantly higher than those before therapy [ $104,1$  ( $89,4-116,9$ ) vs  $119,9$  ( $117,6-122,2$ )  $p < 0.05$ ].

**Conclusion :** Our findings show that the nasal obstruction plays a key role in modulating lower airway responsiveness.

**Support (optional):**

### 0499

#### TEMPORAL ASSOCIATION BETWEEN APPARENT LIFE THREATENING EVENTS AND GASTROESOPHAGEAL REFLUX

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**Introduction :** Apnea episodes during the first year of life have been classified with the term of apparent life threatening events (ALTE). Gastroesophageal reflux (GER) has been considered a factor which can promote the development of ALTE. The aim of this work is to study whether there is a temporal association between ALTE and GER using multichannel intraluminal impedante (MII) technique.

**Methods :** From October 2004 to May 2005, we enrolled consecutive infants, referred to our Department for ALTE. Infants were investigated simultaneously with MII-pH-monitoring and polygraphy. MII patterns, pH and cardio-respiratory (CR) events (apnoea, hypopnoea, arousal, desaturation, bradycardia, periodic breathing) were recorded and analysed. The occurrence of a CR event during 30 sec. preceding or following the beginning of a GER (acid and non acid) was defined as a temporal association.

**Results :** In 11 infants [M 5; median age 2,4 mo (1,3-6,6)], 224 GER episodes were recorded by MII and, out of these, 87 were acid (39%). There were 14 apnoeas, 209 hypopnoeas, 63 desaturations, 19 periodic breathing, 31 arousals and 1 bradycardia. For all the studied CR events, the frequency occurring within +/- 30 sec of a GER (acid and non acid) was not significantly different from that occurring during reflux-free period apart for hypopnoea, that was associated more frequently only with acid GER ( $0,09 \pm 0,2$  min vs  $0,08 \pm 0,07$  min;  $p < 0,02$ ).

**Conclusion :** Our study shows that both GER and CR events are common in children, however we have found only a temporal association with cen-



tral hypopnoeas.

**Support (optional):**

## 0500

### PREDICTING CPAP PRESSURE FROM PSG MEASURES

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**Introduction :** There is often a delay between the diagnostic PSG and CPAP titration. This study looks at predictors of CPAP pressure based on PSG measures.

**Methods :** We studied 83 patients, 69 men and 14 women, with RDI's  $\geq 5$  with both PSG and CPAP titration. One patient was excluded due to TST < 180 min. The mean age was 50. The mean RDI was 31 (6.4 - 98). PSG measures: Age, Gender, BMI, TST, Light Sleep (LS), Deep Sleep (DS), REM sleep, REM and NREM respiratory events, and Lowest SaO<sub>2</sub>. CPAP titration measures: CPAP pressure and RDI at optimal pressure. We used a forward stepwise regression with CPAP pressure as the dependent variable and the above PSG measures or derived variables such as percent Deep Sleep (%DS) as independent variables.

**Results :** The mean CPAP pressure was 11cm, 16 cm at the 90th percentile. The subjects were divided by gender for the regressions. MEN: Significant independent variables in men were BMI and %DS. The r-squared was .29,  $p < .05$ . CPAP pressure =  $5.5 + .22 \cdot \text{BMI} - 11.6 \cdot \% \text{DS}$ . WOMEN: The important independent variable was %DS. The r-squared was .14,  $p > .05$ . CPAP pressure =  $13.2 - 5.7 \cdot \% \text{DS}$ .

**Conclusion :** These results suggest a CPAP pressure for patients when their CPAP titration study is delayed. Simplest is to start at a pressure of 16cm, sufficient for 90% of patients. Another choice is to use the above predictive equation for men. A prediction can be used for women, it is less likely to be close to the titrated pressure. It is difficult to comment on the difference between men and women due to the difference in the numbers of male and female subjects. However, this study also supports the idea that men and women should be looked at differently in OSA.

**Support (optional):**

## 0501

### THE CORRELATION BETWEEN CPAP COMPLIANCE AND AGE IN ADULT MALES DIAGNOSED WITH MODERATE TO SEVERE SLEEP APNEA SYNDROME

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**Introduction :** Sleep apnea affects 6% of the adult population and 20% of the elderly population. Issues with CPAP compliance in the lab environment and home setting can prevent patients from following through with prescribed treatment. We examined the relationship between male subjects of two different age groups with moderate to severe sleep apnea and their compliance to CPAP.

**Methods :** Fifty randomly-selected male patients divided into two groups, Group A (aged 36-50 years) with initial mean AHI 45.9 and Group B (aged 67-99) with mean AHI 55.5. Using post-sleep study questionnaires, perception of sleep quality and comfort during initial titration were considered. Follow-up telephone interviews were conducted to determine home CPAP use. All patients were exposed to the same introduction, study parameters and attended the same sleep facility.

**Results :** Group A mean total sleep time (TST) was 352.4 minutes and mean sleep efficiency (SE) was 76.0 % for initial titration. All patients successfully completed the initial trial, 4 patients claimed the night in the lab was poorer than home, 12 patients claimed it was the same, and 8 patients claimed the night was better. Of 25 middle-aged males, 7 are not using CPAP (non-compliant) and 18 are regularly using CPAP at home

(compliant). Group B mean TST was 238.2 minutes and mean SE was 57.9 % for initial titration. Three patients failed the initial titration, discontinuing the trial. 22 patients were successful, with 7 stating that their sleep was better than home. Twelve patients claimed their sleep was the same as home, while 6 claimed it was poorer. Of 25 elderly-aged males, 8 were non-compliant and 17 were compliant.

**Conclusion :** Findings show that age has little impact on CPAP compliance following the introduction in the lab. A larger sample size may influence results.

**Support (optional):**

## 0502

### PREVALENCE OF CARDIAC ARRHYTHMIAS ON OVERNIGHT PSG AND THEIR ASSOCIATION WITH SDB IN A COMMUNITY SAMPLE OF OLDER MEN

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**Introduction :** The prevalence of nocturnal cardiac arrhythmias detectable by overnight polysomnographs, and their association with SDB in community samples of adults is unclear. We quantified the prevalence of significant cardiac arrhythmias in a community sample of older men, postulating that arrhythmias are increased with SDB in analyses adjusted for age, race, and comorbidity.

**Methods :** We evaluated nocturnal cardiac arrhythmias detected during polysomnography (PSG) scoring at a central Reading Center and SDB in 2911 participants of the Outcomes of Sleep Disorders in Older Men (MrOS) Sleep Study. Participants were  $73.7 \pm 5.9$  [SD] years, 90% Caucasian and 17% had a respiratory disturbance index (RDI) > 30. SDB was quantified using the RDI (continuous variable), and by measures of nocturnal hypoxia (i.e., oxygen desaturation index (ODI) and nadir oxygen saturation). Nocturnal cardiac arrhythmias considered include non-sustained ventricular tachycardia (NSVT), atrial fibrillation (AF) and second and third degree atrioventricular block (AVB).

**Results :** Of 2911 PSGs performed, there was an arrhythmia prevalence of 9.6%:  $n=155$  (5.3%) with AF,  $n=36$  (1.2%) with NSVT, and  $n=24$  (0.8%) with second and third degree AVB. Logistic regression analysis evaluating presence of AF demonstrated a significant association with SDB ( $p=0.004$ ). A 5 unit increase in RDI yielded a 7.2% increase in the odds of AF (OR=1.07, 95% CI: 1.02- 1.13) which persisted after adjustment for age, race, hypertension, angina, myocardial infarction and heart failure (OR=1.06, 95%CI: 1.00-1.11,  $p=0.03$ ). NSVT and AVB were not significantly associated with SDB. There were no significant relationships noted with any of these arrhythmias and measures of nocturnal hypoxia (ODI, nadir oxygen saturation).

**Conclusion :** PSG performed in a community sample of older men reveals a small percentage of clinically significant nocturnal arrhythmias, including 46 (1.6%) cases of AF not previously recognized. Of the arrhythmias examined, AF was associated with SDB even after taking into account cardiovascular comorbidity.

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0503

**GENDER DIFFERENCES IN MMPI-2 DEPRESSION SCORES IN OBSTRUCTIVE SLEEP APNEA PATIENTS**

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**Introduction :** Symptoms of depression are reported as common sequelae of the Obstructive Sleep Apnea Syndrome. The literature suggests that the degree of depression may covary with the severity of the OSAS. There is little in the literature on gender differences in the appearance of depressive symptomatology in OSAS.

**Methods :** The MMPI-2 was administered to 551 patients who had a polysomnographic evaluation for symptoms of OSAS (210 female, 341 male). The patients' ages ranged from 14 to 80 years for females and 20 to 86 years for males. The average age was 47.5 years for females and 49.4 years for males.

**Results :** Females showed a higher depression score than males (females, T = 60.6, SD = 12.8, and males, T = 57.5, SD = 12.5). The AHI was higher in males (females = 17.0, SD = 20.7, and males = 27.8, SD = 26.4). When gender was dichotomized at the mean age, the depressive scores for the younger half of each gender group did not differ from the older half. For the younger females, the T scores were T = 60.6, SD = 13.4, and for the older females, the T scores were T = 60.6, SD = 12.2. For younger males, the T scores were T = 57.3, SD = 12.5, and for the older males, the T scores were T = 57.7, SD = 12.3. The AHI increased with age with the younger half having lower scores (younger females = 11.7, SD = 13.2, and older females = 22.3, SD = 25.0; younger males = 25.3, SD = 25.8, and older males = 30.4, SD = 27.1).

**Conclusion :** The results may contradict the prevailing belief that depressive scores covary with AHI and increase for older male or female OSAS patients.

**Support (optional):**

0504

**VA ASSESSMENT PATHWAY FOR A COMMERCIAL DRIVER LICENSE REFERRAL**

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**Introduction :** Four veterans came to the VA Sleep Clinic with a request from a Medical Examiner (ME) to perform a "PSG/MSLT" within 60-90 days, the extension time for the commercial drivers license (CDL). We sought to discover the rationale, and develop a policy and pathway for such administrative referrals.

**Methods :** We contacted each referring Medical Examiner and the US DOT for instructions for such a referral. Using Internet engines, we identified ~ 103 relevant references for pathway annotation.

**Results :** The MEs use the DOT Medical Examination Report 649-F (6045) on which there is a patient-report checkbox for "Sleep disorders, pauses in breathing while asleep, daytime sleepiness, and loud snoring". Within this document, there are significantly more ME instructions for addressing hypertension (9 paragraphs), diabetes (4 paragraphs), and a cardiovascular condition (4 paragraphs), than for sleep apnea (7 words; p<0.0001). In a footnote, there is a reference to sleep apnea as a diagnosis needing "referral to a specialist for further evaluation and therapy" (<http://fmcsa.dot.gov/rulesregs/medreports.htm>). It is in this reference that contains a recommendation that "drivers with known, treated OSA be evaluated by yearly PSG/MSLT". Review of the current literature suggested no such test would predict accident risk or driver fitness, but that sleepiness from any cause was the correlate to crash risk.

**Conclusion :** A blanket referral for a PSG/MSLT in those with diagnosed OSA is not a rational use of VA resources. A referral could confirm or certify the diagnosis, the appropriateness of management, and the patient's use of and response to therapy. An educational component discussing countermeasures to drowsy driving has also been incorporated. New VA Policy and Procedures will triage patients for clinical examination, compliance monitoring, and/or testing or follow-up. Future ME requests will be responded with this assessment and a description of our educational intervention.

**Support (optional):** The NIH (T32HL07913) and the VA Medical Service

0505

**OBESSE OBSTRUCTIVE SLEEP APNEA PATIENTS WITH TONSIL HYPERTROPHY SUBMITTED TO TONSILLECTOMY**

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**Introduction :** Obstructive sleep apnea-hypopnea syndrome (OSAHS) presents multifactorial physiopathology and obesity has been shown to be one of the main factors correlated with its occurrence. In obese patients with upper airway anatomical alterations, it is often difficult to predict success for surgical correction since obesity is a limiting factor. Therefore the aim of this study was to evaluate the results of tonsillectomy in a uncommon and very specific group of patients, the obese OSAHS patients with tonsil hypertrophy.

**Methods :** Seven obese OSAHS patients presenting obstructive palatine tonsil hypertrophy were submitted to tonsillectomy. Pre and post operative appraisals of body mass index (BMI), otorhinolaryngology examination and polysomnography study were performed for all patients. Data for pre and post operative BMI and polysomnography were appraised using Wilcoxon's test.

**Results :** Patients' average age was 36.4 ± 10.3 and average pre operative BMI was 36.6 ± 6.3 Kg/m<sup>2</sup>. Statistically there were no significant differences between patients' pre and post operative weights (p=0.27). The average preoperative apnea and hypoapnea index (AHI) was 81/hour while the postoperative rate was 23/hour; and average minimum oxyhemoglobin saturation (SaO<sub>2</sub>min) was 69% preoperative and 83% postoperative.

**Conclusion :** Tonsillectomy treatment for OSAHS in obese patients with obstructive palatine tonsil hypertrophy presented a significant reduction in AHI, with improvement in SaO<sub>2</sub> min; it could be eventually considered as an option of treatment for obese OSAHS patients with significant tonsil hypertrophy, when CPAP therapy is not possible as the first choice of therapy.

**Support (optional):** AFIP

0506

**LONG-TERM RECURRENCE OF ATRIAL FIBRILLATION IN OBSTRUCTIVE SLEEP APNEA**

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**Introduction :** Obstructive sleep apnea (OSA) has been linked to increased prevalence and recurrence of atrial fibrillation (AF). We investigated whether OSA is associated with a higher AF recurrence and AF burden in patients with dual-chamber pacemakers implanted for sinus bradycardia who had documented paroxysmal AF, and whether nocturnal

AF episodes predominate in patients with concomitant paroxysmal AF and OSA.

**Methods :** Seventy-two patients (36 M, aged 77±6 years) completed the study. OSA was diagnosed with the Berlin Questionnaire, which is validated to identify patients with OSA. Four-month continuous dual-chamber pacemaker recordings were collected for all patients.

**Results :** OSA was diagnosed in 28% of patients. Patients at high risk for OSA (HR group) and patients at low risk for OSA (LR group) had similar gender, age, and BMI distribution. The rate of hypertension was higher in HR than in LR group (90 vs. 44%,  $p<0.01$ ). The prevalence of paroxysmal AF during the study period was similar in HR and LR group (53 vs. 44%,  $p=NS$ ). Overall number of AF episodes per month was not significantly different between HR and LR group (7±13 vs. 36±122,  $p=NS$ ). Similarly, AF burden was not significantly different between HR and LR group (0.3±0.6 vs. 2.0±4.8,  $p=NS$ ). Circadian distribution of AF episodes was similar in both groups.

**Conclusion :** Continuous 4-month pacemaker recordings of AF recurrence and AF burden is similar in patients with paroxysmal AF at high risk for OSA and those at low risk for OSA, and circadian distribution of AF episodes is similar in both groups.

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## 0507

### EFFECT OF WIRELESS MONITORING ON CPAP ADHERENCE AND TREATMENT EFFICACY: A PILOT STUDY

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**Introduction :** CPAP is the gold standard treatment for OSA and it is generally accepted that adherence to CPAP can be substantially improved. A key advantage to using the CPAP is its ability to objectively measure and store both treatment efficacy and adherence data. Unfortunately, under usual and customary care there is generally a time lag ranging from days to weeks between adherence data collection and data availability to care providers.

**Methods :** This was a randomized, controlled trial of usual care compared to a telemonitoring intervention, in which adherence data were wirelessly transmitted directly and accurately to a remote server/database in 24hr cycles, where they were then accessible to system-authorized care providers. Wireless telemonitoring allowed for the increased speed and frequency with which each patient's nightly CPAP adherence level and efficacy were available and knowable to care providers, enabling early intervention in the treatment initialization process.

**Results :** 41 patients diagnosed with OSA and prescribed CPAP attended were studied. Mean age=59 and mean baseline AHI=39. Nightly CPAP adherence measured over the 2-mo follow-up period was 4.0±1.9 and 3.0±2.4 hrs/night for the telemonitoring and usual care groups, respectively. The telemonitored group had lower mask leak levels than the usual care group (.35±.20 vs .49±.47).

**Conclusion :** Telemonitoring has the potential to be an effective and practical way to improve CPAP adherence and efficacy. Key advantages of telemonitoring CPAP efficacy and adherence data are that the information is objectively measured and easily accessible to providers, enabling them to intervene early in the treatment process to help patients better manage their OSA by helping to establish optimal and enduring patterns of CPAP treatment adherence.

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## 0508

### CPAP ADHERENCE RATES IN A LARGE CLINICAL POPULATION

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**Introduction :** Obstructive sleep apnea (OSA) is a chronic and potentially life threatening disease. CPAP treatment can significantly improve patient outcomes, but rates of CPAP adherence have mainly come from large clinic samples studied outside of the United States. We examined CPAP adherence in newly diagnosed patients over their first 5 months of treatment.

**Methods :** 909 patients at a local sleep clinic were diagnosed with OSA and prescribed CPAP over a two-year period. This study examined the CPAP data downloaded from patients that returned to clinic for follow-up (n=528). The mean follow-up period was 5.2 months. CPAP adherence was defined as the number of hours of use at the prescribed pressure measured objectively via an internal clock. Based on published consensus, CPAP adherence was defined as; poor, less than 4hrs/night; acceptable, 4-6hrs/night; and optimum as greater than 6hrs/night.

**Results :** The mean age was 59yrs and most patients had moderate to severe OSA (AHI=38.8 events/hr sleep). Mean CPAP adherence was 3.1hrs/night (SD=2.5; range=0.1-9.3). 63% of sample (331/528) had poor CPAP adherence; 21% had adequate adherence; and only 16% used CPAP optimally. Baseline disease severity was correlated with higher levels of adherence ( $r=.268$ ;  $p<.0001$ ). Mean change in weight was 0.68lbs (SD=9.9; range=-53-45); mean change in diastolic BP was -1.6mmHg (SD=12; range=-63-44); mean change in systolic BP was -2.6 (SD=19; range=-65-59). Change scores were not statistically different from 0.

**Conclusion :** Adherence to CPAP therapy is suboptimal. Among this subset of CPAP patients who returned to clinic for follow-up (528 /909), over 60% had poor CPAP adherence and less than 20% had optimal adherence. Suboptimal CPAP use results in ineffectively treated patients and increased risk of morbidity/mortality. Continued research to better understand the factors associated with adherence is needed so that effective interventions to increase adherence can be developed and implemented.

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## 0509

### A SELF-MANAGEMENT APPROACH TO IMPROVING CPAP ADHERENCE AND OUTCOMES: PILOT STUDY

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**Introduction :** Low patient adherence to CPAP treatment for OSA limits the effectiveness of treatment. One intervention study examining an intensive support protocol found a 1.5hr improvement in CPAP adherence. However, such intensive support protocols may be too costly and/or time consuming for integration into the existing U.S. healthcare system. This study piloted an intervention that takes a self-management approach toward enhancing CPAP adherence and improving OSA outcomes.

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**Methods :** 12 veterans diagnosed with OSA and prescribed CPAP attended four weekly 2-hour self-management classes. This Sleep Apnea Self-Management Program (SASMP) included information that was both specific to OSA and common across chronic illnesses: understanding OSA symptoms and consequences, problem-solving difficulties with treatment, managing emotional/cognitive symptoms, learning strategies to increase physical activity, improving communication skills, and developing the physician-patient partnership. A major focus was on developing strategies to solve problems patients commonly experience with CPAP. SASMP is a manualized intervention run in a group format that utilizes a variety of different activities, including mini-lectures, brainstorming, action planning, and problem-solving. Measures were assessed at both pre- and post-intervention.

**Results :** Nightly CPAP adherence measured over this 30-day period averaged 5.8 hrs/night (SD=2.5; range=1.0-8.8). Both the Sleepiness Visual Analog Scale (VAS) and the Center for Epidemiological Studies Depression (CESD) showed reductions from pre- to post-intervention (VAS:7.2±2.0 to 5.5±3.0; p=.01; CESD:11.4±8.0 to 6.9±6.4; p=.05). Outcome expectations (e.g., the belief that using CPAP will result in the desired outcomes) increased significantly from pre- to post-intervention (2.7±0.4 to 4.5±0.7; p=.04).

**Conclusion :** The Sleep Apnea Self-Management Program has the potential to be an effective and practical way to improve CPAP adherence and OSA outcomes. A key advantage of the SASMP is its design for integration into current clinical care processes. A larger trial is underway to examine the effect of SASMP on OSA symptoms and health-related quality of life.

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### 0510 USEFULNESS OF PACEMAKER TRANSTHORACIC IMPEDANCE SIGNAL IN SCREENING FOR SLEEP DISORDERED BREATHING

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**Introduction :** A third of patients with permanent pacemakers (PM) have obstructive sleep apnea (OSA). Novel PM utilizes change in transthoracic impedance to determine fluctuations in minute ventilation. We investigated whether this PM algorithm might identify patients with OSA.

**Methods :** We studied 44 patients (27 M, aged 73±9 years) with dual-chamber PM (Talent 3 DR, ELA Medical). This PM detects apnea (A) as the absence of respiratory cycle for >10 sec and hypopnea (H) as a reduction in respiratory amplitude by at least 50% for >10 sec. Six-month continuous pacemaker recordings were collected for all patients. OSA was diagnosed with the Berlin Questionnaire, which is validated to identify patients with OSA.

**Results :** OSA was diagnosed in 56% of patients. Patients at high risk for OSA (HR group) and patients at low risk for OSA (LR group) had similar gender, age, and BMI distribution. Overall number of A+H episodes detected by PM over 6-month period was significantly higher in HR compared with LR group (1040281±19603 vs. 615385±9199, p=0.04). Similarly, A+H index was significantly higher in HR compared with LR group (34±20 vs. 24±12 events/h, p=0.01).

**Conclusion :** Analysis of long-term changes in transthoracic impedance correctly identifies patients with severe OSA. Transthoracic impedance

algorithm may be useful in screening patients with PM for severe sleep disordered breathing.

**Support (optional):**

### 0511 EFFECT OF AGING ON UPPER AIRWAY CLOSING PRESSURE AND AROUSAL THRESHOLD IN RESPONSE TO AIRWAY OCCLUSION DURING SLEEP

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**Introduction :** Aging predisposes to obstructive sleep apnea (OSA), but the underlying mechanisms remain unclear. Recent data in awake normal volunteers show a decrease in the genioglossus negative pressure reflex and an increase in pharyngeal airway length (in women) with increasing age suggesting an age-related predisposition to pharyngeal collapse. However, aging effects on pharyngeal mechanics have not yet been studied adequately during sleep. Arousals likely increase the severity of OSA by promoting greater ventilatory instability, and some data suggest that elderly patients with OSA may arouse more easily during apneic episodes. However, the effect of aging on arousal threshold also has not been studied.

**Methods :** To test the hypotheses that both upper airway closing pressure (Pclose) and arousal threshold (AT) increase (yielding less negative values) with age, we studied 8 healthy individuals aged between 19 and 71 years. Nasal (Pnas) and epiglottic pressures (PEpi), and sleep stage (EEG, EOG, EMG) were monitored while patients wore a nasal mask connected to an occlusion valve. AT was defined as Pepi in breath preceding arousal (stimulus: airway occlusion). Pclose was defined as the pressure at which Pnas plateaued after airway occlusion while Pepi further decreased. Means±SD are presented. Pearson's correlation coefficient was calculated to assess the relationship between age and Pclose/AT.

**Results :** During repetitive occlusions (mean: n=8 per volunteer) Pclose correlated (r=0.71, p=0.047) with age, whereas AT did not correlate with age (r=-0.5, p=0.22).

**Conclusion :** These data suggest an increased upper airway collapsibility may at least partially explain the high predisposition to sleep apnea among older persons. A higher number of volunteers are to be studied to confirm this hypothesis.

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### 0512 REDUCED NASAL RESISTANCE AFTER CONVENTIONAL TONSILLECTOMY IN OBSTRUCTIVE SLEEP APNEA PATIENTS

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**Introduction :** We have often experienced that nasal resistance has the tendency of reduction after tonsillectomy. However, there have been no studies focusing on tonsillectomy with nasal resistance, while several papers focus on nasal surgery. Accordingly, we investigated the effect of nasal resistance on conventional tonsillectomy in obstructive sleep apnea syndrome (OSAS) patients.

**Methods :** Conventional tonsillectomy was performed in 20 patients who were refractory to treatment of continuous positive airway pressure (CPAP). The subjects consisted of 17 men and 3 women (mean age, 32.9 ± 6.3 years; range 23 to 50 years). The effect of tonsillectomy

was evaluated with preoperative and postoperative polysomnography or nasal resistance.

**Results :** After tonsillectomy, nasal resistance (NR) decreased significantly from  $0.39 \pm 0.30$  to  $0.27 \pm 0.16$  Pa/cm<sup>3</sup>/sec ( $P < 0.05$ ). There were no significant correlation between tonsil weight and percentage change of bilateral nasal resistance (BNR) ( $P > 0.05$ ).

**Conclusion :** The reduction of nasal resistance by conventional tonsillectomy could play an important role on the improvement of OSAS, as well as nasal surgery or adenotomy.

**Support (optional):** None

## 0513

### WHAT DISTINGUISHES MIXED SLEEP APNEA FROM PURE OBSTRUCTIVE APNEA?

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**Introduction :** Most patients with obstructive sleep apnea (OSA) syndrome have some concomitant central events. It is unclear why both types of apnea occur in the same individual during the same night. Since patients with OSA usually have an abnormal upper airway resistance during sleep and since both central and obstructive apneas occur at the nadir of respiratory drive, the type of sleep apnea must depend on the degree of reduction of respiratory drive and upper airway structural and functional status. Therefore, we hypothesized that, for patients with equally severe OSA, those with pure OSA may have a more collapsible airway than those with coexisting obstructive and central apneas and/or hypopneas (mixed sleep disorders, MSD), while the MSD group may have more instability of the respiratory controller relative to the pure OSA group.

**Methods :** We studied 18 patients with OSA during non-REM sleep. Among them, 11 had coexisting central apneas and hypopneas ( $28 \pm 6\%$  of total), and 7 had pure OSA. We measured the upper airway collapsibility by assessing the critical closing pressure (Pcrit). The breathing stability was assessed by measuring delta PCO<sub>2</sub> (eupnea-apneic threshold). A ventilator was used in CPAP mode during Pcrit determination to reduce the level of CPAP in a stepwise manner until OSA occurred. In pressure support mode, the ventilator produced a gradual reduction of PaCO<sub>2</sub> until central apnea occurred, revealing the apnea threshold.

**Results :** There was no difference in Pcrit between the two groups ( $2.3 \pm 0.7$  vs  $1.7 \pm 0.6$  cmH<sub>2</sub>O,  $p=0.6$ ); but the delta PCO<sub>2</sub> tended to be smaller in patients with MSD ( $1.5 \pm 0.7$  mmHg) compared to patients with pure OSA ( $3.3 \pm 0.7$  mmHg) ( $p=0.09$ ).

**Conclusion :** The limited data from our ongoing study indicate that breathing stability rather than upper airway collapsibility distinguishes MSD from pure OSA, and a small CO<sub>2</sub> reserve might predispose patients with MSD to a central event.

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## 0514

### A BENCH STUDY TO COMPARE THE PERFORMANCE CAPABILITIES OF CPAP DEVICES FEATURING EXPIRATORY PRESSURE RELIEF ALGORITHMS

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**Introduction :** CPAP devices equipped with an expiratory pressure relief feature are a relatively new addition to the CPAP market. This unique fea-

ture is marketed as a more comfortable option for the OSA patient than standard CPAP therapy. However, what is not widely identified is exactly how these features operate and what differentiates one unit from another. The assumption is that these products perform similarly so purchasing decisions are then based on product reliability, warranty, other features, and price. The objective of this evaluation is to determine the performance capabilities and differences between three current CPAP devices that feature expiratory pressure relief algorithms.

**Methods :** Three separate CPAP machines equipped with an expiratory pressure relief algorithm were tested on a Hans-Rudolph Model 1101 breathing simulator programmed with two distinct breathing patterns and set to record patient flow and airway pressures. Each device was set to operate at 10cmH<sub>2</sub>O therapy pressure and was tested at each expiratory pressure relief setting. The delivered pressures and resulting pressure swings for each of the devices were compared on both breathing patterns. Work of Breathing values were calculated from the pressure deviation and tidal volume data.

**Results :** Each CPAP device exhibited a markedly different response to patient exhalation when the expiratory pressure relief feature was activated. As a result, Work of Breathing and pressure swing values varied greatly under both breathing patterns. Work of Breathing values (per breath) ranged from 0.015 to 0.334 J/L.

**Conclusion :** Each CPAP unit's response to a simulated patient, with expiratory pressure relief activated, was notably dissimilar to other devices in this test. A clinician or physician prescribing a CPAP device equipped with expiratory pressure relief should be familiar with the capabilities of each type of device and be aware of the differences between them.

**Support (optional):**

## 0515

### HYPERTENSIVE PATIENTS AMONG OUR CASES FOLLOWED-UP FOR OSAS

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**Introduction :** Increase of RDI is associated with elevation of systolic (diastolic) blood pressure. This is accompanied by a two- to three-fold escalation of the risk for hypertension during the transition from moderately severe to severe OSAS.

**Methods :** Since 1995, 12,548 questionnaires have been completed by the clients of 4 sleep disorders centers. In 6,356 cases, this was followed by cardiorespiratory polygraphy, intended for assessing the severity of OSAS objectively. After validation, the diagnostic sensitivity of the questionnaire was 90.8%, whereas its specificity was 72.8%. Subjects were categorized according to the following criteria: preclinical OSAS (AHI=5-10); mild OSAS (AHI=11-20); moderate OSAS (AHI=21-40); severe OSAS (AHI>40). The prevalence of hypertension was ascertained in the patient population studied.

**Results :** Verifying the independence of hypertension from severe OSAS using Pearson's chi square test revealed that in this population, the occurrence of hypertension is influenced by OSAS severity (df: 3;  $p < 0.0001$ ). The proportion of patients undergoing treatment for hypertension was 63.2% in the subset with severe OSAS. According to evidence from a prospective study, the risk of concomitant hypertension is 1.5 times higher in severe, than in mild or preclinical OSAS (RR: 1.58). The odds ratio for OSAS accompanied by hypertension was higher for all RDI classes in younger (aged <50 years), than in elderly (>50 years old) patients. Furthermore, the relative influence of BMI was smaller in the subset of

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younger patients.

**Conclusion :** RDI is independently associated with the presence of hypertension - as well as with BMI and age - as seen in our patient population. The odds ratio (OR) for OSAS and hypertension is higher in the younger (<50 years old) age group, than among the elderly. Therefore, young patients suffering from severe OSAS stand a higher chance of undergoing treatment for hypertension.

**Support (optional):**

### 0516

#### HYPERVISCOSITY AS A POSSIBLE CAUSE OF CONTROVERSIAL ACOUSTIC EVOKED POTENTIAL FINDINGS IN SLEEP APNEA PATIENTS

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**Introduction :** Based on our previous findings, we hypothesized that lack or presence of blood hyperviscosity could account for the controversial results observed during electrophysiological evaluation of the brain stem in sleep apnea syndrome.

**Methods :** 610 patients newly diagnosed with severe OSA (apnea/hypopnea index >35/h) by a polysomnographic study underwent hemorheological and brainstem acoustic evoked potential (BAEP) evaluations. All patients were male, aged 30-55 years, with negative results on transcranial and neck Doppler sonography or MRI angiography. Follow up: 239 hyperviscosity patients with positive BAEP findings were followed up. Repeated BAEP and rheological investigation was performed six months after initiation of CPAP therapy. In 80 patients, where in spite of CPAP treatment rheological results remained positive, another course of hemodilution therapy was necessary and a third BAEP test was performed after hemodilution therapy.

**Results :** 282 patients had hyperviscosity and 328 had normal rheological findings. Evoked potential changes - 57 sensorineuronal and 182 brainstem type - appeared only in the hyperviscosity positive subgroup. After six months of follow-up, adequate CPAP therapy normalized hyperviscosity in 159 patients. In 112 of 159 patients (all with brainstem type of lesion), the second BAEP showed normal wave latencies, while in 47 patients (with sensorineuronal lesion) even effective CPAP therapy and normoviscosity were unable to reverse BAEP findings to normal. In 80 patients CPAP therapy was unable to normalize hyperviscosity, and the BAEP results were not different from the initial ones. These patients underwent hemodilution therapy. The third BAEP performed after hemodilution became negative in 61 patients.

**Conclusion :** At present, there are two major implications of our results. Firstly, the role of hyperviscosity in BAEP alterations could settle the matter of controversial BAEP findings in OSA. Secondly, OSA patients should be further followed up to answer, whether pathological BAEP findings reveal a higher risk for cerebrovascular events.

**Support (optional):**

### 0517

#### DEMOGRAPHIC, CLINICAL, AND SLEEP-RELATED CORRELATES OF CENTRAL SLEEP APNEA IN STABLE HF PATIENTS

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**Introduction :** Obstructive (OSA) and central sleep apnea (CSA) are common and often co-exist in heart failure (HF). However, these disorders differ in underlying pathophysiology and likely occur in different subsets of patients. The purpose of this study was to compare the demographic, clinical, and sleep-related characteristics associated with CSA vs. OSA in clinically stable HF outpatients receiving standardized HF management.

**Methods :** The sample included 95 stable Class II-IV HF patients (M age = 58.08, SD = 16.38 years, 68/71.6% male, 58/62% white, ejection fraction (EF) M = 29.87, SD = 13.89%, 46/48% class III/IV). Portable home polysomnography (EEG, chin EMG, EOG, ECG, respiratory effort, nasal airflow, pulse oximetry and nasal cannula) was obtained with the Safiro (Compumedics, Inc.) recorder. Data were scored using Rechtschaffen and Kales and AASM criteria. Participants completed the Pittsburgh Sleep Quality Index and the Epworth Sleepiness Scale. Comorbidity was evaluated with the Charlson Comorbidity Index.

**Results :** Twenty-seven (28.4%) participants had apnea indices (AI)  $\geq$  5. Nine (33.3%) of this subset had predominantly CSA (CSA/AI > 0.5); and 18 (66.7%) had predominantly OSA (CSA/AI < 0.5). The CSA group consisted entirely of men, of whom 6 (66.7%) had class III/IV HF; the OSA group included 14 (78%) men; 9 (50%) had class III/IV HF. CSA participants were older (M = 68.70, SD = 12.70 vs. M = 53.71, SD = 13.76 years,  $p = .009$ ), had lower EF% (M = 22.00, SD = 7.42 vs. M = 33.56, SD = 16.63,  $p = .09$ ) and body mass index (BMI) (M = 25.86, SD = 4.58 vs. 35.44, SD = 9.16,  $p = .007$ ), higher AI (M = 39.3, SD = 11.86 vs. M = 20.12, SD = 17.77,  $p = .007$ ), and percentage wake after sleep onset (M = 51.49, SD = 13.51 vs. M = 19.40, SD = 8.14,  $p = .001$ ). There were no statistically significant group-related differences in comorbidity, NYHA Class, arousal index, daytime sleepiness, or perceived sleep quality.

**Conclusion :** CSA was associated with more advanced age, male gender, lower EF and BMI, a higher percentage of wake after sleep onset, and higher AI. The proportion of HF patients with predominant CSA is low compared with past reports and may reflect the clinically stable status and standardized treatment of this outpatient sample.

**Support (optional):** 5 R01 NR08022

### 0518

#### THE PREDICTOR FOR EVALUATING THE EFFICACY OF THE LATERAL SLEEPING POSITION

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**Introduction :** Lateral sleeping position often improve the number of episodes of apnea or hypopnea per hour (sleep apnea-hypopnea index: AHI) in patients with obstructive sleep apnea syndrome (OSAS). We investigated the predictor for evaluating the efficacy of the lateral sleeping position.

**Methods :** Thirty-five patients who had AHI of 15 or more (age 50.5 $\pm$ 12.2 years mean $\pm$ SD) were enrolled in this study. Standard polysomnography (Alice3: Respironics Inc., Murrysville, PA) was performed in all patients with OSAS. The electroencephalogram (C4-A1, C3-A2, O1-A2, and O2-A1), electrooculogram, electromyogram, and electrocardiogram were recorded continuously, and breathing variables monitored included chest and abdominal movement, diaphragm electromyography.

gram, and airflow. We used 3 categories: the grade of tonsil hypertrophy, the width of posterior pharyngeal cavity and the space of posterior pharyngeal cavity at the base of tongue. Which were graded from 0 to 3 by means of their severities in each. When the grade of the category was 2 or 3, we accounted its score as "+1", and total score by adding up the scores of these three categories was calculated.

**Results :** The patients were classified into 21 positional patients (PP, who decreased AHI on lateral position: Group PP) and 14 non-positional patients (NPP, who did not decrease AHI on lateral position: Group NPP). There were no statistical differences in the age, BMI, Epworth sleepiness scales, AHI, lowest oxygen saturation, and frequency of per hour oxygen desaturation of 3% or more, between Groups PP and NPP. The prevalence of patients with total score of 1 or less in Group PP was significantly higher than in Group NPP (62.0 vs 14.2%,  $p<0.05$ ). The prevalence of patients with total score of 2 or more in Group NPP was significantly higher than that in Group PP (85.8 vs 38.0%,  $p<0.05$ ).

**Conclusion :** Our findings suggest that otorhinolaryngological findings thus provide useful information for the discrimination of PP and NPP in patients with OSAS.

**Support (optional):**

### 0519

#### THE TAIWAN OCCUPATIONAL COHORT STUDY: STRATEGY AND VALIDATION OF A 2-TIER OSA SCREENING MODEL

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**Introduction :** OSA has emerged into an important occupational health issue since it has been found to link with somnolence-induced transportation and occupational incidents. It is urgent to identify OSA employees in order to eliminate the risk of professional liability. The aim of this study is to develop a 2-tier OSA screening model using questionnaires and pulse oximeter to prioritize patients for complete overnight PSG study.

**Methods :** The initial study group consists of 355 patients with symptomatic sleep problems (312 males and 43 females). The mean age is  $44.7\pm 11.3$ , BMI is  $27.4\pm 4.1$ , and RDI is  $38.3\pm 29.9$ . At entry, all patients complete the questionnaires (Snore Outcomes Survey, SOS and Epworth Sleepiness Scale, ESS) and polysomnography. We estimated the predictability of patients' characterizes, SOS, and ESS with an aim to maximize model sensitivity (tier 1). We further randomly selected 100 patients (83 males and 17 females) from the predicted positive population ( $RDI\geq 5$ ) of the 1st tier screening. The mean age is  $43.3\pm 11.5$ , BMI is  $26.5\pm 3.7$  and RDI is  $32.2\pm 28.4$ . We estimate the predictability of pulse oximeter to exclude patients without severe OSA ( $RDI<30$ ) with an aim to maximize the model specificity (tier 2).

**Results :** The receiver operating curve (ROC) analysis revealed that the area under curve (AUC) is 0.88 (standard error=0.026,  $Z=14.62$ ,  $p<0.001$ ) for tier 1 screening when  $ESS=9$  and  $SOS=55$ . The probability (P) of having OSA is:  $P=ek/(1+ek)$ , where as  $k=-4.836 + 1.096Xsex + 0.064Xage+0.264XBMI + 0.039XEES- 0.062 XSOS$ . For the oximeter screening, the ROC analyses indicated that desaturation of 3% is the best predictive threshold for severe OSA; the AUC is 0.951 (standard error=0.024,  $Z=18.792$ ,  $p<0.001$ ). The probability of not having severe OSA is  $P=ek/(1+ek)$ , where as  $k=-3.627 + 0.170XD13$ . With this 2-tier model, we are able to prioritize 86.96% of patients for complete overnight PSG in this cohort.

**Conclusion :** This preliminary data exhibit extreme high OSA prevalence in the middle-age, male dominate and obesity employees. The data may

overestimate the prevalence; this is, in part, the high sensitivity that leads to some false positive. Therefore, we need to use pulse oximeter as the Second-Tier screening tool to increase specificity before the ultimate PSG screening. 2-tier Screening model can look after both sides that include sensitivity and specificity, and identify the high risk OSA employees at an early date.

**Support (optional):**

### 0520

#### ANALYSIS OF REM-LIMITED SLEEP APNEA-HYPOPNEA SYNDROME

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**Introduction :** The pathogenesis of REM-limited Sleep Apnea-Hypopnea Syndrome (REM-limited SAHS), in which the apnea-hypopnea is observed only in REM sleep, is not clear. To help clarify the pathogenesis of REM-limited SAHS we compared nocturnal polysomnography (PSG) data between patients with REM-limited SAHS and those with OSAS diagnosed at the Fukuoka Center for Sleep Respiratory Disorders.

**Methods :** We analyzed 609 patients studied between September 2002 and April 2004. The criteria for diagnosis of REM-limited SAHS were an AHI > 15 in REM sleep and apnea-hypopnea > 66% in REM sleep compared with those in total sleep time (TST). The AHI, arousal index, and desaturation in TST, REM sleep, and non REM (NREM) sleep were compared between the patients with REM-limited SAHS and those with SAHS in TST.

**Results :** (1) Fifteen of the 609 subjects (1.65%) were diagnosed as REM-limited SAHS by nocturnal PSG. (2) Mean age was  $40.1 + 12.8$  and 13 of the 15 (87%) patients with REM-limited SAHS were men. (3) In patients with REM-limited SAHS, AHI was  $10.7 + 6.3$ ,  $44.8 + 17.5$  and  $3.2 + 2.1$  in TST, REM and NREM sleep, respectively. The arousal index was  $11.1 + 5.8$ ,  $18.4 + 9.4$  and  $10 + 5.3$  in TST, REM and NREM sleep, respectively. In addition, the desaturation (%) was  $2.3 + 4.4$ ,  $13.9 + 17.8$  and  $2.3 + 3.9$  in TST, REM and NREM, respectively.

**Conclusion :** The data from our study indicates that patients with REM-limited SAHS have severe nocturnal hypoxia during REM sleep but not during NREM sleep or in TST. CPAP treatment might be indicated in patients with REM-limited SAHS despite the mild sleep apnea-hypopnea syndrome in terms of TST.

**Support (optional):**

### 0521

#### AMBULATORY MANAGEMENT OF OBSTRUCTIVE SLEEP APNEA SYNDROME IMPROVES ALERTNESS AND QUALITY OF LIFE

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**Introduction :** The efficacy of ambulatory management of obstructive sleep apnea to improve the patient's quality of life, QOL, is unclear. We evaluated alertness, QOL, and CPAP therapy compliance using an ambulatory care model.

**Methods :** A prospective longitudinal study with-in subjects design. Convenience sampling was used. Patients completed initial screening questionnaire to document subjective symptoms and an Epworth Sleepiness Scale (ESS). Baseline alertness was assessed by Psychomotor Vigilance Task (PVT), and QOL measures using the SF-36. Ambulatory polysomnography was undertaken with a portable device to obtain recordings of airflow, breathing effort, oxygen saturation, snoring, pulse

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rate, and body position. Patients found to have OSA then underwent an unattended CPAP titration using an auto-titrating CPAP device. After 30 days of treatment, the questionnaires and PVT were repeated. Statistical analyses were performed and statistical significance was defined as 2-tail alpha value of 0.05. Primary outcomes measured were CPAP use and PVT scores. Subjective measures included perception of treatment efficacy (6-point Likert scale), sleepiness by ESS scores, and QOL by SF-36.

**Results :** Fourteen male subjects, age 37-75 years (mean 48.57, S.D. 9.83) completed the study. Apnea Hypopnea Index before treatment was 44.62 events per hour (S.D. 24.13). Quality of life as measured by SF-36 improved significantly for physical health, general health, vitality, social functioning, emotional and mental health subscales. Physical function trended towards improvement. Epworth scores improved from 13.21 (S.D.4.08) to 5.57 (S.D. 3.78) after treatment. Compliance was available for 8 subjects with mean use of 4.04 hours nightly (range 0 - 7.45 hrs). PVT (pretreatment mean = 351.05, S.D. 175.94; posttreatment mean= 304.58, S.D. 102.53) showed a trend towards improvement

**Conclusion :** In selected patients, ambulatory management of obstructive sleep apnea improved the patient's QOL. These improvements are comparable to previously published results using traditional in-laboratory management.

**Support (optional):** This study received support by the ResMed Research Foundation

### 0522

#### LINEAR VERSUS CURVILINEAR TRAJECTORIES FOR INCIDENT SLEEP DISORDERED BREATHING OVER 25 YEARS

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**Introduction :** Previous cross-sectional and longitudinal studies conflict regarding age-dependence of SDB above age 60. We present here longitudinal, natural history data examining incident SDB in non-clinic volunteers.

**Methods :** We recorded in-lab, full PSG in 23 subjects for a total of 166 nts representing 6,736 person-months of observation. Each subject was studied between 3 and 6 occasions. Age at entry ranged from 45 to 73 ( $X = 55.9$ ,  $SD = 7.7$ ); mean follow-up interval from first to last PSG was 24.4 years (range 239 to 361 months).

**Results :** RDI at entry was low ( $X = 2.5$ ,  $SD = 3.6$ ). X difference in RDI between first and last time of measurement was + 11.8 ( $SD = 14.4$ , median 6.6) events per hour. Mean RDI slope was 0.46 events/hr/year. Within subjects regression employed both linear and polynomial functions and used age and age squared, respectively, to curve fit RDI over time. Results indicated 21 of 23 subjects with positive RDI slope. Of those 21 cases, increased RDI was better characterized by linear models, with a median r-squared value of .88; 9/23 of individuals' linear regressions were significant at the .05 level. When slope was expressed as a function of each subject's maximal RDI during the observation period, the mean percentage (% of maximum prorated per year) was 3.1 % ( $SD = 1.1\%$ ).

**Conclusion :** These data confirm incident SDB across the 60's and 70's in elderly volunteers and suggest linear increases with chronologic age. One's likelihood of developing SDB over time appears an inevitable consequence of aging processes when viewed longitudinally over the span of decades. However, the rate of increase exceeds that of many "classic" aging biomarkers (i.e., 0.5% to 0.65% per year) and may also be compatible with age-dependent SDB as a manifestation of disease.

**Support (optional):** AG-020269

### 0523

#### GROUP APPROACH TO CPAP USERS, FAMILY MEMBERS, AND COLLATERALS

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**Introduction :** The objective of the paper in the utilization of appropriate and specific instruments, to prompt the members of the group together with their family members /collaterals to recognize the role of maladaptive cognitive and behavioral aspects in causing OSAH and requiring CPAP.

**Methods :** Two groups of patients accompanied by family members /collaterals took part in four 2-hour sessions at 7-day intervals. Each session included cognitive, behavioral, and educational interventions. The instruments used for evaluation were: PSG, PSG/CPAP, specific questionnaires and subjective reports, and the Epworth Sleepiness Scale (EPW) relating to patient's sleepiness before and after starting treatment, which was filled out by patients and collaterals.

**Results :** There were 29 people in group I, (aged  $52 \pm 10$ ); of which 16 were CPAP users and 13 family members / collaterals and 23 in group II, 12 users and 11 family members (aged  $55 \pm 9$ ). a) the patient's more frequent complaints: fear of psychosocial issues involving family and social interactions; b) partners' more frequent complaints of non-restorative sleep, fatigue and irritability; c) improvements noticed by patients after regular CPAP use: greater predilection for family, occupational and sexual activities; d) improvements noticed by partner after regular CPAP use: better quality sleep and better conjugal relations. There was no difference when comparing EPW forms filled out by collaterals and users before treatment ( $19 \pm 6$  v.  $19 \pm 5$ ) and after starting treatment ( $8 \pm 5$  v.  $7 \pm 6$ ), however, on comparing pre- and post treatment EPW there was difference ( $p < 0.001$ ) in the perceptions of both collaterals and users.

**Conclusion :** Being better informed in relation to the disorder and its treatment, associated with family support, and with cognitive, behavioral, and educational interventions, proved to be effective in ameliorating psychopathological and psychosocial consequences in OSAH patients and in facilitating CPAP acceptance.

**Support (optional):** AFIP, FAPESP/CEPID

### 0524

#### NASOENDOSCOPY DISCLOSES SWALLOWING PROBLEMS IN OSAS PATIENTS

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**Introduction :** OSAS patients may have subclinical swallowing abnormalities due to progressive mechanical trauma of the pharyngeal tissues caused by snoring. Objective: to characterize the function of swallowing in OSAS patients.

**Methods :** We study by nasoendoscopy 11 patients, 6 women, without spontaneous complaints of swallowing,  $48 \pm 14$  years old, with PSG diagnosis of OSAS, IAH  $25,78 \pm 36,82$ . The exams were carried through without anesthetics and nasal vasoconstriction. It was offered to patient diet bolus (5 and 10ml) as thin liquids (L), purée (P), and solids (S). Two examiners had analyzed the anatomical structures and the functional aspects of the swallowing events following the criteria: (1) premature leakage of bolus into the pharynx; (2) laryngeal penetration; (3) traqueal aspiration; (4) bolus residual in the pharynx after swallowing; (5) inefficient pharyngeal cleanliness.

**Results :** We verified that 64% of the patients presented premature leak-



age: 8% for L; 9% for S; 9% for L and P; 18% for P and S; and 9% for L, P and S. We did not observed laryngeal penetration and traqueal aspiration. We verified that 55% of the patients had presented bolus residual after swallowing: 18% for P; 18% for L and P; and 9% for L, P and S. Nine percent of the patients presented inefficacious pharyngeal cleanness for L and P; and 9% for P and S. Were also observed that the patient with more severe problems of swallowing was the not fat one and presented the longer illness time (30 years).

**Conclusion :** OSAS patients presented subclinical manifestations of abnormal swallowing by nasoendoscopy possibly associated to neuromuscular injury caused by snoring. The time of illness and severity of the OSAS seem to be associated to the swallowing dysfunctions in our sample.

**Support (optional):** Center for Clinic and Sciences of Sleep

## 0525

### TREATMENT EFFECT OF CPAP ON CEREBRAL TISSUE OXYGENATION DURING SLEEP IN PATIENTS WITH OSAHS

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**Introduction :** To investigate the CPAP treatment effect on cerebral tissue oxygenation during obstructive sleep apnea.

**Methods :** Cerebral tissue oxygenation reflected by tissue oxygenation index (TOI) in eighteen severe OSAHS patients with a mean AHI of 68±24 was monitored using near-infrared spectroscopy (NIRS) (Niro300, Hamamatsu Japan). Full polysomnography (PSG) and pulse oximetry measuring oxygen saturation (SaO<sub>2</sub>) were conducted simultaneously. The TOI signal was fed into one of the PSG channels and was displayed on the screen at the same time with other PSG tracings. SaO<sub>2</sub> measurements include oxygen desaturation ≥4% index (ODI4), the lowest SaO<sub>2</sub> (LSaO<sub>2</sub>) and the mean SaO<sub>2</sub> (MSaO<sub>2</sub>) during sleep. TOI was given by the ratio of OHb to OHb+HHb. Parameters indicating cerebral tissue desaturation include numbers of TOI decrease ≥4% per hour (TOI4), the lowest TOI (LTOI) and the mean TOI (MTOI) during sleep. TOI, SaO<sub>2</sub> and PSG indexes were also monitored simultaneously during CPAP treatment in fourteen of the 18 patients.

**Results :** AHI, ODI4 and TOI4 correlated very well with each other (AHI vs ODI4 r=0.879; AHI vs TOI4 R=0.568; TOI4 vs ODI4 r=0.729; all p<0.05) in 18 OSAHS patients. However, linear regression did not reveal any relationship between LSaO<sub>2</sub> and LTOI, MSaO<sub>2</sub> and MTOI during sleep. Although the awake SaO<sub>2</sub> after PSG test in the morning returned to the pre-test level (95.4±2.3 vs 95.3±2.0), TOI immediately on morning awakening still maintained to a level lower than that of the pre-test (68.9±4.7 vs 65.4±5.4 p=0.001). With the improvement of sleep apnea during CPAP (mean pressure of 13.2±2.5cmH<sub>2</sub>O) treatment in fourteen patients, SaO<sub>2</sub> and TOI increased significantly. Both the awake SaO<sub>2</sub> (95.3±2.4 vs 95.4±2.1) and TOI (69.7±3.8 vs 69.1±3.8) on morning awakening returned to the pre-test level.

**Conclusion :** Monitoring for cerebral tissue saturation during obstructive sleep apnoea provides additional information to conventional pulse oxygen saturation, and CPAP treatment improve both peripheral and tissue oxygenation.

**Support (optional):** Supported by a grant from National Natural Science Foundation of China (30300120).

## 0526

### EFFECT OF THE NEUROPEPTIDE Y ON THE GENIOGLOSSUS AND DIAPHRAGMATIC EMG ACTIVITIES IN ANAESTHETISED RAT

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**Introduction :** The Neuropeptide Y (NPY) is a central neuromediator involved in the food control via the leptin/orexin pathway. Breathing changes (Vt and FR) were reported after injection of leptin or NPY in animal. The hypothesis is that both obesity and sleep breathing disturbance in OSAS patient can be linked to a central dysregulation of the NPY. The first objective was to study the effects of the NPY on the ventilatory pump (Diaphragm, DIA) and the upper airway muscles (Genioglossus, GG).

**Methods :** The GG and DIA EMG, EEG, O<sub>2</sub> saturation and HR were recorded in 18 anaesthetised rats spontaneously breathing oxygen. The inspiratory time, surface and maximal amplitude of the DIA and GG respiratory activities were analysed after intra-cerebroventricular injection of an Y2 agonist (n=6, 2,4nmol) and Y1 antagonist (n=6, 10nmol) and compared to a control group of NaCl 1M (n=6).

**Results :** A significant decrease of the DIA (-16% ± 4,3% at 48min ) and the GG (-15,7% ± 7% at 48 min) inspiratory time with the Y1 antagonist were observed. The effect was maintained over 50min after injection. No change was observed with a 2,5nmol dose of the Y2 agonist. The anaesthetised state remained constant all over each procedure as shown by a spectral analysis of the EEG.

**Conclusion :** This preliminary result show that the inspiratory time can be modulated by the NPY (Y1 receptor). Two targets can be discussed : (i) the NPY receptors within the NTS (Dorsal Respiratory Group), (ii) the orexin receptors within the XII nucleus. Higher doses of the Y2 agonist must be performed.

**Support (optional):**

## 0527

### SPLIT NIGHT POLYSOMNOGRAPHY IN THE DIAGNOSIS AND TREATMENT OF THE UPPER AIRWAY RESISTANCE SYNDROME

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**Introduction :** The upper airway resistance syndrome (UARS) is a form of sleep-disordered breathing in which transient increases in upper airway resistance result in repetitive EEG arousals. UARS is not associated with apnea or diminished airflow, although snoring and excessive daytime somnolence (EDS) are common. This report describes the use of split night polysomnography with positive airway pressure titration to diagnose and initiate treatment of UARS.

**Methods :** This is a retrospective review of all polysomnographies performed during 2000 at our sleep disorders center, which is located in a large, academic, military medical center and serves military personnel, military retirees, and their dependent families. Esophageal manometry during polysomnography was routinely performed on patients with hypersomnolence (Epworth sleepiness scale > 10) who demonstrated a total arousal index ≥10/h and a respiratory disturbance index of ≤ 5/h on prior polysomnography. UARS was definitely diagnosed in patients who demonstrated repetitive increased upper airway resistance (IUAR) associated with brief EEG arousals followed by normalization of esophageal pressure (Pes). IUAR was defined by a pattern of crescendo negative

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inspiratory Pes of  $\leq$  12 cm H<sub>2</sub>O. Patients then underwent titration with continuous positive airway pressure (CPAP) or bi-level positive airway pressure (BiPAP) to eliminate respiratory-effort related arousals (RERA).

**Results :** During calendar year 2000, we performed 724 polysomnographies in 527 patients. Obstructive sleep apnea was diagnosed in 383 patients (72.6%), and 44 patients (8.4%) were found to have UARS. 23 patients with UARS were diagnosed using split night polysomnography with total elimination of RERAs following CPAP/BiPAP titration.

**Conclusion :** Split night polysomnography with positive airway pressure titration is an effective and cost efficient means to diagnose and initiate treatment of UARS.

**Support (optional):**

### 0528

#### MOTOR RESPONSE OF UPPER AIRWAY DILATOR MUSCLES TO TRANSCRANIAL MAGNETIC STIMULATION IN NORMAL AWAKE SUBJECTS

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**Introduction :** Phasic activities of upper airway (UA) dilator muscles are intimately linked. The motor response to transcranial magnetic stimulation (TMS) has only been characterized for the genioglossus (GG). The objective of this study is to compare the TMS responses of different UA dilator muscles in different respiratory conditions and to compare these responses to that of the diaphragm (Dia).

**Methods :** TMS was applied at the optimal position of the dominant-side area of the scalp for alae nasi (AN), genioglossus (GG), levator palatini (LP), palatoglossus (PG) and diaphragm (Dia) during wakefulness in 8 normal subjects. Motor evoked potential (MEP) were recorded in response to TMS delivered 0.5 s after the onset of expiration (Exp), 0.5 s and 1.5 s after the onset of inspiration (E-Insp, L-Insp) and 1.5 s after the onset of resistively loaded inspiration (Insp+R).

**Results :** UA dilator MEPs were obtained from overlapping cortical areas lateral to Cz, the stimulation of which also elicited an activation of the Dia area. UA dilator MEP latencies were always shorter than that of Dia (in GG area during Exp: AN 7.68±7.93 ms, LP 9.59±4.25 ms, Dia 17.47±1.12 ms, Mean ± SD). Their amplitudes were higher than that of the Dia for GG, LP, and PG (in GG area during Exp: AN 0.60±0.39 mV; LP 0.48±0.36 mV; Dia 0.09±0.07 mV). The characteristics of the GG, LP and Dia responses were differently affected by respiratory maneuvers and tongue protrusion

**Conclusion :** 1) TMS provides a valuable way to evaluate the corticospinal pathway to UA dilator muscles, 2) In response to non focal TMS, UA muscles are consistently activated before Dia, 3) Respiratory maneuvers have facilitatory effects of different nature on the response of these muscles to TMS.

**Support (optional):** Supported by CIHR grant MT 13 768

### 0529

#### HEALTH-RELATED QUALITY OF LIFE OF MILITARY VETERANS WITH OBSTRUCTIVE SLEEP APNEA

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**Introduction :** Several studies suggest poorer quality of life (QoL) to be associated with obstructive sleep apnea (OSA) and related sleep disorders. A majority of these studies have utilized civilian populations. Little is known about relationships between sleep disorders and QoL of veterans, however.

**Methods :** Male veterans 54-85 years old (n=229; 48% Hispanic) completed the Sleep Heart Health Study Sleep Habits and the Centers for Epidemiological Studies—Depression (CES-D) questionnaires. Demographic, health and anthropometric data were also obtained. The MOS SF-12 physical (PCS) and mental composite scores (MCS) provided QoL data. The PCS indicates physical functioning, while the MCS indicates overall mental health. Analysis included standardized PCS and MCS mean scores for comparisons between presence or absence of sleep disorders. Linear regression modeling of the PCS and MCS as dependent variables, and OSA, EDS and Insufficient Sleep as independent variables, controlling for age, education, ethnicity, BMI, smoking, cardiac ischemia, diabetes, and depression was also performed.

**Results :** PCS comparisons for veterans with and without disorders were OSA=32±10 versus 43±10; EDS=32±10 versus 42±10; and Insufficient Sleep=33±7 versus 42±11 (each p<0.0001). MCS comparisons were OSA=50±11 versus 53±10; EDS=51±12 compared to 53±10; and Insufficient Sleep=45±11 to 53±10. Only the MCS comparison for Insufficient Sleep was significant (p=0.003). The three sleep disorders were simultaneously entered into the linear regression modeling for the PCS and MCS. Insufficient Sleep (p<0.0001), OSA (p=0.007) and ischemia (p=0.04) were independently associated with the PCS, accounting for a combined 14% of the variance in the model. Depression was the only variable associated with the MCS, accounting for 46% of the variance in the model.

**Conclusion :** Poorer QoL outcome for veterans with sleep disorders are consistent with civilian studies. Regression modeling suggests that veterans with OSA or Insufficient sleep indicate poorer physical QoL, while depression plays a primary role in poorer mental health.

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### 0530

#### INFLUENCE OF WAKEFULNESS ON PHARYNGEAL MUSCLE ACTIVATION

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**Introduction :** Although it is clear that wakefulness can influence ventilation, it is unclear whether wakefulness per se apart from respiratory/mechanical stimuli can influence pharyngeal dilator muscle activity. We, therefore, assessed the impact of sleep on upper airway muscle activity after minimizing respiratory/mechanical inputs to these muscles.

**Methods :** We have studied to date 3 male and 3 female normal subjects (age 19-49), monitoring genioglossus (GG), tensor palatini (TP), and diaphragm (DIA) EMGs, ventilation, end-tidal PCO<sub>2</sub>, and sleep-wake status. Non-invasive positive pressure ventilation was applied in this study. Expiratory pressure was adjusted to yield the lowest genioglossal tonic activity thereby reducing airway negative pressure effects (EPAP, 6±0 cm H<sub>2</sub>O). Inspiratory pressure, respiratory rate, and inspiratory time were adjusted until the subjects were passively ventilated (assessed by DIA EMG), thereby attenuating respiratory input (IPAP=12.5±0.6 cm

H2O; RR=17±0.1 breaths/minute; Ti, 1.2±0.1 seconds). We evaluated muscle activity during wakefulness, wake-sleep transitions (5 alpha to 5 theta breaths), stable non rapid eye movement (NREM) sleep, and rapid eye movement (REM) sleep in the supine position under these conditions.

**Results :** Under ventilated conditions, none of the muscles demonstrated inspiratory phasic activation. From wakefulness to sleep (alpha to theta), subjects demonstrated decrements in the activity of both GG and TP muscles (1.9±0.8 to 1.5±0.6 % of maximal GGEMG, p=0.046; 6.0±4.1 to 5.0±3.8 % of maximal TP EMG, p=0.063; respectively). Compared with sleep onset, the activity of TP during stable NREM sleep and REM sleep demonstrated further decreases (5.0±3.8 % vs. 4.4±3.7 % vs. 4.4±3.7 %, p<0.001; for onset vs. NREM vs. REM sleep). Activity of GG during stable NREM and REM sleep did not differ from values observed at sleep onset.

**Conclusion :** This study suggests that wakefulness per se, apart from respiratory/mechanical stimuli, can substantially influence pharyngeal muscle activity. However, stable NREM and REM sleep have different further effects on GG versus TP activity.

**Support (optional):** This research was supported by NIH R01HL48531, HL60292.

### 0531

#### THE INFLUENCE OF ABDOMINAL FAT DISTRIBUTION MEASURED BY DEXA ON THE SEVERITY OF SLEEP APNEA IN POSTMENOPAUSAL WOMEN

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**Introduction :** Body fat distribution may influence the severity of sleep apnea. The authors compared abdominal fat distribution seen in postmenopausal women with parameters recorded by cardiorespiratory polygraphy. The objective of this study was to characterize the relationship between the quantity as well as the distribution of abdominal fat and the severity of sleep apnea, in postmenopausal women.

**Methods :** Total and regional fat mass was determined by DEXA (dual energy x-ray absorptiometry). Protocols for measuring total and abdominal fat were used. The quantity of abdominal fat was assessed in the region between the second and fourth lumbar vertebrae. The severity of obstructive sleep apnea was evaluated by cardiorespiratory polygraphy.

**Results :** Sixty-two postmenopausal women suffering from sleep apnea were studied. Mean age of the study population was 57.54±7.48 years. The severity of apnea was categorized as mild-to-moderate, if AHI was in the range of 5 to 30, whereas an AHI above 30 signified severe apnea. Total and abdominal fat content were 44.89±5.86% and 50.15±5.24% in patients with severe OSAS (n=38), whereas these indices were 42.70±7.99% and 46.20±8.42% in the subset with mild-to-moderate sleep apnea. According to Student's two-tailed t-test, the difference between group means was significant for percentage body fat in the abdominal region (p=0.023), but not for total body fat (p=0.13).

**Conclusion :** Excess abdominal fat content aggravates sleep apnea in postmenopausal women.

**Support (optional):**

### 0532

#### PREOPERATIVE SCREENING FOR OBSTRUCTIVE SLEEP APNEA WITH IMPLICATIONS FOR POSTOPERATIVE CARE

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**Introduction :** Patients with obstructive sleep apnea syndrome (OSAS) can be at increased risk for postoperative complications. Screening for OSAS can identify these patients leading to measures reducing postoperative complications. We screened patients using a modification of the Berlin Questionnaire and used continuous positive airway pressure (CPAP) postoperatively in high risk patients attempting to reduce apneic complications.

**Methods :** Our standard self-administered hospital questionnaire includes eleven questions regarding sleep disorders. Patients answering affirmative were asked to complete a modified Berlin Questionnaire. This questionnaire generates a numbered score. Patients with a score greater than 25 are considered high risk for OSAS. High risk patients are placed on CPAP in the postanesthesia recovery unit.

**Results :** 600 patients were screened preoperatively using a modified Berlin Questionnaire. 157 (26.2%) were high risk for OSAS. This corresponds to previous preoperative screening using the Berlin Questionnaire that identified 23.9% of patients to be at high risk. Patients age 50 to 59 had the highest risk of OSAS (44%). There was no difference in risk between men and women. Institution of CPAP postoperatively tended to reduce time patients are intubated and the need for re-intubation.

**Conclusion :** Preoperative screening for OSAS using a modification of the Berlin Questionnaire that generates a number score identifies patients at high risk for OSAS similar to published results. This questionnaire may be easier to use. Risk for OSAS is age but not sex dependent. Placing patients at high risk for OSAS on CPAP postoperatively may reduce prolonged endotracheal intubation and re-intubation and requires further study.

**Support (optional):**

### 0533

#### MECHANISMS OF COMPENSATION FOR UPPER AIRWAY COLLAPSE DURING NREM SLEEP IN OBSTRUCTIVE SLEEP APNEA AND HEALTHY CONTROLS

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**Introduction :** Obstructive sleep apnea (OSA) is characterised by the inability to maintain adequate ventilation (VE) during sleep due to upper airway (UA) collapse. Most OSA patients can compensate for their collapsible UA at least some times during sleep. The aims of this study were to compare: 1) the ability to restore VE and 2) mechanisms of compensation (increased genioglossus muscle activity (EMG<sub>gg</sub>) and duty cycle (Ti/Ttot)) following sudden reduction of continuous positive airway pressure (CPAP) in subjects with and without OSA.

**Methods :** Minute VE, Ti/Ttot, EMG<sub>gg</sub> and epiglottic pressure (Pepi) were measured in subjects with and without OSA who were studied on CPAP sufficient to abolish flow limitation (optimal CPAP). During stable NREM sleep, CPAP was repeatedly reduced between 2 and 10cmH<sub>2</sub>O below optimal CPAP for 5 minutes or until arousal from sleep occurred. Adequate restoration of VE occurred if 1) the subject remained asleep for the 5 minute CPAP drop or 2) if CO<sub>2</sub> and Pepi were stable (<2mmHg increase, <2cmH<sub>2</sub>O decrement) for 30s prior to arousal (regarded as a spontaneous arousal). EMG<sub>gg</sub> and Ti/Ttot prior to arousal or at 5 minutes was calculated to assess compensatory mechanisms.

**Results :** Adequate data were obtained in 10 subjects with OSA (mean±SEM, AHI 63±13 events/hr) and 15 controls. CPAP was reduced 185 times in controls by 5.7±0.1 cmH<sub>2</sub>O and 148 times in OSA patients by 4.2±0.1 cmH<sub>2</sub>O. OSA patients could not restore VE as often as controls (54% versus 66% trials, p=0.04 Chi square). When restoration of VE occurred, EMG<sub>gg</sub> and Ti/Ttot were increased similarly in OSA patients

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and controls (EMG<sub>gg</sub> 267 ± 40 and 199 ± 12 %baseline; Ti/T<sub>tot</sub> 114 ± 2 and 111 ± 2 %baseline respectively).

**Conclusion :** Patients with OSA could restore VE following a drop in CPAP less often than controls. However, the mechanisms used to restore VE were similar.

**Support (optional):** NIH P50HL60292, NCRR GCRC RR01032 and American Heart Association 0425786T.

### 0534

#### UPPER AIRWAY MUSCLE ACTIVITY AND LUNG VOLUME DURING SPONTANEOUSLY OCCURRING STABLE BREATHING PERIODS IN OBSTRUCTIVE SLEEP APNEA

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**Introduction :** Most patients with obstructive sleep apnea (OSA) have periods without apneas/hypopneas at least some of the time during sleep. The mechanisms that enable stable breathing in OSA are currently unknown. We aimed to determine whether the activity of two upper airway dilator muscles, the genioglossus (EMG<sub>gg</sub>) and tensor palatini (EMG<sub>tp</sub>), or end expiratory lung volume (EELV) differ between spontaneous periods of stable and cyclical breathing.

**Methods :** Patients with OSA who had some periods of sleep without apnea on their diagnostic sleep study were recruited. Intramuscular EMG<sub>gg</sub> and EMG<sub>tp</sub>, respiratory effort (epiglottic pressure), ventilation (mask and pneumotachograph), EELV (chest and abdomen magnetometers) and sleep state were monitored during supine sleep without CPAP. A technician blinded to EMG's and EELV scored sleep stage and respiratory events. Peak inspiratory EMG's were expressed as a % of the maximum activity seen during swallowing/tongue protrusion. EMG's and EELV were averaged for all breaths during cyclical breathing periods (>3 minutes with >1 respiratory event/minute) and stable breathing periods (>3 minutes of sleep with no respiratory events or arousals).

**Results :** Four patients have been studied to date. Both cyclical and stable breathing periods were identified during NREM sleep in 2 patients (aged 56 and 34yrs, AHI 62 and 17 events/hr). EMG<sub>gg</sub> was higher in both patients during stable breathing compared to cyclical breathing periods (34±0.5 versus 20±0.5 and 10.6±0.1 versus 6.5±0.3 %max). In contrast EMG<sub>tp</sub> was lower during stable than cyclical breathing (3.7±0.2 versus 10.6±0.7 and 10.2±0.3 versus 11.5±0.5 %max) while EELV results were mixed (394±8 versus 326±21 and 178±8 versus 360±23 mL below waking EELV).

**Conclusion :** If these findings persist in a larger sample it would suggest that elevated EMG<sub>gg</sub> may be a fundamental mechanism by which the upper airway is stabilized such that OSA patients can have periods of sleep free of respiratory events. EMG<sub>tp</sub> and lung volume likely play lesser roles.

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### 0535

#### OSA CONTRIBUTES TO AN INCREASE OF GHRELIN LEVEL INDEPENDENT OF OBESITY

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**Introduction :** Ghrelin and leptin play an important role in hunger regulation, food intake, energy balance and have been associated with the pathogenesis of diabetes, obesity and some cardiovascular diseases which

usually coexist with obstructive sleep apnea (OSA). Recently it had been posited that ghrelin has the opposite effect of leptin. Most studies in OSA patients measuring these metabolic hormones are controversial because obesity represents a confounder factor. To investigate the effect of CPAP on serum level of ghrelin and leptin in obese and non obese OSA patients.

**Methods :** The sample was composed of 13 consecutive patients with OSA (AHI≥10) and 13 volunteers matched for gender (male), age and body mass index (BMI). The exclusion criteria were: patients with metabolic, severe cardiovascular and neoplastic diseases. The protocol included baseline evaluation and after 6 months of CPAP: full night polysomnographic recording along with morning fasting blood sample analyses for ghrelin, leptin, glycemia, insulin, triglycerids, cholesterol (total, LDL, VLDL, HDL), C-reactive protein and fibrinogen.

**Results :** OSA patients compared to volunteers showed (mean/SD) age: 37±7 vs 36±6 years old, p=0.57; BMI: 29±4vs26±4 Kg/m<sup>2</sup>, p=0.08 and AHI: 41±29 vs 2±1, p=0.001. During baseline evaluation, in OSA patients, there was a significant increase in ghrelin level (1642.4±941.6 vs 1009.8±261.9 pg/ml, p=0.043) and there was not a difference regarding leptin levels (20.39±10.86 vs 15.2±5.9 ng/ml). Comparing obese and non obese OSA patients no difference was observed in these measurements. After CPAP treatment there was a significant decrease of ghrelin levels (1642.4±941.6 vs 1031.8±444.3 pg/ml, p=0.04) but no changes occurred in leptin levels (20.39±10.86 vs 22.37±9.7 ng/ml).

**Conclusion :** OSA contributes to an increase in ghrelin level independent of obesity. CPAP treatment is associated with a significant reduction of this hormone.

**Support (optional):** AFIP and FAPESP/CEPID

### 0536

#### CHARACTERIZATION OF BREATHING PATTERNS IN PATIENTS WITH "COMPLEX" SLEEP APNEA SYNDROME

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**Introduction :** While continuous positive airway pressure (CPAP) resolves most sleep disordered breathing in most patients with obstructive sleep apnea (OSA), others develop problematic central apneas (>10/h), a condition we call the Complex Sleep Apnea Syndrome (CompSAS). Their clinical profiles are indistinguishable. Others have drawn focus on the difference in respiratory cycling between patients with OSA and central sleep apnea (CSA). We hypothesized that there should be measurable pre-CPAP differences in respiratory cycling and control between patients with OSA and CompSAS.

**Methods :** Retrospective review of clinical records and polysomnograms of 13 patients with CompSAS, and 8 patients with OSA. In random sections of stage-2 sleep (diagnostic portion), we manually performed 10 measures of apnea and hyperpnea duration, lung to finger circulation time (LFCT), time to peak tidal volume (TTP<sub>v</sub>), and ratio of inspiratory time (Ti) to respiratory cycle length (T<sub>tot</sub>), or duty cycle (Ti/T<sub>tot</sub>). Comparisons of measures between groups were made using Student's t-test.

**Results :** The total apnea-hypopnea index (AHI) was similar between groups (mean±SD: 32.3±29.9 in CompSAS vs. 21.8±5.8 in OSA, p=0.377). CompSAS patients had shorter apneas (20.5±7.4s vs. 24.5±8.1s; p=0.003), and hyperpneas (16.1±5.6s vs. 19.4±8.4s; p=0.004), but LFCT was significantly prolonged (21.1±7.3s vs. 18.2±6.8s; p=0.02) compared to OSA patients. TTP<sub>v</sub> was shorter in CompSAS (0.79±0.4s vs. 2.1±2.8s; p<0.0001) and Ti/T<sub>tot</sub> was higher (0.41±0.1s vs. 0.36±0.1s; p=0.001). The variance in RR was higher (p=0.605), and in Ti/T<sub>tot</sub> was significantly higher in CompSAS than in OSA patients (p<0.0001).

**Conclusion :** Compared to OSA, CompSAS patients demonstrate high

variability in respiratory cycling and more closely mimic patterns observed in CSA. This may allow real-time recognition and prediction of frequent central apneas after the institution of CPAP.

**Support (optional):**

### 0537

#### ONE EDUCATIONAL SESSION CAN IMPROVE OBJECTIVE SLEEP QUALITY AND MASK TOLERANCE OF THE PATIENTS DURING POSITIVE AIRWAY PRESSURE TITRATION

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**Introduction :** The aim of this study is to evaluate if an educational session by PSG technician during the night of PAP titration can improve objective sleep quality and mask tolerance of patients in the sleep laboratory.

**Methods :** The educational program for PSG technician started in September/2003 and its protocol included: 1) patient education about OSAHS, its consequences and treatment; 2) CPAP/BiPAP titration, therapy, and side effects; and 3) patient training with PAP equipment and selection of mask type before the beginning of PSG hook up preparation. Patients were divided in two groups: those previously referred to PSG for CPAP/BiPAP titration (March to August/2003: n=699) and those referred to PSG for PAP titration after the beginning of protocol (March to August/2004: n=782).

**Results :** Demographic data of both groups of patients were similar (2003 vs. 2004): male and female proportion (76:24 vs. 75:25), age (mean  $\pm$  SD) ( $53 \pm 12$  vs.  $52 \pm 12$  years) and BMI ( $31 \pm 6$  vs.  $31 \pm 6$  kg/m<sup>2</sup>). After education session, the number of patients that did not tolerate nasal mask during PSG recording was lower (80 vs. 44) ( $p=0.001$ ). PSG data were different ( $p<0.05$ ) according to: TST ( $312 \pm 81$  vs.  $326 \pm 85$  min), sleep efficiency ( $74 \pm 17$  vs.  $77 \pm 14$  %), Sleep latency ( $22 \pm 24$  vs.  $18 \pm 29$  min), S1 ( $8 \pm 8$  vs.  $6 \pm 5$  %), S3+4 ( $19 \pm 11$  vs.  $21 \pm 13$  %), REM sleep ( $17 \pm 9$  vs.  $18 \pm 9$  %), wake after sleep ( $106 \pm 68$  vs.  $93 \pm 58$  min).

**Conclusion :** One session of patient education by PSG technician can improve objective sleep quality and nasal mask tolerance during the night of PAP titration. It could be an efficient intervention to improve PAP compliance.

**Support (optional):** AFIP and FAPESP/CEPID

### 0538

#### CHARACTERIZATION OF GENIOGLOSSUS AND DIAPHRAGM RESPONSES TO TRANSCRANIAL MAGNETIC STIMULATION IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA AND IN NORMAL INDIVIDUALS

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**Introduction :** Upper airway patency is modulated by tonic and phasic activities of dilator muscles. During wakefulness, these activities are higher in obstructive sleep apnea (OSA) patients than in normal individuals. This study aims at comparing genioglossus (GG) and diaphragm (Dia) responses to transcranial magnetic stimulation (TMS) during wakefulness between OSA and normal subjects.

**Methods :** Motor evoked potential (MEP) of GG and Dia were recorded with TMS applied at vertex (Cz) and dominant-sided antero-lateral (AL) area in 7 OSA and 7 age and body mass index-matched normals. Stimuli

were applied 1 s after inspiratory onset of with and without resistance (Insp+R, Insp) and 0.5 s after expiratory onset with and without maximal tongue protrusion (Exp+P, Exp). Motor threshold (MT) (lowest stimulation intensity associated with a MEP response) was measured in each condition.

**Results :** Dia and GG responses to nonfocal TMS were indissociable in 84% and 52% of twitches in OSA and in normals respectively ( $P<0.0001$ ). In OSA, GG MEP latency was shorter in Exp+P than in other conditions in Cz. Such a difference was not observed in normals. GG MEP amplitude was higher in OSA than in normals in all conditions but Insp (Exp:  $86.4 \pm 44.9\%$  and  $41.1 \pm 28.8\%$  of abductor pollicis-brevis amplitude respectively,  $P<0.01$ ). In OSA GG MT was always lower than that of Dia (Exp values:  $72.1 \pm 12.8\%$  and  $82.0 \pm 9.6\%$  respectively,  $P<0.01$ ). In normals this difference was only found during Exp+P. A significant negative relationship was found between the apnea-hypopnea index and the latency of GG MEP responses in OSA patients.

**Conclusion :** 1) GG and Dia responses to TMS are differently influenced by respiratory conditions in OSAS patients and normals, 2) in OSA patients, GG cortico-motor responses to TMS is higher than that of Dia and 3) this response varies with the frequency of nocturnal breathing disorders.

**Support (optional):** Supported by CIHR grant MT 13 768

### 0539

#### HEALTH CARE UTILIZATION AMONG SNORERS IN A LARGE REPRESENTATIVE POPULATION SAMPLE

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**Introduction :** Snoring is extremely common and might cause significant psychological and physical distress in the general population. Snoring is a hallmark symptom of obstructive sleep apnea syndrome. There is a considerable interest in the association of snoring and health consequences.

**Methods :** We investigated the prevalence of self-reported snoring in the Hungarian population. The "Hungarostudy" is a cross sectional survey enrolling 12668 individuals, as a nationally representative sample of the Hungarian population. As a door-to-door survey, interviews were carried out in 2002. A battery of questionnaires was administered during a home-interview. The battery included questions regarding snoring and health-care use. Utilization of health services was assessed by emergency home visits, number and days of hospitalization, and days on sick leave. Psychosocial and demographic characteristics were also tabulated.

**Results :** 5459 (45%) men and 6753 (55%) women were eligible for the study. The mean age was  $47.6 \pm 17.88$  (sd) years. 37% of the males and 21% of the females reported "loud snoring with breathing pauses". 11% of study participants had requested emergency home visit. 19% had been on sick leave and 19% had been to hospital during the previous year. Hospitalization and emergency home visits were more prevalent in loud snorers compared to non-snorers (23% vs. 17%,  $p<0.001$  and 13% vs. 9%,  $p<0.001$  respectively), and there appears to be a trend between non-snorers, quiet snorers and loud snorers ( $p$  for trend is 0.0001 for both). Negative binomial regression analysis was used to analyze the number of hospitalizations, emergency home visits and the number of days spent in hospital. The odds ratio for loud snoring were 1.36 (95% CI 1.18-1.56,  $p<0.001$ ); 1.38 (95% CI 1.12-1.72) ( $p<0.005$ ); and 1.11 (95% CI 0.88-1.4) (ns), respectively.

**Conclusion :** Several aspects of health care utilization were significantly

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higher among snorers compared to non-snorers in a large representative population sample.

**Support (optional):** Supported by grants from the National Scientific Research Funds (OTKA TS 040889, OTKA T038409, ETT 218/2003).

### 0540

#### CORRELATES OF 12-MONTH ADHERENCE WITH FLEXIBLE CONTINUOUS POSITIVE AIRWAY PRESSURE THERAPY

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**Introduction :** Continuous positive airway pressure (CPAP) is the mainstay therapy for obstructive sleep apnea (OSA), but long-term adherence is often suboptimal despite attempts at patient education and followup. We attempted to establish correlates of 12-month adherence to flexible CPAP therapy in OSA patients.

**Methods :** Patients who were diagnosed with OSA and started on CPAP therapy (REMstar Pro with C-FLEX™, Respironics, Murrysville, PA) in 2004 responded by survey regarding use, perceived benefits, and problems related to their CPAP. Responses to the survey were correlated with usage, as measured after download of data from their CPAP memory cards, and with body mass index, apnea-hypopnea index, and CPAP pressure setting. CPAP adherence was defined for this study as use of CPAP for more than 4 hours per night and more than 4 nights per week.

**Results :** Of 400 patients contacted, 261 (65%) returned surveys and CPAP memory cards. Self-reported CPAP adherence was 77.8%. Download data confirmed that patients reporting adherence, compared with non-adherence, used CPAP for a significantly greater proportion of days (85% vs 40%), and for significantly greater minutes per day (356 vs 182). Adherent patients, compared with non-adherent, had significantly higher apnea-hypopnea index (33.3 vs 24.7) and greater CPAP pressure (11.2 vs 10.1), but no difference in BMI. Adherence was associated with reports of significantly less sleepiness, more energy, less snoring, and less difficulty falling asleep. There was no significant association between adherence and reports of ability to concentrate, depression, irritability, memory loss, or morning headaches. Lack of adherence was not associated with any CPAP-associated problems, including dry mouth, nasal congestion, runny nose, nosebleeds, sores on nose or forehead, eye complaints, or sore throat.

**Conclusion :** Adherence with C-FLEX™ CPAP at 12 months in this patient population was high relative to historical reports, and appeared to correlate significantly with higher apnea-hypopnea index and with perceived improvements in sleepiness, snoring, and energy. CPAP-related problems did not appear to decrease adherence.

**Support (optional):** Unrestricted grant from Respironics.

### 0541

#### INFLUENCE OF TREATING ALZHEIMER'S PATIENTS' SLEEP DISORDERED BREATHING ON THE QUALITY OF CAREGIVERS' SLEEP

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**Introduction :** Sleep disorder breathing (SDB) is common among patients with Alzheimer disease (AD), and may not only effect patients'

functioning, but may also influence quality of life (including sleep) for the patients' caregivers. The present study evaluated whether treating AD patients' SDB would have beneficial effects on the caregivers' sleep quality.

**Methods :** Participants were 27 AD caregivers of patients who had been randomly assigned to receive six weeks of therapeutic Continuous Positive Airway Pressure (CPAP) (n=16) or three weeks of sham CPAP followed by three weeks of therapeutic CPAP (n=11). All caregivers were evaluated with the Pittsburgh Sleep Quality Index (PSQI) at baseline, 3 weeks and 6 weeks. Change scores for PSQI total and sub-scales (all coded such that lower change scores indicated improved sleep quality) among the two groups were compared via t-tests.

**Results :** There were no significant differences in PSQI change scores baseline to 3-weeks, nor were there any significant group differences in total PSQI. However, within the caregivers of the therapeutic CPAP group, after 6-weeks of treatment for the patients, the sleep duration sub-scale at 6-weeks (mean 0.93 vs. 1.25; p=0.019) and the sleep disturbance sub-scale at 6-weeks (mean 1.56 vs. 1.31; p=0.041) significantly improved compared to baseline. There were no significant changes in any PSQI sub-scale scores in the sham CPAP group.

**Conclusion :** These data provide preliminary evidence that treating SDB with CPAP in patients with AD may result in reports of improved sleep in caregivers. Prior research has shown patients' improvements after 3-weeks of CPAP treatment. But as all significant changes in caregivers' sleep quality were evidenced only among those whose patients had received 6-full weeks of therapeutic CPAP, changes in caregivers' sleep may lag behind the beneficial effects seen more immediately among the patients themselves.

**Support (optional):** NIA AG08415, P50 AG05131, M01 RR00827 and the research service of the VASDHS.

### 0542

#### CORRELATIONS BETWEEN BEHAVIOR AND SLEEP BEFORE AND AFTER ADENOTONSILLECTOMY IN CHILDREN WITH SLEEP DISORDERED BREATHING

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**Introduction :** Recent surveys demonstrated that most otolaryngologists do not order objective testing such as polysomnography or neuropsychiatric testing prior to pediatric adenotonsillectomy for sleep disordered breathing (SDB), but instead rely on clinical evaluation skills. Until clinical practice guidelines are established for selecting candidacy for adenotonsillectomy for patients at different points along the spectrum of SDB, alternative methods for identifying at-risk children and evaluating post-operative improvements in sleep and behavior may be useful.

**Methods :** One hundred and seventeen consecutive children (mean[SD] age 6.5[3.1] years, 61 boys, 56 girls) clinically diagnosed with SDB and adenotonsillar hypertrophy who then underwent adenotonsillectomy were enrolled. Parents completed the Pediatric Sleep Questionnaire (PSQ) and Connor's Parent Rating Scale-Revised-S (CPRS-RS) before surgery and again at 6 months post-operatively. Complete follow-up was available in 71/117 (60.6%) patients. Changes in age appropriate T-scores for all four CPRS-RS behavior categories and changes in PSQ scores from a select 22-item sleep-related breathing disorder subscale of the PSQ were determined.

**Results :** Preoperatively, mean [SD] T-scores on CPRS-RS for oppositional, cognitive/inattention, hyperactivity, and ADHD indices were 59.4[13.7], 59.5[13.6], 62[14.4], and 59.9[13.4], respectively. A T-score of 60 in any category places a child in an at-risk group. Postoperatively, T-scores for each category were 51[9.6], 51.2[8.8], 52.4[10.5], and 50.6[7.7]. All changes were found to be statistically significant ( $P < 0.001$ ) and felt to be clinically significant by being reduced approximately one standard deviation from the baseline score on average. For the PSQ, preoperative mean[SD] score was 0.56[0.14] and postoperative mean [SD] score was 0.12[0.14], the scale being between 0 and 1, with scores approaching 1 being most severe in sleep disturbance. Correlations between sleep and behavior scores were found to be statistically significant before and after surgery. Higher baseline T-scores of the CPRS-RS were associated with larger changes in T-scores of the CPRS-RS for all four domains.

**Conclusion :** Children clinically diagnosed with SDB experience significant improvement in both sleep and behavior after adenotonsillectomy. The PSQ and CPRS-RS may be useful adjuncts for screening and following children who undergo adenotonsillectomy for SDB.

**Support (optional):**

### 0543

#### ASSESSING NEUROCOGNITIVE FUNCTION IN MODERATE TO SEVERE OBSTRUCTIVE SLEEP APNEA BEFORE AND AFTER CPAP THERAPY

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**Introduction :** Obstructive Sleep Apnea (OSA) is often accompanied by significant cognitive deficits that extend beyond the effects of sleepiness. In multicentre research studies an additional challenge is to ensure uniformity of procedures and scoring between sites. We are conducting a multicentre randomised controlled trial of a new management paradigm for moderate-severe obstructive sleep apnea during which cognitive function of patients is assessed before and after treatment. We report on our use of the Integneuro testing process, which promises to overcome many of these limitations. In addition we will be comparing the improvement in neurocognitive function after 3 months of CPAP therapy. The large normative database of neurocognitive function available enables comparison between OSA patients both before and after CPAP to normal controls across a wide range of ages and education backgrounds.

**Methods :** The IntegNeuro cognitive battery provides a profile of sensory, motor, language, attention, memory and executive functioning. Testing is completed in 50 minutes using a touch screen computer and linked headphone and microphone set at each investigating site. Data is downloaded and automated scoring available within 1 hour. We report on the results of the baseline tests of 100 patients with moderate-severe OSA. The group had (all results means and SD) a Dip-Rate 52.8 +/- 27.01. Age 50.3 +/- 11.2, BMI 34.3 +/- 7.0 and ESS 13.4 +/- 3.8. Their neurocognitive function was assessed again after 3 months of CPAP therapy

**Results :** OSA patients had significant abnormalities in Psychomotor Speed, Executive function, Sustained attention/vigilance and Memory Recall when compared to a control group matched for age, sex and years of education ( $p < 0.05$  in all cases). 3 months of CPAP therapy led to significant improvements in some aspects of Sustained Attention/Vigilance, short-term memory and psychomotor speed when compared to their pre

treatment results. Those who complied with CPAP therapy improved more than those who did not. Tests were well performed with 92% of patients completing all tests without omission

**Conclusion :** Integneuro test battery is easy to administer, and was well performed by patients with moderate-severe OSA with few omissions. Significant neurocognitive deficits were present, particularly in memory recall, executive functioning and vigilance. CPAP leads to improvements in some of these neurocognitive parameters

**Support (optional):** Brain Resource Company (BRC) supplied tests at discounted rate RESMED supplied CPAP machines and funded BRC test costs Masimo supplied oximeters for measuring OSA

### 0544

#### HIGH FAT/REFINED CARBOHYDRATE DIET DOWN REGULATES INSULIN RECEPTOR MRNA IN RATS EXPOSED TO INTERMITTENT HYPOXIA

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**Introduction :** Exposure to Intermittent hypoxia (IH), such as occurs in sleep-disordered breathing (SDB), is associated with learning deficits, oxidant stress, and increased neuronal cell loss in brain regions underlying learning and memory in rats. High fat/refined carbohydrate (HF/RC) diets enhance the behavioral susceptibility to IH-induced spatial learning deficits and promote lipid peroxidation. Additionally, HF/RC diets are typically associated with insulin resistance. Given that insulin-related growth factors act as an important brake on apoptotic mechanisms, and that neuronal insulin resistance has been proposed as a risk factor for oxidative stress related neurodegenerative disorders, the present study was designed to assess the effects of IH and HF/RC diets on insulin receptor mRNA expression in brain.

**Methods :** Male Sprague-Dawley rats were fed either a HF/RC (40% kcal from fat, 40% kcal from refined carbohydrates) or a low fat/complex carbohydrate diet (13% kcal from fat, 59% kcal from complex carbohydrates) starting on post-natal day (PN) 30 and continuing throughout the duration of the experiment. Starting at PN 120, animals were then exposed to intermittent hypoxia (IH; alternations of 10% O<sub>2</sub> and 21% O<sub>2</sub>), or room air (RA) for 7 days (12 hours/day during light phase). All rats underwent cognitive assessments in the spatial, reference version of the Morris water maze, after which brain tissues were removed for real-time PCR.

**Results :** HF/RC significantly down-regulated insulin receptor in the cortex and hippocampus of both IH and RA rats. In contrast, IH alone had no effect of IR mRNA.

**Conclusion :** HFRC diets are associated with decreased expression of insulin receptor mRNA in the brain, suggesting that anti-apoptotic mechanisms may be down-regulated in response to a HFRC diet. These findings indicate that multiple mechanisms are likely involved in the enhanced susceptibility of HFRC animals to IH, and these may include both increased oxidative stress and decreased cell survival pathways.

**Support (optional):** NIH HL69932

### 0545

#### EXPOSURE TO INTERMITTENT HYPOXIA (IH) AFFECTS STRATEGY SELECTION IN THE MORRIS WATER MAZE

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**Introduction :** Exposure to IH, such as occurs in sleep disordered breathing (SDB), is associated with learning impairments in the rodent that are preceded by neurodegenerative changes in the hippocampus. In rodents, hippocampal damage is often associated with alterations in the cognitive

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strategies used to solve the water maze. The present study was therefore designed to assess the effects of exposure to IH on strategy selection in the water maze.

**Methods :** Male Sprague-Dawley rats were exposed to either Room Air (RA) or to 14 days of IH (i.e., oscillating between 21% and 10% O<sub>2</sub> every 90 seconds during the light phase). Rats were trained in a water maze in which multiple strategies were available to locate a hidden escape platform that was moved to a new location for each set of four learning trials. During acquisition training, a visible floating landmark was always located in a fixed position relative to the platform position. Additionally, fixed extra-maze cues were visible to the animals and surrounded the maze.

**Results :** IH exposures enhanced performance on the initial training trials of the acquisition sessions. However, while removal of the visible landmark during subsequent probe trials had no effect on the performance of RA animals, it significantly disrupted performance in animals exposed to IH. No significant differences were found between groups in regards to swim speeds, indicating that group differences were not due to sensorimotor impairments.

**Conclusion :** These findings indicate that exposure to IH adversely impacts on cognitive learning strategies and may bias against the use of spatial, hippocampal-dependent cognitive strategies in the water maze.

**Support (optional):** NIH HL69932 and Swiss National Foundation.

### 0546

#### CPAP ACCLIMATION: DOES IT MAKE A DIFFERENCE?

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**Introduction :** There are no universally accepted guidelines regarding the use of continuous positive airway pressure (CPAP) before a CPAP titration study. The first exposure to CPAP for many patients occurs during the titration study. Our hypothesis is that patients who used CPAP before the titration study will have a better quality titration study compared to CPAP naive patients.

**Methods :** This was a retrospective chart review. Patients who had a full night CPAP titration study with or without prior CPAP exposure between March and October 2005 were included. The group was stratified by AHI <15 and ≥15. The following parameters were compared between groups: sleep efficiency (SE), sleep latency (SL), wake time after sleep onset (WASO), arousal index (AI), total sleep time (TST), sleep stage percentages and whether an optimal CPAP setting was identified. Statistical analysis was performed using the unpaired t-test and the Mann-Whitney test.

**Results :** There were 202 patients (59% male) who used CPAP prior to their titration study (CPAP+) and 133 patients (51% male) that were CPAP naive (CPAP-). TST was 337.4±70.8 minutes (CPAP+) vs. 316.8±83.6 minutes (CPAP-); p=0.003. SL was 19.6±21.5 minutes (CPAP+) vs. 28.3±38.1 minutes (CPAP-); p=0.01. When comparing the groups by AHI, the TST in the moderate-severe OSA group was 336.4±64.9 minutes (CPAP+) vs. 310.0±85.2 minutes (CPAP-); p=0.003. SL was 18.9±20.1 minutes (CPAP+) vs. 29.7±42.1 minutes (CPAP-); p=0.04. In the mild OSA group, TST and SL were not different based on CPAP use before the titration study. The frequencies of optimal CPAP setting identification in (CPAP+) and (CPAP-) groups were not significantly different.

**Conclusion :** CPAP acclimation before a titration study can increase the TST and SL during CPAP titration studies. This can provide a greater opportunity to identify an optimal pressure.

**Support (optional):**

### 0547

#### EFFECT OF SLEEP DISORDERED BREATHING ON THE SLEEP OF BED PARTNERS IN THE SLEEP HEART HEALTH STUDY

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**Introduction :** Bedpartners of sleep disordered breathing (SDB) patients frequently complain that snoring, breathing pauses, gasping for air and excessive movement disrupt their own sleep. Recently, it has been observed that bedpartners of SDB patients report daytime fatigue and have disturbed sleep on polysomnography. However, there have been no studies where sleep of bedpartners of SDB patients has been recorded in their home sleeping environment.

**Methods :** We compared bedpartners' demographic, polysomnographic (PSG) and questionnaire data from Tucson site of the Sleep Heart Health Study (SHHS). Bedpartners were divided into three different groups, SDB-NoSDB (34 couples), NoSDB-NoSDB (24 couples), and SDB-SDB (26 couples). SDB was defined as a respiratory disturbance index (RDI) > 5.

**Results :** In the NoSDB-NoSDB and SDB-SDB groups there were no significant differences found between bedpartners in any of the variables analyzed. In the SDB-NoSDB group, SDB patients by definition had a higher RDI (17.6 + 2.5 vs. 2 + .23 P = .00001) and snored more loudly (P=.032). However, there were no differences found between bedpartners in the Epworth sleepiness scale, SF-36, insomnia symptoms, sleep latency, sleep efficiency and total sleep time. In comparison to the bedpartner with SDB, NoSDB bedpartners spent less % time in stage 1 (4.4 % + .4 vs. 6.22 + .5 p = .019) and stage 2 sleep (52% + 1.5 vs. 60.6% + P = .0022) and had fewer arousals (13.9 + 1.4 vs. 20.2 + 1.5, P=.0047), but had more % time in delta sleep (21.2% + 1.6 vs. 12.1 + 1.5 P = .0002).

**Conclusion :** NoSDB bedpartners of those with SDB spend less time in lighter stages of sleep, more time in deeper sleep and have less frequent arousals at night than their partners with SDB. However, in this population-based sample, bedpartners of those with SDB did not have an increase in daytime symptoms, lower quality of life or decrease in the quantity of sleep.

**Support (optional):** Supported by HL53938

### 0548

#### ASSOCIATION OF BARRETT'S ESOPHAGITIS WITH HIGH (> 10) EPWORTH SLEEPINESS SCALE

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**Introduction :** A high Epworth Sleepiness Scale (EES) has been associated with Obstructive Sleep Apnea (OSA), and Gastro Esophageal Reflux Disease (GERD) is more common in patients with OSA than in the general population. An ESS score of 6 or less is considered normal, however, a score of 10 or more is considered abnormal and highly suggestive of OSA. GERD has been linked as a risk factor for development of Barrett's Esophagus (BE). Using a high ESS as a surrogate for OSA, we investigated the association between BE and OSA.

**Methods :** A questionnaire was sent to 180 patients diagnosed with Barrett's Esophagus by surgical biopsy at West Virginia University Hospital between March 2001 and May 2004. Fifty-seven (31%) patients responded.

**Results :** Out of 57 patients who responded, 18 (31 %) had ESS of 6 or less (normal), 11 (19%) had score of 7-10 (borderline), and 28 (49%) had a score of more than 10 (abnormal). Forty-one (72%) patients reported



symptoms of GERD and only 11 (19%) patients had been diagnosed with OSA.

**Conclusion :** We conclude that patients diagnosed with BE are more likely to have a higher ESS (> 10) and GERD than the general population. Our study suggests that patients with BE may have OSA, and BE may result from GERD induced by OSA. We also found that despite a high ESS, the majority of patients with BE have not undergone OSA work up.

**Support (optional):** Johns MW et al. Daytime sleepiness, snoring, and obstructive sleep apnea. The Epworth Sleepiness Scale Chest, Jan 1993; 103: 30 - 36 Ing AJ et al. Obstructive sleep apnea and gastroesophageal reflux. Am J Med 2000 Mar 6;108 Suppl 4a:120S-125S Oberg S, Barrett Esophagus; Risk Factors for Progression to Dysplasia. Annals of Surgery. 2005 July Vol 242, No. 1

## 0549

### VENTILATORY RESPONSE TO BRIEF AROUSAL IN MEN WITH AND WITHOUT OBSTRUCTIVE SLEEP APNEA

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**Introduction :** Arousal from sleep frequently accompanies the termination of obstructive respiratory events. The ventilatory response to arousal is greater in men than in women in young healthy adults as well as patients with obstructive sleep apnea (OSA), and in patients where upper airway resistance is increased with suboptimal continuous positive airway pressure (CPAP). We hypothesise that the inherent ventilatory response to arousal is greater in men with OSA compared to gender, age and weight matched control subjects even when upper airway resistance in both groups is controlled using CPAP. Exaggerated brief hyperventilation followed by prolonged hypoventilation following arousal from sleep may play an important role in initiating and perpetuating obstructive respiratory events.

**Methods :** Changes in minute ventilation, end-tidal carbon dioxide, upper airway resistance, upper airway dilator muscle electromyogram, finger photoplethysmography pulse wave amplitude, beat-to-beat heart rate and blood pressure in response to both tone-induced and spontaneous arousal from sleep are being compared between male patients with OSA and control subjects. CPAP has been applied in all subjects to normalize upper airway resistance.

**Results :** The study is in progress but a preliminary analysis of 5 patients with OSA (mean  $\pm$  S.E.M., respiratory disturbance index (RDI)  $43.8 \pm 4.9$  events/h) and 2 control subjects (RDI  $10.6 \pm 4.3$  events/h) showed similar peak inspiratory minute ventilation responses following tone induced arousals between the two groups ( $133.4 \pm 11.4$  and  $135.7 \pm 13.3$  % baseline).

**Conclusion :** While these early data do not support our hypothesis, further data are required to establish if OSA patients have an inherent exaggerated ventilatory response to arousal compared to control subjects.

**Support (optional):** This research is supported by the National Health and Medical Research Council (Australia) grant 324732.

## 0550

### FLOPPY EYELID SYNDROME POSSIBLY ASSOCIATED WITH OBSTRUCTIVE SLEEP APNEA IN CAUCASIANS AND AFRICAN AMERICANS

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**Introduction :** Floppy eyelid syndrome is an uncommon condition characterized by easily everted and flaccid upper lids related to reduced elastin. Literature indicates the possibility of association of Floppy eyelid syndrome and OSA. This study investigates the prevalence of floppy eyelid syndrome in patients referred for an evaluation to a sleep center as possibly an additional factor for the prediction of OSA.

**Methods :** 326 consecutive patients referred to a sleep center for a consultation have been examined and interviewed for a history of floppy eyelid syndrome. Results of clinical evaluation and overnight polysomnograms have been analyzed.

**Results :** The history of floppy eyelid syndrome was found in three patients. One patient was African-American and two were Caucasians. They were 49, 52, and 55 year old males with a body mass index of 46.6, 47, and 30 respectively. All of them snore. They tested 6, 14, and 9 on the Epworth sleepiness scale, and subsequent apnea-hypopnea index was 75.4, 95.2, and 20.1.

**Conclusion :** 1) All three of our patients, with a history of floppy eyelid syndrome, have moderate to extremely severe obstructive sleep apnea syndrome. 2) Possible association present not only in Caucasians, as was described by literature, but also in African-Americans, although prevalence of floppy eyelid syndrome in a group of patients referred to a sleep center for evaluation is rare and larger group is necessary for more reliable conclusion. 3) For two out of three patients, the results of the Epworth sleepiness scale were below 10. Subsequently, the possibility of obstructive sleep apnea syndrome in patients with floppy eyelid syndrome should be evaluated even in the category of patients without significant sleepiness. 4) Primary care physicians and ophthalmologists should be aware about possible association and should refer patients with a history of floppy eyelid syndrome and snoring to a sleep center.

**Support (optional):** McNab AA, Floppy eyelid syndrome and obstructive sleep apnea. Ophthalm Plast Reconstr Surg 1997;13(2):98-114

## 0551

### THE ESTIMATED PREVALENCE OF SDB IN HIGH-RISK POPULATION AS SCREENED BY SLEEP-SPECIFIC QUESTIONNAIRES

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**Introduction :** Using sleep-specific survey, we applied an established screening model to identify possible SDB employees from a petrochemical company in Taiwan.

**Methods :** 1057 employees (1005 males and 52 females, age= $44.50 \pm 7.70$ , BMI= $23.79 \pm 4.64$ ) were administered a snore-specific (Snore Outcomes Survey, SOS) and a sleepiness-specific (Epworth Sleepiness Scale, ESS) outcomes surveys. We used the previously developed multiple regression model to estimate RDI. The equation  $-13.914 + 8.179X_{sex} + 0.269 X_{age} + 2.228XBMI + 0.538XE_{SS} - 0.573 XSOS$  was used to predict RDI. Responders of SOS less than 55 was considered of having sleep respiratory problems; and ESS of 9 was used as a threshold to pin-point responders with day-time sleepiness. RDI of 5 episodes/hr or over was considered of having OSA. RDI of 30 episodes/hr or over was considered of having severe OSA.

**Results :** Of all the employees screened, 79 (7.5%) have SOS<55, indicating the presence of sleep respiratory problems. A total of 257 (24.3%) have ESS>9, indicating the presence of day-time sleepiness problems, with or without sleep respiratory problems. When introducing the patients' characteristics and survey information into the prediction model,

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1007 (95.3%) would have  $RDI \geq 5$ , 531 (50.2%) would have  $RDI \geq 30$ . In this middle-aged, male-dominant, and relatively obese population, we estimated there would be 95.3% to have SDB, 7.5% would be snorers, 45.0% would have mild to moderate apnea, and 50.2% would have severe apnea. 24.3% of the day-time sleepiness may not be attributable to SDB.

**Conclusion :** The estimated prevalence of SDB in the high-risk population appears to be high. Employer should be aware of the potential threat to health that may incur from somnolent employees. Effective measures should be taken to reduce the risks of occupational safety.

**Support (optional):**

### 0552

#### CENTRAL SLEEP APNEA AND CENTRAL PERIODIC BREATHING DURING SLEEP IN ACUTE ISCHEMIC STROKE

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**Introduction :** Central sleep apnea and central periodic breathing (CPB) in sleep are present in 20-40% of patients with acute ischemic stroke and often spontaneously recover during the following weeks. The underlying pathophysiological mechanisms, clinical, and prognostic implications of CPB in sleep remain still poorly known. The aim of our study is to better characterize CPB in sleep and its relevance in acute ischemic stroke.

**Methods :** We included patients admitted within 96 hours after stroke onset. Stroke severity on admission (NIH Stroke Scale, Scandinavian Stroke Scale) and stroke outcome at discharge (modified Rankin Disability Scale) were assessed. Nocturnal breathing was assessed with an ambulatory device the first night after admission. Sleep apnea was defined by an apnea-hypopnea-index  $\geq 10/h$ , a differentiation between obstructive and central apneas was undertaken according to standard criteria. CPB was defined as  $\geq 3$  cycles of regular crescendo-decrescendo breathing associated with reduction of  $>50\%$  in nasal airflow and respiratory effort lasting  $>10$  seconds. CPB severity was represented as percentage of recording time.

**Results :** 55 patients were included. 23 (48%) patients showed CPB during  $\geq 10\%$  of recording time. The mean CPB duration in all patients was  $18 \pm 22\%$  [0-74%]. CPB severity was associated with age ( $p=0.016$ ), stroke severity at day1 ( $p=0.034$ ) and day3 ( $p=0.006$ ) and duration of hospitalisation ( $p=0.034$ ). CPB was also associated with ECG abnormalities ( $p=0.011$ ) and with a lower left ventricular ejection fraction ( $p=0.001$ ). CPB severity was significantly lower in patients with stroke in the insular region ( $n=8$ ,  $p=0.001$ ).

**Conclusion :** CPB in sleep is a frequent phenomenon in acute ischemic stroke, occurs much frequently in older patients, and is associated with more severe stroke on admission, longer duration of hospitalisation and cardiac abnormalities. The lower occurrence of CPB in sleep in insular strokes suggests an implication of this region in the modulation of respiratory response to acute ischemic brain damage.

**Support (optional):**

### 0553

#### ACUTE ISCHEMIC STROKE AND SLEEP APNEA: EVOLUTION OF RADIOLOGICAL PARAMETERS WITHIN 3 DAYS AFTER STROKE ONSET

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**Introduction :** Sleep apnea (SA) is present in about 50-70% of patients

with acute ischemic stroke. Hypoxia and hemodynamic changes accompany SA and may have a detrimental effect on not yet irreversibly damaged ischemic brain areas (penumbra). The aim of the study is to test the hypothesis that in the acute phase of stroke SA leads (especially if moderate-severe) to an enlargement of the ischemic lesion that is more pronounced than in patients without SA.

**Methods :** We studied patients admitted within 24 hours after stroke onset. Stroke severity on admission (NIH Stroke Scale, Scandinavian Stroke Scale) and stroke outcome at discharge (modified Rankin Disability Scale) were assessed. Nocturnal breathing was assessed by an ambulatory device the first night after admission. SA was defined by an apnea-hypopnea-index (AHI)  $\geq 10/h$ , moderate-severe SA (MSSA) by an AHI  $>30/h$ . A differentiation between obstructive and central apneas was undertaken according to standard criteria. MR imaging (T2-weighted, MR-angiography, DWI, PWI) was performed on admission (day 1) and at day 3. Stroke volumes were measured on DWI.

**Results :** 27 patients were included. SA was found in 17 (63%, AHI  $34 \pm 16$  [14-77]), MSSA in 9 patients (30%, AHI  $46 \pm 15$  [32-77]). Patients with higher degree of obstructive apneas (obstructive apnea index [OAI]  $\geq 5$ ) showed a smaller regression of perfusion deficit (PWI) within the first 3 days after stroke ( $p=0.028$ ), and OAI was significantly higher in patients showing a regression of perfusion deficit  $<20\%$  ( $11 \pm 9$  versus  $3 \pm 5$ ,  $p=0.032$ ), respectively. In contrast, no relationship between sleep apnea severity (estimated by AHI) or type and enlargement of the ischemic lesion (DWI) was found.

**Conclusion :** Severity of obstructive sleep apnea was associated in the acute stroke phase with a smaller regression of the perfusion deficit in the ischemic penumbra, but not with an enlargement of the ischemic lesion as estimated by DWI.

**Support (optional):**

### 0554

#### SLEEP APNEA AND BLOOD PRESSURE LEVELS IN ACUTE ISCHEMIC STROKE AS PREDICTORS OF CLINICAL OUTCOME AFTER 3 MONTHS

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**Introduction :** Sleep apnea (SA) is frequent in acute ischemic stroke and is associated with increased blood pressure (BP) levels. The aims of our study are to determine 1) the evolution of SA severity and type (obstructive vs. central) and 2) the evolution of BP after acute ischemic stroke, 3) whether severity and type of SA in the acute stroke phase may affect BP evolution and clinical outcome.

**Methods :** We studied 20 consecutive patients admitted within 96 hours after stroke onset. Stroke severity on admission (NIH Stroke Scale, Scandinavian Stroke Scale) and stroke outcome at discharge (modified Rankin Disability Scale) were assessed. Nocturnal breathing was assessed by an ambulatory device the first night after admission. SA was defined by an apnea-hypopnea-index (AHI)  $\geq 10/h$ . A differentiation between obstructive (OAI) and central (CAI) apnea index was undertaken according to standard criteria. BP was registered using an ambulatory device during 36 hours starting the first night. The above investigations were again performed 3 months after discharge.

**Results :** 1) AHI ( $p=0.041$ ) and CAI ( $p=0.016$ ) were higher during the acute stroke phase compared to 3 months thereafter. 2) Systolic and diastolic BP values during night and day were higher ( $p \leq 0.001$ ) in the acute phase compared to 3 months later. 3) Higher BP values in the acute phase were associated with a) severity of obstructive apneas ( $r=0.715$ ,  $p=0.001$ ) and b) worse functional outcome at 3 months ( $r=0.667$ ,  $p=0.003$ ). The severity of obstructive apneas (OAI) in the acute phase was associated

with worse functional outcome at 3 months ( $r=0.477$ ,  $p=0.045$ ).

**Conclusion :** SA severity (AHI), degree of central apneic events (CAI), and BP values improve after the acute stroke phase. Increased BP values and severity of obstructive apneas in the first 3 days after stroke predict a worse clinical outcome.

**Support (optional):**

## 0555

### OBSTRUCTIVE SLEEP APNEA AND QUALITY OF LIFE

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**Introduction :** While obstructive sleep apnea (OSA) is defined by both polysomnographic abnormalities and clinical symptoms, severity is quantified primarily by the apnea-hypopnea index (AHI) alone. Clinically, we have noted discordance between the severity indicated by polysomnography results and the degree of symptoms reported by some patients with OSA. The aim of this study was to assess the quality of life (QOL) in patients with OSA, and the relationship between the QOL, and self-reported measures and polysomnographic measures.

**Methods :** We reviewed the clinical data and night polysomnography results in 117 patients with OSA at our sleep disorder clinic. QOL was assessed with the Medical Outcome Study 36-Item Short-Form Health Survey (SF-36). Demographic data were obtained via structured interview and medical record review. Self-reported measures included Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality index (PSQI), Insomnia Severity Index (ISI), Berlin Questionnaire (BQ), and Beck Depression Inventory (BDI). All subjects underwent full overnight in laboratory polysomnography for the diagnosis of OSA. OSA was defined by an apnea-hypopnea index scoring more than five. Patient's data were compared to normative data of general population. The associations between each domain on the SF-36, and self-reported measures or polysomnographic measures were examined by Spearman correlation coefficients, and regression analysis.

**Results :** In comparison with general population, scores for QOL were decreased in OSA patients. The parameters of SF-36 of the patients with OSAS correlated well with self-reported measures. The parameters of polysomnographic measures of patients with OSA did not show correlation with that of SF-36.

**Conclusion :** Although OSA is independently related to lower general health status, the parameters measured by polysomnography may do not reflect the severity of patients with OSA and sleep apnea disease burden should be quantified with both physiologic and subjective measures.

**Support (optional):**

## 0556

### SLEEP APNEA SCREENING FOR DENTISTS - POLITICAL MEANS AND PRACTICAL PERFORMANCE

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**Introduction :** 95 % of patients with sleep apnea go undiagnosed. There is a need to involve additional specialties into the diagnostic process. Here we see a new role of dentists. Trained sleep disorders dentists, e.g. members of the national Dental Sleep Medicine Academies (American, European, German, Japanese, British associations are existing) , can use innovative easy screening monitors to screen their normal dental patients and identify those suffering from sleep-related breathing disorders.

**Methods :** Based on a patient history with snoring and excessive daytime sleepiness in the dental examination we used the screening device Apnea Link in a dental office in 35 patients (28 m, 7 f, mean age 42.7 yrs) to receive a pretest probability for the risk of OSA. This minimal one channel screening device collects the respiratory information by means of nasal cannula with a highly sensitive pressure sensor. Automatic analysis of apneas, hypopneas, flow limitations and snoring present a pretest probability for the risk of OSA based on an RDI > 5.

**Results :** 33 out of 35 screened patients had a risk for OSA (RDI > 5). They were referred to sleep specialists and underwent portable home monitoring and/or PSG for further diagnostic procedure. In all patients mild to severe sleep disordered breathing could be confirmed. Treatment was initiated either with mandibular advancement device or with CPAP.

**Conclusion :** Sleep disorders dentists see as many patients as general practitioners. Additionally they see young adults on a regular base who do not often see their GP. These dentists have the unique chance to diagnose patients with SDB and refer them for polysomnography. Dentists trained in sleep medicine play an increasing role in the diagnosis of sleep-related breathing disorders.

**Support (optional):**

## 0557

### QUANTITATIVE MORPHOMETRIC ANALYSIS OF THE EFFECTS OF CHRONIC INTERMITTENT HYPOXIA ON THREE BRAINSTEM NUCLEI IN A DEVELOPMENTAL RODENT MODEL

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**Introduction :** Chronic intermittent hypoxia (CIH), one of the prominent manifestations of sleep-disordered breathing (SDB), is common during childhood and plays a pathophysiological role in cognitive morbidity of SDB. While cognitive sequelae of SDB have recently received considerable attention, little is known about the effects of CIH on cardio-respiratory regulation. We have previously shown that CIH during early development promotes long-lasting respiratory plasticity in an age-dependent manner. The aim of this study was to use unbiased stereological tools to assess for the presence of morphologic alterations within three brainstem nuclei implicated in upper airway motor control and/or cardio-respiratory regulation.

**Methods :** Altogether 48 rats of both genders were exposed to a CIH profile consisting of alternating room air and 10% oxygen every 90 seconds during sleep during postnatal days 10-25. Animals were divided into three groups and sacrificed by perfusion fixation at age 4, 8 and 20 weeks. Stereological techniques: optical dissector, nucleator, and Cavalieri were used to determine total number of neurons, glial cells, neuronal nuclear volumes and volumes of the compact and semicompact formations of nucleus ambiguus (NA), hypoglossal (XII) and dorsal motor vagal (DMV) nuclei.

**Results :** Following CIH treatment, the most prominent changes emerged in XII: neuronal nuclear volume was significantly reduced in 2 out of the 3 age groups ( $p=0.004$ ,  $0.001$ , and  $0.07$  at 4, 8 and 20 weeks respectively). Reduced numbers of glial cells were also found in XII at 4 and 8 weeks ( $p=0.04$  and  $0.01$  respectively) and DMV at 4 weeks ( $p=0.03$ ). No changes in neuronal numbers were observed in any of the structures studied at any of the time points apart from borderline significant increases in XII in females at 4 weeks of age ( $p=0.04$ ).

**Conclusion :** Brainstem structures involved in upper airway motor con-

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tol, and/or cardio-respiratory regulation are morphometrically sensitive to CIH exposures and the changes in cellular characteristics may partly underlie components of the respiratory plasticity that develops following CIH.

**Support (optional):** Supported by grants from Babes in Arms and National Institutes of Health HL-69932

### 0558

#### PULSE WAVE AMPLITUDE MEASURED BY PHOTOPLETHYSMOGRAPHY IN CONTINUOUS FLOW LIMITATION PERIODS DURING SLEEP

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**Introduction :** Sleep-disordered breathing patients (SDB) may present only snoring and a pattern of flow limitation (FL), without ASDA arousal or AASM defined respiratory events. The purpose of this study was to assess hemodynamic response to periods of continuous FL during sleep using pulse wave (PW).

**Methods :** Patients with SDB (n = 18, F:M = 1:1, age = 36 ± 11, BMI = 25.7 ± 5.0) were evaluated with RDI < 5 events/h. We selected a total of 124 events, 53 five-minute windows of continuous FL (not associated with arousal or oxygen desaturation); and 71 five-minute windows of normal breathing (NB), both during slow wave sleep. The PW was measured from the finger photoplethysmography signal obtained from the EMBLA@ polysomnography system oximeter. The maximum PW amplitude, peak-to-peak PW value and the power spectrum of three frequency bands (FB1: 0.05-0.08 Hz, FB2: 0.15-0.35 Hz and FB3: 0.70-1.50 Hz) were calculated for each 5-minute period of normal and continuous FL during SWS.

**Results :** Maximum PW amplitude: NB = 225.65 ± 38.83, FL = 205.64 ± 29.38 (p = 0.002). Peak-to-peak PW: NB = 194.18 ± 58.39, FL = 160.47 ± 46.84 (p < 0.001). FB1: NB = 3.71 ± 4.92, FL = 1.80 ± 2.64 (p = 0.01). FB2: NB = 101.38 ± 141.85, FL = 182.07 ± 279.20 (p = 0.04). FB3: NB = 9071.86 ± 6223.07, FL = 5384.48 ± 3276.62 (p < 0.001).

**Conclusion :** The increase in FB2 and the decrease in baseline oscillation (FB1), peak-to-peak PW amplitude value, and FB3 found in prolonged-FL events, without ASDA arousal, evidence that this unrecognized respiratory pattern may lead to an hemodynamic repercussion.

**Support (optional):** AFIP, FAPESP/CEPID

### 0559

#### CAP RATE ANALYSIS IN OBSTRUCTIVE SLEEP APNEA PATIENTS

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**Introduction :** CAP is an EEG activity that may indicate sleep instability and it may be used to describe sleep fragmentation associated with different sleep disorders. It has been suggested that CAP may be more sensitive parameter for sleep disorders consequences. It has been also demonstrated that conventional sleep parameters do not show good correlation with clinical complains in patients with OSA. The purpose of this study was to investigate the correlation of CAP rate to polysomnographic parameters in OSA patients.

**Methods :** A group of 60 OSA patients (Groups: 1:20 mild, 2:20 moderate, 3:20 severe) was evaluated with clinical sleep history and nocturnal polysomnography. Airflow was measured with nasal pressure cannula. Parameters evaluated were: AHI, arousal index, total number of arousals and sleep architecture. CAP automatic analysis was performed for each

patient (Science software, Embla System). Parameters used were total CAP rate and CAP index. Statistical analysis was performed with Pearson correlation and Stepwise Regression Analysis (SPSS).

**Results :** Patients were matched for age and BMI. Age: 30 to 50 years old, BMI: 25 to 27 mgKg<sup>2</sup>. Polysomnographic results: AHI: group 1: 9.6±3.4; group 2: 21± 3.7; group 3: 40.5 ± 11.2. CAP rate: group 1: 57.2±19.8; group 2: 60.6±17.5; group 3: 72±14.1. CAP rate did not show significant correlation with other polysomnographic values (AHI, arousal index, total number of arousals and sleep stages).

**Conclusion :** Cap rate did not show to be significant correlated with conventional polysomnographic values indicated by routine PSG in OSA patients (AHI, arousal index, total number of arousals and sleep stages percentage). Evaluation of the different CAP types may show different results. It may be suggested that CAP rate analysis represents a more sensitive parameter and is probably related to other aspects not routinely evaluated in a conventional sleep study. Larger studies are necessary to establish CAP parameters and associated comorbidity.

**Support (optional):** AFIP

### 0560

#### GENDER DIFFERENCE IN THE SLEEP PATTERNS BEFORE AND DURING CPAP TITRATION

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**Introduction :** The objectives of this study were to characterize gender differences of PSG and related measurements in sleep apnea patients and to identify the effects of CPAP titration on these patients.

**Methods :** The study included 81 (60 males and 21 females) sleep apnea patients. Two consecutive overnight PSG recordings and a CPAP titration, about one month later, were carried out for each subject. These patients were free of psychotropic medications at the time and for the two weeks prior to the sleep studies. To avoid a "first night effect", the first night was disregarded. At baseline and during CPAP titration, measurements included age, body mass index, respiratory disturbance index in total sleep time (RDITST), oxygen desaturation, sleep onset latency (SOL), sleep efficiency, wake, stage 1 sleep (S1), stage 2 sleep, slow wave sleep (SWS), REM latency (REML), and REM sleep. Other measurements included the score of the Center for Epidemiological Studies-Depression Scale (CES-D) at baseline and the CPAP pressure during CPAP titration. Student t-test was used for statistic analyses.

**Results :** At baseline, RDITST (P = 0.042) and S1 (P = 0.003) were higher in males than in females; CES-D (P = 0.004) was higher in females than in males. During CPAP titration, CPAP pressure (P = 0.001) and S1 (P = 0.009) were higher in males than in females; SOL (P = 0.017), SWS (P = 0.013) and REML (P = 0.009) were higher in females than in males.

**Conclusion :** The results indicate that in this group of sleep apnea patients, males were less depressed at baseline, but had more light sleep. This may be a consequence of their higher baseline RDITST. Mixed results were found on the effects of CPAP titration with regard to gender.

**Support (optional):**

### 0561

#### AUTOCPAP IN OBSTRUCTIVE SLEEP APNEA (OSA) PATIENTS WITH POOR COMPLIANCE TO STANDARD CPAP TITRATION

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**Introduction :** CPAP is considered the standard treatment for the management of OSA patients, but this is often intrusive and poorly accepted

by patients. Standard laboratory full polysomnography (PSG) CPAP titration is still considered the gold standard for determining the level of pressure required for each patient. However a proportion of patients remain untreated because of the lack of acceptance to this treatment. Several studies demonstrated that auto-titrating positive airways pressure (APAP) devices improve compliance, comfort and therefore adherence to treatment, with no differences in functional outcomes compared to CPAP. Aim of this study was to evaluate acceptance and compliance to APAP in a population of OSA patients in which standard manual titration failed and therefore have been considered “untreatable”.

**Methods :** Three hundred and seventy six consecutive severe OSA patients (AHI $\geq$ 20) referred to our sleep disorders center in 1-year period underwent one full-night PSG manual CPAP titration. Based on compliance (time spent with CPAP on), patients were classified as: compliant (C; >4 hours) and not compliant (NC) including those who were poorly compliant (NC1; between 2 and 4 hours) and those not compliant (NC0; less than 2 hours). The night after manual titration, these NC patients received treatment with APAP (REMstar® Auto Respironics Inc.).

**Results :** Characteristics of the whole sample (n=376) were: 320M,56W; mean age: 54.2 $\pm$ 12.8 yrs., Mean Oxygen Desaturation Index (ODI): 41.82 $\pm$ 2.3 per hour; minimal SaO<sub>2</sub>% :73.81 $\pm$ 0.2. Forty-six patients (12.2%; 39M,7W; mean age: 53.1 $\pm$ 13.2 yrs., mean ODI: 48.51 $\pm$ 9.6; minimal SaO<sub>2</sub>%: 70.71 $\pm$ 1.1) were classified as NC (NC0:n=32; NC1: n=14) and therefore were treated with APAP. Of them, 3 patients showed no compliance also to APAP. Nine patients still had a compliance < than 4 hours (mean average use: 2.1 $\pm$ 1.7hours, average pressure: 5.81 $\pm$ 1 cmH<sub>2</sub>O; 90th centile pressure: 8.2 $\pm$ 1.6 cmH<sub>2</sub>O) while 34/46 (73.9%) patients showed a good compliance to APAP (mean average use: 6.7 $\pm$ 1.5 hours; average pressure: 8.4 $\pm$ 1.9 cmH<sub>2</sub>O; 90th centile pressure: 10.2 $\pm$ 2.2 cmH<sub>2</sub>O).

**Conclusion :** The vast majority of patients in which manual CPAP titration failed, precluding eventual treatment, surprisingly showed good compliance to APAP. Our data suggest that APAP could be a valid therapeutic alternative in those patients judged “untreatable” with conventional respiratory devices before considering other treatment options (weight loss, ENT surgery etc.).

**Support (optional):**

## 0562

### DEMOGRAPHIC & POLYSOMNOGRAPHIC CHARACTERISTICS IN PATIENTS WITH REM-RELATED OBSTRUCTIVE SLEEP APNEA: A RETROSPECTIVE ANALYSIS OF 226 PATIENTS

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**Introduction :** Obstructive sleep apnea (OSA) has a 5% prevalence with a male:female of 3:1. The disease differs clinically and polysomnographically for men and women. Women tend to have respiratory events in REM sleep. In the following proposal, we discuss the demographic and polysomnographic characteristics of subjects with REM OSA.

**Methods :** A retrospective review was performed of patients having undergone polysomnography at the CCSDC between 11/04 and 11/05. Inclusion criteria were age >18 and diagnosis of REM OSA. REM OSA was defined as AHI > 5, NREM AHI < 15 and REM AHI : NREM AHI > 2. Data were collected from the PSG report and medical records and included sleep latency, REM latency, TST, AHI, REM AHI, NREM AHI, sleep stage %, age, gender, BMI, ESS, neck circumference, history cardiovascular risk factor, psychiatric disease and antidepressant usage. Data were analyzed for descriptive statistics and logistical analysis. Pearson’s chi-square and the student’s t- test were used for comparison of means and proportions. Oneway ANOVA tests were used to detect any correla-

tions. P values < 0.05 were statistically significant.

**Results :** There were 226 subjects (151 F, 75 M) with female:male ratio of 2:1. The following variables were significantly different: age (52.2w vs. 46.3m), BMI (38.0w vs. 31.3m), neck circumference (38.6w vs. 41.9m[cm]), number cardiovascular risk factors (1.5w vs 0.9m) and REM index (40.6w vs. 35.7m). Variables which were not significantly different when stratified by gender included: ESS, REM latency, TST, AHI, NREM AHI, percentage REM sleep and depression.

**Conclusion :** To our knowledge, this is the first study to delineate characteristics of patients with REM OSA. We hypothesize that distinct mechanisms of REM OSA exist for men and women. Female hormones may limit sleep-disordered breathing to REM sleep in obese females. The pathophysiology of REM OSA in men is less clear. Further investigation is necessary.

**Support (optional):**

## 0563

### CORRELATION BETWEEN CLINICAL SYMPTOMS AND CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) COMPLIANCE FROM SMART CARD DOWNLOADS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA (OSA)

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**Introduction :** CPAP compliance in patients with obstructive sleep apnea has been variable and excessive daytime sleepiness has been one of the few symptoms that have been shown to correlate positively with increased compliance. Subjective compliance data obtained from questioning patients has also been shown to differ significantly from objective data downloaded from Smart Cards which store data about the actual daily use. Identifying prognostic factors for good CPAP compliance early can be used to reduce mortality and morbidity due to OSA.

**Methods :** Clinical symptoms, polysomnographic data and also compliance (overall and daily use) from Smart Card downloads from 117 patients followed over the past year at our Sleep Center was collected. Maximal follow up time was about a year. Clinical symptoms and polysomnographic data was correlated with objective (Smart Card) compliance.

**Results :** An overall compliance of over 50% was seen in 77.8% of patients with 46.1% demonstrating over 75% compliance. Most of the patients had over 50% daily compliance. Forty nine (41.8%) patients had complained of significant daytime sleepiness, 52 (44.4%) had fatigue and 42 (35.9%) had nonrestorative sleep. Objective compliance did not correlate with any of these symptoms.

**Conclusion :** Objective compliance was not shown to correlate with any symptom even though 77.8% of the patients followed had a compliance over 50%. The exact reason(s) is unclear. It is possible that patient education and motivation and prescribing the lowest effective CPAP pressure may be among the answers.

**Support (optional):**

## 0564

### USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE INTERVENTIONS BY PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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**Introduction :** Use of complementary and alternative medicine (CAM) interventions in the US population has increased over the past decade. The prevalence of CAM use among patients with obstructive sleep apnea (OSA) is unknown.

**Methods :** We developed a survey regarding previous and current use of the 20 most common CAM interventions and administered it to consecutive patients undergoing polysomnography between 1/27/05 and 3/4/05 at our center.

**Results :** Of 457 patients (80.8%) who completed questionnaires, 344 patients (222 M, 122 F, mean  $\pm$  SD age 57.1 $\pm$ 14.3 years) had OSA (mean AHI 25.1 $\pm$ 27.1). Nasal strips (23.5%), weight loss programs (6.7%), throat sprays (5.8%) and relaxation (4.6%) were the most common CAM therapies used for sleep problems in the past by the patients with OSA. There were no gender differences with respect to previous (32.0% vs 30.3%,  $p=0.81$ ) or current (10.4% vs 11.5%,  $p=0.86$ ) CAM use, yet men with OSA more commonly used nasal strips (27.5% vs 16.4%,  $p=0.024$ ), and less commonly used relaxation (2.2% vs 9.0%,  $p=0.007$ ), homeopathy (0.4% vs 4.1%,  $p=0.02$ ), or therapeutic audio tapes (0.4% vs 4.1%,  $p=0.02$ ) than women with OSA. Regarding future CAM plans OSA patients were most commonly interested in weight loss (42.2%), massage therapy (27.9%), relaxation (20.4%), and stress management (17.2%) for sleep-related symptoms.

**Conclusion :** CAM interventions are frequently used by OSA patients. While use of CAM therapies for sleep problems was similar for men and women with OSA, men more commonly used nasal strips, an intervention specifically aimed at the reduction of snoring.

**Support (optional):**

### 0565

#### HOME DIAGNOSTIC PORTABLE MONITORING: AN EFFECTIVE SCREENING TOOL IN A COMMUNITY- BASED PRIMARY CARE POPULATION

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**Introduction :** The waiting period for laboratory testing with polysomnography for sleep disordered breathing may exceed three months. Portable, in-home monitoring may be useful for screening but studies have been limited by lack of risk stratification, ethnicity and gender, and exclusion of co-morbid conditions. This Cross-sectional study followed by a prospective cohort, investigates the utility of portable, in-home diagnostic testing for screening sleep disordered breathing (SDB) in a low-risk primary care patient population.

**Methods :** 810 multi-ethnic, adult patients were selected from a community-based primary care clinic population. Patients were stratified into low ( $n=408$ ) and high-risk groups ( $n=402$ ) using the Berlin questionnaire. Low risk patients (LR) were tested initially with the portable, in-home Eden trace Plus II™ device and if positive underwent confirmatory testing with in-lab polysomnography (PSG). Portable monitor negative patients were then re-evaluated at one year and symptomatic patients were re-tested with laboratory PSG. High risk (HR) patients underwent initial in-lab PSG.

**Results :** SDB was detected by portable monitoring in 24% (99) of LR patients (CI 20.1-28.4%) and 80.8% (80/99) were confirmed by PSG resulting in a sensitivity of 86.4% and a specificity of 80.8%. At 1-year follow-up, 87 portable monitor negative patients developed symptoms and 48% (42) had SDB confirmed by PSG. Overall, 13.5%, (42/309) of portable monitor negative patients had SDB at one-year.

**Conclusion :** Portable monitoring is useful as an initial screening test for

detecting SDB in low-risk patients. Eighty percent of SDB diagnosed by portable monitoring was confirmed by PSG. Patients who are initially negative by portable monitoring should be followed for development of symptoms and further evaluation may be necessary.

**Support (optional):**

### 0566

#### ERP STUDY OF INVOLUNTARY ATTENTION SWITCHING IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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**Introduction :** In patients with obstructive sleep apnea syndrome (OSAS), attentional capacity and executive function are altered. These deficits are assumed to be related to a (pre)frontal lobe dysfunction. Few ERP studies have been conducted to assess cognitive impairment in OSAS. The aim of the study was to measure ERP to better characterize attentional deficits in OSAS patients.

**Methods :** Thirteen OSAS patients and 14 age-matched controls (age: 41.5  $\pm$  11y and 42.2  $\pm$  10y, respectively) (AHI: 46.0 and 1.6, respectively) were recorded for one night of sleep. Each subject underwent an ERP paradigm where standard (90%, 1000Hz), high deviant (2.5%, 1250Hz) and low deviant (2.5%, 1050Hz) tones were presented by earphones. Subjects were asked to ignore the stimuli and read during the task. Mismatch negativity (MMN) and P3a peak amplitudes and latencies were measured by subtracting the standard from each deviant waveform. A three-way ANOVA with two independent variables (Group and Tone) and one repeated measure (Electrode) was done on Fz, FCz and Cz in order to compare the groups.

**Results :** A significant Group effect was found for the amplitude of the P3a component ( $p<0.05$ ): OSAS patients had a reduced amplitude in comparison with control subjects. This difference was not influenced by the magnitude of the tone deviance or by the electrodes. This reduced amplitude was not observed for the MMN. No between-group differences were found for the MMN and the P3a latencies.

**Conclusion :** Anomalies were observed in the ERP in OSAS patients and are specific to the P3a amplitude. Thus, automatic auditory processing appears to be preserved in OSAS, but deficits in the later stage of information processing are present and can possibly reflect impaired brain functioning in the frontal lobe, the area considered responsible for that type of processing.

**Support (optional):**

### 0567

#### CAN OBSTRUCTIVE SLEEP APNEA BE PREDICTED IN BARIATRIC SURGERY CANDIDATES?

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**Introduction :** Our goal was to identify clinical characteristics predictive of obstructive sleep apnea (OSA) in bariatric surgery candidates.

**Methods :** Overnight polysomnography (PSG) records were reviewed from September 2003 to December 2004. Patients with AHI (apnea-hypopnea index)  $> 5$  met criteria for OSA. An obstructive apnea was defined as a  $> 90\%$  reduction in airflow for more than 10 seconds in the presence of continued respiratory effort. Hypopneas were defined as a reduction in the amplitude of the nasal pressure transducer signal below 50% of baseline level during sleep, lasting longer than 10 seconds and associated with an EEG arousal or oxygen desaturation  $> 3\%$ .

**Results :** Of 1982 overnight PSGs reviewed, 38 were patients referred prior to bariatric surgery. Female:male ratio was 6.6:1. Age was 42.0  $\pm$  9.6

years (mean  $\pm$  standard deviation). Mean total AHI was  $24.1 \pm 27.9$ , NREM AHI was  $24.0 \pm 29.9$ , and REM AHI was  $31.7 \pm 27.3$ . The mean minimal oxyhemoglobin saturation was  $76.5 \pm 12.8$ . Of the 38 patients, 32 (84.2%) had AHI  $> 5$  and received treatment with CPAP prior to surgery. Even in the 6 (15.8%) patients with AHI  $< 5$ , the minimal oxyhemoglobin saturation was 75%, and patients had predominantly REM related respiratory events (REM AHI  $17.6 \pm 25.4$ ). Symptoms included excessive daytime sleepiness (n = 31, 81.6%), snoring (n = 36, 94.7%), witnessed apneas (n = 14, 36.8%), repeated nocturnal awakenings (n = 30, 78.9%) and fatigue (n = 25, 65.8%). None distinguished OSA from non-OSA patients.

**Conclusion :** These data confirm previous reports that the prevalence of OSA is extremely high in this subgroup of patients, and support overnight PSG as an integral part of the preoperative evaluation. Even patients without witnessed apneas or fatigue may have OSA, most likely due to its almost universal prevalence in this population.

**Support (optional):**

## 0568

### DETERMINING CLINICAL MARKERS TO PREDICT OBSTRUCTIVE SLEEP APNEA TO IMPROVE ACCESS TO POLYSOMNOGRAPHY IN A VETERANS HOSPITAL

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**Introduction :** There is a high prevalence of obstructive sleep apnea (OSA) among Veterans compared to the general population. Limited access to polysomnography at VA hospitals results in diagnostic delays. The aim of this study is to improve access to polysomnography in a VA hospital by developing a prediction score based on patients' BMI and ESS score.

**Methods :** Retrospective analysis of patients who had a sleep study between 2003 -2005. Data on ESS (Epworth Sleepiness scale) score, BMI (body mass index) and AHI (apnea-hypopnea index) were collected. ESS and BMI were converted to binary variables using cutoff values of  $>10$  (ESSBIN) and  $>30$  (BMIBIN), respectively. Pearson correlations were computed between variables and logistic regression was used to model OSA as a function of ESSBIN and BMIBIN.

**Results :** Of the 261 sleep studies done between 1/1/2003 and 10/31/2005, ESS scores were available for 126 patients and these are used for data analysis. 101 (80%) patients had OSA and 25 (20%) did not. Mean BMI was  $33.46 \pm 5.83$  kg/m<sup>2</sup>. Mean ESS score was  $12.58 \pm 5.48$ . 94 (74.6%) patients had BMI  $> 30$  kg/m<sup>2</sup>. 83 (65.9%) patients had ESS  $> 10$ . Significant correlations were noted between BMI and OSA ( $r = 0.29$ ,  $P=0.001$ ), BMIBIN and OSA ( $r = 0.34$ ,  $P<0.001$ ) and ESS and OSA ( $r = 0.28$ ,  $P=0.001$ ). 88% of patients with BMI  $> 30$  had OSA vs. 56% of patients with BMI  $\leq 30$ , and 66% of patients with ESS  $> 10$  had OSA vs. 34% of patients with ESS  $\leq 10$ . Logistic regression, using BMIBIN and ESSBIN to predict OSA, yielded odds ratio of 6.78 and 3.81, respectively.

**Conclusion :** BMI  $> 30$  kg/m<sup>2</sup> and ESS score  $> 10$  show strong correlation with presence of OSA in Veterans. These parameters may be used to prioritize polysomnography for symptomatic patients awaiting sleep studies.

**Support (optional):** None

## 0569

### TREATMENT EXPERIENCE OF PATIENTS WITH COMPLEX SLEEP APNEA SYNDROME: A RETROSPECTIVE COMPARATIVE REVIEW

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**Introduction :** Many patients who demonstrate apparent obstructive sleep apnea syndrome (OSA) develop problematic central apneas or Cheyne-Stokes pattern with acute application of CPAP (herein called Complex Sleep Apnea Syndrome or CompSAS), suggesting that CPAP will not be a successful treatment strategy. We sought to compare treatment approach and experience of patients with CompSAS versus OSA. We hypothesized that CompSAS patients would find CPAP less effective and have more problems with adherence compared with OSA patients.

**Methods :** Retrospective review of consecutive CompSAS and OSA patients studied in a sleep disorders center over a one month period. We recorded clinical and polysomnographic data from baseline and all follow-up contacts for the six months after diagnosis.

**Results :** There were 133 with OSA (mean age=  $57.6 \pm 12.2$  years; males= 63.9%), and 34 patients with CompSAS (mean age=  $54.4 \pm 16$  years; males= 82.4%). They had similar total apnea-hypopnea indices (AHI=  $26.3 \pm 24.8$  in OSA vs.  $33.4 \pm 26.5$  in CompSAS patients;  $p=0.16$ ). CPAP was prescribed in 93.7% vs. 87.9% of OSA vs. CompSAS patients ( $p=0.284$ ), with no significant difference in required CPAP pressures ( $p=0.112$ ). There was no difference in prescription frequency of positional, pharmaceutical, or oxygen therapy. Mean time to first follow-up was shorter in CompSAS ( $46.2 \pm 47.3$  vs.  $53.8 \pm 36.8$  days;  $p=0.022$ ), and they tended to have more follow-up visits in the first 6 months ( $0.8 \pm 0.9$  vs.  $0.5 \pm 0.8$ ,  $p=0.15$ ). CPAP adherence ( $5.1 \pm 1.6$  vs.  $6.1 \pm 1.5$  hr/night,  $p=0.156$ ) and improvement in Epworth Sleepiness Scale ( $-4.6 \pm 4.8$  vs.  $-5.9 \pm 6.9$ ,  $p=0.483$ ) was similar between OSA and CompSAS patients. However, interface problems were more common in CompSAS patients, especially "insufficient air" (0.75 vs. 8.8%;  $p=0.017$ ), and inadvertent mask removal (2.6 vs. 17.7%;  $p=0.002$ ).

**Conclusion :** Physicians prescribed similar treatments to patients with CompSAS and OSA. CompSAS patients have more CPAP interface problems and require closer follow up to achieve similar adherence.

**Support (optional):**

## 0570

### NASAL INFLAMMATION AND CARRIAGE OF STAPHYLOCOCCUS AUREUS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA TREATED WITH NASAL CPAP

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**Introduction :** Patients with obstructive sleep apnea treated with nasal continuous positive airway pressure (CPAP) often complain of nasal side effects. We previously reported that patients showing increased numbers of neutrophils in their nasal scrape were at increased risk of discontinuing nasal CPAP because of nasal side effects. We also found increased numbers of bacteria in the scrapes of patients with increased neutrophils. The present study tested the hypothesis that nasal carriers of *Staphylococcus aureus* (Staph) would have increased numbers of neutrophils and that CPAP use would be less in Staph carriers than in non-carriers.

**Methods :** Nasal symptom scores, nasal scrapes for cytology and nasal cultures were obtained at baseline and one month following initiation of nasal CPAP. Compliance with CPAP therapy was measured by time-at-pressure recordings.

**Results :** Seventeen patients completed the one month follow-up visit, 7 of them having positive Staph cultures. Nasal neutrophil counts were

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greater in the carriers than the non-carriers ( $p = 0.05$  by one-tailed Mann-Whitney test). There was no significant difference in hours of CPAP use or in nasal symptom scores between carriers and non-carriers. Nor were any significant correlations found between hours of CPAP use, nasal symptom scores and nasal neutrophil counts.

**Conclusion :** In patients with obstructive sleep apnea nasal carriers of *Staphylococcus aureus* have increased nasal inflammation manifested by increased neutrophils in their nasal scrapes. However this inflammation is not associated with increased nasal symptoms or with reduced compliance with nasal CPAP.

**Support (optional):** This work is supported by the Scripps Clinic Academic Affairs. CPAP units for compliance monitoring were provided by Respironics.

### 0571

#### ROLE OF EMPIRIC TREATMENT WITH AUTOTITRATING CPAP IN PATIENTS SUSPECTED OF HAVING OBSTRUCTIVE SLEEP APNEA (OSA)

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**Introduction :** There is a high prevalence of obstructive sleep apnea (OSA) among Veterans compared to the general population. Limited access to diagnostic testing leads to treatment delays. Untreated OSA is associated with adverse consequences on quality of life. We evaluated efficacy of empiric treatment with autotitrating CPAP in patients suspected of having OSA.

**Methods :** Randomized controlled trial comparing treatment with autotitrating CPAP with sham CPAP for 3 months in patients referred for evaluation of OSA who have BMI > 30kg/m<sup>2</sup> and Epworth sleepiness scale score (ESS) > 12. Outcome variables evaluated: ESS, Functional outcomes in sleep (FOSQ) and health related quality of life (SF-36).

**Results :** 5 of the 16 patients enrolled have completed the treatment period of 3 months and their data is presented. Both groups were matched at baseline with respect to BMI, ESS, SF 36 and FOSQ scores. In the Auto CPAP group baseline and after 3 months values respectively were: ESS:  $16 \pm 5.29$ ,  $13 \pm 6.88$ ,  $p = 0.03$ ; FOSQ total score:  $13.22 \pm 7.11$ ,  $12.73 \pm 4.94$ ,  $p = 0.07$ ; and SF 36 physical health scores:  $41.31 \pm 10.31$ ,  $32.23 \pm 8.01$ ,  $p = 0.09$ ; mental health scores:  $32.10 \pm 9.84$ ,  $40.11 \pm 13.76$ ,  $p = 0.08$ . In the sham CPAP group baseline and after 3 months: ESS:  $15 \pm 1.41$ ,  $11 \pm 5.65$ ,  $p = 0.57$ ; FOSQ total score  $13.14 \pm 4.65$ ,  $17.25 \pm 1.77$ ,  $p = 0.53$ ; and SF 36 physical health scores:  $33.28 \pm 2.47$ ,  $38.6 \pm 3.08$ ,  $p = 0.40$ ; mental health scores:  $54.9 \pm 11.65$ ,  $52.6 \pm 15.52$ ,  $p = 0.56$ . No statistical difference was noted at 3 months between the 2 groups.

**Conclusion :** The limited data available does not support empiric treatment with auto CPAP in patients suspected of having OSA. However, final outcome may differ when more data is available.

**Support (optional):** None

### 0572

#### IMPACT OF PRE STUDY ACCLIMATIZATION WITH AUTOTITRATING POSITIVE PRESSURE IN PATIENTS UNDERGOING NASAL CPAP TITRATION

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**Introduction :** In most communities treatment of obstructive sleep apnea by fixed continuous positive airway pressure (CPAP) requires an in laboratory titration procedure to determine therapeutic pressure. Auto Titrating Positive Pressure in patients (APAP) is a technology with a growing number of clinical applications with some evidence of improved compliance and more ideal pressure delivery than standard CPAP. The aim of this study is to assess if outcome of nasal CPAP titration study is improved if preceded by previous acclimatization to APAP therapy.

**Methods :** We randomly selected charts of 50 patients with a diagnosis of OSA on baseline PSG never having previously been on nasal CPAP. Group A consisted of 25 patients undergoing CPAP titration. Group B consisted of 25 patients who were on APAP therapy for at least two weeks prior to CPAP titration. We assessed the nasal CPAP titration study in both groups with respect to sleep latency, REM latency, arousal index per hour (ARI), wake after sleep onset (WASO), total sleep time, percentage of sleep time in stage 3 and 4, and percentage of sleep in REM. We also assessed minutes on final pressure, apnea hypoapnea index (AHI) on final pressure, and as well as parameters of subjective tolerance to the air pressure titration.

**Results :** Analysis of data between two groups suggested that patients acclimatized to APAP had improved subjective tolerance to nasal CPAP, lower AHI on final pressure and reduced WASO. We also found good correlation between APAP trial pressure calculation and laboratory measured pressure requirements.

**Conclusion :** Our data suggested that patients undergoing nasal CPAP titration may benefit from a prior trial of acclimatization with APAP therapy in order to improve data derived during the nasal CPAP titration.

**Support (optional):**

### 0573

#### EVALUATION OF THE PERFORMANCE OF CPAP HEATED HUMIDIFIERS FOR USE IN SLEEP APNEA THERAPY; A COMPARATIVE STUDY OF HUMIDIFICATION EFFECTIVENESS USING A LUNG MODEL

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**Introduction :** Humidification performance of seven commercially available CPAP devices with heated humidifiers was evaluated under simulated-use conditions using moisture output methods from international standards ASTM 1690 and ISO 8185 and moisture loss methods from ISO 9360 test lung model.

**Methods :** Moisture output of heated humidifiers and corresponding moisture loss of a test lung were determined over one-hour periods using a mass-loss method. Medically relevant and standardized test conditions were limited to CPAP pressures of 10 cm H<sub>2</sub>O, and four humidifier settings (no humidification, unheated humidification, medium heater setting, and maximum heater setting). Airway temperatures and breathing tube condensation were recorded. Single measurements of water content in delivered air used a novel hybrid capacitive humidity sensor.

**Results :** Moisture output varied directly with the application of heat. Unheated moisture output ranged from 2.9 mg/L to 11.8 mg/L. Medium heat moisture output ranged from 7.1 to 20.3 mg/L. Maximum heat moisture output ranged from 19.1 to 29.0 mg/L. Moisture loss from the test lung decreased with increased levels of humidification and heat from the CPAP humidifiers. Unhumidified moisture loss ranged from 20.2 to 25.6 mg/L. Unheated humidification moisture loss ranged from 15.3 to 18.9 mg/L. Medium heat moisture loss ranged from 7.4 to 16.5 mg/L. Maximum heat moisture loss ranged from 2.6 mg/L to 9.7 mg/L.



**Conclusion :** At maximum heat setting, all CPAP humidifiers met and exceeded the minimum requirements for moisture output as defined by international standards as “at least 10mg/L”. Some devices appear capable of approaching the requirements for intensive care ventilator heated humidifiers of “at least 33 mg/L”. All CPAP humidifiers met or exceeded the moisture loss expectations of standard calibration heat and moisture exchangers in one test condition. Test data from international standards should be included in the informed decision to buy and use these devices.

**Support (optional):**

## 0574

### CHARACTERISTICS, POLYSOMNOGRAPHIC FINDINGS, AND TREATMENT OUTCOMES OF RAPID EYE MOVEMENT-PREDOMINANT OBSTRUCTIVE SLEEP APNEA

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**Introduction :** To compare patient characteristics, polysomnographic (PSG) findings, and continuous positive airway pressure (CPAP) responses in rapid eye movement (REM)-predominant obstructive sleep apnea (R-OSA) and OSA not confined to REM (control-OSA).

**Methods :** Retrospective, single-institution case-control study. R-OSA cases were randomly selected between 2001-04 and defined by a REM apnea-hypopnea index (AHI) > 10 yet total AHI <10. Control-OSA patients were defined by a total AHI > 10 as studied consecutively during a month in 2004.

**Results :** 104 R-OSA (mean age: 51 ± 13 years; 38% men; mean BMI: 38.3 ± 8.4 kg/m<sup>2</sup>) and 84 control-OSA (mean age: 59 ± 12 years; 66% men; mean BMI: 36.3 ± 9.8 kg/m<sup>2</sup>) cases were reviewed. Snort arousals and morning headache were more common in R-OSA patients (69.9% vs 53.6%; p = 0.036 and 55.1% vs 14.3%; p = <0.0001, respectively). Epworth Sleepiness Scores (ESS) were similar (11.1 ± 5.7 vs 10.6 ± 5.3; p = 0.58). Mean and lowest REM oxyhemoglobin saturations were higher in R-OSA patients (93 ± 2.5% vs 92 ± 2.4%; p = 0.0008 and 82 ± 6.5% vs 78 ± 11.5%; p = 0.01, respectively). CPAP was prescribed in 93.5% R-OSA and 95.2% control-OSA cases with R-OSA patients requiring a lower pressure (6 ± 4 cm H<sub>2</sub>O vs 9.7 ± 2.6 cm H<sub>2</sub>O; p = <0.0001). CPAP adherence rates (324 ± 107 mins/night vs 317 ± 97.5 mins/night; p = 0.83), ESS change (-2.5 ± 5 vs. -4.5 ± 5.5; p = 0.139) and frequency of CPAP interface problems at follow-up were similar.

**Conclusion :** R-OSA was distinguished from control-OSA by greater female gender representation, more reports of snort arousals and morning headaches, higher oxyhemoglobin saturations during polysomnography, and lower CPAP levels. CPAP compliance, improvements in ESS, and the frequency of CPAP interface problems were similar between the groups.

**Support (optional):**

## 0575

### OXIDATIVE STRESS IN PERIODIC BREATHING: IT'S RELATIONSHIP WITH INTERMITTENT HYPOXEMIA

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**Introduction :** Periodic breathing has been described in patients with CHF for many years. More recently, this association has been linked to increased mortality. The underlying mechanisms leading to worsening in outcome of CHF patients with periodic breathing haven't yet been estab-

lished. One potential mechanism involves the frequent drops in oxygen saturation associated with periodic breathing. This research aims to quantify oxidative stress in CHF patients with periodic breathing and intermittent hypoxemia.

**Methods :** Subjects with CHF confirmed by NYHA ≥ 2 and EF ≤ 40% were studied. Inclusion criteria included EF <40%, stable clinical symptoms and absence of underlying OSA or home oxygen requirement. All patients had periodic breathing (or Cheyne-Stokes Respiration - CSR) confirmed and measured by overnight polysomnography. Variables measured included CSR duration in hours and % sleep time, oxygen desaturation index (ODI), arousal index, duration of sleep at SaO<sub>2</sub> <90%, urine isoprostane and reactive oxygen species (ROS) formation by flow cytometry. Patients with periodic breathing and ODI <10 were used as controls. Variables are shown as mean ± SD.

**Results :** Seventeen patients were included in this preliminary analysis. Baseline characteristics were: age 69 ± 9.6, EF 30 ± 9.7%, CSR(h) 3.9 ± 1.1, ODI 32.8 ± 21, ROS (MFI) 4212 ± 985. Periodic breathing was strongly associated with intermittent hypoxemia (ODI) (r=0.80, p<0.005). Oxidative stress was increased in patients with CHF and periodic breathing. There was a strong relationship between the overnight duration of CSR and the severity of oxidative stress (r=0.77, p<0.005). Patient with CSR also had high levels of isoprostane when compared to controls.

**Conclusion :** This study demonstrates a significant increase in oxidative stress as measured by urine isoprostane levels and by ROS formation in CHF patients with periodic breathing and intermittent hypoxemia. The strong correlation between the severity of CSR and oxidative state is an important factor and may lead to better understanding of the processes leading to increased mortality in CHF patients with periodic breathing. Further research in this area is warranted.

**Support (optional):** AHA, NIH M01RR00096

## 0576

### EVALUATION OF SUBJECTIVE MEASURES OF SLEEPINESS IN OBSTRUCTIVE SLEEP APNEA PATIENTS PRE- AND POST-TREATMENT WITH CPAP AND COMPARISON TO HEALTHY CONTROLS

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**Introduction :** Self-report is widely used to measure sleepiness in research and clinical practice, but may be inaccurate due to patients' inability to gauge their level of sleepiness. Two standardized subjective measures, the Epworth Sleepiness Scale (ESS) and the Visual Analog Scale (VAS), are commonly used to assess sleepiness, although their reported correlations with objective measures are weak.

**Methods :** Obstructive Sleep Apnea (OSA) patients (n=135, mean RDI=48.1, range 5-149) were evaluated at baseline and at 2-, 4-, 8- or 12-weeks post-treatment with CPAP and compared to 46 controls. The Alertness and Memory Profiler (AMP) was used to quantify impairments in memory and alertness as measured by EEG and performance on neurocognitive tests. The ESS was administered prior to each AMP session, and the VAS was administered repeatedly throughout the AMP sessions.

**Results :** ESS scores were significantly different at baseline (mean OSA=11.8, healthy=4.3) and were significantly correlated with objective measures of sleepiness (r= 0.31, p<0.01). VAS scores (mean OSA=7.4, healthy=3.3) also correlated with the objective measures pre-treatment (r= 0.25, p<0.01). OSA patients evidenced progressively less sleepiness at each of the post-treatment timepoints for both the objective measures and VAS scores (t=4.03, p<0.01; t=3.07, p<0.05), however, ESS scores showed no significant improvement after the initial post-treatment

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test. The VAS but not the ESS scores were significantly correlated with the composite objective alertness measures post-treatment ( $r=0.36, p<0.01$ ).

**Conclusion :** Within the context of the AMP testing, VAS scores better reflected changes in the objective measures of sleepiness than the ESS scores. This suggests that when patients are asked to gauge their sleepiness following completion of challenging cognitive tasks, it may facilitate their ability to rate their sleepiness. The ESS proved useful in measuring sleepiness pre-treatment, but was not sensitive to the incremental improvements in alertness observed with both the VAS and multiple objective measures obtained over the three-month treatment.

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### 0577

#### RELATIONSHIP BETWEEN DURATION AND FREQUENCY OF OBSTRUCTIVE RESPIRATORY EVENTS

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**Introduction :** Diagnosis of the sleep apnea-hypopnea syndrome depends upon an index that measures the frequency of respiratory events without accounting for event duration, conceivably misrepresenting disease severity, in particular among patients with longer, less frequent apneas.

**Methods :** We retrospectively reviewed 71 consecutive overnight, attended polysomnograms performed in our sleep lab that were manually scored by licensed technicians. A board-certified sleep medicine physician approved all reports. Data points collected included total sleep time, RDI, total number of apneas and hypopneas, average hypopnea time, and average apnea time. Using these variables we calculated a composite index of total event time as a percentage of total sleep time (RDI%).

**Results :** For this cohort of adult patients (25 female, 46 male), the mean AHI was  $29.4 \pm 27.7$ . Mean duration of apneas and hypopneas was 14.7 seconds ( $\pm 9.7$ ) and 17.8 ( $\pm 4.1$ ). Using the Excel data analysis package, we calculated a Pearson correlation between RDI% and RDI of 0.96. The correlation between RDI and total event time independent of total sleep time was 0.90.

**Conclusion :** The close correlation between RDI% and RDI suggests that incorporating data about apnea and hypopnea duration into the commonly used RDI adds little valuable information. Our preliminary data suggest that the RDI adequately reflects any variations in mean apnea and hypopnea duration. Further studies should be done to validate this correlation in a larger population of patients. It would be interesting to see if the RDI% is a more accurate predictor of cardiovascular mortality associated with Sleep Disordered Breathing.

**Support (optional):**

### 0578

#### A MULTI-CENTER, RANDOMIZED CONTROLLED TRIAL OF THE FIRST AUTOMATICALLY TITRATING BILEVEL POSITIVE AIRWAY PRESSURE DEVICE DURING POLYSOMNOGRAPHY

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**Introduction :** Several automatically titrating nasal continuous positive airway pressure devices are available for the treatment of obstructive sleep apnea. A technologically unique and innovative device that automatically adjusts inspiratory and expiratory pressures (Auto Bilevel, Respironics, Inc.) is evaluated in a randomized, controlled trial.

**Methods :** Seventeen patients (10 males, Mean age  $39.7 \pm 1.2$ , BMI  $35.6 \pm 5.5$ ) with a previously identified apnea-hypopnea index of  $\geq 15$  events/hr-1 participated. Patients were medically stable and did not exhibit other sleep disorders. Patients were naive to treatment and had three sleep studies. The first night's PSG determined conventional bilevel (inspiratory and expiratory) pressures following a standardized titration protocol. On the second and third night, therapy was randomized. One night conventional bilevel therapy using pressures determined on night 1 was used. On the other night patients received Auto Bilevel therapy set to deliver between 4 and 20 cm H<sub>2</sub>O. PSG data were reviewed and scored. Results were compared with a paired t-test with significance set  $p \leq 0.05$ .

**Results :** (Data: auto bilevel, fixed pressure bilevel night; mean  $\pm$  standard deviation). There were no significant differences in sleep architecture (TST  $330 \pm 21$  and  $331.7 \pm 31$  min., SE  $86.4 \pm 7.4$  and  $83.5 \pm 10.4\%$ , REM (%TST)  $17.5 \pm 11$  and  $18.3 \pm 7\%$ ). Compared to the diagnostic night, both auto and conventional bilevel reduced the AHI significantly from  $42.4 \pm 24$  to  $2.61 \pm 3$  and  $4.8 \pm 7.8$  ( $p < 0.001$ ). There were no significant differences in the mean saturation and lowest saturation on both nights. The 90% IPAP pressure was  $11 \pm 3.1$  and conventional IPAP was  $11.88 \pm 3.3$  (ns). Average IPAP was significantly lower ( $9 \pm 2.6$ ,  $11.9 \pm 3.3$ ,  $p < 0.01$ ). 90% EPAP was  $8.1 \pm 3.6$  and  $6.4 \pm 2.8$  ( $p = 0.03$ ). Comparing average EPAP to the conventional EPAP, there were no significant differences.

**Conclusion :** These data suggest that Respiration's new Auto Bilevel device treats obstructive sleep apnea as well as effectively as manually titrated, conventional bilevel positive airway pressure therapy.

**Support (optional):** Respiration, Inc.

### 0579

#### DEPRESSION AND OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH CORONARY HEART DISEASE

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**Introduction :** Depression is a risk factor for adverse cardiac events in patients with coronary heart disease (CHD) but the mechanism underlying this association is unknown. Depression and Obstructive sleep apnea/hypopnea syndrome (OSAHS) are frequently comorbid. OSAHS is a risk factor for cardiac events in patients with coronary heart disease (CHD). Undetected OSAHS could explain the increased risk associated with depression.

**Methods :** CHD patients with major (MD, N=53), minor (md, N=36), or no depression (ND, N=43) who were medically stable, were evaluated for two nights in a sleep medicine laboratory.

**Results :** There was no difference in prevalence of OSAHS across groups (MD 66%, md 69%, ND 77%;  $p > 0.05$ ). Patients with MD had a greater frequency of apneic events, desaturations per hour and a significantly longer duration of apneas and hypopneas than those with md, but there were no differences with MD and ND patients in frequency of apneic events or desaturations. Males with MD had a greater frequency of episodes than males with ND, whereas females with MD had fewer episodes than ND females. Apnea duration was longer in patients with

MD as compared with ND patients. There was no difference in the mean duration of apnea per hour between md and ND patients.

**Conclusion :** OSAHS is not more common in depressed CHD patients. However, MD is associated with a longer obstructive sleep apneic episodes in both men and women, with a higher frequency of episodes in men.

**Support (optional):**

## 0580

### MODERATORS OF COGNITIVE DYSFUNCTION IN OBSTRUCTIVE SLEEP APNEA: APPLYING THE COGNITIVE RESERVE THEORY

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**Introduction :** Obstructive Sleep Apnea (OSA) is a serious medical disorder with extensive daytime consequences. Cognitive compromise is often reported in OSA, but not all patients demonstrate deficits. The theory of cognitive reserve suggests that above average intelligence may be a moderator of dysfunction. This study examines the role of cognitive reserve in OSA as a moderator of dysfunction in several cognitive domains.

**Methods :** One-hundred-ninety-six participants (129 men, 67 women; mean age=50.4) with moderate to severe OSA (mean respiratory disturbance index=43.8) were administered a battery of standardized neuropsychological tests prior to and after 3 months of positive airway pressure treatment. Participants were dichotomized into High IQ and Normal IQ groups using a standard clinical cutoff based on estimated verbal IQ. T-scores were calculated using published normative data to determine clinical impairment. Comparisons of the rate of impairment were then made between the two IQ groups at both time points to determine cognitive response to treatment.

**Results :** Groups did not exhibit differences in OSA severity or key demographic factors. At baseline, high IQ participants demonstrated less likelihood of impairment compared to normal IQ participants on tests of executive function ( $\eta^2=6.8$ ,  $p<.01$ ), memory ( $\eta^2=22.1$ ,  $p<.01$ ), and vigilance ( $\eta^2=9.9$ ,  $p<.01$ ), but no other cognitive tests. Results were similar at 3 months. Although greater impairment was observed at baseline in normal IQ participants, high IQ participants demonstrated a greater tendency to improve on tests of memory ( $\eta^2=4.0$ ,  $p<.05$ ) and executive function ( $\eta^2=6.6$ ,  $p<.02$ ) following 3 months of treatment.

**Conclusion :** The findings suggest that cognitive reserve, as measured by IQ, moderated cognitive dysfunction in only certain domains in this clinical sample. High cognitive ability was also shown to moderate response to treatment, showing an advantage for the domains of memory and executive function. These findings extend cognitive reserve theory to recovery of cognitive function in individuals with OSA.

**Support (optional):** Research supported by the National Heart, Lung, and Blood Institute (R01 HL67209).

## 0581

### SATISFACTION AND COMPLIANCE WITH CPAP : SPLIT-NIGHT VS TWO NIGHT PROTOCOL

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**Introduction :** We hypothesized 1. that there would be a correlation

between compliance to therapy with the satisfaction the patients experienced after the first night of sleep with the CPAP in the laboratory and 2. that the satisfaction experienced by patients after a full night's sleep with the CPAP would be greater than that experienced after a split-night protocol for the prescription of CPAP.

**Methods :** Retrospective database review was performed for patients who underwent CPAP prescription sleep studies in our laboratory in 2003. Group I underwent a full diagnostic polysomnogram and returned for a full titration night. Group II underwent a split-night protocol using standard Medicare criteria (April 1,2002) for the administration of CPAP. Patients were assigned to one group or the other based on clinical judgment. Satisfaction measures were based on post-sleep questionnaires completed in the morning after the CPAP titration. Compliance measures were based on phone or mail follow up questionnaires.

**Results :** Group I, N=109, vs Group II, N=79, was older (54vs47\*), had lower BMI (35vs45\*), had lower ESS scores pre-CPAP (11vs14\*), lower baseline AHI (34vs67\*), longer baseline SL (10vs7\*). There were no significant differences in compliance between the groups although there was a tendency for Group I to be more compliant with CPAP compared with Group II (65.1 vs 54.4%). There were no significant differences in satisfaction between the groups. There was no correlation between CPAP compliance and the responses to the satisfaction questionnaires.

**Conclusion :** In this retrospective review, there was no correlation between compliance to therapy with the satisfaction the patients experienced after the first night of sleep with the CPAP in the laboratory. The satisfaction experienced by patients after a full night's sleep with the CPAP was not greater than that experienced after a split-night protocol for the prescription of CPAP. (\*  $p<.05$ )

**Support (optional):**

## 0582

### INFLUENCE OF POSTURE IN THE CEPHALOMETRIC PARAMETERS USED TO EVALUATE UPPER AIRWAY OBSTRUCTION IN SLEEP APNEA PATIENTS

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**Introduction :** A systematic evaluation of upper airway in patients with sleep apnea seems to be crucial to select patients for surgery and improve clinical outcomes. Cephalometric radiograph is the simplest and most practical upper airway imaging technique. One of its limitations is that the patient is evaluated while awaked and seated. The possibility to perform cephalometric films in supine position could improve the evaluation of the upper airway during sleep. The aim of our study was to examine the influence of postural changes on the main cephalometric parameters used in sleep apnea surgical protocols, and its impact on selection criteria.

**Methods :** One hundred fifty-six consecutive patients were analysed. All patients had a detailed examination of the upper airway, a conventional polysomnography, and cephalometric radiographs in supine and seated positions. The cephalometric parameters included: palate length (P), posterior airway space (PAS), distance of hyoid from inferior mandible (MP-H), maxilla to cranial base angle (SNA), mandible to cranial base angle (SNB). Mean and standard deviation values were calculated for each parameter. A Wilcoxon test was used to compare the values. A  $p<.05$  was considered as statistically significant.

**Results :** The mean age of the sample was  $50.32 \pm 11.08$  (range, 17-78), with a body mass index of  $28.55 \pm 4.29$ . The comparison between groups showed a slight increment of P value ( $p=.01$ ) and a consistent reduction in SNB ( $p<.000$ ) in the supine position. Parameters like PAS or MP-H, that have been widely used to select patients for palate surgery alone, did not change significantly in our study.

## Category I—Sleep Disorders-Breathing

**Conclusion :** Changes on cephalometric parameters obtained in a group of sleep apnea patients in two different awake situations (seated or supine) are minimal except for the SNB, suggesting that selection criteria protocols based on SNB values could be underestimated.

**Support (optional):**

### 0583

#### COGNITIVE FUNCTION AND CHRONIC INTERMITTENT NOCTURNAL HYPOXEMIA IN OBSTRUCTIVE SLEEP APNEA

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**Introduction :** Obstructive sleep apnea (OSA) is associated with chronically fragmented sleep and intermittent oxyhemoglobin desaturation, or hypoxemia. Although impairments across a range of cognitive functions have been demonstrated in individuals with OSA, their pathogenesis remains poorly understood. The objective of this study was to examine the contribution of hypoxemia in OSA to performance on tests of cognitive function independent of the effects of sleep fragmentation.

**Methods :** One-hundred-nineteen participants (80 men, 39 women; mean age=50.4) with moderate to severe OSA (mean respiratory disturbance index (RDI)=48.5) were dichotomized into low hypoxemia (< 6% total sleep time below 90% blood oxygenation; n=40) and high hypoxemia (> 20% total sleep time below 90% blood oxygenation; n=79) groups based on the top and bottom third of the hypoxemia distribution of a larger sample of 197 participants. All participants were administered a battery of standardized cognitive tests prior to initiation of OSA treatment.

**Results :** There were no group differences on age, IQ, education, or subjective measures of daytime sleepiness or daily functioning. ANCOVA covarying for RDI, body mass index, and total sleep time revealed significant group differences on learning, total recall, and delayed recall indices of a test of memory (F=15.0 to 6.31, p<0.01 to p<0.02), but not on performance on any other cognitive test. Post-hoc analyses indicated that individuals in the low hypoxemia group performed relatively worse on the memory test compared to the high hypoxemia group.

**Conclusion :** Untreated, newly diagnosed OSA participants with high levels of hypoxemia demonstrate relatively better performance on a test of verbal memory compared to participants with low levels of hypoxemia, independent of the effects of other clinical and demographic variables. The mechanism through which this relationship occurs requires further elucidation. One potential speculation is that individuals with more severe hypoxemia may develop compensatory mechanisms at the cellular level, such as pre-conditioning.

**Support (optional):** Research supported by the National Heart, Lung, and Blood Institute (R01 HL67209).

### 0584

#### EFFECTS OF TREATMENT FOR OSA ON MR SIGNAL DURING A WORKING MEMORY TASK

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**Introduction :** Obstructive Sleep Apnea (OSA) has been associated with both medical and psychological consequences and has even been reported as a predictor of stroke. Cognitive correlates of OSA have been reported in several cognitive domains, but a clear picture of cognitive dysfunction has not yet been determined. Treatment for OSA has demonstrated

improvement in certain cognitive functions. Our objective was to determine the degree to which treatment affected MR signal in OSA during the completion of a working memory task.

**Methods :** Ten individuals with moderate to severe OSA were recruited from a larger clinical sample. Participants completed a working memory task called the 2-back task. Participants completed this task during fMRI sessions after effective treatment and after withholding treatment for 2 consecutive nights. Adherence to treatment was monitored objectively. Conditions were delivered in a counterbalanced manner and participants were practiced on the cognitive activation task before each session.

**Results :** Multiple regression was used to identify regions where activation was associated with task condition after controlling for head movement. Nine regions of interest were identified as activated in either of the two experimental conditions (on or off treatment). These nine regions were then examined using paired t-tests comparing treatment condition. Three regions showed greater intensity of activation with treatment: (1) the right posterior parietal cortex (PPC); (2) bilateral cingulate, and (3) the right dorsolateral prefrontal cortex. In contrast, the left dorsolateral prefrontal cortex showed greater intensity of activation without treatment. Moreover, the left PPC showed greater voxel recruitment without treatment and a trend toward greater activation within those voxels. There were no other volumetric changes associated with treatment condition.

**Conclusion :** This study has implications for a better understanding of the neurofunctional underpinnings of OSA and the effects of treatment on brain function.

**Support (optional):** Research supported by the Ittleson Foundation.

### 0585

#### EFFECT OF AGE ON SLEEPINESS IN MORBIDLY OBESE PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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**Introduction :** It has been well established that the prevalence of obstructive sleep apnea (OSA) among patients with morbid obesity is much higher compared to the general population. The relationship between age and the subjective perception of sleepiness in morbidly obese patients with OSA merits further investigation. The purpose of this study was to determine if younger morbidly obese patients with OSA have lower Epworth scores than older morbidly obese patients with OSA.

**Methods :** Patients in the study with suspected OSA were referred from their primary physician to the sleep disorders center for the purposes of a sleep evaluation. A complete sleep history was obtained on all patients. It was at this point that clinical lab values for the Body Mass Index (BMI) and Epworth scores (EP) were obtained. A full nocturnal polysomnogram was performed on all patients using a standard 16-channel montage. For the purposes of the study, patients were considered positive for OSA if the apnea-hypopnea index (AHI) was greater than 15 events per hour. Patients were considered morbidly obese if their BMI was greater than 40. Patients were grouped into 3 age brackets of Less than 30, 30 - 50, Greater than 50. The average Epworth score was calculated for each group. The average BMI and AHI of each group was also calculated.

**Results :** Of 105 patients with morbid obesity and documented OSA, 21 had ages <30, 52 had ages between 30-50, and 32 had an age >50. The difference in Epworth Scores between the 30-50 age group and the Over 50 age group was not statistically significant. The Under 30 Age group had an Epworth of only half of the other two groups.

**Conclusion :** For the same degree of OSA and morbid obesity there is a trend for the average Epworth score to increase significantly as age increases past the 30 year mark. Further investigation may be helpful in discovering the reason for this finding. Epworth scores viewed alone might not warn the clinician of the presence of significant OSA in the

younger morbidly obese patient.

**Support (optional):** AGE<30 AGE 30-50 AGE>50 AVG AGE 22.8 41.4 60.0 AVG AHI 57.1 60.9 49.3 AVG BMI 44.9 45.2 46.7 AVG EP 5.6 11.2 11.4

## 0586

### HIGH PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH UNCONTROLLED HYPERTENSION

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**Introduction :** Among individuals with systemic arterial hypertension (SAH) a high proportion has obstructive sleep apnea (OSA). In cases of resistant hypertension (RH; BP>140/90mmHg in treatment with three or more correct drugs) the prevalence of OSA reaches 83%. The diagnosis of RH can be confused by poor adherence to treatment, white coat hypertension, and masked hypertension. Previous studies lacked control for these biases. In this study we controlled for confounders, confirmed RH with ambulatory blood pressure monitoring (ABPM) and diagnosed OSA with portable polysomnography (PP).

**Methods :** We studied 95 consecutive patients, 67 women, attending the hypertension unit, by means of ABPM and PP level III with SomnoCheck (Weinmann, Germany), 59 with controlled (CH) and 36 with uncontrolled hypertension (UH) defined by 24-hour BP>130/80mmHg. We excluded patients with heart failure, cancer, stroke, chronic lung disease, and those with confirmed inadequate adherence to treatment of hypertension.

**Results :** The proportion of patients with more than 10 AH/h in the CH group was 33% and in the UH group it was 56% ( $p=0.026$ ). The apnea-hypopnea index (AHI) significantly correlates with systolic ( $r=0.221$ ;  $p=0.041$ ) and diastolic blood pressure PAS ( $r=0.259$ ;  $p=0.016$ ). In a step-wise linear regression analysis, AHI is the single variable included in the model to explain systolic ( $p=0.041$ ) and diastolic ( $p=0.025$ ) BP in the ABPM, when controlling for age, gender, and BMI.

**Conclusion :** This is the first study to employ a control group, ABPM and portable polysomnography to assess the association of OSA with uncontrolled hypertension. The findings suggest that OSA may be associated with higher prevalence of RH confirmed by ABPM. This emphasizes the need for excluding OSA in the hypertensive population

**Support (optional):**

## 0587

### A NOVEL TWO-MINUTE MEASURE OF BREATHING VARIABILITY AROUND SLEEP ONSET PREDICTS SLEEP DISORDERED BREATHING

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**Introduction :** The pathogenesis of Sleep Disordered Breathing (SDB) is believed to relate to the instabilities in the respiratory chemical/neuromuscular control systems. These instabilities can be particularly pronounced at the wake-sleep transition due to the removal of the wakefulness stimulus. It was thus hypothesized that a marker for the individual's propensity for SDB could be developed by a spectral-based quantification of respiratory variability around the sleep onset time. A measure, termed "Apnea Propensity Index (API)" was derived and assessed for its ability to predict SDB.

**Methods :** The general derivation of API is based on characterization of the time-varying power spectral density (spectrogram) of a respiratory signal during a short window of time. For this study, API was calculated

from the normalized variance of the spectrogram of the abdominal inductance signal in specific frequency bands during a 2-minute period around the very first wake-sleep transition. API was then independently computed from the previously recorded overnight Polysomnography data (abdominal inductance plethysmography) of 599 subjects (age  $40.4\pm 19.7$  yrs, 58% females, mean AHI  $13.0\pm 19.9$ ) who had participated in the Cleveland Family Study.

**Results :** Unadjusted correlations showed that the API was significantly associated with: male gender, age, body mass index, hypertension, and diabetes, as well as with the AHI, arousal index, and indices of overnight desaturation. Of all covariates, the API was most strongly associated with the AHI ( $r=0.38$ ,  $p<.001$ ). Multiple linear regression analysis showed that the API significantly predicted the AHI after adjusting for other covariates ( $p<0.001$ ). Logistic regression analysis for predicting SDB (defined as AHI >5) showed that each 0.5 standard deviation increase in the API was associated for a 50% increased likelihood of SDB (Odds Ratio: 1.5; 95% CI: 1.35-1.66;  $p < 0.0001$ )

**Conclusion :** The novel API computed from a 2-minute window around the wake-sleep transition demonstrates a good potential to be used as the predictor of SDB.

**Support (optional):** 1R43 HL076986-01A1 and HL 46380

## 0588

### SLEEP DISORDERED BREATHING IS COMMON IN PATIENTS WITH SCLERODERMA-ASSOCIATED PULMONARY COMPLICATIONS

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**Introduction :** Sleep disordered breathing (SDB) rates in patients with scleroderma have been reported to be low. However, the subset of patients with pulmonary complications, including interstitial lung disease (ILD) and pulmonary hypertension (PH), may be susceptible to SDB and ventilatory instability. Our objectives were to determine the rates of SDB in patients with scleroderma and pulmonary complications.

**Methods :** Scleroderma patients, recruited from the outpatient setting of a large tertiary academic hospital, were included if 1) stable medical condition for the previous 4 weeks; and 2) no change in medications in the previous 4 weeks; and 3) presence of ILD (by computed tomography or biopsy) and/or PH (by transthoracic echocardiogram with estimated right ventricular systolic pressure>40 mm Hg or cardiac catheterization with mean pulmonary arterial pressure>25 mm Hg). Standard nocturnal polysomnography was performed on all subjects. Airflow was monitored using nasal cannula. In addition to standard sleep indices, breathing pattern was analyzed during samples of quiet wakefulness and stable non-REM sleep throughout the night.

**Results :** Of the first ten subjects (9 female, 1 male) studied, 9 had PH and 4 had ILD (3 had both), with overall median age 58.6 years (IQR 52.7-62.0 years) and median body-mass index 25.7 kg/m<sup>2</sup> (IQR 24.6-30.6). Seven of ten subjects had an apnea-hypopnea index >5 events/hr (median 6.9/hr; IQR 3-23.4/hr). Four subjects had a respiratory rate (RR) >20 (mean 23.9/min, SD 4.8/min) during quiet wakefulness, and five subjects had a paradoxical increase in RR from wake to non-REM (wake: mean 18.3/min, SD 2.8/min; mean increase in RR in non-REM 1.6/min SD 0.5/min).

**Conclusion :** Scleroderma patients with pulmonary complications exhibit high rates of disordered breathing and abnormal breathing patterns during sleep, which may contribute to disrupted sleep architecture and daytime symptoms of sleepiness and fatigue.

**Support (optional):** NIH HL72126

0589

**THE EPWORTH SLEEPINESS SCALE PREDICTS DOZING OFF AT THE WHEEL AND AT WORK; SLEEP DISORDERED BREATHING DOES NOT**

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**Introduction :** Excessive daytime sleepiness (EDS) is the primary symptom of several sleep disorders, including sleep disordered breathing (SDB). Subjective measures of daytime sleepiness may not correlate with objective manifestations. This study sought to determine the association between the Epworth Sleepiness Scale (ESS), SDB, and two daytime manifestations of sleepiness.

**Methods :** This cross-sectional retrospective chart review examined subjects, age  $\geq 18$ , who underwent polysomnography. Each subject completed the ESS and a questionnaire, which included the two questions: "Have you nodded off at the wheel?" and "Have you dozed off at work?" Subjects were divided into two groups based on ESS score (Group 1: ESS  $< 10$ ; Group 2: ESS  $> 15$ ). Two subgroups of each group were determined by apnea-hypopnea index (Non-SDB: AHI  $< 5$ ; SDB: AHI  $\geq 20$ ). Percent of "yes" responses to each of the above questions was calculated for Groups 1 and 2 and each subgroup.

**Results :** Fewer subjects in group 1 (n=101) admitted to nodding off at the wheel than in group 2 (n=119) (28% vs. 70%;  $P < .0001$ ). Fewer subjects in group 1 admitted to dozing off at work than in group 2 (30% vs. 74%,  $P < .0001$ ). Within group 1, there was no significant difference between subjects with SDB (n=15) and those without SDB (n=41) in nodding off at the wheel (13% vs. 28%,  $P = .2606$ ) or dozing off at work (13% vs. 25%,  $P = .3392$ ). Within group 2, there was no significant difference between subjects with SDB (n=15) and those without SDB (n=60) in nodding off at the wheel (71% vs. 68%,  $P = .8004$ ) or dozing off at work (60% vs. 69%,  $P = .4856$ ).

**Conclusion :** These findings demonstrate a strong association between the ESS and dozing behind the wheel and at work. SDB itself did not appear to predispose to these manifestations.

**Support (optional):**

0590

**INDIVIDUAL DIFFERENCE IN PATTERNS OF ADHERENCE TO PAP IN OBSTRUCTIVE SLEEP APNEA**

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**Introduction :** Positive airway pressure (PAP) is the most common form of treatment for OSA. PAP is effective but adherence is often poor. Adherence is a complex behavior and difficult to characterize with a complete appreciation for individual differences. To date, few studies have attempted to address individual differences in adherence to PAP. We applied time series data analysis techniques to highlight and attend to individual differences in long-term PAP adherence.

**Methods :** Seventy-one participants with moderate to severe OSA (21 women, AHI =  $44 \pm 23$ ) had their PAP adherence monitored objectively over the course of a year. Daily adherence data were plotted on 365-day

graphs, which were then grouped into categories by two independent raters. Raters reached 82% agreement in their groupings and disagreement was decided by consensus. This method is consistent with time series data analysis procedures. Time series statistics were calculated for each grouping including the level (mean nightly use), variance, and slope.

**Results :** Seven distinct categories of users were identified and given the following descriptors: 1) good users (24% of the participants), 2) slow improvers (13%), (3) slow decliners (14%), (4) variable users (17%), (5) occasional attempters (8%), (6) early drop-outs (13%), and (7) non-users (11%). Good users had high average use (6.55 hrs/nt) and little variability (2.06 hrs/nt) or slope over time. Slow improvers demonstrated a positive slope with time, occurring between 3 and 6 months of use. Slow decliners demonstrated a negative slope, occurring at the same period. Variable users had many good and bad nights of use with a non-systematic high range.

**Conclusion :** This is the first study to identify multiple adherence groups, suggesting that PAP use can be approached in several ways over the course of a year. These results have implications for the development and evaluation of different approaches to target different reasons for poor adherence.

**Support (optional):** Research supported by the National Heart, Lung, and Blood Institute (R01 HL67209).

0591

**SUSTAINED HYPOXIA DECREASES SENSORY PROCESSING TO BRIEF PULSES OF NEGATIVE UPPER AIRWAY PRESSURE DURING NREM SLEEP**

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**Introduction :** Hypoxia is common in several respiratory disorders including sleep apnea and sleep hypoventilation syndrome. Sustained hypoxia has been shown to have depressant effects on ventilation, respiratory load sensation and cough and therefore may have deleterious effects in hypoxic respiratory disorders. Using respiratory related evoked potentials (RREP)s hypoxia has recently been shown to depress sensory processing to brief respiratory resistive loads during wakefulness. We hypothesized that sustained hypoxia would similarly depress respiratory sensory processing during sleep.

**Methods :** On two separate occasions, 9 healthy males slept overnight in the sleep laboratory instrumented with scalp EEG electrodes (C3, Cz, C4, Fz and Pz) and standard EOG and EMG recordings for sleep staging and arousal scoring. In random order, subjects breathed normoxia (medical air) or isocapnic hypoxia ( $\text{SaO}_2 \approx 85\%$ ) via a nasal mask and pneumotachograph throughout each visit. Upper airway negative pressure pulses ( $\approx -12$  cmH<sub>2</sub>O mask pressure, 250 msec) were delivered during early inspiration via a computer-controlled rapid actuating solenoid valve system during stable NREM sleep and the following morning during wakefulness to elicit RREPs. Approximately 75 pulses per subject were identified that were not associated with ASDA arousal or movement artifact. The EEG responses to these pulses were ensemble averaged across NREM sleep stages to generate RREP waveform components in each condition. Similarly, approximately 55 pulses under each gas condition were averaged to generate RREP components during wakefulness.

**Results :** Stimulus magnitude was well matched between hypoxia and normoxia during sleep (minimum mask pressure  $-12.0 \pm 1.5$  vs.  $-13.6 \pm$

1.9 cmH<sub>2</sub>O) and wakefulness ( $-12.1 \pm 1.2$  vs.  $-12.7 \pm 2.2$  cmH<sub>2</sub>O respectively). Whilst data collection remains ongoing, the main finding of this preliminary analysis was a decrease in the amplitude of the P2 component of the RREP at Cz during hypoxia compared to normoxia during both sleep ( $32.4 \pm 4.3$  vs.  $37.9 \pm 4.0$   $v$   $p=0.04$ ) and wakefulness ( $32.5 \pm 4.3$  vs.  $39.2 \pm 2.5$   $v$   $p=0.03$ ).

**Conclusion :** Hypoxia-induced depression of respiratory sensory processing during sleep, as demonstrated in this study, extends previous wakefulness findings and suggests that respiratory sensory depression may be impaired across a range of hypoxic-respiratory disorders including sleep apnea and sleep hypoventilation syndromes.

**Support (optional):** This work was funded by the National Health and Medical Research Council, Australia

## 0592

### ESTIMATING THE IMPACT OF THE U.S. OBESITY EPIDEMIC ON TRENDS IN PREVALENCE OF SLEEP DISORDERED BREATHING

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**Introduction :** Obesity, a cause of sleep-disordered breathing (SDB), is increasingly prevalent in the U.S. Consequently, prevalence of SDB may also be expanding. We investigate the influence of the obesity epidemic on SDB from 1992 to 2004.

**Methods :** Using data from 1359 participants of the Wisconsin Sleep Cohort, a population-based longitudinal study of laboratory-assessed SDB initiated in 1989, we estimated age- and sex-specific risks of having SDB ( $\geq 5$  apnea+hypopnea events/hr) attributable to excess body weight for 4 body mass index (BMI) categories:  $<25$  (reference), 25-29, 30-39, and  $\geq 40$  kg/m<sup>2</sup>. Then, using both U.S. Census and Centers for Disease Control and Prevention data, we extrapolated the Wisconsin Sleep Cohort prevalence and risk estimates to the 1992 and 2004 U.S. age, sex and BMI distributions of 30- to 69-year-olds (the age span represented in the Sleep Cohort). From this extrapolation we calculated point estimates (confidence intervals are not presented here because parameter variances are affected by the multiple data sources) of U.S. prevalences of SDB in 1992 and 2004, as well as the proportion of SDB due to excess weight.

**Results :** In 1992, we estimate that, among 30-49 year-olds, 17% of men and 6% of women had SDB; for 50-69 year-olds, 37% of men and 14% of women. An estimated 40% of SDB cases were due to excess weight. In 2004, due to expanding prevalence of excess weight, we estimate that SDB prevalence had increased: among 30-49 year-olds, 21% of men and 9% of women had SDB; among 50-69 year-olds, 40% of men and 17% of women. The estimated proportion of SDB cases due to excess weight grew to 69%.

**Conclusion :** In response to the U.S. obesity epidemic, the prevalence of SDB in adults is likely to be rising precipitously and will continue to do so if the obesity epidemic does not abate.

**Support (optional):** Grants R01HL62252, RR03186, and R01AG14124 from the National Institutes of Health

## 0593

### CCK-B ANTAGONIST REDUCES RESPIRATORY RHYTHM DISTURBANCES DURING SLEEP

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**Introduction :** Inhibition of vagal afferents by peripherally acting sero-

tonin antagonists increases upper airway muscle activity in English bulldogs and reduces obstructive and central sleep apnea expression in bulldogs and rats, respectively. Endogenous CCK is a potent activator of vagal afferent neurons and here, we test the impact of a CCK-B antagonist (CR2945) on sleep and breathing in rats.

**Methods :** In chronically instrumented Sprague-Dawley rats, we recorded (09:00 - 15:00) sleep and breathing (plethysmograph) on 5 occasions separated by at least 3 days: following sham injection (i.p. DMSO 1 ml/kg), and after injection with 0.005, 0.05, .05, or 5.0 mg/kg CR2945 (in DMSO). Injection sequence was randomized in each animal. Sleep was staged on 10 s epochs and apneas (pauses  $> 2.0$  s) were associated with sleep stage of occurrence and according to the presence (post-sigh, PS) or absence (spontaneous, SP) of an immediately preceding sigh.

**Results :** Sleep architecture was unchanged from baseline by any dose ( $p > 0.1$  for %W, %NREM and %REM for each dose versus sham). SP apnea index was reduced to 42% and 31% of the placebo value by the 0.5 and 5.0 mg/kg doses, respectively ( $p < 0.03$  for each), but apnea duration was not affected by any dose ( $p = 0.7$ ). Similar reductions were observed for NREM SP apnea index ( $p < 0.05$  for 0.5 and 5.0 mg/kg). REM SP apnea index was significantly reduced by all 4 doses tested ( $p < 0.04$  for each).

**Conclusion :** The frequency of spontaneous central apnea expression is significantly reduced in all sleep stages in rats by systemic administration of a CCK-B receptor antagonist. We speculate that this results from inhibition of vagal afferent neurons. These findings support further exploration of the target tissue and receptor subtype specificity of these effects.

**Support (optional):**

## 0594

### THE USE OF THE BERLIN SCREENING QUESTIONNAIRE IN A BARIATRIC SURGERY POPULATION

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**Introduction :** Bariatric surgeries are increasingly used as a means for weight reduction. The morbidly obese patients that pursue bariatric surgery have high rates of obstructive sleep apnea (OSA). Although bariatric surgery can be a successful treatment for OSA via weight loss, untreated OSA at the time of surgical intervention may lead to complications in the perioperative period. Thus, identification of patients who may have OSA prior to surgery and general anesthesia is important. This investigation was intended to evaluate the Berlin Questionnaire as a screening tool for OSA in the bariatric surgery population.

**Methods :** Patients evaluated for bariatric surgery from April 2005 to November 2005 were administered a Berlin questionnaire to assess risk for sleep apnea. Patients having positive responses in at least 2 of 3 categories were deemed to be high risk for OSA and underwent attended overnight polysomnography in the standard fashion. PSG scoring was performed using R&K and AASM standards using a hypopnea definition of 30% airflow reduction and 4% or greater oxygen desaturation. OSA was considered present if the apnea hypopnea index was greater than 5/hr with symptoms or 15/hr without symptoms.

**Results :** 139 consecutive patients who were deemed high risk by Berlin questionnaire screening underwent PSG. 105 patients met criteria for OSA leading to a specificity of 75.5% when comparing the Berlin questionnaire to the gold standard of PSG. All patients had a body mass index of greater than 40.

**Conclusion :** The Berlin screening questionnaire for OSA is a useful tool when evaluating bariatric surgery patients preoperatively. Future directions should involve the evaluation of bariatric surgery patients who do

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not have high risk Berlin questionnaire screening in order to gain a better understanding of the sensitivity of this tool in this specific patient population.

**Support (optional):**

### 0595

#### INCIDENCE OF OBSTRUCTIVE SLEEP APNEA IN CHEMICAL EXPOSED POPULATION

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**Introduction :** The data on chemically exposed patients in the past suggests that there is a high correlation between sleep disturbance and chemical exposure. The purpose of this study to evaluate the subjects using polysomnography.

**Methods :** This is a retrospective study in which 165 patients (26 female, 139 male) who suffered exposure to Hydrochloric acid, chlorinated methanes (methylene chloride, methyl chloride) underwent one night of diagnostic polysomnography. The mean age of the patient group was  $38 \pm 10$  and the mean body mass index was  $28.3 \pm 5.6$ . The parameters monitored were left / right oculogram, central / occipital electroencephalography, chin / leg electromyography, nasal / oral airflow measured by thermister, chest / abdominal inductance plethysmography, and oxygen saturation.

**Results :** Sleep efficiency in this population was reduced with a mean of  $77\% \pm 15.5$ . The mean respiratory disturbance index was  $9.32 \pm 18$  and the REM RDI was  $12.8 \pm 20.8$ . Although the mean BMI is low at 28, the percentage of subjects with sleep apnea (RDI  $\geq 5$ ) was high at 38.7% as opposed to the 5% in the normal population.

**Conclusion :** This study indicates that exposure to certain chemicals can cause sleep apnea in otherwise normal patients and future studies may clarify the specific chemicals associated with this syndrome.

**Support (optional):**

### 0596

#### IMPLEMENTATION OF A SLEEP APNEA SCREENING PROTOCOL IN AN INPATIENT POPULATION

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**Introduction :** A higher prevalence of sleep apnea may be present in an inpatient population due to a greater prevalence of co morbidities putting patients at greater risk of poor outcome due to acute cardiovascular, pulmonary and neurologic complications of sleep apnea. To address this issue a clinical pathway was implemented to identify patients with sleep apnea to assess need and provide intervention.

**Methods :** A new clinical pathway, PRAIS (Protocol for Recognition of Apnea in Sleep), was implemented in 2004 at a large tertiary care center. Patients were screened using a three item nurse administered questionnaire. A sleep medicine assessment was ordered if at least one positive answer was given or if there was 1) witnessed apnea; 2) clinical history suggesting sleep apnea; and/or 3) presence of high risk co-morbidity such as recent stroke or active cardiopulmonary disease. The assessment of patients with suspected sleep apnea included overnight oximetry recording when appropriate. Patients were excluded if their health status was inappropriate for testing or treatment e.g. DNR orders present, sinus surgery, etc., they refused testing or treatment, or they were discharged or expired before assessment could be conducted (n = 93).

**Results :** 631 inpatients were evaluated between January 2004 and

September 2005. Age range was from 17 to 92, with a mean age of 59, and 56% were male. Of 232 receiving oximetry testing 86% were positive for significant desaturation episodes. Four percent did not have sleep apnea, 39% had past sleep apnea and 56% had a new diagnosis of sleep apnea. Of these 631, 27% (n=169) made follow up appointments at our outpatient clinic, 11% (n=72) did not wish to make follow up appointments, and 6% (n=36) were referred to other sleep centers.

**Conclusion :** An inpatient sleep apnea screening protocol can be successfully implemented with significant identification of newly diagnosed sleep apnea patients in need of CPAP treatment.

**Support (optional):**

### 0597

#### PREDICTIVE EQUATION INADEQUATE FOR ESTABLISHING THERAPEUTIC CONTINUOUS POSITIVE AIRWAY PRESSURE LEVELS

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**Introduction :** In our sleep laboratory ~40% of patients undergoing split night protocol require an additional study to titrate CPAP potentially delaying treatment. A predictive formula for CPAP pressure may be helpful in establishing an initial CPAP level for home use. The purpose of our study is to evaluate the predictability and clinical usefulness of such a formula proposed by Miljeteig et al. (1993) in Obstructive Sleep Apnea (OSAS) patients.

**Methods :** 37 newly diagnosed OSAS patients were studied. Predicted CPAP pressure was calculated using the formula  $-5.12 + 0.13 * \text{BMI} + 0.16 * \text{Neck} + 0.04 * \text{AHI}$  (Miljeteig and colleagues). These results were compared with therapeutic CPAP (to reduce AHI  $< 5$ ) level obtained during PSG

**Results :** Body mass index (kg/m<sup>2</sup>), neck circumference (cm) and AHI were obtained and used in the equation to predict the therapeutic CPAP pressures. Predicted value was compared with the actual CPAP pressure established during CPAP titration study. The formula was predictive in 43% (16 out of 37) within +2.5 cm. and in only 16% (6 out of 37) of patients within +1 cm. The formula underestimated the therapeutic pressure majority of the time. The formula predicted the therapeutic CPAP value in fewer patients in our study compared to Miljeteig et al. (43% vs 71%, respectively). However, we considered an optimal therapeutic pressure to be achieved when the AHI  $< 5$  rather than  $< 10$  in the original study.

**Conclusion :** The formula was predictive only 43% of time within a +2.5 cm pressure range. Higher CPAP pressures can be associated with many problems (CPAP intolerance, oral/mask leaks, airway dryness, etc). Suboptimal pressures can leave patients at continued risk for the health consequences associated with sleep apnea. The formula is inadequate in predicting a therapeutic pressure. CPAP titration in the sleep laboratory remains the gold standard for establishing therapeutic pressure. Our study is still ongoing. References: Miljeteig H, Hoffstein V. Determinants of Continuous Positive Pressure Level for Treatment of Obstructive Sleep Apnea. American Review of Respiratory Diseases 1993; 147:1526-1530.

**Support (optional):**

### 0598

#### HYPNOTIC ADMINISTRATION MAY IMPROVE SPLIT-NIGHT PROTOCOL OUTCOMES IN A SUBSET OF OSA PATIENTS: PRELIMINARY STUDY

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**Introduction :** Polysomnography is used for diagnosis and treatment of OSAS. Split night (SN) protocols have been used to reduce time from diagnosis to treatment, minimize patient inconvenience, and reduce cost. It may be difficult to complete both portions of the test in a single night due to the unfamiliar laboratory environment (first night effect). We have developed a protocol to provide a hypnotic (zolpidem) for individuals with sleep difficulties in the laboratory. We investigated the hypothesis that hypnotic administration improves SN protocol outcomes.

**Methods :** Participants: 915 newly diagnosed OSA patients (661m, 254f; mean age 56.7yrs) (AHI=>15) evaluated in four sleep laboratories in our health care system. Hypnotic was available for administration in two of the centers. Group 1 (hypnotic available) 838 patients; 602m, 236f; mean age 56.7yrs; Group 2 (no hypnotic available) 77 patients; 59m, 18f; mean age 56.5yrs. Group 1 received a hypnotic if they were awake over one hour or unable to reach consolidated sleep before 0200.

**Results :** Groups did not differ significantly in gender, age, or success of SN protocol outcome (Group1-60% vs Group2-58%). Of the 838 patients in Group 1, 100 (mean AHI= 37) received a hypnotic the night of their sleep study (12%). The SN was successfully completed in 55 patients (mean AHI=45) and unsuccessful in 45 patients (mean AHI=27).

**Conclusion :** A minority of patients attending a sleep laboratory has difficulty initiating and maintaining sleep. The administration of a hypnotic without myorelaxant properties or significant respiratory suppression allowed 55% of individuals in this study to complete testing in one night preventing a delay in treatment. These individuals had significant OSAS and were at significant risk for motor vehicle accidents and other known health consequences of OSAS if left untreated. This study is ongoing. A more robust effect may be seen with a larger sample size.

**Support (optional):**

## 0599

### ROLE OF CHLORIDE-MEDIATED INHIBITION IN THE NEUROCHEMICAL CONTROL OF AIRWAY MOTONEURONS DURING NATURAL SLEEP IN BEHAVING RATS

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**Introduction :** Muscle tone is suppressed in sleep, particularly in REM sleep. Disturbances of muscle tone underlie most of the major sleep disorders including obstructive sleep apnea as well as bruxism, narcolepsy and REM-sleep behaviour disorder. In order to develop effective pharmacological treatments for such disorders, it is imperative to understand the neurochemical mechanisms that mediate muscle control during sleep. It is hypothesized that muscle activity is suppressed in sleep because motoneurons are actively inhibited by sleep-related neural circuitry. This study aims to understand the role that chloride-mediated inhibition plays in regulating airway motoneuron excitability and hence muscle activity during natural sleep.

**Methods :** GABAergic and glycinergic antagonists (strychnine and bicuculline, respectively) were focally applied onto trigeminal airway motoneurons while masseter muscle activity was monitored in freely behaving rats. Male Sprague-Dawley rats (350-400g; n=6) were implanted with EEG and EMG (masseter and neck) electrodes to determine sleep states. Microdialysis probes were implanted in the left trigeminal motor nucleus for dialysis of artificial cerebral spinal fluid (ACSF) or 0.1mM strychnine and bicuculline onto trigeminal motoneurons across the natural sleep-wake cycle.

**Results :** Application of ACSF onto trigeminal motoneurons had no effect on masseter muscle activity (P=0.548); however, blockade of GABAA and glycine receptors caused a significant increase in masseter muscle activity in all states (two-way ANOVA, P<0.05), and particularly in sleep.

Compared to baseline levels during waking, strychnine/bicuculline application significantly increased masseter muscle activity in NREM sleep by 133% and in REM sleep by 127%.

**Conclusion :** These results suggest that chloride-mediated inhibition plays a key role in mediating trigeminal motoneuron excitability and hence masseter muscle activity during natural sleep. Therefore, neuropharmacological blockade of GABAergic and glycinergic receptors on airway motoneurons could be used as an effective method for reversing the sleep-dependent suppression of airway muscle activity that ultimately underlies obstructive sleep apnea.

**Support (optional):**

## 0600

### LONG TERM FACILITATION IN WAKEFULNESS AFTER REPEATED EPISODIC HYPOXIA

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**Introduction :** Intermittent hypoxia during sleep can evoke long term facilitation of ventilatory motor output(LTF). Manifestations of LTF are decreased upper airway resistance, increased minute ventilation and activation of the genioglossus activity. We wished to determine whether sleep, per se, is required to manifest LTF. We hypothesized that LTF of the genioglossus muscle can occur in wakefulness following repetitive episodes of eucapnic hypoxia.

**Methods :** We studied 5 healthy participants, (1F& 4M) during wakefulness, confirmed by continuous EEG recording. We measured tidal volume, respiratory frequency, minute ventilation and genioglossus EMG. After a control period, 15 brief episodes of hypoxia (< 1 minute each) were induced. Hypoxia was alternated with 1 minute of RA breathing. Isocapnia was maintained by bleeding in CO<sub>2</sub>. Findings are expressed as % of control and averaged for the 5 participants. We compared findings during the RA control and after 20 minutes of recovery (R20).

**Results :** Nadir oxyhemoglobin saturation during trials was 83.4+/-2.0%. Minute ventilation at R20 was 113+/-23.7% of control. Peak and phasic genioglossus activity at R20 were 114.7+/-28.5% and 160.4+/-71.0% of control respectively. Statistical analysis using a paired t-test comparing control and R20 values for minute ventilation and peak and phasic genioglossus EMG did not show a significant difference.

**Conclusion :** 1) There was no evidence of genioglossus or ventilatory LTF in awake humans. 2) We conclude that sleep state, per se, is required for LTF to manifest. 3) We speculate that sleep-related serotonergic changes may contribute to the development of LTF during sleep only.

**Support (optional):**

## 0601

### CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) LEVEL IN OBSTRUCTIVE SLEEP APNEA (OSA): THE AFTERMATH OF VARIOUS MATHEMATICAL MODELS

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**Introduction :** Several anatomic and functional characteristics have been shown to be independent determinants of the effective level of CPAP to treat OSA: body mass index (BMI), neck circumference (NC) and apnea-hypopnea index (AHI). We studied a large cohort of patients with OSA who underwent CPAP titration, and modeled the prescribed level of CPAP by different characteristics.

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**Methods :** 576 consecutive CPAP titration studies for OSA performed at Cleveland Clinic Sleep Disorders Center were retrospectively analyzed. CPAP (n=316), BiPAP (n=28), mixed CPAP/BiPAP (n=29) titrations and split-night (n=202) polysomnographic studies were included. We recorded the demographic and polysomnographic characteristics of these patients and used them for the predictive models. We also analyzed the correlation between the optimal CPAP setting determined in the titration studies and various equation-derived CPAP levels. JMP 5.0.1 software (SAS Institute, Cary, NC) was used for the statistical analysis.

**Results :** 498 patients had complete records; this group was split randomly into a derivation lot of 344 patients and a validation lot of 154 patients. In the derivation lot the following linear regression equation was constructed:  $CPAP = -1.78 + 0.078BMI + 0.196NC + 0.006AI$ , where AI represents the apnea index (number of apnea episodes per hour of sleep). In the validation lot the correlation coefficient was 0.47, which was slightly stronger for severe OSA. We also analyzed 3 other predictive equations, including 2 which were previously published and found the above equation to be superior, and the main predictors were: BMI, NC and AI.

**Conclusion :** We proposed a different equation for predicting the level of CPAP needed to effectively treat OSA and compared its predictive value against previously published or similar regression equations. After the derivation and the validation process in distinct patient lots, we found that hypopneas contribute less than apneas in the linear regression model and found poor correlations for other predictive models.

**Support (optional):** None

### 0602

#### THE PREVALENCE OF OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH CORONARY HEART DISEASE

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**Introduction :** In patients with coronary heart disease (CHD), obstructive sleep apnea (OSA) increases the risk for myocardial infarction. Recognizing the prevalence of OSA in patients with CHD is essential for optimal treatment of these patients.

**Methods :** One hundred thirty-two patients with either a prior history of a myocardial infarction or angiographically verified coronary artery disease were recruited to participate in a study of heart disease and sleep disorders. Two nights of polysomnographic data were obtained, including EEG, pulse oximetry, and oronasal thermistors. The main outcome measures were the frequency of apneas and hypopneas, the desaturation index, the maximum oxygen desaturation, and the duration of apneic and hypopneic episodes.

**Results :** The prevalence of OSA, defined as 5 or more episodes of obstructive apnea or hypopnea per hour, in patients with CHD was 70%.

**Conclusion :** OSA is quite common in patients with CHD. The high prevalence of OSA in patients with CHD reported here, even higher than previously published prevalence estimates, emphasizes the importance of screening this patient population for OSA.

**Support (optional):**

### 0603

#### THE SIGNIFICANCE OF GENDER AND PARTNER-REPORTING ON THE LAY-DIAGNOSIS, MANAGEMENT, AND TREATMENT OF APNEA: A PERSPECTIVE FROM ANTHROPOLOGY

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**Introduction :** Research has shown that men and women can vary in their decisions as to when and where to seek medical advice. When advice is sought, symptoms of the same illnesses can be presented to physicians very differently, patterned by gender or marital relationships. These social and cultural components of sleep apnea, however, are relatively little understood. This cross-sectional, exploratory, qualitative study illuminates the significance of gender and partner-reporting in shaping the lay diagnosis, management, and treatment of sleep apnea.

**Methods :** Patients clinically diagnosed with sleep apnea were recruited by a physician and offered participation in the study. A medical anthropologist then arranged in-depth, semi-structured, qualitative interviews in patient homes (n=18 at the time of submittal; this should increase to n=28 at the time of presentation), in order to make observation of the sleeping environment. Interviews were recorded, transcribed, and coded with the qualitative software package Atlas Ti. Content analysis followed standard inductive strategies, allowing emic patterns to emerge from the data independent of predetermined analytical approaches in order to provide an understanding of how participants identify and organize factors related to apnea. A content coding system was developed in which words or themes are coded according to their contextual significance. Relationships between categories were examined, as were trends that emerged across sub-groups.

**Results :** 67% of the patients were men; 33% were female; spouses were 67% male/ 33% female. Medical care was sought only after the insistence of the spouse in 92% of all cases. 50% of spouses located apnea as a cause of problems within the marital relationship; 0% of patients reported this. 29% of men, vs. 20% of women, located apnea as a problem within their relationship. 55% of men and 65% of women (patients or spouses) mention dissatisfaction with CPAP machines; 75% of these cases mention non or partial compliance with medical advice concerning the machines. Women's dissatisfaction centered around a perceived lack of femininity associated with use of the machine.

**Conclusion :** Given the small proportion of adults estimated with apnea that currently see a physician for care, an anthropological perspective attempts to reveal new insight into the lay diagnosis, management, and treatment of sleep apnea.

**Support (optional):**

### 0604

#### THE DIFFERENCE OF CORTICO-SPINAL EXCITABILITY BETWEEN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA AND UPPER AIRWAY RESISTANCE SYNDROME

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**Introduction :** A pathological alteration of neuromotor control of pharyngeal muscles may play a role in the development of obstructive sleep apnea syndrome (OSAS) or upper airway resistance syndrome (UARS). With single pulse transcranial magnetic stimulation (TMS) we studied the electrophysiology of the corticospinal projection to hand muscles in nine OSAS and five UARS patients, and investigate the underlying pathophysiological difference between the two.

**Methods :** Seven age- and sex-matched normal subjects were selected (control) in the wake state. The parameters of apnea/hypopnea index (AHI; >30, <50 in OSAS vs <5 in UARS), body mass index (BMI; >25, <29 in OSAS and <25 in UARS), age/sex (M:F = 5:4 in OSAS and 2:3 in UARS) were matched. The following morning of overnight polysomnography, figure of eight shaped double coil was applied above the right motor cortex and MEPs were recorded from the left first dorsal interosseus (FDI) muscle. Single pulse TMS parameter measured were the amplitude and duration resting motor threshold (rMT), silent period (SP). **Results :** TMS revealed no changes between two groups, except more lengthening of the central silent period (SP) in OSA group comparing to control or UARS group (  $P < 0.001$ ). In UARS group, the SP was more shortened than control group, but not statistically significant ( $P > 0.1$ ).

**Conclusion :** This supports a steady imbalance of motor cortical interneuronal activities towards a state of enhanced inhibition in OSAS, on the contrary decreased or normal inhibition in UARS group. It also indicates the changes were detected outside the pharyngeal district, suggesting a widespread dysfunction of the cortico-subcortical connection in the OSAS, but not in UARS patients.

**Support (optional):**

### 0605

#### VASCULOPATHY IN SLEEP DISORDERED BREATHING: PAI-1 AND E-SELECTIN CORRELATE WITH SAS SEVERITY

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**Introduction :** Vascular endothelial dysfunction is suspected to be part of the mechanisms responsible for vascular morbidity and mortality associated with obstructive sleep apnea syndrome (OSAS). Therefore, we investigated in OSAS patients and control subjects, markers of the fibrinolytic system, soluble adhesion molecules and cytokine IL-18 whose overexpression was shown to be associated with the development of atherosclerosis.

**Methods :** 43 patients, referred to our sleep laboratory, were evaluated for sleep disordered breathing (SDB) by polysomnography. Major vascular risk factors were determined. Blood samples were collected before and after polysomnography and assessed for plasma concentrations of t-PA, PAI-1, soluble adhesion molecules sE-selectin, sP-selectin, sICAM-1 and sVCAM-1 as well as IL-18.

**Results :** Patients were separated in three groups according to polysomnographic criteria: group 1, snoring or upper-airway resistance syndrome or mild OSAS with AHI <15/h (n=12); group 2, moderate OSAS  $15 \leq \text{AHI} < 30$  (n=15); group 3, severe OSAS with  $\text{AHI} \geq 30$  (n=16). After controlling for covariate factors (BMI, age), morning t-PA and PAI-1 were found to be significantly increased in patients of group 2 [ $m \pm \text{SD}$ ] [8.9±3ng/ml; 33±22ng/ml], and group 3 [11.5±4ng/ml; 52±37ng/ml] as compared to group 1 [5.6±3ng/ml; 16±9ng/ml]. Circadian variation of PAI-1 was higher in group 2 and 3 with a peak secretion in the morning (200 to 500 % increase of basal level). No significant difference in the sVCAM-1, sICAM-1, sP-selectin, and IL-18 concentrations was observed between groups. In contrast, sE-selectin concentrations [88±70ng/ml] are significantly increased in severe OSAS patients (group 3) as compared to patients of group 2 [40±26 ng/ml] and group 1 [31±21ng/ml].

**Conclusion :** Both PAI-1 and sE-selectin are markedly elevated in OSAS suggesting that severe OSAS patients might display endothelial dysfunction that could play a key role in the pathogenesis of vasculopathy associated to SDB.

**Support (optional):**

### 0606

#### MANDIBULAR ADVANCEMENT IS LIMITED IN BRAZILIAN JAPANESE DESCENDENT

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**Introduction :** Obesity is a major risk factor for obstructive sleep apnea (OSAS), but we have treated many non-obese Brazilian Japanese with moderate to severe OSAS. Besides Japanese OSAS patients are less obese than Caucasian Brazilian patients, in Japanese SAOS is frequently severe.

**Methods :** The craniofacial structures of 36 OSAS patients (12 Japanese 50±12.4 years; and 24 Brazilians 45±11.6 years) were evaluated using standard cephalometric analysis. The radiographs were obtained in the same patient in two positions: teeth together and in maximum comfortable mandibular advancement (MA). We analyzed the following variables between groups: body mass index (BMI), apnea hypopnea index (AHI), SNB angle, PAS (pharyngeal airway space), soft palate length (distance from posterior nasal spine to the tip of soft palate), MP-H (distance from mandibular plane to the hyoid bone), C3-H (distance from third cervical vertebrae to hyoid bone). We used Student t Test for statistical analysis.

**Results :** Japanese patients presented BMI=24±1.4kg/m<sup>2</sup> and Brazilian patients 27.3±4.6kg/m<sup>2</sup> (p=0.36); in Japanese AHI was 22.7/h±14.8 and in Brazilian group 14.8/h±12 (p=0.12). SNB angle with MA for Brazilian patients were 84.2±3.8 degrees and for Japanese group 82.3 ±3.5degrees (p=0.16). PAS in MA condition was 13.3±5.1mm for the Brazilian and 11.1±4.9mm for Japanese group (p=0.22). C3-H without MA in the Japanese was 40±4.1mm and in Brazilian group 44±7.8mm (p=0.05). When in MA the C3-H in Japanese was 41.5±7.3mm and in Brazilian group 48.2±9.9mm (p=0.03)

**Conclusion :** This initial study demonstrated that MA procedure produce a lesser displacement in the C3-H in Japanese compared to Brazilians, and also a lesser change in PAS in Japanese. We think that structural and dynamic features regarding mandibular advancement in Japanese might bring less benefit to them when considering titrating oral appliances to treat OSAS in this group.

**Support (optional):** Center for Clinic and Science of Sleep.

### 0607

#### PREVALENCE OF SLEEP DISORDERS IN ATHLETES OF WHEELCHAIR BASKETBALL IN SÃO PAULO, BRAZIL

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**Introduction :** There are some controversies surrounding the prevalence of sleep disorders in the physically challenged population. Sleeping patterns might be associated with morbidities, according to disability etiology, to life style, and to individual's general conditions. Physical activity is important for its relation with healthier behaviors and improvement in sleeping quality and efficiency. Wheelchair basketball is one of the most popular sports practiced by physically challenged people among other sports. Objective: To investigate sleep disturbances in wheelchair basketball athletes.

**Methods :** A cross-sectional study carried out during the State of Sao Paulo Basketball Wheelchair Tournament, from April 19th to April 21th, 2005, in Caraguatuba, São Paulo, Brazil. We interviewed 99 athletes (92 men) from 15 teams, mean age 31 years. The athletes were identified

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according to the disability etiology, functional classification, and a questionnaire about sleep disorder.

**Results :** The athletes presented a total sleep time of 7:30 hours a day. About etiology: 37.4% have poliomyelitis sequels, 35.4% spinal cord injury, 13.13% amputation, and 14.15% other etiologies. About sleep: 48.5% report sleep disorders complaints, and the athletes with spinal cord injury show more sleep disorders than other athletes. The main sleep disorders were snoring (32.5%), night awakenings (14.3%), impaired day performance (7.8%), insomnia and apnea (6.5%), sleep talking, myoclonus and daytime sleepiness (5.2%).

**Conclusion :** Our preliminary data showed that although young adult athletes form the studied population, the prevalence of snoring is high. We need to compare our data to a similar group of athletes without physical challenges.

**Support (optional):**

### 0608

#### ZOLPIDEM: SUCCESSFUL AND SAFE TREATMENT FOR IDIOPATHIC CENTRAL SLEEP APNEA

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**Introduction :** The purpose of this investigation was to extend our previous findings demonstrating the beneficial effects of zolpidem on idiopathic central sleep apnea. Additionally, central and obstructive events were evaluated separately to address concerns about potential worsening of obstructive sleep apnea with hypnotics.

**Methods :** We conducted an open label trial of zolpidem in 14 patients with newly diagnosed idiopathic central sleep apnea (central apnea-hypopnea index  $\geq 10$  and symptoms of snoring and/or excessive daytime sleepiness). Patients were started on zolpidem 10 mg at bedtime. In 11.4 +/- 7.4 weeks a repeat 8 hour polysomnogram and assessment of daytime sleepiness by the Epworth Sleepiness Scale (ESS) were performed.

**Results :** On zolpidem the AHI decreased from 32 +/- 21(SD) to 16 +/- 13 ( $p < 0.005$ ). Central apnea-hypopnea index decreased from 27 +/- 20 to 9 +/- 14 ( $p < 0.001$ ) without change in obstructive apnea-hypopnea index (pre 5 +/- 5, with zolpidem 7 +/- 10). Mean lowest NREM arterial oxygenation saturation was the same (pre 87 +/- 4%, with zolpidem 87 +/- 4%). Sleep efficiency, NREM, REM and slow wave sleep percents did not change. Percent stage 1 sleep decreased from 40 +/- 23 to 26 +/- 14 ( $p < 0.003$ ) and percent stage 2 increased from 52 +/- 25 to 64 +/- 16 ( $p < 0.001$ ). ESS improved from 14 +/- 5 to 8 +/- 5 ( $p < 0.002$ ).

**Conclusion :** Zolpidem improved idiopathic CSA, sleep continuity, and subjective daytime sleepiness in individuals with idiopathic central sleep apnea without worsening obstructive apnea or oxygenation. These results extend earlier findings. We speculate that zolpidem stabilizes sleep, lessening the cyclic sleep-arousal-sleep pattern and thereby reducing repetitive central apneas.

**Support (optional):**

### 0609

#### RESPIRATORY PATTERN MODULATION FOLLOWING LESION OF DORSAL RAPHE OR LOCUS COERULEUS PROJECTIONS

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**Introduction :** The present study was performed to test the impact of selective chemical axotomy of noradrenergic or serotonergic neurons on

sleep and breathing in conscious animals.

**Methods :** In 9 chronically instrumented Sprague-Dawley rats, we recorded sleep, pontine waves (P-waves) and breathing (plethysmograph) during baseline, following sham injection (i.p. 1 ml/kg), and 1, 7, 14, 21, 28 and 35 days following injection with a systemic neurotoxin. Locus coeruleus (N = 5) or raphe (N = 4) axons were lesioned by a single dose (i.p. 50 mg/kg) of DSP-4 or by two injections of PCA (i.p. 6 mg/kg) 24 h apart, respectively. Sighs (50% augmentation of tidal volume) and apneas (two "missed" breaths) were detected.

**Results :** Sleep architecture was unchanged from baseline by PCA or DSP-4 ( $p > 0.1$  for %W, %NREM and %REM for each). At baseline, the frequencies and durations of spontaneous (SP) and post-sigh (PS) apneas were equivalent during NREM and REM ( $p \geq 0.2$  for each). PCA injection produced an immediate and sustained increase of NREM PS apnea index ( $F = 8.18$ ;  $p = 0.002$ ) and apnea duration ( $F = 5.00$ ,  $p = 0.02$ ), but NREM SP apnea index ( $F = 2.65$ ;  $p = 0.09$ ) and REM SP and PS indexes ( $p > .5$  for each) remained unchanged. The frequency ( $F = 2.03$ ;  $p = 0.09$ ) and volume ( $F = 0.72$ ; 0.66) of sighs were unaffected by PCA, but the percent of sighs producing apnea increased five-fold ( $F = 9.8$ ;  $p = 0.001$ ), and the proportion of PS apneas preceded by P-waves increased by 10% ( $p = 0.05$ ). DSP-4 caused NREM PS apnea duration to exceed SP apnea duration beginning 21 days after injection ( $p = 0.0001$ ).

**Conclusion :** Our findings suggest an important role for serotonin in determining the vulnerability and stability of the respiratory pattern generator.

**Support (optional):** This work was supported by NIH Grant AG16303.

### 0610

#### BLOCKADE OF NMDA RECEPTORS IN THE PONTINE INTERTRIGEMINAL REGION INCREASES BREATHING VARIABILITY FOLLOWING REFLEX APNEA IN RATS

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**Introduction :** Vagal reflex apnea can be induced by intravenously injected 5-HT in anesthetized rats. We have shown previously that this breathing disturbance was increased by microinjection of kynurenic acid (KYN), a broad spectrum glutamate (Glu) receptor antagonist, into the intertrigeminal region (ITR) of the lateral pons. In this experiment we aimed to determine whether specific blockade of NMDA receptors by microinjection of D-AP5 into the ITR can affect breathing following intravenous infusion of 5-HT. This was of interest since NMDA receptors have been shown to be essential in glutamatergic neurotransmission in the lateral pons.

**Methods :** In 8 anesthetized Sprague-Dawley rats a catheter was inserted into the femoral vein for the infusion of 5-HT (0.05 M) using an infusion pump. Four-barrel micropipettes, aimed at ITR, were filled with Glu (10 mM), D-AP5 (1 mM), PBS and oil red-O dye. In three separate intervals 5-HT was infused to induce reflex apnea. After that, Glu was microinjected into the ITR and evoked immediate apnea. Following the recovery of the breathing pattern, a bolus of D-AP5 was injected into the ITR apneic site. After that, three intravenous 5-HT infusions were repeated at equal intervals.

**Results :** Following 5-HT induced reflex apnea, coefficient of variation of breath duration (CVTT) increased 950% during the first 30 s following injection ( $p < 0.0001$ ) and remained elevated by 44% for 5 minutes ( $p = 0.0003$ ). Injection of D-AP5 produced no change in CVTT ( $p > 0.5$ ) but prolonged respiratory variability associated with reflex apnea: CVTT increase in the first 30 s following 5-HT was not altered ( $p = 0.83$ ) but remained above the matching pre D-AP5 injection levels during 150 s ( $p$

= 0.025) and 300s ( $p = 0.0001$ ) post-injection analysis intervals.

**Conclusion :** Endogenous glutamatergic tone in the ITR is important for respiratory stability, since Glu and particularly NMDA antagonism exacerbates respiratory disturbance. This protective role of ITR agrees with general damping function of pontine structure in autonomic activities including respiration.

**Support (optional):** This work was supported by NIH grants HL70870 and AG16303

## 0611

### BILATERAL OOPHORECTOMY: A CONTRIBUTING RISK FACTOR FOR SLEEP APNEA SEVERITY IN WOMEN?

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**Introduction :** Post-menopausal women appear to have a higher risk of developing obstructive sleep apnea (OSA) syndrome than premenopausal women (Bixler et al, 2001). Women with hysterectomies and bilateral oophorectomies (HBO) have increased mortality (Parker et al., 2005). Little data exists regarding the presence of sleep apnea in women who have undergone HBO.

**Methods :** We reviewed polysomnograms requested for a clinical suspicion of OSA during a six-year period. We identified fourteen cases of women who had had a documented HBO. The remaining women were not included because complete medical records were not available to us.

**Results :** The mean age in this series was  $58.5 \pm 10.2$  years (s.d.) and mean body mass index (BMI) was  $42 \pm 7$  kg/m<sup>2</sup>. Time from the surgery to the diagnostic polysomnogram was  $12 \pm 9$  years. The mean apnea-hypopnea index (AHI) was  $92.2 \pm 51.9$  events/hr; the mean minimum oxygen saturation was  $71.1 \pm 15.8\%$ .

**Conclusion :** Our sample of women with HBO had severe OSA. Though they comprise a small proportion of our clinic population, they constitute a proportionally large percentage of women with remarkably high AHIs. Our sample's AHI of 92.2 events/hr is higher than previously reported in the Resta et al (2004) series of women (AHI of 33.8 events/hr) who had BMIs similar to those of our patients. Women with HBO may have a higher risk of severe OSA, at an earlier age than expected, possibly due to the removal of ovaries. This finding could suggest that the increased mortality after HBO may be in part related to the increased risk of severe OSA. Routine evaluation of patients who have undergone HBO for signs and symptoms of sleep-disordered breathing should be considered.

**Support (optional):**

## 0612

### EFFECTIVENESS OF ORAL APPLIANCES FOR OBSTRUCTIVE SLEEP APNEA IN REM VS. NON-REM SLEEP

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**Introduction :** Oral appliances (OAs) that advance the mandible are used increasingly as a treatment option for mild to moderate obstructive sleep apnea (OSA). However, their effect on specific sleep stages, and effectiveness during these stages remain largely unstudied.

**Methods :** We reviewed sleep studies performed for clinical purposes before and during OA use between January 1999 and August 2005. Approximately 130 patients received OAs during that time; many had split-night studies or did not complete both a pre-OA and post-OA study and were not included in this study. Virtually all of the OA were the DeSRA or TAP-adjustable models. Polysomnographic methods and scoring have been described previously (Chervin and Aldrich, Sleep 1998;21:799-806).

**Results :** A total of 67 patients (51 men) had polysomnograms first without and then with an OA. The mean interval between both studies was  $23 \pm 7$  (s.d.) months. OA usage was associated with reduction in REM sleep latency from 151 to 117 minutes (paired t-test,  $p = .004$ ); decreased stage 1 sleep (85 to 69 min,  $p = .008$ ), mildly increased stage 2 (175 to 191 min.,  $p = .070$ ), essentially unchanged stage 3-4 (23 to 20 min,  $p = .425$ ), and increased stage REM (50 to 59 min,  $p = .040$ ). The mean number of apneas or hypopneas per hour of sleep (AHI) decreased with use of an OA from 24 to 13 (46% reduction,  $p < .001$ ). The AHI decreased from 22 to 12 (45%,  $p < .001$ ) during non-REM sleep, but only from 24 to 18 (25%,  $p = .008$ ) during REM sleep. Minimum oxygen saturation remained unchanged on average at 84%.

**Conclusion :** Data from this clinical series suggest that OAs improve sleep architecture and reduce the AHI, more effectively during NREM sleep than REM sleep, but oxygen saturation may not improve. These findings may aid in prediction of patient response to OA treatment.

**Support (optional):**

## 0613

### PASSIVE AUTOMATIC DETECTION OF SLEEP APNEA AND AROUSALS COMPARED TO STANDARD POLYSOMNOGRAPHY: PRELIMINARY VALIDATION

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**Introduction :** According to the NIH Sleep Research Plan, current methods for measuring breathing abnormalities have little predictive power, do not allow for screening of large populations, are cumbersome, and expensive. The NAPS (Non-invasive Analysis of Physiological Signals) System is designed to obtain physiological measurements passively while the subject is in bed. It consists of two pressure sensitive pads which are connected to a base unit that converts minute body movements into electrical signals. The pads and sensors can be placed on any bed in order to measure pulse, breathing, and movement from the test subject.

**Methods :** The study was approved by the University of Virginia's Institutional Review Board and the General Clinical Research Center (GCRC). Forty generally healthy adult subjects who had signed an informed consent underwent an overnight sleep study with conventional polysomnography, while simultaneously monitored by the passive system, at the University of Virginia's GCRC. Twenty of the subjects were found to have an apnea-hypopnea index greater than 10. Preliminary analysis involved two three minute blocks of data from each subject selected at random with one set containing no apneas or arousals and the other set containing at least one apnea. Apnea and arousal events were manually scored by the technician while data from the passive system was automatically scored using our algorithm with manual event detection using a set of rules we developed.

**Results :** Two-way contingency table analysis showed that the passive apnea detection capability exhibited 89.2% sensitivity, 94.6% specificity and kappa correlation coefficient of 82.8%. Additionally, arousals were detected with 77.3% sensitivity, 96.2% specificity and kappa of 73.0%.

**Conclusion :** The preliminary results of this study demonstrated the validity of the passive system's ability to provide clinically meaningful automated apnea and arousal detection. Further validation will be performed on data collected from the full nights of sleep.

**Support (optional):** This work was supported in part by a grant to the University of Virginia's General Clinical Research Center, 5 M01 RR00847.

0614

**COMPLIANCE WITH CONTINUOUS POSITIVE AIRWAY PRESSURE USED AS PREOPERATIVE TREATMENT IN CHILDREN WITH OBSTRUCTIVE SLEEP APNEA**

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**Introduction :** Adenotonsillectomy (A&T) is the first line of therapy for children with obstructive sleep apnea (OSA), but the procedure has been associated with an increased risk of perioperative complications in children with serious illness. The preoperative use of continuous positive airway pressure (CPAP) might decrease the perioperative risk. The aim of the study was to evaluate compliance with CPAP in children diagnosed with severe OSA before T&A, as well as the occurrence of surgical complications .

**Methods :** Twenty-four otherwise healthy children with severe OSA programmed for A&T were enrolled. The diagnosis of OSA was made with a simplified monitor which registered oxygen saturation (SaO<sub>2</sub>), snoring, body position and nasal flow. They were assigned by convenience, to use either a continuous positive airway pressure (CPAP), or an auto-titrating positive airway pressure (APAP) devices, for at least one month prior to surgery. Compliance was assessed by data obtained from the machines, and perioperative complications were analyzed with follow-up of each patient.

**Results :** Data for 24 patients (19 men) are presented as median and interquartile range. Age was 5 years (3); body mass index: 19.6 kg/m<sup>2</sup> (8.24); respiratory disturbance index: 75.45 (39.95); mean nocturnal SaO<sub>2</sub>: 85.60% (2.88); median pressure required was 9.3 cmH<sub>2</sub>O (3.9). Total days of use was 26 (26), days without use: 2 (6), hours per night 5.42 (5.13). We found no significant differences among children using fixed-pressure CPAP vs APAP. One patient presented surgical rebleeding.

**Conclusion :** Compliance to preoperative treatment with CPAP / APAP is satisfactory, and can contribute to prevent complications due to the illness.

**Support (optional):** None

0615

**CASE STUDY ON RDI VARIABILITY DURING TREATMENT WITH AN ORAL APPLIANCE**

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**Introduction :** Reports of night-to-night variability in sleep-disordered breathing (SDB) have focused primarily on differences in diagnostic results. Few investigations have included repeated measures assessments to identify factors that influence treatment outcomes.

**Methods :** A case study of a 48 year-old male with OSA. The patient completed four Apnea Risk Evaluation System (ARES) unattended in-home sleep studies prior to treatment with a TAP II self-adjusting oral appliance. The baseline adjustment was at maximum active protrusion. Additional adjustments were made at one-half turn increments, for a total adjustment of two turns or 0.66 mm. An additional 18 ARES sleep studies were acquired over a 45-day titration period. Alcohol consumption within three-hours prior to sleep and the TAP adjustment setting were recorded.

**Results :** The mean recording time across the 22 sleep studies was

6.2+1.1 hours. The supine and non-supine RDI and percent time snoring above 40 dB were stratified into four conditions, pre-treatment (n=4) increased adjustment nights (n=3), and non-adjustment nights with alcohol (n=8)(mean alcohol consumption 1.6 drinks/night) or without alcohol (n=7). Across the four conditions, the mean overall RDI based on the Chicago Criteria for each of the four conditions were 27, 16, 12 and 9. The mean supine RDI for each of the four conditions were 51, 21, 21 and 11. The mean percent time supine were 5, 4, 9 and 16. The mean non-supine RDI were 25, 16, 12 and 9. The mean percent time snoring above 40 dB were 49, 26, 13 and 5.

**Conclusion :** This case study suggests that alcohol consumption and appliance adjustment can affect the RDI, percent time supine and percent time snoring. Assessing the treatment outcome immediately after an adjustment may not reflect the true benefit of the appliance. This report suggests the benefit of studying patients on multiple nights under realistic conditions to obtain a more accurate assessment of treatment outcomes.

**Support (optional):** This research was funded in part by NIH NIDCR grant number DE016772.

0616

**INFLUENCE OF SLEEP-DISORDERED BREATHING ON NEUROCOGNITIVE FUNCTIONS PRE- AND POST-TREATMENT WITH CPAP**

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**Introduction :** Controversy exists regarding the cause (hypoxemia versus sleep fragmentation) of the cognitive impairments seen in Obstructive Sleep Apnea (OSA) patients, and their reversibility following treatment. In a large group of patients, we examined the association of hypoxemia and RDI to neurocognitive impairment pre- and post-treatment.

**Methods :** The Alertness and Memory Profiler (AMP) quantified EEG/performance during: 3-Choice-Vigilance-Test, Verbal/Image Paired-Associate-Memory tests, and Sternberg-Verbal-Memory-Scan. Epworth scales assessed self-reported sleepiness. OSA patients (n=135,mean RDI=48.1, range 5-149) were evaluated with AMP pre-treatment and 4-weeks post-treatment with CPAP and compared to 46 controls. RDI and hypoxemia levels (SpO<sub>2</sub><80%,80-85%,85-90%) were quantified based on pre-treatment polysomnography.

**Results :** Factor analysis of AMP variables resulted in four Neurocognitive Factor Scores: processing speed (PS), visuospatial memory (VSM), sustained attention (SA) and verbal memory (VM). Pre-treatment OSA factors revealed significant impairments relative to controls: PS[t=-3.797,p<0.001]; VSM[t=-2.318,p=0.022]; SA[t=-4.403,p<0.001]; VM[t=-4.812,p<0.001]. PS, SA, and VM significantly improved post-treatment (n=124), t=4.158,p<0.001,t=4.339,p<0.001,t=3.133,p=0.002, respectively. Post-treatment PS, VSM, and SA no longer significantly differed between groups (VM remained impaired in OSA, t=-2.204,p=0.029). Stepwise multiple regression examined the relative importance of RDI, hypoxemia, Epworth and age on the factors. Pre-treatment, RDI/Epworth predicted PS(R=0.336), Epworth predicted SA(R=0.225) and SpO<sub>2</sub>85-90% predicted VSM(R=0.225). Post-treatment VM was predicted by hypoxemia SpO<sub>2</sub>80-85% (R=0.309) and PS by a combination of Epworth/Age/SpO<sub>2</sub><80% (R=0.440).

**Conclusion :** These data suggest that hypoxemia is closely related to learning and memory impairment pre-treatment while alertness factors (PS, SA) were predicted by subjective sleepiness (Epworth). Surprisingly, RDI related only to PS. Post-treatment, hypoxemia was an important

determinant of the residual neurocognitive impairments observed in VM. The findings support the theory that the various manifestations of OSA differentially affect neurocognitive functioning and that some impairments persist even after successful amelioration of sleep-disordered breathing. The AMP proved useful as an easy-to-administer method to quantify OSA-related cognitive impairments and verify treatment efficacy.

**Support (optional):** This work was supported by NIH NHLBI grant number HL70484. Nasal CPAP equipment, training and support were provided by ResMed Inc., Poway, CA.

## 0617

### A PRELIMINARY ASSESSMENT OF AUTOMATICALLY TITRATED BILEVEL POSITIVE AIRWAY PRESSURE: IS THERE A VENTILATORY EFFECT?

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**Introduction :** Automatically adjusted positive airway pressure is frequently prescribed for the treatment of Obstructive Sleep Apnea (OSA). Pressure is adjusted based on inspiratory flow patterns. Bilevel positive airway pressure treats obstructive sleep apnea with independently adjusted inspiratory and expiratory pressure levels. An automatically adjusted bilevel positive airway pressure device (BiPAP Auto, Respironics, Inc.) was evaluated to determine if therapy affected ventilation measured by non-invasive monitoring of CO<sub>2</sub>.

**Methods :** Four subjects (3 males), age 58.3±15.4 (mean ± SD), BMI 40.9±13.7, with known OSA (AHI>15) were studied using BiPAP Auto during attended polysomnography. The device delivered between 4 and 25 cm H<sub>2</sub>O. Maximum pressure support was 8 cm H<sub>2</sub>O and minimum was 2 cm H<sub>2</sub>O. End tidal CO<sub>2</sub> (EtCO<sub>2</sub>) measurements were made during quiet breathing after the application and stabilization of a transcutaneous carbon dioxide monitor (TcCO<sub>2</sub>). TcCO<sub>2</sub> was monitored continuously during polysomnography. EtCO<sub>2</sub> was repeated upon awakening and correlated with TcCO<sub>2</sub>.

**Results :** Subjects slept an average of 262±27.9 minutes. Sleep efficiency was 74.3±10%, Stage 2 sleep 74.4±16% and REM 19.2±13%. Arousal index was 4.5 ±2.4. SpO<sub>2</sub> averaged 93.5±1.3 and minimum SpO<sub>2</sub> was 86.8±2.4. Treatment with BiPAP Auto resulted in an AHI of 2.3±0.53. The average EPAP was 9.2±3.9 cm H<sub>2</sub>O and the 90% EPAP was 11.9±4.1 cm H<sub>2</sub>O. The average IPAP was 12.9±6 cm H<sub>2</sub>O and the 90% IPAP was 14.1±3.2 cm H<sub>2</sub>O. The average pressure support was 2.7±0.22 cm H<sub>2</sub>O. There was no significant difference between the two EtCO<sub>2</sub> measurements (37.5±2.1 and 38.8±2.4 mm Hg). The average TcCO<sub>2</sub> was 44.9±6 mm Hg.

**Conclusion :** The BiPAP Auto effectively controlled OSA. Based on non-invasive measurement of carbon dioxide, there was no tendency to over-ventilate the patients. This suggests that the BiPAP Auto should not adversely affect respiratory control or contribute to complex sleep apnea.

**Support (optional):** Respironics, Inc.

## 0618

### EPIDEMIC SURVEY OF THE MIDDLE AND AGED WOMEN RELATED OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME IN BEIJING

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**Introduction :** To find out the prevalence and risk factors related obstructive sleep apnea hypopnea syndrome(OSAHS) in Chinese women aged

40 years and older.

**Methods :** and methods Participants living in communities must be of age≥40 years and were given questionnaires, which developed a scale of 11 questions. Subjects were divided into three groups by scale scores. Those with higher scores were oversampled(2.4%, 14.8%, 42.1% respectively) and subjects of this community-based sample were recorded in the sleep laboratory to ascertain patients(apnea hypopnea index,AHI≥5/h and daytime sleepiness). Contrasting patients with the others as a control group,explored differences in symptoms. Stepwise logistic regression was used to determine the principal covariates affecting AHI.

**Results :** 33.4% of 1336 eligible women admitted various degree of snoring and 91.0% of those completed questionnaires. Cronbach's coefficient of scale reached 0.7025. Factor Analysis reduced 11 questions of scale to four common factors as we have designed: snoring,apneas,other symptoms,risk factors. Fifty-nine subjects experienced polysomnography evaluation. The ratios of patients to controls were 2:25,4:18,10:16 from low scores group to higher. We estimated the prevalence of AHI 5,10,15/h and OSAHS in this population were 41.1%, 24.0%,17.0% and 11.1%, respectively.As far as the frequency of sleep choking, xerostomia or pharyngoxerosis in the morning, these were significant differences between the OSAHS and non-OSAHS groups. Stepwise multiple logistic regression analysis identified serum level follicle-stimulating hormone and BMI as predictors of AHI.

**Conclusion :** This scale has good validity and reliability. Snoring and OSAHS are very common in Chinese women 40 years of age and older. Women with OSAHS did report sleep choking, xerostomia or pharyngoxerosis in the morning. BMI and sex steroids all play a role in OSAHS.

**Support (optional):**

## 0619

### SIGNIFICANCE OF APNEA HYPOPNEA TIME INDEX IN OBSTRUCTIVE SLEEP APNEA HYPOPNEA SYNDROME PATIENTS AND POSSIBLE CORRELATION BETWEEN POLYSOMNOGRAPHIC PARAMETERS AND SEVERITY OF THE DISEASE

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**Introduction :** To find out the polysomnography (PSG) indexes that reflex the degree of pathology of obstructive sleep apnea hypopnea syndrome (OSAHS).

**Methods :** Six hundred and twenty-one male OSAHS patients, aged over 21, underwent measurement of weight, height, and neck circumference. Polysomnography was conducted to detect the apnea and hypopnea index (AHI), apnea and hypopnea time (AHT), and apnea and hypopnea time index (AHTI). A questionnaire survey based on Epworth sleep scaling (ESS) was conducted among 392 patients to assess the symptoms, such as excessive daytime sleepiness. 324 patients with an AHTI of 68.4 +/- 17.16 events/hour were regarded as severe group, and those with an AHTI >or= 7 events/hr were regarded as very severer group. The relationship among clinical characteristics and polysomnographic parameters were analyzed.

**Results :** The AHI, AHTI, and lowest SaO<sub>2</sub> of the patients were significantly correlated with the ESS7 scores, morning mouth dryness, daytime fatigue (all P < 0.01), and significantly correlated with sour regurgitation, and heartburn, (all P < 0.05). AHTI was significantly correlated (r = 0.317), morning mouth dryness (r = 0.239); and sour regurgitation, and heartburn (r = 0.137). AHT was significantly correlated (r = 0.344), morning mouth dryness (r = 0.261); and sour regurgitation, and heartburn (r = 0.138). Very significant differences existed in morning mouth dryness, sour regurgitation and heartburn, and ESS7 scores between the severe and very severe patients (all P < 0.01).

## Category I—Sleep Disorders-Breathing

**Conclusion :** Among the PSG indexes, AHTI is better associated with sleepiness and other clinical symptoms than AHI. In severe OSAHS patients, there are significant differences in their clinical symptoms between the AHI < 70 events/hr group and AHI ≥ 70 events/hr group.  
**Support (optional):**

### 0620

#### ARE OPIOID MEDICATIONS ASSOCIATED WITH SLEEP RELATED HYPOVENTILATION/HYPOXEMIA?

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**Introduction :** Opioids have different effects on the respiratory pattern depending on whether or not pre-inspiratory neurons (pre-I) are present in sections of the pre-Botzinger complex in experimental animals. When pre-I are absent, respiration slows. When pre-I are present, there is step-like slowing of breathing similar to the pattern that occurs in sleep apnea. While opiates have been associated with central sleep apnea, we hypothesized that opiates might cause sleep related hypoventilation/ hypoxemia without sleep apnea.

**Methods :** We conducted a retrospective analysis of 98 consecutive patients on opioid medications who were referred for overnight polysomnography for diagnostic purposes. We defined hypoventilation/hypoxemia by the criteria described in the International Classification of Sleep Disorders, 2nd edition, 2005: oxygen saturation by pulse oximetry (SpO<sub>2</sub>) of <90% for 30% of total sleep time or SpO<sub>2</sub> of < 90% for > 5 min with a nadir of < 85%.

**Results :** Of these 98 patients, 40% had obstructive sleep apnea, 20% had central sleep apnea, 24% had both central and obstructive sleep apnea, and 17% had no sleep apnea. Of 17 patients without sleep apnea, 7 patients had nocturnal hypoventilation/hypoxemia, 1 patient was excluded because of uncertain quality of the oximetry signal. Of those 7 patients, 3 were also hypoxemic in the awake state (SpO<sub>2</sub> < 90%), 1 had chronic obstructive pulmonary disease and 2 had a body mass index of > 35 suggestive of obesity hypoventilation syndrome.

**Conclusion :** We conclude that in patients, opioid medications are associated predominantly with obstructive and central sleep apnea. When sleep related hypoventilation/hypoxemia does occur, it is associated with other conditions that are already known to be associated with hypoxemia/hypoventilation. Therefore, opioid medications may aggravate but do not appear to cause sleep related hypoventilation.

**Support (optional):** UB Divisional funds

### 0622

#### MODEL DRIFT IN A QUESTIONNAIRE THAT PREDICTS SEVERITY OF OBSTRUCTIVE SLEEP APNEA

*Grant B,<sup>1,2</sup> Choi Y,<sup>2</sup> Sathananthan A,<sup>2</sup> Magalang UJ,<sup>3</sup> Grant GB,<sup>4</sup> El-Solh AA<sup>2</sup>*

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**Introduction :** Model drift is defined as the deterioration in a model's predictive properties over time. Previously, we developed a questionnaire that predicts the apnea-hypopnea index (AHI) of patients suspected of obstructive sleep apnea (El-Solh et al, Sleep 22:105-110, 1999) using an artificial neural network (ANN) and retested its diagnostic accuracy with data obtained from another group of patients six years later.

**Methods :** The ANN was developed on 189 patients and validated on another 80 patients who underwent full night polysomnography in 1996.

We collected data in 2002 from a different laboratory on 529 patients for model development and another 200 patients for validation. Diagnostic accuracy was assessed from the area under receiver operator characteristic curve: 0.5 would be expected by chance, 1.0 would indicate perfect accuracy.

**Results :** Diagnostic accuracy for 1996 ANN deteriorated from 0.96 (95%CI: 0.90-0.99) with 1996 data to 0.63 (95%CI:0.55-0.71) with 2002 data. Another ANN was developed from 2002 data but it did not improve accuracy: 0.64 (95%CI: 0.56-0.71). A predictive model developed using multiple adaptive regression splines (MARS) on the 1996 data suffered a similar loss in accuracy over time from 0.92 (95%CI: 0.83-0.97) to 0.77 (95%CI: 0.70-0.82). A MARS model developed from the 2002 data had better predictive properties than ANN and was less susceptible to model drift: 0.80 (95%CI: 0.68-0.88) and 0.77 (95%CI: 0.70-0.82) for 1996 and 2002 data respectively. All the results reported used a cutoff of AHI of 15/hr, results were similar with cutoffs of 5 and 30/hr.

**Conclusion :** We conclude (1) that MARS may be less susceptible than the ANN to model drift and (2) the pattern of results suggest changes in the patient characteristics are most likely to be the primary cause of the model drift.

**Support (optional):** UB Divisional funds.

### 0623

#### EXPLORATORY STUDY OF A POSSIBLE TWO-FACTOR MODEL OF THE EPWORTH SLEEPINESS SCALE (ESS)

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**Introduction :** Kim & Young reported on the multi-factorial nature of daytime sleepiness. Based on their research, one can derive two scores from the ESS, one for sleepiness in active situations and one for sleepiness in passive situations. This study was a retrospective chart review to assess sleepiness as determined by these factors in a cohort of OSA patients. The Dallas ESS (a modified ESS that determines sleepiness in the morning, afternoon, and evening) was used to assess active and passive sleepiness across the day.

**Methods :** 475 consecutive patients attending sleep medicine consultation completed the ESS and the Dallas ESS (295 M/ 180 F). Sleepiness was defined using a cutoff of ≥ 10 on the ESS. Repeated measures MANOVAs were run on the Dallas ESS scores of both factors by gender.

**Results :** A main effect of sleepiness was derived for both the active and passive factors on the Dallas ESS (p<.001). Increasing levels of sleepiness were documented across the day (p<.001). No interactions were noted. Interestingly, a gender effect was noted for the passive sleepiness scores with females reporting higher levels of sleepiness in the morning (p< 0.05) with similar sleepiness later in the day. No gender differences were noted in the active sleepiness scores. The proportion of endorsed sleepiness to total possible ESS score was compared for each factor. Patients endorsed a higher proportion of sleepiness in passive rather than active situations (p<.001). For the passive factor only, there was a higher proportion of sleepiness in the evening than at other times of the day (p<.001).

**Conclusion :** The results of this study indicate that use of two factors on the ESS allows for differentiation of sleepiness in passive and active situations such that either a one or two factor structure of the ESS and Dallas ESS may be viable for clinical use.

**Support (optional):**



## 0624

**PEDIATRIC OBSTRUCTIVE SLEEP APNEA: OUTCOME OF ADENOTONSILLECTOMY**

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**Introduction :** Long term follow-up was conducted on children (3 of whom were teenagers) previously treated with adenotonsillectomy during the prepubertal period. Post-operative pediatric subjects demonstrated a persistent and pathological number of apneas and hypopneas.

**Methods :** One hundred successively seen children, age 2 to 12 (mean: 6.8) years were diagnosed with obstructive sleep apnea (OSA). This diagnosis was based on clinical complaints (including fatigue, nocturnal sleep disruption, chronic sleepwalking, sleep terror, enuresis, bruxism, hyperactivity, inattention, decline in school performance, morning headache, delayed sleep phase) and the presence of an apnea hypopnea index (AHI) >1 at polysomnography with nasal cannula pressure transducer. All children had adenotonsillectomy with or without simultaneous radiofrequency treatment of nasal turbinates. Three surgeons participated in this study. Surgical technique was different, with one surgeon performing wound suturing after tonsil removal. Follow-up polysomnography was performed with similar equipment and procedure 3 to 4 and 1/2 months post-operatively.

**Results :** Despite improvement in all cases, 32 children presented persistence of abnormal breathing and an AHI > 1, with residual events seen in 50, 40 and 26% respectively of each surgeon's cases. Factors involved in the persistence of OSA included lateral soft tissue due to surgical technique in 10 cases and the presence of skeletal factors in 22 cases. These skeletal factors involved a narrow maxilla in 8 cases, mandibular retro-position in 7 cases, and maxillo-mandibular retro-position in 7 cases.

**Conclusion :** Skeletal analysis is necessary in OSA (non-syndromic) children before performing surgery. Such analysis will allow the physician to determine if there is either lateral narrowing or a combination of both anteroposterior and lateral impairment. Most appropriate management will then become evident, and a joint orthodontic and surgical treatment approach can be devised. Furthermore, such analysis can help to guide technical approach on soft tissues to attain the greatest results.

**Support (optional):**

## 0625

**RESPONSE TO CPAP THERAPY IN SLEEPY AND NON-SLEEPY OSA PATIENTS**Rosenthal L,<sup>2</sup> Dolan DC,<sup>1,2</sup> Taylor DJ<sup>1</sup>

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**Introduction :** Adherence to CPAP therapy is critical to the therapeutic outcome of OSA patients. It has been speculated that sleepy OSA patients might achieve higher adherence with CPAP. This study evaluated the adherence to therapy and change in sleepiness levels in sleepy and non-sleepy OSA patients using the Dallas ESS to assess sleepiness at morning (am), afternoon (noon), and evening times (pm).

**Methods :** Consecutive patients (N=82) with complaints of sleep disordered breathing were diagnosed with OSA from Jan to July 2005 and included in the study. Of those, 53 completed the ESS and Dallas ESS and had follow-up Dallas ESS and compliance data available. Patients were grouped into non-sleepy (N=22) and sleepy (N=34) groups by ESS score using a cutoff of  $\geq 10$ . The groups were comparable on age (54.5 $\pm$ 2.7 vs. 54.2 $\pm$ 12.4;  $p = .94$ ), gender (16M/6F vs. 23M/11F;  $\chi^2 = .69$ ), AHI (49.2 $\pm$ 26.5 vs. 54.9 $\pm$ 30.2;  $p = .47$ ) and BMI (37.1 $\pm$ 8.3 vs. 35.7 $\pm$ 8.5;  $p = .53$ ). Follow-up was at an average of 32.4 days (SD = 10.5).

**Results :** Both groups used CPAP therapy for an equivalent percentage of

nights out of total nights (88% $\pm$ 11% vs. 91% $\pm$ 16%;  $p = .49$ ) and for an equivalent average hours of use on nights CPAP therapy was used (5.5 $\pm$ 1.7 vs. 5.7 $\pm$ 1.6;  $p = .7$ ). Scores for the Dallas ESS at baseline were 2.4 $\pm$ 2.4 (am), 4.6 $\pm$ 2.9 (noon), and 6.5 $\pm$ 3.7 (pm) for non-sleepy patients and 9 $\pm$ 4.6, 14 $\pm$ 4.9, and 15.8 $\pm$ 4.3 for sleepy patients. There was a main effect of sleepy/non sleepy groups for the change in Dallas ESS scores ( $p < .001$ ). The follow-up scores for each group were 1.8 $\pm$ 2.6, 3.8 $\pm$ 2.9, and 5.5 $\pm$ 3.4, and 3.9 $\pm$ 4.3, 6.5 $\pm$ 4.2, and 9 $\pm$ 4.5, respectively. No interaction was found.

**Conclusion :** Both sleepy and non-sleepy OSA patients achieved similar CPAP adherence. The results of the study demonstrate that sleepiness is not necessarily a determining factor in the adherence to CPAP therapy.

**Support (optional):**

## 0626

**CHANGES IN LEFT VENTRICULAR MASS IN CHILDREN WITH SLEEP DISORDERED BREATHING AFTER ADENOTONSILLECTOMY**Amin RS,<sup>1</sup> Somers VK,<sup>2</sup> Kimball T,<sup>1</sup> Jeffries J,<sup>1</sup> Witt S,<sup>1</sup> Daniels S<sup>1</sup>

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**Introduction :** Children with Sleep disordered breathing (SDB) develop structural and functional changes of the left ventricle. The aim of the study is to determine the changes in left ventricular mass after treatment of SDB by adenotonsillectomy (T & A).

**Methods :** Twenty four children age 10  $\pm$  2 (54% whites and females) with polysomnography proven SDB were followed for one year after T & A. Polysomnography and echocardiography were obtained before and 1 year after surgery. Left ventricular mass index (LVMI) and relative wall thickness (RWT) were measured at the two time points. Paired t test was performed to compare the changes in echocardiographic measures before and after surgery.

**Results :** Nine children had resolution of SDB defined as AHI  $\leq 2$ /hour. LVMI in the whole study population decreased from 37  $\pm$  8 to 34  $\pm$  7 ( $p = 0.003$ ) and RWT decreased from 0.35  $\pm$  0.04 to 0.33  $\pm$  0.05 (NS). In children who had resolution of SDB, apnea hypopnea index (AHI) decreased from 4  $\pm$  2 to 0.8  $\pm$  0.6, BMI remained at 19  $\pm$  5 and LVMI decreased from 32.8  $\pm$  6 to 28.5  $\pm$  6 ( $p = 0.03$ ). In children with partial resolution of SDB, AHI decreased from 9  $\pm$  10 to 5  $\pm$  4, BMI changed from 25  $\pm$  6 at baseline to 27  $\pm$  5.5 at 1 year and LVMI decreased from 39.7  $\pm$  9 to 37  $\pm$  7 ( $p = 0.04$ ).

**Conclusion :** Complete and or partial resolutions of SDB in children 1 year after T & A are accompanied by a decrease in left ventricular mass index.

**Support (optional):** RO1HL070907 and MO1 RR 08084-08

## 0627

**THE EFFECT OF BMI AND UPPER AIRWAY ANATOMY ON RDI ACCORDING TO POSITION IN KOREAN OBSTRUCTIVE SLEEP APNEA PATIENTS**Moon B,<sup>1</sup> Lee J,<sup>1</sup> Jang Y,<sup>1</sup> Lee B,<sup>1</sup> Lee S,<sup>2</sup> Chung Y<sup>1</sup>

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**Introduction :** Avoidance of the supine position during sleep is a simple behavioral therapy for many patients with obstructive sleep apnea (OSA), and the efficacy of this positional therapy is influenced by RDI and BMI. In Asians, however, little is known about the effect of anatomic characteristics of the upper airway and BMI on positional OSA. We aimed to investigate the effect of BMI and upper airway anatomy (the degree of tonsil-

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lar hypertrophy and obstruction of the oropharynx and hypopharynx) on RDI according to sleep position in Korean OSA patients.

**Methods :** Using overnight polysomnography, we evaluated 112 patients with RDI over 5 and whose sleep time in the supine/non-supine position was over 30 minutes. We measured their BMI, tonsillar hypertrophy and obstruction of the oropharynx and hypopharynx by Müller maneuver. We analyzed their RDI according to position, BMI, tonsillar hypertrophy and obstruction of the oropharynx and hypopharynx.

**Results :** 76.8% of Korean OSA patients had positional sleep apnea. The mean reduction rate according to BMI was lower in obese class II group than other groups ( $p = 0.001-0.028$ ). The mean RDI reduction rate according to tonsil grade was significantly lower in patients with grade II and III than in patients with grade I tonsils ( $p < 0.001$ ). Following the Müller maneuver at oropharynx, the mean RDI reduction rate was RDI was significantly decreased in patients with grade IV ( $p < 0.001$ ). The most significantly predicted positional non-dependency was high grade obesity (OR = 9.61,  $p = 0.034$ ), followed by grade IV oropharyngeal obstruction (OR = 4.68,  $p = 0.029$ ).

**Conclusion :** Positional therapy may be more effective in Korean than in Western OSA patients. However, in obese class II patients and those with grade IV oropharyngeal obstruction, the effect of the position change on RDI was lower than in other groups.

**Support (optional):**

### 0628

#### SOFT PALATE IS A MAJOR SOURCE OF PHARYNGEAL EVOKED POTENTIALS

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**Introduction :** Pharyngeal sensitivity participates to the control of pharyngeal patency and has been shown to be impaired in apneic patients. However, measurement of pharyngeal sensitivity is currently based on patient's subjective response. Moreover, the contribution of the different pharyngeal regions in the neurogenic regulation of upper airway is unclear. To address these issues, we developed a novel procedure allowing to record cortical evoked potentials from various pharyngeal regions.

**Methods :** Nine healthy adult volunteers were equipped for EEG recordings and for pharyngeal stimulation. Using a device previously developed for measuring pharyngeal sensation by the psychophysical method of limits, and combined to an air source delivering small air puff stimuli, different oropharyngeal regions were tested. Pharmacological modulation of the cortical response was assessed by topical anesthesia.

**Results :** Air-pulse stimuli were well-tolerated in all participants but one. The sensory stimulation elicited consistent and reproducible electrophysiological patterns, with a good signal-to-noise ratio, as well as intra- and intersession repeatability, enabling an objective and quantitative assessment of pharyngeal sensitivity. The complete evoked response was a W-shaped waveform complex, with succession of negative and positive peaks, morphologically resembling the sensory potentials elicited by electrical or mechanical stimuli of hand, leg and face. Among the different tested regions, soft palate stimulation elicited the largest and the most complete response, that was decreased or abolished by topical xylocaine application.

**Conclusion :** We have developed a simple procedure to record pharyngeal evoked potentials using air-puff stimuli. Among the different pharyngeal regions tested, and based on electrophysiological responses, soft palate appeared as the main source of sensory information from pharynx. Easy to adapt to standard evoked potential machine, this new technique may

represent a powerful tool for studying the neurogenic regulation of the upper aerodigestive tract, and the role of pharyngeal sensitivity in the pathophysiology of sleep disordered breathing.

**Support (optional):** Supported by a grant from ANTADIR and AGIRaDOM Scientific Council.

### 0629

#### RESULTS OF PREOPERATIVE OVERNIGHT AIRWAY PRESSURE MEASUREMENTS PREDICT THE SURGICAL OUTCOMES FOR PATIENTS WITH OBSTRUCTIVE SLEEP APNEA SYNDROME

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**Introduction :** The distribution of obstructive sites of upper airway can be identified quantitatively and dynamically using continuous airway pressure measurements in obstructive sleep apnea syndrome (OSAS) patients. Its predictive value, along with several other variables, for surgical procedures extending the retropalatal level airway was evaluated.

**Methods :** Proportions of obstruction located transpalatal and subpalatal were preoperatively assessed by overnight pressure measurements during polysomnography (PSG) in 26 males and 2 females with OSAS. All patients were follow-up by PSG. The relationship between the percentage of transpalatal obstruction events, age, tonsil size, preoperative apnoea hypopnoea index (AHI) and body mass index (BMI) and the reduction in AHI was analyzed.

**Results :** Except for the three who had transpalatal plus genioglossus advancement, 25 subjects with an average of  $38.05 \pm 7.63$  years underwent site specific operations and were follow-up at  $6.30 \pm 0.84$  months, twenty three had uvulopalatopharyngoplasty (UPPP), two had transpalatal advancement pharyngoplasty. The AHI (times/hr) falls down from  $64.94 \pm 17.64$  to  $27.46 \pm 24.88$ . The response rate was 56% (definite as 50% reduction in AHI). Correlation between the percentage of oropharynx obstruction (Op%) and the percentage of reduction in AHI was significant at the 0.01 level ( $r = 0.611$ ), so was the degree of the tonsil size ( $r = 0.541$ ). Patients with Op% > 70% had a success rate of 90% and all patients with Op% < 60% response poorly to the operation. Other factors showed marginal statistical significance with the reduction in AHI include age ( $r = 0.404$ ) and pre-operative AHI ( $r = 0.397$ ,  $p < 0.05$ ). The baseline nadir O<sub>2</sub> saturation show a negative correlation for the improvement of O<sub>2</sub> saturation ( $r = -0.714$ ,  $p < 0.01$ ).

**Conclusion :** The distribution of UA obstructive sites, along with the tonsil size has significant predictive value to the outcome of transpalatal level surgery in OSAHS patients. The presence of a Op% < 60% are predictors of failure of UPPP.

**Support (optional):**

### 0630

#### OVERNIGHT TREND OF UPPER AIRWAY OBSTRUCTIVE SITES IN OBSTRUCTIVE SLEEP APNEA PATIENTS AND IT'S INFLUENCING FACTORS

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**Introduction :** Understand how the sites of upper airway (UA) obstruction change during overnight sleep in patients with obstructive sleep apnea syndrome (OSAS) and the various influencing factors as sleep stage and position. Investigate whether positional patients had special obstructive pattern compare to nonpositional patients.

**Methods :** 54 OSAS patients underwent overnight upper airway pressure measurements during polysomnography. The levels of the UA obstruction

were determined by the observed pressure pattern. The involvement of different UA segments and the relationship between sleep stage, position and site of obstruction were analyzed.

**Results :** 23,176 respirative events were recorded and analyzed, 65.65% were located at the oropharynx, 23.54% were located at the tongue base, and 10.02% events with extension of obstructive sites, the remaining 0.81% events located at hypopharynx or other. Age of patients showed statistical significance with the distribution of obstructive sites ( $r=0.353$ ,  $0.389$ ). 2) Compare to NREM sleep, REM sleep was associated with a tendency for obstruction to extend towards lower levels of UA. The portion of tongue base obstruction increased ( $t=8.790$ ), the percentage of tongue base obstruction was higher ( $t=6.189$ ). 3) Sleep position affected little on distribution of obstructive site. Increased frequency of the UA collapses was observed on all levels in supine position and was most obvious on the level of post oropharynx (with an average of 7.08 times/hr). Positional patients had similar distribution of obstructive site to nonpositional patients.

**Conclusion :** 1) Obstructive sites tend to extend to lower level of UA during REM sleep. 2) Sleep position has little effect on distribution of obstructive sites. Collapses of UA on the post oropharynx level contribute more to the increased AHI when the subjects were in supine position.

**Support (optional):**

### 0631

#### USE OF NASAL CPAP FOR SLEEP APNEA AFTER PRESCRIPTION IN A PUBLIC REFERRAL HOSPITAL

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**Introduction :** Continuous Positive Airway Pressure (CPAP) is the treatment of choice for obstructive sleep apnea syndrome (OSAS). CPAP decreases mortality and morbidity associated with this disorder. Our aim was to analyze the onset of treatment after prescription, and the long-term compliance to CPAP in patients with OSAS in a referral hospital in Mexico. A secondary aim was to identify predictors of CPAP pressure.

**Methods :** We analyzed a total of 304 OSAS patients with CPAP prescription. Diagnosis was made by polysomnography (PSG) ( $n=270$ ) or by a simplified study ( $n=34$ ), and CPAP titration was made during the PSG, or with an automatic CPAP device. All patients received a general education session on CPAP use and functioning. CPAP compliance was evaluated during monthly follow-up visits or by telephone, when patients did not attend the consult

**Results :** Only 169 (55.5%) of the patients acquired the equipment within 1.5 months (median), predictive factors were severe disease (respiratory index  $>30$ /hr) and having social security. Compliance was 80% after three years, with respiratory index as the unique compliance predictive factor by Cox regression analysis. Body mass index, Epworth scale, respiratory index and mean SpO<sub>2</sub> during PSG, were predictive factors of prescribed pressure. Besides the well known restricted availability of diagnostic methods for OSAS, we have to take into account a limited access to CPAP in diagnosed patients without social security in Mexico.

**Conclusion :** Almost half of patients with CPAP prescription, did not start the treatment, but most of those who acquired the device, had an acceptable compliance after three years. CPAP compliance was better in patients with high respiratory index.

**Support (optional):** None

### 0632

#### COGNITIVE FUNCTIONING IN OBSTRUCTIVE SLEEP APNEA (OSA) PATIENTS: EFFECT OF AUTOCPAP AND STANDARD CPAP

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**Introduction :** OSA is known to be associated with neuropsychological deficits and CPAP treatment has been shown to improve performances in specific cognitive domains, although data are still controversial. Recently, a possible correlation between treatment compliance and cognitive improvement has been suggested. Aim of this study was to compare changes in neurocognitive functioning in OSA patients after treatment with AutoCPAP and standard CPAP.

**Methods :** Fifty consecutive patients with severe OSA (RDI  $>30$ ), were randomly assigned to one of two treatment groups. Group A received one-month treatment with AutoCPAP followed by one-month standard CPAP while group C received treatment in the opposite order (all patients received REMstar® Auto Smart CPAP System, Respiroics Inc., set in Auto or standard CPAP modes). All patients underwent full nocturnal polysomnography as well as a wide battery of neuropsychological tests at baseline (before treatment), at T1 (after one month) and at T2 (after two months). Global cognitive functioning, attention, vigilance, language, memory, executive function, constructional and psychomotor abilities were blindly assessed.

**Results :** Forty patients (37M, 3F; mean age  $53.1 \pm 10.4$ ) completed the study. The two groups were similar in terms of demographic and clinical features. Most of the neurocognitive tests showed an effect of time indicating a treatment improvement on cognition (Anova by repeated measures;  $p < .001$ ). An effect of group was also observed indicating that Group A had a better improvement in executive function (Stroop error [ $F(1,37)=4.507$ ;  $p=0.041$ ]) and divided attention (TEA [ $F(1,37)=4.241$ ;  $p=0.047$ ]) than Group C. Moreover a time by group interaction was found for flexibility [ $F(2,74)=3.174$ ;  $p=0.048$ ] and a trend toward significance for divided attention [ $F(2,74)=2.603$ ;  $p=0.081$ ]. Objective compliance was very good in both two groups (average time of use per night over two-months: 395 min. in Group A versus 420 min. in Group C). A trend towards a positive correlation between objective compliance and cognitive performances was obtained in some cognitive domains ( $r=0.29$ ;  $p=0.08$ ).

**Conclusion :** Our data showed that most cognitive functions significantly improved over time, regardless the type of CPAP, although AutoCPAP may have a better impact on some cognitive domains. Cognitive improvement might be related to treatment compliance (objectively evaluated). Therefore adherence to treatment should always be measured when assessing cognitive functioning changes.

**Support (optional):**

### 0633

#### A COMPARATIVE STUDY OF AMBULATORY BLOOD PRESSURE MONITORING IN CHILDREN WITH SLEEP-DISORDERED BREATHING

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**Introduction :** Sleep-disordered breathing (SDB) in children is associated with cardiovascular morbidities. High blood pressure in children with SDB is generally missing in the routine pediatric practice. Our aim was to

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determine the frequency of hypertension and non-dipping in this disorder

**Methods :** Thirty-one children (21 male), between 6 to 12 years of age were enrolled, in this cross-sectional study. According to polysomnography criteria (apnea/hipopnea/index, mean oxygen saturation and percentage of sleep with < 90 % oxygen saturation) were divided in 3 groups: primary snoring, mild/moderate obstructive sleep apnea (OSA), and severe OSA. All underwent a 24-hours ambulatory blood pressure monitoring by an oscillometric device with appropriate cuff for age. Hypertension was defined as mean systolic or diastolic pressure superior to 95 th percentile, and systolic or diastolic load >25%. Non-dipping was defined as mean nocturnal blood pressure falling < 10 % relative to diurnal measurements

**Results :** We observed 16 primary snoring, 10 mild/moderate OSA and 5 severe OSA. Results are presented as median and interquartile range, for primary snoring, mild/moderate OSA and severe OSA respectively. Age: 7.03 ( 2.56), 8.02 (4.51) and 6.10 (0.55) years. Body mass index: 17.43 (6.24), 17.63 (8.25), and 21.24 (3.78) Kg/m<sup>2</sup>. (p=0.17); daytime systolic load: 0 (2.35), 0 (0) and 6.20 (8.4) % (p=0.002); nighttime systolic load: 6.2 (7.3), 0 (7.3) and 43 (58.2) % (p=0.03); 24 hours systolic load: 0 (4.22), 0 (5.3) and 35 (31.30) % (p=0.007) There were five (16%) hypertensive children (4 severe OSA and 1 primary snoring) There were twenty (64.5%) non-dipper children ( 10/16 primary snoring, 6/10 mild/moderate OSA, and 4/5 severe OSA)

**Conclusion :** Systemic hypertension in children with SDB is frequent. We found a major proportion of hypertension and non-dipping in severe OSA group in comparison with other groups

**Support (optional):**

### 0634

#### PREVALENCE OF OBSTRUCTIVE SLEEP APNOEA (OSA) IN UK HEAVY GOODS VEHICLE (HGV) DRIVERS

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**Introduction :** OSA affects approximately 1-4% of the middle aged male population. Previous research has shown that the demographics of UK HGV Drivers pre-dispose this group to increased OSA risk factors and therefore they are more likely to suffer from OSA.

**Methods :** A questionnaire was used as a basis for screening for OSA and Fatigue Risk and used to stratify subjects into risk groups and to direct therapeutic intervention. Overall, 940 drivers were recruited in the study from five diverse freight companies. Drivers were initially screened based on responses to a questionnaire and were categorised as positive, likely or negative. Diagnosis was only confirmed after further investigation by experienced clinicians. Those judged on screening as positive for OSA were started on non-invasive therapy immediately with their GP consent and the data from the Positive Airways Pressure (PAP) machine was used to confirm the diagnosis. Individuals who appeared likely to have sleep apnoea were sent a respiratory monitor to wear during sleep to confirm or refute the diagnosis. Of the individuals who appeared negative on questionnaire response, a random sample of 10% were asked to wear the respiratory monitor to assess for false negatives. All therapeutic interventions were initiated if the individual met the SIGN guidelines for treatment of OSA.

**Results :** 373 (40%) questionnaires were returned. All respondents were male. Of the 373 drivers, 149 completed the protocol to diagnosis. The results showed that 11-16% of drivers had moderate/severe OSA requiring therapy (lowest limit/lowest prevalence) and 17-38% had some severity of OSA (lowest limit/lowest prevalence).

**Conclusion :** This study suggests that up to 16% of UK HGV drivers suffer from OSA, which requires PAP therapy according to the SIGN guidelines. Previous evidence suggests that 19 -27% of patients with OSA have had a motor vehicle accident due to falling asleep at the wheel and that

there are more fatal accidents on the roads caused by sleepiness each year than by drink-driving. With approximately 500,000 active UK HGV drivers this presents a significant road safety risk. With the current limitations within the UK Healthcare System and the existing vehicle licensing procedures there is an acute need for a simple, low-cost system that can fast-track the screening, diagnosis and management of these drivers. It is imperative that this approach is sensitive to the needs of the drivers and their employers.

**Support (optional):**

### 0635

#### GENDER DIFFERENCES IN THE RELATIONSHIP BETWEEN THE EPWORTH SLEEPINESS SCALE AND INDICES OF SLEEP APNEA

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**Introduction :** Previously published studies have reported that there may be gender differences in how patients describe their presenting symptoms and respond to the Epworth Sleepiness Scale. We examined the association between objective polysomnography measures of respiratory disturbance and subjective reports of sleepiness in sleep apnea patients. We hypothesized that the relationships among the ESS and sleep variables would differ between men and women.

**Methods :** The data presented are part of a larger study of 1135 consecutive patients referred to our sleep center. Patients completed nocturnal polysomnography, a quality of life questionnaire, a list of chief complaints, a sleep survey, the ESS, and a medication list. Data from 515 men and 258 women with sleep apnea were examined. The relationships between ESS and polysomnography measures were analyzed for the full sample and for males and females separately.

**Results :** In the present study, ESS scores did not differ between men and women (mean=11.46, SD=5.0, men; mean=12.07, SD=5.05, women); however, significant correlations were present between ESS scores and objective measures of respiratory disturbances for men, but not women. Respiratory arousal index, respiratory disturbance index, minimum oxygen saturation, mean oxygen saturation, and number of obstructive apneas ( $r = .23, .23, -.19, -.24, .30$ , respectively;  $p < .001$  tt) were significantly correlated with ESS for men. For women, the ESS was significantly correlated only with minimum oxygen saturation ( $r = -.21, p < .001$ ).

**Conclusion :** Although women reported being as sleepy as men, the subjective measures of sleepiness were related to the objective measures of apnea more so in men than women. Thus, subjective sleepiness in women may be accounted for by other factors. The significance of these findings, as they relate to other health and quality of life measures, will be explored further.

**Support (optional):**

### 0636

#### PATTERNS OF SLEEP DISORDERED BREATHING DURING THE ACUTE AND RECOVERY PHASES OF STROKE

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**Introduction :** The relationship between sleep disordered breathing and stroke is increasingly recognized as an important modifiable risk factor prior to occurrence of a vascular event. Much less is known about the effect of acute cerebrovascular injury stroke on disordered breathing and whether acute treatment might alter the functional outcome of these

patients. The occurrence of acute brain injury whether as ischemic or hemorrhagic stroke will affect sleep disordered breathing depending on the localization of the stroke, and the presence, type and severity of sleep disordered breathing prior to the event. Many patients simultaneously exhibit several forms of sleep disordered breathing which evolve during the acute and recovery phases. The study was undertaken to determine the predominant patterns of sleep disordered breathing in stroke and correlate these patterns related neuroanatomic damage.

**Methods :** Six patients with acute stroke were studied in the acute and recovery phases of either hemorrhagic and ischemic stroke. Baseline demographic and cardiovascular risk data were obtained as well as overnight polysomnograms to document the patterns of disordered breathing. Clinical MRI and CT scans were done to determine the localization extent of the strokes and the evolution of these lesions over time.

**Results :** Three distinct patterns emerged of the stroke patients with respect to the presence of sleep disordered breathing. In the first group, both obstructive and central sleep apnea were present during the acute phase of the stroke with resolution of central sleep apnea and persistence of the obstructive sleep apnea during the recovery phase. In the second group, mainly central sleep apnea was present during the acute phase, but it subsequently resolved. In the third group, obstructive sleep apnea was present during the acute and recovery phases and responded appropriately to conventional therapies such as CPAP.

**Conclusion :** This study shows that there are at least three patterns of sleep disordered breathing found in patients with acute stroke. The patterns vary according to localization and size of the lesions and are also influenced by the premorbid status of the patients. Further detailed stratified studies are required to determine if the treatment of the different types and patterns of sleep disordered breathing in the acute and recovery phases has a significant impact on functional outcomes.

**Support (optional):**

### 0637

#### SLEEP APNEA MORTALITY IN MIDDLE-AGED VERSUS GERIATRIC VETERANS

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**Introduction :** Untreated obstructive sleep apnea (OSA) appears to increase mortality, and OSA treatment reduces mortality. Some have postulated that the mortality risk attributable to OSA and the benefit of OSA treatment are less in geriatric compared to middle-aged patients. We tested these hypotheses.

**Methods :** This retrospective inception cohort study included all patients diagnosed with OSA in any Veteran Affairs (VA) inpatient facility 1991 - 2001 or outpatient facility 1997 - 2001. Subjects were identified by ICD9 diagnostic codes in the VA inpatient and outpatient treatment files. Treatment status (None versus CPAP/UPPP) was determined by ICD9 or CPT procedure codes in these databases. Patients without a code for CPAP or UPPP were considered untreated. Sleep apnea severity data were not available. The Charlson Comorbidity Index was calculated from ICD-9 diagnostic codes from the year prior to inception into the cohort. Mortality data were extracted from VA Death Files. Middle-aged (<60 years) and geriatric (60+ years) patients were compared on mortality hazard with Cox regression, adjusting for age, sex, race, comorbidity, and inception year, and using time-dependent exposure for treatment analysis.

**Results :** The cohort consisted of 82,625 middle-aged (mean 48+/-8 years, 95% male) and 65,163 geriatric (mean 69+/-6 years, 98% male) veterans. After adjusting for the variables listed, untreated middle-aged patients had a similar hazard of dying relative to untreated geriatric patients (hazard ratio 0.96, 95%CI 0.90-1.02, p=0.17). Accounting for the

time-dependent nature of treatment, treated middle-aged patients had 0.80 the hazard of dying at any time relative to untreated middle-aged patients; similarly, treated geriatric patients had 0.79 the hazard of dying at any time relative to untreated geriatric patients.

**Conclusion :** The independent mortality risk of OSA and the benefits of treatment are similar between middle-aged and geriatric patients. These data suggest that OSA should be treated comparably in geriatric patients.

**Support (optional):** VA Epidemiology Research and Information Center grant, American Geriatrics Society Jahnigan Award (funded by the John A. Hartford Foundation of NYC and Atlantic Philanthropies), and NIH K23 HL068849.

### 0638

#### PATIENT SATISFACTION WITH EMPIRIC CPAP THERAPY FOR SUSPECTED OBSTRUCTIVE SLEEP APNEA

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**Introduction :** Limited resources have resulted in a lack of timely access to diagnostic polysomnography (PSG) for patients with suspected obstructive sleep apnea (OSA) in Saskatchewan. The lengthy wait time for completion of diagnostic PSG has prompted the practice of prescribing empiric continuous positive airway pressure (CPAP) therapy for patients who are assessed as having a high pre-test probability for OSA based on clinical assessment and/or positive results on overnight oximetry testing. A quality assurance project was undertaken to assess patient satisfaction with the initiation of empiric CPAP, subjective response to the therapy and followup by the prescribing physician.

**Methods :** Patients who had been prescribed empiric CPAP therapy for suspected OSA were asked to complete a questionnaire on the morning following completion of diagnostic or split night protocol PSG. Patients completed the survey anonymously. The responses were reviewed by a physician who was not involved in prescribing empiric CPAP therapy.

**Results :** A total of 43 patients completed the questionnaire during a 3 month period. The average age of the respondents was 50.5 years (range 29-70). The average duration of use of empiric CPAP therapy prior to completion of diagnostic PSG was 11.8 months (range 1.5-72). Twenty two of the patients met with a nurse educator prior to initiation of empiric CPAP therapy. Twenty patients were seen in followup by the prescribing physicians. Patient adherence with empiric CPAP therapy was good with 72.1%(31/43) demonstrating regular nightly use prior to diagnostic PSG. The majority of patients (28/43 65.1%) reported significant improvement in sleep quality, daytime somnolence and energy level with use of empiric CPAP therapy. 75.6% of the respondents felt that treatment with empiric CPAP was appropriate during the period prior to completion of diagnostic PSG.

**Conclusion :** The majority of patients who are prescribed empiric CPAP therapy for suspected OSA report a high degree of satisfaction with this practice. Most patients experience a significant subjective improvement in sleep quality and daytime somnolence. Patient satisfaction with empiric CPAP therapy may be further improved by meeting with a nurse educator prior to initiation of therapy and regular followup by the prescribing physician.

**Support (optional):**

### 0639

#### CLINICAL AND POLYSOMNOGRAPHIC FEATURES OF BARIATRIC SURGERY CANDIDATES WITH SUSPECTED SLEEP APNEA

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## Category I—Sleep Disorders-Breathing

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**Introduction :** Morbidly obese patients are more likely to have obstructive sleep apnea (OSA) than nonobese patients due to the known relationship between body weight and the apnea-hypopnea index (AHI). This study is part of a prospective study evaluating the prevalence of OSA and its predictors in morbidly obese patients.

**Methods :** This was a retrospective chart review between March and November 2005 of patients undergoing evaluation for bariatric surgery at the Cleveland Clinic Foundation. Subjects in whom sleep apnea was suspected based on clinical suspicion were referred for polysomnography (PSG). Demographic and PSG data were collected. Sleep apnea was classified as mild ( $5 \leq \text{AHI} < 15$ ), moderate ( $15 \leq \text{AHI} < 30$ ), or severe ( $\text{AHI} \geq 30$ ). REM-related apnea was defined as an overall  $\text{AHI} \geq 5$  and  $\text{REM-AHI/NREM-AHI} > 2$ . Univariate and multivariate regression analyses were performed using JMP 5.0.1 (SAS Institute, Cary, NC).

**Results :** Eighty-eight patients (83% females) were included. Mean age was  $44 \pm 11$  (range 16-69) years. Mean body mass index (BMI) was  $52.4 \pm 12.9$  (31.8-121.4). Mean neck circumference (NC) was  $42.9 \pm 4.6$  cm; 52% of the patients had a  $\text{NC} \geq 43$  cm. Mean Epworth Sleepiness Scale score (ESS) was  $11.2 \pm 5.2$ ; of note, 60 patients (68%) had an  $\text{ESS} \geq 10$ . Mean AHI was  $33 \pm 35$  (range 0.3-142.5). Overall, OSA was found in 84% patients including 26% with mild OSA, 19% with moderate OSA, and 38% with severe OSA. REM-related apnea was found in 30% of patients (92% females). The ESS did not correlate with AHI ( $R^2=0.11$ ,  $p=0.21$ ). There was no correlation between NC and AHI ( $R^2=0.19$ ,  $p<0.0001$ ) or between NC and REM-AHI ( $R^2<0.01$ ,  $p=0.98$ ). The BMI did not correlate with the AHI ( $R^2=0.005$ ,  $p=0.48$ ).

**Conclusion :** OSA is common in morbidly obese patients. REM-related OSA was seen almost exclusively in women. No single clinical or physical characteristic was predictive of OSA in this patient population.

**Support (optional):**

### 0640

#### PRETREATMENT FACTORS INFLUENCING CPAP ADHERENCE

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**Introduction :** It has been established that pattern of CPAP use is determined during first week of treatment. It remains unclear what pre-treatment factors are operative during this time period, influencing treatment adherence. As CPAP is nonsurgical treatment of choice for OSA, identifying causes of nonadherence is central clinical concern. We explored several pre-treatment demographic and self-efficacy variables to identify factors related to CPAP use during first week of treatment.

**Methods :** 55 subjects (mean age  $48.52 \pm 12.09$  yrs) with  $\text{AHI} \geq 15$  were prescribed CPAP treatment, completed actigraphy, and battery of tests pre-treatment: Functional Outcomes of Sleep Questionnaire (FOSQ); Epworth Sleepiness Scale (ESS) and Self-Efficacy Scale for Sleep Apnea (SEMSA) which included subscales of Perceived OSA Risk, Outcome Expectancies for CPAP treatment, and Treatment Self-Efficacy. CPAP adherence measured by AutoSet Clinical system (ResMed Corp, San Diego, CA) in constant mode, circumventing autoadjust feature thus delivering constant CPAP pressure. AutoSet Clinical System selected not as autoadjusting device, but to utilize its monitoring capabilities.

**Results :** First day of treatment considered as acclimatizing experience and not used in analysis. Mean CPAP use from Day 2-7 was  $3.41 \pm 2.67$  hrs/day. On first step of multiple regression (ANOVA), pretreatment variables included gender, education level, race, AHI, full time employment, ESS total, and Total FOSQ score. This model accounted for

36% of variance ( $F_8 = 2.84$ ,  $p = 0.01$ ). Independent predictors were being of black race ( $p = 0.002$ ) and Total FOSQ score ( $p = 0.01$ ). Self-efficacy subscales included in subsequent steps, each entered separately. Pre-treatment self-efficacy variables were not independent predictors of CPAP use. Final reduced model accounting for 25% of variance ( $F_3 = 5.93$ ,  $p = 0.002$ ) included being of black race, male sex, and Total FOSQ score. Being black ( $p = 0.0037$ ) and Total FOSQ score ( $p = 0.046$ ) were independent predictors of nightly duration of CPAP use. CPAP use was 1.6 hours less/night if black and male.

**Conclusion :** This study demonstrated pretreatment predictors of CPAP use are race and daily functional level. Further investigation needed as to basis for racial differences in CPAP and contribution of functional level to adherence. Unclear is whether racial difference reflects socio-cultural perspective rather than race itself. Understanding these relationships can lead to tailored interventions addressing socio-cultural differences applying to CPAP use.

**Support (optional):**

### 0641

#### PREVALENCE OF FLOPPY EYELID SYNDROME IN OBSTRUCTIVE SLEEP APNEA-HYPOPNEA SYNDROME

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**Introduction :** Floppy eyelid syndrome (FES) refers to a constellation of findings, including increased eyelid laxity, papillary conjunctivitis, and lash ptosis. There have been several reports suggesting an association between obstructive sleep apnea-hypopnea syndrome (OSAHS) and FES. Our goal was to determine the frequency of FES in a group of patients with OSAHS.

**Methods :** Ophthalmologic tests, including slit lamp exams, a subjective measure of lid eversion ease, and quantification of lid laxity via strain gauge, were performed just before polysomnography on 59 patients with a suspected sleep disorder.

**Results :** Forty-four (75%) patients had OSAHS and 15 patients did not (controls). The OSAHS group was older (mean [SD] age 62.7 [15.0] years vs 43.2 [11.8] years,  $p=0.0001$ ) while body mass indices (BMI) were similar (mean [SD] BMI 33.9 [5.9] kg/m<sup>2</sup> vs 33.2 [6.6] kg/m<sup>2</sup>,  $p=0.68$ ). FES was found in 1 (2.3%) of the OSAHS patients, and not in any control patients. Adjusting for age and BMI, apnea-hypopnea index (AHI) was correlated with subjectively easy lid eversion (odds ratio 2.38;  $p=0.025$ ). However, combined lid force measurements were not statistically different in OSAHS and non-OSAHS patients (mean [SD] force 20.7 [8.9] grams vs 18.2 [9.6] grams,  $p=0.37$ ).

**Conclusion :** The frequency of FES in 2.3% of OSAHS patients matches that from the largest series studied to date. Subjective lid eversion data correlated with AHI while objective lid force measurements did not.

**Support (optional):**

### 0642

#### THE NASAL AIRWAY AS A PREDICTOR OF CPAP OUTCOMES

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**Introduction :** Limited data suggest that the baseline nasal airway before treatment with continuous positive airway pressure (CPAP) may be associated with subsequent CPAP outcomes. We tested the hypotheses that the pre-CPAP nasal cross-sectional area is associated with CPAP tolerance, use, and outcome.

**Methods :** The Seattle Sleep Cohort is an ongoing prospective inception

cohort study of patients newly diagnosed with obstructive sleep apnea in the UW Sleep Laboratory and recommended for CPAP therapy. Baseline minimal nasal cross-sectional area was measured using acoustic rhinometry after 10 minutes supine on the evening of initial polysomnography. Six months later, CPAP tolerance (visual analog scale) and objective CPAP use (minutes with pressure on), and change in Epworth Sleepiness Scale (ESS) and Sleep Apnea Quality of Life Index (SAQLI) were measured. Multivariate linear regression was used to test associations between the pre-CPAP nasal airway and CPAP tolerance/use, and between CPAP tolerance/use and outcome, adjusting for age, sex, race, body mass index, baseline apnea-hypopnea index, and CPAP humidity type.

**Results :** The cohort consists of 322 newly diagnosed sleep apnea patients (58% male) with baseline mean age 46+/-12 years, apnea-hypopnea index 51+/-35 events/hour, nasal cross-sectional area 0.4+/-0.1 cm<sup>2</sup>, ESS 10+/-5, and SAQLI 4.3+/-1.0. At six months, mean CPAP tolerance was 57+/-35, CPAP use 2.8+/-2.9 hours, and improvement in ESS 2+/-5 and SAQLI 0.3+/-0.9. After adjustment, pre-CPAP nasal area was associated with CPAP tolerance ( $p<0.02$ ) and CPAP use (only in middle-aged <60 years [87% of cohort],  $p=0.05$ ). CPAP tolerance and use was each strongly associated with improvement in ESS and SAQLI (all  $p<0.001$ ).

**Conclusion :** The baseline nasal airway dimensions are associated with subsequent CPAP tolerance and, in middle-aged sleep apnea patients, CPAP use. The improvement in tolerance and use translate into improved sleepiness and quality of life.

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0643

WEIGHT LOSS TRENDS IN SODIUM OXYBATE TREATED PATIENTS

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**Introduction :** Sodium oxybate is indicated for cataplexy treatment in narcolepsy. The drug has demonstrated efficacy in the fragmented sleep and excessive daytime sleepiness of narcolepsy. This is a study to examine weight loss trends in 86 individuals taking sodium oxybate as of August 31, 2005.

**Methods :** 86 patients at one sleep clinic on sodium oxybate therapy were studied. Chart audits were conducted at two different time intervals to obtain baseline, 1st, and 2nd office visit weights. No patients taking sodium oxybate were excluded from the review. Most patients in the data set were on stimulant therapy, which remained unchanged.

**Results :** Within the group of 86 patients, there were 22 males (ages 20-76) and 64 females(ages 16-76). The dates for drug initiation ranged from 2002-2005. Current dose ranged from 3 grams to 10.8 grams. Means with standard deviations are reported. Initial chart review revealed at first office visit (mean 1.7 months)that there were 48 with weight loss (11 men /37 women), 28 with weight gain (5 men /23 women) and 10 with no change. The range of weight loss was 1-16 lbs and there were 10 with weight loss over 10 lbs. The mean weight at baseline for the group was 174(41) and at first office visit post therapy initiation 173(41). T-test comparing weight loss at baseline and first office visit post-therapy was not significant p=0.4. Comparison of mean weight loss was for men 2.5lbs(3) and women 4.9lbs(5). T-test comparing weight loss between men and women was statistically significant p<0.01. A subsequent chart review performed three months later to obtain data from second office visit(mean 5 months) found 76 in the group with 57 women, 19 men, and 10 who either stopped therapy or had not been back for follow-up visit. There were 46 with weight loss (36 women/10 men), 27(20 women/7 men)with weight gain, and 3 with no change. The mean weight loss for the group was baseline 173(39) and at 2nd office visit was 166(3). T-test comparing weight loss at baseline and second office visit post-therapy was not significant p=0.2. Weight loss was compared between men 8.3lbs(4) and women 14lbs(10). T-test comparing weight loss between men and women was statistically significant p<0.04.

**Conclusion :** There is variable weight loss in the short term with sodium oxybate therapy. Subgroups of individuals studied had more substantial weight loss. Women tended to have more weight loss than men. As a group there was no significant weight change after 5 months of therapy.

**Support (optional):**

0644

HYPERSOMNIA CASES DUE TO PARAMEDIAN THALAMIC STROKES HAD NORMAL HYPOCRETIN (OREXIN) LEVELS

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**Introduction :** Bilateral paramedian thalamic strokes (PTS) are characterized by disturbance of consciousness, followed by persisting dementia, decreased spontaneity, apathy and amnesia. The paramedian thalamus is also believed to play an important role in the regulation of sleep, and the disturbances of sleep/wake regulation are known to occur in patients with

PTS. However, it is not known that the hypocretin (orexin) system is involved in these conditions. We experienced two hypersomnia cases with bilateral PTS and discussed with 4 other reported cases.

**Methods :** Case study.

**Results :** Case1: A 45-year-old man admitted to our hospital with chief complaint of disturbed consciousness. MRI revealed bilateral PTS. There was no lesion in the hypothalamus and midbrain. His symptoms were alleviated for 2 months course but he cannot work because of decreased motivation for work, memory disturbance and hypersomnia. Seven months after the onset, when the hypersomnia was still persistent, nocturnal polysomnography revealed to be normal range, but the MSLT showed borderline sleep latency (10 min) with twice SOREMPs. His hypocretin-1 levels were 322 pg/ml in acute stage and 255pg/ml in chronic stage (normal range: >200pg/ml). The hypersomnia of this patient was dramatically disappeared by 20 mg of methylphenidate. Case2 was a 15 year-old male who suffered from bilateral PTS. He exhibited transient coma at the onset, followed by persisting decreased spontaneity, apathy, amnesia and hypersomnia. MRI showed symmetric PTS. There was no lesion in the hypothalamus and midbrain. His hypocretin level was 274pg/ml in ten days after onset. Unfortunately, no objective sleep studies were performed in this case.

**Conclusion :** Dauvilliers (2003) reported one case with hypersomnia and thalamic infarction. His mean sleep latency by MSLT was 9 min and hypocretin level was 265 pg/ml. Miyamoto (2004) reported 3 cases with PTS and normal hypocretin level. Since the lesions of infarctions did not include the posterior hypothalamus, their hypocretin levels seemed to be normal. Although, it is not known whether the other hypocretin systems (projections or receptive sites) are still involved in hypersomnia with PTS, it seemed that hypocretin cell damages are not directly involved in hypersomnia associated with bilateral PTS.

**Support (optional):**

0645

NARCOLEPSY IN ISRAEL - IS IT SO RARE

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**Introduction :** Narcolepsy is a central nervous system disorder, diagnosed both clinically and by an overnight polysomnography (PSG) followed by the mean sleep latency test (MSLT), according to ICSD definition. Narcolepsy prevalence is estimated to occur in 0.02% to 0.18% of the general population. A much lower prevalence was suggested in Israeli Jews (Lavie 1986). 1,526 patients complaining of excessive daytime sleepiness were evaluated both clinically and polysomnographically. The prevalence of narcolepsy-cataplexy among the "sleepy" patients was 0.39%. An extrapolated prevalence of 1:500,000 in the general population was suggested. Since our impression was that the disease is not as rare, we investigated the prevalence of narcolepsy among "sleepy" patients seen in the Institute for Fatigue and Sleep Medicine in the Chaim Sheba Medical Center, Tel Hashomer, Israel.

**Methods :** Since mid 2001, 15,279 patients were assessed for various sleep disorders. 5,160 patients complained of tiredness and excessive daytime sleepiness. Patients suspected of sleep related breathing disorders (SRBD), periodic limb movements in sleep (PLMS), circadian rhythm sleep disorders (CRSD), insufficient sleep syndrome and insomnia were eliminated by medical history. Other 449 of the "sleepy" patients were assessed by PSG and MSLT.

**Results :** 26 patients (5.8%) were diagnosed with narcolepsy according to ICSD criteria and sleep study results (PSG + MSLT), of them, 8 patients (1.8%) had cataplexy. Demographic data, clinical features and HLA typ-



ing will be presented. Other diagnoses were CRSD (20.5%), SRBD (18%), Idiopathic Hypersomnia (8.2%), PLMS (4.9%) and others

**Conclusion :** Our findings suggest that narcolepsy in Israel is not as rare as was determined previously. Our 8 patients are probably part of a larger group, seen in other sleep clinics in Israel. Moreover, the disease is probably under diagnosed in Israel, due to unawareness of sleep disorders and due to health insurance companies policy in referring to sleep clinics.

**Support (optional):**

## 0646

### GENE EXPRESSION PROFILING IN POSTMORTEM POSTERIOR HYPOTHALAMIC TISSUE REVEALS NARCOLEPSY SPECIFIC GENES

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**Introduction :** Narcolepsy-cataplexy affects 1 in 2,000 people. It is tightly associated with HLA-DQB1\*0602 and hypocretin (orexin) deficiency. Its main symptoms include excessive daytime sleepiness, cataplexy and other abnormalities of REM sleep. Although autoimmune etiology is suggested, there are no confirmed immunological abnormalities in narcolepsy; how hypocretin cells are destructed is not known.

**Methods :** A postmortem analysis of transcripts expression was conducted. Eight controls and 6 narcolepsy postmortem posterior hypothalamic samples were selected after verification of brain tissue quality. Age and sex did not differ significantly between the two groups. Total RNA was extracted and 5-16 microgram used for hybridization onto Affymetrix U133A and B microarrays, covering approximately 40,000 transcripts. Data were statistically analyzed using the Microarray Suite 5.0 (Affymetrix) and Significant Analysis of Microarray (Stanford University). To verify expression differences, Quantitative Real-Time Polymerase Chain Reaction (RT-PCR) was performed using Taqman probes (Applied Biosystems). ACTB and B2M were used as housekeeping controls, as determined by the geNorm software.

**Results :** Forty-five candidate genes were selected from the microarray data analysis (up and down regulated transcripts). Of those, nine were confirmed by quantitative RT-PCR; all were down regulated in narcolepsy versus controls. Hypocretin was by far the most significantly decreased transcript (60 times lower in patients versus controls). We also found several additional genes consistently down-regulated in narcolepsy brains. In situ hybridization on mice hypothalamic section is being conducted using c-DNA probes derived from all other down-regulated genes. Probable colocalization within hypocretin containing cells is likely in at least two cases.

**Conclusion :** Gene expression profiling in postmortem human brain sample using microarray is a new and controversial area. Our procedure was validated by the observation that, among over 40,000 transcripts tested, hypocretin is the top down-regulated transcript in the hypothalamus of narcoleptic patients. Several novel narcolepsy specific candidate genes were also identified and are being characterized. The study of these genes is likely to provide insight into the pathophysiology of narcolepsy. Our work also validates the use of postmortem samples for the study of neurological disorders, providing careful selection of the neuroanatomical region of interest is first performed.

**Support (optional):**

## 0647

### STUDIES OF HUMORAL IMMUNITY TO HYPOCRETIN RECEPTOR 1 AND 2 IN HLA DQB1\*0602 POSITIVE NARCOLEPTICS WITH CATAPLEXY

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**Introduction :** Canine models for narcolepsy have mutations of the hypocretin (orexin) receptor 2 gene and preprohypocretin knock out murine lines exhibit narcoleptic-like behaviors. Human narcolepsy with cataplexy is associated with HLA DQB1\*0602 positivity and reduced hypocretin levels in cerebrospinal fluid (CSF) suggesting an autoimmune diathesis. We tested the hypothesis that HLA DQB1\*0602 positive narcoleptics with cataplexy have antibodies against human hypocretin receptors 1 and 2.

**Methods :** Serum samples were obtained from 44 HLA DQB1\*0602 positive narcoleptics with cataplexy and 58 controls. CSF samples were obtained from 22 of the narcoleptics and 20 of the controls. We tested for antibodies to hypocretin receptor 1 and 2 using immunofluorescence staining of CHO cells transfected with receptor 1 or 2 encoding cDNA in pcDNA3.1-myc-His and by immunoprecipitation of proteins derived from these cells using serum and CSF. We also did immunoprecipitation assays with patient and control serum and CSF using 125-I radiolabeled N-terminal and extracellular segments 1, 2, and 3 of hypocretin receptors 1 and 2.

**Results :** The immunofluorescence staining with narcoleptic serum and CSF yielded a staining pattern that was similar to vector transfected CHO cells and unlike that staining seen with positive control serum. Similarly, immunoprecipitation studies yielded no evidence of autoantibodies reactive to these receptors. However, the immunoprecipitation assay with serum using the first extracellular loop of receptor 2 revealed a significant difference that was counter to the hypothesis: narcoleptic serum had less immunoreactivity than controls. There was no evidence for antibodies to either receptor by any of the tests employed here.

**Conclusion :** The hypothesis that HLA DQB1\*0602 positive narcoleptics with cataplexy have antibodies against human hypocretin receptor 1 and 2 is not supported.

**Support (optional):** This research was supported by NIMH R01 MH62599, by the Mayo Clinic small grants fund, and by the Ruan Family Grant for Proteomic Research to the Mayo Clinic.

## 0648

### SEVERITY OF REBOUND CATAPLEXY IS WORSE FOLLOWING THE DISCONTINUATION OF TRICYCLIC ANTIDEPRESSANTS (TCAS) THAN SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS)

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**Introduction :** Rebound cataplexy following the discontinuation of anti-cataplectic medications is a well-known clinical phenomenon, which has

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never been systematically studied in a population of narcoleptics. A recent double-blind, placebo-controlled study with sodium oxybate (Xyrem) for treating cataplexy included tapering previously used antidepressants, which provided a unique opportunity to evaluate rebound phenomenon and compare differences between two classes of antidepressants: TCAs and SSRIs.

**Methods :** Patients were weaned from antidepressants over a 21-day withdrawal period followed by a washout period of 5 days or 5 times the half-life of the discontinued drug, but not exceeding 18 days; 2 additional weeks were permitted for withdrawal from fluoxetine. This was followed by a 14-21 day baseline period, after which the 8-week double-blind placebo treatment phase started. Of the 71 patients using anticataplectic medications, 37 patients were on TCAs and 20 patients were on SSRIs.

**Results :** Median weekly cataplexy frequency at the beginning of the Withdrawal Period (Visit 2) for both groups was comparable (16 VS 18). Median weekly cataplexy frequency increased to 55 for TCA-treated patients and to 35 for SSRI-treated patients by the End of Washout Period (Visit 5). A nonparametric analysis using the 2-sample Wilcoxon test showed that the increase in cataplexy frequency between Visit 2 and Visit 5 for the TCA group was significantly greater than the increase in the SSRI group during the same time period ( $p < 0.05$ ).

**Conclusion :** Even gradual withdrawal from antidepressants resulted in a marked rebound cataplexy, which was of significantly greater magnitude in patients withdrawn from TCAs. Although the rebound cataplexy has long been believed to be worse following withdrawal from TCAs, it has never been previously demonstrated. This observation has important clinical and safety implications in situations requiring discontinuation of a particular antidepressant in a narcoleptic patient.

**Support (optional):** This study was supported by Orphan Medical, Inc./Jazz Pharmaceuticals

### 0649

#### LEG MOVEMENTS DURING SLEEP IN NARCOLEPSY/CATAPLEXY HAVE A TIME STRUCTURE DIFFERENT FROM THAT OF RESTLESS LEGS SYNDROME

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**Introduction :** Periodic leg movements (PLM) during sleep in patients with narcolepsy are more numerous than in normal controls and different papers have indicated that up to 70% of narcoleptics have a PLM index  $\geq 5$ . This might suggest an important role for a decreased dopamine (DA) function in this clinical condition, similarly to Restless Legs Syndrome (RLS). For this reason, we analyzed PLM in a group of HLA DQB1\*0602-positive patients with narcolepsy/cataplexy and compared the results with those obtained in age-matched normal controls and subjects with RLS.

**Methods :** A total of 84 subjects were recruited for this study, 40 with narcolepsy/cataplexy, 22 with RLS and 22 controls. The time structure of their polysomnographically recorded PLM was analyzed by means of a recently reported approach particularly able to consider their periodicity.

**Results :** Twenty-eight patients with narcolepsy (70.0%) were found with a PLM index  $> 5$ . The distribution of inter-LM intervals was clearly bimodal in RLS and narcoleptics, with one peak at 2-4 s and another at

around 22-26 s; In the range between 22 and 40 s (probably representing PLM), RLS patients had values significantly higher than patients with narcolepsy/cataplexy. Also all of our periodicity parameters were significantly lower in the narcolepsy group. Finally, the distribution of number of PLM per hour of sleep was inverse U-shaped in normal controls and narcolepsy/cataplexy patients; on the contrary, RLS patients showed a progressive decrease throughout the night.

**Conclusion :** Narcoleptic patients show during sleep a high number of LMs which are significantly less periodic than those observed in patients with RLS. The eventual role suggested for a decreased DA function in narcolepsy is probably less important than reported previously. Our results represent also a clear example of the inadequacy of the classical criteria for the description of the periodicity of leg motor activity during sleep. PLM are known to be modulated by a periodic sleep phenomenon called cyclic alternating pattern (CAP) which has recently been reported as reduced in patients with narcolepsy. The reduction in CAP might be one of the factors responsible for the reduction in periodicity of the occurrence of LMs during sleep in patients with narcolepsy and, therefore, these two phenomena might share some common mechanisms based on orexin deficiency which may reflect in reduced activity of cortical arousal regions, reduced CAP rate in NREM sleep and disorganization of LMs.

**Support (optional):**

### 0650

#### CORRELATES OF SLEEP ONSET REM PERIODS DURING THE MULTIPLE SLEEP LATENCY TEST IN COMMUNITY ADULTS

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**Introduction :** The diagnosis of narcolepsy without documented cataplexy is entirely based on the observation of 2 or more Sleep Onset REM periods (SOREMPs) during the Multiple Sleep latency Test (MSLT). We report on the prevalence and correlates of SOREMPs in the community-based Wisconsin Sleep Cohort Study.

**Methods :** MSLTs were conducted following nocturnal polysomnography (NSPG) and daily sleep diaries in 289 men and 267 women (age 35-70, 97% Caucasians).

**Results :** Multiple SOREMPs were observed in 13.1 % of men and 5.6 % of women. An MSLT mean sleep latency  $\leq 8$  minutes and  $\geq 2$  SOREMPs (diagnostic of narcolepsy) was observed in 5.9% (men) and 1.1% (women), all without cataplexy. Because of significant sex interactions, analyses were stratified by sex. Increased prevalence of HLA-DQB1\*0602, a marker of narcolepsy, was observed in men but not women with  $\geq 2$  SOREMPs. Men with multiple SOREMPs compared to those with no SOREMPs had shorter REM latency during NSPG, were sleepier on the MSLT, and reported increased sleepiness, hypnagogic hallucinations and cataplexy-like symptoms, suggesting a narcolepsy-like phenotype. In men only, the occurrence of SOREMPs increased with shift work and some indirect markers of sleep restriction such as shorter sleep a day prior to NSPG. SOREMPs were unrelated to age, body mass index, depression (Zung Scale), anxiety (State-Trait Anxiety Scale), and the number of apnea and hypopnea events per hour of sleep (AHI), but were associated with decreased mean lowest oxygen saturation in men. Finally, we found that both men and women with SOREMPs reported taking more antidepressants, but those were of the types known not to suppress REM sleep.

**Conclusion :** These results suggest a high prevalence of narcolepsy without cataplexy, as defined by the International Classification of Sleep

Disorders, and/or a large number of false positive for the MSLT.

**Support (optional):**

### 0651

#### SWISS NARCOLEPSY SCALE: A VALID TOOL FOR THE DIAGNOSIS OF NARCOLEPSY

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**Introduction :** In a recent study in the *J Sleep Res* 2004 we reported the high sensitivity (96%) and specificity (98%) of a new scale based on 5 questions for the diagnosis of narcolepsy with cataplexy. The aims of the present study are: 1) To assess the value of the Swiss Narcolepsy Scale (SNS) in a new series of patients with narcolepsy with cataplexy and 2) to compare its sensitivity and specificity with the Ullanlinna Narcolepsy Scale (UNS) and the Epworth Sleepiness Scale (ESS).

**Methods :** We prospectively studied by a standard questionnaire - which includes the SNS, the UNS and the ESS - patients with narcolepsy with cataplexy (n=33, 24 of them with assessment of CSF hypocretin-1 levels) and patients with excessive daytime sleepiness (EDS, n=142) of other origin. The diagnosis of narcolepsy was made according to international criteria. Causes of EDS included restless legs syndrome (n=44), sleep disordered breathing (n=40), chronic sleep insufficiency (n=27), idiopathic hypersomnia (n=15), NREM-parasomnias (n=11), circadian sleep disorders (n=5).

**Results :** For the diagnosis of narcolepsy the following sensitivities and specificities were found: SNS (score <0) 79% and 92%; UNS (score ≥14) 94% and 77%; ESS (score ≥14) 81% and 73%. For the diagnosis of narcolepsy with low/absent CSF hypocretin-1 the sensitivities and specificities were: SNS 92% and 92%, UNS 100% and 77%, ESS 90% and 73%.

**Conclusion :** The preliminary results of this on-going study confirm that an Epworth Sleepiness Scale ≥14 and an Ullanlinna Narcolepsy Scale ≥14 are suggestive of narcolepsy. The Swiss Narcolepsy Scale (with a cut-off <0) appears to be superior to ESS and UNS in the diagnosis of narcolepsy with cataplexy and allows, in addition, the identification of hypocretin-1 deficient patients.

**Support (optional):**

### 0652

#### HLA-DQB1\*0602 AND HYPOCRETIN IN KOREAN NARCOLEPTICS WITH CATAPLEXY

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**Introduction :** Cataplexy is one of the most pathognomonic symptoms in narcolepsy. This study was designed to investigate the clinical features, frequency of DQB1\*0602 and CSF hypocretin levels in Korean narcoleptics with cataplexy to compare with those who have not cataplexy.

**Methods :** 72 narcoleptic patients were selected by nocturnal polysomnography and multiple sleep latency test(MSLT) as well as their history and clinical symptoms at Sleep Disorders Clinic of St. Vincent's Hospital, the Catholic University of Korea. The patients were divided into 56 cataplexy-positive narcolepsy group and 12 cataplexy-negative group. All patients were subjected to HLA typing for the presence of DQB1\*0602 and spinal tapping for measuring the level of CSF hypocretin.

**Results :** 1. Mean positivity of HLA-DQB1\*0602 of all narcoleptic patients were 83.3%(60 subjects). In cataplexy-positive patients, compared with cataplexy-negative patients, the positivity of HLA-DQB1\*0602 was found to be significantly increased(51 subjects, 91.9% vs. 9 subjects, 56.3%)(P=0.003). 2. In 48 out of 56 cataplexy-positive

patients(85.7%), hypocretin levels were decreased(≤110 pg/ml) or below the detection limit of assay(<40 pg/ml). However, only 6 out of 16 cataplexy-negative patients(37.5%) exhibited decreased hypocretin level. And the difference between two groups was statistically significant(P=0.000). 3. Cataplexy-positive group(mean age; 25.3 ± 10.4, 34 men and 22 women), compared with cataplexy-negative group(mean age; 29.8 ± 14.8, 13 men and 3 women), showed more frequent hypnagogic hallucinations(36 subjects, 64.3% vs. 4 subjects, 25.0%)(P=0.005). 4. In MSLT findings, average sleep latency was 2.4 ± 2.0 minutes and average frequency of SOREMPs(sleep-onset REM periods) was 3.0 ± 1.2 in all narcolepsy patients. Cataplexy-positive group, compared with cataplexy-negative group, only manifested decreased sleep latency tendency(2.3 ± 2.1 min. vs. 2.6 ± 1.7 min.) and increased frequency of SOREMPs tendency(3.0 ± 1.2 vs. 2.9 ± 1.0).

**Conclusion :** High frequency of HLA-DQB1\*0602 and low hypocretin level in cataplexy-positive groups suggest that cataplexy-positive narcoleptics may be a etiologically different disease entity from cataplexy-negatives. Additionally, Current criteria prevail for the diagnosis of narcolepsy need to be reclassified according to the presence of cataplexy or not.

**Support (optional):** St.Vincent's Hospital, Catholic University of Korea

### 0653

#### PREVALENCE OF NARCOLEPSY IN KOREAN ADOLESCENTS

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**Introduction :** Narcolepsy is a chronic disorder which typically begins between adolescence and early adulthood, and causes severe neuropsychiatric impairments. Although many prevalence studies of narcolepsy have been reported, there have been few studies of adolescent narcoleptics. We investigated the prevalence of narcolepsy in adolescents with laboratory confirmation.

**Methods :** Total 20,407 students, ages 14-19 years, participated in this study. Ullanlinna Narcolepsy Scale (UNS) was performed by all the subjects, and then subjects with UNS score ≥ 14 were contacted by phone for semi-structured interview. Subjects suspected of narcolepsy based on the semi-structured interview took part in laboratory investigations including nocturnal polysomnography and multiple sleep latency test (MSLT), and HLA typing. Revised diagnostic criteria of International Classification of Sleep Disorders (ICSD-2) was used.

**Results :** Subjects scoring UNS equal to or more than 14 were numbered 4,535 (22.2% of all the participants). Twenty subjects participated in the laboratory examinations, and 9 subjects (7 female and 2 male) were finally diagnosed as narcoleptics. Among them, 8 (89%) had cataplexy or cataplexy-like symptoms and 3 (33.3%) were HLA DQB1\*0602 and DRB1\*1501 positive. The prevalence of narcolepsy in Korean adolescence was 0.044% (95% confidence interval = 0.015-0.073%). Although narcoleptics were more prevalent in female than male adolescents, male narcoleptics showed severe sleepiness and REM sleep abnormality on MSLT.

**Conclusion :** The prevalence of narcolepsy in Korean adolescence is similar to those of other studies in adult or general population. Considering that the cases with onset after adolescence were not included, the prevalence in our study is higher than expected. Higher prevalence could be explained by the application of the revised diagnostic criteria of ICSD-2, chronic sleep deprivation in adolescents, and possibly ethnic difference. That narcoleptics with mild symptomatology were included in the study might be related with female predominance and low HLA positivity

**Support (optional):** Choongwae Pharma Corporation

### 0654

#### HOMEOSTATIC SLEEP REGULATION IN NARCOLEPSY-CATAPLEXY: BASELINE SLEEP AND EFFECT OF 40 HOURS OF WAKEFULNESS ON SLEEP-ONSET REM SLEEP AND NREM SLEEP REGULATION

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**Introduction :** To study the effects of 40 hours wakefulness on REM sleep (REMS) and on homeostatic nonREM sleep (NREMS) regulation in patients with narcolepsy-cataplexy (NC)

**Methods :** The baseline and recovery sleep recordings before and after 40 hours sleep deprivation were compared between seven drug-free NC-patients and seven healthy controls. Sleep stages were visually scored and EEG power spectra were calculated for consecutive 20-s epochs (derivation C3A2).

**Results :** In both baseline and recovery sleep all NC-patients, yet no healthy control showed a sleep-onset REMS episode (SOREMS). The SOREMS lasted longer in the recovery night than in the baseline night ( $p=0.01$ ). Sleep deprivation increased slow-wave activity (SWA; power in the 0.75-4.5 Hz range) during recovery sleep in both groups and SWA declined similarly across the first three NREMS episodes in both baseline and recovery nights (group x cycle x condition;  $p=0.5$ ). The build-up of SWA during the first 30 min was similar in both groups in NREMS episode 1, but slower in the NC-patients in NREMS episode 2 (cycle x group  $p=0.009$ ).

**Conclusion :** Even after increasing NREMS pressure by 40 hours of prolonged waking all patients initiated recovery sleep with a SOREMS. Notwithstanding, SWA in NREMS episode 1 of the recovery night did not differ between the groups. The similar increase of SWA from baseline to recovery sleep, and the similar declining trend of SWA in baseline and recovery sleep episodes demonstrate that the homeostatic facet of NREMS regulation is functional in NC-patients.

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### 0655

#### CLINICAL ASPECTS OF EARLY ONSET NARCOLEPSY

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**Introduction :** To compare the clinical and polysomnographic features of early onset (symptoms occurred at age of <15 years old) and late onset ( $\geq 15$  years old) narcolepsy.

**Methods :** The histories and clinical and polysomnographic features of 105 consecutive patients diagnosed as narcolepsy between April 2004 and March 2005 were reviewed. Among them, 63 were early onset narcolepsy with a mean onset age of  $9.7\pm 3.1$  years; and 42 were late onset narcolepsy with a mean onset age of  $22.8\pm 9.3$  years.

**Results :** All 105 patients showed daytime sleepiness. Cataplexy occurred in 92% of the early onset narcolepsy group, and in 76% of the late onset group ( $p=0.023$ ). However, the two groups had no significant differences in the rates of sleep paralysis, hypnagogic hallucinations and disturbed nocturnal sleep. Compared to the late onset patients, MSLT revealed a

shorter mean sleep latency ( $4.5\pm 4.0$  vs  $7.0\pm 5.7$  min,  $p=0.018$ ) and a shorter REM sleep latency ( $3.4\pm 3.2$  vs  $4.8\pm 2.2$  min,  $p=0.02$ ), but increased numbers of sleep onset REM ( $3.4\pm 2.0$  vs  $2.5\pm 1.9$ ,  $p=0.009$ ) in early onset narcoleptic patients. The late onset patients had sleep disordered breathing as indicated by an AHI level ( $9.2\pm 16.5$  vs  $1.9\pm 6.3$ ,  $p=0.009$ ). Three cases in the early onset group had close family members with sleepiness and cataplexy vs none in the late onset group.

**Conclusion :** Early onset narcolepsy patients had more severe daytime sleepiness and higher rate of cataplexy. A genetic effect might play an important role in the development of symptoms.

**Support (optional):**

### 0655

#### OBSERVATION OF NARCOLEPTIC PATIENTS IN HUNGARY

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**Introduction :** The diagnosis of narcolepsy can be especially difficult, not only because of its low prevalence, but also because the elements of its characteristic tetrad occur seldom together. However, the solitaire occurrence of hypersomnia is frequent. The most common complain of our 5-6000 patients is daytime sleepiness, which can be caused by OSAS, UARS, RLS/PLMD, idiopathic hypersomnia and by the inefficient night's sleep besides narcolepsy.

**Methods :** According to the national protocol, the diagnosis of the narcoleptic patients begins with subjective sleepiness scales (Epworth, Ullanlinna), followed by polysomnography (to obtain the efficient amount of sleep and to monitor the quality of sleep), and MSLT. At the MSLT, naps were checked 4-5 times a day, 20 minutes each. Sleep latencies under 5 minutes were considered as serious sleepiness. The examinations were completed with HLA-analysis. Hypersomnias occurring after a good night's sleep were treated with modafinil. Patients were controlled yearly by sleepiness scales and MSLT.

**Results :** With hypothetical narcolepsy 97 patients (55 male, 42 female, aged 17-80, average 46) were tested, 245 (diagnostic and control) examinations were done. 51 patients proved to be narcoleptic, in 46 cases hypersomnia was caused by other diseases (REM-dependent obstructive hypopnoe 76%, UARS 11%, PLMS 4%, other 9%). Hypersomnia was a typical symptom of narcolepsy, it occurred in every patient (100%), 42% of the patients complained of hypnagogic hallucinations, 40% of sleep paralysis, and 28% of cataplexy. As a treatment for hypersomnia modafinil therapy was applied (200-300 mg), which led to improvement of the average sleep latency in the MSLT from 4,25 to 17,02 min.

**Conclusion :** Based on our results it is clear, that modafinil is effective in the treatment of hypersomnia, and that the co-occurrence of all the symptoms of narcolepsy is extremely rare, but, however, the solitaire occurrence of hypersomnia is definitely frequent.

**Support (optional):**

### 0656

#### MAGNETIC RESONANCE SPECTROSCOPY IN NARCOLEPSY

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**Introduction :** Two previous magnetic resonance spectroscopy (MRS) studies in narcolepsy exist in the literature. These studies examine different regions of interest. In the first one no metabolic changes were observed in the ventral pontine area. The second study showed a reduc-

tion in N-acetylaspartate (NAA)/creatine-phosphocreatine (Cr) in the hypothalamus of narcolepsy patients with cataplexy. The aim of our study is to test for metabolic changes in specific brain areas, "regions of interest", thought to be involved in sleep regulation and pathophysiology of narcolepsy: hypothalamus, pontomesencephalic junction and both amygdalas.

**Methods :** In 8 narcolepsy patients with clear-cut cataplexy, CSF hypocretin deficiency (3/3) and HLA-DQB1\*0602 positivity (5/5) and 5 age, gender and body mass index matched controls MRS was performed. Patients were treatment naive or off therapy for at least 14 days before scanning. MRS was performed on a Philips Intera 3.0 T scanner. Single-voxel proton MR spectra were acquired from the regions of interest and processed to determine metabolite concentration ratios. The concentration ratios of NAA/Cr, (total NAA)/Cr, (total Choline)/Cr and myo-Inositol (mI)/Cr were determined. The patient group was compared with the control group on the basis of these results.

**Results :** A trend towards lower (total NAA)/Cr ratios in the right amygdala was observed in patients ( $1.1 \pm 0.3$ ) in comparison to controls (mean  $1.5 \pm 0.4$ ). Surprisingly a trend towards higher NAA/Cr ratios in the pontomesencephalic junction was found in patients (mean  $1.4 \pm 0.4$ ) compared to control subjects ( $1.05 \pm 0.3$ ). No metabolic differences were observed concerning the other voxels of interest.

**Conclusion :** Our preliminary results suggest the presence of metabolic changes in the right amygdala and the pontomesencephalic junction in narcolepsy patients.

**Support (optional):** EFNS Grant to RP, SNF Grant to CB

## 0657

### SYMPTOMS OF EATING DISORDERS IN NARCOLEPSY WITH CATAPLEXY

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**Introduction :** Patients with narcolepsy have a higher Body Mass Index (BMI) than controls. The cause of obesity in narcolepsy is unknown as of yet. Several mechanisms may be responsible, including differences in energy balance, decreases in mobility due to sleepiness, or differences in eating habits. Interestingly, the hypocretin system seems to be involved in all these processes. In this study, we assessed eating habits and symptoms of eating disorders in a group of narcoleptic patients.

**Methods :** We examined 21 patients who fulfilled the ICSD-2 criteria for narcolepsy with cataplexy. We used the eating disorders section of the Schedules of Assessment in Neuropsychiatry (SCAN 2.1). As controls, we used previously acquired population data of 314 subjects from the REGIO-2 study, matched for age, sex, and community size.

**Results :** In our cohort, BMI scores did not significantly differ between groups (mean BMI in patients: 25.8 (confidence interval 18.20-33.40) and in controls: 24.41 (c.i.: 17.57-31.25)). The narcoleptic patients reported significantly higher (Fishers exact test  $P < .0001$ ) on the following symptoms: gain of weight, weight problem, dread of becoming fat, earlier episode of undereating, irresistible and persistent craving for food, avoidance of fattening foods, actions to loose weight through self restriction, binge eating with a sense of loss of control, restrictive actions to correct binging. Furthermore, patients reported a significant interference with activities due to eating disorder symptoms.

**Conclusion :** Patients with narcolepsy clearly have more symptoms of eating disorders than controls. A possible relation with the increased prevalence of obesity in narcolepsy remains to be elucidated. Furthermore, a formal diagnosis of specific eating disorders could not be made. Currently, we are assessing this issue in a prospectively acquired

patient and control group, using the Eating Disorder Examination Questionnaire (EDE-Q) and the Structured Clinical Interview for DSM Axis I disorders (SCID-I/P).

**Support (optional):**

## 0658

### CAP REDUCTION AS AN EEG MARKER OF HYPOAROUSABILITY IN NARCOLEPSY WITH CATAPLEXY

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**Introduction :** Narcolepsy is a sleep disorder with clinical symptoms attributed to a reduced activation of the arousal system. CAP (cyclic alternating pattern) is the expression of rhythmic arousability during NREM sleep. CAP parameters, arousals and conventional sleep measures, were studied in narcoleptic patients with cataplexy.

**Methods :** Data were collected from all-night PSG recordings and the MSLT on the intervening day of 25 drug-naive patients (10 males and 15 females; mean age:  $34 \pm 16$  years) after adaptation and exclusion of other sleep disorders. Clinical and neurological examination was integrated by laboratory blood chemistry with identification in all subjects of the HLA DQB1\*-0602, and by MSLT evaluation during the day with at least 2 SOREMPs. A group of 25 age- and gender-matched normal sleepers were selected as controls. Each PSG recording was subdivided into sleep cycles. Analysis of CAP included classification of A phases in subtypes A1, A2, A3.

**Results :** There was an increase of the sleep period time mainly due to an increased wake time after sleep onset. REM latency was sharply reduced. The percentage of NREM sleep was slightly reduced and the balance between light sleep (S1 + S2) and deep sleep (S3 + S4) showed a curtailment of the former, while deep sleep was slightly increased. Excluding sleep cycles with SOREMPs, the duration of ordered sleep cycles was not different between narcoleptics and controls. The two groups showed similar values of arousal index, while CAP time, CAP rate, number of CAP cycles and of phase A subtypes (in particular subtypes A1) were significantly lower in narcoleptic patients.

**Conclusion :** The reduced periods of CAP in narcoleptic NREM sleep could be the EEG expression of a general hypoarousability that parallels the hypocretin/orexin deficiency. This can explain some of the clinical correlates of the disorder, i.e., excessive sleepiness, short sleep latency and impaired attentive performances, without evidence of arousal-induced sleep fragmentation. The increased intrasleep wake time could be instead related to the enhanced percentage of REM sleep that shares common neurophysiological substrates with wakefulness.

**Support (optional):**

## 0659

### INTEROBSERVER RELIABILITY IN THE ASSESSMENT OF DISABLEMENT IN PATIENTS WITH NARCOLEPSY

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**Introduction :** Narcolepsy (N) is a disabling chronic disease with a major impact on quality of life. The psychosocial and socioeconomic impact of N have been investigated, but a severity scale of the degree of disablement (DD) due to N is lacking. The Italian Social Security System guarantees

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benefits to disabled people referring to the DD (range 33% to 100%) and to the handicap condition (H) ascertained by deputed an ad hoc Medical Commission. This study aimed to estimate the interobserver reliability of the assessment of DD and H in patients with N.

**Methods :** Four Medical Commissions (composed of 3 specialists in legal medicine and 1 specialist in occupational medicine) from three Italian towns independently classified 15 patients with N of different degrees of severity according to the DD (divided into five degrees: 0-33-45-75-100%) and H (non-H, H, severe-H). Clinical interviews were monitored by an independent observer to evaluate possible sources of variance. Interobserver reliability was calculated by Kappa statistics, and interpreted according to standard classification (0.0-0.20 = slight agreement; 0.21-0.40 = fair; 0.41-0.60 = moderate; 0.61-0.80 = substantial; 0.81-1.00 = almost perfect).

**Results :** The observed raw agreement ranged from 20.0% to 53.1% for DD, and from 13.3% to 60.0% for H between each pair of raters; the interobserver reliability for both DD and H ranged from "slight" ( $\kappa = 0$ ) to "fair" ( $\kappa = 0.35$  and  $0.36$  respectively).

**Conclusion :** Our study discloses a poor agreement in assessing both the DD and H in patients with N. This finding may reflect the scant knowledge of N and/or a general cultural difficulty in accepting sleepiness as a disabling symptom. A standardized multidisciplinary procedure (including sleep medicine specialists) is needed to purpose a social and occupational medicine oriented severity scale for N.

**Support (optional):**

### 0660

#### ALTERED SKIN TEMPERATURE REGULATION RELATES TO SLEEP PRESSURE IN NARCOLEPSY

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**Introduction :** In healthy subjects, sleep propensity is related to the thermoregulatory state of the skin. Sleep pressure is enhanced when the distal skin temperature increases relative to the proximal skin temperature. This is the result of inhibition of the sympathetic vasoconstrictor tone, leading to increased blood flow in the skin of the extremities. In relation to sleep, this thermoregulatory state occurs during the circadian phase just prior to habitual nocturnal sleep onset, but is not associated with homeostatic buildup of sleep pressure. We studied the diurnal skin thermoregulatory state and its relation to the increased sleep propensity that characterizes narcolepsy.

**Methods :** Distal and proximal skin temperature and their gradient (DPG) were measured in fifteen unmedicated narcolepsy patients with cataplexy and fifteen controls during a Multiple Sleep Latency Test. The protocol allowed temperature averages during wakefulness in an upright position, during wakefulness in a supine position and during sleep.

**Results :** While awake, narcoleptic patients maintained a strongly increased DPG throughout the day (time  $\times$  group,  $p < 0.0001$ ), due to increased distal temperature and decreased proximal temperature as compared to young subjects. An elevated DPG during wakefulness was associated with an accelerated subsequent sleep onset ( $p = 0.02$ ). Once asleep, narcoleptics maintained elevated distal skin temperature and DPG ( $p < 0.0001$ ), whereas proximal skin temperature increased to reach normal levels.

**Conclusion :** This is the first demonstration of a dramatic activation of distal skin blood flow in narcolepsy. Even during wakefulness, narcoleptic

patients show a DPG level that is not even reached during sleep in healthy controls. As in healthy subjects under controlled conditions, heat loss activation is associated with increased sleep propensity. This association warrants further research into a possibly causal contribution of skin temperature to sleep propensity in narcolepsy, as was recently demonstrated to exist in healthy subjects.

**Support (optional):**

### 0661

#### FRONTAL WHITE MATTER INTEGRITY IN YOUNG NARCOLEPTIC PATIENTS

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**Introduction :** The objective of the current study is to explore differences in frontal white matter integrity between young narcoleptic patients and healthy comparison subjects.

**Methods :** Twelve narcoleptic patients (9 men;  $24.5 \pm 4.3$  year old) and 15 healthy comparison subjects (11 men;  $27.7 \pm 5.8$  year old) were recruited. Inclusion criteria for narcoleptic patients include presence of cataplexy, HLA allele DQB1 \*0602, and two or more sleep onset rapid eye movement sleep in multiple sleep latency test. Exclusion criteria include age over 35 years and comorbid sleep disorders or major psychiatric/medical disorders. Fractional anisotropy values, a scalar index of the white matter integrity, were calculated for regions-of-interest in bilateral deep frontal white matter and the corpus callosal genu on diffusion tensor images.

**Results :** Relative to healthy comparison subjects, narcoleptic patients had significantly lower fractional anisotropy values in the right and left deep frontal white matter and the corpus callosal genu ( $t=2.73$ ,  $p=0.011$ ;  $t=2.52$ ,  $p=0.018$ ;  $t=3.22$ ,  $p=0.003$ , respectively).

**Conclusion :** The current findings show that narcoleptic patients had compromised frontal white matter integrity.

**Support (optional):**

### 0662

#### CLOCK GENE POLYMORPHISMS AND NARCOLEPSY IN HLA-DQB1\*0602 POSITIVE AND NEGATIVE PATIENTS

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**Introduction :** Narcolepsy is a sleep-wake disabling disorder that affects about 1 in 2,000 people throughout the world. It is well known that the disorder is linked to the human leukocyte antigen system (HLA) mainly the DQB1\*0602 allele that is in tight linkage disequilibrium with DRB1 alleles. A recent report established a genetic linkage between HLA-DRB1 positive Japanese narcoleptic patients and the chromosomal region 4p13-q21 that contains, among others, the Clock gene. The Clock gene has been proposed as a participatory agent in the regulation of sleep-wake cycle in which it may possibly modulate human diurnal preference.

**Methods :** We studied the T257G and T3111C SNPs in the Clock gene in 43 HLA-DQB1\*0602 positive and negative narcoleptic patients and 87 healthy controls in order to check whether these SNPs have any association with the disease in our narcoleptic patients.

**Results :** The allelic and genotypic frequencies of the T257G and T3111C SNPs in the patients group did not differ significantly neither from the general population nor between the HLA-DQB1\*0602 positive and neg-

ative patients.

**Conclusion :** We conclude that these two Clock SNPs are not associated with narcolepsy.

**Support (optional):** AFIP, FAPESP/CEPID

## 0663

### REM SLEEP REGULATION IN NARCOLEPTICS AND NORMAL CONTROLS

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**Introduction :** REM sleep (REM) propensity is known to be high in the early morning. REM duration, REM latency and number of interventions to prevent REM are major markers to explore REM regulation. In the present study we attempted to specify the role of REM regulation in narcoleptics and healthy controls by studying daytime sleep under varying sleep pressure (SP).

**Methods :** 5 narcoleptics with cataplexy (NC, age: 28.2y ±3.2 (SEM) and 4 healthy controls (C, age: 31.8±4.2) underwent a four session crossover balanced sleep protocol with 2 sessions with a night of sleep deprivation to increase SP and 2 sessions with a 4h nighttime sleep episode (23:00-3:00h) to reduced SP, followed by daytime sleep (DS, 7:00-15:00h). In 2 sessions (one with high and one with low SP) subjects were repeatedly awakened during the first 4h of the DS episode to prevent REM. DS was undisturbed in the other 2 sessions.

**Results :** The number of interventions to prevent REM was significantly increased in NC (25.6±7.2) compared to C (8.8±2.3, p<0.001), whereas different SP did not (in NC: 26.8 (high SP) vs.24.4 (low SP) interventions, in C: 7.5 (high) vs. 10.3 (low)). The amount of accumulated REM (within the first 4h) in the undisturbed DS with low SP was significantly increased by 70% compared to the high SP condition in C (p<0.03). Chances in NC were minor (23%, p>0.34). Additionally, a low SP shortened REM latency in C (low SP: 63±20 min, high SP: 119±8 min p<0.07).

**Conclusion :** Our preliminary results suggest that markers of REM regulation (i.e., number of interventions during its deprivation and accumulated REM duration) may behave different in respect of its regulation and between NC and C.

**Support (optional):**

## 0664

### MATHEMATICAL MODELING OF FRAGMENTED SLEEP-WAKE BEHAVIOR IN OREXIN KNOCKOUT MICE

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**Introduction :** Behavioral states of wake, REM sleep, and NREM sleep and the transitions among them are regulated by a network of neurons in the brainstem and hypothalamus. Mutually inhibitory connections between wake- and sleep-active neuronal populations result in a “sleep-wake switch” that helps generate clearly defined bouts of each state with little time spent in intermediate states. Behavioral states are poorly regulated in narcolepsy. Loss of the hypothalamic neurons that produce orexin/hypocretin results in excessive daytime sleepiness, rapid transitions into REM sleep, and, in many cases, sudden episodes of cataplexy. Since sleep homeostasis is normal in narcolepsy, these features may best be considered examples of behavioral state instability. We modeled loss of

state-dependent excitation to the wake-active population as a potential source of this instability.

**Methods :** We used a network of coupled Morris-Lecar-type relaxation oscillators to model the dynamics of the mouse sleep-wake switch; the network includes parameters to explore potential effects of orexin. Data from normal and narcolepsy phenotype orexin knockout mice were used for testing model results.

**Results :** The model qualitatively reproduces features of mouse sleep-wake architecture including daily percentages of time spent in each state, bout durations, and probabilities of transitions between states. Decreasing state-dependent excitation to the wake-active population creates excessive switching behavior consistent with the orexin knockout mouse phenotype. Time constants associated with sleep homeostasis are not altered, but durations of wake and sleep bouts are reduced.

**Conclusion :** The model predicts that reduced excitation of wake-active populations is sufficient to account for the fragmented wakefulness and sleep of orexin deficiency. Mathematical analysis of the model equations provides a geometric perspective on state transition mechanisms and stabilization of the sleep-wake switch by orexin. To gain better quantitative agreement between model output and experimental data, our next step will be to incorporate circadian effects into the model.

**Support (optional):** National Physical Science Consortium, Burroughs Wellcome Fund, NSF: DMS-0109427, DMS-0211505; NIH: MH62589, HL60292, DAO15644

## 0665

### SPECIFICITY OF DIRECT TRANSITION FROM WAKE TO REM SLEEP IN OREXIN/ATAXIN-3 NARCOLEPTIC MICE

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**Introduction :** Hypocretin neuron ablated narcoleptic mice (C57BL/6-DBA1 hybrid) have been reported to exhibit sleep fragmentation, cataplexy and direct transitions from wake to REM sleep (DREM). In contrast to cataplexy, DREM can be more objectively evaluated. In the current study, we have assessed the specificity and sensitivity of DREM for narcolepsy as well as other sleep characteristics using the C57BL/6 congenic mice line.

**Methods :** Orexin/ataxin-3 TG mice (N8, backcrossed to C57BL/6) and respective WT littermates (n=9 for each group) were used. The mice were surgically prepared for EEG and EMG recording. They were maintained in a 24-hr light-dark cycle (LD12:12) within separate compartments with a running wheel in a sound-attenuated stainless steel recording chamber. Sleep data for 24 hours for each animal was scored visually, and each 10-second epoch is classified as wake, REM, or NREM sleep.

**Results :** Generally, similar sleep abnormalities compared to those reported in 75% C57BL/6 25% DBA1 background were observed in the congenic line. Narcoleptic mice spend less time in wakefulness and more time in sleep during the active period. Abnormal sleep characteristics were most typically characterized by fragmentation of wake/sleep states reflecting an inability to maintain consolidated wakefulness (and sleep). However, DREM, when analyzed with original data with 10-second epoch lengths, was observed in both narcoleptic and wild-type animals during the light period (when animals sleep most of time). These DREMs are often characterized as sequences that REM sleep episodes are interrupted by a brief wake episode. This pattern of transition contrasts from that of DREM in narcoleptic mice during the dark period. A rule for the length of preceding wake epochs was then applied for the definition of DREM. Applying 4 preceding wake length rules (i.e., at least 40 seconds of wake needs to be preceded before DREM) results in the best specificity and eliminated

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almost all pseudo-DREM in wild-type animals.

**Conclusion :** Defined DREM is specific for narcolepsy and occurs during the active period. This phenotype may share common pathophysiological mechanisms with cataplexy, and may be a good electrophysiological measure for cataplexy-equivalent episodes.

**Support (optional):**

### 0666

#### THE DIAGNOSIS OF HYPERSOMNIA AT KURUME UNIVERSITY HOSPITAL

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**Introduction :** The number of patients complaining of excessive daytime sleepiness, or dozing off several times a day, and the number of patients referred from other hospitals has increased in recent years. The disorders that cause hypersomnia include intrinsic disorders, extrinsic ones, and disorders accompanied by psychiatric illness and so on. Differing opinions are advocated when diagnosing hypersomnia in consideration of the International Classification of Sleep Disorders diagnosis and coding manual (ICSD).

**Methods :** We have investigated patients who have complained about EDS or were referred due to hypersomnia, (except those suffering from sleep apnea syndrome or restless leg syndrome), from April 2004 to November 2005. On the first visit to the hospital the patients were required to report the condition of their sleepiness using the Pittsburgh's Sleep Quality Index and the Epworth Sleepiness Scale. Moreover, the patients had to wear an actigraphy and maintain a sleep diary. Several days later, polysomnographies (PSG) were conducted followed by multiple sleep latency tests (MSLT).

**Results :** Thirty-four patients were diagnosed using this method. On the basis of the diagnostic criteria of ICSD-2, nine patients suffered from idiopathic hypersomnia, three of narcolepsy, while eight were diagnosed with insufficient sleep syndrome. Excepting these diagnoses, hypersomnia accompanied with psychosis, insufficient sleep of long duration sleepers, delayed sleep phase syndrome(DSPS), narcolepsy without cataplexy, and DSPS with insufficient sleep were diagnosed. On the basis of ICSD-1, our cases of idiopathic hypersomnia satisfied the diagnostic criteria. However, the polysomnographic features are prolonged sleep duration and increased slow wave sleep (SWS). Increased SWS was not discovered among the patients.

**Conclusion :** One reason of increasing hypersomnia in Japan may be a deeper comprehension of hypersomnia, therefore making it easier to diagnose. Another reason may be chronic insufficient sleep time that may appear to be hypersomnia.

**Support (optional):**

### 0667

#### MODAFINIL-INDUCED HIPPOCAMPAL ACTIVATION IN NARCOLEPSY

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**Introduction :** We studied the cerebral glucose metabolism of narcoleptics with FDG-PET to elucidate the pathophysiology of Narcolepsy. Also, effects of modafinil on the brain glucose metabolism of narcoleptic patients were investigated. Few studies have been reported to find out changes in brain functions of narcoleptics using FDG-PET after modafinil administration.

**Methods :** Eight narcoleptic patients, 6 women and 2 men, ages 15-18 ( $16.4 \pm 0.7$ ; mean  $\pm$  SD) and 8 normal controls, 6 women and 2 men, ages 20-24 ( $22.3 \pm 1.6$ ; mean  $\pm$  SD) participated in the study. Baseline FDG-PET scans were obtained both in narcoleptics and healthy controls, and another FDG-PET scan was acquired in narcoleptics 2 weeks after modafinil administration. All studies were conducted in the morning between 9:30 to 10:30 AM. Voxels with a p-value of less than 0.005 (uncorrected) were considered to be significantly different.

**Results :** In comparison analysis between pretreatment scans of patients and healthy controls, the significant decrease of glucose metabolism was observed in the midbrain, bilateral hypothalamus, bilateral thalamus, right parahippocampus, temporal cortex, and cerebellum. Paired-t-test between pre- and post-treatment FDG-PET scans demonstrated a significant increase of glucose metabolism in the left hippocampus after 2 week-treatment. No change was observed in glucose hypometabolism of the hypothalamus after treatment.

**Conclusion :** Midbrain, hypothalamus, and thalamus in which decreased glucose metabolism was observed in narcoleptics, are known as neural systems generating wakefulness. Hypometabolism in the hypothalamus, where hypocretin neurons are mainly located, could explain hypocretin deficiencies in narcoleptics. Increased hippocampal metabolism after modafinil administration in the study might be related with activation of septohippocampal pathway through modafinil-induced hypocretin release. As glucose uptake mainly occurs in dendrites and axon terminals, activation of cell bodies in the hypothalamus might not be demonstrated in the study.

**Support (optional):** Choongwae Pharma Corporation

### 0668

#### CSF LIPOCALIN-TYPE PROSTAGLANDIN D SYNTHASE (BETATRACE) IS DECREASED IN IDIOPATHIC HYPERSOMNIA AND NARCOLEPSY

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**Introduction :** Until now, no neurochemical indicators of hypersomnia/excessive daytime sleepiness (EDS) are known. Lipocalin-type prostaglandin D synthase (L-PGDS, also known as betatrace) catalyzes the production of sleep-promoting prostaglandin D<sub>2</sub>. The aim of the study was to test whether cerebrospinal fluid (CSF) L-PGDS concentrations are altered in patients with hypersomnia/EDS.

**Methods :** L-PGDS was determined in the CSF of nine patients with narcolepsy-cataplexy, eight patients with idiopathic hypersomnia, and eight healthy age- and gender-matched controls.

**Results :** We observed significantly decreased CSF L-PGDS levels in patients with hypersomnia disorders (narcolepsy-cataplexy: mean 10.1 mg/l, SD 8.4, range 2.2-30.5; idiopathic hypersomnia: mean 6.8 mg/l, SD 4.4 1.5-13.4) compared to controls (mean 18.4 mg/l, SD 4.9, range 12.3-27.8;  $p < 0.005$ ). Mean levels did not differ significantly between narcolepsy-cataplexy and idiopathic hypersomnia patients ( $p = 0.32$ ).

**Conclusion :** Our results indicate that L-PGDS may be an indicator for hypersomnia/EDS. The role of L-PGDS in the pathophysiology of hypersomnia disorders (downregulation?) remains unclear at present time.

**Support (optional):**



0669

**CSF VERSUS SERUM LEPTIN IN NARCOLEPSY: IS THERE AN EFFECT OF HYPOCRETIN DEFICIENCY?**Arnulf I,<sup>1,2</sup> Lin L,<sup>1</sup> Zhang J,<sup>1</sup> Ripley B,<sup>1</sup> Einen M,<sup>1</sup> Nevsimalova S,<sup>3</sup> Bassetti C,<sup>4</sup> Bourgin P,<sup>1</sup> Nishino S,<sup>1</sup> Mignot E<sup>1,5</sup>

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**Introduction :** Patients with narcolepsy-cataplexy have higher body mass index (BMI) than controls. We asked whether hypocretin deficiency is associated with abnormally low serum leptin levels, a putative cause of increased BMI.**Methods :** In this cross-sectional controlled study, 370 subjects completed the Stanford Sleep Inventory and underwent spinal tap and blood sampling for measurement of CSF leptin and hypocretin-1, HLA DQB1\*0602 phenotyping, and serum leptin and C-reactive protein levels. There were 111 healthy controls, 93 narcoleptic subjects with hypocretin deficiency (CSF hypocretin-1 levels <110 pg/ml), 72 narcoleptic subjects with normal hypocretin levels, and 89 subjects with other sleep disorders**Results :** Serum leptin levels were similar in narcoleptic subjects, whether hypocretin-deficient (13.2±1.7 ng/ml, mean ±SE) or not (13.0±1.8 ng/ml), controls (10.1±1.1 ng/ml) and subjects with other sleep disorders (11.5±1.6 ng/ml). Similarly, the CSF leptin levels and the CSF:serum leptin ratio (an indicator of brain leptin uptake) were not different between groups. Serum and CSF leptin levels were higher in women and in subjects with higher BMI. Leptin brain uptake decreased in women, in the aged and in more obese subjects. In contrast with a presumed inhibitory effect of leptin on hypocretin-containing cells, CSF leptin levels tended to correlate positively with CSF hypocretin-1 levels. C-reactive protein was higher (4.2±0.9 mg/l) in narcoleptic subjects with hypocretin deficiency than in controls (1.4±0.3 mg/l, p=0.0055), a difference still significant after adjustment on confounding factors.**Conclusion :** Our data does not support a role for leptin in mediating increased BMI in narcolepsy. A moderate but selective increase in C-reactive protein in hypocretin-1 deficient subjects should prompt research on inflammation in narcolepsy.**Support (optional):** Study supported by grants MH-073435 and HL-62252

0670

**ABSENCE OF AVERSIVE STARTLE REFLEX POTENTIATION IN HUMAN NARCOLEPSY-CATAPLEXY: IMPLICATIONS FOR AMYGDALA DYSFUNCTION**Khatami R, Birkmann S, Poryazova R, Bassetti C  
Neurology, University Hospital, Zuerich, Switzerland**Introduction :** Cataplexy arises from the recruitment of REM atonia mechanisms, which may also involve reticulospinal pathways. These pathways can be tested in humans with the acoustic startle reflex (ASR). The blink reflex of ASR is modulated by emotions. The absence of ASR potentiation during unpleasant stimuli has been reported in humans following amygdala lesions.**Methods :** ASR and its emotional modulation were studied in narcoleptic patients with definite cataplexy (NC). ASR and the affective modulation of the blink reflex of ASR were assessed during the presentation of standardized emotional pictures in drug free NC (n=12, mean age 34 years SD 12) and in age- and gender-matched controls (n=7, mean age 31 years SD 8). Subjective ratings of emotional valence, emotional arousal

and heart rate were also measured.

**Results :** ASR could be evoked in seven NC. ASR responses (latencies, recruitment pattern of involved muscles as well as habituation) were similar in both groups, although the magnitude was more variable in NC. While both groups had a mild enhancement of startle magnitude during pleasant pictures (relative to neutral pictures, p=0.56), NC failed to evoke a potentiation of ASR during unpleasant pictures (p=0.02). Startle potentiation during unpleasant pictures was consistently found in each individual control subject, but was absent in 3 of 7 NC-patients irrespective to the individual level of ASR magnitude. Subjective rating on the valence (p=0.10) and emotional arousal (p=0.12) were comparable in both groups (suggesting normal emotional perception and arousal following unpleasant pictures). Likewise no differences were found in autonomic arousal as assessed by heart rate activation (p=0.35).**Conclusion :** The absence of aversive startle potentiation gives further support to the hypothesis, suggested by animal data, of an amygdala dysfunction in NC.**Support (optional):** Swiss National Science Foundation grant 3200B0-104100/1 (to RK).

0671

**ARMODAFINIL IMPROVES SUBJECTIVE MEASURES OF SLEEPINESS IN PATIENTS WITH EXCESSIVE SLEEPINESS ASSOCIATED WITH OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME, NARCOLEPSY, AND SHIFT WORK SLEEP DISORDER**Hayduk R,<sup>1</sup> Harsh J,<sup>2</sup> Roth T<sup>3</sup>

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**Introduction :** Excessive sleepiness (ES) is a characteristic symptom of many sleep disorders, including obstructive sleep apnea/hypopnea syndrome (OSA/HS), narcolepsy, and shift work sleep disorder (SWSD). Armodafinil, a wake-promoting agent, is the R-enantiomer of racemic modafinil and has a longer half-life than the S-enantiomer. This analysis evaluated the effects of armodafinil on patient-rated sleepiness in these sleep disorders.**Methods :** Four 12-week, double-blind, placebo-controlled studies were conducted to evaluate the efficacy and tolerability/safety of armodafinil in 993 patients. Two of the studies were in patients with OSA/HS. Patients were randomized to receive armodafinil 150 or 250 mg/day (OSA/HS and narcolepsy), 150 mg on nights worked (SWSD), or placebo. The change from baseline to week 12 (or final visit) on the patient-completed Epworth Sleepiness Scale (ESS; 24-point scale; OSA/HS and narcolepsy) or the Karolinska Sleepiness Scale (KSS; 9-point scale; SWSD) was analyzed. On both scales higher scores indicate greater sleepiness. Patients' self-assessments were completed at weeks 4, 8, and 12.**Results :** Armodafinil significantly improved ESS scores compared with placebo at final visit in patients with OSA/HS (mean change from baseline: 150 mg, -5.4 points; 250 mg, -5.5; placebo, -3.1; P<.001) and in patients with narcolepsy (mean change from baseline: 150 mg, -4.1 points; 250 mg, -3.8; placebo, -1.9; P<.01). The differences in ESS scores at final visit between armodafinil and placebo were of similar magnitude in the OSA/HS and narcolepsy populations. Armodafinil significantly improved KSS scores compared with placebo at final visit in patients with SWSD (mean change from baseline: 150 mg, -1.8 points; placebo, -1.0; P<.001). Improvement was observed at the first visit at week 4 and was maintained throughout the study (P<.01 vs placebo).**Conclusion :** Armodafinil significantly improved patient-rated sleepiness in patients with ES associated with OSA/HS, narcolepsy, and SWSD.**Support (optional):** Sponsored by Cephalon, Inc.

0672

**TNF AND IL-6 LEVELS IN NARCOLEPTIC PATIENTS**

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**Introduction :** Narcolepsy is characterized by excessive daytime sleep and cataplexy. An important feature is an increase in the HLA-DQB1\*0602 allele along with the decrease of hypocretinergic cells in the hypothalamus thereby adding weight to the possibility of a different physiopathology between patients with or without cataplexy. Until now there has been a dearth of information centring on clinical and laboratory differences between narcoleptic subjects.

**Methods :** Our study was prospective and controlled with 22 patients diagnosed as being narcoleptic using DSM4 criteria and 17 health control subjects without sleep related disorders. All patients underwent a night-time polysomnographic recording (PSG), MSLT and a study of the HLA-DQB1\*0602. The levels of TNF and IL-6 of the controls and the patients were quantified.

**Results :** The presence of allele HLA DQB1\*0602 was found in 10 patients with cataplexy, and 2 patients without cataplexy (p=0.24). Significant increase of TNF in patients with rare cataplexy when compared with control subjects was found (p=0.009). A similar finding was established between patients without cataplexy versus patients with frequent cataplexy (p<0.0001). Differences of IL-6 levels were however not identified.

**Conclusion :** Discrepancies from a clinical standpoint in narcoleptic patients may stem from subtle changes in the physiopathological mechanism undergirding the illness. This could indeed be surmised from our findings. We further believe that our findings fortify the hypothesis of narcolepsy as an immunological illness with different expressions or associated features which could be observed in the clinical context. This phenomenon can be justified in part by the immunological differences observed among narcoleptic patients.

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0673

**ARMODAFINIL REDUCES DAYTIME FATIGUE ASSOCIATED WITH EXCESSIVE SLEEPINESS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA/HYPOPNEA SYNDROME OR NARCOLEPSY**

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**Introduction :** Excessive sleepiness (ES) is often accompanied by fatigue, which can negatively impact quality of life. Armodafinil, a wake-promoting agent, is the R-enantiomer of racemic modafinil and has a longer half-life than the S-enantiomer. The effects of armodafinil on the severity of daytime fatigue and its impact on daily living in adults with ES associated with obstructive sleep apnea/hypopnea syndrome (OSA/HS) or narcolepsy are reported.

**Methods :** Three randomized, 12-week, double-blind, placebo-controlled studies were conducted; 2 in patients with OSA/HS and 1 in patients with narcolepsy. Patients received armodafinil 150 or 250 mg/day or placebo. The Brief Fatigue Inventory, a 9-item questionnaire, was used to assess the severity of fatigue and impact on daily functioning using an 11-point scale (0-10). Higher scores indicated greater severity or impact. Changes in scores for global fatigue (average of all 9 items) and worst fatigue during the past 24 hours were analyzed.

**Results :** 777 patients were evaluable (OSA/HS, n=601; narcolepsy,

n=176). Armodafinil (150 and 250 mg/day) significantly improved global fatigue at final visit versus placebo in patients with OSA/HS or narcolepsy (P<.01). In patients with OSA/HS, the armodafinil 150 mg group showed significantly greater improvement than the placebo group in worst fatigue during the past 24 hours (mean±SD change from baseline, -1.4±2.7 vs -0.7±2.72; P=.0044). In patients with narcolepsy, numerical improvement in worst fatigue scores was observed with armodafinil compared with placebo, but the differences did not achieve statistical significance.

**Conclusion :** Armodafinil reduces the severity and impact of patient-reported fatigue in patients with ES associated with OSA/HS and narcolepsy.

**Support (optional):** Supported by Cephalon, Inc.

0674

**ARMODAFINIL DOES NOT AFFECT INTENDED SLEEP AS DETERMINED BY POLYSOMNOGRAPHY IN PATIENTS WITH EXCESSIVE SLEEPINESS**

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**Introduction :** Armodafinil, a wake-promoting agent, is the R-enantiomer of racemic modafinil and has a longer half-life than the S-enantiomer. The effects of armodafinil on desired sleep as measured by polysomnography variables in patients with excessive sleepiness associated with narcolepsy, obstructive sleep apnea/hypopnea syndrome (OSA/HS), or shift work sleep disorder (SWSD) are reported.

**Methods :** Patients with narcolepsy, OSA/HS, or SWSD participated in 1 of 4 randomized, double-blind, placebo-controlled studies. Patients received armodafinil 150 or 250 mg/day (narcolepsy, OSA/HS), 150 mg on work nights (SWSD), or placebo. Sleep variables (latency to persistent sleep, sleep efficiency, wake after sleep onset [WASO], number of arousals) were assessed at baseline and week 12 (or final visit) by nocturnal (narcolepsy, OSA/HS) or daytime (SWSD) polysomnography.

**Results :** In total, 1090 patients were evaluated from the narcolepsy (armodafinil, n=131; placebo, n=63), OSA/HS (armodafinil, n=391; placebo, n=260), and SWSD (armodafinil, n=123; placebo, n=122) studies. Mean change from baseline in the latency to persistent sleep was -0.6, -1.6, and 3.1 minutes in the armodafinil group and 7.2, -0.3, and 1.1 minutes in the placebo group in the narcolepsy, OSA/HS, and SWSD studies, respectively. The mean change from baseline in sleep efficiency was -0.6%, -0.4%, and -2.1% in patients receiving armodafinil and -0.9%, -0.7%, and 0.5% in patients receiving placebo in the narcolepsy, OSA/HS, and SWSD studies, respectively. The mean change from baseline in WASO was not clinically meaningful for armodafinil compared with placebo (narcolepsy, 3.5 vs -3.6 min; OSA/HS, 1.7 vs 1.7 min; SWSD, 6.2 vs -4.7 min). For patients receiving armodafinil, the mean number of arousals was reduced from baseline by -0.7 in narcolepsy, -1.7 in OSA/HS, and -0.5 in SWSD compared with -1.5, -0.4, and -0.1, respectively for placebo.

**Conclusion :** Armodafinil did not affect intended sleep when sleep was desired in patients with narcolepsy, OSA/HS, or SWSD.

**Support (optional):** Sponsored by Cephalon, Inc.

## 0675

## SODIUM OXYBATE IMPROVES SLOW WAVE SLEEP AND DAYTIME SLEEPINESS IN NARCOLEPSY

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**Introduction :** A recent trial demonstrated that sodium oxybate significantly improves excessive daytime sleepiness (EDS) in patients with narcolepsy as demonstrated by improved scores in the Maintenance of Wakefulness Test (MWT) and Epworth Sleepiness Scale (ESS). The mechanism of this improvement is unknown. Polysomnographic data from this trial was analyzed to test the hypothesis that a significant correlation exists between changes in sleep parameters total sleep time (TST), nocturnal awakenings and slow wave sleep (SWS) and the improvements in sleepiness as measured by the MSW and ESS.

**Methods :** In this 8-week, double-blind, placebo-controlled trial, patients with narcolepsy received 4.5, 6 or 9 g of sodium oxybate, or placebo nightly. Sodium oxybate was administered in equally-divided doses at bedtime and 2.5-4 hours later. Patients receiving 6 and 9 g doses received weekly 1.5 g increments. Placebo was also administered with a mock dose titration schedule. Nocturnal polysomnograms were performed at the beginning and end of double-blind phase (steady doses). The intent-to-treat population included 228 patients; 206 patients completed the trial.

**Results :** After 8 weeks, sodium oxybate significantly improved SWS across all three doses. Additionally, sodium oxybate increased TST and decreased nocturnal awakenings at 6 and 9 g doses. SWS improvements across all doses significantly correlated with decreased ESS scores ( $p=0.004$ ), and nocturnal awakenings ( $p=0.0006$ ). Improved MWT scores also correlated with decreased Epworth Sleepiness Scale scores ( $p=0.0032$ ). The most commonly reported adverse events included headache (17.1%), nausea (14.2%), dizziness (13.0%), nasopharyngitis (7.7%), and enuresis (6.9%).

**Conclusion :** The strong correlation found between measures of improved EDS and sodium oxybate-induced increases in SWS and decreased awakenings suggest that improved sleep quality may be responsible for some of the improvement in EDS. Further investigation is required to determine whether the increase in SWS, often considered to be the most restorative stage of sleep, or other improvements in sleep quality are mediating this effect.

**Support (optional):** This study was sponsored by Orphan Medical, a subsidiary of Jazz Pharmaceuticals.

## 0676

## TNF-ALPHA GENE EXPRESSION AND EFFECTS OF THALIDOMIDE (HYPNOTIC WITH TNF-ALPHA INHIBITION) ON SLEEP IN OREXIN/ATAXIN-3 NARCOLEPTIC MICE

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**Introduction :** TNF-alpha (a cytokine involved in sleep regulation)-mediated mechanisms may be involved in the pathophysiology of narcolepsy. Polymorphism of TNF-alpha and its receptor genes are associated with human narcolepsy, and thalidomide (a hypnotic with TNF-alpha inhibition), induces status cataplectus in canine narcolepsy. We have therefore assessed the TNF-alpha gene expression and effects of thalidomide administration in hypocretin-deficient narcoleptic mice.

**Methods :** Orexin/ataxin-3 TG mice (N8, C57BL/6-DBA1 backcrossed to C57BL/6) and respective WT littermates were used. Eight TG and 8

WT mice were implanted with EEG and EMG electrodes and were maintained in LD12:12 cycle. The mice were administered with 2 doses (10, 40 mg/kg p.o.) of thalidomide and vehicle at ZT18, and the effects on NREM and REM sleep during the 4-hour post treatment were analyzed. The expression of TNF-alpha gene in the cortex was analyzed using RT-PCR in TG and WT mice at the baseline (50 and 200 days old) and 2 hr after the thalidomide (10, 40 mg/kg p.o., 200 days old) administrations.

**Results :** Thalidomide dose-dependently increased NREM and REM sleep in both WT (142% [NREM] and 192% [REM], 4-hours after 40 mg/kg) and TG (138% and 180%) mice with higher incidences of direct transition from wake to REM sleep in TG mice. TNF-alpha gene expressions in the cortex did not differ between the genotype. Thalidomide also reduced TNF-alpha gene expression similarly in both TG and WT mice.

**Conclusion :** We have previously shown that REM enhancements by thalidomide are likely to be mediated by the inhibition of TNF-alpha. No alternation of TNF-alpha gene expression was observed in TG mice. REM sleep was similarly increased in both WT and TG mice after thalidomide administration. A higher incidence of DREM in narcoleptic mice after thalidomide administration may explain the reason why narcoleptic dogs exhibit status cataplectus from thalidomide. Although no alternation in TNF-alpha mechanisms are found in hypocretin-deficient narcoleptic mice model, this negative result does not preclude the possibility that TNF-alpha mechanisms are involved in the pathogenesis of human narcolepsy.

**Support (optional):**

## 0677

## ASSOCIATION BETWEEN REM SLEEP BEHAVIOR DISORDER AND NARCOLEPSY WITH AND WITHOUT CATAPLEXY

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**Introduction :** Rapid eye movement (REM) Sleep Behavior Disorder (RBD) is a parasomnia characterized by a loss of REM sleep muscle atonia leading to complex and vigorous behaviors. An association between RBD and Narcolepsy has been described, although only two studies have estimated its prevalence. We aimed to assess the clinical and polysomnographic (PSG) frequency of RBD and to quantify REM sleep muscle activity in narcoleptic patients with and without cataplexy.

**Methods :** Twenty-five consecutive narcoleptic patients (14M, 11F; mean age: 40.3±14.5) and 13 age and sex-matched control subjects entered the study. Subjects underwent to a semi-structured interview to assess the presence of RBD followed by one-night PSG recording. Percentage of 10-sec mini-epochs containing chin EMG activity longer than 0.5 sec with amplitude exceeding two times the background activity was calculated in narcoleptic patients and controls by a scorer blind to the condition. Between-group differences in clinical and PSG variables have been assessed by means of T-Student and Mann-Whitney.

**Results :** Thirteen of our narcoleptic patients (52 %) reported a history of RBD. Furthermore, RBD symptoms were present in 11/14 (79%) of narcoleptic patients with cataplexy (Cat) and in 2/11 (18 %) of those without cataplexy (Cat-; Chi-square: 0.003). Narcoleptic patients showed a higher % of epochs with muscle activity during REM sleep compared to controls (19.5±19.8 vs. 8.5±3.9;  $p=0.009$ ). Cat+ patients showed a greater number of epochs with muscle activity compared to Cat- (26.7±23.7 vs. 13.2±11.4;  $p=0.009$ ). RBD was equally distributed among males and females in Narcolepsy and no gender difference was found in muscle

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activity during REM sleep.

**Conclusion :** Our study showed that RBD is quite common in Narcolepsy and that patients with cataplexy are much more likely to have RBD than those without cataplexy. Narcoleptic patients should be routinely questioned about RBD symptoms. The peculiar association between RBD (loss of atonia during REM sleep) and cataplexy (loss of muscle tone during wake) could help in understanding the pathophysiology of these conditions and deserves further studies.

**Support (optional):**

### 0678

#### WAKE PROMOTING EFFECTS OF NON-IMIDAZOLIN HISTAMINE H3 ANTAGONIST IN OREXIN/ATAXIN-3 NARCOLEPTIC MICE

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**Introduction :** Recent experiments demonstrated that the histaminergic system is one of the important executive systems of hypocretin signaling for promoting wakefulness. An impaired histaminergic system is also suggested in human and canine narcolepsy. We have reported that thioperamide (an imidazolin histaminergic H3 autoreceptor antagonist), promotes wakefulness in the mouse narcoleptic model. Since thioperamide may also act on non-histaminergic imidazolin receptors, this property may influence the observed pharmacological effects. Therefore, we have further assessed the therapeutic effects of a non-imidazolin H3 antagonist in the mouse model.

**Methods :** Orexin/ataxin-3 TG narcoleptic mice (N8, C57BL/6 congenic line) and WT littermates (n=5-8 for each group) were used. The mice were surgically prepared for EEG and EMG recording, and they were maintained in LD12:12 within separate compartments in a sound-attenuated stainless steel recording chamber. The mice were subjected to oral administration of three doses (0.3, 3 and 10 mg/kg) of RWJ662733 and one vehicle administration during light and dark periods. Drug administrations were made either at ZT 2 and ZT 16. Six-hour post drug data were analyzed, and each 10-second epoch is scored visually as wake, REM, or NREM sleep.

**Results :** RWJ662733 increased wake and reduced NREM and REM sleep in a dose dependent manner in TG and WT mice. Larger wake-promoting effects were observed during light period when the animal sleep most of the time at the baseline, and wake promoting potency of 3 mg/kg p.o. of RWJ662733 roughly corresponds to that of 200 mg/kg p.o. modafinil. Interestingly, wake-promoting effects of RWJ662733 in light period were more prominent in TG mice and 153% of wake from the vehicle session in TG vs. 140% in WT after 10mg/kg p.o. Wake-promoting effects of RWJ662733 during dark period was subtle (110% to 116%), but, the mean bout length of wake in TG and WT mice became longer after RWJ662733 administration.

**Conclusion :** The non-imidazolin H3 antagonist, RWJ662733, significantly promotes wakefulness in both hypocretin-deficient narcoleptic (TG) and WT type mice. TG mice were however, more sensitive to RWJ662733, and larger wake-promoting effects during light period were observed. Although smaller wake-promoting effects were observed in TG mice during dark period, RWJ662733 is likely to consolidate wakefulness in these animals. H3 antagonists may thus be another therapeutic choice to manage excessive daytime sleepiness associated with narcolepsy.

**Support (optional):**

0679

**CLONIDINE AS A TREATMENT FOR PRIMARY INSOMNIA**Bonnet MH,<sup>1,2,4,3</sup> Arand DL<sup>3,4,2</sup>

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**Introduction :** Numerous studies have documented elevated physiological arousal as indexed by heart rate and heart rate variability, metabolic rate, and increased cortisol and norepinephrine in patients with primary insomnia. It was hypothesized that clonidine, which is commonly used to modify sympathetic activity, would reduce central arousal and improve sleep and daytime function in these patients.

**Methods :** Twelve insomnia patients, identified by having a sleep efficiency of less than 85% (and no other sleep disorder) on two screening nights spent an additional four nights (baseline followed by blinded administration of clonidine .2 mg hs and .1 mg qam or placebo on two randomized weeks) and the following days in the laboratory. On the day following clonidine and placebo administration, subjects had an MSLT and performance testing.

**Results :** Clonidine administration was associated with significant increases in stage 2 and decreases in REM. Nonsignificant increases in total sleep and decreases in sleep latency were also found. Significant decreases in low frequency heart rate variability and increases in high frequency heart rate variability were accompanied by a reduction of MSLT from 14.2 to 12.4 minutes and significant decreases in tension/anxiety and depression. Significant change in performance was not found.

**Conclusion :** Administration of low doses of clonidine bid produced expected decreases in arousal and improved subjective mood without producing hypothesized significant increases in total sleep. The sleep effects may have been secondary to individual differences in response (increases of 100+ min in TST in some Ss compared to 70+ min decreases in other Ss) and could imply multiple mechanisms in “primary” insomnia or that reducing arousal may be related to improved symptoms independent of large changes in objective EEG parameters.

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0680

**INSOMNIA AS RISK-FACTOR FOR PERMANENT WORK DISABILITY**Sivertsen B,<sup>1</sup> Overland S,<sup>2</sup> Neckelmann D,<sup>3</sup> Glozier N,<sup>4</sup> Krokstad S,<sup>5</sup> Pallesen S,<sup>6,7</sup> Nordhus IH,<sup>1,7</sup> Bjorvatn B,<sup>7,8</sup> Mykletun A<sup>2,4,9</sup>

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**Introduction :** Chronic insomnia is common in the general population. Its effect upon an individual’s functioning and disability is usually attributed to an underlying condition and so the diagnosis of insomnia does not

qualify for the award of a disability pension in the US or Europe. The aim of this study was to investigate whether DSM-IV defined insomnia contributed to long-term work disability.

**Methods :** Employing an historical cohort design, baseline data were gathered from a population based Norwegian health study of 37 308 working age people not claiming disability pension through 1995-97. The outcome was a subsequent award of a disability pension (18 to 48 months after the health screening), as registered in the National Insurance Administration.

**Results :** Insomnia was a strong predictor of subsequent permanent work disability (adjusted odds ratio (OR) 3.90, 95% confidence interval (CI): 3.20, 4.76). Socio-demographic and shift work characteristics had little confounding effect (adjusted OR = 3.69, 95% CI: 3.00, 4.53), and this association remained significant after adjustment for psychiatric and physical morbidity, and health-related behaviours (adjusted OR=1.75, 95% CI: 1.40, 2.20).

**Conclusion :** This suggests that insomnia should receive increased attention as a robust and independent risk factor for subsequent work disability.

**Support (optional):**

0681

**IMPAIRED SLEEP-RELATED MEMORY CONSOLIDATION IN PRIMARY INSOMNIA**Nissen C,<sup>1,2</sup> Kloepfer C,<sup>2</sup> Nofzinger EA,<sup>1</sup> Voderholzer U,<sup>2</sup> Riemann D<sup>2</sup>

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**Introduction :** Preclinical and clinical evidence indicate that sleep can contribute to the consolidation of memories. The present pilot study tested the hypothesis that the pre-post sleep consolidation of procedural memory traces may be impaired in patients with primary insomnia.

**Methods :** 7 patients with primary insomnia and 7 gender, age and IQ matched healthy controls spent one night in the sleep laboratory. Performance on a mirror tracing task was measured before and after sleep.

**Results :** Polysomnography did not reveal a significantly disturbed sleep profile in the patients compared to the control group (MANOVA: F(10,3) = 8.7, p = 0.050, univariate tests not significant). Pre-sleep performance in the mirror tracing task did not differ significantly between the groups. Both groups performed significantly better in the post-sleep recall session (MANOVA for factor test session: F(9,4) = 31.8, p = 0.000). However, healthy controls showed an improvement of 42.8 ± 5.8 % in the mirror tracing draw time, whereas patients with insomnia showed only an improvement of 20.4 ± 14.8 % (MANOVA test session \* group interaction: F(9,4) = 10.9, p = 0.002).

**Conclusion :** These findings support the view that sleep-associated consolidation of procedural memories may be impaired in patients with primary insomnia.

**Support (optional):**

0682

**BEHAVIORAL SLEEP INTERVENTION FOR BEREAVED FAMILY CAREGIVERS: A PILOT STUDY**

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**Introduction :** By 2007 thirty-nine million households will be giving care to persons aged 50 an older with chronic illnesses. The psychiatric and physical health effects of family caregiving are well documented; however the after effects during bereavement are only now being docu-

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mented. Bereavement is a complex process in which sleep plays a vital role. Insomnia is a common complaint among bereaved caregivers. This study evaluated the feasibility of a behavioral sleep intervention designed for family caregivers (CASI) for use with bereaved caregivers.

**Methods :** Bereaved caregivers of persons who died from chronic illness at least 3 weeks, but no more than 3 months prior were invited to participate. Ten individuals have completed the 5-week protocol. Depression (CESD) and Insomnia (PSQI & actigraphy) were assessed at baseline, 3 & 5 weeks. The intervention included stimulus reduction, sleep hygiene, relaxation, and cognitive behavioral education elements. A Master's prepared research nurse delivered content in two 2-hour sessions (Weeks 2 & 4) in the participant's home. Goal setting and monitoring were used to individualize the intervention.

**Results :** Participants were Caucasian (100%), primarily male (57%), spouses (57%) and adult children (30%) and ranged in age from 47-79 (M=62). Baseline CESD and PSQI mean scores were 19.2 and 9.3 respectively. Average latency was 42 minutes, duration was 5.2 hours, and efficiency averaged 78%. Following the intervention all participants' scores improved. On average, latency improved 20 minutes, duration increased 45 minutes, and efficiency increased to 82%. PSQI and CESD scores decreased to 7.2 and 15 respectively.

**Conclusion :** Working one-on-one with bereaved caregivers using a behavioral sleep intervention and personal goal setting during the early stages of bereavement provided the caregiver with skills and knowledge to improve their sleep quality. Improved sleep quality resulted in improved levels of energy needed to actively engage in the tasks of bereavement.

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### 0683

#### ATTENTION BIAS IN PI TO 'NEGATIVE' SLEEP STIMULI

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**Introduction :** Experimental evidence has confirmed an attentional bias to sleep-related stimuli in PI and explanations of the processes driving this bias have been reviewed, but not tested. Being unable to sleep may drive an attentional bias through threat. Indeed, being unable to sleep might be experienced as a threat. To directly assess whether threat is involved in the attentional bias shown by PI we have modified a Posner paradigm by generating two forms of sleep words, those that are intrinsically threatening i.e. fatigue, and others that are intrinsically non-threatening i.e. pillow.

**Methods :** A between group (PI, GS, DSPS) by within group factorial design has been employed, whereby each individual completes a modified Posner paradigm. Within this modified paradigm, threatening sleep, non-threatening sleep words and neutral words cue attention and will be presented either in the same spatial location as the target (valid) or at a different spatial location as the target (invalid). All factors associated with the Posner paradigm (Word, Validity and Cue exposure) will be within participant factors.

**Results :** The RT data was subjected to a 3 (group: PI, DSPS, GS) X 2 (location: valid, invalid) X 3 (word valence: positive/ non threatening, negative/threatening, neutral) ANOVA. There was a main effect of valid vs invalid trial on neutral words  $F(1,88) = 10.095$ ,  $p < 0.01$ , with participants responding, on average, 63.37ms faster on valid trials relative to invalid trials. There was also a significant main effect of group  $F(2,126) = 6.363$ ,  $p < 0.01$ . Scheffe Post Hoc analyses revealed that PI were significantly slower to respond to invalid trials than GS  $t(15) = 10.32$ ,  $p < 0.01$ ,

and DSPS  $t(15) = 8.70$ ,  $p < 0.05$ . A significant interaction was revealed between group and word valence  $F(2,126) = 3.803$ ,  $p < 0.01$ . Scheffe Post Hoc analyses revealed that PI were significantly slower on invalid negative word trials than GS  $t(15) = 20.31$ ,  $p < 0.0001$ , and DSPS  $t(15) = 13.58$ ,  $p < 0.01$ , and PI were significantly slower on negative word trials than neutral word trials  $t(15) = 17.15$ ,  $p < 0.001$ .

**Conclusion :** When the cue word was a negative sleep word, PI took longer to categorize the target on invalid trials relative to when the cue was either a positive sleep word or a neutral word. Furthermore, PI took longer to categorize a negative sleep word on invalid trials relative to both GS and DSPS. This data is the first evidence to suggest that the attentional biases detected in PI to sleep salient stimuli may be driven by threat.

**Support (optional):**

### 0684

#### A DOUBLE-BLIND PLACEBO-CONTROLLED PHASE III STUDY OF THE LONG-TERM EFFECTS OF RAMELTEON ON ENDOCRINE FUNCTION IN ADULTS WITH CHRONIC INSOMNIA

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**Introduction :** The chronohypnotic Rozerem™ (ramelteon) is a highly selective and potent MT1/MT2-receptor agonist indicated for the treatment of insomnia. The long-term effects of ramelteon on endocrine function were evaluated in adults with chronic insomnia.

**Methods :** In a double-blind, placebo-controlled, multicenter trial, 122 adults (18 to 45 years of age) with primary insomnia (DSM-IV™ criteria) received placebo or ramelteon 16 mg nightly for 6 months. The primary variable was total serum thyroxine (T4) change from baseline. Secondary variables included thyroid and adrenal function measures, and reproductive endocrine assessments. Endocrine variables were measured monthly. Safety (eg, physical exams, vital signs, ECG, and clinical labs) was monitored throughout the study.

**Results :** No consistent statistically significant differences between treatments were observed on measures of thyroid function (total T4, free T4, TSH and total T3), adrenal function (AM cortisol and ACTH), or on most reproductive endocrine measures (LH, FSH, estradiol [women], total and free testosterone [men]). The mean change in prolactin levels from baseline differed significantly between ramelteon (2.9  $\mu\text{g/L}$ ; 22.8% change) and placebo (-0.6  $\mu\text{g/L}$ ; 4.4% change). This effect was only observed in women and appeared to be transient. No clinical signs of elevated prolactin were reported. There was no difference between placebo and ramelteon 16 mg groups in the length of the average menstrual cycle length, the duration of menses, or the probability of ovulation. The frequency of adverse events (AEs) was similar between the placebo and ramelteon 16 mg groups; most AEs were mild or moderate (3 patients had serious AEs unrelated to study drug).

**Conclusion :** In adults with chronic insomnia, long-term treatment with ramelteon did not produce any consistent effects on a range of endocrine function measures. Observed alterations in prolactin levels occurred in women, but were small, transient and had no clinically significant effect.

**Support (optional):** This research was funded by Takeda Pharmaceutical Company, Ltd.

## 0685

## LONG-TERM SAFETY OF RAMELTEON TREATMENT IN ADULTS WITH CHRONIC INSOMNIA: A 1-YEAR STUDY

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**Introduction :** Rozerem™ (ramelteon) is a highly selective agonist of MT<sub>1</sub>/MT<sub>2</sub> receptors and is indicated for insomnia treatment. Adults with chronic insomnia were administered ramelteon for 1 year to assess the long-term safety of this chronohypnotic agent.

**Methods :** Adults (N=1213) diagnosed with primary insomnia (DSM-IV-TR™ criteria) and reporting symptoms for ≥3 months received ramelteon every night for 1 year. Ramelteon treatment was followed by a 3-day placebo run-out. Older adults ≥65 years of age received ramelteon 8 mg (n=248); adults 18 to 64 years of age received ramelteon 16 mg (n=965). Safety was evaluated over the course of the study at monthly clinic visits.

**Results :** A total of 597 subjects completed 6 months of ramelteon treatment and 473 completed 1 year of treatment. The primary reasons for early discontinuation were lack of efficacy (19.7%), adverse events (AEs) (12.2%), and consent withdrawal (11.9%). The overall incidence of AEs was similar at 6 months and 1 year; AEs were predominantly mild or moderate. At 1 year, the AEs most frequently reported with ramelteon 8mg and 16mg were nasopharyngitis (10.5% and 14.9%), somnolence (9.5% and 8.1%), upper respiratory tract infection (7.6% and 11.1%), headache (1.9% and 13.5%), and sinusitis (1.9% and 7.8%). Of 38 subjects (3.1%) reporting a serious AE, only 3 AEs were possibly treatment related. There were no clinically meaningful changes in vital signs, physical exams, clinical chemistry, hematology, or urinalysis values and no ECG trends to suggest adverse effects on cardiac function over 1 year of treatment. No notable changes in endocrine function and sexual/reproductive function were observed except for mean free and total testosterone, which had a slight decrease in older men (8mg group) that returned to normal by the Final Visit.

**Conclusion :** Over 1 year of treatment, ramelteon was well tolerated and did not adversely affect safety measures in adults.

**Support (optional):** This research was supported by Takeda Pharmaceutical Company, Ltd.

## 0686

## DOES CO-MORBID OSA IMPACT ON INSOMNIA TREATMENT OUTCOME?

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**Introduction :** Obstructive sleep apnoea and primary insomnia are usually regarded as discrete sleep disorders with few symptoms in common and different demographic characteristics. However, research is indicating a degree of overlap between the two disorders that may have etiological importance and treatment consequences. The presence of co-morbid OSA may impair the treatment of insomnia. The aim of the study was to evaluate the degree of OSA in patients referred to an outpatient cognitive/behavioural insomnia treatment program, and to determine the impact of this co-morbidity on the response to insomnia treatment.

**Methods :** The first 60 patients (35 females, 25 males, Mean age = 52.7 (13.4)yrs, Mean BMI = 25.4 (3.6)) attending an outpatient cognitive/behavioural treatment program for insomnia had full nocturnal home polysomnography. Treatment response was determined from 7-day

sleep/wake diaries at baseline, 5 week and 3 month follow-up.

**Results :** To date, 37% of insomnia patients also presented with a Respiratory Disturbance Index (RDI) of at least 15 (mild OSA). The patients were divided into a 'No OSA' group (RDI < 15; M=7.8 (3.6)) and an "OSA" group (RDI > 15; M=25.6 (7.1)). There were no significant differences between groups on BMI or gender. For the entire group as a whole there were significant improvements in sleep onset latency (F(2,51)=14.7, p<0.001), wake time after sleep onset (F(2,48)=51.8, p<0.001), total sleep time (F(2,51)= 32.2, p<0.001), and sleep efficiency (F(2,48)=70.3, p<0.001). There was a significant interaction effect between groups only in the improvement of total sleep time (F(1,52)=4.38, p<0.05), however, it was the OSA group that improved more.

**Conclusion :** More than a third of patients referred for the treatment of insomnia had at least mild OSA. Following a non-drug treatment program for insomnia, those with some OSA showed improvements in sleep at least as great as those without OSA. The presence of mild to moderate comorbid OSA does not impair the treatment of insomnia.

**Support (optional):**

## 0687

## THE CONTRIBUTION OF ANXIETY TO SLEEP QUALITY REPORTING IN INSOMNIA SUBTYPES

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**Introduction :** The Pittsburgh Sleep Quality Index is used as a subjective measure of sleep quality. Although this is a well-validated and widely used tool it has not been investigated in the context of different diagnostic insomnia subtypes.

**Methods :** To assess for insomnia and rule-out other sleep disorders, participants completed the Duke Structured Interview for Sleep Disorders (DSID), 2 weeks of sleep logs, and 2 nights of polysomnography. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) was used to assess for mental disorders; the Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-16) Sleep Worry subscale assessed worry about sleep and the Beck Anxiety Inventory (BAI) assessed general anxiety. Two groups were formed on the basis of DSM-IV-TR criteria: Primary Insomnia (PI) and Insomnia related to a Mental Disorder (IMD).

**Results :** An analysis of variance (ANOVA) revealed IMD had higher PSQI scores than PI; however, after covarying the BAI, there were no differences. To determine if sleep-specific worry could account for these results, we covaried for Sleep Worry only, and found significant group differences. A final ANOVA indicated that there was not a statistically significant difference between the groups on mean Sleep Diary ratings of Sleep Quality over two weeks.

**Conclusion :** The elevated PSQI scores in IMD patients were removed by controlling for anxiety but not by controlling for sleep worry, thus supporting a key role for general anxiety in driving reported sleep quality on the PSQI in such patients. Sleep Diary ratings of sleep quality were not different between the groups, thus these ratings may not be as determined by emotional state as the PSQI. It would be important for those using the PSQI in patients with a comorbid mental disorder to take into account the extent to which the index reflects anxiety.

**Support (optional):** National Sleep Foundation Pickwick Fellowship; Classifying Psychiatric, Medical, and Primary Insomnias (NIH R01, MH067057).

0688

**ARE INSOMNIA PATIENTS PATHOLOGICALLY WORRIED OR SIMPLY WORRIED ABOUT SLEEP?**

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**Introduction :** People with insomnia have been described as dispositionally anxious and worried; although these studies have not examined carefully identified diagnostic insomnia subtypes.

**Methods :** To assess for insomnia and rule-out other sleep disorders, participants completed the Duke Structured Interview for Sleep Disorders (DSID), 2 weeks of sleep logs, and 2 nights of polysomnography. The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) was used to assess for mental disorders; the Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS-16) Sleep Worry subscale assessed worry about sleep; the Penn State Worry Questionnaire (PSWQ) assessed general worry; and the Beck Anxiety Inventory (BAI) assessed general anxiety. Two groups were formed based on diagnosis: Primary Insomnia (PI; N = 58) and Insomnia related to Mental Disorder (IMD; N = 20).

**Results :** A multivariate analysis of variance (MANOVA) tested whether PI and IMD differed on BAI, PSWQ, or Sleep Worry. ANOVAs followed-up a significant MANOVA, and revealed higher anxiety and worry in the IMD group; there were no significant differences on Sleep Worry. A MANOVA on BAI items revealed that items typical of Panic Disorder (e.g., heart pounding, lose control) discriminated PI from IMD. A MANOVA on PSWQ items revealed that discriminating items related to Generalized Anxiety Disorder diagnostic criteria: namely, worry frequency, controllability and pervasiveness.

**Conclusion :** Unlike the IMD group, the PI group was not characterized by pathological worry and anxiety (e.g., scores above the clinical cutoff). Moreover, there were no group differences on sleep-specific worry. Together the findings suggest that it is inaccurate to consider those with PI as a necessarily pathologically worried or anxious group; rather, their worry pertains to sleep.

**Support (optional):** National Sleep Foundation Pickwick Fellowship; Classifying Psychiatric, Medical, and Primary Insomnias (NIH R01, MH067057).

0689

**SLEEP PROBLEMS, COMORBID MENTAL DISORDERS, AND ROLE FUNCTIONING IN THE NATIONAL COMORBIDITY SURVEY REPLICATION (NCS-R)**

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**Introduction :** Little is known about the prevalence of different types of disturbed sleep and whether the associations of sleep problems with role impairment are due to comorbid mental disorders.

**Methods :** The associations of 12-month sleep problems of difficulty initiating sleep(DIS), difficulty maintaining sleep(DMS), early morning awakenings(EMA), and nonrestorative sleep(NRS) with role impairment were analyzed in Part II of the National Comorbidity Survey Replication (n = 5692) controlling for 12-month DSM-IV anxiety, mood, impulse-control, and substance disorders. The WHO Composite International Diagnostic Interview was used to assess sleep problems and DSM-IV disorders. The WHO Disability Schedule II(WHO-DAS) was used to assess

role impairment.

**Results :** Twelve-month prevalence estimates are 16.4% for DIS, 19.9% for DMS, 16.7% for EMA, 25.0% for NRS, and 36.3% for any of the four sleep problems. Mean duration of sleep problems in the past 12 months ranged from 25 to 29 weeks, depending on the specific sleep problem, with 32.1% of cases reporting short durations (2-4 weeks) and 28.0% long durations (51-52 weeks). The sleep problems were all significantly comorbid with all the 12-month DMS-IV disorders (median OR: 3.4; 25th-75th percentile: 2.8-3.9) and related to substantial role impairment that generally remained significant after controlling for comorbid mental disorders.

**Conclusion :** Each of the four sleep problems considered here have great public health significance because of their high prevalence and significant associations with role impairment even in the absence of comorbid psychiatric disorders.

**Support (optional):** Supported by NIMH (U01-MH60220),NIDA, SAMHSA, the Robert Wood Johnson Foundation, and the John W. Alden Trust with a supplemental grant from Eli Lilly and Company.

0690

**LONG-TERM THERAPEUTIC EFFECTS OF RAMELTEON TREATMENT IN ADULTS WITH CHRONIC INSOMNIA: A 1 YEAR STUDY**

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**Introduction :** Rozerem™ (ramelteon), a chronohypnotic agent, is a highly selective and potent MT1/MT2-receptor agonist. The long-term safety and efficacy of ramelteon was evaluated in adults with chronic insomnia.

**Methods :** Adults (N=1213) diagnosed with primary insomnia (DSM-IV-TR™ criteria) and reporting symptoms for ≥3 months received ramelteon each night for 1 year. Ramelteon treatment was followed by a 3-day single-blind placebo run-out. Adults 65 years of age and older received ramelteon 8mg (n=248); adults 18 to 64 years received ramelteon 16mg (n=965). At monthly clinic visits, safety was assessed and efficacy was evaluated by Clinical Global Impression (CGI) assessments performed by the investigator. Subject-reported efficacy was also evaluated by daily sleep diaries.

**Results :** The ramelteon 8mg and 16mg groups had similar baseline mean sleep latencies (85.1 and 88.8 min, respectively) and total sleep times (TST) (293.8 and 304.1 min, respectively). With ramelteon 8mg and 16mg, sleep latency improved from baseline at Month 1 by 34.0% and 35.1%, respectively, and continued to improve through Month 6 (44.7% and 49.1%) and Month 12 (50.3% and 52.1%). Improvements in TST at Month 1 (15.2% and 16.9%), Month 6 (21.6% and 22.7%), and Month 12 (25.5% and 23.9%) were also reported with ramelteon 8mg and 16mg. During the placebo run-out, no notable changes in sleep latency were reported. At 6 months and 1 year, CGI indices showed an improved insomnia condition, a moderate and sustained improvement in severity of illness, and a moderate therapeutic effect in both treatment groups. Consistent with previous studies, adverse events were primarily mild or moderate and reported at a low frequency in both groups.

**Conclusion :** In adults with chronic insomnia, ramelteon improved sleep latency, TST, and CGI at Month 1, and sustained these improvements through 1 year of treatment. Ramelteon was also well tolerated and did not result in rebound insomnia.

**Support (optional):** This research was supported by Takeda Pharmaceutical Company, Ltd.



0691

## LONG-TERM FOLLOW-UP OF A SELF-HELP TREATMENT FOR INSOMNIA

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**Introduction :** Self-help interventions represent a promising alternative to make effective insomnia treatments more readily accessible. This study reports long-term follow-up data on the efficacy of a self-help treatment for insomnia.

**Methods :** This report is based on participants (N = 192) who initially took part in a self-help intervention study. Treatment consisted of six booklets of cognitive-behavior therapy mailed weekly. Outcome assessment was based on sleep diaries and questionnaires completed at baseline, post-treatment, 6-, and 18-month follow-ups. At each assessment, participants were classified in one of three subgroups, using an algorithm based on DSM-IV and ICD-10 diagnostic criteria for insomnia: good sleepers, insomnia symptoms, and insomnia syndrome. The present analyses are based on participants who completed post-treatment assessment (N = 172; treatment group [Tx], n = 89, no-treatment control group [CI], n = 83; 65.3% women; aged 18-76, M = 46.1). Analyses were conducted separately for participants who were good sleepers (Tx, n = 39, CI, n = 36) and those who had insomnia symptoms or syndrome (Tx, n = 41, CI, n = 51) at post-treatment; Tx and CI groups were compared on sleep parameters and sleep status at 18-month follow-up.

**Results :** First, for participants who were good sleepers at post-treatment, there was no significant difference between Tx and CI groups for the percentage of participants who developed insomnia symptoms (17.2% vs. 23.3%) or syndrome (10.3% vs. 13.3%) at 18-month follow-up. There were no between-group differences for sleep diary parameters (i.e., sleep efficiency, total sleep time, total wake time, sleep quality) at 18-month follow-up. Second, for participants who had insomnia symptoms or syndrome at post-treatment, there was no significant difference between Tx and CI groups for the percentage of participants who became good sleepers at 18-month follow-up (37.5% vs. 32.6%). Sleep diary parameters at 18-month follow-up did not differ between groups.

**Conclusion :** These results suggest that a self-help minimal intervention for insomnia did not reduce relapse rates or enhance long-term recovery rates over an 18-month follow-up period. Whether these findings are due to poor compliance with self-help recommendations after treatment or to other factors remain unclear. Follow-up treatment reminders or even consultation visits might be more effective to maintain initial therapeutic benefits.

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0692

## DAYTIME FUNCTIONING AND INSOMNIA COMPLAINTS IN PEOPLE NOT HAVING INSOMNIA

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**Introduction :** The relationship between sleep and daytime functioning remains unclear. Three proposed relationships are: sleep quality predicts daytime functioning, daytime functioning predicts sleep quality, and sleep and daytime functioning are weakly related.

**Methods :** A random digit dialing survey collected sleep diaries for 14 days, as well as measures of health and daytime functioning, from 772 participants. The sleep diaries provide six measures of sleep quality: total

sleep time, sleep onset latency (SOL), wake time after sleep onset (WASO), number of nighttime awakenings, sleep efficiency, and time spent napping. Subjects also reported perceived sleep quality. Daytime functioning variables collected in the study were: Insomnia Impact Scale, Epworth Sleepiness Scale (ESS), Fatigue Severity Scale, State-Trait Anxiety Inventory (STAI), and Beck Depression Inventory (BDI). Participants who exhibited mean SOL and WASO < 31 minutes were classified as good sleepers.

**Results :** Criteria that matched subjects on sleep variables were empirically derived, so that daytime functioning could be compared in equivalent groups of good sleepers who did not complain of insomnia (PNI) and good sleepers who had an insomnia complaint (CGS). Individuals who complained of sleep disruptive health problems were excluded from the analysis. The results revealed that PNI (N=85) and CGS (N=7) had significant differences in BDI [t(90)=3.01, p=.003], M=11.9, SD=6.5 for CGS and M=5.6, SD=5.2 for PNI; STAI [t(90)=3.01, p=.003], M=44.1, SD=7.6 for CGS and M=33.9, SD=8.7 for PNI; and ESS [t(90) 2.35, p=.021] with M=11.43, SD=4.43 for CGS and M=7.71, SD=4.00 for PNI.

**Conclusion :** After matching subjects based on sleep, individual differences lead some subjects to perceive themselves as insomniacs, and these individuals have a greater propensity to report impaired daytime functioning. Possible explanatory factors to account for differential daytime impairment are hypersensitivity to small sleep decrements or a predisposition to emotional disability.

**Support (optional):** This Research was supported by the National Institute on Aging grants AG12136 and AG14738.

0693

## SLEEP PATTERN DIFFERENCES BETWEEN PEOPLE NOT HAVING INSOMNIA, COMPLAINING GOOD SLEEPERS, AND PERSONS WITH INSOMNIA

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**Introduction :** Three sleep groups can be identified: people not having insomnia (PNI), people with insomnia (PWI), and complaining good sleepers (CGS): people that have a sleep complaint, but do not meet quantitative requirements for insomnia. PNI and CGS both do not meet sleep criteria for insomnia, but CGS have a subjective sleep complaint. The goal of this paper is to compare the sleep patterns of CGS to both PNI and PWI.

**Methods :** We garnered participation from at least 50 men and 50 women in each decade from age 20 to 89 using random-digit dialing. They completed 14 days of sleep diaries and were grouped based on data collected from the diaries and the presence or absence of sleep and daytime functioning complaints. To qualify for an insomnia label, participants must have been self identified as having insomnia, complained of impaired daytime functioning, and shown a sleep pattern characterized by sleep latency  $\geq$  31 minutes or wake time after sleep onset  $\geq$  31 minutes, at least three times per week for six months.

**Results :** Of 772 participants, there were 137 PWI, 401 PNI, and 76 CGS. These groups were compared on six sleep variables: sleep onset latency, number of awakenings, wake time after sleep onset, total sleep time, sleep efficiency, nap time, and sleep quality rating. A MANOVA on this set of dependent variables was significant, Wilks'  $\lambda$  = .352, F(14,1210)=59.28, p<.01. PWI had significantly worse sleep on all six variables than CGS, who in turn had significantly worse sleep than PNI on all variables except for nap time.

## Category K—Sleep Disorders-Insomnia

**Conclusion :** Complaining good sleepers have significantly worse sleep than non-complaining good sleepers. This may indicate the existence of a sub-clinical insomnia group that are not just “complainers,” but have legitimate distressing sleep difficulties that are not severe enough to meet research grade insomnia criteria.

**Support (optional):** Research supported by National Institute on Aging grants AG12136 and AG14738.

### 0694

#### DAYTIME FUNCTIONING DIFFERENCES BETWEEN PEOPLE NOT HAVING INSOMNIA, COMPLAINING GOOD SLEEPERS, AND PERSONS WITH INSOMNIA

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**Introduction :** Three sleep groups can be identified: people not having insomnia (PNI), people with insomnia (PWI), and complaining good sleepers (CGS): people that have a sleep complaint, but do not meet quantitative requirements for insomnia. Few data exist comparing CGS to PNI. PNI and CGS both do not meet sleep criteria for insomnia, but CGS have a subjective sleep complaint. The goal of this paper is to compare CGS to both PNI and PWI on daytime functioning variables.

**Methods :** We garnered participation from at least 50 men and 50 women in each decade from age 20 to 89 using random-digit dialing. They completed 14 days of sleep diaries and a series of daytime functioning questionnaires. Participants were grouped based on data collected from the diaries and the presence or absence of sleep and daytime functioning complaints. To qualify for an insomnia label, participants must have been self identified as having insomnia, complained of impaired daytime functioning, and shown a sleep pattern characterized by sleep latency  $\geq$  31 minutes or wake time after sleep onset  $\geq$  31 minutes, at least three times per week for six months.

**Results :** Out of 772 participants, there were 137 PWI, 401 PNI, and 76 CGS. Participants in these groups were compared on six daytime functioning measures: IIS, FSS, STAI, BDI, ESS, and SSS. A MANOVA on this set of dependent variables was significant, Wilks'  $\eta^2 = .721$ ,  $F(12, 1212) = 17.92$ ,  $p < .01$ . CGS had significantly worse daytime functioning than PNI on all seven variables. There were no significant differences between PWI and CGS on any daytime functioning measure.

**Conclusion :** Based upon perceived daytime impairment, CGS are significantly worse than PNI but do not differ from PWI. Daytime functioning complaints are subjective, which may indicate that CGS are “complainers,” or they may have legitimate daytime functioning concerns attributed to perceived sleep difficulties.

**Support (optional):** Research supported by National Institute on Aging grants AG12136 and AG14738

### 0695

#### EFFECT OF TRANQUILIZER AND HYPNOTICS IN SLEEP ARCHITECTURE AND AUTONOMIC STATUS IN SHORT AND LONG TERM USAGE IN TREATMENT OF INSOMNIA

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**Introduction :** Benzodiazepines (BZ) are known for their dependence and addiction qualities. However, its effect on sleep architecture and autonomic conditions have not been clearly documented. Non-benzodiazepines (nBZ) hypnotics generally have a safer side effect profile; however, they have not been recommended by the FDA for chronic use. Their effect on sleep architecture and autonomic is also unclear.

**Methods :** This retrospective study of insomnia was performed by using cases from the sleep disorder clinic. Overnight polysomnography was performed in each patient to exclude cases involving sleep-related breathing disorders or any systemic diseases. All cases were divided into four groups: the first group took no medications, the second group took BZ tranquilizers, the third group took BZ hypnotics, the fourth took nBZ hypnotics. The polysomnography was analyzed for percentage of Wake After Sleep Onset (WASO), sleep stage 1, 2, 3 & 4, and REM. The autonomic status was evaluated with heart rate variability(HRV) in each group.

**Results :** In stage 3 & 4, Its percentage was  $5.63 \pm 6.51$  in cases not taking medicine,  $5.57 \pm 6.87$  (less than 3 months) and  $1.80 \pm 4.35$  (more than 3 months) in taking BZ tranquilizers, and  $3.05 \pm 5.71$  (less than 3 months) and  $2.83 \pm 5.20$  (more than 3 months) in taking BZ hypnotics. These results revealed remarkable differences between not taking medicine and taking BZ hypnotics or long term use of BZ tranquilizer. In status of WASO percentage, it was  $16.74 \pm 12.40$  in cases not taking medicine,  $20.63 \pm 14.50$  (less than 3 months) and  $26.79 \pm 8.21$  (more than 3 months) taking BZ hypnotics, and  $19.53 \pm 13.60$  in long term use of nBZ hypnotics. These findings revealed higher WASO with BZ and nBZ use than with not taking medicine. The HRV studies showed reduction of total power in nBZ group as compared with not taking medicine.

**Conclusion :** BZ tranquilizers reduced slow wave sleep if used more than 3 months, while BZ hypnotics reduced slow wave sleep and increased WASO for any duration of use. nBZ hypnotics did not affect slow wave sleep but increased WASO during chronic use. Therefore, long term use of tranquilizers or hypnotics for insomnia should be cautious.

**Support (optional):**

### 0696

#### THE CORRELATIONS BETWEEN DYSFUNCTIONAL SLEEP BELIEFS AND ATTITUDES, MALADAPTIVE SLEEP PRACTICES, AND PRE-SLEEP AROUSALS

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**Introduction :** Dysfunctional sleep beliefs and attitudes have been shown to be a contributing factor of insomnia. The dysfunctional thoughts may enhance emotional arousals that further exacerbate sleep, or may lead to maladaptive behavioral practices. Understanding the ways by which dysfunctional cognitions influence sleep may facilitate the assessment and treatment of insomnia. This study aimed to examine the associations of different dysfunctional cognitions with arousals and sleep-related behaviors.

**Methods :** Participants were 97 patients with primary insomnia. The Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS), the Pre-sleep Arousal Scale (PSAS), and a self-constructed rating scale for maladaptive sleep practices were administered. Pearson correlations were conducted between each item of the DBAS and scores of the other scales.

**Results :** Eight DBAS items, most related to consequences of insomnia and control over sleep, were associated with both poor sleep practices and pre-sleep arousals. Six of the eight items (DBAS items 8, 10, 17, 18, 22, 23) were associated with worry-enhancing behaviors, one with alcohol

use (item 4), and one with irregular and extended time in bed (item 2). Three items (21, 25, 29), all related to consequences of insomnia, correlated with pre-sleep arousals but not with behavioral practices. Seven DBAS items correlated with maladaptive sleep behaviors alone, and not with pre-sleep arousals. The associated behaviors included doing sleep-unrelated activities in bed (item 11), irregular and extended time in bed (item 30), coffee drinking (items 11), alcohol use (item 19, 26), and worry-enhancing behaviors (items 11, 12, 16, 28). The rest of the items did not correlate with either pre-sleep arousals or maladaptive sleep practices.

**Conclusion :** Different dysfunctional sleep cognitions may interfere with sleep in different ways. Thoughts regarding the consequences of insomnia tend to increase arousals with or without worrying behaviors. Thoughts regarding control over sleep increase arousals as well as worry-enhancing behaviors. Some other thoughts are associated with different maladaptive sleep practices, but do not generate pre-sleep arousals.

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## 0697

### INFORMATION PROCESSING DURING THE BEGINNING OF SLEEP IN PATIENTS WITH PRIMARY INSOMNIA: AN ERP STUDY

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**Introduction :** Patients with insomnia often report awareness of environmental activities during the prolonged time lying in bed trying to fall asleep. Also, they tend to report longer sleep onset latency compared to polysomnographic sleep onset latency. It was suggested that the sleep difficulties in insomniacs may result from enhanced information processing around sleep onset. The present study examined information processing during the beginning of sleep in insomniacs by the measurement of event-related potentials (ERPs).

**Methods :** Fifteen patients with primary insomniacs and 15 normal controls participated in the study. Oddball paradigm was conducted to elicit ERPs during sleep. Pure tones, 1500 and 1000 Hz alternating as rare (20/100) and standard (80/100) tones across subjects, at 80 db were presented via earphone throughout the night. ERPs during the first 5 minutes of continuous stage 2 sleep were analyzed. Since N350 and P900 were found to be associated with the inhibitory processes that serve to facilitate sleep initiation and maintenance, ANOVAs were conducted to compare mean amplitudes of these two components between insomnia and control groups and between the two types of tones.

**Results :** Significant group x type-of-tone interactions were obtained (Fz:  $F = 8.66, p < .01$ ; Cz:  $F = 7.46, p < .01$ ). The amplitudes of N350 induced by standard tones were smaller in insomniacs comparing to normal controls (Fz:  $t = 2.51, p < .05$ ; Cz:  $t = 1.84, p = .081$ ); the N350 responding to rare tones was not different between the two groups (Fz:  $t = -.31, N.S.$ ; Cz:  $t = .03, N.S.$ ).

**Conclusion :** Insomniacs generate smaller N350 toward standard tones during the beginning part of sleep than good sleepers. Since N350 was suggested to be associated with the inhibition of sensory process, the findings support the hypothesis that insomnia patients have an elevated level of information processing around sleep onset.

**Support (optional):** National Science Council, Taiwan (Grant no. NSC92-2413-H-030-014).

## 0698

### SELF-REPORTED EFFICACY OF 8 MG RAMELTEON IN ELDERLY CHRONIC INSOMNIA PATIENTS WITH SEVERE SLEEP-INITIATION DIFFICULTY

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**Introduction :** This study assessed the sleep-promoting effects of Rozerem™ (ramelteon), a chronohypnotic that acts via MT<sub>1</sub>/MT<sub>2</sub> receptors, in elderly chronic insomnia subjects with severe sleep-initiation difficulty.

**Methods :** In a previous Phase III trial, 5-weeks of nightly administration of ramelteon was evaluated in 829 elderly subjects (>65 years) with chronic primary insomnia (DSM-IV-TR™). This subanalysis included 327 subjects who had a baseline self-reported sleep latency  $\geq 60$  min and who were randomized to receive double-blind ramelteon 8 mg (n=157) or placebo (n=170). Subjects completed daily sleep diaries; change from baseline sleep latency was assessed at Weeks 1, 2, 3, 4, and 5. The potential for rebound insomnia was assessed during a 7-day single-blind run-out period. Least-squares means were calculated for comparison analyses.

**Results :** Compared to placebo, administration of ramelteon 8 mg resulted in statistically significant reductions from baseline sleep latency at Week 1 (-7.5 vs. -23.2 min;  $P=0.002$ ), Week 2 (-15.7 vs. -29.3;  $P=0.006$ ), Week 3 (-19.8 vs. -33.7 min;  $P=0.005$ ), Week 4 (-23.7 vs. -34.2;  $P=0.041$ ), and Week 5 (-17.1 vs. -37.4;  $P<0.001$ ). No rebound insomnia was observed during the run-out period; the ramelteon group sustained a similar reduction in baseline sleep latency compared to placebo group. The most common adverse events were dizziness, dysgeusia, myalgia, and headache; no individual adverse event was reported in >9% of subjects in either group. Most of the adverse events were rated as mild or moderate.

**Conclusion :** In this subanalysis, elderly chronic insomniacs with severe sleep-initiation difficulty experienced statistically significant reductions in sleep latency over 5 weeks of ramelteon 8 mg treatment with a low incidence of adverse events. Rebound insomnia was not observed following discontinuation of ramelteon treatment.

**Support (optional):** This research was supported by Takeda Pharmaceutical Company, Ltd.

## 0700

### EFFECT OF MULTIPLE DOSES OF ESCITALOPRAM ON THE SYSTEMIC EXPOSURE OF RAMELTEON, A SELECTIVE MT<sub>1</sub>/MT<sub>2</sub> RECEPTOR AGONIST, IN HEALTHY ADULTS

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**Introduction :** The chronohypnotic Rozerem™ (ramelteon) is a highly selective MT<sub>1</sub>/MT<sub>2</sub> receptor agonist indicated for insomnia. Since sleep medications are likely to be taken with antidepressants, this study examined the potential interaction of ramelteon and the SSRI escitalopram.

**Methods :** In this open-label study, 48 healthy adults received single dose ramelteon 8 mg (n=24) or escitalopram 10 mg (n=24) on Day 1. Following a 6-day washout period, subjects received the alternate treatment once daily for 6 days. On Day 14, all subjects received combined treatment of escitalopram 10 mg and ramelteon 8 mg. Blood samples were collected post-dose on Days 1 and 14. Least-squares means were calculated for comparison analyses.

**Results :** Compared to ramelteon alone, coadministration with escitalopram increased ramelteon systemic exposure (AUC<sub>0-inf</sub>: 2.03 vs. 2.58 ngH/mL, 90%CI: 102.6%,156.7%; C<sub>max</sub>: 1.54 vs. 2.08 ng/mL, 90%CI:

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101.2%,180.3%). Escitalopram had no effect on systemic exposure of ramelteon's metabolite, M-II (AUC<sub>0-inf</sub>: 144.7 vs. 155.1 ng/h/mL, 90%CI: 99.5,115; C<sub>max</sub>: 54.4 vs. 52.0 ng/mL, 90%CI: 85.6,106.9). Compared to escitalopram alone, coadministration with ramelteon had no effect on systemic exposure of escitalopram (AUC<sub>0-inf</sub>: 288.5 vs. 298.5 ng/h/mL, 90%CI: 93.7%,114.2%; C<sub>max</sub>: 10.37 vs. 9.53 ng/mL, 90%CI: 76.5%,110.5%) or its metabolite, desmethylcitalopram (AUC<sub>0-inf</sub>: 170.5 vs. 167.1 ng/h/mL, 90%CI: 92.2%,104.3%; C<sub>max</sub>: 1.69 vs. 1.49 ng/mL, 90%CI: 77.2%,100.6%). The number of subjects who experienced adverse events was 24, 16, and 15 in the escitalopram, ramelteon, and combined treatment groups, respectively. Most adverse events were considered mild. No clinically meaningful changes in clinical laboratory, physical examination, or electrocardiogram results were observed.

**Conclusion :** The presence of escitalopram resulted in a 27% increase in AUC<sub>0-inf</sub> and 35% increase in C<sub>max</sub> for ramelteon. These increases were not considered clinically relevant due to ramelteon's highly variable inter-subject pharmacokinetic profile and wide safety margin. Ramelteon had no effect on systemic exposure of escitalopram. These results suggest that no dosage adjustments are required when these drugs are taken together.

**Support (optional):** This research was supported by Takeda Pharmaceutical Company, Ltd.

### 0701

#### EFFECT OF RAMELTEON, A SELECTIVE MT1/MT2 RECEPTOR AGONIST, IN A FIRST-NIGHT-EFFECT MODEL OF TRANSIENT INSOMNIA

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**Introduction :** The chronohypnotic Rozerem™ (ramelteon) is a novel, highly selective MT1/MT2 receptor agonist indicated for insomnia treatment. This study evaluated the efficacy of ramelteon in a first-night-effect model of transient insomnia.

**Methods :** In this double-blind, randomized, parallel-group study, 289 healthy adults (mean age, 28.8 years) naïve to the sleep laboratory environment received ramelteon 8 mg, 16 mg, or placebo 30 min before bedtime. Sleep was assessed with overnight polysomnography (PSG) and a next-morning questionnaire. Subjects also completed next-morning residual effect assessments. Least-squares means were calculated for comparison analyses.

**Results :** Compared to placebo, latency to persistent sleep, as measured with PSG, was decreased with ramelteon 8 mg (19.7 vs. 12.2 min) and 16 mg (19.7 vs. 14.8 min), with the 8 mg dose showing statistical significance (P=0.004). Similarly, total sleep time was increased with ramelteon 8 mg (419.7 vs. 436.8 min; P=0.009) and 16 mg (419.7 vs. 433.1 min; P=0.043). Ramelteon was not associated with next-morning residual effects, as measured with Digit Symbol Substitution Test, memory tests for immediate and delayed recall, and visual analog scales for mood and feeling. Adverse event rates were 12.4%, 13.3%, and 6.4% for the placebo, ramelteon 8 mg, and ramelteon 16 mg groups, respectively. No clinically meaningful changes in laboratory value, vital sign, or electrocardiogram results were observed.

**Conclusion :** In this model of transient insomnia, ramelteon promoted sleep with no evidence of next-morning psychomotor or memory effects.

**Support (optional):** This research was supported by Takeda Pharmaceutical Company, Ltd.

### 0702

#### SLEEP-PROMOTING EFFECTS OF RAMELTEON, A SELECTIVE MT1/MT2 RECEPTOR AGONIST, IN OLDER ADULTS WITH CHRONIC INSOMNIA

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**Introduction :** The chronohypnotic Rozerem™ (ramelteon) is a novel, highly selective MT1/MT2 receptor agonist indicated for insomnia. This study determined the efficacy of ramelteon in older adults with chronic insomnia.

**Methods :** In this double-blind, randomized, 3-way crossover study, 100 older adults (mean age, 70.7 years) with primary insomnia (DSM-IV-TR™) for at least 3 months received ramelteon 4 mg, ramelteon 8 mg, and placebo on 2 consecutive nights with 5- to 12-day washout periods between each treatment. Sleep was evaluated by overnight polysomnography (PSG) and by next-morning sleep questionnaire. Subjects also completed next-morning residual effect assessments. Least-squares means were calculated for comparison analyses.

**Results :** Compared with placebo, statistically significant decreases in latency to persistent sleep (LPS), as measured with PSG, were seen with ramelteon 4 mg (38.4 vs. 28.7 min, P<0.001) and ramelteon 8 mg (38.4 vs. 30.8 min, P=0.005). Similarly, PSG total sleep time was increased with 4 mg (350.4 vs. 359.4 min, P=0.036) and ramelteon 8 mg (350.4 vs. 362.0 min, P=0.007). Self-reported sleep latency was decreased with ramelteon 4 mg (48.2 min) and 8 mg (50.9 min) compared to placebo (58.2 min); with the 4 mg group showing statistical significance (P=0.037). Self-reported total sleep time was similar between treatment groups. Ramelteon was not associated with next-morning residual effects, according to the Digit Symbol Substitution Test, memory recall tests, and self-reported alertness or ability to concentrate. The incidence of adverse events was 14%, 7%, and 9% in the 4 mg, 8 mg, and placebo groups, respectively. No clinically important changes in laboratory values, vital signs, or electrocardiogram results were observed.

**Conclusion :** In this study of older adults with chronic insomnia, ramelteon resulted in statistically significant decreases in LPS and increases in total sleep time, as measured with PSG, with no evidence of next-morning residual psychomotor or memory effects.

**Support (optional):** This research was supported by Takeda Pharmaceutical Company, Ltd.

### 0703

#### THE EFFECT OF ESZOPICLONE 3 MG COMPARED WITH PLACEBO IN PATIENTS WITH RHEUMATOID ARTHRITIS AND CO-EXISTING INSOMNIA

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**Introduction :** Patients with rheumatoid arthritis (RA) often report co-existing insomnia. This pilot study was conducted to evaluate the efficacy and safety of eszopiclone 3mg in patients with RA and co-existing insomnia.

**Methods :** This multicenter, double-blind, study enrolled patients aged 25-64 years with ACR-defined RA (receiving treatment for ≥3 months) who reported insomnia (wake time after sleep onset (WASO) ≥45 min & total sleep time (TST) ≤6.5 hr). After placebo run-in, patients were ran-

domized to eszopiclone (n= 77) or placebo (n=76) nightly for 4 weeks, followed by a 2-week run-out. Patient reports of sleep (sleep latency [SL], WASO, TST), Insomnia Severity Index (ISI), daytime function, pain, and RA assessments were evaluated.

**Results :** Eszopiclone (vs placebo) significantly reduced SL ( $p<0.0001$ ), WASO ( $p=0.0002$ ), and nocturnal awakenings ( $p=0.0065$ ), and significantly increased TST ( $p=0.0001$ ), sleep depth ( $p=0.0003$ ), sleep quality ( $p<0.0001$ ), daytime alertness, ability to function, and ability to concentrate (all  $p<0.04$ ). ISI total scores were significantly better ( $p<0.0001$ ) with eszopiclone vs placebo, as were individual items of sleep quality, feeling rested, daytime fatigue, relationship enjoyment, and sleep difficulties (all  $p<0.02$ ). Change scores on the Arthritis Self Efficacy Scale were clinically and statistically significant for overall score ( $p=0.046$ ), pain ( $p=0.0064$ ), and pain and other symptoms ( $p=0.018$ ). No differences in duration or severity of morning stiffness were noted, though subjects' assessment of pain severity was significantly reduced with eszopiclone ( $p=0.023$ ). Number of tender joints was also significantly reduced in the eszopiclone group ( $p=0.035$ ). Subject global assessments were also better with eszopiclone, though not statistically significant ( $p=0.072$ ).

**Conclusion :** In this pilot study of RA and co-existing insomnia, eszopiclone 3mg improved all sleep efficacy measures and daytime function over the treatment period. In addition, patients treated with eszopiclone experienced reductions in some measures of pain and RA disease activity.

**Support (optional):** for this study provided by Sepracor Inc.

## 0704

### THE RELATIONSHIP BETWEEN ESZOPICLONE'S EFFECTS ON SLEEP AND DEPRESSION IN PATIENTS WITH NEW ONSET MAJOR DEPRESSIVE DISORDER (MDD) AND INSOMNIA: SURROGATE MARKER ANALYSIS

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**Introduction :** In a double-blind study, 545 patients who met DSM-IV criteria for new onset MDD and insomnia were randomized to receive either eszopiclone (ESZ) or placebo (PBO) in addition to fluoxetine (FLX). At Weeks 4 and 8, patients receiving FLX+ESZ demonstrated significant improvements in HAM-D17 and in subjective sleep parameters relative to those receiving FLX+PBO. This analysis assesses the extent to which the improvements in depression scores may be explained through improvements in sleep.

**Methods :** Patient-reported sleep parameters were captured weekly, and included sleep latency (SL), wake time after sleep onset (WASO), total sleep time (TST), sleep quality (SQ) and the Insomnia Severity Index (ISI), a validated instrument designed to assess the multiple dimensions of insomnia. HAM-D17 was assessed at Weeks 4 and 8. To assess the percent of the treatment effect (PTE) on the HAM-17 attributable to the effect of ESZ on sleep, two statistical models were used. Model 1 had treatment as the only explanatory variable for NDF improvements (estimated treatment effect beta1). In Model 2, both treatment and the post-dose sleep parameters were explanatory variables (estimated effect beta2). Estimates from both models were used in the following equation:  $PTE=100(\beta_1-\beta_2)/\beta_1$ . (PTEs > 100% were set to 100%).

**Results :** At Week 4, PTEs were ISI (69%), SQ (54%), WASO (49%), SL (28%), and TST (19%). At Week 8, PTEs decreased for all parameters: ISI (44%), SQ (5%), WASO (15%), SL (0%), and TST (0%).

**Conclusion :** In this analysis, more of the treatment effect on depression at Week 4 was explainable through changes in sleep than at Week 8, and the sleep parameters having the greatest effects were the ISI, SQ, and WASO.

**Support (optional):** for this study provided by Sepracor Inc.

## 0705

### ESZOPICLONE TREATMENT DURING MENOPAUSAL TRANSITION: SLEEP EFFECTS, IMPACT ON MENOPAUSAL SYMPTOMS AND MOOD

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**Introduction :** This study evaluated 1) eszopiclone 3mg in the treatment of insomnia associated with menopausal transition, and 2) the impact of treating insomnia on changes in mood, menopause-related symptoms, and quality of life (QOL).

**Methods :** This double-blind, placebo-controlled study included 410 women meeting menopause STRAW criteria stages -2, -1, or 1a (a perimenopausal population), who reported sleep latency (SL)  $\geq 30$  minutes and total sleep time (TST)  $\leq 6$  hours/night. Patients received eszopiclone or placebo nightly for 4 weeks. Sleep endpoints were reported daily. Physician global evaluations of menopause (PGE), menopause-specific QOL questionnaire (MenQOL), Greene Climacteric Scale (GCS), the Montgomery Asberg Depression Rating Scale (MADRS), and the Sheehan Disability Scale (SDS) were collected at baseline and end of treatment.

**Results :** Patients receiving eszopiclone reported significantly greater improvements in SL, sleep maintenance (awakenings and time awake after sleep onset), TST, sleep quality (all  $p$ -values  $<0.0001$  vs placebo), and awakenings due to hot flushes ( $p=0.001$ ). No differences in the number or severity of daytime hot flushes were found. Patients treated with eszopiclone had significantly greater improvements in MADRS scores ( $p<0.03$ ) and PGEs ( $p<0.0001$ ) compared with patients treated with placebo; total GCS score (baseline scores were 14.8 in each group; change scores were -2.18 for placebo and -3.57 for eszopiclone) and the vasomotor and psychological subscales ( $p<0.05$  vs placebo); vasomotor and physical domains of the MenQOL ( $p<0.05$ ); and family life/home disability domain using the SDS ( $p<0.05$ ). The most common adverse event was unpleasant taste in those receiving eszopiclone (18.1% vs 0.5%). Other adverse events (ie, headache, pain) were similar in the two groups.

**Conclusion :** In this study, eszopiclone produced significant improvements in sleep and positively affected mood, QOL, and menopause-related symptoms in peri-menopausal women.

**Support (optional):** for this study provided by Sepracor Inc.

## 0706

### EFFICACY AND SAFETY OF DOXEPIN 1, 3, AND 6MG IN ELDERLY ADULTS WITH PRIMARY INSOMNIA

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**Introduction :** Previous research demonstrated that the sedative-hypnotic properties of doxepin are retained at low doses. This randomized, placebo-controlled cross-over study evaluated the efficacy and safety of doxepin 1, 3, and 6mg in elderly adults with insomnia.

**Methods :** Randomized patients (n=76) reported  $\geq 3$  months of DSM-IV

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primary insomnia, and had  $\geq 60$  minutes of wake-time-during-sleep (WTDS), 240-410 minutes of total-sleep-time (TST), and  $\geq 10$  minutes of latency-to-persistent-sleep (LPS), confirmed by polysomnography (PSG). Patients received a random sequence of doxepin 1mg, 3mg, 6mg and placebo. Treatment periods consisted of two PSG assessment nights with a 5- or 12-day drug-free interval. Primary endpoint was WTDS; secondary endpoints included wake-after-sleep-onset (WASO), sleep efficiency (SE), LPS, and subjective sleep assessment.

**Results :** All three doxepin groups had dose-related significant improvements in WTDS ( $p < 0.0001$ ), WASO ( $p < 0.0001$ ), and overall SE ( $p < 0.0001$ ) versus placebo. In the 6mg dose-group, SE was significantly increased during all thirds-of-the-night ( $p < 0.005$ ). SE was significantly increased in the 3mg dose-group during the 2nd and final third-of-the-night ( $p < 0.005$ ). LPS was numerically reduced; subjective sleep latency was significantly reduced ( $p = 0.017$ ) in the doxepin 6mg dose-group. Other subjective efficacy results were consistent with PSG results. There were no significant group differences in next-day residual sedation and sleep architecture was generally preserved. There were no adverse events occurring at an incidence  $> 2\%$  in the doxepin dose-groups; incidence of all events was comparable to placebo.

**Conclusion :** In elderly adults with insomnia, doxepin 1, 3, and 6mg was well-tolerated and produced dose-related significant improvement in PSG-defined and patient-reported sleep maintenance and duration endpoints that persisted through the final third-of-the-night with no reported anti-cholinergic effects or significant hangover/next-day residual effects. Effects on sleep onset were also observed at the highest doses. These data suggest that doxepin 1, 3, and 6mg may improve sleep maintenance, sleep duration, and sleep onset in elderly adults with primary insomnia.

**Support (optional):** This study was fully funded and supported by Somaxon Pharmaceuticals, Inc., San Diego, CA.

### 0707

#### ANALYSIS OF INDIVIDUAL ITEMS OF THE HAMILTON DEPRESSION SCALE IN A STUDY OF ESZOPICLONE/FLUOXETINE CO-THERAPY

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**Introduction :** Results of a co-morbid insomnia and depression study of eszopiclone and fluoxetine demonstrated that initiation of co-therapy produced greater improvements in sleep and depression compared with fluoxetine monotherapy. To determine if the changes in the HAMD17 were due only to sleep, the individual HAMD17 items were evaluated.

**Methods :** Patients ( $n = 545$ ) met DSM-IV criteria for MDD and insomnia, with screening HAMD17 (excluding the sleep items)  $> 14$ . All patients received fluoxetine QAM for 10 weeks, and randomly received double-blind eszopiclone 3mg or placebo QHS for 8 weeks, followed by a single-blind placebo 2-week run-out to evaluate discontinuation effects. HAMD17 was completed at Weeks 4, 8, and 10. Individual items were compared with ANCOVA using an LOCF approach.

**Results :** Mean baseline HAMD17 scores were 22 for each group. At Week 4, differences were noted between treatment groups in the total score, and the individual items of insight, and insomnia early, middle, and late ( $p < 0.02$  vs monotherapy), with a trend for guilt ( $p = 0.07$ ). At Week 8, significant changes were noted in the total score ( $p = 0.0005$ ), the three insomnia items ( $p < 0.001$ ), guilt, work/activities, and anxiety psychic ( $p < 0.05$ ), and a trend in retardation ( $p = 0.07$ ). At Week 10, the total score,

guilt, insomnia early, middle, and late, work/activities, retardation, agitation, anxiety psychic, general somatic symptoms, and hypochondriasis demonstrated significant improvements ( $p < 0.05$  vs monotherapy) despite discontinuation of eszopiclone.

**Conclusion :** Eszopiclone/fluoxetine co-therapy resulted in significant improvements in the insomnia items of the HAMD17. In addition, several items related to core depressive symptoms were also improved with co-therapy compared with monotherapy, and these differences increased over time. Co-therapy led to an enhancement of the antidepressant response that was not sleep-specific but evident across the range of depression symptoms, and affected an increasing number of aspects of depression over time for at least 10 weeks.

**Support (optional):** for this study provided by Sepracor, Inc.

### 0708

#### DOES INSOMNIA KILL THE ELDERLY?

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**Introduction :** This study examined whether chronic insomnia and use of prescribed sedatives were independent predictors of mortality in a population-based sample of older adults. This extended previous research to older adults and further refined the clinical definition of insomnia.

**Methods :** A total of 2087 participants in the Australian Longitudinal Study of Ageing provided sleep and health information in a baseline interview conducted in 1992 with participants ranging in age from 65 to 103 years ( $M = 78.2$ ,  $SD = 6.7$ ). A series of Cox proportional hazards regression analyses was conducted to examine whether chronic insomnia and use of prescribed sedatives independently predicted mortality at a 13 year follow-up, when adjusting for the effects of demographic (e.g., age, sex, educational level) and health risk variables (e.g., stroke, chronic bronchitis, hypertension, smoking status, etc.). Ten different definitions of chronic insomnia, based on combinations of questions about frequency of sleeping difficulties, typical SOL and WASO, and daytime symptoms, ranged from mild insomnia (including 28.1% of the sample) to severe insomnia (only 2.8% of sample). Each definition was included in a separate Cox regression analysis.

**Results :** When controlling only for age at entry to the study, chronic insomnia was not associated with an increased risk of death for any of the ten insomnia definitions. The mean hazard ratio (HR) was 1.03 and ranged from  $HR = 0.95$  (95% confidence interval (CI) = 0.713-1.263,  $p = 0.72$ ) to  $HR = 1.14$  (CI = 0.998-1.295,  $p = 0.054$ ). Furthermore, when the other demographic and health risk variables were controlled, insomnia still did not predict mortality; the mean HR was 1.10 and ranged from  $HR = 0.96$  (CI = 0.649-1.412,  $p = 0.83$ ) to  $HR = 1.17$  (CI = 0.905-1.502,  $p = 0.24$ ). Conversely, the use of prescribed sedatives was associated with an increased risk of death, when controlling for insomnia and the other covariates. This relationship was evident for all ten insomnia models examined with an overall mean HR of 1.12, ranging from  $HR = 1.12$  (CI = 1.047-1.197,  $p = 0.001$ ) to  $HR = 1.13$  (CI = 1.053-1.203,  $p < 0.001$ ).

**Conclusion :** Insomnia in the elderly was not associated with an increased risk of death at 13 year follow-up when controlling only for the effect of age at baseline, nor when the effects of other demographic and health covariates were also taken into account. However, when controlling for covariates, greater use of prescribed sedatives did increase the risk of death by an average of 12%.

**Support (optional):**

## 0709

**BRIEF BEHAVIORAL TREATMENT FOR INSOMNIA IN OLDER ADULTS: PRELIMINARY EFFICACY FINDINGS***Buysse DJ, Germain A, Franzen P, Moul D, Reynolds CF, Monk T*Clinical Neuroscience Research Center, University of Pittsburgh  
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**Introduction :** The efficacy of manualized behavioral treatments for insomnia has been well-demonstrated, but their use in usual care settings has been limited. Dissemination may be limited by the length and complexity of available treatments, the need for relatively highly-trained therapists, and the use of highly-screened subjects in previous studies. We report here on preliminary findings from a Brief Behavioral Treatment for Insomnia (BBTI) in older adults with insomnia.

**Methods :** Subjects included 25 older adults (20F, 5M; mean age 70 years) who met DSM-IV criteria for insomnia disorder, recruited from medical practices and the community. Only subjects with untreated current psychiatric disorders or sleep apnea were excluded; medications, treated depression, and other medical disorders were permitted. After baseline clinical, sleep diary, and polysomnographic assessments, subjects were randomly assigned to BBTI (n=13) or information control (IC) (n=12) consisting of printed pamphlets. BBTI included a single session focusing on four main techniques: limiting time in bed, regularizing wake-up time, not going to bed until sleepy, and not staying in bed unless asleep. Subjects received a booster session after two weeks, and outcome was assessed four weeks after start of treatment.

**Results :** Subjects had an average of six comorbid medical conditions, with no difference between groups. At the end of four weeks, the BBTI group had significantly better outcomes on the Pittsburgh Sleep Quality Index (PSQI) and on sleep diary measures of sleep latency, wakefulness after sleep onset, and sleep efficiency ( $p < .05$  for each). Using a categorical definition of PSQI score  $< 5$  or sleep efficiency  $> 85\%$  post-treatment, 9 of 12 BBTI subjects but no IC subjects were considered remitted.

**Conclusion :** These preliminary findings suggest that a very brief form of behavioral insomnia treatment has short-term efficacy for older adults with comorbid illnesses. Further evaluation of a larger sample and other outcome measures is warranted.

**Support (optional):** Supported by AG20677, MH24652, RR00056, AG00972, MH71944, MH37869

## 0710

**FATIGUE AND SLEEPINESS IN PATIENTS WITH PRIMARY INSOMNIA COMPARED TO GOOD SLEEPERS***Combs A, Perlis ML, Matteson S, Pigeon WR*

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**Introduction :** The diagnostic distinction between fatigue and excessive daytime sleepiness (EDS) is thought to differentiate between DIMS and DOES, with fatigue being a primary daytime sequelae of insomnia. Little empirical work, however, has been conducted to assess whether sleepiness is a feature of insomnia.

**Methods :** Archival data from 70 subjects with Primary Insomnia (PIs) and 18 Good Sleepers (GSs) were used for the present analysis. All data were collected at intake and included the Pittsburgh Sleep Quality Index (PSQI) and the Insomnia Severity Index (ISI). In addition the two groups were compared on the Epworth Sleepiness Scale (ESS) and the Multidimensional Fatigue Inventory (MFI) using t-tests, contingency analyses, and Cohen's d for effect size determination.

**Results :** Groups did not differ with respect to age, gender or BMI. Subjects with PI reported a higher level of EDS ( $p = .02$ ; Effect Size: .65) and fatigue on all MFI dimensions (physical fatigue, reduced activity,

reduced motivation, mental fatigue; all  $p < .01$ ; Mean Effect Size: 1.27), except for general fatigue ( $p = .18$ ). In the PI group, 31% had ESS  $> 10$  compared to only 7% in the GS group (Fishers Exact  $p = .03$ ) and 20% (vs 0% of GS) had at least one fatigue scale  $> 1$  standard deviation above healthy norms.

**Conclusion :** PIs have higher levels of fatigue and EDS and they are more likely to be pathologically sleepy or fatigued than GSs. Fatigue and EDS are not, however, associated with disease severity. While not surprising in relation to global sleep disturbance, the absence of a relationship between fatigue and insomnia severity is puzzling. At the group level, effect sizes for fatigue are twice that of sleepiness. At the individual level, the findings highlight that sleepiness is a daytime sequelae for some patients with insomnia, which warrants monitoring during treatment, especially when utilizing sleep restriction that can exacerbate sleepiness.

**Support (optional):** NIH Support NS049789 (Dr. Pigeon)

## 0711

**DOES INSOMNIA CAUSE HYPERTENSION OR CARDIOVASCULAR DISEASE?***Phillips BA, Mannino DM*

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**Introduction :** We prospectively investigated odds ratios (OR's) for development hypertension or cardiovascular disease by endorsement of sleep complaints.

**Methods :** The Atherosclerosis Risk in Communities (ARIC) Study is a prospective, population-based study of cardiovascular disease. Our study sample was 7281 ARIC participants without hypertension and 9710 ARIC participants without cardiovascular disease at baseline. We applied multivariate regression analysis to predict the OR's of development of hypertension or cardiovascular disease over 6 years of follow-up by endorsement of symptoms of difficulty falling asleep (DFA), waking up repeatedly (SCD), awakening tired and fatigued (NRS), combinations of these symptoms, or use of hypnotics. We defined insomnia as a complaint of difficulty falling asleep or difficulty staying asleep plus nonrestorative sleep. We defined hypertension as physician-diagnosed hypertension, use of antihypertensives, or BP  $> 160$  mmHg systolic or  $> 95$  mmHg diastolic. We defined heart disease as physician-diagnosed myocardial infarction (MI) or probable MI, or EKG findings of MI. We controlled for age, sex, alcohol intake, income, smoking, diabetes, heart disease, menopausal status, depression, educational level, Body Mass Index, respiratory symptoms, pulmonary function, and hypnotic use.

**Results :** Neither insomnia as we defined it nor any single insomnia symptom predicted an increased risk for development of hypertension or cardiovascular disease at 6 years of follow-up. Endorsement of all three sleep complaints predicted increased risk of cardiovascular disease (OR 1.44, 1.05-1.98), but not hypertension. Hypnotic use was not associated with increased risk of development of hypertension or cardiovascular disease at follow-up.

**Conclusion :** 1. The definition of insomnia affects its impact. 2. A combination of 3 sleep complaints (DFA, SCD, NRS) predicted increased risk of cardiovascular disease but not hypertension. 3. A single sleep complaint (DFA or SCD) with daytime impact (NRS) did not predict increased cardiovascular or hypertensive risk. 4. Hypnotic use did not increase cardiovascular or hypertensive risk.

**Support (optional):**

0712

DAYTIME SYMPTOMS IN PRIMARY INSOMNIA: PROSPECTIVE ANALYSIS USING ECOLOGICAL MOMENTARY ASSESSMENT

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**Introduction :** Recent diagnostic criteria for insomnia disorders emphasize daytime symptoms and impairments. However, daytime symptoms and their diurnal patterns have not been studied as carefully as sleep symptoms. We used ecological momentary assessment techniques to examine daytime symptoms in insomnia patients, and to compare those symptoms to standard clinical and sleep diary measures.

**Methods :** Participants included 47 volunteers with primary insomnia (PI) (22M, 25F, mean age 35.9) and 18 good sleeper controls (GSC) (3M, 15F, mean age 27.2). None had current psychiatric or significant medical disorders. Following diagnostic and baseline symptom evaluations, participants completed visual analog scale symptom ratings on hand-held computers (HHC) four times per day for one week. Functional principal components analysis (FPCA) was conducted to identify factors among the 19 items in PI subjects, accounting for time of day, multiple days, and individual subjects. FPC scores derived from PI alone were then used to contrast PI and GSC, and to compare daytime symptom ratings with baseline clinical and sleep diary ratings.

**Results :** Subjects completed 95% of HHC ratings. FPCA of daytime symptoms in PI subjects identified four FPCs accounting for 67% of total variance, termed alert cognition, negative mood, positive mood, and fatigue/sleepiness. PI had significantly worse scores than GSC on all four FPCs ( $p<.001$ ), showing different mean levels and diurnal patterns. Among PI subjects the FPCs correlated modestly with retrospective symptom ratings of depression, anxiety, and hyperarousal (13/40 correlations significant with  $\rho>.3$ ,  $p<.05$ ). Fatigue/sleepiness and positive mood FPCs correlated with diary sleep efficiency; negative mood and alert cognition correlated with sleep latency ( $\rho$  0.30-0.40,  $p<.05$ ).

**Conclusion :** Prospective daytime symptom ratings showed robust differences between PI and GSC subjects, not only in mean level, but also in diurnal pattern. These symptom patterns may yield insights into the pathophysiology of insomnia and provide more informative outcome measures.

**Support (optional):** Supported by MH24652, AG20677, AG00972, RR00056

0713

PREDICTOR OF OUTCOME TO GROUP CBTI IN A SLEEP CLINIC SETTING

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**Introduction :** The efficacy of cognitive behavioral therapy for primary insomnia (CBTI) has been demonstrated in randomized controlled trials. Less is known about predictors of outcome when CBTI is delivered in an outpatient sleep clinic. This study explores the impact of four predictors of response to group CBTI: medication use, depression symptoms, chronotype, and age.

**Methods :** Participants were 214 men and 293 women (age 48.9 14.4 years) who sought group CBTI, provided sleep diary at baseline, and attended at least two group sessions. At baseline participants also completed the Morningness Evenness Scale, and the Beck Depression

Inventory (BDI). Modified intent-to-treat analyses were performed (last observations carried forward).

**Results :** Baseline differences were present for each of the four predictors. Insomniacs taking medications prescribed for sleep (62.4%) spent more time in bed (TIB,  $p<0.05$ ) and more time asleep (TST,  $p<0.05$ ) than those not taking medications for sleep. Patients with elevations in depression (BDI>13) had longer sleep onset ( $p<0.01$ ) and lower sleep efficiency ( $p<0.05$ ). Compared with larks, owls had more TIB ( $p<0.05$ ) and more TST ( $p<0.05$ ). Older age was also associated with less TIB ( $p<0.05$ ), less TST ( $p<0.0001$ ), more wakefulness (WASO  $p<0.001$ ) and lower sleep efficiency ( $p<0.001$ ). A series of repeated measures ANOVAs conducted on sleep efficiency and WASO separately revealed no significant interaction between time and any of the four predictors. Significant predictor group effect was present only for age ( $p<0.01$ , split at 48.8 yrs). A series of regression analyses revealed that at the end of treatment, after controlling for baseline values, only older age and depression were associated with lower sleep efficiencies ( $p<0.05$ ) and more WASO ( $p<0.05$ ).

**Conclusion :** Whereas elevation in depression scores and taking medications prescribed for sleep were common, neither hindered response to treatment. Nevertheless, more depressed individuals and older people remained more symptomatic than their counterparts at the end of treatment.

**Support (optional):**

0714

DAYTIME COMPLAINTS AND INSOMNIA IN THE GENERAL POPULATION

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**Introduction :** Although daytime impairment stands among the criteria necessary to diagnose insomnia, studies examining the prevalence and nature of daytime complaints in insomnia are sparse. The aim of the present study was to explore areas of daytime impairment associated with insomnia in a large population-based sample.

**Methods :** Participants were involved in a longitudinal study of the natural course of insomnia. A random sample of 2000 individuals completed an initial telephone survey and a sub sample completed four follow-up postal evaluations conducted over a two-year period. Of the 765 participants who returned their questionnaires at the two-year follow-up, 29 were excluded because they reported another sleep disorder. The final sample included 736 adults (mean age = 46.2 years, 61.6% women) which were categorized into three groups using an algorithm based on DSM-IV and ICD-10 criteria for insomnia: good sleepers (GS;  $n=425$ ), individuals with insomnia symptoms (INS-Sx;  $n=229$ ) and individuals with insomnia syndrome (INS-Dx;  $n=82$ ). Daytime impairment was assessed by the Multidimensional Fatigue Inventory (MFI), the SF-12 Health Survey, and six additional items from the Insomnia Severity Index (5-point Likert scale) about the impact of insomnia on quality of life, fatigue, mood, memory/concentration, leisure/social activities, and relationships.

**Results :** For each of the MFI and the SF-12 subscales, the INS-Dx group reported more severe impairment compared to the INS-Sx group, which in turn reported more impairment than GS, except for the Reduced Activity scale of the MFI for which INS-Sx and GS did not differ. The proportion of individuals reporting at least moderate impairment for at least one domain of daytime functioning was greater in the INS-Dx group (85.4%) compared to the INS-Sx group (69.9%), in which it was higher than in the GS group (54.1%). The most frequent complaints were about mood disturbances, cognitive problems, and fatigue; complaints regarding interference with social/leisure activities and relationships were less frequent. Impaired quality of life was more frequently reported by INS-



Dx (50.0%) and INS-Sx (34.7%) compared to GS (6.7%).

**Conclusion :** Results confirm that daytime complaints regarding fatigue, cognitive functions and mood are frequent among insomnia sufferers. However, such complaints may not be specific to insomnia as they also appear relatively frequently in good sleepers.

**Support (optional):** Research supported by the Canadian Institutes of Health Research (MT42504)

## 0715

### PHARMACOLOGICAL CHARACTERISATION OF AGONISTS AT $\alpha_1$ -CONTAINING GABAA RECEPTORS: FUNCTIONAL SELECTIVITY FOR EXTRASYNAPTIC RECEPTORS IS DEPENDENT ON ABSENCE OF $\alpha_2$

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**Introduction :** Studies using  $\alpha_1$ - or  $\alpha_2$ -containing GABAA receptors expressed in cell systems suggest that the pharmacological profiles of a series of GABAA receptor agonists are highly dependent on the  $\alpha_1$  subunit but not on the  $\alpha_2$ , or the  $\alpha_3$  subunits. The present study was conducted to clarify the role of the  $\alpha_1$  subunit in determining the potency and efficacy of a series of GABAA agonists.

**Methods :** Using two-electrode voltage clamp technique, a series of full agonists, partial agonists and antagonists were characterised at  $\alpha_1$ ,  $\alpha_2$ ,  $\alpha_3$ , and  $\alpha_4$ -containing GABAA receptors expressed in *Xenopus* oocytes.

**Results :** Little or no difference in both potency and efficacy was seen, when the compounds were tested at  $\alpha_1$ ,  $\alpha_2$ , or  $\alpha_3$ -expressing oocytes, whereas a significant reduction in both potency and relative efficacy was observed, when compared to  $\alpha_4$ -containing receptors as previously described by this lab. These data clearly confirm that the presence of the  $\alpha_1$  subunit in heterotrimeric receptors is a strong determinant of the increased pharmacological activity of agonists. The very similar agonist pharmacology of  $\alpha_1$ ,  $\alpha_2$ , and  $\alpha_3$ -containing receptors, which is significantly different from  $\alpha_4$ -containing receptors, show that whereas the presence of a  $\alpha_1$  subunit reduces the response to agonist stimulation of the  $\alpha_1$ -receptor complex, the  $\alpha_2$  subunit does not affect this in any way.

**Conclusion :** Taken together, these data are well in line with the idea that  $\alpha_1$  may contribute to the pharmacological action of exogenously applied agonists and may explain why systemically active compounds like gaboxadol and muscimol in vivo appear to act as selective extrasynaptic GABAA agonists (SEGA).

**Support (optional):** This research was supported by H. Lundbeck A/S.

## 0716

### RELATIVE EFFECTIVENESS OF COGNITIVE BEHAVIOR THERAPY FOR PRIMARY AND COMORBID INSOMNIA: PRELIMINARY REPORT

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**Introduction :** Cognitive-Behavioral Therapy (CBT) has proven efficacious for primary insomnia (PI) and for insomnia comorbid with some sleep-disruptive medical or psychiatric conditions. The current study was conducted to determine if PI and comorbid insomnia (CMI) patients derive similar benefits from CBT.

**Methods :** Outpatients with insomnia were screened via structured interviews, a sleep diary, and polysomnography to select those who met Research Diagnostic Criteria for insomnia disorder and had an average

diary total wake time (TWT) > 60 minutes. Eight-one enrollees completed pre-therapy sleep diaries (2 weeks), actigraphy (1 week), the Insomnia Symptom Questionnaire (ISQ), and Pittsburgh Sleep Quality Index (PSQI). They then were stratified into PI and CMI groups, and comparable numbers of each subtype were randomized to CBT (total n = 41) or a generic sleep hygiene (SH; total n = 40) therapy. Following 4 biweekly therapy sessions, all pre-therapy measures were repeated. Outcome measures included ISQ and PSQI scores, and total sleep time (TST), TWT, and sleep efficiency (SE) from diary and actigraphy. Linear mixed models were used to compare pre-post change among the 4 treatment x patient subgroups (CBT/PI, CBT/CMI, SH/PI, SH/CMI).

**Results :** All 4 subgroups showed significant PSQI improvements. All except the SH/PI subgroup reported significant ISQ improvements. Only SH/CMI patients showed no improvements in their diary TWT and SE. CBT produced significantly greater reductions in diary TWT among CMI patients than did SH. CBT also led to significantly greater reductions on actigraphic TWT than did SH among PI patients. Moreover, CBT produced significantly greater improvements in the PI group than in the CMI cohort across all three actigraphic measures.

**Conclusion :** CBT is more effective than SH for PI patients. PI and CMI patients show similar subjective CBT benefits, but PI sufferers may have relatively better objective CBT responses.

**Support (optional):** Department of Veterans Affairs Health Services Research and Development Grant # IIR 00-091

## 0717

### LACK OF GENERALISATION BETWEEN THE GABAA RECEPTOR AGONIST, GABOXADOL, AND ALLOSTERIC MODULATORS OF THE BENZODIAZEPINE BINDING SITE IN THE RAT DRUG DISCRIMINATION PROCEDURE

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**Introduction :** Gaboxadol (4,5,6,7-tetrahydroisoxazolo(5,4-c)pyridin-3-ol;) is a selective extrasynaptic GABAA agonist (SEGA) that has demonstrated improvements in both sleep onset and maintenance measures in patients with insomnia. The binding sites for GABA and GABAA receptor agonists are located differently from the binding site for benzodiazepines and benzodiazepine site agonists. Furthermore, gaboxadol interacts primarily with extrasynaptically located  $\alpha_1$ -containing GABAA receptors while benzodiazepines interactions with the synaptically located  $\alpha_1$ ,  $\alpha_2$  containing receptors. The aim of the present study was to address if this in vitro functional selectivity was reflected in vivo. We therefore used the drug discrimination paradigm, which previously has been able to detect receptor selectivities.

**Methods :** A two-lever liquid reinforced operant discrimination procedure was conducted. Two groups of rats were trained to discriminate gaboxadol (5.5 mg/kg i.p.) and zolpidem (0.7 mg/kg i.p.), respectively, from vehicle.

**Results :** Substitution tests showed that animals trained with gaboxadol did not recognize diazepam (0.75-1.5 mg/kg), zolpidem (0.4-0.7 mg/kg), zopiclone (2.5 mg/kg), zaleplon (1.0-1.5 mg/kg) or indiplon (0.31). In contrast, all benzodiazepine site agonists, but not gaboxadol (4.5-5.5 mg/kg), substituted for zolpidem in zolpidem-trained animals. In agreement with these data, the competitive benzodiazepine site antagonist flumazenil (10 mg/kg s.c.) prevented recognition of zolpidem in zolpidem-trained animals, but not of gaboxadol in gaboxadol-trained animals. For both groups of trained animals, tests for pharmacological interaction were carried out and showed that no synergistic interaction was present when gaboxadol and zolpidem were administered simultaneously.

**Conclusion :** Previous studies have found that gaboxadol and benzodi-

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azepines are interacting with different receptor populations and the present study confirms that in vivo functional consequences of this receptor selectivity exist in the form of differential behavioural responses in rats.

**Support (optional):** This study was supported by H. Lundbeck A/S.

### 0718

#### SPECTRAL PROFILES DURING NREM SLEEP FOR GABOXADOL AND ZOLPIDEM IN THE TREATMENT OF PATIENTS WITH PRIMARY INSOMNIA

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**Introduction :** Gaboxadol, a selective extrasynaptic GABAA agonist (SEGA), has produced acute improvements in sleep onset and maintenance measures in primary insomniacs. The objective of this analysis was to evaluate the spectral profiles of differing doses of gaboxadol and zolpidem with placebo in patients with Primary Insomnia, aged 18-65 years.

**Methods :** The spectral analysis was performed on data collected from two separate randomised, double-blind, crossover, polysomnograph (PSG) studies designed to compare the dose response characteristics of gaboxadol (GBX) to placebo (PBO) after 2 nights of treatment. Study 1 (GBX10mg, GBX20mg and zolpidem 10mg as an active reference drug) included 38 patients; study 2 (GBX5mg, GBX15mg) included 23 patients. Both studies were conducted at the same site. Spectral power after 2 treatment nights was evaluated during NREM sleep relative to baseline.

**Results :** Compared to placebo and in contrast to zolpidem, gaboxadol clearly and significantly increased spectral power in the lower frequency bands (slow wave activity [0.5-3.5Hz]; theta activity [4-7.5Hz]) in a dose-dependent manner within study (all  $p < 0.05$ ; GBX5mg not significant). Zolpidem significantly reduced theta activity ( $p < 0.05$ ). Alpha activity [8-12.5Hz] showed a borderline increase with GBX20 ( $p = 0.051$ ) and a reduction with zolpidem ( $p < 0.05$ ) in study 1. However, gaboxadol showed no effect on alpha activity in study 2. Power in the spindle frequency range [11.5-15Hz] was either not affected by gaboxadol (study 1) or reduced ( $p < 0.05$  for GBX15;  $p = 0.072$  for GBX5 in study 2). Zolpidem showed a non-significant increase in power within the spindle frequency range. There were no consistent effects on beta activity [13-30Hz] with any drug.

**Conclusion :** Gaboxadol clearly and consistently increases SWA and theta activity in an apparently dose-dependent manner. In contrast, zolpidem did not affect SWA and reduced theta activity. These observed differences in EEG power spectra are likely consequences of the differential mechanisms of action for gaboxadol and zolpidem.

**Support (optional):** This research was supported by H. Lundbeck A/S.

### 0719

#### GABOXADOL IMPROVES SLEEP ONSET AND MAINTENANCE AND ENHANCES LOW FREQUENCY COMPONENTS OF NREM SLEEP EEG IN A MODEL OF TRANSIENT INSOMNIA

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**Introduction :** Gaboxadol is a selective extrasynaptic GABAA agonist (SEGA) that has demonstrated improvements in both sleep onset and maintenance measures in patients with insomnia. The present study was designed to evaluate the efficacy of gaboxadol in a model of transient insomnia.

**Methods :** 109 healthy subjects (18-58 y) completed a randomized, double-blind, crossover study in a 4h phase advance model of transient insomnia. Sleep was assessed using polysomnographic (PSG) and self-reported measures following gaboxadol 5, 10 and 15mg (GBX5, GBX10, GBX15) versus placebo (PBO). Zolpidem 10 mg (ZOL10) was used as an active reference.

**Results :** Efficacy analysis was based on 82 per protocol subjects. Wakefulness after sleep onset (WASO) and total sleep time (TST) were significantly improved in all active treatments compared with PBO (WASO-all  $p < 0.05$ ; TST-all  $p < 0.001$ ), with no apparent dose response for gaboxadol. Latency to persistent sleep was significantly shorter than PBO for GBX10 and GBX15 (both  $p < 0.05$ ) and ZOL10 ( $p < 0.001$ ), but not with GBX5. GBX10 and GBX15 increased ( $p < 0.05$ ) slow-wave (SWA; 0.75-4.5 Hz) and theta (4.75-7.75 Hz) activity in NREM sleep EEG in a dose dependent manner. In contrast, zolpidem did not enhance SWA ( $p = 0.8$ ) and reduced theta activity ( $p < 0.0004$ ). Self-reported (s) measures of sleep maintenance showed improvements in both sWASO ( $p < 0.05$ ) and sTST ( $p < 0.05$ ) for all active treatments compared with PBO. Self-reported sleep onset was significantly reduced following all active treatments except GBX5. Neither drug treatment was associated with residual effects at 30 minutes or 3 hours after lights-on. The majority of adverse events were mild or moderate with no SAEs.

**Conclusion :** Gaboxadol 10mg and 15mg improved sleep on PSG and self-reported efficacy measures in this model of transient insomnia. In contrast to zolpidem, gaboxadol enhances low frequency components of sleep EEG. There were no next day residual effects and the treatments were well tolerated.

**Support (optional):** H. Lundbeck A/S, Copenhagen, Denmark.

### 0720

#### GABOXADOL IMPROVES SLEEP MAINTENANCE AND, IN CONTRAST TO ZOLPIDEM, ENHANCES SLOW WAVE SLEEP IN ADULT PATIENTS WITH PRIMARY INSOMNIA

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**Introduction :** Gaboxadol is a selective extrasynaptic GABAA agonist (SEGA) in development for the treatment of insomnia. This study was designed to evaluate its acute efficacy and safety in the treatment of primary insomnia (PI).

**Methods :** This was a randomised, double-blind, 4-way crossover, polysomnograph (PSG) study comparing gaboxadol 10mg (GBX10) and 20mg (GBX20) to placebo (PBO) in 40 adult patients with PI. Zolpidem 10mg (ZOL10) was used as an active reference drug. Treatment was administered on two consecutive nights in each treatment session. Patients were enrolled after confirmation of DSM-IV criteria for PI and specific PSG inclusion criteria for sleep onset and maintenance. Next day residual effects were evaluated 2h after lights on.

**Results :** The efficacy analysis ( $n = 38$ ) was based on data from the second night of each treatment session. Both gaboxadol doses and ZOL10 significantly reduced wakefulness after sleep onset (all  $p < 0.05$ , log transformed). GBX20 and ZOL10 increased total sleep time (all  $p < 0.05$ ). Both doses of gaboxadol but not zolpidem, reduced the number of night awakenings ( $p < 0.001$ ). Neither drug reduced sleep onset latency. Gaboxadol dose dependently enhanced slow wave sleep (SWS;  $p < 0.01$  for GBX10 and GBX20). Neither drug treatment was associated with next day residual effects the morning after treatment. The majority of adverse events (AEs) were mild or moderate with no SAEs. Compared to placebo, the incidence and severity of AEs were higher with GBX20.

**Conclusion :** Acute administration of gaboxadol improves sleep maintenance and enhances SWS in a dose dependent manner in adult patients

with PI. Effects on sleep induction need further evaluation considering the lack of effect of the reference drug zolpidem. Gaboxadol 10mg and 20mg doses were not associated with next day residual effects. Gaboxadol was generally well tolerated although gaboxadol showed a dose dependent increase in incidence and severity of AEs.

**Support (optional):** This research was supported by H. Lundbeck A/S.

## 0721

### LONG-LASTING HEAT REDISTRIBUTION FROM THE CORE TO THE SHELL IS RELATED TO LONG SLEEP LATENCY IN VASOSPASTIC SYNDROME

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**Introduction :** Sleep Onset Insomnia frequently occurs in psychiatric disorders but also in the general population. Primary Vasospastic Syndrome is a functional disorder of vascular regulation in otherwise healthy subjects (main symptom: cold hands and feet). In an ongoing controlled laboratory study we are investigating whether women who report both symptoms (VS) have prolonged sleep latency due to stronger distal vasoconstriction before bedtime compared with controls (C).

**Methods :** After an adaptation night, 13 healthy women (N=6 VS, 7 C; age: 20-34yr; luteal phase) entered the laboratory 2h before usual bedtime and lay down 30min before lights off. Skin temperatures (ST, 8 probes) and core body temperature (CBT, rectal) were recorded in 20-s intervals. The EEG was recorded continuously, sleep stages were visually scored according to Rechtschaffen and Kales, and results analyzed by ANOVA (significance set at  $p=0.05$ ).

**Results :** CBT began at the same level, but the CBT minimum induced by lying down was reached later in VS than C (VS:118±14min; C:55±7min). Distal ST was lower before lights off in VS than C - this difference disappeared 2.5h after lights off. VS exhibited a longer sleep latency to stage1 (VS:35±6min; C:17±3min) and stage2 (VS:48±6min; C:27±4min). No differences were found in the sleep stage analyses. Preliminary EEG spectral analysis revealed no differences in the delta range but VS had lower power density in the beta range of the parietal derivation (Pz) during nonREM sleep.

**Conclusion :** VS showed colder distal ST before lights off and longer heat redistribution thereafter than C, which could be the cause of their longer SL. However, sleep per se in VS was not largely disturbed.

**Support (optional):** Research supported by the Swiss National Science Foundation to K.K.(SNF# 33100a0-102182/1)

## 0722

### NON-PHARMACOLOGICAL TREATMENT OF INSOMNIA: A GROUP THERAPY MODEL WITH A COGNITIVE-BEHAVIORAL AND PSYCHODRAMATIC APPROACH

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**Introduction :** The non-pharmacological approach to insomnia, has been used frequently, however considering that the individual cognitive-behavioral treatment is very expensive, we propose a group therapy model with psychodramatic approach.

**Methods :** This study examined the treatment of chronic insomnia in eight patients submitted to group therapy using a cognitive-behavioral approach associated with psychodramatic techniques. Duration of treatment was one session per week for eight weeks. Patients were evaluated before, during and after treatment using sleep diary, the Beck depression

inventory, the SF-36, the State-Trait Anxiety Inventory, and a questionnaire on anxiety prior to sleep.

**Results :** The analysis of sleep diary, before and after treatment, showed improved of sleep efficiency (61.2±21.9 and 77.3±17.2) and sleep latency (77.3± 83.9 and 30.0±23.2). We can observe improve of sleep satisfaction, a reduced daytime symptoms and reduction or withdrawal of benzodiazepine use by patients taking this drug. After the treatment the SF-36 showed a improved of functional capacity (65.0±13.6 and 74.0±18.6), vitality (40.6 ±29.4 and 50±28.5) and social aspects (49.7± 26.4 and 73.4± 20.5).

**Conclusion :** The findings show the effectiveness of the treatment proposed here with the greatest advantages being in the greater ease of assimilation of the cognitive component by using psychodrama and in the attention paid to individual experiences, not only in relation to insomnia but also to the entire psycho-social context involved in each case. It is believed that greater use of a brief exposition and discussion of particular themes in relation to the ways patients find to cope with stressful situations, instead of diverting focus away from insomnia, will assist in understanding and possibly eliminating factors that may be predisposing, triggering and/or perpetuating insomnia. Furthermore there are advantages inherent to most group situations such as the enriching exchange of experiences and greater accessibility due to the lower cost in comparison with individual therapies.

**Support (optional):** AFIP, FAPESP/CEPID

## 0723

### EPIDEMIOLOGY OF INSOMNIA AND MEDICAL DISORDERS

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**Introduction :** Insomnia prevalence rates range from 9-17%. Few studies have analyzed the relationship between insomnia and medical illnesses. Fewer still have controlled for depression, anxiety and organic sleep disorders, all of which could be confounds. This study compared the prevalence of (a) insomnia in people with and without specific medical disorders and (b) medical disorders in people with and without insomnia. Analyses controlled for depression, anxiety, and organic sleep disorders.

**Methods :** A random digit dialing protocol was used to recruit 772 participants. Participants were excluded if they had significant symptoms or a diagnosis of any sleep disorder except insomnia, leaving a final sample of 538. Participants completed a 14-day sleep diary, health survey, depression and anxiety measures.

**Results :** People with the following medical disorders were more likely to have insomnia than people without these disorders: hypertension (OR = 2.24), breathing problems (OR = 3.26), chronic pain (OR = 2.27), and gastrointestinal problems (OR = 2.57), and urinary problems (OR = 2.25), all  $p$ 's < .05. People with insomnia were more likely than people without insomnia to have the following medical disorders: hypertension (OR = 3.08), heart disease (OR = 2.88), cancer (OR = 3.47), breathing problems (OR = 4.52), neurological disease (OR = 4.50), urinary problems (OR = 3.56), chronic pain (OR = 3.43), and gastrointestinal problems (OR = 3.96). Prevalence rates will be presented at APSS.

**Conclusion :** These results demonstrate significant relationships between insomnia and medical disorders. It is impossible to determine a causal relationship with this data, but these results indicate more research is needed examining the role of insomnia in instigating or exacerbating these disorders, and determining if insomnia is treatable when co-morbid with these disorders.

## Category K—Sleep Disorders-Insomnia

**Support (optional):**

### 0724

#### SLEEP PERCEPTION INDEX IN INSOMNIACS AND SLEEP APNEA/HYPOPNEA SYNDROME PATIENTS

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**Introduction :** An intriguing fact in relation to insomnia patient is their misperception of sleep. Systematic use of polysomnography (PSG) recording followed by sleep perception reports from patients is crucial in this respect. We recorded estimated number of minutes slept and minutes asleep as recorded by PSG expressed this ratio as a sleep perception index (SPI), and we observed this ratio in insomnia and obstructive sleep apnea syndrome patients.

**Methods :** We studied 209 patients, 124 men and 85 women, who were being treated for insomnia or probable sleep respiratory disorder. All patients were submitted to PSG and then administered a questionnaire on their perception of the recording night's sleep. We defined the sleep perception index (SPI) as the ratio between total sleep time as perceived by the patient and total sleep time as recorded by PSG. We compared SPIs for three groups of patients: an insomniac group, a sleep respiratory disorder (SRD) group, and insomniac/SRD group.

**Results :** The insomniac group comprised 47 individuals, average age 46.7 ( $\pm 14.7$ ), the SRD group contained 78 patients with an average age of 49.1 ( $\pm 13.7$ ) and the insomniac/SRD group comprised 84 individuals with an average of age of 49.0 ( $\pm 13.7$ ). The SPI distribution was: insomniac group 0.82 ( $\pm 0.37$ ), SRD group 0.97 ( $\pm 0.26$ ) and insomniac/SRD group 0.87 ( $\pm 0.28$ ). On comparing groups, we found that insomnia patients' SPIs were significantly lower than those of the SRD patients' group.

**Conclusion :** We found that insomniacs showed less perception of sleep than SRD patients. Similarly to obstructive apnea/hypopnea sleep syndrome, we may take insomnia as a symptom that is also part of a set of other clinical manifestations, constituting a syndrome. SPI is a parameter of severity and a marker of the evolution and effectiveness of the therapeutic modality used in treating insomnia.

**Support (optional):** AFIP, FAPESP/CEPID

### 0725

#### NATURAL COURSE OF INSOMNIA IN THE PENN STATE COHORT

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**Introduction :** Although many studies have assessed the prevalence of insomnia, there are few studies on the longitudinal course of insomnia, with most of them conducted in clinical populations for a short period (1-3 years). The purpose of this study was to assess the natural course of insomnia in a large random sample of the general public.

**Methods :** 1,741 individuals were interviewed at baseline to assess for the presence of sleep disorders. A total of 1395 or 80.1% were interviewed at about 7.5 years later (10.3 years for men, and 4.5 years for women). Insomnia was defined by a complaint of insomnia of at least one year. Difficulty sleeping was defined as difficulty falling asleep, difficulty staying asleep, early final awakening or unrefreshing sleep. No sleep difficulty was defined as the absence of either of these two categories.

**Results :** The incidence of insomnia was 7.8% and of sleeping difficulties

13.3%. Of those with insomnia at baseline, 38.6% continued to have insomnia, 29.7% changed from insomnia to sleeping difficulties and 31.7% no longer had sleep difficulty. Nearly half of those with sleeping difficulty at baseline, 48.6%, had no sleep difficulty at follow-up, but 35.4% continued to have sleep difficulty, and 16.0% progressed to insomnia. Of those with no sleep difficulty at baseline, 6.2% developed new insomnia, and 15.5% reported having sleep difficulty.

**Conclusion :** The results show that insomnia, particularly its more severe form, tends to be chronic. However, a large number of patients with insomnia or sleep difficulty were asymptomatic at follow-up, whereas we observed a large number of incident cases within a 5-10 year period. Identifying risk factors associated with the chronicity of insomnia and its incidence, as well as beneficial factors associated with its remission/recovery may lead to new preventative and therapeutic strategies for insomnia in primary care.

**Support (optional):** NIH R01: HL 40916 HL 51931

### 0726

#### PREDISPOSING FACTORS IN INSOMNIA

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**Introduction :** It has been hypothesized that stress acts as a precipitating factor in the development of insomnia. Not everyone experiences insomnia during times of stress, likely reflecting individual differences in underlying predisposition. A number of factors are thought to predispose an individual to develop insomnia but little empirical evidence exists. The purpose of this study was to take a first step at identifying predisposing factors in insomnia.

**Methods :** Fifty-three undergraduate students without current insomnia were recruited from introductory psychology courses. Subjects completed a battery of questionnaires. The Ford Insomnia Response to Stress Test (FIRST) was utilized as a measure of individual tendency towards difficulty sleeping when under stress. To measure putative predisposing factors subjects completed measures of depression (Center for Epidemiological Studies Depression Scale), trait anxiety (State-Trait Anxiety Inventory), tendency to worry (Penn State Worry Questionnaire), tendency towards cognitive arousal (Arousal Predisposition Scale), and use of coping strategies (Brief COPE). Correlations between FIRST scores and other variables were computed.

**Results :** FIRST scores were significantly related to depression ( $r=.44$ ), worry ( $r=.49$ ), trait anxiety ( $r=.43$ ), and cognitive arousal ( $r=.52$ ). FIRST scores were weakly related to use of action-oriented ( $r=-.31$ ) and emotion-focused ( $r=.30$ ) coping strategies.

**Conclusion :** A number of variables are known to be elevated in individuals with insomnia, such as anxiety, worry and depression. The current correlational analyses demonstrate that these factors may also act as predisposing factors for insomnia in healthy sleepers. Identifying those at risk for experiencing insomnia when under stress can help direct efforts to prevent the development of chronic insomnia in at-risk individuals. Simple interventions such as coping skills training may be effective preventive measure.

**Support (optional):**

0727

**CHARACTERISTICS OF EXCESSIVE DAYTIME SLEEPINESS IN PATIENTS WITH INSOMNIA**Grieser EA,<sup>1</sup> Taylor DJ,<sup>1</sup> Meixner R,<sup>2</sup> Dolan DC,<sup>1</sup> Rosenthal LD<sup>3</sup>

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**Introduction :** The assessment of Excessive Daytime Sleepiness (EDS) among patients with insomnia (PWI) has yielded mixed results. Few studies have examined within-group differences among PWI. The present study explored the prevalence of EDS in PWI and compared excessively sleepy PWI to alert PWI on subjective sleep parameters and diagnoses.

**Methods :** Consecutive PWI (N=131; 83 female) aged 19-84, were interviewed by a board certified sleep disorders specialist, and completed the Symptoms Checklist-90-Revised (SCL-90-R), Epworth Sleepiness Scale (ESS), and Sleep-Wake Activity Inventory (SWAI). Patients were defined as "Alert" if their ESS and SWAI scores both showed no evidence of EDS [ESS ≤10, SWAI ≥50], "Sleepy" if their ESS and SWAI both showed EDS [ESS >10, SWAI <50] and "Mixed" if their ESS and SWAI scores disagreed. **Methods:** Consecutive PWI (N=131; 83 female) aged 19-84, were interviewed by a board certified sleep disorders specialist, and completed the Symptoms Checklist-90-Revised (SCL-90-R), Epworth Sleepiness Scale (ESS), and Sleep-Wake Activity Inventory (SWAI). Patients were defined as "Alert" if their ESS and SWAI scores both showed no evidence of EDS [ESS ≤10, SWAI ≥50], "Sleepy" if their ESS and SWAI both showed EDS [ESS >10, SWAI <50] and "Mixed" if their ESS and SWAI scores disagreed.

**Results :** More PWI were Alert (76%) than Sleepy (13%) or Mixed (11%),  $\chi^2(2) = 85.47, p < 0.001$ . MANOVA comparing the three groups on five subjectively-reported sleep variables (average time in bed, number of nighttime awakenings, number of daytime naps, and average sleep onset latency) was significant, Wilkes'  $\Lambda = .784, F(8,146) = 2.364, p < 0.05, \eta^2 = .115$ . Post-hoc testing revealed Alert PWI took fewer naps than Mixed ( $P = 0.017$ ) and Sleepy ( $P < .001$ ) groups. No differences were seen between groups on SCL-90 global severity or subtests, or insomnia diagnoses (primary, secondary to medical, or secondary to psychiatric).

**Conclusion :** This study showed a high rate of agreement between the ESS and SWAI regarding levels of sleepiness/alertness in PWI. Consistent with other literature, we found a large number of PWI are alert during the day. Efforts to determine how these PWI were different from sleepy or mixed only showed that alert PWI took fewer daytime naps, which would be expected if they were not sleepy.

**Support (optional):**

0728

**COMBINING MINDFULNESS MEDITATION WITH CBT FOR INSOMNIA: A PRELIMINARY REPORT**Ong J,<sup>1</sup> Manber R,<sup>1</sup> Shapiro S<sup>2</sup>

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**Introduction :** Mindfulness-based interventions have been used in the treatment of a variety of disorders involving arousal (e.g., chronic pain, anxiety disorders). Although these interventions have been hypothesized to improve symptoms of insomnia, no study has examined its impact on both arousal and sleep. The aim of this study was to investigate the feasibility and the treatment effects of combining a mindfulness-based intervention with cognitive-behavior therapy for insomnia (CBT-I).

**Methods :** Fifteen participants (60% female, age = 19-53) recruited from

both university and community settings participated in 6 weekly, 90-minute group sessions. All participants met criteria for psychophysiological insomnia and were screened for other sleep disorders, mental disorders, and medical conditions. Treatment sessions included mindfulness meditations in addition to the standard CBT-I components (e.g., sleep restriction, stimulus control) with particular emphasis given to the application of these meditations for reducing cognitive arousal associated with sleep disturbances. Participants maintained weekly sleep diaries along with the Pre-Sleep Arousal Scale (PSAS). In addition, self-report measures of dysfunctional sleep-related cognitions and sleep effort were completed at baseline and the end of treatment.

**Results :** Results examining baseline to end-of-treatment effects from sleep diary data revealed significant improvements on sleep efficiency ( $p < .001$ ) and reductions in total wake time in bed ( $p < .001$ ) but no significant difference on total sleep time. In addition, significant reductions from baseline to the end of treatment were found on the PSAS ( $p < .05$ ) as well as measures of sleep effort ( $p < .01$ ) and dysfunctional sleep-related cognitions ( $p < .01$ ).

**Conclusion :** These preliminary results support the feasibility of integrating mindfulness with standard CBT-I. Moreover, the evidence suggests that the combined intervention improves sleep efficiency and decreases unwanted wake time, state measures of arousal scores, and dysfunctional sleep-related cognitions.

**Support (optional):**

0729

**SLEEP RESTRICTION MECHANISMS IN INSOMNIA: PRELIMINARY OUTCOMES ON SLEEP EFFICIENCY STABILISATION**Vallieres A,<sup>1,2</sup> Gardani M,<sup>3</sup> Espie CA<sup>3</sup>

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**Introduction :** Sleep restriction therapy is recommended as a non-pharmacological treatment for insomnia. However, there is little attention concerning its efficacy when used alone and the underlying biological and psychological treatment mechanisms. Therefore, the main goal of this study was to evaluate the efficacy of sleep restriction alone and to explore its mechanisms in insomnia treatment.

**Methods :** The sample included 5 participants (4 women, mean age of 41.1 years, range 22-62 years) meeting diagnostic criteria for primary insomnia. A multiple baseline across subjects design was used. Participants completed daily sleep diaries. Sleep was considered stabilised when sleep efficiency (SE) was higher than 85% with a reduced SE night-to-night variability relative to baseline. Sleep restriction therapy consisted of curtailing the time spent in bed to the actual amount of time estimated to sleep. A first sleep window was determined using the average of total sleep time reported by participants in their two last baseline weeks using sleep diaries. The sleep window was increased for 15 minutes, contingent upon reaching a SE of 85% or more. Frequently asked questions (FAQ) and answers were prepared in advance to ensure treatment integrity.

**Results :** Each participant presents an increase in SE and a decrease in total wake time. Four seem to sustain these improvements after treatment. An average of 5 treatment sessions over 7 to 8 weeks duration were delivered. The first sleep window varied from 5 hours to 6h40 duration. The number of days to get a stabilised sleep pattern was different for each successfully treated participant (6, 9, 16, and 25 days). One participant did not seem to present sleep stabilisation, although an increase in SE was observed. The most FAQ reported were related to daily tiredness, difficul-

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ties of going out of bed, and change in mood.

**Conclusion :** These preliminary results suggest that sleep restriction is effective when used alone. In addition, it indicates that the treatment response and duration may differ among patients. Attention to common FAQ may aid effective home implementation. Further analyses are needed to evaluate biological and psychological mechanisms related to sleep improvements.

**Support (optional):** Research supported by CIHR

### 0730

#### MMPI CHARACTERISTICS OF INSOMNIA IN A GENERAL POPULATION SAMPLE

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**Introduction :** Previous studies using the Minnesota Multiphasic Personality Inventory (MMPI), have reported a high degree of psychopathology with a preponderance of depression and anxiety in clinical insomnia samples. The goal of this study was to assess for degree and pattern of psychopathology using MMPI in insomnia in a random sample of the general public.

**Methods :** 1,741 men and women of a wide-age range (Penn State Cohort) were evaluated in the sleep laboratory. 1,300 completed the MMPI. The sample was not different from the overall sample of 1,741 in terms of age, gender, body mass index (BMI), or sleep complaint. Insomnia was defined by a complaint of insomnia of at least one year duration. No sleep difficulty was defined in the absence of any sleep complaints.

**Results :** The prevalence of insomnia was 7.3%. Insomniacs vs. those with no sleep difficulty had significantly higher scores in all 8 clinical MMPI scales ( $P < 0.05$ ). However, their scores were significantly lower compared to clinical samples ( $P < 0.05$ ). Sixty-two percent of the subjects had one or more MMPI scales elevated to a pathological degree. The scales most elevated were, in order, hypochondriasis, depression, and hysteria with hypochondriasis being the most frequently elevated scale.

**Conclusion :** In the general population, chronic insomnia is associated with emotional stress but to a significantly lesser degree than in a clinical setting. Furthermore, the predominant pattern is preoccupation with physical symptoms and depression, different from the depression-anxiety pattern reported in clinical samples. We conclude that in general samples, insomnia is associated with psychological distress, physical disorders/complaints, and physiological vulnerability. It appears that in a primary care setting, a large number of insomniacs can be effectively treated with behavioral interventions, including education and sleep hygiene, and appropriate use of medication rather than a rigorous psychiatric intervention.

**Support (optional):** R01 Grants: HL 40916 HL 51931

### 0731

#### DAYTIME FUNCTIONING AND INSOMNIA COMPLAINTS IN PEOPLE WITH POOR SLEEP

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**Introduction :** To explore the relationship between daytime functioning

and poor sleep, we extracted sleep equivalent groups from non-complaining poor sleepers (NPS) and people with insomnia (PWI).

**Methods :** A random digit dialing survey collected for 14 days of sleep diaries and measures of health and daytime functioning from 772 participants. The sleep diaries provided the following measures: total sleep time (TST), sleep onset latency (SOL), wake time after sleep onset (WASO), number of nighttime awakenings, sleep efficiency, time spent napping and perceived sleep quality. Participants also completed the following daytime functioning measures: the Insomnia Impact Scale (IIS), Epworth Sleepiness Scale, Fatigue Severity Scale, State-Trait Anxiety Inventory (STAI), and Beck Depression Inventory (BDI). Participants who exhibited mean SOL or WASO > 31 minutes were classified as poor sleepers.

**Results :** Criteria that matched subjects on sleep variables were empirically derived, so that daytime functioning could be compared in equivalent groups of PWI and NPS. Individuals who reported cancer were excluded from the analysis because the groups had a significant difference in cancer rates. The results revealed that PWI (N=16) and NCI (N=21) had significant differences in BDI [ $t(35)=2.04$ ,  $p=.049$ ],  $M=13.5$ ,  $SD=8.6$  for PWI and  $M=8.3$ ,  $SD=6.2$  for NCI; STAI [ $t(35)=3.59$ ,  $p=.001$ ],  $M=45.0$ ,  $SD=10.5$  for PWI and  $M=34.4$ ,  $SD=7.5$  for NCI; and IIS [ $t(35) 2.24$ ,  $p=.031$ ],  $M=116.6$ ,  $SD=27.4$  for PWI and  $M=98.0$ ,  $SD=23.1$  for NCI.

**Conclusion :** Two groups were formed based on presence or absence of an insomnia complaint from a sample of people who satisfy the sleep detriment criteria for insomnia. Groups were then matched based on sleep using empirically derived criteria. People who complained of insomnia reported more impaired daytime functioning. Possible explanatory factors to account for differential daytime impairment are lower sensitivity to sleep detriments among NPS or lesser propensity to emotional difficulties among NPS.

**Support (optional):** This Research was supported by the National Institute on Aging grants AG12136 and AG14738.

### 0732

#### HYPNOTIC DISCONTINUATION IN CHRONIC INSOMNIA: IMPACT OF READINESS TO CHANGE, SELF-EFFICACY AND PSYCHOLOGICAL DISTRESS

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**Introduction :** About a third of chronic hypnotic users are unable to discontinue their sleep medication when they undergo medically supervised, systematic hypnotic taper. Prochaska and DiClemente's transtheoretical model of change (TTM) proposes that readiness to change can account for success or failure in changing health-related behaviors. This study aimed to compare readiness to change, self-efficacy, insomnia severity and distress symptoms among individuals reaching different outcomes after a hypnotic taper intervention.

**Methods :** Secondary data from a hypnotic withdrawal study involving 53 chronic users of hypnotics (34 women; mean age = 55,  $SD = 11$ ) were used. Mean duration of hypnotic use was 14 years ( $SD = 10$ ). Most participants ( $n = 44$ ) used benzodiazepine hypnotics and 17 used zopiclone. The taper intervention comprised two medical visits and eight weekly phone follow-ups aimed at guiding participants to comply with their individualized medication withdrawal schedule. In addition, half of the participants received a self-help format of cognitive-behavior therapy for insomnia.

**Results :** Results showed no distinctions on baseline measures between individuals who were drug-free and those who were still using sleep medication at the end of the taper intervention. Differences in symptoms (insomnia and withdrawal), psychological distress (depression, anxiety, and perceived mental health) and self-efficacy appeared mid-way through

the eight-week withdrawal and were accentuated after the intervention. Contrary to expectations, there were no differences between drug-free and non drug-free participants on both readiness to change and stages of change.

**Conclusion :** Present findings did not support the TTM's basic assumptions concerning stages of change and readiness to change. It is unclear whether this was due to psychometric flaws of the instruments or to the fact that the TTM's assumptions may not apply to the context of hypnotic withdrawal. Still, decrease of symptoms and distress, and increase of perceived health and self-efficacy during withdrawal were related to successful hypnotic discontinuation.

**Support (optional):**

### 0733

#### TWO DOUBLE-BLIND, PLACEBO-CONTROLLED, 6-MONTH TRIALS OF ESZOPICLONE FOR INSOMNIA: POOLED ANALYSIS BY RACE/ETHNICITY

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**Introduction :** To corroborate and extend the findings from a 6-month insomnia trial of eszopiclone, a second randomized, double-blind, 6-month study was conducted. Reported are endpoints analyzed by race/ethnicity from pooled data from these two large studies.

**Methods :** Patients (1195 Caucasian, 236 African American, 150 Hispanic) were adults (21-64 years) with DSM-IV primary insomnia with total sleep time (TST) <6.5 hours and/or sleep latency (SL)>30 minutes who received nightly placebo (n=462) or eszopiclone 3mg (n=1119 for ITT) for 6 months. Sleep and daytime function data were captured weekly with an interactive voice response system.

**Results :** At baseline, for Caucasians, African Americans and Hispanics, respectively, median SL was 60, 88, 76 min; WASO was 41, 60, 38 min; and TST was 306, 290, 300. Baseline measures of daytime function were similar across races. Change from baseline calculations for Caucasians, African American and Hispanics, respectively, vs placebo for SL were -26.7 vs -14.7; -39.5 vs -20.1; -36.5 vs -16.5; (p<0.02 for all); for WASO were -17.6 vs -4.3 (p<0.0001); -28.5 vs -12.0 (p<0.002); -20.0 vs -11.7 (p=0.178); for TST were 72.8 vs 30.0 (p<0.0001); 85.6 vs 45.5 (p<0.002); 86 vs 42.9 (p=0.1789). For measures of daytime function, the magnitude of differences in change from baseline scores between eszopiclone and placebo for Caucasians, African Americans, and Hispanics varied with Hispanics having the smallest differences between eszopiclone and placebo (daytime alertness 0.86, 0.87, 0.57; ability to function 0.67, 1.14, 0.35; sense of well-being 0.67, 0.99, 0.21, respectively).

**Conclusion :** In these studies, for all parameters, response to eszopiclone was significantly better than response to placebo for Caucasians and African Americans; these differences, while similar in magnitude in Hispanics did not reach statistical significance, most likely due to small numbers.

**Support (optional):** for this study provided by Sepracor Inc.

### 0734

#### ESZOPICLONE CO-ADMINISTERED WITH FLUOXETINE FOR INSOMNIA CO-EXISTING WITH MAJOR DEPRESSIVE DISORDER (MDD): ANALYSIS BY SEVERITY OF INSOMNIA

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**Introduction :** Initiation of eszopiclone/fluoxetine co-therapy produced greater improvements in sleep and depression compared with fluoxetine monotherapy in an insomnia and depression study. This analysis was conducted to determine whether baseline sleep severity influenced response.

**Methods :** Patients (n=545) met DSM-IV criteria for MDD and insomnia, received fluoxetine QAMx10 weeks, and randomly received double-blind eszopiclone 3mg or placebo QHSx8 weeks. Post hoc, patients were stratified by baseline insomnia severity (moderate=ISI score<18; severe=ISI score≥18) and changes in sleep and depression were evaluated.

**Results :** ISI scores, patient-reported sleep latency (SL), wake after sleep onset (WASO), and total sleep times (TST), and Hamilton Depression-17 (HAMD17) scores were worse in the severe subgroup (ISI=21.7; SL=147 minutes, WASO=85 minutes, TST=231 min; HAMD=23) compared with the moderate subgroup (ISI=14.4; SL=90 minutes, WASO=49 minutes, TST=285 minutes; HAMD=21). Week 8 HAMD scores were 7.3±5.7 vs 9.5±6.8 (p=0.06) for co-therapy vs monotherapy, respectively, in the moderate subgroup, and 9.4±7.0 vs 11.0±7.2 (p=0.03) for the severe subgroup. Depression response rates were similar between co-therapy subgroups (~58%), but remission rates were slightly higher in the moderate co-therapy group (50% vs 39%). Within subgroups, differences in remission rates between co-therapy and monotherapy were 12% for moderate (p=0.2) and 9% for severe (p=0.06). At Week 1 and at Week 8, statistically significant treatment differences were observed in both the severe and moderate subgroups for SL, WASO, and TST. Treatment differences were of similar magnitudes in both subgroups [eg, differences in the medians (ESZ minus PBO) at Week 1 were -36, -15, and 62 minutes for SL, WASO, and TST, respectively, versus -25, -19, and 88 minutes for the moderate subgroup.]

**Conclusion :** Eszopiclone/fluoxetine co-therapy resulted in significant improvements in sleep and depression measures in patients with moderate and severe insomnia relative to monotherapy.

**Support (optional):** for this study provided by Sepracor Inc.

### 0735

#### EFFICACY AND SAFETY OF SIX-MONTHS OF NIGHTLY ESZOPICLONE IN PATIENTS WITH PRIMARY INSOMNIA: A SECOND LONG TERM PLACEBO-CONTROLLED STUDY

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**Introduction :** Eszopiclone is a non-benzodiazepine insomnia treatment. The results of a second long-term study are presented.

**Methods :** In this randomized, double-blind study, adults (21-64 years) with DSM-IV primary insomnia sleeping ≤6.5 hours and/or having sleep latency ≥30 minutes received nightly placebo (n=280) or eszopiclone 3 mg (n=550) for 6-months followed by a two-week placebo run-out period. Patient-reported endpoints collected with IVRS included sleep [latency, total sleep time (TST), wake time after sleep onset (WASO), sleep quality] and daytime function (alertness, daytime sleepiness, ability to function/concentrate, physical well-being). Withdrawal effects (rebound insomnia and CNS adverse events) were carefully and prospectively assessed after 180 nights of continuous nightly therapy using a 2-week single-blind placebo-substitution run-out phase.

**Results :** At all monthly assessment points, eszopiclone 3 mg significantly improved sleep latency, WASO, TST, and sleep quality versus placebo

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( $p < 0.0001$ ). Patients taking eszopiclone had average changes from baseline vs placebo of -38.3 vs -21.7; -22.03 vs -7.5; and 79.38 vs 41.6 minutes for latency, WASO, and TST, respectively. Eszopiclone 3 mg also significantly improved all monthly daytime parameters ( $p < 0.05$ ) at all assessment points versus placebo. Pharmacologic tolerance was not observed. No rebound insomnia was noted as the medians for all sleep parameters remained below baseline during the entire 2-week run-out period. No withdrawal CNS effects were noted (as assessed by spontaneously-reported adverse events during the discontinuation phase and the Benzodiazepine Withdrawal Questionnaire). Eszopiclone was well tolerated; the most common adverse event was unpleasant taste.

**Conclusion :** Results from this study are consistent with a previous 6-month study and indicate that the nightly use of eszopiclone produced consistent and sustained improvements across all sleep and daytime function parameters, and was well tolerated with no pharmacologic tolerance, withdrawal CNS adverse events or rebound insomnia.

**Support (optional):** for this study provided by Sepracor Inc., Marlborough, MA

### 0736

#### SWS TIME AND DELTA POWER IN PATIENTS WITH PRIMARY INSOMNIA

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**Introduction :** Some 30 years ago it was proposed that insomnia might be a disease of Slow Wave Sleep (SWS) deficiency. Yet, few studies have been published which show that patients with insomnia exhibit reduced amounts of SWS or Delta activity (under normal sleep or sleep deprivation conditions). The present study addresses this proposition.

**Methods :** A sample of 11 Primary Insomnia subjects (PIs) and 11 Good Sleeper (GS) controls were assessed over 4 consecutive PSG nights. Inclusion was based on clinical interview, two weeks of sleep diary and by sleep continuity variables from PSG. EEG's were recorded from 6 sites (bi-lateral derivations for frontal, central and parietal sites). Studies were scored according to R&K criteria and subjected to power spectral analysis with values reported as relative power. For individual sites and time points t-tests were conducted and all variances were shown to be equal by Levines Test. Effect sizes given are for Cohen's  $d$ .

**Results :** Groups did not differ with respect to age, BMI, or gender. Although all differences for R&K scored SWS were in the expected direction (PIs had less SWS effect sizes ranged from .23 to .92), there were no significant differences in either S3 or S4 total minutes or stage percent between PIs and GSs on any night. In contrast, delta power was significantly lower in PIs for virtually all sites and time points (total effect size for all nights and sites of 1.45). Frontal delta power was significantly lower and consistently so across all 4 nights (with effect sizes ranging from 1.07 to 1.73). For both central and parietal power there was a trend to increase across successive nights in the laboratory such that by Night 3, the groups exhibited more comparable levels of Delta activity.

**Conclusion :** While having similar levels of R&K-scored SWS, the patients with insomnia in this sample tend to exhibit reduced Delta power. This observation supports the contention that SWS (and arguably sleep homeostasis) is altered in PIs and suggests that PSA is required to identify this alteration. Given both that Delta activity tends to be maximal within the frontal region and that the effect observed was largest within this region, it suggests that primary insomnia may indeed be a "disease of slow wave sleep". The trend toward increased Delta activity across nights, while requiring further exploration, suggests that sleeping in the laboratory (and the attendant imposed sleep wake schedule) may exert a positive effect on sleep wake regulation in insomnia.

**Support (optional):** NIH support from NS049789-02 (Dr. Pigeon) and MH59392-02 (Dr. Perlis)

### 0737

#### EVALUATION OF PATIENT SATISFACTION: REGIMEN OF ESZOPICLONE SLEEP SATISFACTION TRIAL (RESST)

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**Introduction :** Eszopiclone has been extensively studied in well-controlled trials of primary and secondary insomnia, but patient satisfaction with eszopiclone has not been evaluated. The Regimen of Eszopiclone Sleep Satisfaction Trial (RESST) was conducted to assess patient satisfaction with eszopiclone in a more naturalistic setting in a broad patient population.

**Methods :** This open-label, Phase 4 study included 2606 patients 18-85 years who reported nighttime sleep disturbance (difficulty falling asleep, staying asleep, non-refreshing sleep) that interfered with daytime functioning or caused daytime distress at least 3 times/week. At baseline, patients completed questionnaires to capture sleep symptom importance index, the types of treatments used historically to treat these symptoms, and satisfaction with their current sleep aid regarding 8 specific insomnia symptoms. All patients received 10 tablets of commercially available eszopiclone and returned to the office 2 weeks later, at which time they completed questionnaires to evaluate satisfaction with eszopiclone.

**Results :** Most patients were female (68%) and Caucasian (91%), 84% reported insomnia duration  $> 1$  year, and 56% had secondary insomnia. Most reported both sleep onset and sleep maintenance symptoms (73%), 50% reported TST  $< 4$  hours/night, and 43% used a prescription sleep aid nightly. The items that were most important to patients were "feel rested and refreshed in the morning" (96%) and "feel alert and think clearly" (96%). After treatment with eszopiclone, approximately 2-2.5 times as many patients were extremely or very satisfied with eszopiclone for treatment of all 8 insomnia symptoms as were satisfied with their previous sleep aid. The majority of patients reported better overall satisfaction, better satisfaction considering the benefits and side effects, and that eszopiclone worked better in the treatment of the 8 specific insomnia symptoms.

**Conclusion :** In this large effectiveness study, more than twice as many patients were satisfied with eszopiclone as were satisfied with their previous sleep aid.

**Support (optional):** for this study provided by Sepracor Inc.

### 0738

#### DOSE-RESPONSE ANALYSIS OF THE EFFECT OF INDIPLON ON SUBJECTIVE MEASURES OF SLEEP MAINTENANCE

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**Introduction :** Indiplon, a new generation GABAA potentiator, is in development for the treatment of insomnia using two formulations, immediate release (IR) capsules and modified release (MR) tablets, the latter targets patients with more severe sleep maintenance difficulties. This dose-response analysis was conducted to describe the effect of indiplon on subjective total sleep time (sTST) and wake after sleep onset (sWASO).

**Methods :** Data were pooled from Phase 2 crossover and Phase 3 paral-



lel studies, with daily data measured up to 3 months. Doses ranged from 5 to 40 mg. Dose response was modeled using nonlinear mixed effects models.

**Results :** A total of 2492 (sTST) or 2187 (sWASO) patients were included, with ages ranging from 18 to 85 years. Baseline values were dependent on gender (women having less severe insomnia), study population (MR studies having more severe insomnia), and age (elderly having more severe insomnia). Indiplon increased sTST with a maximum response of 386 min, and 50% of the value observed at a dose (ED50) of 7.8 mg. Indiplon decreased sWASO with a nadir of 56 min (IR), and ED50 of 16.6 mg. For both endpoints, drug response was larger in women, smaller in elderly patients, and greater with the MR tablets relative to the IR capsules (11.4% for sTST and 39.6% for sWASO). The efficacy of indiplon was observed following the first dose and was sustained over time.

**Conclusion :** The magnitude of response on sTST and sWASO is dependent on dose, disease severity, gender, age, and formulation. Increased benefit is observed between doses of 10 mg to 15 mg. The MR tablet provides increased benefit over a similar dose of the IR capsule, particularly in patients with more severe sleep maintenance difficulties. Elderly differ in disease severity and response and a lower dose may be required.

**Support (optional):** Research funded by Pfizer Inc and Neurocrine Biosciences.

### 0739

#### HEART RATE VARIABILITY IN PATIENTS WITH PRIMARY INSOMNIA COMPARED TO GOOD SLEEPER CONTROLS

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**Introduction :** Hyperarousal is considered to be a main feature of, and etiological factor for, insomnia. It has been assessed along three dimensions (cognitive, cortical and physiologic). In order to further explore one measure of physiologic arousal, we evaluate Heart Rate Variability (HRV) in a sample of 11 Primary Insomnia subjects (PIs) and 9 Good Sleeper (GS) controls.

**Methods :** All subjects were categorized based on clinical interview and data drawn from two weeks of sleep diaries and by PSG-based data drawn from 4 consecutive sleep studies. Data for the current study were gathered from Night 2 of PSG. HR was derived from Type-II ECG lead placement and recorded at 256 hz. ECG segments were identified from the first 5 minutes of the first, second and last NREM periods beginning with stage 2 sleep and from the first 5 minutes of the REM periods following the selected NREM periods. Each of these segments was subjected to an HRV routine using Somnologica software which identified r-r intervals and had built-in artifact rejection. Variance in HR was measured by the following frequency domain indices: low frequency [0.04-0.15 hz (LF)], high frequency [0.15-0.40 hz (HF)], LF/HF ratio (LF/HF) and Normalized LF (LF/(LF+HF)). Independent samples t-tests were conducted for each index at each time point and for combined NREM segments and REM segments.

**Results :** Groups did not differ with respect to age, BMI, gender or mean nightly heart rate. Groups did not differ with respect to HF power, nor were there any differences for any measure during REM. Significant findings included that PIs had elevated LF power and LF/HF ratio in each of the NREM periods (all  $p < .05$ ). PIs also had elevated Normalized LF power in the first NREM period, but the group difference did not reach significance for NREM2 ( $p = .18$ ) or the last NREM ( $p = .12$ ).

**Conclusion :** Combined, these findings suggest that the balance between sympathetic and parasympathetic regulation of heart rate is more heavily influenced by sympathetic inputs in PIs than in GSs during NREM sleep (predominantly Stage 2 sleep). This is consistent with various hypotheses

related to increased hyperarousal in insomnia and further demonstrates that HRV can be a useful, non-invasive measure of this phenomenon.

**Support (optional):** Support for this project comes from NIH F32 NS049789 (Dr. Pigeon) and R01 MH59392 (Dr. Perlis).

### 0740

#### RELATIONSHIP OF DYSFUNCTIONAL SLEEP-RELATED THOUGHTS AND BEHAVIORS, PRE-SLEEP AROUSAL, CANCER SYMPTOMS, AND MOOD TO SLEEP IN BREAST AND LUNG CANCER PATIENTS WITH INSOMNIA

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**Introduction :** Insomnia is a common and distressing issue reported by cancer patients, but little research has focused on this issue. The purpose of this study was to examine the relationship of dysfunctional sleep-related thoughts and behaviors, pre-sleep arousal, cancer symptoms, and mood to sleep in cancer patients with insomnia.

**Methods :** Participants were 38 breast and 32 lung cancer patients. 39 patients met diagnostic criteria for insomnia and 31 were a comparison group with no sleep complaints. Participants completed sleep logs for 7 days assessing pre-sleep arousal, pain, fatigue, sleep efficiency, sleep quality, and restfulness upon awakening. They also completed questionnaires assessing dysfunctional sleep-related thoughts and behaviors, depressive symptoms, and anxiety. Before correlational analyses were conducted, 2 (insomnia v. comparison group) x 2 (breast v. lung cancer) ANOVA's were conducted to ensure that there were only significant differences between those in the insomnia and comparison groups and not significant differences between lung and breast cancer patients on the variables of interest. Results revealed that the insomnia group reported significantly higher levels of dysfunctional sleep-related thoughts and behaviors, pre-sleep arousal, fatigue, depressive symptoms, and anxiety than the comparison group. There were no significant differences between breast and lung cancer patients on these variables.

**Results :** Correlational analyses revealed that patients reporting higher levels of sleep inhibitory behaviors reported lower levels of sleep efficiency, sleep quality, and restfulness (all  $p < .01$ ). Patients with higher levels of pre-sleep arousal reported lower levels of sleep quality ( $p < .05$ ). Finally, patients reporting higher levels of depressive symptoms reported lower levels of sleep efficiency ( $p < .05$ ), and patients reporting higher levels of fatigue and anxiety reported lower levels of restfulness ( $p < .05$ ).

**Conclusion :** These findings suggest that sleep inhibitory behaviors, pre-sleep arousal, fatigue, and mood relate to sleep in breast and lung cancer patients with insomnia.

**Support (optional):**

### 0741

#### ASSOCIATIONS BETWEEN SLEEP AND MEMORY IN HYPNOTIC DEPENDENT OLDER ADULTS

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**Introduction :** Older adults are disproportionately high users of hypnotic medications and are particularly vulnerable to medication side effects,

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including impaired daytime functioning. Older insomniacs frequently complain of daytime memory and learning difficulties. We examined the relationship between sleep and memory performance in hypnotic dependent older adults.

**Methods :** This is a secondary data analysis of baseline measures obtained from 79 community-dwelling older adults ( $M=63.39$ ,  $SD=8.57$ ) recruited from the Memphis, TN metropolitan area to participate in a study of hypnotic dependent older adults. Average duration of hypnotic use was 4.47 years ( $SD = 4.50$ ; range-6 months-20 years). Participants completed sleep diaries, Rey-Osterreith Complex Figure (Rey-O), and California Verbal Learning Test (CVLT). Subjective sleep variables examined: wake time after sleep onset (WASO), number of nighttime awakenings (NWAK), sleep efficiency (SE), total sleep time (TST), and sleep quality rating (SQR).

**Results :** Multiple correlations were run to examine the relationships between sleep and memory. WASO was positively associated with time to draw the Rey-O ( $r=.301$ ,  $p<.05$ ). NWAK was negatively related ( $r=-.374$ ,  $p<.01$ ), while SE was positively related ( $r=.323$ ,  $p<.05$ ) to Rey-O cued recall. TST was positively associated with initial recall number on the CVLT ( $r=.277$ ,  $p<.05$ ). SQR was positively related to Rey-O copy and delayed scores ( $r=.285$ ,  $p<.05$ ;  $r=.287$ ,  $p<.05$ ), negatively related to time to draw Rey-O immediate and delayed ( $r=-.289$ ,  $p<.05$ ;  $r=-.307$ ,  $p<.05$ ), and positively associated with CVLT long-delayed free-recall ( $r=.342$ ,  $p<.05$ ).

**Conclusion :** Sleep and memory are associated in hypnotic dependent older adults. Better sleep was correlated with better visual/verbal memory performance. Perceived sleep quality showed the most consistent association across memory variables, highlighting the importance of the relationship between perceptions of good sleep quality and memory in older insomniacs. An important question that remains to be addressed is whether hypnotic withdrawal and subsequent improvements in sleep will result in improved memory functioning.

**Support (optional):**

### 0742

#### SLEEP MEDICATIONS CHRONICALLY USED BY OLDER ADULTS WITH HYPNOTIC-DEPENDENT INSOMNIA

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**Introduction :** A 2004 editorial in *SLEEP* attempted to summarize drug treatment for insomnia with a survey of 29 medical specialties. The data were interpreted as showing Trazodone the most used drug for treatment of insomnia. The editorial defined treatment of insomnia by assuming that every time a physician prescribed a drug with a desired action related to promoting sleep or to promoting nighttime sedation, the physician was treating insomnia. This definition fails to address the fact that prevalent medical disorders, such as depression, are common in medical practice and have associated difficulty sleeping. Clinically, anti-depressants are perceived to help people sleep. It is likely that anti-depressants are often prescribed, at least in part, for their sleep-promoting capacities. It is problematic to study all patients with difficulty sleeping if interested in patients with an insomnia disorder. Chronic insomnia is a better population for studying persistent insomnia. The present study examined hypnotic-dependent insomnia. We predicted Trazodone would be used less often among patients with hypnotic-dependent insomnia than among all patients with difficulty sleeping.

**Methods :** Participants were in a sleep medication withdrawal study.

They were 79 older adults with hypnotic-dependent insomnia. All had used prescription sleep medication for over 6 months, and all had symptomatic insomnia when joining the study.

**Results :** The majority of the participants were using hypnotics (58%). The second most frequent category was anxiolytics (29%). Anti-depressants were uncommonly used among the hypnotic-dependent insomnia sample (13%).

**Conclusion :** Trazodone was not a common treatment among older people with hypnotic-dependent insomnia. In order to study medical practice patterns of drug selection for treatment of insomnia, samples of carefully selected insomnia patients should be examined. Broad questions about the nature of prescribing practices for all patients with a complaint of difficulty sleeping should be broken down into questions more capable of being well answered.

**Support (optional):** Research supported by National Institute on Aging grant AG14738.

### 0743

#### QUANTITY OF SLEEP DYSFUNCTION AND CORRESPONDING LEVELS OF DAYTIME FUNCTION

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**Introduction :** Quantitative criteria for diagnoses of health problems are often established by finding thresholds for key variables at which morbidity risk increases. The goal of the current study is to establish such thresholds for variables associated with the diagnosis of insomnia.

**Methods :** Sleep diary and daytime function data were collected from 772 participants recruited via random digit dialing. Sleep onset latency (SOL), wake time after sleep onset (WASO), and sleep efficiency (SE), were among the sleep variables computed. Daytime function measures included: the Insomnia Impact Scale (IIS), Fatigue Severity Scale (FSS), State-Trait Anxiety Inventory (STAI), and Beck Depression Inventory (BDI). 5 minute (or 5% in the case of SE) increments were used to explore quantitative thresholds for SOL, WASO, and SE at which pre-established criteria for daytime impairment were crossed. This was done for persons who described themselves as good sleepers (GS) and persons who described themselves as having chronic insomnia (CI).

**Results :** CI reported clinically relevant BDI and STAI scores ( $\geq 10$  and  $\geq 37$  respectively) at relatively modest levels of sleep impairment (SOL = 5, WASO = 5, SE = 90%). GS reported sub-threshold BDI and STAI scores regardless of sleep dysfunction. As measures of sleep moved toward higher levels of dysfunction (SOL = 60, WASO = 60, SE = 70%) BDI and STAI scores remained below established cut-offs among GS. Both diagnostic groups never crossed pre-established morbidity scores for the IIS or FSS. CI reported clinically relevant BDI and STAI scores ( $\geq 10$  and  $\geq 37$  respectively) at relatively modest levels of sleep impairment (SOL = 5, WASO = 5, SE = 90%). GS reported sub-threshold BDI and STAI scores regardless of sleep dysfunction. As measures of sleep moved toward higher levels of dysfunction (SOL = 60, WASO 60, SE = 70%) BDI and STAI scores remained below established cut-offs among GS. Both diagnostic groups never crossed pre-established morbidity scores for the IIS or FSS.

**Conclusion :** There was no measure of SOL, WASO or SE that served as a threshold at which daytime impairment became problematic. Thresholds could not be established because sleep measures appear to be disengaged from daytime function measures. Daytime function measures are most closely related to the self-perception that one has chronic insom-

nia versus healthy sleep.

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## 0744

### RACE AND SLEEP COMPLAINTS: ANALYSIS OF THE NATIONAL SLEEP FOUNDATION DATA

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**Introduction :** The present study examined racial differences in sleep complaints using data from the National Sleep Foundation (NSF).

**Methods :** Data presented in this report came from a national study of sleep habits sponsored by the NSF. A total of 1,506 telephone interviews (lasting approximately 20 min) were conducted in 2002 using a random sample of American adults (ages 55 to 84 years). Telephone numbers were purchased from Affordable Samples; quotas were established by region and age based on U.S. Census household data. About 80% of the interviews were conducted on weekdays. Women comprised 58% of the sample, and men, 42%. Results of age and sex effects on sleep habits have been reported. The present analysis focuses on differences in sleep patterns between Black (n=92) and White (n=960) respondents.

**Results :** We found no significant difference in the rate of insomnia complaints (i.e., DIS, DMS, or EMA) of Blacks and Whites [60% and 56%,  $\chi^2=0.47$ ]. We also found no significant race differences regarding reported sleep durations either during work days [6.97 ± 1.87hrs vs. 6.99 ± 1.33hrs,  $F=1.14$ , NS] or non-work days [6.99 ± 1.57hrs vs. 7.19 ± 1.32hrs,  $F=1.57$ , NS]. However, a greater proportion of Blacks reported daytime napping [18.5% vs. 14.2%,  $\chi^2=9.27$ ,  $p<0.05$ ]. Within the Black race, 9% of respondents with insomnia complaints used prescribed sleep medications, whereas 18% used OTC medications; within the White race 12% used prescribed sleep medications, whereas 15% used OTC medications.

**Conclusion :** Results of the NSF survey suggest that Black and White Americans do not differ significantly regarding insomnia complaints or sleep durations. Most of the epidemiologic studies have shown greater rates of insomnia among older White respondents compared to Blacks. Discrepancies might reflect methodological differences and/or differing insomnia definition. The lack of adequate representation of Blacks in the national sample should be considered when interpreting these data.

**Support (optional):** Funding from the National Sleep Foundation supported this work.

## 0745

### SLEEP AND HEALTH COMPLAINTS AMONG OLDER WOMEN: DOES ETHNICITY MATTER?

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**Introduction :** This study compared rates of sleep and health complaints

in a community-based sample of Hispanic, White, and Black women.

**Methods :** A total of 1440 women (mean age=59.36 ± 6.53 yrs) living in Brooklyn, NY, participated in the study; Hispanics=12%, Whites=25%, and Blacks=63%. Participants were recruited using a stratified, cluster sampling technique and provided data during face-to-face interviews. Questionnaires were used to acquire demographic data. Physical health was measured with the CARE; six sub-scales were included: sleep disorder, heart disease, respiratory disease, arthritis, vision problems, and hypertension.

**Results :** The rate of difficulty initiating sleep among Hispanics was significantly different from both Whites and Blacks [34%; 42%; and 16%, respectively  $\chi^2=95.34^*$ ]. Regarding difficulty maintaining sleep, Hispanics reported greater rates than Blacks [62% vs. 40%,  $\chi^2=74.32^*$ ], but rates were comparable to those of Whites [62% vs. 64%]. Rates of early morning awakening were significantly greater for Hispanics compared to Blacks [54% vs. 27%,  $\chi^2=101.90^*$ ], but they were similar to those of Whites [54% vs. 53%]. Rates of daytime sleep were significantly greater for Hispanics compared to Whites [8% vs. 4%,  $\chi^2=10.20^*$ ], but they were similar to those of Blacks [8% vs. 9%]. The percentage of Hispanic, White, and Black women reporting respiratory problems was: 60%; 52%; and 28%, respectively ( $\chi^2=97.92^*$ ). For hypertension, rates were: 54%; 41%; and 57%, respectively ( $\chi^2=25.78^*$ ). For heart problems, rates were: 58%; 55%; and 41%, respectively ( $\chi^2=30.88^*$ ). For arthritis, rates were: 80%; 73%; and 67%, respectively ( $\chi^2=12.71^*$ ). For vision problems, rates were: 9%; 28%; and 54%, respectively ( $\chi^2=168.05^*$ ). \*  $p < 0.01$ .

**Conclusion :** Our results show appreciable differences in insomnia symptoms between Hispanic and White women, but rates of insomnia in those races were significantly greater compared to rates reported by Black women. Interestingly, Hispanic and Black women reported similar rates of daytime sleep, which is usually more common among ethnic minorities.

**Support (optional):** This research was supported by grants to the second author from the National Institute on Aging (KO7 AG00921), the National Institutes of Health General Medical Science (2SO6 GM54650) and the National Cancer Institute (1P20 CA 91372).

## 0746

### COGNITIVE-BEHAVIORAL AND HYPNOTIC TREATMENT OF CHRONIC PRIMARY INSOMNIA AMONG THE ELDERLY. A RANDOMIZED CONTROLLED TRIAL

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**Introduction :** Insomnia is a common condition in older adults and is associated with a number of adverse medical, social and psychological consequences. Previous research has suggested beneficial outcomes of both psychological and pharmacological treatments, but blinded, placebo-controlled trials comparing the effects of these treatments are lacking. The present study was designed to examine both short- and long-term clinical efficacy of cognitive-behavior therapy and pharmacological treatment in patients suffering from late-life primary insomnia.

**Methods :** 47 subjects were randomized into either cognitive-behavior therapy (CBT, n=18), hypnotics (7.5 mg Zopiclone, n=12), or placebo treatment (n=16). All treatments lasted 6 weeks with follow-ups conducted at 6 months. Patients in the placebo condition were randomized into the to active treatment conditions after 6 weeks. Ambulant clinical

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polysomnography (PSG) and sleep diaries were used on all three assessment points.

**Results :** CBT was associated with significantly better short- and long-term outcome than Zopiclone and placebo condition. No significant outcome differences were observed between Zopiclone and placebo. Post-treatment between-group effect-sized (ES) ranged from 1.2 to 1.7 in favor of CBT, depending on the outcome measures. For example, CBT-recipients improved their sleep efficiency by 10.8% at post-treatment, as compared to only 1.8% in the Zopiclone condition. These differences were maintained at follow-up. Furthermore, subjects in the CBT group spent significantly more time in stage 3 or/and stage 4 as compared to the other conditions, as well as spending less time awake during the night.

**Conclusion :** The findings indicate that CBT are superior to pharmacological treatments, both in terms of short- and long-term management of late-life insomnia.

**Support (optional):**

### 0747

#### LONG-TERM USE OF INDIPLON IN ELDERLY PATIENTS WITH CHRONIC INSOMNIA

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**Introduction :** Indiplon is a highly alpha-1-selective GABA-A receptor potentiator that has been shown to be effective and well tolerated in several 2-week studies of adult and elderly patients with chronic insomnia. This study was undertaken to evaluate the long-term safety of indiplon in elderly chronic insomnia sufferers who had previously completed a 2-week, double-blind, placebo-controlled study of indiplon 5mg and 10mg capsules, taken nightly.

**Methods :** This was a 6-month open-label extension study which enrolled 121 patients aged 65-80 years with a minimum 3-month history of DSM-IV primary insomnia. Patients were required to have a latency to sleep onset >45 minutes and a subjective total sleep time <6.5 hours on at least 3 nights/week to enter the preceding 2-week double-blind study. All patients took either indiplon 5mg or 10mg capsules, as needed, at bedtime. Assessments included patient evaluation of benefit, indiplon use, and safety (including treatment-emergent adverse events; AEs).

**Results :** 67% (n=81) of patients (mean age 71 years) remained in the study for the full 6 months (59% of patients taking indiplon 5mg and 78% of patients taking indiplon 10mg). Overall, 81% of patients reported that indiplon treatment had benefited their insomnia (72% on 5mg, 92% on 10mg). The mean number of indiplon doses in each treatment group was similar and remained constant over time, at approximately 22 doses/month. Indiplon was well tolerated by the elderly patients in this study; AEs were generally mild or moderate, and only three patients (2.5%) discontinued treatment due to an AE. No treatment-related serious AEs were reported, and no safety concerns or evidence of tolerance emerged over time.

**Conclusion :** Indiplon 5mg and 10mg capsules, taken as needed for the long-term treatment of chronic insomnia, was well-tolerated and perceived as beneficial by elderly patients. No safety or tolerability issues were identified.

**Support (optional):** Supported by funding from Neurocrine Biosciences Inc., and Pfizer Inc.

### 0748

#### SUBLINGUAL ZOLPIDEM COMPARED TO ORAL ZOLPIDEM IN THE POST-NAP SLEEP MODEL OF INSOMNIA

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**Introduction :** OX22 is a sublingual, mucoadhesive zolpidem tablet with a more favorable pharmacokinetic profile in terms of shorter t first and tmax than oral tablets. This polysomnographic, post-nap study was initiated to evaluate if OX22 gives shorter latency to persistent sleep (LPS) compared to oral zolpidem.

**Methods :** This was an open randomized, three-period crossover study. Twenty-one healthy volunteers (17 women and 4 men) 18 to 40 years without any history of sleep disorder were enrolled after a medical screening and a five-day actigraphy assessment demonstrating regular sleep schedule (11 pm to 7 am +/- 1 h). Each study period, sleep was recorded (polysomnography) 11 pm to 7 am during two consecutive nights and during a 4 pm to 6 pm nap before the second night. Treatment (OX22 5 mg, 10 mg or oral zolpidem 10 mg) was administered 30 min before lights-out the second night to subjects demonstrating at least 30 min sleep during the afternoon.

**Results :** OX22 10 mg significantly reduced LPS compared to oral zolpidem 10 mg (12.8 +/- 9.9 min vs. 18.4 +/- 11.3 min; p <0.05). There was no difference between OX22 5 mg and oral zolpidem 10 mg (19.5 +/- 11.5 min vs. 18.4 +/- 11.3 min). No differences were evidenced on total sleep time, time awake after sleep onset and sleep architecture parameters. All treatments were well tolerated and did not induce next-day residual effects, as evaluated by Bond & Lader visual analogue scale, digit symbol substitution test and Leeds psychomotor tests.

**Conclusion :** OX22 is a novel tablet formulation of zolpidem, enabling rapid absorption over the sublingual mucosa. In a post-nap sleep model, OX22 10 mg significantly reduced LPS compared to oral zolpidem 10 mg. There was no difference in total sleep time. OX22 was well tolerated and did not induce next-day residual effects.

**Support (optional):**

### 0749

#### INSOMNIA: PREVALENCE, COMORBIDITIES, COSTS IN A TREATED INSURED POPULATION

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**Introduction :** Insomnia occurs as a primary condition and also comorbid with a variety of physical and psychiatric conditions. The objective of this study is to examine the prevalence of treated insomnia, associated comorbidities and costs in an insured population.

**Methods :** We identified subjects who had an ICD-9 insomnia-related medical claim or a prescription for a hypnotic or low-dose sedating antidepressant from a nationally representative administrative claims database. The index date was assigned as the most recent insomnia related-medical claim or prescription that occurred between January 1 2002 and Dec 30 2003. A control group (5 controls:1 case) that did not meet the inclusion criteria for insomnia was also identified. All subjects were required to be continuously enrolled for at least 1 year before and after index date to be included in the study. Comorbidities associated with insomnia in the 6-month period prior to and after index date were examined and subjects were classified as primary insomnia, insomnia comorbid with a physical condition, insomnia comorbid with a mental condition

and insomnia comorbid with physical & mental conditions. Insomnia-related and overall healthcare costs were compared across the insomnia subtypes and a control group using t-tests for bivariate comparisons and generalized linear models with a gamma function for multivariate comparisons.

**Results :** Of the 319,183 subjects with insomnia (mean age=54.5+/- 14.8 years, female: 66.6%) 15.1% did not have any comorbidities, 25.1% had a physical comorbidity, 19.3% had a mental comorbidity and 40.5% had both. Mean unadjusted insomnia-related and total medical costs in the 1-year following index date were lowest for the control group (\$0, \$3355), followed by primary insomnia (\$141, \$4,135) insomnia comorbid with mental condition (\$197, \$6431), insomnia comorbid with physical condition (\$169, \$11,637) and insomnia comorbid with both (\$237, \$16,772) ( $p < .000$  for all comparisons to the control group). After controlling for age, gender, pre-period comorbidity index, healthcare costs prior to the index date the magnitude of differences diminished but remained statistically significant for all comorbid groups.

**Conclusion :** The high prevalence and increased healthcare costs in comorbid insomniacs suggests that treatment of insomnia in comorbid patients could result in higher cost savings. This hypothesis needs testing in randomized clinical trials of insomnia treatments.

**Support (optional):** Funded by Eli Lilly

## 0750

### A PLACEBO CONTROLLED, RANDOMISED, DOUBLE-BLIND, 4 WAY CROSS-OVER STUDY OF 3 DOSES OF EVT201 (2.5MG, 5MG AND 10MG) ON ASPECTS OF SLEEP AND MORNING AFTER PERFORMANCE USING A TRAFFIC NOISE MODEL OF SLEEP DISTURBANCE

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**Introduction :** EVT201 is a novel partial positive allosteric modulator of the GABAA benzodiazepine receptor complex. The aim of this study was to assess the hypnotic efficacy of this novel therapeutic in a model of situational insomnia and cognitive performance the next morning.

**Methods :** A randomised, double-blind, 4-way crossover study comparing the effects of 3 doses (2.5mg, 5mg and 10mg) of EVT201, with placebo in a traffic noise model of insomnia. Standard sleep PSG was recorded and residual effects were measured with a psychomotor test battery at 8, 10 and 12 hours post dose.

**Results :** All three doses of EVT201 reduced the number of awakenings ( $P < 0.05$ ) and increased the duration of Slow Wave Sleep ( $P < 0.05$ ). Furthermore, 2.5mg and 5mg significantly reduced the duration and percentage of wake after sleep onset ( $P < 0.05$ ) and the 2.5mg dose led to a significant improvement in sleep efficiency ( $P < 0.05$ ). Only the 5 and 10mg doses increased latency to REM sleep ( $P < 0.01$ ) and reduced REM duration ( $P < 0.01$ ). All three doses had a tendency to improve the ease of getting to sleep and significantly improved the quality of sleep ( $P < 0.0001$ ). The 2.5mg dose also increased self-assessed alertness and mood the following day. The 5mg and 10mg doses impaired several aspects of psychomotor performance, whereas 2.5mg had very limited residual effects and only at the 8 hour time-point.

**Conclusion :** EVT201, in doses up to 2.5mg, could prove to be a useful drug in the management of insomnia. EVT201 has the potential to sustain sleep free of residual effects beyond the sleep period. At this dose the compound increases slow wave sleep and is free of adverse effects on REM sleep. Further studies are underway with a dose range up to 2.5mg.

**Support (optional):**

## 0751

### EFFICACY OF INDIPLON DURING THE FIRST TREATMENT NIGHT IN STUDIES OF PRIMARY INSOMNIA

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**Introduction :** To evaluate the efficacy of indiplon, a GABAA receptor potentiator with selectivity for receptors with the  $\alpha 1$  subunit, during the first night of treatment.

**Methods :** Efficacy data were combined from 4 studies evaluating the efficacy of indiplon in treating adult and elderly patients meeting DSM-IV criteria for primary insomnia. All studies had similar designs (double-blind, placebo-controlled, outpatient trials with nightly treatment). Treatment durations ranged from two weeks to three months. ANOVA was performed on patient self-assessments of sleep initiation (latency to sleep onset; LSO, mins), and sleep maintenance and duration (wake time after sleep onset; sWASO, mins; and total sleep time (sTST, mins).

**Results :** Significantly shorter LSO (+ se) was observed on the first night of treatment with indiplon 5 mg (34.7 + 3.0), 10 mg (35.6 + 1.8), and 15 mg (26.3 + 1.6) vs. placebo (45.7 + 1.8). Similarly, shorter sWASO was observed on the first night of treatment with indiplon 5 mg (68.4 + 6.2), 10 mg (53.4 + 3.6), and 15 mg (54.2 + 4.4) vs. placebo (74.2 + 2.8). sTST was significantly longer on indiplon 5 mg (342.5 + 9.1), 10 mg (364.4 + 5.3), and 15 mg (378.4 + 6.4) vs. placebo (326.5 + 4.2). Efficacy was observed on the first night of treatment regardless of clinical and demographic variables such as baseline insomnia severity, age, and gender.

**Conclusion :** Treatment with indiplon achieved rapid effects regardless of insomnia severity and these effects persisted throughout the study duration.

**Support (optional):** Neurocrine Biosciences, Inc, and Pfizer Inc.

## 0752

### SAFETY AND TOLERABILITY OF LONG-TERM TREATMENT WITH INDIPLON: RESULTS OF A RANDOMIZED 12-MONTH STUDY

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**Introduction :** There have been relatively few studies conducted to evaluate the safety of long-term treatment of insomnia. We summarize here the results of a long-term study of the safety of indiplon, a novel,  $\alpha 1$  subunit-selective, GABA-A receptor potentiator.

**Methods :** Adult patients (n=536) who met DSM-IV criteria for primary insomnia were randomized to 12 months of double-blind, as-needed, treatment with either indiplon 10 mg or 20 mg. Safety assessments included evaluation of adverse events, ECGs, clinical laboratory testing, and vital signs. Patients provided a global assessment of whether treatment was helping their insomnia.

**Results :** The 3 most frequent adverse events (incidence, median day of onset, median duration, respectively) on indiplon 10 mg were headache (11.8%; day 29; 8 days), back pain (7.9%; day 114; 23 days), and somnolence (7.9%; day 2; 29 days). The 3 most frequent adverse events on indiplon 20 mg were headache (8.7%; day 10; 5 days), URI (6.5%; day 180; 10 days), and nasopharyngitis (5.9%; day 136; 7 days). No dose-response effect was observed for adverse events. No clinically meaningful changes were observed in vital signs or ECG parameters, and there were only isolated abnormal lab values that were not clinically signifi-

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cant. At month 2, study treatment was rated as helping insomnia by 80% of patients on indiplon 10 mg, and 85% of patients on indiplon 20 mg. These levels were maintained through month 12. Frequency of indiplon dosing did not increase over time.

**Conclusion :** Long-term treatment with indiplon was found to be safe and well-tolerated; no unexpected adverse events occurred. Indiplon maintained high levels of patient-rated therapeutic effectiveness across 12 months of treatment with no increase in dosing frequency.

**Support (optional):** Neurocrine Biosciences, Inc, and Pfizer Inc.

### 0753

#### RANDOMISED CONTROLLED CLINICAL EFFECTIVENESS TRIAL OF COGNITIVE BEHAVIOUR THERAPY (CBT) VERSUS TREATMENT AS USUAL (TAU) FOR INSOMNIA IN CANCER PATIENTS

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**Introduction :** Epidemiologic studies have shown that insomnia is particularly common amongst cancer patients, with many continuing to report sleeping difficulties one year after completion of cancer treatment. Conventional wisdom on the natural history of insomnia has recently been applied in the context of cancer, suggesting the appropriateness of a biopsychosocial treatment model. There is emerging evidence that intervening at the psychosocial level using cognitive behavioural therapies (CBT) can be effective for insomnia associated with cancer. We aim therefore to assess the benefits of CBT for insomnia in a cancer population.

**Methods :** 150 individuals from four cancer groups (breast, prostate, colorectal and gynaecological) participated in the study. All had completed anti-cancer treatment and satisfied the diagnostic criteria for chronic insomnia. The mean age of the sample was 61 years and the mean duration of their insomnia was 53 months. A 2:1 randomisation process in favour of the intervention (100 in CBT and 50 in TAU) was in operation.

**Results :** For the CBT group, baseline (BL) and post treatment (PT) comparisons yielded statistically significant differences ( $p < 0.05$ ) on all subjectively assessed sleep variables [sleep onset latency (SOL), wake time after sleep onset (WASO), total sleep time (TST), time in bed (TIB) and sleep efficiency (SE)]. SOL reduced from 49mins at BL to 21mins at PT; WASO reduced from 80mins (BL) to 38mins (PT); TST increased from 389mins (BL) to 416mins (PT); TIB reduced from 517mins (BL) to 475mins (PT) and SE increased from 75% (BL) to 87% (PT). Analyses on measures of psychopathology and fatigue also generated significant results for the CBT group. Comparisons on the same variables within the TAU group produced no significant differences.

**Conclusion :** These findings demonstrate the effectiveness of using CBT to treat severe and persistent insomnia in cancer populations. This effectiveness does not diminish due to the existence of physical symptoms such as pain or treatment side effects.

**Support (optional):**

### 0754

#### EFFICACY AND TOLERABILITY OF INDIPLON IN PRIMARY INSOMNIA: RESULTS OF A DOUBLE-BLIND, PLACEBO-CONTROLLED, 4-WEEK TRIAL

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**Introduction :** The present study evaluated the efficacy and safety of indiplon, a novel,  $\alpha 1$  subunit-selective, GABA-A receptor potentiator, in adults diagnosed with primary insomnia characterized by sleep maintenance difficulties.

**Methods :** Patients (N=248) who met DSM-IV criteria for primary insomnia were randomized to 4 weeks of double-blind, nightly treatment with either indiplon 15mg or placebo. Subjective assessments included total sleep time (sTST, primary), wake time after sleep onset (sWASO), number of awakenings after sleep onset (sNAASO), latency to sleep onset (LSO), and sleep quality. Responder status was defined as much-to-very-much improved on the Investigator Global Rating, Change scale (IGR-C). Daytime drowsiness and ability to function were both rated on single-item 6-point scales.

**Results :** Treatment with indiplon was associated with significantly greater improvement than placebo on sTST over the 4-week treatment period (364.7 + 5.3 mins vs. 336.6 + 5.3 mins;  $p = 0.0002$ ), as well as on all secondary sleep measures. Improvement in sleep onset and sleep maintenance parameters on indiplon was associated with significant improvement in sleep quality ( $p < 0.0001$ ) and a significantly higher rate of IGR-C responders (65% vs. 33%;  $p < 0.001$ ). Treatment with indiplon was associated with a significant improvement in daytime functioning relative to placebo (LS-mean 4-week ANCOVA, 3.9 + 0.04 vs. 3.7 + 0.04;  $p = 0.014$ ), and was also associated with a significant reduction in daytime drowsiness (LS-mean 4-week ANCOVA, 3.7 + 0.05 vs. 3.5 + 0.05;  $p = 0.0282$ ). Indiplon was well-tolerated, with only somnolence occurring with an incidence of at least 5% with an incidence greater than placebo (10.6% vs. 4.1% on placebo).

**Conclusion :** The 15 mg dose of indiplon was safe and effective in inducing and maintaining sleep in patients with primary insomnia.

**Support (optional):** Neurocrine Biosciences, Inc, and Pfizer Inc.

### 0755

#### PSYCHOLOGICAL AND BEHAVIORAL TREATMENT OF INSOMNIA: UPDATE OF RECENT EVIDENCE (1998-2004)

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**Introduction :** Recognition that psychological and behavioral factors play an important role in insomnia has led to increased interest in therapies targeting these factors. This review provides an update of the evidence (1998-2004) regarding the efficacy of psychological and behavioral treatments for persistent insomnia. The review was conducted by a task force commissioned by the American Academy of Sleep Medicine in order to update its practice parameters on insomnia treatment.

**Methods :** Thirty-seven treatment studies (N = 2246 subjects) published between 1998 and 2004 and identified through PsycInfo and Medline searches were selected for review. Criteria for inclusion were: (a) a diagnosis of insomnia, (b) the content of treatment was psychological or behavioral, (c) the sample included a minimum of 10 subjects, and (d) the primary outcome variable included at least one of the following: sleep latency, number and/or duration of awakenings, total sleep time, sleep efficiency, or sleep quality. Each study was systematically rated by two reviewers for the design, sample, diagnosis, type of treatments and controls, primary and secondary measures, and main findings.

**Results :** The data indicated that psychological and behavioral therapies produced reliable changes in both sleep continuity and sleep quality. There was evidence of efficacy among individuals with primary insomnia

(28 studies) or insomnia associated with medical and psychiatric disorders (13 studies). Nine studies documented the benefits of treatment for insomnia in older adults or for facilitating discontinuation of medication among chronic hypnotic users. Sleep improvements were well sustained over time. With the exception of reduced psychological symptoms, there was limited evidence that improved sleep led to clinically meaningful changes in morbidity. Five treatments met criteria for empirically-supported psychological therapies for insomnia: Stimulus control therapy, relaxation, paradoxical intention, sleep restriction, and cognitive-behavior therapy.

**Conclusion :** These findings provide additional evidence in support of the efficacy and generalizability of psychological and behavioral therapies for persistent insomnia. Additional research is needed to examine the effectiveness of those therapies when implemented in clinical settings and by non-sleep specialists.

**Support (optional):**

## 0756

### SLEEP LABORATORY ASSESSMENT OF INDIPLON IN PRIMARY INSOMNIA: RESULTS OF A DOUBLE-BLIND, PLACEBO-CONTROLLED, CROSSOVER TRIAL

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**Introduction :** To evaluate the efficacy of indiplon, a novel, -1 subunit-selective, GABA-A receptor potentiator, in patients diagnosed with primary insomnia characterized by sleep maintenance difficulties.

**Methods :** Patients (N=100; mean age, 51 years, range, 22-78 years; female, 63%) who met DSM-IV criteria for primary insomnia, and who reported >60 minutes of wake time after sleep onset, were randomized to a double-blind, 2-period, 2-night crossover sleep lab comparison of indiplon 15mg and placebo. Polysomnographic (PSG) assessments included wake time during sleep (WTDS, primary outcome), wake time after sleep onset (WASO), latency to persistent sleep (LPS), total sleep time (TST), and sleep quality. Comparisons were made using a crossover ANOVA model.

**Results :** Treatment with indiplon was associated with significantly reduced WTDS (60.4 + 3.5 min vs. 71.5 + 3.6 min; p=0.0036), reduced WASO (73.9 + 4.0 min vs. 83.0 + 4.0 min; p=0.0190), significantly shorter LPS (12.5 + 1.1 min vs. 26.1 + 2.4 min; p<0.0001), and significantly longer TST (389.8 + 4.9 min vs. 362.8 + 5.0 min; p<0.0001) relative to placebo. Sleep quality was rated as significantly improved on indiplon (3.3 + 0.1) compared to placebo (4.0 + 0.1; p<0.0001). The overall incidence of adverse events was similar on indiplon (8.0%) and placebo (10.4%).

**Conclusion :** The 15 mg dose of indiplon was safe and effective in inducing and maintaining sleep in patients with primary insomnia as demonstrated by both objective PSG measures, and by subjective diary-based measures.

**Support (optional):** Neurocrine Biosciences, Inc, and Pfizer Inc.

## 0757

### INSOMNIA: THE QUARTER OF AN HOUR RULE (QHR), A SINGLE COMPONENT OF STIMULUS CONTROL, IMPROVES SLEEP

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**Introduction :** Although multi-component cognitive behavioural therapy (CBT) is an effective insomnia treatment and stimulus control (SC) is a core component of CBT and the single intervention with most empirical evidence, little is known about SC mechanism of effect, and whether all its elements are critical to sleep improvement. This study investigated the impact on sleep of the QHR - a single, situational element considered central to SC for insomnia.

**Methods :** Forty GP and self referred volunteers, aged 20-70 years, with onset (SOL) and/or maintenance (WASO) sleep complaints, 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'. Sleep diary pre- (two weeks) and post-(three weeks) treatment and polysomnography (four nights, two pre and two post) data were collected. Compliance with the QHR was measured objectively (actigraphy) and subjectively (compliance diary). ANOVAs were conducted on sleep diary data to evaluate changes in sleep patterns.

**Results :** Following the QHR treatment, statistically significant i) reduction in SOL (only QHRout) and WASO (both QHRin and QHRout), ii) increase in total sleep time, and sleep efficiency (both QHRin and QHRout) and iii) decrease in PSQI score were found (all ps <.05 for these subjective data). Clinical significant improvements (SOL and WASO shorter than 31 minutes or reduced by 50%, SE greater than 84%) were obtained in around 50% of active groups participants.

**Conclusion :** The QHR, a single instruction administered in thirty minutes was found to improve subjective reported sleep both statistically and clinically. The finding that both QHRin and QHRout were efficacious for WASO, sheds doubt on the argument that for difficulties maintaining sleep, the QHR component works solely via SC principles. In contrast leaving the bedroom maybe a critical aspect of QHR during the sleep initiation phase. Further research seems worthwhile.

**Support (optional):**

## 0758

### SYMPTOM RESPONSE AND REMISSION IN INSOMNIA: ANALYSIS OF HOW VARIOUS CRITERIA PERFORM

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**Introduction :** Response and remission are the two most commonly utilized measures of outcome in treatment studies of many psychiatric disorders (e.g., depression, anxiety), yet consensus regarding such criteria in the treatment of insomnia are lacking. The goal of this analysis was to test how various response and remission criteria for insomnia perform with respect to one another.

**Methods :** Month 1 efficacy data were analyzed from a prospective, double-blind, placebo-controlled trial utilizing indiplon 10 mg and 20 mg. Response and remission were evaluated using the following 4 outcome measures: (1) the 7-item, Investigator Global Rating of Change (IGR-C); (2) the self-administered 7-item Insomnia Severity Index (ISI); (3) normative values for sleep onset and total sleep time from a community survey (Lichtstein et al, 2004); and (4) no longer meeting insomnia severity criteria required for study entry, consisting of latency to sleep onset >45 mins, wake time after sleep onset >45 mins, and total sleep time <330 mins.

**Results :** At Month 1, the 2 candidate responder criteria yielded the following response rates: IGR-C <2 (indiplon 10 mg, 45% vs. indiplon 20 mg, 58% vs. PBO, 23%), and ISI-total score <15 (indiplon 10 mg, 69% vs. indiplon 20 mg, 70% vs. PBO, 53%). At Month 1, the 4 remission criteria yielded the following remission rates: IGR-C=1 (indiplon 10 mg,

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18% vs. indiplon 20 mg, 28% vs. PBO, 8%); no longer meeting insomnia severity criteria for study entry (indiplon 10 mg, 32% vs. indiplon 20 mg, 33% vs. PBO, 17%); ISI-total score <10 (indiplon 10 mg, 36% vs. indiplon 20 mg, 46% vs. PBO, 22%); and return to community norm levels of sleep (indiplon 10 mg, 29% vs. indiplon 20 mg, 25% vs. PBO, 12%).

**Conclusion :** Empirical data provide an important first step for establishing consensus clinical criteria for response and remission in the treatment of insomnia.

**Support (optional):** Neurocrine Biosciences, Inc, and Pfizer Inc.

### 0759

#### MAGNITUDE OF SLEEP CHANGES DURING PLACEBO ADMINISTRATION IN INSOMNIA TREATMENT TRIALS

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**Introduction :** Insomnia is presumed to be a condition susceptible to placebo effects. However, few studies have systematically examined how sleep changes with the administration of a placebo, and no study has compared these changes with those observed in wait-list control conditions. Accordingly, a meta-analysis was conducted to assess the magnitude of sleep changes observed in placebo conditions (pharmacological and psychological) and wait-list conditions in insomnia treatment trials.

**Methods :** Reference databases (1990 -2004) were searched for primary insomnia treatment studies using a randomized controlled parallel-group design. Combination of effect sizes for each end-point variable was done within each assessment subtype (PSG versus diary) and each control condition subtype (pharmacological, psychological, wait-list) using a random effects model approach. Results of the meta-analysis are presented as raw differences, expressed in minutes, along with their effect sizes (ES).

**Results :** Thirty-four studies (1392 subjects) met inclusion criteria; twenty-three used a pharmacological placebo (1163 subjects), four used a psychological placebo (81 subjects), and seven used a wait-list condition (148 subjects). The following statistically significant findings were observed. Pharmacological placebo condition: 7.5 min decrease of PSG SOL (-0.41) and 19.6 min of diary SOL (-0.54); 21.4 min decrease of diary WASO (-0.35); 18.3 min increase of PSG TST (0.31) and 31.1 min of diary TST (0.41); and 6.16% increase of diary sleep quality (0.42). Psychological placebo condition: 6.07% increase of diary sleep quality (0.52). Wait-list condition: 6.86 min decrease of diary WASO (-0.18) and a decrease of 0.37 of diary awakenings/night (-0.35).

**Conclusion :** These findings provide some evidence that a placebo effect may indeed be operating in clinical trials of insomnia when a pharmacologic agent is used as placebo. The observation that changes were greater on subjective endpoints is consistent with results of other meta-analyses conducted across different conditions. Further research on effects associated with the use of psychological placebos remains necessary.

**Support (optional):**

### 0760

#### AN OPEN TRIAL OF COGNITIVE-BEHAVIORAL TREATMENT FOR INSOMNIA ASSOCIATED WITH ALCOHOL DEPENDENCE: EFFECTS ON SLEEP OUTCOMES

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**Introduction :** Insomnia during recovery from alcohol dependence is

prevalent, persistent, and may contribute to relapse. Limited evidence exists for the efficacy of hypnotics to treat insomnia in alcoholic patients. Physicians may additionally be reluctant to prescribe these medications and patients in early recovery may want to avoid using medications for sleep. In an open pilot study, we evaluated the efficacy of cognitive-behavioral treatment for insomnia in abstinent alcoholic patients (CBTI-A).

**Methods :** Five abstinent alcoholic patients (3 women, mean age 39.6 ± 5.8 years, median 246 days sober, range 27-433 days) recruited from local outpatient facilities met DSM-IV criteria for insomnia due to alcohol dependence (median insomnia duration 18 months, range 1-84 months) and participated in the 8-session individual CBTI-A. Participants were otherwise free of medical, psychiatric, and sleep disorders. Daily sleep diaries were completed beginning two weeks before treatment until two weeks post-treatment. The Dysfunctional Beliefs and Attitudes about Sleep Scale-Short Form (DBAS-SF) and clinician- and patient-rated Insomnia Severity Index (ISI) were completed pre-treatment, mid-treatment, and post-treatment.

**Results :** Repeated measures ANOVA indicated diary-rated improvements in the frequency of nighttime awakenings (FNA; F(2,8)=6.60, p=0.02), total wake time (TWT; F(2,8)=52.54, p<.001), sleep efficiency (SE; F(2,8)=21.77, p=0.001), and morning restfulness ratings (F(2,8)=6.04, p=0.02). Relative to pre-treatment, TWT (p=0.003) and SE (p=0.01) improved by mid-treatment, and these gains were maintained through post-treatment (p<.001 for TWT; p=0.007 for SE). Improvements in sleep diary measures were also reflected on the patient-rated ISI (F(2,8)=32.25, p<.001), clinician-rated ISI (F(2,8)=29.51, p<.001), and the DBAS-SF (F(2,8)=9.96, p=0.007).

**Conclusion :** In this small-scale uncontrolled pilot study of abstinent alcoholics with mild to moderate insomnia, an 8-week individual CBTI-A produced post-treatment improvements in insomnia severity, sleep beliefs and attitudes, and sleep diary measures of sleep consolidation. An ongoing randomized clinical trial will determine the efficacy of CBTI-A for improving sleep and reducing relapse in abstinent alcoholic patients.

**Support (optional):** Research supported by the National Institute on Alcohol Abuse and Alcoholism (R21 AA014408).

### 0761

#### VALIDATION OF THE INSOMNIA SEVERITY INDEX

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**Introduction :** Although insomnia is a highly prevalent health problem, it is infrequently diagnosed or treated. Brief and valid instruments are needed for both screening and outcome assessment. The Insomnia Severity Index (ISI) is a 7-item self-report instrument which quantifies insomnia severity according to several indicators including sleep difficulties, sleep satisfaction, daytime impairment, distress, and noticeability of impairment. Total ISI scores are usually broken down into four categories: no insomnia (0-7), sub clinical insomnia (8-14), moderate (15-21), or severe insomnia (22-28). This study examined the ISI reliability, convergent validity, sensitivity, and specificity.

**Methods :** Subjects were 183 adults (mean age: 41.2 years; range: 19-72; 48.4% men) meeting criteria for primary insomnia and 62 self-defined good sleepers (mean age: 50.8 years; range: 30-72; 38.8% men). They completed the ISI, daily sleep diaries, and a semi-structured clinical interview to determine their insomnia or good sleeper status. Sensitivity and specificity were assessed through receiver-operator characteristic (ROC) curves comparing ISI scores with clinical interview and diary data.

**Results :** The reliability coefficient (Cronbach's alpha) for the total ISI was .91. Items targeting sleep onset and maintenance difficulties were positively correlated with diary measures of total wake time (rs = .19 to



.29) and negatively correlated with total sleep time and sleep efficiency ( $r_s = -.18$  to  $-.28$ ). A cutoff score of 15 (moderate severity) yielded sensitivity and specificity indexes of 78.1% and 100% respectively, while a cutoff score of 8 (sub clinical insomnia) yielded indexes of 99.4% and 91.8% respectively.

**Conclusion :** These findings provide additional evidence that the ISI is a valid and reliable instrument to discriminate between individuals with insomnia and self-defined good sleepers. Additional research is needed to examine other cutoff points for identifying insomnia cases in primary care and for detecting clinically meaningful changes with treatment.

**Support (optional):**

## 0762

### CORRELATES OF SLEEP ESTIMATES IN INSOMNIACS AND CONTROLS

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**Introduction :** The purpose of this research was to investigate the correlates of sleep latency estimates in a sample of insomniacs. Actigraphy, sleep diary, and an Anticipatory Sleep Questionnaire (ASQ), were used to measure sleep onset latency in a sample of insomniacs and controls. The ASQ measures the anticipation of poor sleep just prior to bedtime.

**Methods :** A sample of 13 healthy insomniacs (mean age 36 yrs old, 62% F) and 10 healthy normal controls (mean age 31 yrs old, 70%F) were recruited from the Detroit tri-county area. All insomniacs were diagnosed with primary insomnia based on DSM-IV criteria. Across a 2-week period, actigraphy, sleep diary, and ASQ assays of sleep latency were collected while the subject slept at home. Correlation coefficients were determined between morning diary sleep latency estimates, actigraphically determined sleep latency, as well as, subjective estimates of anticipation of difficulty falling asleep.

**Results :** In controls, the sleep diary estimate of sleep onset latency (SOL) correlated comparably with actigraphy SOL ( $r=.47$ ,  $p=.17$ ) and anticipation of sleep latency ( $r=.57$ ,  $p=.08$ ). In contrast, among insomniacs there was no correlation between actigraphy and the anticipatory estimate ( $r=.09$ ,  $p=.77$ ), but a robust correlation between diary and anticipatory estimates ( $r=.72$ ,  $p=.006$ ).

**Conclusion :** Insomniacs and controls exhibit a high correlation on both subjective sleep latency measures taken before and after sleep. However, in controls nocturnal measures of subjective and objective sleep latency are highly correlated with morning diary whereas, insomniacs do not predict sleep latency accurately, as defined by actigraphy. Although, insomniacs anticipate sleep latency consistent with what they report on morning diaries, this anticipation may not always reflect their nocturnal sleep pattern.

**Support (optional):** Research supported by Grant MH068372 to Drake

## 0763

### AN OPEN TRIAL OF COGNITIVE-BEHAVIORAL TREATMENT FOR INSOMNIA ASSOCIATED WITH ALCOHOL DEPENDENCE: EFFECTS ON MOOD, FATIGUE, AND QUALITY OF LIFE

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**Introduction :** Chronic insomnia is associated with affective symptoms, daytime fatigue, and decreased quality of life. Among alcohol dependent patients, insomnia is common, persistent, and may contribute to relapse.

We evaluated changes in mood, fatigue, and quality of life following a cognitive-behavioral treatment for insomnia (CBTI-A) in abstinent alcoholic patients.

**Methods :** Five abstinent alcoholics (3 women, mean age  $39.6 \pm 5.8$  years, median 246 days sober, range 27-433 days) recruited from outpatient facilities who met DSM-IV criteria for insomnia due to alcohol dependence (median insomnia duration 18 months, range 1-84 months) participated in the 8-session individual CBTI-A. Participants did not meet DSM-IV criteria for other Axis I disorders and were otherwise medically healthy without evidence of other sleep disorders as confirmed by polysomnography. Before and after the 8-week CBTI-A, participants completed the Beck Depression Inventory (BDI), State Trait Anxiety Inventory (STAI), Multidimensional Fatigue Inventory (MFI-20), and SF-36 Health Survey.

**Results :** Compared to pre-treatment, post-treatment BDI scores ( $24.2 + 9.7$  vs.  $10.8 + 3.4$ ,  $t(3)=3.78$ ,  $p=0.03$ ) and State ( $41.8 + 9.39$  vs.  $34.20 + 6.6$ ,  $t(4)=3.6$ ,  $p=.024$ ) and Trait ( $49.60 + 10.9$  vs.  $41.40 + 12.36$ ,  $t(4)=4.1$ ,  $p=.014$ ) subscales of the STAI declined significantly. The General Fatigue ( $12.8 + 1.8$  vs.  $7.6 + 2.4$ ,  $t(4)=5.10$ ,  $p=0.007$ ) and Reduced Activity ( $10.0 + 2.4$  vs.  $8.0 + 1.6$ ,  $t(4)=2.83$ ,  $p=0.05$ ) subscales of the MFI-20 also decreased significantly. There were no significant changes on the SF-36 or any of the subscales.

**Conclusion :** These preliminary findings suggest that abstinent insomniacs undergoing CBTI-A may experience reductions in the daytime sequelae of their insomnia. Caution is advised in interpreting the results given the small sample size and the lack of control group. An ongoing randomized controlled trial that includes follow-up assessments of these outcomes and drinking status at 3 and 6 months will provide insight into the relationship between insomnia, daytime function, and relapse.

**Support (optional):** Research supported by the National Institute on Alcohol Abuse and Alcoholism (R21 AA014408 and T32 AA07477).

## 0764

### ANTIBIOTICS MAY BE INSOMNOGENIC

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**Introduction :** It is well established that medications which alter CNS neurotransmission may produce acute insomnia. The most common insomnogenic agents are SSRIs, beta adrenergic antagonists, alpha-2 adrenergic agonists, calcium channel blockers, corticosteroids, and adenosine antagonists. The extent to which insomnia may occur as a side effect of other classes of medications is less well known. In the present report, we call attention to data which suggest that antibiotics may be insomnogenic.

**Methods :** A survey was undertaken using the Physicians' Desk Reference to document the occurrence of insomnia with seven classes of antibiotics including the cephalosporins (n=14), quinolones (7), penicillins (n=7), tetracycline (n=1), aminoglycosides (n=2), macrolides (n=4) and B-lactam (n=2) antibiotics.

**Results :** While the occurrence of insomnia as an iatrogenic effect was found to be relatively uncommon (< 7% incidence), five of the classes were found to reliably have insomnia as a side effect. 100% of the quinolones, 57% of the penicillins, 50% of the B-lactam medications, 37% of the cephalosporins, and 25% of the macrolides have insomnia as a potential side effect. No such association existed for tetracycline and aminoglycosides. Insomnia occurred most reliably with the penicillin

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zoysn (6.6%) and the quinolone floxin (3%).

**Conclusion :** These data suggest that antibiotics are not benign with respect to sleep and that they may serve as a precipitating factor for insomnia. Further research is needed to determine 1) what factors predispose the individual to this particular stress-diathesis, 2) precisely what aspects of sleep continuity are affected (sleep initiation, maintenance, or both) and 3) how such medications, at a mechanistic level, result in sleep continuity disturbance. With respect to the last of these points, it has been suggested that antibiotics may cause delirium and/or seizures via the inhibition of GABA activity. A similar mechanism may be responsible for the occurrence of insomnia as a side effect, and particularly with the quinolones and zosyn.

**Support (optional):**

### 0765

#### COMPARISON BETWEEN ACTIGRAPHY AND SLEEP DIARIES IN ELDERLY INSOMNIA PATIENTS UNDERGOING LONG-TERM LIGHT THERAPY

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**Introduction :** Measurement of sleep in insomniacs is problematic at best. Actigraphy and sleep diaries are frequently used for this purpose, though each has limitations. The current study is a component of a large, randomized, single-blinded, placebo-controlled study to determine the effectiveness of light and behavioral therapy for elderly insomnia patients. The goal of the study is to determine the differences between an objective measure (actigraphy) and a subjective measure (sleep diaries) in a specific population (elderly insomniacs) over time (3 months of treatment).

**Methods :** Forty-nine subjects  $\geq 55$  years old with a primary insomnia complaint completed 7 nights of actigraphic recordings and sleep diaries at baseline, mid-treatment, and end of treatment 3 months later. Parameters analyzed were sleep latency (SL), total sleep time (TST), sleep efficiency (SE), and wake after sleep onset (WASO). Paired t-tests were performed to assess sleep diary/actigraphy differences at each time point. A repeated measures ANOVA was used to assess differences (actigraphy - sleep diary) for each sleep parameter by condition across the 3 time points.

**Results :** Sleep diaries and actigraphy sleep parameters were significantly different at all time points. For SL, the mean difference at baseline was 13.2 minutes, 0.4 at mid-treatment, and 4.3 at end-of-treatment. For TST, they were 63.9, 15.8, 18.8. For SE, they were 12.2, 3.3, 2.2. For WASO, they were 7.8, 4.8, 11.7. There were no differences between treatment groups that would account for this change.

**Conclusion :** The differences between sleep diaries and actigraphy followed a similar trend from baseline to mid-treatment: major differences were found during baseline and these differences were reduced at mid-treatment. At end-of-treatment, these differences either slightly increased or decreased. Overall, the subjective and objective measures converged over time independent of treatment effects, perhaps suggesting elderly insomniacs may become more accurate in their quantitative perception of sleep parameters over time.

**Support (optional):** Medical Research Service of the Palo Alto Veterans Affairs Health Care System, Department of Veterans Affairs Sierra-Pacific MIRECC, and AG 12914.

### 0766

#### REGIONAL CEREBRAL METABOLIC CORRELATES OF WASO DURING NREM SLEEP IN INSOMNIA

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**Introduction :** Sleep maintenance problems are the most common complaints of insomnia patients although the mechanisms of these problems are not known. In order to begin to address this question, we correlated NREM sleep-related regional cerebral metabolism with self-reported wake after sleep onset (WASO) in primary insomnia patients. We hypothesized that subjective difficulty maintaining sleep correlates with increased metabolism during NREM sleep in distributed thalamocortical networks.

**Methods :** Fifteen patients (7 women / 8 men, mean age + s.d. = 36.9 + 10.5 years) who met DSM-IV criteria for primary insomnia completed 1-week diary assessments of WASO and regional cerebral glucose metabolic assessments during NREM sleep using [18F]fluoro-2-deoxy-D-glucose positron emission tomography (PET). Whole brain voxel-by-voxel correlations were performed between WASO and relative regional cerebral metabolism using the statistical software SPM2.

**Results :** Self-reported WASO positively correlated with NREM sleep glucose metabolism in the pontine tegmentum and in thalamocortical networks in a frontal, anterior temporal, and anterior cingulate distribution.

**Conclusion :** Increased relative metabolism in these brain regions during NREM sleep in insomnia patients is associated with increased severity of self-reported WASO. This may reflect ascending effects of increased neural activity in basic arousal systems in the brainstem/hypothalamus. This may also reflect a persistence of higher order cognitive or emotional processes during sleep which may decrease arousal thresholds and/or increase perceptions related to awakenings in primary insomnia.

**Support (optional):** This research was supported in part by MH61566, MH66227, MH01414, MH30915, RR00056, and MH24652

### 0767

#### ATTITUDE AND BELIEFS OF 111 INSOMNIACS REPORTED ON A SELF-ADMINISTERED QUESTIONNAIRE

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**Introduction :** A web-based system is developed for evaluation, diagnosis, and internet based Cognitive Behavior Therapy (CBT) of insomniacs. Approximately 60000 individuals visited the web-site. 19935 individuals completed a short self-test for the first assessment of their sleep problem. 5594 of these individuals felt that their sleep problem is serious enough to complete a detailed sleep interview. 111 insomniacs were selected to evaluate the attitude and beliefs about their sleep.

**Methods :** A questionnaire to assess faulty beliefs and negative attitude consisting of 21 items was administered. The responses were collected on a 5-point scale ranging between fully agree to fully disagree. The chi-square non-parametric test was performed to test the hypothesis that all subjects will respond with negative attitudes and beliefs.

**Results :** In 7 statements there were significantly more agreements with the expected response ( $p < 0.001$ ). In 4 statements there was no difference in the distribution of responses over the 5 response classes. Strikingly, on 9 statements the subjects responded in a direction opposite to the expectations ( $p < 0.001$ ). Subjects agreed with statements concerning the positive effect of sleeping aids, staying in bed longer to catch more sleep and

they showed concern that their sleep was getting worse. However, they did not agree with statements that were more concerned with possible detrimental effects of their insomnia on daytime functioning, and with negative effects of the insomnia on their future. The responses on the statement the positive effect of taking naps were equally divided over 'Agree' and 'Disagree' categories.

**Conclusion :** The internet based system is a good instrument to reach many people with possible insomnia. The attitude and belief questionnaire gives information, needed for the cognitive component of the CBT. The fact that the subjects did not agree with several of the statements can most probably be explained by the fact that these subjects were actively seeking help and showed a positive approach towards these issues.

**Support (optional):**

## 0768

### WILLINGNESS TO PAY FOR INSOMNIA TREATMENT

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**Introduction :** Decisions regarding the investment of resources for treatment may be improved by balancing outcome data with the cost of the interventions and patient preferences for treatment. Willingness to pay (WTP) methods measure treatment preferences as well as the burden of a clinical problem in economic terms. We used a contingent valuation method to estimate the amount persons with insomnia would be willing to self-pay for behavioral treatment to achieve varying degrees of reduction in their sleep difficulty.

**Methods :** The data used in the analyses were from a non-pharmacological intervention study for insomnia in breast cancer survivors. Women, 18 years and older, with breast cancer who were at least 3 months post completion of primary cancer treatment and without active disease were eligible to participate. Women were considered for inclusion if they met the study definition of insomnia. Exclusion criteria included cognitive impairment or suspicion of sleep disorders other than insomnia. A WTP questionnaire was developed based on similar questionnaires found in the literature and modified for insomnia treatment.

**Results :** The 69 women who completed the WTP questionnaire at pre-treatment had a mean age of 57.9 years (SD=9.9), were 5.5 years (SD=5.0) post primary cancer treatment, and had a mean insomnia duration of 4.8 years (SD=6.4). At pre-treatment, 45% of the women were willing to pay for a 25% reduction in insomnia, 77% were willing to pay for a 50% decrease in insomnia, and 97% would pay for a 75% reduction in sleep difficulty. In actual dollar amounts, 27% to 62% of the women were willing to pay \$125 to \$250 to achieve a 25% or 50% reduction in insomnia. When the hypothetical insomnia improvement rate rose to a 75% reduction in insomnia, 40% to 68% of the women were willing to self-pay up to \$500. There were significant but low correlations between family income and WTP \$250 to \$500 for a 50 and 75% reduction in insomnia (rs=.28 to .35).

**Conclusion :** Breast cancer survivors with chronic insomnia are willing to self-pay for the non-pharmacological treatment of their sleep difficulty. This exploration of WTP reveals it may have potential as a method to assess the value of treatment for a prevalent clinical problem. Research is needed to further develop the WTP questionnaire and include other time points for measurement.

**Support (optional):** National Cancer Institute CA91869

## 0769

### SELF-REPORTED IMPROVEMENT OF SLEEP BY INTERNET BASED MULTI-COMPONENT INDIVIDUALIZED CBT OF INSOMNIA

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**Introduction :** A web-based system was developed for the evaluation, diagnosis and treatment of insomnia patients with an internet based version of Cognitive Behavior Therapy (CBT). Approximately 50000 individuals visited the internet site www.somnio.nl during the last four years. 19935 individuals were aware of their sleep problems and completed a short self test for the first assessment of sleep. 5594 of these individuals felt that their sleep problem was serious enough to complete a detailed sleep interview. This paper reports data on self reported improvement of sleep of 50 insomniacs.

**Methods :** The treatment plan consists of eight sessions and provides various components of CBT: sleep hygiene, sleep restriction, stimulus control and cognitive therapy. For each session, the patients had to keep a diary of sleep wake schedule and their subjective perception of sleep. After each week this information was analyzed and a personalized treatment plan was proposed. Patients were also encouraged to send their personal comments and questions that were handled confidentially by a CBT therapist. This method is called mi-CBT (multi-component, individualized CBT). All individuals followed the treatment anonymously and no solicitation or proactive evaluation was performed to keep them under treatment. The effectiveness of mi-CBT was assessed by self-reported sleep quality and feeling in the morning on VAS, nap duration during the day, sleep latency, number of awakenings and minutes awake during sleep. these parameters after the eighth mi-CBT session were compared with the assessment of the first mi-CBT session.

**Results :** The multi-component individualized CBT led to significant improvement of all sleep parameters (p<0.025 Mann-Whitney U test) except the duration of daytime naps.

**Conclusion :** Internet based Cognitive Behavioral Therapy is a valid treatment procedure for insomnia.

**Support (optional):**

## 0770

### CONTINUOUS GLUCOSE MONITORING IN SUBJECTS WITH INSOMNIA

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**Introduction :** Blood glucose levels (BGL) fall in subjects awake in recumbent position, and during sleep deprivation without activity but decreases minimally across a fast night sleep. Hence sleep "protects" glucose metabolism. Does insomnia disturb this metabolism? This is an ongoing study investigating glucose metabolism and autonomic nervous system activity in insomniacs.

**Methods :** Subjects Fifteen chronic insomniacs (8 women, 7 men) and 2 normal women. Procedure Subjects were confined to a semi-constant routine, resting semi-reclined on the bed, with relatively dim light, not allowed to sleep during the day. They received around 8 am a glucose load (77 g dextropure) and had constant caloric intake every 3 hours. The following day subjects could proceed with their activities keeping two more days the recording instruments. Blood glucose was measured continuously (CGMS, System Gold MiniMed), averaging values every 5 min (calibration 3 times daily). Heart activity, body temperature and movements were monitored continuously, blood pressure was measured automatically at regular intervals. Polysomnography started in the evening.

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**Results :** Following glucose load BGL decreased in all subjects. - Pronounced insomniacs had enhanced response with steeper and longer decrease. - BGL was lower (20-50 %) during bedrest day than during the following days in all but 2 subjects. - BGL decreased during the first sleep hours. - This decrease was often interrupted by an increase in the middle of the sleep period - Phasic variations occurred, specially in the second half of the sleep, sometimes related to REM or awakenings, without however consistent relationships. - Subjects with marked insomnia presented more pronounced phasic variations

**Conclusion :** - BGL are not stable during sleep. - Severe insomniacs seem to have increased glucose intolerance during late part of sleep. - While bedrest usually results in insulin resistance, our study suggests that in insomniacs bedrest enhances blood glucose response.

**Support (optional):**

### 0771

#### A LONGITUDINAL ASSESSMENT OF MENOPAUSAL STATUS AND NIGHTLY FREQUENCY OF SLEEP PROBLEMS

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**Introduction :** Previous studies have shown that peri- and postmenopausal women report more insomnia-related sleep problems on one-time surveys. To address whether sleep problems reported on daily diaries were related to menopausal status or HRT use, we used data from 149 midlife women participating in a sub-study of the Wisconsin Sleep Cohort.

**Methods :** Study participants completed diaries and had biannual in-home polysomnography. The diaries included daily accounts of menstrual cycles and sleep problems, and monthly questions about HRT use, gynecologic surgery, and sleep medications. Body habitus and other health data were obtained biannually. For this analysis, we selected women who completed 2 to 6 years of diaries (a total 8,224 diaries from 149 women) and at least one polysomnography study. Sleep problems were characterized by the nights/month of difficulty initiating, maintaining, or restless sleep. Menopausal status was classified using WHO criteria. Mixed-effect models accounted for multiple diaries per woman while controlling for age and BMI, and were used to estimate least squares means $\pm$ s.e. nights/month of sleep problems.

**Results :** Premenopausal women experienced difficulty initiating sleep  $0.5\pm 0.1$  nights/month. Perimenopausal women experienced  $0.9\pm 0.2$  nights/month (0.4 more than premenopausal,  $p=0.02$ ); and postmenopausal women experienced  $1.3\pm 0.2$  nights/month (0.8 more,  $p=0.001$ ). HRT users experienced 0.3 ( $p=0.02$ ) fewer nights/month difficulty initiating sleep than non-users. Premenopausal women experienced difficulty maintaining sleep  $1.4\pm 0.4$  nights/month. Perimenopausal women experienced  $2.6\pm 0.4$  nights/month (1.2 more,  $p=0.004$ ); and postmenopausal women experienced  $2.9\pm 0.4$  nights/month (1.5 more,  $p=0.002$ ). HRT users experienced 0.9 ( $p<0.001$ ) fewer nights/month difficulty maintaining sleep than non-users. Premenopausal women experienced restless sleep  $1.4\pm 0.2$  nights/month. Perimenopausal women experienced  $2.0\pm 0.3$  nights/month (0.6 more,  $p=0.05$ ); and postmenopausal women experienced  $2.6\pm 0.3$  nights/month (1.2 more,  $p=0.001$ ). HRT users experienced 0.5 ( $p=0.2$ ) fewer nights/month restless sleep than non-users.

**Conclusion :** Compared to premenopausal women, postmenopausal women experienced an approximate doubling of nightly sleep problem frequency. Perimenopausal women had an intermediate frequency. HRT use may partially mitigate sleep problems.

**Support (optional):** Grants R01HL62252, RR03186, and R01AG14124 from the National Institutes of Health.

### 0772

#### SLEEP BEHAVIOR PROFILE OF 5594 VOLUNTARY SELF REPORTED SLEEP DISTURBED INDIVIDUALS

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**Introduction :** A web-based system is developed for evaluation, diagnosis, and internet based Cognitive Behavior Therapy (CBT) of insomniacs. The evaluation and diagnosis is free of charge, whereas CBT is provided by paid subscription. Approximately 60000 individuals visited the site. 19935 individuals completed a short self-test for a first assessment of their sleep problem. 5594 of these individuals felt that their sleep problem was serious enough to complete a detailed sleep interview. 1150 (20.6%) of these individuals were reported to be suffering from insomnia. This paper presents the self-assessed sleep behavior of insomniacs determined from sleep interview.

**Methods :** The profile of the sleep behavior of this group of self assessed insomnia patients was determined by analyzing the questions from the sleep interview.

**Results :** The answers from the sleep interview revealed that 32.6% of the patients complained about initiating sleep, 24.1% about maintaining sleep and 11.6% complained about early morning awakening. 31.1% had a combination of these problems. 44.7% of the patients never felt sleepy during the day, but 55.3% felt sometimes or often sleepy. 29.2% of the patients reported to actually take a nap. Actually falling asleep when it was not appropriate was reported by only 4.5% of the patients, whereas 95.5% never fell asleep. The use of sleeping aids was reported by 54.5% of the insomnia patients and 78.8% used alcohol. For 59% of the patients the sleep problem had started with a period of stress. 19.6% of the patients admitted that they stayed in bed after awakening in the morning and 24.3% worried in bed.

**Conclusion :** Although about 50% of the insomnia patients answered that they felt sleeping during the day, only 30% sometimes were taking a nap and less than 5% felt so sleepy that they would fall asleep at inappropriate timings. Sleeping aids were used by more than 50% of the patients. The web-based system simplifies these measurements and allows rapid data collection with least interference to the subjects.

**Support (optional):**

### 0773

#### PRIMARY INSOMNIA STUDY PARTICIPANTS COMPARED WITH PARTICIPANTS OF A MEMORY TRAINING STUDY

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**Introduction :** Given the stringency of primary insomnia criteria, we questioned if and how the sleep of healthy older ( $\geq 55$ ) individuals meeting this diagnosis differed from the sleep of other older, non-demented, community-dwelling individuals with a different chief complaint.

**Methods :** Light treatment study participants with a complaint of insomnia (INS, N=60) were compared with individuals with memory complaints in a memory training/drug augmentation study (MMH, N=50) using baseline screening questionnaires, cognitive testing and 7 days of actigraphy (MMH: Ambulatory Monitoring, MicroMini, 60-sec epochs; INS: Mini-Mitter, Actiwatch-L, 30-sec epochs).

**Results :** Both samples had more women than men: INS 44 vs 16, MMH 30 vs 20. No significant between-group differences were found for age: INS  $63.7 \pm 6.9$  years, MMH  $65.7 \pm 7.7$  years; education: INS  $16.4 \pm 2.4$

years, MMH  $16.0 \pm 2.2$  years; Body Mass Index: INS  $25.4 \pm 3.3$ , MMH  $25.7 \pm 4.6$ ; MMSE: INS  $28.7 \pm 1.3$ , MMH  $28.5 \pm 1.2$ . Executive function (EXIT) scores: INS  $2.8 \pm 2.1$ , MMH  $3.8 \pm 2.6$  and Geriatric Depression Scale (GDS) scores: INS  $4.1 \pm 3.1$ , MMH  $6.0 \pm 4.2$  were significantly worse for MMH. There were no between-group differences on total sleep time (INS  $397.7 \pm 57.0$ , MMH  $385.1 \pm 106.1$ ); sleep efficiency (INS  $79.2 \pm 7.8$ , MMH  $80.1 \pm 20.1$ ); sleep latency (INS  $21.1 \pm 15.3$ , MMH  $22.5 \pm 19.9$ ). However, MMH participants had significantly more wake after sleep onset (WASO  $101.2 \pm 110.8$  vs  $64.5 \pm 30.8$ ).

**Conclusion :** EXIT and GDS differences were in the expected direction for individuals experiencing memory difficulties. MMH depression inclusion criteria were more lenient than INS. Despite device and measurement differences, sleep parameters were similar except for greater MMH WASO. These data suggest primary insomnia subjects had less fragmented sleep than other older community-dwelling individuals, which raises questions regarding the meaningfulness of studying primary insomnia in older age.

**Support (optional):** Medical Research Service of the Palo Alto Veterans Affairs Health Care System, Department of Veterans Affairs Sierra-Pacific MIRECC, AG 12914, and MH 35182.

## 0774

### THE EFFECTS OF PROPRANOLOL ON HEART RATE AND AUTONOMIC AROUSAL IN INSOMNIA

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**Introduction :** Many individuals with chronic insomnia experience high levels of autonomic arousal as compared to individuals with normal sleep patterns. It was hypothesized that a drug that could reduce autonomic arousal might therefore improve the sleep of a group of chronic insomniacs.

**Methods :** Twenty-one individuals with chronic insomnia participated. These individuals completed three polysomnographic (PSG) studies. Heart rate data was also acquired for spectral analysis. The first PSG was for adaptation and confirmation of insomnia. The final two PSGs were preceded by one week of treatment with either propranolol or placebo, in random order. Subjects were treated with either propranolol at 40 mg ( $n = 10$ ) or 80 mg ( $n = 11$ ) in order to assess any dose response effect. Spectral analysis of heart rate variability provided an index of autonomic arousal. A series of mixed between subjects by within subjects ANOVAs were conducted on these data.

**Results :** Propranolol significantly reduced heart rate in all stages of sleep and during wake. There was no significant difference between the 40 mg and the 80 mg dose. There was no effect of propranolol on autonomic arousal as measured by the LF/HF ratio. Sleep onset latency, sleep efficiency, and other objective sleep measures were not affected by propranolol. Subjective sleep measures of sleep quality and sleep onset latency were not significantly affected by propranolol.

**Conclusion :** Reduction of autonomic arousal, as measured by heart rate and heart rate variability, did not improve measures of sleep in these participants with insomnia. It is likely that hyperarousal is not a general characteristic of insomniacs, but rather a characteristic of a subset of these patients. Future studies that specifically selected insomniacs with hyperarousal could address this issue.

**Support (optional):**

## 0775

### SUBTYPING PRIMARY CHRONIC INSOMNIA: CLASSIFICATION DIFFERENCES AMONGST EVALUATIONS FOR 'PSYCHOPHYSIOLOGICAL' INSOMNIA SUFFERERS

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**Introduction :** After a phone interview, chronic primary insomnia subtypes (initial, maintenance, terminal or mixed) are usually obtained through structured or semi-structured diagnostic interview. The goal of this study was to examine the reliability classification offered by four different instruments (PSG, morning estimates- ME, semi-structured Insomnia Diagnostic Interview -SSIDI, ISI) quantifying sleep variables related to insomnia subtypes.

**Methods :** The sample included 24 chronic primary insomniacs. Following a multi-step assessment evaluation (questionnaires - ISI, 2 weeks of sleep diaries, clinical evaluation - SSIDI), participants meeting criteria for 'psychophysiological' insomnia were invited to undergo three consecutive nights of PSG recordings. Participants completed sleep estimates upon arising (ME) each morning. At each evaluation step, participants were 'subtyped' according to estimated or observed sleep difficulties (SOL, WASO and EMA).

**Results :** PSG and ME of Night 2 and 3 were retained for analysis. The insomnia subtype diagnosis reliabilities were 46% (PSG vs SSIDI), 41% (PSG vs ISI), 33% (PSG vs ME), 33% (PSG vs Diaries), 63% (SSIDI vs ME), 77% (SSIDI vs ISI), 79% (SSIDI vs Diaries), 82% (ISI vs Diaries), 50% (ISI vs ME) and 58% (Diaries vs ME). Non-parametric tests revealed that the SSIDI classified subtypes similarly than both the ISI and the Diaries and the ISI and the Diaries had also similar classifications (all  $ps < .01$ ). Other comparisons were non-significant. If only PSG had been considered, 8% of participants would have been classified as 'good sleepers'. The most consistent subtype across assessments was mixed difficulties while EMA was the least consistent one.

**Conclusion :** Although only psychophysiological insomniacs participated in this study, discrepancies were found between diagnoses on the different measures. However, these findings highlight once more the multifactorial nature of chronic insomnia, the need for multi-step clinical evaluations and suggest the usefulness of developing a reliable instrument to differentiate insomnia subtypes.

**Support (optional):** Research supported by the Canadian Institutes of Health Research (# 49500).

## 0776

### CHRONIC PRIMARY INSOMNIA AND COGNITIVE EVENT-RELATED POTENTIALS (ERPs): PRELIMINARY RESULTS FROM A MULTI-ASSESSMENT PROTOCOL

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**Introduction :** Chronic primary insomnia has been hypothesized to result from conditioned arousal or the inability to initiate normal sleep processes. The event-related potentials (ERPs) components N1, P2 and N350, reflecting respectively attention, inhibition and sleepiness, are useful index of arousal levels. In the present study, these ERPs amplitudes and latencies are compared in primary chronic insomniacs (INS) and good sleepers (GS).

**Methods :** Participants were 15 INS (mean age= 46 years, SD = 7.5) and 16 GS (mean age=37 years, SD = 10.1). Following a multi-step clinical evaluation, participants meeting criteria for 'psychophysiological' insomnia underwent four consecutive nights of PSG recordings (N1 to N4). ERPs in the evening and upon awakening were recorded on N3 and N4,

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with the addition of sleep-onset recordings on N4. Auditory stimuli consisted of ‘standard’ frequent (70 dB, 2000 Hz, .85 probability) and ‘deviant’ rare stimuli (90 dB, 1500 Hz, .15 probability). The ISI was 2 s. Participants received the explicit instruction to ignore all stimuli at all times.

**Results :** Repeated measures MANOVAs were computed for each ERP component (amplitudes and latencies) at each assessment phase (evening, sleep onset, morning) for each stimulus. As expected, the amplitude of all components was greater for the deviant than for the standard stimulus in both groups. However, the amplitudes of N1 and N350 differ between INS and GS at night and morning. N350 was larger in GS than in INS in the evening for the deviant stimulus while N1 amplitude was especially greater in the morning for deviant stimuli in INS compared to GS.

**Conclusion :** Although insomniacs appear electrophysiologically sleepy at night, they are not as sleepy as good sleepers. Signs of greater cortical arousal in insomniacs were also observed, especially upon awakening in the morning. These results suggest that both an inability to initiate normal sleep processes and a higher cortical activation might interfere with sleep in insomniacs.

**Support (optional):** Research supported by the Canadian Institutes of Health Research (# 49500).

### 0777

#### SLEEP, SUB-CLINICAL ANXIETY SYMPTOMS, AND DAYTIME DYSFUNCTION IN OLDER ADULTS WITH PRIMARY INSOMNIA

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**Introduction :** Insomnia complaints and anxiety-related distress often coexist in older adults, and both have been associated with poor daytime function. Even low levels of anxiety can lead to functional disability in the elderly. This study investigated the extent to which insomnia and sub-clinical anxiety symptoms were associated with impaired function in older adults. We hypothesized that disturbed sleep and trait anxiety would each independently contribute to daytime dysfunction.

**Methods :** Participants were 60 adults ( $63.7 \pm 6.9$  years) with primary insomnia. They completed the State Trait Anxiety Inventory (STAI, Form X), RAND 36-Item Health Survey 1.0 (SF-36) and 7 nights of sleep diaries. Participants’ mean wake after sleep onset (WASO) was  $69 \pm 8.9$  min; mean sleep efficiency (SE) was  $.68 \pm .10$ ; and mean STAI-trait score was  $34.4 \pm 8.9$ . Spearman rank correlation coefficients were calculated among WASO, SE, STAI-trait scores and SF-36 subscales.

**Results :** Significant correlations were obtained between STAI-trait scores and the following: WASO ( $r = .29, p < .05$ ), SF-36 Social Function ( $r = -.39, p < .01$ ) and General Health ( $r = -.27, p < .05$ ) subscales. Based on these correlations, regression analyses were conducted. STAI-trait scores, sleep diary WASO, and their interaction were entered as independent variables; SF-36 subscales were dependent variables. The combination of WASO, STAI-trait anxiety, and WASO x STAI-trait interaction contributed significantly to variance in SF-36 Social Function score ( $R^2 = .36, p < .001$ ). Beta weights for WASO and the WASO x STAI-trait interaction each accounted for statistically significant variance in daytime function.

**Conclusion :** Sub-clinical levels of anxiety and self-reported sleep disturbance may interact to impact social functioning. Inclusion of anxiety-reduction components in non-pharmacologic treatments for insomnia in older adults might improve functional outcomes, even in patients with

sub-clinical levels of anxiety.

**Support (optional):** Medical Research Service of the Palo Alto Veterans Affairs Health Care System, Department of Veterans Affairs Sierra-Pacific MIRECC, and AG 12914.

### 0778

#### SUBJECTIVE AND OBJECTIVE MEASURES OF SLEEP AND DAYTIME PERFORMANCE IN PATIENTS WITH PRIMARY INSOMNIA AS COMPARED TO NORMAL CONTROLS

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**Introduction :** Insomnia has as a common ancillary feature the subjective report of memory and concentration problems as well as decreased ability to perform daily activities. While complaints of cognitive impairment are common in this population, few studies have found evidence that insomnia is reliably associated with deficits in daytime functioning.

**Methods :** Subjects ( $n=48$ ; 32 primary insomnia [PI], 17 good sleepers [GS];  $39+/-11$ yo; 35F) were evaluated on self-report measures of daytime performance, a week of sleep diary data, and neuropsychological (NP) test battery results. For this study we analyzed group differences on subjective/objective measures of sleep and daytime performance.

**Results :** PIs reported greater levels of sleepiness on the Epworth (total score,  $p=.031$ ) and more difficulty falling asleep (PSQI-SL,  $p<.001$ ), longer sleep latency ( $p=.033$ ) and greater WASO ( $p=.003$ ) on sleep diaries. Importantly, PIs reported significantly reduced activity levels ( $p<.001$ ), reduced motivation ( $p=.028$ ), and greater mental fatigue ( $p=.030$ ) on the Multidimensional Fatigue Inventory. PIs also reported poorer physical well being ( $p=.046$ ) and worse overall sleep quality ( $p=.008$ ) as measured on their sleep diaries (5-point Likert scale). When tested on a comprehensive NP battery, PIs and GSs were found to perform equally well on all NP measures, except for preservations on the Hopkins Verbal Learning Test ( $p=.015$ ).

**Conclusion :** Overall, patients with primary insomnia report diminished activity levels, greater mental fatigue, and reduced motivation. These complaints do not, however, appear to be paralleled by objectively measured deficits on neuropsychological measures. Provided that the NP measures are ecologically valid, this mismatch suggests that the subjective report of diminished performance may not correspond to “output” so much as it corresponds to “effort”. That is, a consequence of insomnia is that more cognitive effort is expended to accomplish normal levels of performance. Functional imaging of subjects engaged in NP tasks may be useful towards supporting this proposition.

**Support (optional):** NIH RO1 MH59392

### 0779

#### INSOMNIA AND SELF-TREATMENT REGIMENS: NEW PERSPECTIVES FROM MEDICAL ANTHROPOLOGY

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**Introduction :** Medical Anthropology can show how sleep patterns and disorders take place against social as well as physical contexts, during the evaluation of symptoms or symptom severity, the process of seeking help, self-medication, the construction of a home sleep environment, and patient compliance with medically prescribed treatment. This is relative-

ly rare in the field of sleep medicine. We will present data from a qualitative, exploratory anthropological study of a cross-sectional cohort of insomnia patients (n=24).

**Methods :** Patients clinically presenting with chronic insomnia were recruited by physicians at two different locations and offered participation in the study. A medical anthropologist then arranged in-depth, semi-structured, qualitative interview in the patients homes, in order to make observation of the sleeping environment. Interviews were recorded, transcribed, and coded with the qualitative software package Atlas Ti. Content analysis followed standard inductive strategies, allowing emic patterns to emerge from the data independent of predetermined analytical approaches in order to provide an understanding of how participants identify and organize factors related to their insomnia. A content coding system was developed in which words or themes are coded according to their contextual significance. Relationships between categories were examined, as were trends that emerged across sub-groups.

**Results :** Patients' underlying beliefs about the nature of their insomnia and the efficacy of medical treatment had dramatic influences on self-treatment regimens and health-seeking behavior. Insomniacs employed a wide-range of self-treatment strategies, including supplementing medically prescribed medication with personally decided upon alternative therapies and over-the-counter medications (91% reported complementary and alternative therapies; 50% reported supplementing current prescriptions with over-the counter medications). Personalized sleep regimens ranged widely, including some done against medical advice. Observation of the home environment yielded information of clinical relevance to the sleep physician.

**Conclusion :** Given the small proportion of adults estimated with insomnia that currently see a physician for care, the anthropology of insomnia promises to reveal new insight into patient beliefs and behaviors related to problem sleeping.

**Support (optional):**

## 0780

### UNDERSTANDING INSOMNIA FROM THE PATIENT'S PERSPECTIVE: A VIEW FROM MEDICAL ANTHROPOLOGY

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**Introduction :** The elicitation of patient "explanatory models" for chronic illnesses has revealed important insight into socially constructed patient beliefs about illness etiology, expected course, and patient compliance with medically prescribed treatment. Such consideration has not heretofore been given, however, to insomnia. We will present data from a qualitative, exploratory anthropological study of a cross-sectional cohort of insomnia patients.

**Methods :** Patients clinically presenting with chronic insomnia were recruited by physicians at two different locations and offered participation in the study. A medical anthropologist then arranged in-depth, semi-structured, qualitative interviews in the patient homes, in order to make observation of the sleeping environment (n=24). Interviews were recorded, transcribed, and coded with the qualitative software package Atlas Ti. Content analysis followed standard inductive strategies, allowing emic patterns to emerge from the data independent of predetermined analytical approaches in order to provide an understanding of how participants identify and organize factors related to their insomnia. A content coding system was developed in which words or themes are coded according to their contextual significance. Relationships between categories were examined, as were trends that emerged across sub-groups.

**Results :** Only 30% of chronic insomniacs interviewed understood the

chief problem with themselves as insomnia; 70% considered their insomnia to be a secondary symptom of an alternate problem, with a widely diverse etiology ranging from heart problems, depression, work-related stress, hormonal changes, childhood trauma, to supernatural influences. This self-diagnosis impacted health-seeking behavior (66% of the sample was referred to a sleep clinic by either primary care physicians or other specialists), as well as the patient's anticipated course of illness, self-treatment, valuations of the efficacy of their medical treatment, and compliance with medical advice.

**Conclusion :** Eliciting a patient's explanatory model for insomnia can be useful as a window to understanding patient treatment-seeking behavior. Given the small proportion of adults with insomnia that currently see a physician for care, the anthropology of insomnia promises to reveal new insight into patient beliefs and behaviors related to problem sleeping.

**Support (optional):**

## 0781

### THE NATURAL HISTORY OF INSOMNIA IN A POPULATION-BASED SAMPLE

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**Introduction :** The natural history of insomnia is poorly documented. This paper presents preliminary findings from an ongoing longitudinal study examining persistence, remission, and relapse of insomnia in a population-based sample.

**Methods :** Two thousand randomly selected adults from the general population took part in a telephone survey and a sub sample of 700 subjects completed postal evaluations at 0, 6, and 12-month follow ups. Subjects were classified in one of three subgroups using standard diagnostic criteria for insomnia: (a) good sleepers (n = 394); (b) insomnia symptoms (n= 207); and (c) insomnia syndrome (n= 99). The present analyses included subjects (123 men; 183 women, mean age = 45.5 years) who presented insomnia (symptoms or syndrome) at baseline. Rates of persistence, remission, and relapse were computed over a 12-month period. Persistent insomnia was defined as being present at each assessment, remission as a change of status (improvement) at one or more assessments relative to baseline, and relapse as a return to an insomnia status after achieving complete remission.

**Results :** Of the 306 participants with insomnia at baseline, 46.1% continued to report (persistent) insomnia throughout the subsequent 12-month period. The remaining participants experienced either partial (5.6%) or complete remission (48.4%). Of the complete remission group, 30.4% returned to an insomnia symptoms or syndrome status at the 12-month follow-up (relapses). The natural course of insomnia was similar for those with insomnia symptoms and a syndrome at baseline and across genders. Although not statistically significant, the older age group (55+ years) displayed a higher rate (52.6%) of persistent insomnia relative to the rate (37.3%) in younger age group (18-35 years). Remission rate was also lower in the older age group (26.3%) relative to the younger group (43.3%).

**Conclusion :** These results suggest that the natural course of insomnia is quite variable, with nearly equal proportions showing persistence and remission over a one-year period. Additional analyses are planned to examine which factors are associated with new onset, persistence, and with remission or relapse.

**Support (optional):** Research supported by the Canadian Institutes of Health Research (MT42504).

0782

**QUANTITATIVE EEG AND EKG MEASURES SHOW GREATER STABILITY THAN TRADITIONAL POLYSOMNOGRAPHIC (PSG) SLEEP MEASURES IN PRIMARY INSOMNIA (PI)**

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**Introduction :** Traditional PSG measures do not consistently distinguish PI from control subjects, and variability across nights further limits the utility of PSG-defined phenotypes. We collected traditional PSG, quantitative EEG, and quantitative EKG data over three consecutive nights in PI and good sleeper controls (GSC) to examine group differences and night-to-night stability within each domain.

**Methods :** Subjects were 54 volunteers with clinically-defined PI (mean age 34.6, 46F) and 22 GSC (mean age 26.5, 12F). None had current psychiatric or significant medical disorders. PSG and EKG were collected over 3 nights. PSG outcomes included total sleep time (TST), sleep latency (SL), and sleep efficiency (SE). Quantitative EEG outcomes included power in delta (0.5-4 Hz) and beta bands (16-32 Hz) during NREM. Heart rate variability was measured in low (.04-.15 Hz) and high frequency (.15-.4 Hz) bands during NREM; outcome measures were power in high frequency variability (HFV) and the ratio of the low-to-high frequency (LF-HF) variability. ANCOVAs were used to test group differences, covarying for age and sex. Stability of measures across nights 1-2, 2-3, and 1-3 was evaluated with Pearson correlations.

**Results :** PI and GSC differed on PSG, quantitative EEG, and EKG measures in expected directions; after controlling for age and sex, only beta power differed significantly ( $F(3,70)=6.4, p<.01$ ). Quantitative EEG and EKG measures correlated highly across nights in PI: delta power  $r=.82-.94$ ; beta power  $r=.77-.86$ ; HFV power  $r=.89-.94$ ; LF-HF power  $r=.83-.93$  (all  $p<.001$ ). Across-night correlations for PSG measures were lower in PI: TST  $r=.52-.62$ ; SL  $r=.21-.74$ ; SE  $r=.44-.57$ . Correlations were similar for the combined PI-GSC sample.

**Conclusion :** PI and GSC differed on PSG, quantitative EEG and EKG measures, but only beta EEG was significant. Quantitative measures had larger night-to-night correlations than PSG measures, suggesting that they define a more stable electrophysiologic phenotype than traditional PSG measures.

**Support (optional):** Supported by MH24652, AG20677, AG00972, AG019362, RR00056

0783

**PSYCHOSOCIAL FEATURES OF SLEEP STATE MISPERCEPTION IN BRAZILIAN PATIENTS**

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**Introduction :** According to International Classification of Sleep Disorders (ICSD), Sleep State Misperception (SSM) is a disorder in which a complaint of insomnia occurs without objective evidence of sleep disturbance. The present study aims to identify psychosocial features of patients with SSM, investigating their life history, and social-familial environment.

**Methods :** We studied SSM patients from Center for Clinic and Science of Sleep of Departments of Neurology and Internal Medicine of Federal University of São Paulo (UNIFESP), Brazil. They were interviewed following a script of questions about their lives, biographical information, from childhood, exploring their perception about SSM. We provided

analysis of interviews, searching patients perception, feelings, thoughts, and social and familiar insertion.

**Results :** In this study, until now, we identified 60 patients (33 females, 23 to 76 years old) with confirmed SSM diagnosis among 2000 medical files and 1735 PSG studies. We observed that 80% was not native of Sao Paulo City. Preliminary data of 14 interviews reveal similar features of these patients. They reported unsafe and threatened environment, uprooting feelings, complacency and methodical behavior; non-adaptation and isolation, recurrent feelings of loss and grief, and problems of attachment.

**Conclusion :** Psychosocial features of SSM patients are an important information to diagnosis and treatment of this disease.

**Support (optional):**

0784

**OBJECTIVE AND SUBJECTIVE MEASURES OF DAYTIME FUNCTIONING IN LATE-LIFE INSOMNIA**

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**Introduction :** Insomniacs complain of reduced daytime functioning and sleepiness, and in particular the complaint is found in elderly insomniacs. Studies have shown that insomniacs do not differ from normal sleepers on measures of vigilance and sleepiness. The present study aims to investigate whether a group of primary insomniacs screened for other sleep disorders, a group of insomniacs with comorbid symptoms of apnea and periodic leg movement in sleep (PLMS; the sleep disorder group) and a group of healthy elderly with no sleep complaints differ on a subjective and objective measure of daytime functioning.

**Methods :** Forty-eight elderly insomniacs (55+) were compared to a sample of elderly insomniacs who displayed clinical significant symptoms of sleep apnea and PLMS (N=14) and to an age-matched sample who reported no sleep problems (N =20). The samples were compared on an objective measure of vigilance (Vigil 5.0) and on a subjective measure of sleepiness, the Epworth sleepiness scale (ESS). The samples were also asked a question about to which degree they had problems with staying awake during the day.

**Results :** Both the insomnia group and the sleep disorder group reported significantly more problems with staying awake during the day than the normal sleepers. No significant differences were observed between the groups on the ESS. No significant differences were observed on the raw score of reaction time, as measured by Vigil 5.0. However, the insomnia group displayed a larger increase in reaction time when compared to the sleep disorder group.

**Conclusion :** The study supports previous findings that insomniacs self-reported problems of staying awake cannot be accounted for by objective measures of vigilance. The study also indicates that patients displaying symptoms of sleep disorders do not perform worse than normal sleepers or insomniacs on subjective and objective measures of daytime functioning.

**Support (optional):**

0785

**DEXAMETHASONE ATTENUATES EFFECTS OF SLEEP DEPRIVATION ON ALERTNESS IN PRIMARY INSOMNIA**

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**Introduction :** We have proposed that central corticotropin releasing hormone (cCRH) activity is elevated in primary insomnia (PI). One prediction of this model is that manifestations of PI should be alterable by glucocorticoids (GC). Data in animals suggest that, unlike endogenous cortisol, dexamethasone (dex) does not readily reach cCRH neurons, but



rather attenuates feedback inhibition of cCRH neurons by inhibiting GC production exclusively at peripheral sites. The resultant disinhibition of cCRH activity may underlie the alerting effects of dex reported during sleep deprivation. Evidence that this effect is exaggerated in PI would provide important corroboration of a pathogenic role of cCRH in this disorder.

**Methods :** Ten patients with PI (6f, mean age = 35.2) and ten age- and gender-matched controls (mean age 31.9) were studied during two 48-hour laboratory visits separated by 7-14 days. Using a double-blind, cross-over design, participants received either dex 4 mg or placebo at 23:00 on the second night. Subjects were deprived of sleep from 23:00 until 18:00 the following evening. MSLTs were conducted at 2-hour intervals beginning at 10:00 on the first day and continuing throughout the second day until 18:00. Log-transformed MSLTs were analyzed using repeated-measures MANOVA (JMP, SAS Institute, Inc.).

**Results :** As previously reported, dex 4 mg significantly increased sleep latency during sleep deprivation in both groups ( $F=6.48$ ,  $p<0.02$ ), with separation from placebo apparent after 10:00 AM (time x drug,  $F=2.71$ ;  $p<0.01$ ). PI subjects showed significantly greater MSLTs than controls under both conditions ( $F=4.98$ ;  $p<0.04$ ) and a slightly larger drug effect (drug x diagnosis,  $F=1.54$ ,  $p=0.2$ ). Greater baseline MSLT was associated with a larger drug effect for both groups ( $F=4.24$ ,  $p<0.05$ ).

**Conclusion :** Dex attenuates the increase in sleepiness following sleep deprivation in both PI and normals. The effect of dex was most pronounced in those PI subjects with higher baseline MSLTs, suggesting that cCRH may be particularly relevant in patients with PI and physiological hyperarousal.

**Support (optional):** Supported by MH63968 (GSR).

## 0786

### PRIMARY INSOMNIA WITH HYPERAROUSAL IS ASSOCIATED WITH A HISTORY OF CHILDHOOD STRESS

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**Introduction :** A subset of patients with primary insomnia exhibit signs of physiological hyperarousal on a variety of measures including daytime sleep latency, catecholamines, cortisol, basal metabolic rate, and high frequency EEG. We hypothesize that hyperactivity of central stress mechanisms underlie both the insomnia and physiological hyperarousal. While the origins of this increased activity remain unclear, data from animal models and studies in depression suggest that stress during development may be an important risk factor.

**Methods :** 70 adults (35f; mean age = 32.6y) with primary insomnia (PI) and 90 normal sleepers ( were assessed with PSG, MSLT, urine hormone assays, and multiple questionnaire assessments. PI with hyperarousal (PIhyper) was operationally defined as a complaint of insomnia with sleep efficiency <85% and MSLT > 8.0 minutes (population median). 21 subjects met these criteria (6f; mean age = 32.3y).

**Results :** Relative to other subjects with PI, PIhyper showed increased levels of urine epinephrine ( $F=3.74$ ,  $p<0.05$ ). Other endocrine measures did not differ statistically. Subjective estimates of sleep quality were worse in PIhyper, including latency ( $p<0.01$ ) and TST ( $p<0.01$ ). On questionnaire results, the Home Environment Questionnaire (HEQ) assessment of childhood stress history was elevated in PIhyper, both for total score ( $p<0.04$ ) and for the sexual abuse subscale ( $p<0.01$ ).

**Conclusion :** Evidence for hyperarousal in the setting of PI is associated with higher scores on standard assessments of childhood stress exposure. These data are consistent with a model in which stress during development permanently alters central systems regulating sleep and physiological arousal.

**Support (optional):** Supported by MH63968 (GSR).

0787

**SLEEP PARALYSIS IN KOREAN YOUNG ADULTS: KAWINULLIM PHENOMENON**

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**Introduction :** The mythological term Kawinullim in Korea is descriptively and symptomatically identical to sleep paralysis (SP). The etymology of the term Kawinullim derives from Kawi (ghost enters our body during sleep and scares it ) plus nulim (being squeezed or pressed), meaning that scaring ghost enters and squeezes body during sleep. We examined the characteristics of Kawinullim phenomenon that Korean male teenagers have suffered.

**Methods :** 482 Korean male army draftees were selected by simple random selection method and a questionnaire package including Sleep Paralysis Questionnaire, the Epworth Sleepiness Scale (ESS), and questions about sleep-wake schedule were applied. Mean age was 19.2±1.0. Subjects were divided into SP and non-SP experienced groups.

**Results :** Of all subjects, 150 subjects (33.9%) had experienced at least one attack of SP in their lifetime. 147 (98.0%) of SP and 192 (67.4%) of non-SP had admitted to have heard of the term so-called Kawinullim and showed significant difference between them ( $\chi^2=53.6$ ,  $p<0.0001$ ). The peak age of onset was at the range of 14-19 years old (78.4%). SP group was significantly more complaining of daytime sleepiness and was also significantly more complaining of disturbed sleep than non-SP. 14.2% of SP group reported they were under unusual conditions preceding the attacks such as fatigue, psychological pressure, sleep deprivation, stressful event, or alcohol. Most respondents, including SP and non-SP subjects, interpreted the cause of Kawinullim to be associated with physical weakness (43.4%), psychological stress (38.7%), mental illness (9.5%), and irregular sleep habits (8.4%).

**Conclusion :** Our results show that prevalence of SP among Korean male teenagers is high and SP subjects have more sleep-related complaints. Taken into consideration that physical and psychological stress can induce frequent arousal, it seems that both arousals from either physical or psychological stress and the disruption of the usual sleep schedule may predispose such sleep state dissociation.

**Support (optional):**

0788

**TOPIRAMATE THERAPY OF SLEEP RELATED EATING DISORDER (SRED)**

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**Introduction :** The anticonvulsant topiramate is reported to promote weight loss, control binge-eating disorder, and control SRED (2 cases). We now report on 17 consecutive patients treated with topiramate for SRED.

**Methods :** The 17 patients presented clinically over a 2.5 year period; weight gain & non-restorative sleep from SRED were the chief complaints in all pts; some also had major metabolic/dental complications. PSG was completed in 12 pts. Topiramate was prescribed for 9 pts who failed prior therapies for SRED & for 8 pts as first-line therapy. Initial

dose was 25 mg qhs, with weekly 25 mg increases as needed and as tolerated, up to a maximum of 400 mg. Weight loss from control of SRED was a primary outcome measure in these pts.

**Results :** N=6 (35.3%) pts discontinued topiramate due to lack of efficacy (n=4) or side-effects (n=2: pruritis, weight gain). Data on the other n=11 (64.7%) pts are now reported: mean age 45.0 +/-SD 12.8 yrs, range 20-62; females, 9/11; duration of SRED, 3-45 yrs; nightly SRED episodes, 10/11 pts. SRED- induced overweight status, using NIH criteria (>20% in excess of desirable weight): 9/11 pts. Idiopathic SRED: 45.5% (5/11); (presumed) symptomatic SRED, 54.5% (6/11 pts; total of 8 other sleep disorders: RLS/PLMD, n=5; SW, n=1; narcolepsy, n=1; primary insomnia, n=1). Axis I psychiatric disorders, 45.5% (5/11; total of 8 disorders: mood d/o, n=4; chemical dependency, in remission, n=1; anxiety d/o, n=2; paranoid d/o, n=1). When starting topiramate therapy, 8/11 pts were taking other hs medications (total of 13): benzodiazepines/agonists, n=5; dopaminergics, n=3; trazodone, n=3; anti-psychotics, n=2. 4/11 pts were also taking daytime psychotropics. Topiramate treatment data: mean follow-up interval, 1.9 +/-SD 0.9 yrs (range, 6 months-3 yrs); mean dose, 104.5 +/- 52.2 mg qhs (n=3, 50-75 mg; n=6, 100 mg; n=2, 200 mg). All pts reported that SRED episodes were fully/substantially controlled (as noted by pts & spouses/family), sleep became restorative, and meaningful weight loss was achieved. Mean weight loss from controlling SRED (10/11 pts; indeterminate in n=1 pt): 9.4 +/- 5.1 kg (range, 5.9-21.4). Side effects were reported by 3/11 pts: paresthesias, n=2; vitreal floaters, n=1.

**Conclusion :** Topiramate was effective in promoting weight loss & controlling frequent, recurrent episodes of eating in nearly two-thirds of pts with chronic, nightly SRED, in combination with pharmacotherapy of various associated sleep and psychiatric disorders. Topiramate was usually well-tolerated.

**Support (optional):**

0789

**CONFIRMING CLINICAL RBD: COMPARISON OF PATIENTS WITH AND WITHOUT REM SLEEP WITHOUT ATONIA**

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**Introduction :** REM sleep behavior disorder (RBD) is defined as abnormal nocturnal motor behaviors with increased skeletal muscle tone in REM sleep during polysomnography. The condition is associated with neurodegenerative disorders, specifically the synucleinopathies, or may be idiopathic. Polysomnography criteria for diagnosis are not clearly established. Untreated obstructive sleep apnea (OSA) with agitated REM sleep arousals can mimic RBD. The purpose of this study was to examine patients in whom RBD was considered likely based on clinical history, but could not be confirmed on polysomnography. Our hypotheses were that patients with confirmed RBD would have more REM sleep time recorded on polysomnography and be more likely to have coexisting neurodegenerative disorders, whereas those with unconfirmed RBD would have more severe OSA during REM sleep.

**Methods :** We reviewed evaluations of patients diagnosed with clinically probable or definite RBD from 2003-2005. Of 267 patients that met criteria and underwent polysomnography, 33 (12.4%) had normal REM atonia. We matched these patients by age and gender to 33 patients with RBD confirmed on polysomnography.

**Results :** Patients with confirmed RBD were significantly more likely than the unconfirmed patients to have neurological disorders known to be associated with RBD (58% vs 26%, Fishers exact test = 0.01), whereas

patients with unconfirmed RBD had more severe OSA in supine REM (apnea/hypopnea index, 37 vs 17,  $P=0.05$ ). There was no significant difference in mean REM sleep duration (55.5 vs 54.5 minutes).

**Conclusion :** Patients with clinically probable RBD are significantly more likely to have the condition confirmed on polysomnography if they have a neurodegenerative disease. They are significantly less likely to have RBD confirmed if severe OSA during supine REM sleep is present. Their nocturnal motor behaviors likely represent agitated REM sleep related arousals due to OSA. Minutes of REM sleep recorded did not influence the likelihood of confirming RBD.

**Support (optional):**

## 0790

### EEG SYNCHRONIZATION FOR THE DIFFERENTIAL DIAGNOSIS BETWEEN PAROXYSMAL AROUSALS (NOCTURNAL FRONTAL LOBE EPILEPSY) AND CONFUSIONAL AROUSALS (PARASOMNIA)

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**Introduction :** Confusional arousals (CA), paroxysmal arousals (PA), as part of the nocturnal frontal lobe epilepsy (NFLE), and normal arousals and awakenings from NREM sleep are frequently a challenge for their differential diagnosis. Based on recent reports of different patients in whom the analysis of the synchronization between different EEG channels allowed us to clarify the epileptic nature of their nocturnal episodes, the functional interactions between the different EEG channels during the nocturnal seizures were analyzed by means of the so-called Synchronization Likelihood (SL). SL is a measure of the dynamical (linear and nonlinear) interdependencies between a time series (EEG channel) and one or more other time series.

**Methods :** We studied 3 groups of patients including 14 with PA (NFLE), 3 with CA (parasomnia) and 7 cases in whom video-PSG was not able to clarify the nature of their nocturnal attacks. Moreover, also 4 normal controls (aged 20 to 26 years) presenting short arousals/awakenings were included. SL was measured for 5 different EEG bands from 20 s before the onset of the attacks to 60 s after. The first 10 s were used to assess the baseline level of SL, all subsequent values of SL were statistically compared to the baseline.

**Results :** First of all, we detected 4 different attack-related SL patterns: 1 - significant increase of SL in more than 1 EEG band; 2 - significant increase of SL in 1 EEG band; 3 - significant decrease in 1 or more EEG bands; 4 - no significant change of SL. Pattern 1 was exclusively found in patients with PA (n=4); also pattern 2 was almost exclusively found in patients with PA (n=3), but also in 1 subjects with CA; pattern 3 was present in 6 patients with PA, 1 with CA and 3 with doubtful attacks. Finally, pattern 4 was found in the 4 normal controls, in 2 patients with PA, 1 with CA and 4 with doubtful episodes.

**Conclusion :** Clinically similar ictal motor patterns might be generated by different neurophysiological mechanisms, characterised by different patterns of synchronization and involving multiple or single frequency bands. However, the results obtained in our patients with CA and doubtful episodes induce us to use some caution in the interpretation of episodes where we find short significant increases in SL or no significant changes of SL because of the possibility of some confounding conditions. The significant increase or decrease in SL may be more frequent in epileptic seizures than in CA or normal awakenings from NREM sleep.

**Support (optional):**

## 0791

### REM SLEEP BEHAVIOR DISORDER IN PATIENTS WITH PARKINSON'S DISEASE

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**Introduction :** REM sleep behavior disorder (RBD) affects up to one-third of the patients with Parkinson's disease (PD), and may precede parkinsonian motor symptoms. It, however, has not been clearly established that there are any clinical and polysomnographic differences between parkinsonian patients with developed RBD and those without RBD.

**Methods :** Fifty patients with PD (22 males, age  $60.6 \pm 6.35$ , Hoehn and Yahr stage  $2.7 \pm 0.87$ ) were recruited, and history for RBD and related factors were evaluated. Neurological examinations and polysomnographic studies were performed on patients taking routine antiparkinsonian medications. We divided patients into the group with RBD and without RBD, and further the group with clinically overt RBD and subclinical RBD (tonic EMG activities, but no movement during REM sleep). Based on polysomnographic findings, patients with RBD could also be divided into 2 groups. One had loss of atonia during REM sleep and the other additional extra movements. Demographic and clinical characteristics of patients were analyzed between groups to correlate with RBD.

**Results :** Twenty-six patients were suspected of having RBD with clinical interview, and of these, 10 patients reported RBD developed prior to parkinsonian symptoms (mean 7.5 years) and 12 patients had history of injury caused by dream enactments. We could not find significant correlation in clinical, demographic, and polysomnographic characteristics between above groups except age- and education-controlled mini mental status examination (K-MMSE) score, which was significantly decreased in patients with RBD ( $p=0.005$ ). On polysomnography, 12 patients, who had no clinical symptoms, showed tonic EMG activities during REM sleep, but there was no significant difference between these patients with subclinical RBD and patients with clinically overt RBD.

**Conclusion :** Our results confirmed that RBD was prevalent in patients with PD. We also found significantly low K-MMSE scores in patients with RBD compared to those without RBD, and further studies will be needed to clarify the correlation between cognitive dysfunction and RBD.

**Support (optional):**

## 0792

### PHENOMENOLOGY OF SOMNAMBULISM

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**Introduction :** Sleepwalking is a NREM parasomnia characterized by mental disorientation, motor behavior, poor response to stimulation, and variable retrograde amnesia. Somnambulistic actions take many forms, ranging from mundane or stereotyped behaviors to complex activities such as playing a musical instrument or driving a car. Relatively little is known, however, about the phenomenological aspects of this parasomnia.

**Methods :** Participants were 34 adult patients (17 men, 17 women, mean age =  $29.7 \pm 7.9$  years) referred to our sleep disorders clinic for chronic sleepwalking. Twenty-nine patients (85%) reported that their sleepwalking began during childhood or early adolescence while 6 (18%) reported adult onset. All underwent at least one screening night in the laboratory and were free of any other major sleep disorder. Participants completed a

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detailed questionnaire assessing various aspects of their sleepwalking, including history, suspected precipitating factors, nature and frequency of somnambulistic behaviors, and recall of accompanying sleep mentation.

**Results :** Perceptual elements from the sleeper's actual environment during somnambulistic episodes were sometimes (29%), often (35%) or always (12%) recalled by the sleepwalkers. Twenty-five patients (74%) reported that various forms of mental content or sleep mentation (e.g., images, thoughts, emotions) often or always accompanied their episodes. Furthermore, episodes were described by 41% of the sample as being often or always triggered by some form of sleep mentation. Only 5 of the patients (15%) reported that their somnambulistic behaviours were never related to an underlying logic, motivation, or sense of urgency. Emotions were described by 22 sleepwalkers (65%) as being often or always experienced during their episodes. The most commonly reported emotions were fear, panic, confusion, anger, frustration and helplessness.

**Conclusion :** Although sleepwalking is often characterized in terms of its automatic behaviors, the present results suggest that perceptual, cognitive and affective dimensions play an important role in the subjective experience of adult sleepwalking. Morning recall of somnambulistic episodes may also be greater than generally believed. The displayed behaviors are construed by most patients as being motivated by an intrinsic sense of urgency or underlying logic that accounts for their actions during actual episodes.

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### 0793

#### SEXUAL BEHAVIOUR IN SLEEP: AN INTERNET SURVEY

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**Introduction :** Sexual Behaviour in Sleep (SBS, sexsomnia, sleepsex) covers almost all aspect of human sexual behaviour, often presenting in peculiar or bizarre circumstances and occasionally involving minors. Previous studies involved mostly adult males, while anecdotal evidence suggests more even distribution across age groups and genders. The goal of the present study was to test this premise.

**Methods :** A 28-item Internet survey was designed to query potential participants visiting a reference site for SBS ([www.sleepsex.org](http://www.sleepsex.org)). Data were collected for a period of three months (April-June 2005). Upon termination, a total of 226 responses were screened, and n=219 responses were validated and analyzed (152 males, 67 females, mean age 30.4+/-8.87, age range 15-67 years).

**Results :** A total of 186 respondents identified themselves as heterosexual (84.9%), 25 homosexual (11.4%) and 6 bisexual (2.7%). The vast majority (n=202, 92.2%) reported multiple SBS episodes, versus a single episode (n=17, 7.8%). A variety of sexual behaviours were reported, including intercourse in sleep (n=105, 48%), this by both genders (24 females and 81 males). A total of 181 respondents (82.6%) reported exhibiting different behaviours, and 14.6% reported alcohol, 4.3% drugs, 41.1% fatigue, 52.5% stress and 64.4% physical contact as precipitating factors (multiple answers were allowed). Diagnosis of a psychiatric disorder was reported by 32%, physical illness by 16.9%, family history of a sleep disorder by 22.8% and personal history of another sleep disorder by 47% respondents. There were 13 respondents (5.9%, 10 males and 3 females) who reported sexual contact with minors, in majority cases (males only) resulting in legal repercussions.

**Conclusion :** In spite of known limitations of such surveys, the study provides much-needed information regarding the SBS. In contrast to previ-

ous studies, the study shows wider distribution across age groups and genders, report of specific precipitators and smaller involvement of minors as victims of such behaviour.

**Support (optional):**

### 0794

#### EMG VARIANCE DURING POLYSOMNOGRAPHY AS AN ASSESSMENT FOR REM SLEEP BEHAVIOR DISORDER (RBD)

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**Introduction :** Previous work by our group suggested that a quantitative, polysomnographic assessment of RBD severity is both valid and reliable in patients at risk for RBD because of neurodegenerative disorders. As the required visual scoring of surface EMG activity is labor-intensive, we developed a computerized metric to assess digital sleep recordings in these patients. We then compared the performance of this algorithm to results of visual scoring, bed partner-rated RBD symptom-scores, and likelihood of RBD as judged through interviews by board-certified sleep specialists using International Classification of Sleep Disorders criteria.

**Methods :** Subjects included 17 with neurodegenerative disorders and 6 controls as reported previously (reference above). Two consecutive nocturnal polysomnograms for each subject were staged and scored for RBD features as described by Lapierre and Montplaisir. For each polysomnogram, a computer calculated the variance of the chin EMG signal during all 3-second mini-epochs. An upper limit for background activity was defined as four times the 5th percentile of the variance observed during all non-REM epochs. The percentage of REM mini-epochs with mean variance above this threshold was computed as the new metric. A score for each subject was computed as a REM sleep duration-weighted average of results on the two nights.

**Results :** The new variance-based metric correlated well with the visually-derived score for RBD severity (Spearman rho = 0.85, p < 0.0001). A clinical impression of probable or possible RBD (n=9 subjects) was associated to similar extents with both the variance metric (T test, p=0.035) and the visually-derived score (p=0.023). The RBD symptom score also correlated with the variance metric (rho=0.43, p=0.039) about as strongly as it did with the visual score (rho=0.42, p=0.048).

**Conclusion :** These results suggest that a new, automated assessment for RBD may provide as much utility as a more time-consuming manual approach that is subject to interscorer variability.

**Support (optional):**

### 0795

#### A CONTROLLED CLINICAL TRIAL ON MELATONIN IN RBD-PATIENTS

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**Introduction :** REM-sleep behaviour disorder (RBD) is clinically impressive by virtue of its vigorous sleep behaviours, usually accompanying vivid, striking dreams which often result in injuries to the patients themselves or to people sleeping nearby. We earlier reported of good clinical improvement of RBD patients treated with Melatonin in an open-labelled study. The aim of the study was to confirm this finding in a controlled clinical trial.

**Methods :** Eight consecutive male RBD patients with a polysomnographically confirmed diagnosis of RBD (according to ICSD criteria) were included in two consecutive, randomized, double-blind, placebo-controlled, parallel design clinical trials. Patients received 3mg Melatonin

daily, administered between 22.00 and 23.00 hours for four weeks. Three patients suffered from idiopathic RBD, three had concomitant narcolepsy and PLMD, one suffered from Parkinson's disease and two from concomitant idiopathic insomnia. Polysomnographic (PSG) recordings were performed in all patients, at baseline as well as at both endpoints of four weeks' placebo and Melatonin treatment period. Besides R+K scoring, REM-sleep was scored according to the criteria of Lapière and Montplaisir.

**Results :** There was no placebo effect in any of the patients. With melatonin six out of eight patients were clinically much improved according to their own as well as their partners' reports. Whereas most of the general PSG measures were basically unchanged, most REM-sleep parameters were significantly improved with Melatonin. With Melatonin there was a significant reduction of 30-second epochs scored as REM-sleep without muscle atonia, a significant reduction of stage shifts in REM and a significant reduction in epochs considered as movementtime in REM. REM density was basically unchanged.

**Conclusion :** Today, the therapy of choice in RBD is Clonazepam. Clonazepam reduces phasic activity in RBD-patients but does not affect muscle tone. In contrast, Melatonin seems to restore REM-sleep associated muscle atonia in RBD patients and thus may have a more direct impact on the basic mechanism of their disorder than Clonazepam.

**Support (optional):**

### 0796

#### NIGHTMARE FREQUENCY DIMINUTION OVER A SIX-MONTH PERIOD USING A DAILY RECORDED PHONE QUESTIONNAIRE AND COGNITIVE-BEHAVIORAL DRAWING TECHNIQUE: PRELIMINARY RESULTS

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**Introduction :** Major psychological problems and sleep disorders affect nightmare sufferers. However, techniques used to treat this parasomnia are limited in their application. Most imply patient training, a group setting and professional skills. This preliminary study examines the efficacy of a recorded phone questionnaire (RPQ) and a simple cognitive-behavioral drawing technique on nightmare frequency.

**Methods :** 11 subjects (9 women, 2 men;  $M=32.36 \pm 6.55$  years) suffering from at least one weekly nightmare over 6 months completed the study. Subjects were screened by phone, evaluated by a psychologist and randomly assigned to an immediate ( $N=9$ ) or a delayed treatment group ( $N=2$ ). The study lasted respectively 8 and 14 weeks during which patients had to complete a daily RPQ allowing a weekly measure of prospective nightmares. They also drew their nightmares for 6 weeks (treatment period) following mornings with nightmares according to specific instructions. For the present analyses, mean weekly nightmare estimates for all patients together were assessed for four time periods: pre-treatment: 1) questionnaire (Pre-Q); 2) Pre-RPQ; 3) treatment; 4) post-treatment (follow ups at 3 and 6 months) using Friedman non-parametric test.

**Results :** A significant effect was found for time periods ( $X^2(3)=21.29$ ;  $p<0.0001$ ). Wilcoxon post-hoc tests revealed differences between all times ( $p<0.03$ ) except the two pre-treatment measures ( $p=0.29$ ). Weekly nightmare frequencies decreased from pre-treatment (combined  $M=2.44$ ;  $SD=1.56$ ; Range=0.67 to 6.18) to treatment ( $M=1.10$ ;  $SD=1.31$ ; Range=0 to 3.80) and again post-treatment (combined  $M=0.56$ ;  $SD=0.97$ ; Range=0 to 3.36).

**Conclusion :** Although sample size is modest, preliminary results support the efficacy of both the RPQ and drawing techniques in treating night-

mares, with nightmare frequency decreasing from 2.6/week to about 0.5/week at six-month follow up. Both techniques are economical, applied in the home and require minimal interventions by a therapist.

**Support (optional):** Research supported by the Canadian Institutes of Health Research (CIHR) and the Fonds de la recherche en sante du Quebec (FRSQ)

### 0797

#### EARLY-ONSET IDIOPATHIC RAPID EYE MOVEMENT SLEEP DISORDER (RBD): ASSOCIATIONS WITH SECONDARY FACTORS

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**Introduction :** RBD in young patients has been associated with medications and other factors, but these associations have never been investigated systematically.

**Methods :** We reviewed the records of consecutive patients diagnosed with RBD between 2002 and 2005. After extracting those without neurodegenerative disorders at the time of diagnosis, we compared patients with an age at diagnosis < 50 years to a group of age and gender matched patients without RBD (all with diagnoses of OSA), investigating for numerous associations. Data were abstracted, and Fisher's exact and Wilcoxon rank sums tests were used for statistical analyses.

**Results :** Twenty-two early-onset idiopathic RBD patients were identified (mean age at diagnosis =  $35.13 \pm 11.44$ , 10 females) and were age- and gender-matched with 22 non-RBD controls (mean age =  $35.63 \pm 11.26$ , 10 females). Younger RBD patients had a significantly higher frequency of psychiatric diagnoses (77% versus 18%), and antidepressant use (86% versus 27%) compared to the non-RBD controls. There were no significant intergroup differences with respect to other assessed variables.

**Conclusion :** This study demonstrated a higher occurrence of psychiatric diagnoses and antidepressant use in the early onset RBD group as compared to non-RBD controls. As this is a retrospective study, direct causality cannot be inferred. It remains unclear as to whether RBD in young patients may be caused by antidepressants or psychiatric disease, whether similar underlying factors may predispose to both conditions, or whether psychiatric disease is a consequence of RBD. It also remains uncertain as to whether the underlying pathophysiology of RBD differs depending on the age of presentation, and whether the younger cohort possesses the same risk of developing a neurodegenerative disorder as their older counterparts.

**Support (optional):** Piscopo Funds (Mayo Foundation)

### 0798

#### IDENTIFICATION OF RESTLESS LEGS SYNDROME DURING POLYSOMNOGRAPHY

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**Introduction :** Restless Legs Syndrome (RLS) is primarily a clinical diagnosis as defined by the International Restless Legs Syndrome Study Group. It is estimated that the prevalence of RLS is 5%. Although scoring guidelines have been established for Periodic Limb Movements (PLM), none exist for RLS. We hypothesize that a restless leg syndrome index (RLSI) can be developed for polysomnography (PSG) to help identify

## Category L—Sleep Disorders-Parasomnias

patients who may have undiagnosed RLS.

**Methods :** A case control study was designed to review 23 consecutive polysomnograms performed at Tampa General Hospital from January-April 2005. A screening question that conformed to the general clinical definition for RLS was utilized to assign cases and controls. Cases were selected if patients' responses conformed to the general clinical definition for RLS; controls were respondents answering "no" to this screening question. The interpreter was blinded to scoring leg movements awake or asleep. Leg movement was defined using AASM practice parameter criteria. The PLM index was also recorded for each case.

**Results :** The RLSI was reported as the ratio of leg movements from Lights Out on the PSG to Lights On divided by total awake time. Group 1 subjects (cases, N=11) were defined as those who answered "yes" to the screening question for RLS, whereas Group 2 (controls, N=12) were subjects who responded "no" to the same question. Comorbid obstructive sleep apnea was noted in 7 and 10, Group 1 and 2 patients respectively. The mean RLSI for Group 1 was 48/hr. The mean RLSI for Group 2 was 34/hr. There was a correlation between RLSI and respondents answering "yes" to the screening question for restless legs syndrome ( $p = 0.09$ ). There was also a correlation between RLSI and PLM index ( $p=0.015$ ).

**Conclusion :** Undiagnosed RLS may be identified in the sleep laboratory using subjective criteria (questionnaires) and possibly confirmed by objective criteria (RLSI). Further studies are needed to correlate the RLSI with outcomes, in a larger group of unselected patients.

**Support (optional):**

### 0799

#### CARDIAC AUTONOMIC REGULATION DURING SLEEP IN SUBJECTS WITH REM SLEEP BEHAVIOUR DISORDERS

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**Introduction :** REM behaviour sleep disorders (RBD) is a parasomnia characterized by abnormal motor activity associated with dream mentation. Previous studies showed a reduced heart rate response to motor activity during NREM and REM sleep, suggesting an autonomic nervous system dysfunction in patients with idiopathic RBD. The current study aimed to assess the cardiac autonomic changes from stage 2 NREM (NREM) to REM sleep by spectral analysis of heart rate variability in subjects with idiopathic RBD compared controls.

**Methods :** Eight subjects with idiopathic RBD (2 females, age  $63 \pm 7$  years) and 8 sex and age matched controls were studied. One night polysomnography was used to assess R-R variability during NREM and REM sleep. Time domain variables (mean RR, standard deviation of RR, sdRR) and frequency domain variables (low frequency and high frequency components in normalized units, LFn and HFn; LF/HF ratio) were obtained from 5-minute ECG segments selected during NREM and REM sleep, while in stable conditions (stable breathing pattern, no micro-arousals or leg movements). Values obtained were then averaged for each stage and analysed by 2x2 ANOVA with group (RBD and controls) as factor and state (NREM and REM) as repeated measures.

**Results :** RR interval decreased from NREM to REM in both groups (state effect  $p=0.02$ , no group by state interaction). No changes were observed in sdRR. LFn increased significantly (~11%) in controls but not in RBD (~1%) (State effect  $p=0.01$ , interaction  $p= 0.1$ ). HFn decreased

significantly (~13%) in controls and a little (~2%) in RBD (state effect  $p=0.06$ , interaction,  $p=0.1$ ). Finally, LF/HF increased markedly from NREM to REM in controls while remained stable in RBD (interaction  $p=0.01$ ).

**Conclusion :** REM-related sympathetic response and parasympathetic withdrawal are blunted in subjects with idiopathic RBD. These findings further support the hypothesis of a presence of autonomic dysfunction in this condition.

**Support (optional):**

### 0800

#### IDIOPATHIC REM SLEEP BEHAVIOR DISORDER - A FOLLOW UP OF 39 PATIENTS

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**Introduction :** REM sleep behavior disorder (RBD) is characterized by loss of normal skeletal muscle atonia associated with excessive nocturnal motor behaviors that commonly occurs in association with vivid, distinctly altered dreams. It occurs most commonly in a chronic form that is either idiopathic or associated with neurologic, most often neurodegenerative disorders, such as the synucleinopathies of Parkinson's disease, multiple system atrophy, or dementia with Lewy bodies. Schenck et al have reported subsequent development of a parkinsonian disorder or dementia in 65% of patients with idiopathic RBD (Sleep 2003;26:A316). We aimed to identify the percentage of patients with idiopathic RBD who subsequently develop a neurodegenerative disorder.

**Methods :** With approval of the institutional IRB, questionnaires were mailed to 39 patients diagnosed with idiopathic RBD at the Mayo Clinic Sleep Disorders Center between 1988 and 1995. If the patient was deceased, the questionnaire was mailed to surviving relatives.

**Results :** The mean follow-up period was 11.2 years. The response rate was 59%, 12 patients or relatives could not be located. Of the 27 patients who returned the questionnaire, 23 agreed to participate in the study. Five patients had developed a neurodegenerative disorder (22%). Those included Parkinson's disease (1 patient), and dementia (4 patients, with 3 of the 4 patients carrying the diagnosis of dementia with Lewy bodies). Ten other patients (43%) reported developing neurological symptoms highly suggestive of parkinsonism and/or dementia.

**Conclusion :** Of 23 patients with idiopathic RBD 15 (65%) developed a physician-diagnosed neurodegenerative disorder or symptoms highly suggestive of a parkinsonian or dementing disorder at a mean follow up of 11.2 years. Our findings confirm previous reports that patients with idiopathic RBD frequently develop neurodegenerative disorders. It can be speculated that chronic idiopathic RBD represents an evolving neurodegenerative disorder in a significant percentage of patients, which usually is a synucleinopathy.

**Support (optional):**

0801

**EFFICACY OF IRON IN PATIENTS WITH RESTLESS LEGS SYNDROME AND A LOW-NORMAL FERRITIN: A RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY. JAMES Y WANG, MD(ASSOCIATE); VINCENT MYSLIWIEC, MD; COLLIN FISCHER, MD; PATRICIA DEHAAN, MD; DAVID OWSHALIMPUR MD; ANGELA MYSLIWIEC, MD. MADIGAN ARMY MEDICAL CENTER, TACOMA, WA**

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**Introduction :** The prevalence of RLS is increased in conditions associated with iron deficiency such as pregnancy and end stage renal disease. Prior studies have shown a relationship between serum ferritin and RLS symptom severity, and improvements have been described treating RLS patients with ferritins in the “low-normal” range (15-75mcg/l). To this date there has not been a placebo-controlled study of oral iron replacement in symptomatic RLS patients with low-normal ferritin levels using a validated RLS symptom scale. The purpose of this study was to determine if these patients truly benefit from iron replacement.

**Methods :** This was a prospective, randomized, placebo-controlled, double blinded study. Patients attending routine outpatient visits to the internal medicine, pulmonology, hematology/oncology, neurology, and family practice clinics were asked to complete a survey and give consent to be contacted if they met study eligibility. Patients meeting diagnostic criteria for RLS and with a score of at least 11 using the validated scale developed by the IRLSSG(International Restless Legs Syndrome Study Group) were contacted and a CBC, iron panel, and ferritin were drawn. Subjects with a ferritin of 15-75mcg/l and no recent iron replacement were then randomized to iron(ferrous sulfate 325mg PO BID) or placebo. Patients were followed at 6 and 12 weeks with a repeat RLS severity survey, CBC, ferritin, and iron panel.

**Results :** Interim evaluation was performed on 373 completed and reviewed RLS surveys. 42% met diagnostic criteria for RLS. The mean RLS severity score in these patients was 20.2 +/- 9.0. Of the 38 subjects who consented to participate in the study, 17 met all inclusion criteria and were enrolled. 8 patients have completed the study to date (4 placebo, 4 on iron supplementation). Mean baseline RLS scores for iron and placebo groups were 27.3 +/- 6.2 and 22 +/- 4.2, and mean baseline ferritin was 45.4 +/- 18.3 and 44.2 +/- 21.9(ng/ml), respectively (p= NS for all). Mean change in ferritin after 12 weeks was 43.5 +/- 17 and 3.6 +/- 17.7(ng/ml) for iron and placebo groups (p=.02). No significant change in RLS score was observed between groups although subjects on iron replacement were more likely to report improvement in the general quality of their lives.

**Conclusion :** Preliminary data analysis suggests that treating RLS patients with low-normal ferritin with PO iron may improve RLS symptoms and overall quality of life. This study is ongoing.

**Support (optional):**

0802

**AN EXPLORATORY TRIAL OF ISTRADefylline FOR THE TREATMENT OF RESTLESS LEGS SYNDROME**

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**Introduction :** Studies of istradefylline (KW6002), an adenosine A2a receptor antagonist, have provided evidence in favor of its potential as a novel, non-dopaminergic anti-parkinson's drug. In light of the proven efficacy of anti-parkinson's drugs in Restless Legs Syndrome (RLS), we

sought to explore whether this non-dopaminergic drug having anti-parkinsonian effects might also benefit patients with RLS.

**Methods :** We performed a short-term polysomnographic, open-label trial in 5 patients with moderate to severe idiopathic RLS.

**Results :** A single daily dose of 80 mg istradefylline for up to 6 weeks resulted in a reduction of either the motor or sensory component of the disorder in 4 of 5 subjects as measured by the International RLS Study Group Severity Scale (IRLSRS), periodic leg movements index, (PLMI), PLM arousal index, Visual Analog Scale, or Clinicians Global Impression. Only one of the five subjects clearly failed to exhibit a response to any of the parameters tested. Two of five subjects experienced unequivocal reductions in either PLMI, or IRLSRS only to experience worsening in either variable when study drug was withdrawn. Two subjects reported a treatment-emergent increase in insomnia.

**Conclusion :** In this small exploratory trial, istradefylline appears to provide a reduction of both the motor and sensory component of RLS. A larger controlled clinical trial is underway.

**Support (optional):** Kyowa Pharmaceutical Inc.

0803

**EVOLUTION OF SLEEP DISTURBANCES IN MULTIPLE SYSTEM ATROPHY (MSA)**

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**Introduction :** The aim of this study was to evaluate the evolution of sleep dysfunction in comparison with the disease progression in multiple system atrophy (MSA) by means of the Parkinson's disease sleep scale (PDSS) and a range of additional scales.

**Methods :** The PDSS is a visual analogue scale addressing 15 commonly reported features associated with sleep disturbances with a resulting maximum cumulative score of 150 (best state). The following scales were applied in addition: Unified MSA Rating Scale (UMSARS) part I and the Schwab & England Activities of Daily Living (ADL) scale (both for ADL), UMSARS part II (for motor performance), as well as UMSARS part IV and Hoehn & Yahr (H&Y) Staging (both for global disability).

**Results :** 17 MSA patients diagnosed according to published clinical diagnostic criteria were analysed. Mean interval between baseline and follow up was 7.0 (SD: 1.0) months. Median disease duration was 4.2 (range: 3.1 to 6.3) years. The mean total PDSS score at baseline was 103.1 (SD: 30.4) and at follow up 107.5 (SD: 28.7). As compared to published controls, the baseline total PDSS scores (p=0.030) and the baseline PDSS items 8 (getting up to pass urine (p= 0.040), 9 (urinary incontinence due to the inability to move) (p= 0.002), 11 (painful muscle cramps at night) (p= 0.028) and 13 (tremor on walking) (p= 0.034) were found to be lower in MSA. Although there was no significant change in the PDSS total score (or its single items) between baseline and follow up, we found a deterioration in the UMSARS II (24.8 [SD: 8.3] vs. 33.6 [SD: 10.1], p= 0.003), UMSARS I (26.9 [SD: 8.2] vs. 31.9 [SD: 8.5], p= 0.0001), S&E ADL (42.9 [range: 30.7 to 62.5] vs. 33.3 [range: 19.0 to 61.3], p= 0.025), UMSARS IV (3.3 [range: 2.3 to 4.3] vs. 4.0 [range: 3.1 to 4.8], p= 0.034) and H&Y staging (3.5 [range: 2.7 to 4.4] vs. 4.3 [range: 3.4 to 5.0], p= 0.014).

**Conclusion :** This study confirms that sleep disturbances, in particular nocturia and nocturnal motor symptoms, are common in MSA. Although the motor, functional and global status deteriorated during this short follow up period, there was no change in the PDSS scores. Despite the known progression of sleep disturbances in objective measures, the relative non-progressiveness as shown in this study could be due to the fact that the PDSS assesses self perceived sleep dysfunction. Also the respon-

## Category M—Sleep Disorders-Movement Disorders

siveness to change of the PDSS in MSA is not established yet and further studies with longer follow ups are certainly warranted.

**Support (optional):**

### 0804

#### EFFICACY AND TOLERABILITY OF LEVETIRACETAM IN THE TREATMENT OF RESTLESS LEGS SYNDROME: A DOUBLE-BLIND PLACEBO CONTROLLED CROSSOVER TRIAL

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**Introduction :** Restless Legs Syndrome (RLS) is a sensory-motor neurological disorder characterized by a compelling urge to move, which is present with immobility, improved with movement and worse at night. Dopaminergic agonists are considered first line treatments, though anti-convulsant medications such as gabapentin and clonazepam are also widely employed. We assessed the therapeutic value of levetiracetam (Keppra®), currently approved for the treatment of refractory partial seizures, in the treatment of RLS in a single site, randomized placebo-controlled crossover trial, employing both subjective and objective measurements.

**Methods :** 20 subjects (15 female and 5 male) with primary RLS, an IRLSSG severity score greater than 15, and with a PLMS index > 15 at baseline were randomized to either levetiracetam or placebo for six weeks of treatment, followed by a one week washout, and then by the opposite treatment for six weeks. Levetiracetam was begun at 500 mg 1-3 hours before bed, and increased by 500 mg per week as tolerated up to a maximum of 1500 mg per day. Polysomnography was performed at the beginning and end of each treatment period (weeks 0, 6, 7, 12). The primary outcome variables were the IRLSSG severity score and the Clinical Global Impression of Improvement (CGI-I). Secondary variables included polysomnographic measures of sleep quantity and quality and periodic leg movements of sleep (PLMS).

**Results :** Mean IRLS severity scores at baseline were 18.5 and 18.8 for placebo and levetiracetam, respectively. There was no difference in the change in IRLSSG scores between levetiracetam (1.89) and placebo groups (3.94). Clinician based ratings were also not different between the two groups. Levetiracetam did not improve polysomnographic recorded sleep parameters. Adverse events were more common with levetiracetam, with somnolence, mood changes, and dizziness occurring in at least 20% of subjects.

**Conclusion :** Levetiracetam does not appear to have a beneficial therapeutic effect on the symptoms of RLS, as measured by subjective or objective measures.

**Support (optional):** Support for this study was provided by UCB Pharma.

### 0805

#### EVENT-RELATED POTENTIALS IN RESTLESS LEGS SYNDROME AND PARKINSON'S DISEASE

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**Introduction :** Restless legs syndrome (RLS) may be a condition of impaired CNS dopamine function. Certain dopamine deficiency states are associated with bradykinesia and impaired attention (eg Parkinson's disease [PD] and attention deficit disorder [ADD]), and dopamine restoration or excess associated with normal or excessive movement and with

improved attention (eg treatment of PD with L-DOPA and ADD with amphetamine). RLS symptoms are decreased by movement, especially by walking. Some patients also report that increased mental activity, focused concentration, or being distracted decrease RLS. The P3a and P3b event-related brain potential (ERP) components were used to assess frontal attention engagement (P3a) and temporal-parietal memory storage (P3b) cognitive operations in unaffected controls (CN), patients with RLS, and patients with PD.

**Methods :** Subjects (n=7/group) were matched on age (63.2 years), education (15.0 years), and balanced for gender (~F=30%, ~M=70%). Patients had mild to moderate PD or RLS and were not on CNS medications. Reliable daytime P3a (distracter) and P3b (target) components were elicited using a visual ERP task, with 275 stimuli presented on a gray computer screen at 2 second intervals. Subjects were instructed to ignore the distracter (15 cm square checkerboard, P=0.15), press a button in response to occurrence of the target (5 cm diameter circle, P=0.15), and ignore the standard (4.5 cm circle, P=0.70).

**Results :** Task performance was comparable across subject groups. P3a amplitude was significantly different (P<0.02) among the groups, with CN>RLS>PD. P3b amplitude did not differ reliably among groups (P>0.30) but the CN and RLS subjects yielded similar amplitudes compared to the low amplitude PD subjects.

**Conclusion :** P3a amplitude variation suggests that relative to unaffected CN subjects, RLS patients demonstrate somewhat impaired, and PD patients strongly impaired, frontal dopamine-mediated attention mechanisms. P3b amplitude variation suggests that CN and RLS subjects reflect no impairment, whereas PD subjects may reflect deficits for memory storage.

**Support (optional):** This work was supported by the Scripps Clinic Brain Research and Treatment Center and NIH Grant RO1-DA018262. We thank Maya Cano for her superlative research assistance.

### 0806

#### THE DRLS: A NEW 24-HOUR RATING SCALE FOR RESTLESS LEGS SYNDROME

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**Introduction :** Recent studies on RLS have utilized the IRLSSG scale (IRLS) to rate RLS severity. The IRLS is a research tool for global impressions of the syndrome. It was the goal of this project to develop a clinically relevant scale for RLS similar to the ESS while also developing a tool to reveal augmentation. A new scale, Dallas Restless Legs Scale (DRLS), is compared to the IRLS.

**Methods :** Treated patients completed the IRLS and DRLS to assess the urge to move in 8 situations during three time periods (04:01-14:00, 14:01-20:00, and 20:01-04:00). The patient rates "0"=no chance to "3"=high chance of having an urge to move over 60 minutes ("sitting and reading," "watching television," "sitting in a public place," "as a passenger in a car"), 30 minutes ("sitting with arms relaxed at sides", "lying down to rest or relax"), and also "trying to sleep or nap" and "sitting in the center seat on an airplane." The scale tallies each time period, and final score sums the 3 period scores. Regression analysis was then performed to assess time period and final scores against the IRLS.

**Results :** 71 patients (F=59%, mean age 61.3) completed both scales. 64 reported moderate to good response to RLS therapy. IRLS mean score: 14.67+SD 9.35 (range: 0-38). DRLS results and regression analysis to IRLS are below. DRLS Mean + SD Range Correlation to IRLS P value 04:01-14:00 5.89+0.83 0-24 r=0.3036 p<.01 14:01-20:00 10.31+0.87 0-24 r=0.3922 p<.001 20:01-04:00 11.43+0.96 0-24 r=0.5288 p<.001



TOTAL 27.62±2.23 0-72 r=0.4916 p<.001

**Conclusion :** The DRLS correlates well with the IRLS but is simpler to administer, provides temporal information, and addresses situations that impact a patient's quality of life. Further study is ongoing with controls, polysomnographic data, and longitudinal assessment.

**Support (optional):** NONE

## 0807

### CAN THE DYSESTHESIAS OF RESTLESS LEGS SYNDROME BE MEASURED ON INSTRUMENTS FOR PAIN?

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**Introduction :** The sensations of Restless Legs Syndrome (RLS) are described as paraesthesias and dysesthesias, sensations which also occur in neuropathic pain. Whether descriptors of pain can be used to measure the quality and severity of RLS sensations is not known.

**Methods :** Subjects with RLS (n=25) completed the RLS severity scale of the International Restless Legs Syndrome Study Group (IRLSSG), the John Hopkins severity scale for RLS, the McGill Pain Questionnaire (MPQ) and visual analogue scales (VAS) assessing current and lifelong pain. Words chosen from the MPQ were used to calculate indices of severity including the pain rating index (PRI) and number of words chosen (NWC). Words chosen frequently were also compared to those describing nociceptive and neuropathic pain types.

**Results :** There were no gender differences in RLS severity measures or severity indices from the MPQ. There were also no significant correlations between the severity measures for RLS or pain and duration or age of onset of RLS. IRLSSG RLS severity scale scores correlated significantly with the John Hopkins scale as well as with the PRI, the NWC, but not with either VAS estimate of pain intensity. The most common words chosen from the MPQ by RLS subjects were “tingling” and “nagging” (56% of subjects) and “annoying” and “tiring” (48% of subjects). There were similarities between these words and those chosen by patients with neuropathic pain.

**Conclusion :** The quality and severity of the sensation of RLS can be measured on the MPQ, and severity calculated from MPQ indices correlates significantly with a standard RLS severity measure. RLS may comprise a mild type of neuropathic pain and have similar neurological origins.

**Support (optional):** Wits Dial.a.Bed Sleep Laboratory

## 0808

### CORTICAL AND AUTONOMIC ACTIVITIES PRECEDING PERIODIC LIMB MOVEMENT IN SLEEP

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**Introduction :** Periodic limb movements in sleep (PLMs) are frequently associated with excessive daytime sleepiness (EDS). However, recent studies have reported that PLMs alone are not the cause of EDS. Other conditions underlying PLMs may produce EDS. In particular, cerebral and autonomic activities preceding the onset of the PLMs could be related to this underlying condition.

**Methods :** 12 cases of PLMs without other sleep disorders or systemic diseases were collected. These cases were arbitrarily divided into 4 types according to inter-PLM interval. Type I had a PLM interval less than 20 seconds. Type II had an interval between 20-30 seconds. Type III had an interval more than 30 seconds. Type IV presented with a period of time free of PLM prior to clustered PLMs. The cortical activities were evaluated with FFT spectral analysis. The autonomic activities were evaluated with an analysis of the R-R interval in heart rate variation (HRv).

**Results :** Evaluation of autonomic activities with HRv showed a strong, progressive elevation of sympathetic excitation at least 3 beats prior to the onset of PLMs. The analysis of HRv between 3 and 10 beats prior to the onset of PLMs revealed no significant change in type I and II, was fairly steady in type III, and demonstrated an oscillation pattern in type IV. Evaluation of cerebral EEG activities captured strong beta activity 2-3 seconds prior to the onset of the PLM in type I, and sigma band in type II, III, and IV.

**Conclusion :** These results demonstrate the activation of cerebral sigma EEG band and autonomic excitation approximately 3 seconds prior to the onset of PLM. These findings are compatible with activation of certain subcortical activities prior to the onset of PLM. Subcortical activation may be related to the cause of PLMs and subsequent EDS.

**Support (optional):**

## 0809

### ROPINIROLE IMPROVES RESTLESS LEGS SYNDROME (RLS) SYMPTOMS IN PATIENTS WITH RLS AND A HISTORY OF PERIODIC LIMB MOVEMENTS IN SLEEP (PLMS)

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**Introduction :** Restless Legs Syndrome (RLS), a chronic neurological disorder, may result in sleep disturbance; approximately 80% of patients experience periodic limb movements in sleep (PLMS). Requip® (ropinirole), a dopamine agonist approved to treat moderate-to-severe primary RLS, has been shown to significantly reduce PLMS, as measured using polysomnography and actigraphy. The efficacy of ropinirole was assessed in patients with a self-reported history of PLMS.

**Methods :** Three 12-week, double-blind studies (TREAT RLS 1, 2, and US) included adults aged 18 years or older with moderate-to-severe primary RLS. Patients were randomized to ropinirole (n=465), 0.25-4.0mg/day, titrated as needed and tolerated, or placebo (n=469), once-daily 1-3 hours before bedtime, for 12 weeks. Efficacy was assessed (post-hoc) in patients with a history of PLMS using mean change from baseline in the International Restless Legs Scale (IRLS) total score (primary endpoint) and the proportion of patients classified as responders (much/very much improved) on the Clinical Global Impression-Improvement (CGI-I) scale, at Week 12, using pooled data from the three studies.

**Results :** 214 patients taking ropinirole and 225 taking placebo (~50% of the total study population) reported a history of PLMS; treatment groups were well matched for demographic and baseline characteristics. At Week 12, a statistically significant treatment difference was observed in favor of ropinirole on the IRLS (last observation carried forward; adjusted mean treatment difference: -3.0; 95%CI: -4.7, -1.4; p<0.001). Similarly, significantly more patients receiving ropinirole compared with placebo were classified as CGI-I responders (61% versus 45%; adjusted odds ratio: 2.1; 95%CI: 1.4, 3.1; p<0.001). Statistically significant differences in favor of ropinirole were apparent on both scales at each visit, beginning as early as within 2 nights of treatment.

**Conclusion :** Ropinirole provides symptom relief in patients with moderate-to-severe RLS who have a history of PLMS, a common characteristic

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of RLS.

**Support (optional):** Study supported by GlaxoSmithKline Research and Development.

### 0810

#### ROPINIROLE IS EFFECTIVE IN PATIENTS WITH MODERATE-TO-SEVERE PRIMARY RESTLESS LEGS SYNDROME (RLS) IRRESPECTIVE OF FAMILY HISTORY OF RLS OR PERIODIC LEG MOVEMENTS IN SLEEP (PLMS)

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**Introduction :** Restless Legs Syndrome (RLS) is a chronic neurological disorder characterized by an irresistible urge to move the legs. Two phenotypes are hypothesized: early-onset (<45 years), which is slowly progressive and often familial, and late-onset, non-familial with more rapid symptom progression. Underlying pathophysiologies may differ between these phenotypes, as may treatment response. This analysis of data from three large clinical trials (protocols: 101468/190, 194, and 249) assessed the efficacy of ropinirole, a dopamine agonist, in patients with moderate-to-severe primary RLS with/without a family history of RLS or periodic leg movements in sleep (PLMS).

**Methods :** Patients with primary RLS and a baseline International Restless Legs Scale (IRLS) total score  $\geq 15$  were randomized to ropinirole, 0.25-4.0 mg titrated as needed and tolerated, or placebo once daily for 12 weeks. Family history (first-degree relative) of RLS/PLMS was reported at screening. Efficacy was determined by change in IRLS total score (primary endpoint) and proportion of responders (“much improved” or “very much improved”) on the Clinical Global Impression - Improvement (CGI-I) scale (key secondary endpoint).

**Results :** A total of 402/934 patients randomized reported a family history of RLS/PLMS (ropinirole=206; placebo=196). In this post-hoc analysis, mean improvements from baseline in IRLS total score at each assessment point, from within 2 nights up to and including Week 12, were statistically significantly greater for patients receiving ropinirole than for those receiving placebo (e.g. Week 12 last observation carried forward adjusted mean treatment difference: -4.3; 95% CI: -6.0, -2.6;  $p < 0.001$ ). The proportions of CGI-I responders were also statistically significantly higher for ropinirole patients at all assessment points. Similar findings were evident for the patient subgroup with no family history of RLS/PLMS.

**Conclusion :** Ropinirole is effective for the treatment of moderate-to-severe primary RLS, irrespective of a family history of RLS/PLMS.

**Support (optional):** Study supported by GlaxoSmithKline Research and Development.

### 0811

#### EFFECT OF ROPINIROLE TREATMENT ON SEXUAL INTEREST AND ACTIVITY IN PATIENTS WITH RESTLESS LEGS SYNDROME (RLS)

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**Introduction :** Restless Legs Syndrome (RLS) is a chronic neurological disorder characterized by an irresistible urge to move the legs. RLS has been associated with anxious and depressed mood and a reduced libido. This analysis examined the effect of Requip® (ropinirole, a dopamine agonist, FDA-approved for moderate-to-severe primary RLS) on sexual interest and activity among patients with moderate-to-severe primary

RLS.

**Methods :** Analyses were performed on pooled data from three 12-week pivotal studies (TREAT RLS 1, 2, and US). Patients were randomized to ropinirole (n=465), 0.25-4.0 mg/day, titrated as needed and tolerated, or placebo (n=469), once daily, 1-3 hours before bedtime. Changes in sexual interest and activity were assessed by post-hoc analyses using Questions 11 (level of interest in sexual activity) and 12 (level of disturbance or reduction in sexual activities) of the RLS Quality of Life (RLSQoL) questionnaire (rated from “none” to “a lot”).

**Results :** The intention-to-treat population comprised 930 patients (ropinirole=464, placebo=466); 59% of the ropinirole group and 64% of the placebo group were women. Mean (SD) ages were 53.5 (11.8) years and 54.5 (12.2) years. At baseline, the distribution of responses for those answering Question 11 (ropinirole=419, placebo=419) and 12 (ropinirole=417, placebo=414) were similar. Among those responding at Week 12 (ropinirole=397, placebo=402), there was no difference in patients’ reported interest in sexual activity ( $p=0.942$ ). In addition, a statistically significantly greater proportion of ropinirole-treated patients compared with placebo-treated patients reported that their RLS did not reduce or disturb their sexual activities (Question 12) ( $p=0.04$ ; 74% [294/396] and 68% [274/401], respectively; odds ratio=1.4; 95%CI: 1.0, 1.9) at Week 12.

**Conclusion :** The percentage of patients reporting that RLS disturbed or reduced sexual activity was significantly less for ropinirole- than placebo-treated groups.

**Support (optional):** Study supported by GlaxoSmithKline Research and Development.

### 0812

#### ROPINIROLE IMPROVES OBJECTIVE MOTOR SYMPTOMS OF RESTLESS LEGS SYNDROME (RLS) THROUGHOUT THE NIGHT

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**Introduction :** Restless Legs Syndrome (RLS) is characterized by sensory and motor symptoms, including periodic limb movements during sleep (PLMS) that cause sleep disturbance in approximately 80% of patients. The dopamine agonist ropinirole (Requip®) is the only FDA-approved treatment for moderate-to-severe primary RLS. This study evaluated response of actigraphically defined PLMS in patients with symptom onset earlier in the evening.

**Methods :** The 12-week, double-blind, flexible-dose study 101468/100013 involved patients with primary RLS, a baseline International Restless Legs Scale total score of  $\geq 20$ , and symptom onset no earlier than 5pm. Patients were randomized to ropinirole (n=176), 0.5-6.0 mg/day, or placebo (n=187), in divided doses; the first taken 1 hour before usual symptom onset and the second within 3-8 hours of the first. Leg movements were measured objectively via actigraphy, during the last 3 consecutive nights prior to baseline and Week 12. Changes from baseline in PLMS/hour of sleep (Periodic Limb Movement Index, PLMI) at Week 12 were examined in the actigraphy population (ropinirole, n=69; placebo, n=80) - patients with average  $\geq 10$  PLMs/hour (PLM when supine throughout night) in at least one leg during the 3-night pre-baseline assessment.

**Results :** Week 12 (observed cases) PLMI was analyzed in 66/69 patients receiving ropinirole and 71/80 receiving placebo. There was a statistically significantly greater improvement in PLMI (adjusted mean treatment difference: -14.2; 95%CI: -18.8, -9.6;  $p < 0.001$ ) with ropinirole over placebo. Even though PLMI was higher in the first half of the night com-

pared with the second half, there was a statistically significant improvement with ropinirole over placebo during both halves of the night ( $p < 0.001$ ).

**Conclusion :** Throughout the entire night, ropinirole reduces leg movements during sleep in patients with RLS.

**Support (optional):** Study supported by GlaxoSmithKline Research and Development.

### 0813

#### ROPINIROLE REDUCES SLEEP DISTURBANCE IN PATIENTS WITH PRIMARY RESTLESS LEGS SYNDROME (RLS) WHO REPORT AN INSUFFICIENT AMOUNT OF SLEEP

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**Introduction :** Sleep disturbances are the primary presenting complaint among patients with Restless Legs Syndrome (RLS). RLS often results in sleep disturbances, reducing the amount of restful sleep. This analysis examined the efficacy of ropinirole in patients with RLS reporting impaired sleep at baseline.

**Methods :** Data were pooled from three 12-week pivotal trials of patients with moderate-to-severe primary RLS (TREAT RLS 1, 2, and US; protocols 101468/190, 194, and 249, respectively). Patients were randomized to ropinirole, 0.25-4.0 mg/day titrated as needed and tolerated, or placebo, once daily, 1-3 hours before bedtime. This post-hoc analysis included patients responding at baseline on the Medical Outcomes Study (MOS) Sleep Scale Question 12: "getting the required amount of sleep you need" as "a little" or "none" of the time. The primary endpoint for each study was the mean change from baseline in International Restless Legs Scale (IRLS) total score at Week 12 (last observation carried forward). The proportion of patients classed as responders (much or very much improved) on the Clinical Global Impression-Improvement (CGI-I) scale was a secondary endpoint.

**Results :** At baseline, 502/930 (54%) patients reported impaired sleep on MOS Question 12. At Week 12, there was a statistically significant treatment difference in this group in favor of ropinirole for mean change from baseline in IRLS total score, compared with placebo (adjusted mean treatment difference: -3.6; 95%CI: -5.2, -1.9;  $p < 0.001$ ). In addition, the proportion of CGI-I responders was significantly greater in the ropinirole treatment group compared with placebo at Week 12 (61% [150/246] versus 43% [109/254], respectively; odds ratio: 2.2; 95%CI: 1.5, 3.1;  $p < 0.001$ ).

**Conclusion :** In patients with primary RLS who report not getting their required amount of sleep, ropinirole (the only FDA-approved treatment for moderate-to-severe primary RLS) improves RLS symptoms, compared with placebo.

**Support (optional):** Study supported by GlaxoSmithKline Research and Development.

### 0814

#### RAPID ONSET OF CLINICIAN- AND PATIENT-ASSESSED EFFICACY WITH ROPINIROLE IN PATIENTS WITH RESTLESS LEGS SYNDROME REQUIRING EXTENDED TREATMENT COVERAGE

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**Introduction :** Restless Legs Syndrome (RLS) is a chronic neurological

disorder characterized by an irresistible urge to move the legs. Requip® (ropinirole), a dopamine agonist, taken once daily, 1-3hrs before bedtime, is the only FDA-approved treatment for moderate-to-severe primary RLS. Some patients, with onset of symptoms in the late afternoon/early evening, may benefit from extended treatment coverage. A recent study has examined the efficacy, including the rapidity of clinician- and patient-assessed symptom relief in such a population.

**Methods :** This was a 12-week multicenter, double-blind, placebo-controlled, flexible-dose study (protocol 101468/100013). Patients with primary RLS, a baseline International Restless Legs Scale (IRLS) total score of  $\geq 20$ , and symptom onset no earlier than 5:00pm were randomized to ropinirole ( $n=176$ ), 0.5-6.0 mg/day in divided doses, or placebo ( $n=187$ ). First dose was 1hr before usual onset of symptoms and second dose was 3-8hrs after the first. Efficacy was assessed via change in IRLS total score and the proportion of patients classed as responders (much/very much improved) on the Clinical Global Impression-Improvement (CGI-I) and Patient Global Improvement (PGI) scales.

**Results :** Mean IRLS total score at baseline was 26.0 in both treatment groups. At Day 3 (observed case), improvement in IRLS total score was statistically significantly greater in the ropinirole group compared with placebo (mean treatment difference: -2.8; 95%CI: -4.5,-1.2;  $p < 0.001$ ), as was the proportion of CGI-I scale responders (odds ratio: 2.6; 95%CI: 1.5,4.4;  $p < 0.001$ ). At Days 1-7, the proportions of PGI scale responders were significantly greater among ropinirole- vs. placebo-treated patients ( $p \leq 0.016$ ). Ropinirole also demonstrated statistically significant benefits on each of these measures at all assessments through Week 12.

**Conclusion :** Ropinirole provides rapid RLS symptom relief, as assessed by both clinicians and patients. Efficacy was sustained through the end of the 12-week study.

**Support (optional):** Study supported by GlaxoSmithKline Research and Development.

### 0815

#### ROPINIROLE PROVIDES EARLY AND SUSTAINED REDUCTION IN SYMPTOM SEVERITY IN PRIMARY MODERATE-TO-SEVERE RESTLESS LEGS SYNDROME (RLS)

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**Introduction :** Restless Legs Syndrome (RLS) often causes sleep disturbance, leading to reduced quality of life. Overall reduction in severity of illness is therefore key to successful treatment. This analysis investigates the effects of treatment on symptom severity in patients with moderate-to-severe primary RLS.

**Methods :** Pooled data were analyzed from three 12-week pivotal studies: TREAT RLS 1, 2, and US (protocols: 101468/190, 194, and 249, respectively). Patients with moderate-to-severe primary RLS were given ropinirole ( $n=465$ ), 0.25-4.0 mg, titrated as needed and tolerated, or placebo ( $n=469$ ) once daily. The proportions of patients with a score of 1 (normal, not at all ill) or 2 (borderline ill) on the Clinical Global Impression - Severity of Illness (CGI-S) scale were analyzed post hoc, as were patient responses to International Restless Legs Scale (IRLS) Items 6 ("severity of RLS as a whole") and 8 ("average severity of symptoms judged by duration per day"), each rated on a scale from "none" to "very severe" (0-4).

**Results :** At Weeks 1 (the earliest common assessment for IRLS and CGI-S) through 12, a statistically significantly greater proportion of ropinirole-treated patients, compared with placebo, were rated normal or borderline ill on the CGI-S scale ( $p < 0.001$ ). Additionally, an analysis of patients with moderate or greater responses on IRLS Item 6 and/or 8 at baseline was performed at Week 12. For Item 6, more ropinirole patients (64%) report-

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ed an overall RLS severity of “none”/“mild” versus placebo (48%) ( $p<0.001$ ). For Item 8, more ropinirole patients (51%) reported an average RLS symptom severity as judged by duration per day of “none” or “mild” versus placebo (40%) ( $p<0.001$ ).

**Conclusion :** Ropinirole treatment for RLS reduced severity of illness (on both global and disease-specific measures) as early as within 1 week, with efficacy sustained throughout the study.

**Support (optional):** Study supported by GlaxoSmithKline Research and Development.

### 0816

#### POSITIVE RESPONSE TO ROPINIROLE TREATMENT FOR INDIVIDUAL INTERNATIONAL RESTLESS LEGS SCALE ITEMS AND OVERALL RESTLESS LEGS SYNDROME (RLS) SEVERITY: RESULTS FROM PLACEBO-CONTROLLED TRIALS

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**Introduction :** The International Restless Legs Scale (IRLS), a validated tool for assessing symptom severity in Restless Legs Syndrome (RLS), comprises ten items scored 0-4, indicating increasing severity. A positive relationship has been reported between response on individual IRLS items and IRLS total score (measure of overall severity), but this has not been investigated in a double-blind, placebo-controlled study.

**Methods :** An analysis of changes in individual IRLS items at Week 12 last observation carried forward (LOCF) was performed post hoc on pooled data from three 12-week studies (TREAT RLS 1, 2, and US) of Requip® (ropinirole) in patients with moderate-to-severe primary RLS. Primary endpoint was change from baseline in IRLS total score at Week 12 LOCF. Patients with a baseline IRLS total score  $\geq 15$  were randomized to receive ropinirole, 0.25-4.0 mg/day titrated as needed and tolerated, or placebo, once daily, 1-3 hours before bedtime.

**Results :** At baseline, mean (SD) IRLS total scores were 23.2 (5.6) for the ropinirole group ( $n=464$ ) and 23.6 (5.5) for placebo ( $n=465$ ). At Week 12 LOCF, adjusted mean (2SE) changes from baseline in IRLS total score were -11.9 (0.8) and -8.7 (0.8), respectively (adjusted mean treatment difference: -3.2; 95%CI: -4.3, -2.1;  $p<0.001$ ). For each individual IRLS item, ropinirole-treated patients had less severe symptoms at Week 12 LOCF, compared with placebo ( $p<0.040$ - $<0.001$  for all items). For each item, among those with moderate-to-very-severe symptoms at baseline (score 2-4), a greater proportion receiving ropinirole had mild or no symptoms (score 0-1) at Week 12 LOCF, compared with placebo. The greatest treatment difference for change from baseline was seen for item 4 (sleep disturbance).

**Conclusion :** Each individual item of the IRLS (especially sleep disturbance) showed statistically significant treatment differences in favor of ropinirole in patients with moderate-to-severe primary RLS.

**Support (optional):** Study supported by GlaxoSmithKline Research and Development.

### 0817

#### ROPINIROLE IMPROVES MOOD AND SYMPTOMS OF ANXIETY AND DEPRESSION IN PATIENTS WITH RESTLESS LEGS SYNDROME (RLS) REQUIRING EXTENDED TREATMENT

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**Introduction :** RLS can impact negatively on patients' mood and is associated with anxiety; improvements in both have been shown following once-daily ropinirole treatment for RLS. The effect of ropinirole, a dopamine agonist, on mood disturbance, anxiety, and depression was studied in patients with RLS requiring extended treatment coverage.

**Methods :** In this 12-week, flexible-dose study (protocol: 101468/100013), patients with primary RLS, International Restless Legs Scale (IRLS) total score  $\geq 20$ , Insomnia Severity Index  $\geq 15$ , and symptom onset no earlier than 5PM were randomized to placebo ( $n=187$ ) or ropinirole ( $n=176$ ), 0.5-6 mg/day in divided doses (first dose 1 hour before usual symptom onset and the second dose 3-8 hours later). The primary endpoint was change from baseline at Week 12 last observation carried forward (LOCF) on the IRLS. Secondary efficacy assessments included the Profile of Mood State (POMS) and Hospital Anxiety and Depression Scale (HADS).

**Results :** At Week 12 LOCF, improvement in IRLS total score was significantly greater for ropinirole compared with placebo (adjusted mean treatment difference [AMTD]: -4.1; 95%CI: -6.1, -2.1;  $p<0.001$ ). In addition, there was a significantly greater reduction in POMS Total Mood Disturbance with ropinirole than placebo (AMTD: -6.3; 95%CI: -12.0, -0.5;  $p=0.032$ ). A significant treatment difference in favor of ropinirole was also seen for change from baseline in the HADS anxiety (AMTD: -0.9; 95%CI: -1.5, -0.3;  $p=0.003$ ) and depression scores (AMTD: -0.8; 95%CI: -1.4, -0.2;  $p=0.006$ ).

**Conclusion :** Ropinirole improves RLS symptoms in patients requiring extended treatment. In addition, mood disturbance and symptoms of anxiety and depression are reduced.

**Support (optional):** Study supported by GlaxoSmithKline Research and Development.

### 0818

#### XP13512 IMPROVES SYMPTOMS AND SLEEP DISTURBANCE IN RLS PATIENTS: RESULTS OF A 2-WEEK, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CROSS-OVER POLYSOMNOGRAPHY TRIAL

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**Introduction :** Gabapentin has been reported to improve symptoms and sleep disturbance in RLS but suffers from sub-optimal pharmacokinetics. XP13512 is a prodrug of gabapentin in sustained-release formulation that provides dose-proportional exposure to gabapentin for an extended period after oral dosing. Therefore, this study was conducted to compare the efficacy and safety of XP13512 with placebo over 2 weeks as a treatment of patients with RLS.

**Methods :** Study XP021 is a multi-center, randomized, double-blind, placebo-controlled, cross-over Phase 2a trial of XP13512. 36 patients were treated for 2 weeks with placebo or 1800 mg of XP13512 (600 mg at 5PM; 1200 mg 1 hour before bed) with a one week wash-out between treatments. The primary endpoint was the change from baseline in International Restless Legs Scale (IRLS) total score at week 2. Secondary endpoints included: the change in IRLS total score at week 1; patient and investigator Clinical Global Impression (CGI) of Change and subjective measures of sleep at the end of 2 weeks. Polysomnography (PSG) and

Suggested Immobilization Tests (SIT) were conducted at baseline and at the end of each treatment period.

**Results :** Compared to placebo, treatment with XP13512 significantly improved IRLS score at the end of 2 weeks (-12.1 vs. -1.9;), IRLS score at the end of 1 week (-11.7 vs. 3.7;), both patient and investigator CGI, overall quality of sleep, the number of awakenings per night due to RLS symptoms and the number of hours awake per night due to RLS symptoms (all  $p < 0.0001$ ). XP13512 treatment led to significant reductions in Leg Discomfort Score during SIT. Compared to placebo, XP13512 treatment statistically significantly increased PSG-determined total sleep time (+25.2 min;  $p = 0.0317$ ), Stage 3/4 sleep (+21.3 min;  $p = 0.0002$ ) and reduced the time awake after persistent sleep onset (-28.2 min;  $p = 0.0009$ ). XP13512 reduced the number of periodic limb movements with arousals (PLMA) (46.3 for placebo; 29.3 for XP13512;  $p = 0.0082$ ) and awakenings (5.9 for placebo, 3.8 for XP13512;  $p = 0.0172$ ). XP13512 was generally well tolerated. The most common side effects were somnolence and dizziness.

**Conclusion :** In this exploratory study of 2 weeks duration, XP13512 was effective in reducing symptoms and sleep disturbances in RLS patients.

**Support (optional):** Xenoport, Inc.

## 0819

### EFFECT OF SELECTIVE HISTAMINE H3 RECEPTOR ANTAGONISM ON PERIODIC LIMB MOVEMENTS IN THE RAT

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**Introduction :** Histamine mechanisms have been implicated in the control of sleep and motor activity. Allen et al. (2005) showed that RLS patients treated with a histamine H1 receptor blocker exhibit increased numbers of PLM episodes. The histamine H3 receptor, which regulates the release and synthesis of histamine, has been proposed as a novel therapeutic target for sleep disorders, but the effects of its modulation in sleep-related motor disorders have not been studied.

**Methods :** Male Sprague-Dawley rats, aged 12-22 months, were used for the experiment ( $n = 8$ ). Chronic EEG and EMG electrodes were implanted to monitor their behavioral states and muscle activity in hind limbs. The histamine H3 antagonist thioperamide and H3 agonist  $\alpha$ -methylhistamine were administered at 10 mg/kg intraperitoneally (i.p.) during the light period (ZT2 or ZT8) of LD 12:12, and the effects were compared with the injections of control vehicle at the same circadian time. Sleep was scored visually in 10-sec epochs for the 8-hour post-injection period; PLM was scored according to criteria defined by International Classification of Sleep Disorders for humans.

**Results :** Spontaneous PLM episodes in sleep were seen in 4 of 8 aged rats under baseline conditions. Among the animals displaying PLM, average PLM index (PLMI) was 5.7 counts per hour of NREM sleep with control injections ( $n = 7$ ). Thioperamide decreased (PLMI = 2.9,  $n = 4$ ) while  $\alpha$ -methylhistamine increased PLM episodes (PLMI = 12.3,  $n = 3$ ) ( $p = 0.05$ , ANOVA). Thioperamide also increases wakefulness by about 30% at the expense of NREM sleep, and  $\alpha$ -methylhistamine produced the opposite effect and suppressed REM sleep by 22%. The effects on sleep are consistent with those previously reported in the literature.

**Conclusion :** The selective histamine H3 antagonist thioperamide suppressed periodic limb movements during sleep in rats. This finding is relevant to the development of treatments for PLM-related disorders in humans.

**Support (optional):**

## 0820

### A SINGLE QUESTION FOR THE RAPID SCREENING OF RESTLESS LEGS SYNDROME IN THE NEUROLOGICAL CLINICAL PRACTICE

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**Introduction :** Restless legs syndrome (RLS) is a sensory-motor disorder characterized by discomfort of and urge to move the legs, primarily during rest or inactivity, partial or total relief with movement, with presence or worsening exclusively in the evening. RLS is a relatively common but often unrecognized disorder. The aim of this study was to assess the specificity and sensitivity of a single question "When you try to relax in the evening or sleep at night, do you ever have unpleasant, restless feelings in your legs that can be relieved by walking or movement?" for the detection of RLS in a group of adult-elderly patients with a range of clinical conditions in the field of neurology.

**Methods :** We evaluated a group of 413 consecutive subjects (202 F, mean age 61.9 y and 211 M, mean age 60.3 years) who accessed our neurology clinics. Patients with dementia or other types of disease affecting their capabilities to understand our simple battery of tests and questions were discarded. The following items were collected, beside the answer to the single question: 1) the four criteria for RLS set by the International RLS Study Group, 2) the Epworth Sleepiness Scale, 3) the Clinical Global Impression of Severity, and 4) the Mini-Mental State evaluation. For patients diagnosed to be affected by RLS, also the International RLS Study Group Rating Scale was obtained.

**Results :** 84 patients were affected by RLS: 48 F and 36 M, mean age 60.7 years, range 26-88. RLS was idiopathic in 53 patients and secondary/associated in the remaining 31 subjects (diabetes, OSAS, extrapyramidal disease, hemiparesis, narcolepsy, etc). All patients with RLS answered "yes" to the single question, together with other 14 subjects not affected by RLS. These results indicate a sensitivity of 100% and a specificity of 95.7% of the single question for the detection of RLS. NonRLS subjects who answered "yes" to the single question were: 1 normal control (2.6%), 5 OSAS (5.0%), 4 depressed (12.5%), 1 NFLE (25.0%), 1 RBD (14.3%), 1 insomniac (5.9%), and 1 with cerebrovascular disease (5.3%).

**Conclusion :** The screening of RLS can be simple and reliable by means of our single question. However, the positive answer in some subjects without diagnosis of RLS and with other diseases (false positives) suggests that in these cases the single question needs to be followed by the application of the International criteria for RLS; on the contrary, no further work is needed in those who answer "no".

**Support (optional):**

## 0821

### PARKINSONS DISEASE AND SLEEP DYSFUNCTION

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**Introduction :** Sleep related problems in Parkinsons patients include difficulty initiating sleep, fragmented sleep, nocturnal akinesia, painful cramps, obstructive sleep apnea, REM sleep behavior disorder, frequent awakenings and urinary bladder problems.

**Methods :** Patients with Idiopathic Parkinsons disease (29;13 M and 16 F) were divided into two groups i.e. with disease duration up to 3 years

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and greater than 3 years. The Epworth Sleepiness scale (ESS), Scopa Sleepiness Scale (SSS) evaluating daytime sleepiness (DS-SSS) and nighttime sleep problem (NS-SSS), and the Pittsburgh Sleep Quality Index (PSQI) were done on all patients. The spouses served as controls and filled the scales. Polysomnogram (PSG) with MSLT in 5 patients and actigraphy in 4 patients were performed.

**Results :** SSS, ESS and PSQI scores were higher in patients than controls ( $p<0.05$ ) indicating disruption of sleep quality and excessive daytime sleepiness. NS-SSS was higher in group 2 compared to group 1 ( $p<0.05$ ) indicating a greater night time sleep dysfunction as the disease progressed. 7 patients and 1 control had history suggestive of REM sleep behavior disorder and 8 patients and 1 control had symptoms suggestive of restless legs syndrome. 2 patients had sleep apnea on PSG. Actigraphic recording showed disruption of sleep wake schedule with daytime sleepiness and prolonged awakenings across the night which correlated with the duration of the disease.

**Conclusion :** Patients with Parkinsons disease present a significant deterioration in sleep quality as the disease progresses.

**Support (optional):**

### 0822

#### MOTOR PATTERN OF PERIODIC LIMB MOVEMENTS IN SLEEP AND WAKEFULNESS

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**Introduction :** There have been scattered reports of motor patterns and morphology of PLMS but no generally accepted standardized and validated criteria for PLMS and PLMW emerged.

**Methods :** We analyzed electromyographic (EMG) characteristics recorded during polysomnography (PSG) in 14 patients with restless legs syndrome (RLS). We recorded EMGs of right and left tibialis anterior and gastrocnemius, masseter, submental, sternocleidomastoideus, biceps, triceps, rectus abdominis, lumbar paraspinal and quadriceps muscles. We counted the first 100 EMG bursts during sleep and wakefulness if there are at least 4 consecutive bursts with an interval of 4 -90 seconds even if the amplitude is less than 25% of the calibration signal and the duration is beyond 0.5 to 5 seconds.

**Results :** We found myoclonic, polymyoclonic and dystonic patterns of morphology. The burst duration ranged from very short (0.1 to < 0.5 sec) to very long (> 5 to 15 secs). Most common is the intermediate duration (1-3 secs) and PLMW frequently showed very long duration bursts. The bursts are symmetrical, asymmetrical, synchronous, asynchronous or alternating between two sides and sometimes multiple. Agonist and antagonist muscle bursts are mostly synchronous but occasionally asynchronous and rarely alternating. Tibialis anterior muscle bursts are most frequent showing the highest amplitude but occasionally gastrocnemius or quadriceps bursts are frequent with the highest amplitude. Sometimes tibialis or gastrocnemius muscles had low amplitude bursts synchronous with others. Occasionally periodic muscle bursts were seen in the submental, masseter or trunk muscles synchronously with the leg muscle bursts.

**Conclusion :** The pattern of inconsistent and variable recruitment and independent occurrence of bursts in arms or legs or even occasionally in cranially innervated muscles suggest presence of multiple or independent oscillators for the origin of PLMS and PLMW.

**Support (optional):**

### 0823

#### HEART RATE RESPONSE TO RESPIRATORY EVENTS WITH OR WITHOUT LEG MOVEMENTS

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**Introduction :** The aim of this protocol was to examine the effects of leg movement (LM) on heart rate (HR) response to the termination of apnea/hypopnea.

**Methods :** Twenty-one patients with obstructive sleep apnea who had respiratory event (RE) both with and without associated LMs were selected. HR was measured for 15 R-R intervals before (T-15 to T-1) and after (T+1 to T+15) the termination of RE as a change from the baseline rate, defined as the average of 10 R-R intervals occurring before the termination of each RE (T-15 to T-6). Individual HR changes of the 21 patients were then averaged separately, for 10 RE with, and 10 without, associated LM.

**Results :** Maximal HR rise for RE with LM (7.9 beats/min) was significantly greater than for RE without LM (5.1 beats/min) ( $p<0.0001$ ). The area under the curve for heart rate increase from T-5 to T+9 was 50.1% higher for RE with LM than without LM. When REs with and without accompanying LMs were compared, there were no significant differences in mean duration of RE, mean post-RE oxygen desaturation, mean duration of EEG arousal following RE, or mean HR during the baseline period. HR rise did correlate with duration of the LM ( $p<0.001$ ) in those RE with LM. The odds ratio of having a HR greater than 71.8 (mean HR for RE with LM at T+4) was 3.95 (95% CI: 2.54-6.16) for RE with LM compared to RE without LM, when potential confounding variables were added to a multivariate regression.

**Conclusion :** Cardiac activation is significantly greater when the termination of RE is associated with LM compared to those without LM. This exaggerated HR response may be a consequence of the LM itself, as other features of the REs and associated arousal were not different in the two conditions.

**Support (optional):**

### 0824

#### IMPROVEMENTS IN SYMPTOM-RELATED SLEEP DISTURBANCE DURING ROPINIROLE TREATMENT IN PATIENTS WITH RESTLESS LEGS SYNDROME (RLS)

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**Introduction :** Restless Legs Syndrome (RLS) is a neurological disorder, the symptoms of which often result in impaired sleep. Effective RLS symptom relief may reduce sleep disruption. This analysis evaluated changes in overall symptom severity and measures of sleep disturbance in patients with RLS treated with Requip® (ropinirole), a dopamine agonist.

**Methods :** Pooled data from three 12-week pivotal trials (TREAT RLS 1, 2, and US) were analyzed. Patients with moderate-to-severe primary RLS were randomized to ropinirole (n=465), 0.25-4.0 mg/day titrated as needed and tolerated, or placebo (n=469), once daily, 1-3 hours before bedtime. Symptom severity was assessed via International Restless Legs Scale (IRLS) total score (primary endpoint for each study). Sleep impairment was assessed using the Medical Outcomes Study (MOS) Sleep Scale (secondary endpoint) and post hoc analyses of responses to IRLS Items 4 'sleep disturbance' and 5 'daytime tiredness or sleepiness' (0-4, none-very severe).

**Results :** At Week 12 last observation carried forward (LOCF), there was a statistically significant treatment difference in favor of ropinirole, com-

pared with placebo, for change from baseline in IRLS total score (treatment difference: 3.2; 95%CI: 4.3, 2.1;  $p < 0.001$ ). Patients receiving ropinirole also had significantly greater improvements in MOS Sleep Scale domains relating to Sleep Disturbance, Sleep Adequacy, Sleep Quantity, and Daytime Somnolence at Week 12 LOCF ( $p < 0.001$  for each). Among patients reporting at least moderate baseline sleep disturbance (IRLS Item 4), ropinirole-treated patients had significantly less severe sleep disturbance at Week 12 LOCF, vs. placebo ( $p < 0.001$ ). Among patients reporting at least moderate baseline daytime tiredness (IRLS Item 5), those receiving ropinirole had significantly less severe daytime tiredness at Week 12 LOCF, vs. placebo ( $p < 0.001$ ).

**Conclusion :** Ropinirole treatment reduces RLS symptom severity and is associated with improvements in sleep measures in patients with primary RLS.

**Support (optional):** Study supported by GlaxoSmithKline Research and Development.

## 0825

### EFFECTS OF PRAMIPEXOLE ON SUBJECTIVE MEASURES OF SLEEP QUALITY AND SYMPTOM SEVERITY IN PATIENTS WITH RESTLESS LEGS SYNDROME

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**Introduction :** Patients with restless legs syndrome (RLS) frequently present with sleep problems related to their symptoms. Pramipexole, a D2/D3 dopamine agonist, improves polysomnographic measures of sleep disturbance in RLS. The objective of this study was to evaluate the effects of pramipexole on subjective measures of sleep quality and symptom severity in patients with moderate to severe RLS.

**Methods :** Data were collected as part of a 12-week, multicenter, double-blind, randomized, placebo-controlled trial of fixed doses of pramipexole (0.25 mg, 0.50 mg, and 0.75 mg) in 344 patients; data from 338 patients were included in the analysis. Subjective ratings of sleep quality and symptom severity were assessed with four 100-mm visual analogue scales regarding the severity of RLS symptoms while trying to get to sleep, during the night, and during the day, in addition to satisfaction with sleep. The change from baseline to the end of the study (last observation carried forward [LOCF]) was analyzed by an analysis of covariance model, with factors treatment and center, and baseline as covariate.

**Results :** Pramipexole reduced symptom severity more than placebo (adjusted mean) while getting to sleep (pramipexole: -43.1 mm vs placebo: -29.0 mm;  $P = .0001$ ), in the course of the night (-41.3 vs -24.6;  $P < .0001$ ), and during the day (-16.0 vs -9.2;  $P = .0081$ ) relative to baseline. Patients in the pramipexole group also reported significantly improved satisfaction with sleep relative to baseline (-38.4 vs -25.8;  $P = .0016$ ). The fact that pramipexole reduced daytime RLS symptoms is particularly noteworthy, given that symptoms often occur at a low rate during the day.

**Conclusion :** Pramipexole significantly improved RLS symptoms while getting to sleep, during the night, and during the day, and it substantially improved satisfaction with sleep in patients with moderate to severe disease.

**Support (optional):**

## 0826

### RESTLESS LEGS SYNDROME AND PERIODIC LIMB MOVEMENTS OF SLEEP IN PREGNANT WOMEN

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**Introduction :** Restless legs syndrome has been reported to be common during pregnancy. However, few studies have examined characteristics of RLS in pregnancy or determined whether women with RLS are likely to have periodic limb movements during sleep.

**Methods :** We recruited 126 pregnant women from the obstetrics practices at our institution. Each woman completed a 4-item questionnaire about the presence and frequency of symptoms of restless legs syndrome and underwent full overnight polysomnography (PSG) during the first trimester. 84 women have also completed questionnaires and PSGs during the third trimester (31-39 weeks). Comparisons were made using unpaired t-tests, chi-squared or Fisher's exact tests and logistic regression as appropriate.

**Results :** Mean subject age was 27.3 (7.2) years. 76% of subjects were African-American. 40% of subjects were primigravidas. In the first trimester, the prevalence of RLS (symptoms  $\geq 2$ -4x/month) was 20.6%, increasing to 31.0% by the third trimester with a trend towards statistical significance ( $p = 0.09$ ). Mean periodic limb movement index (PLMI) increased significantly from the first to third trimester (1.4/hr v. 3.1/hr,  $p = 0.03$ ). The proportion of subjects with PLMI  $\geq 15$ /hr increased significantly from the first to the third trimesters (PLMI: 4.8% v. 14.3%,  $p = 0.02$ ); however, subjects with a PLM Arousal Index (PLMAI)  $\geq 15$ /hr did not increase significantly (2.4% v. 6.0%,  $p = 0.12$ ). We did not observe a significant relationship between the presence of RLS symptoms and either the PLMI or PLMAI. In bivariate analyses (controlled for pregnancy trimester), age, Epworth Sleepiness Score, daytime naps and marital status showed trends towards prediction of RLS symptoms ( $p < 0.10$ ). Primiparity, nocturnal sleep time, race, tobacco/alcohol use and use of multivitamins/iron were not predictive of RLS.

**Conclusion :** The prevalence of restless legs syndrome increased in our subjects with advancing pregnancy. Only a small proportion of women were noted to have periodic limb movements. The presence of PLMS did not correlate with RLS symptoms.

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## 0827

### CEREBROSPINAL FLUID MINUS SERUM MAGNESIUM DIFFERENCES ARE GREATER IN RESTLESS LEGS SYNDROME PATIENTS THAN CONTROLS

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**Introduction :** Cerebrospinal fluid (CSF) levels of Magnesium (Mg) have not been previously studied in Restless Legs Syndrome (RLS). Previous studies have shown that serum Mg is low in patients with RLS.

**Methods :** Eleven patients with idiopathic RLS (9 F, 2M, 56.8 yrs) and 9 controls (6F, 3M, 58.7 yrs) were tapered off all medications that might affect RLS for one week and then serum and CSF were drawn simultaneously between 6:00 and 8:00 pm. Analysis was performed in a blinded

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fashion.

**Results :** The mean CSF Mg levels are higher in RLS patients than controls (2.87 vs. 2.60 mg/dL). However, consistent with previous literature, serum levels of Mg are lower in RLS patients than controls (2.11 vs 2.22 mg/dL). The CSF-serum difference for Mg is thus significantly greater for RLS patients than controls ( $p < .05$ ). There is a positive correlation for CSF and serum Mg for controls ( $r = + 6.75$ ,  $p < .05$ ), whereas there is no meaningful correlation for RLS patients ( $r = -.086$ ,  $p = 0.8$ ). Results were similar when the familial RLS patients were analyzed separately.

**Conclusion :** These results suggest increased active transport from serum to CSF in RLS patients as compared to controls and that the transport is not done in a linear fashion in RLS patients as opposed to the linear transport in controls. Previous studies have implicated iron, dopamine and endogenous opioid deficiencies as pathogenetic in RLS. The known interaction of Mg with the iron transport system and with dopamine and opioid receptors is a possible way that Mg may modulate the symptoms of RLS.

**Support (optional):** This research was supported by the German Restless Legs Syndrome patient support group, the German Federal Ministry of Education and Research and the Department of Pathology and Laboratory Medicine, University of Louisville, KY.

### 0828

#### RESTLESS LEGS SYNDROME IN SCLERODERMA PATIENTS

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**Introduction :** Restless Legs Syndrome (RLS) is a neurological disorder associated to dopamine and iron metabolism problems. The patients have unpleasant sensations in the lower limbs with dysesthesia resulting in an urge to move the legs, mostly at night. Scleroderma is a rare progressive systemic sclerosis of unknown etiology, characterized by endothelial lesions and fibrosis of the skin and other organs. In a previous study we suggested that scleroderma patients were more allowed having RLS, but at that time we did not exclude from analysis patients with scleroderma and associated rheumatic condition. The objective of this study is to verify the prevalence of RLS in "pure" scleroderma patients compared to osteoarthritis patients.

**Methods :** 90 consecutive patients with scleroderma and 90 with osteoarthritis for control group will be evaluated for RLS symptoms. The scleroderma group must not have other comorbidities. All patients were interviewed for RLS and had filled in a sleep log for 6 weeks, to observe total sleep time (TST) and wake up after sleep onset (WASO).

**Results :** Until this moment, 19 patients with scleroderma (48±11 years old) and 14 with osteoarthritis (62±7years old) had been evaluated. In the scleroderma group 3/19 (16%) patients presented RLS symptoms and 3/14 (21%) in the group osteoarthritis ( $p=0.51$ ). The TST was 6h48min ±1h51min for scleroderma patients and 5h32min ±2h25min for osteoarthritis patients ( $p=0.17$ ). The WASO was 27min ±33min for scleroderma patients and 1h20min ±1h3min for osteoarthritis patients ( $p=0.02$ ).

**Conclusion :** Our preliminary data showed that RLS is equally prevalent in the scleroderma and osteoarthritis groups. The osteoarthritis groups presented a WASO greater than scleroderma group. The sample was not enough to conclude for the association

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### 0829

#### PREVALENCE OF HEADACHE AND NECK PAIN IN A SLEEP BRUXISM POPULATION INVESTIGATED IN A SLEEP LABORATORY

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**Introduction :** Sleep bruxism (SB) has been studied for over a decade in our sleep research laboratory. The objective of this retrospective analysis is to report the prevalence of headaches, neck or shoulder pain and morning fatigue in SB subjects.

**Methods :** SB subjects were selected according to tooth-grinding history (>3 nights/week), without trauma or chronic pain history. All subjects completed questionnaires for SB/pain diagnostic and sleep disorders (Canadian Sleep Society). SB diagnosis and absence of other sleep disorders were confirmed by 2 nights of polygraphic recordings. Sleep and SB variables were analyzed based on previously validated criteria. The following polygraphic criteria were used to identify SB subjects: > 4 SB episode/hour of sleep, > 25 SB bursts/hour of sleep and > 1 episode with grinding noise. SB subjects were divided in 2 groups based on the afore mentioned criteria: low SB subjects failed in 2 out of the 3 criteria and high SB subjects met at least 2 criteria. A total of 21 controls (mean age±SEM: 22.90±0.65), 38 low SB (26.71±0.88) and 41 high SB (24.78±0.70) subjects were selected. Chi-square and odds ratios (OR), with their 95% confidence intervals were used to compare answers between both SB groups and between each SB groups and the control group.

**Results :** Headaches or migraines, occurring occasionally to frequently, were reported twice more often in SB groups (low SB: 52.6%; high SB: 51.2%) than in controls (19%), with OR of 4.7 [1.3-16.7] and 4.5 [1.3-15.6] respectively. Reported morning headaches were also significantly higher in SB groups (low SB: 32.4%; high SB: 17.6%) than in controls (0%). Furthermore, neck or shoulder pain were reported more frequently in both SB groups (low SB: 68.4%; high SB: 68.4%) in comparison to controls (23.8%), with high OR (low SB: 6.9 [2.1-23.3], high SB: 5.7 [1.8-18.9]). Fatigue upon awakening was reported 5 times more in SB groups (low SB: 43.8%; high SB: 41.2%) than in controls (8.3%), with nearly significant OR (low SB: 8.6 [0.98-74.4], high SB: 7.7 [0.89-66.6]).

**Conclusion :** High prevalence of reported headache/migraine and neck/shoulder pain in SB subjects support the need for further investigations to study possible common mechanisms and association.

**Support (optional):** CIHR, FRSQ, CFI

### 0830

#### MYOCLONIC HEAD JERKS IN REM SLEEP: A COMMON AND AGE DEPENDENT FEATURE IN A SLEEP LABORATORY PATIENT POPULATION

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**Introduction :** Myoclonic events are common in wake-sleep transition (hypnic jerks). During REM sleep movements are rare because of physiologic muscle atonia, but both random myoclonic twitching and sleep myoclonus are well known phenomenons during REM sleep. We intended to quantify the occurrence of myoclonic jerks in REM-sleep and focused on head jerks since these movements are readily identified in EMG and videographic recording.

**Methods :** We examined REM sleep of all patients admitted to our sleep



laboratory in a course of six months. From January to June 2004 205 patients underwent polysomnographic recording (one to four nights). 147 patients (71.7%) were men, 58 (28.3%) were women, mean age was 50±14.4 years (range 14 to 82). REM sleep was examined visually in the PSG (occurrence of movement artifacts or myoclonic muscle activity) and by video by one scorer.

**Results :** 472 nights of 205 patients were analyzed. 112 patients (54.6%) showed head jerks during REM sleep, 93 patients (45.4%) did not. Patients with head jerks had a mean of 3.29±5.16 (range 1 - 44) jerks. We compared the occurrence of head jerks in different age groups. In the youngest patient group aged below 45 years (n=72) head jerks were detected in 48 patients (66.7%), in the group between 45-60 years (n=72) head jerks were present in 39 patients (54.2%) and in the oldest patient group above 60 years (n=61) head jerks were seen in 25 patients (41%). The association between head jerks and age was significant (chi-square test, p=0.012).

**Conclusion :** Our data confirm previous observations that head jerks are frequent in REM sleep and might represent a physiological phenomenon. Furthermore a significant difference in the occurrence of head jerks in different age groups was observed with a higher prevalence in younger individuals.

**Support (optional):**

### 0831

#### PRAMIPEXOLE TREATMENT RAPIDLY IMPROVES PATIENT RATINGS OF RESTLESS LEGS SYNDROME SYMPTOMS

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**Introduction :** Pramipexole (PPX) has been shown to be effective in several multicenter clinical trials in restless legs syndrome (RLS). This data analysis describes the rapid onset of action of pramipexole during a 12-week, randomized, double-blind, placebo-controlled, forced-titration, clinical trial conducted in the United States.

**Methods :** Three hundred forty-four patients with moderate to severe RLS were randomized to placebo, 0.25, 0.50, or 0.75 mg/d PPX. Doses were up-titrated weekly, beginning with 0.125 mg PPX. Data from the Patient Global Impression (PGI) scale were used in this analysis. The PGI is a 7-point scale in which patients rate themselves from “very much better” (score = 1) to “very much worse” (score = 7).

**Results :** Pramipexole significantly improved PGI ratings relative to placebo. When data in the pramipexole group were collapsed across doses, 61.4% of patients were PGI responders (“very much better” or “much better”) after 12 weeks, compared with 44.7% in the placebo group (P = .0056). The effects of pramipexole on PGI responder rates were evident within the first week of treatment, at which point in titration, all patients were receiving 0.125 mg PPX. After 1 week, the PGI responder rate was significantly higher (P<.0001) in the pramipexole group (42.5%) compared with the placebo group (14.1%).

**Conclusion :** Pramipexole, at a low titration dose of 0.125 mg, significantly improved PGI scores by week 1. This improvement in patient rat-

ings was maintained throughout the 12-week trial. As the therapeutic effects of low-dose pramipexole were apparent at the 0.125-mg dose, patients may achieve rapid effectiveness with minimal side effects.

**Support (optional):**

### 0832

#### ROLE OF CYTOKINES IN PATIENTS WITH RESTLESS LEGS SYNDROME(RLS)

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**Introduction :** Restless Legs Syndrome (RLS) can have a course of remission and recurrence which seems similar to certain immunological diseases with elevated cytokines levels such as Multiple Sclerosis. Cytokines levels have not been determined previously in RLS.

**Methods :** We included 11 patients (M=6,F=5, Avg age-51.5 yrs) with RLS and 11 age and sex matched controls (M=6,F=5, Avg age-51.2yrs) in the study. We excluded RLS patients and controls with illnesses that can cause raised cytokine levels. The patients were maintained on RLS medications to maintain adequate sleep and matched against controls for total sleep time (TST) by a sleep log. The samples were collected from serum at the same time (i.e. 10 am) for all the patients and the controls. The samples were then analyzed blindly for the presence and the levels of the following cytokines Interferon Gamma, TNF alpha, IL1B, IL 6, IL12 and IL 4.

**Results :** We did not find any difference in the levels of the 6 cytokines in the patients vs the controls after matching for age, sex and TST. We found no difference in cytokines levels in 5 RLS patients treated with dopaminergic agents and the 6 RLS patients treated with nondopaminergic agents. We did not find any correlation between the cytokine levels of all the RLS patients as well as those with only a family history of RLS and the severity of RLS as determined by the IRLS scale and a visual analogue scale. For the patients with a positive family history for RLS, we also correlated the subscales of the IRLS (Impact and symptom subscales) and the single question 3 from the IRLS scale (that is not on any subscale) to the levels of different cytokines but again did not find any statistical significance.

**Conclusion :** We did not find any relation of the 6 cytokine levels to the presence or severity of RLS. Other immunological factors such as TCD4 lymphocytes, TCD8 lymphocytes and CD19 B cells need also to be studied to see if they have a relation with RLS.

**Support (optional):**

### 0833

#### PREVALENCE OF RLS AND DEPRESSION IN TYPE 2 DIABETES

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**Introduction :** Diabetes is the 5th leading cause of death affecting 6.2% of the population, with direct costs of \$91.8 billion dollars and indirect costs of \$40.2 billion dollars (1). Restless Legs Syndrome is a sleep disorder affecting up to 15% of the population (2-4) and may compromise diabetic control due to sleep deprivation, fatigue, and depression. Twenty-one per cent of persons with RLS have diabetes (5), a prevalence over three times that of the general population. There are no reports on the prevalence of RLS in the diabetic population. RLS is significantly associ-

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ated with self-reported diminished general health and poor mental health, and significantly correlates with age, increasing BMI, and low exercise, all factors that contribute to poor glycemic control. This abstract presents preliminary findings of a study to estimate the prevalence of RLS and depression in type 2 diabetics.

**Methods :** The study design is a descriptive, comparative study of type 2 diabetics with and without RLS. The sample was recruited from the PENN Rodebaugh Diabetes Center and the PENN Sleep Center.

**Results :** Preliminary findings suggest that 44 of 102 (43%) participants who were screened for the study have RLS; 30 participants completed the surveys with 53% of the diabetics with RLS depressed compared to 43% of non-RLS. Only 25% of RLS participants who were depressed were being treated for depression compared to 33% of the non-RLS group.

**Conclusion :** Based on our sample, this study indicates that the incidence of RLS in type 2 diabetics may be higher than previously reported. Rates of depression in persons with RLS are higher than non-RLS diabetics and may affect self-care treatment of diabetes. Larger studies need to be performed to confirm these findings. Health care providers should be aware that RLS may impact cost and effectiveness of treatment for diabetes and depression.

**Support (optional):** This study was funded by Sigma Theta Tau International Society and the American Association of Diabetic Educators 1. Clearinghouse NDI. National Diabetes Statistics. National Institute of Health. May 2003. Accessed September 24, 2003, 2003. 2. Ohayon MM, Roth T. Prevalence of restless legs syndrome and periodic limb movement disorder in the general population. *Journal of Psychosomatic Research.* 2002;53(1):547-554. 3. Earley CJ, Allen RP, Beard JL, Connor JR. Insight into the pathophysiology of restless legs syndrome. *Journal of Neuroscience Research.* 2000;62(5):623-628. 4. Allen RP, Earley CJ. Restless legs syndrome: a review of clinical and pathophysiologic features. *Journal of Clinical Neurophysiology.* Mar 2001;18(2):128-147. 5. Phillips B, Young T, Finn L, Asher K, Hening WA, Purvis C. Epidemiology of restless legs symptoms in adults. *Archives of Internal Medicine.* Jul 24 2000;160(14):2137-2141 2228-2139.

### 0834

#### INTERMITTENT DOSING OF ROPINIROLE FOR TREATMENT OF MILD TO MODERATE RESTLESS LEGS SYNDROME: TOLERABILITY AND EFFICACY

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**Introduction :** Dopamine agonists are prescribed for nightly use, in RLS, due to the risk of side effects and the delayed onset of action of some of these agents. We conducted a 12-week, prospective, open-label, study of 27 consecutive patients with mild to moderate RLS symptoms using the non-ergot D2/D3 agonist ropinirole on an as needed basis, rather than nightly, to determine the efficacy and tolerability of this unconventional dosing regimen.

**Methods :** Patients with mild to moderate RLS symptoms who required only intermittent use of medication were enrolled for treatment and evaluation. Patients were evaluated at baseline and every 4 weeks for 12 weeks with a physical exam and multiple subjective rating scales.

**Results :** 21 patients completed the 12-week testing period. The group as a whole evidenced significant improvement in the two primary outcome measures of RLS symptom severity; IRLS-scale score decreased from 17.9+/-5.1 at baseline to 14.9+/-3.2 ( $p < 0.01$ ) at 12 weeks, and mean RLS VAS decreased from a baseline score of 44.3+/-20.6 to 29.3+/-13.4 ( $p < 0.01$ ). Secondary outcome measures that improved included, but were not limited to: insomnia severity, frequency of sleep maintenance insomnia, and reports of non-refreshing sleep. There was no improvement in the Epworth Sleepiness Scale and subjective measures of sleep-onset insomnia.

At the end of the study, the mean dose of ropinirole was 0.5+/-0.38 (range 0.125-2.0) and mean dosing frequency was 3.2+/-1.5 (range 1-9) doses per week. No significant orthostatic vital-sign changes were seen over the course of the study. Somnolence (11.11%), nausea (7.41%), disturbed sleep (25.93%), and headache (18.52%) were the most commonly reported side effects, no patients withdrew from the study due to side-effects, and no serious adverse events occurred.

**Conclusion :** Dopamine agonists, such as ropinirole, may be effective and well-tolerated when used intermittently on a pro re nata (prn) basis for the treatment of mild to moderate and/or intermittent RLS symptoms.

**Support (optional):** This study was investigator initiated and sponsored in-part by a research grant by GlaxoSmithKline, Inc.

### 0835

#### CIRCADIAN VARIATION OF THE SYMPTOMS OF RESTLESS LEGS SYNDROME (RLS): AN EFFECT OF MELATONIN ?

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**Introduction :** A recent study conducted in our laboratory showed that melatonin secretion started approximately two hours before the worsening of RLS symptoms at night and could perhaps explain their circadian variation. The aim of this study was to verify the hypothesis of the direct involvement of melatonin in this phenomenon. The effects on RLS symptoms of the administration of melatonin and conversely those of its suppression by the exposure to bright light were studied.

**Methods :** Seven RLS subjects (2 men, 5 women, mean age = 21.4±9.7 years,) were studied in three conditions. First, the control condition allowed to measure the PLMS index and the severity of the sensory and motor symptoms during the Suggested Immobilization Test (SIT). The second and third conditions were the administration of melatonin (3 mg at 7:00 pm) and the exposure in the bright light (3000 lux from 7:00 pm to midnight), respectively. These two experimental nights were separated by one week and the order of those conditions was inverted for half the subjects. The SIT was administered twice for each condition: before the habitual appearance of symptoms (from 7:30 pm till 8:30 pm) and after (from 11:00 pm till 00:00 am).

**Results :** The administration of exogenous melatonin and exposure to bright light did not significantly influence sleep architecture, PLMW, PLMS or the sensory symptoms experienced during the SIT. However, a weak difference on motor symptoms during the 1st SIT was observed between the two experimental conditions (exogenous melatonin increased the number of leg movements whereas the bright light decreased it;  $p = 0.046$ ). No effect was found for the second SIT.

**Conclusion :** Although melatonin may have a certain influence, notably on motor symptoms, other mechanisms could explain in a more direct way, the circadian variation of RLS symptoms.

**Support (optional):** Supported by the Canadian Institutes of Health Research (CIHR) and the Fonds de Recherche en Santé du Québec (FRSQ).

### 0836

#### ACCURACY OF THE SINGLE ITEM SCREENING QUESTION FOR RESTLESS LEGS SYNDROME WITHIN A COMMUNITY HOSPITAL SLEEP CENTER

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**Introduction :** Our aim was to test the accuracy of a single question to

screen for Restless Legs Syndrome (RLS). The question was developed through consensus by members of the International Restless Legs Syndrome Study Group (IRLSSG). As a gold standard, we used four questions that corresponded to the four diagnostic criteria recommended by the IRLSSG.

**Methods :** In the Summer of 2005, 150 sequential patients who were referred to the Akron General Medical Center Sleep Disorders Center were administered the questionnaire. Patients first answered the single item, "When you try to relax in the evening or sleep at night, do you ever have unpleasant, restless feelings in your legs that can be relieved by walking or movement?" On the reverse side of the questionnaire, patients then answered four questions which corresponded to the four criteria outlined by the IRLSSG.

**Results :** Of the 149 completed questionnaires, 54% were female. The average age was 52 (range: 24-82) and the average BMI was 35 (range: 22-71). Over 46% endorsed the single item, while only 28% endorsed all 4 criteria. Overall, the sensitivity of the single item was 93% (95% CI: 89-97%) and the specificity was 70% (CI: 63-77%). The positive predictive value was 54% (CI: 46-62%) and the negative predictive value was 96% (CI: 93-99%). The overall accuracy of the single question was 77% (CI: 70-84%). The sensitivity was higher for women [97%; (CI: 93-100%)] than for men [80%; (CI: 70-90%)]. The specificity did not differ between groups. There were no clear patterns for age or BMI group differences.

**Conclusion :** Overall, the sensitivity of the single question was very good while the specificity was adequate. These data suggest the single item measure would be useful in clinical settings to rule out cases but would overestimate cases if used in epidemiological studies estimating prevalence.

**Support (optional):**

### 0837

#### REBOUND OF SLEEP DISTURBANCE AFTER RAPID DISCONTINUATION OF PRAMIPEXOLE IN PATIENTS WITH RESTLESS LEGS SYNDROME

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**Introduction :** Recent clinical trials (manuscripts under review) have shown that pramipexole is effective in treating symptoms of restless legs syndrome (RLS), including sleep problems, for up to 12 weeks. However, RLS is a chronic condition that may require longer-term treatment. The objective of this analysis was to determine the effects of pramipexole withdrawal on symptoms.

**Methods :** Data in this analysis were collected as part of a randomized, double-blind, parallel-group, placebo-controlled, multicenter, pramipexole withdrawal study of 3 months' duration. During a preceding 6-month period (Period 1), open-label pramipexole was up-titrated to individually optimized dosage (0.125, 0.25, 0.50, or 0.75 mg once daily) (N = 224). At the end of this run-in phase, patients who met predefined criteria for drug response (N = 150) were randomized to receive 3 months of either placebo or the optimized dosage of pramipexole (Period 2). Symptom and sleep-related data collected with 100-mm visual analogue scales are presented. Patients rate the severity of their symptoms while trying to get to sleep, during the night and during the day, as well as their satisfaction with sleep.

**Results :** At the start of Period 2, the median scores on all scales were low relative to baseline (Period 1), indicating high satisfaction with sleep and a low severity of RLS at all times of day. Although ratings remained virtually unchanged in patients continuing on pramipexole, the placebo group exhibited large increases in the median for all scales, including a 48-mm increase for RLS severity while going to sleep and a 47-mm increase for its severity during the night (P<.0001).

**Conclusion :** This study showed that disruption or withdrawal of a successful treatment with pramipexole leads to prompt worsening of RLS symptoms and reoccurrence of sleep disturbance. Patients who remained on pramipexole during the double-blind period experienced sustained benefit on symptoms, as well as sleep satisfaction.

**Support (optional):**

### 0838

#### RESTLESS LEGS, PERIODIC LIMB MOVEMENT AND OTHER SLEEP PROBLEMS IN PATIENTS WITH BEHAVIOR DISORDERS

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**Introduction :** It has been suggested that sleep problems including restless legs syndrome (RLS) and periodic limb movement during sleep (PLMS) are highly prevalent among patients with attention deficit hyperactivity disorders (ADHD). However, systematic investigation of sleep problems among the patients with behavior disorders has not been conducted. The aim of the study was to investigate the prevalence of restless legs, periodic limb movement (PLM) and other sleep problems among patients with behavior disorders.

**Methods :** 134 patients between the ages of 4 to 11 years ( mean age 9.3 SD 1.5 years) with behavior disorders were included in the study. RLS/PLMD Pediatric Screening Questionnaire (RPSQ) and Children's Sleep Habits Questionnaire (CSHQ) were filled out by their parents. Patients were divided into ADHD group (33 patients, 26.8%), PDD group (39 patients, 31.7%) and mental retardation (MR) group (40 patients, 32.5%) according to the DSM-IV. Presence of restless legs and PLM symptom were judged to be present with predetermined criteria using RPSQ, and the prevalence was estimated in each groups. In addition, total sleep disturbance score and subscale scores of CSHQ were also calculated and compared among the three groups.

**Results :** Restless legs symptom was present in 39.4% of ADHD group while PDD group and MR group had restless legs symptom in 12.8% and 17.5% respectively. 27.3% of patients in the ADHD group had PLM symptoms while only 5.1% and 10.0% of patients had PLM symptom in the PDD and MR group respectively. ADHD group showed significantly higher total sleep disturbance score and parasomnia subscale score on CSHQ than the PDD and MR group.

**Conclusion :** Not only restless legs and PLM symptom but also other sleep problems were highly prevalent in ADHD than in other behavior disorders. Presence of sleep disorders should always be considered in the management of ADHD.

**Support (optional):**

0839

**DOPAMINE RECEPTOR D3 POLYMORPHISM IN PATIENTS UNDERGOING TREATMENT WITH DOPAMINE RECEPTOR AGONIST ROPINIROLE FOR RESTLESS LEG SYNDROME**

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**Introduction :** Dopamine receptor agonists are regarded as the treatment of choice for idiopathic restless leg syndrome (RLS). Exploring the efficacy of individual agents, as well as their relationship with dopamine receptors is a potential mean for better characterization of the underlying neuro-bio-chemical dysfunction in RLS. Dopamine receptor D3 (DRD3) plays an essential role in the pharmacology of dopaminergic neurotransmission. This study was undertaken to determine whether DRD3 polymorphism has any influence on the efficacy of ropinirole, a D2/D3 receptor agonist therapy in idiopathic RLS.

**Methods :** Thirty-one patients diagnosed and cared as outpatients with idiopathic RLS were enrolled in this study. Mean age of male patients (n=12) was 57.3±16.1 years, and it was 58.2±12.1 years in females (n=19). Following screening, subjects received ropinirole - binding affinity to D2/D3 receptors - in an average daily dose of 0.25 to 1.5 mg. Genomic DNA was extracted from peripheral blood. The PCR reaction was carried out in the presence of appropriate primers. The PCR product was digested with restriction endonuclease MspI. The electrophoresis was carried out on 5% acrylamide/bis acrylamide gel. The bands were visualized by ethidium bromide under UV light. The therapeutic effect of ropinirole was monitored using a questionnaire (International Restless Leg Syndrome Study Group Rating Scale) and actigraphy, both performed at baseline as well as after 2 months of ropinirole treatment.

**Results :** DRD3 Ser/Ser genotype was ascertained in 11 patients, whereas 18 had Ser/Gly and 2 had Gly/Gly genotypes. Therapeutic efficacy in relation to DRD3 receptor polymorphism was analyzed with paired, two-tailed t-testing. Assuming a p<0.05 limit of significance, the scores obtained using the questionnaire reflected significant improvement in patients with Ser/Ser (p=0.0015, df: 15) or Ser/Gly genotype (p=0.0026, df: 24). Non-significant improvement was observed in patients with the Gly/Gly genotype (p=0.212 df: 1). Actigraphic work-up, by contrast, showed significant improvement in all three subsets: Ser/Ser p=0.031, df: 15; Ser/Gly p=0.025, df: 24; Gly/Gly p=0.031 df: 1.

**Conclusion :** Ropinirole was effective in all three subsets with different genotypes with idiopathic RSL.

**Support (optional):**

0840

**PRAMIPEXOLE DOES NOT CAUSE DAYTIME SLEEPINESS IN PATIENTS TREATED FOR RESTLESS LEGS SYNDROME**

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**Introduction :** Dopamine agonists are now considered first-line treatment for patients with daily or weekly symptoms of restless legs syndrome (RLS). Studies have shown that these agents are effective and generally well tolerated, but some have expressed concern that these medications cause daytime sleepiness. The purpose of this analysis was to determine the effects of the dopamine agonist, pramipexole, on daytime sleepiness in patients with RLS.

**Methods :** Data used for this analysis were collected as part of a multinational, randomized, controlled trial of pramipexole on clinical parameters of RLS during 6 weeks of treatment. In total, 345 patients were randomized 1:2 to receive either placebo (n = 115) or individually optimized

doses of pramipexole (0.125-0.75 mg/d) (n = 230) 2-3 hours before bedtime. Daytime sleepiness was assessed with Item 5 of the International RLS Study Group Rating Scale (IRLS), a 10-item, patient self-rating instrument that assesses the severity of RLS symptoms in 5 degrees, ranging from 4 ("very severe") to 0 ("none"). Question 5 of the IRLS asks patients, "How severe was your tiredness or sleepiness during the day due to your RLS symptoms?"

**Results :** For tiredness or sleepiness during the day (IRLS Item 5), both treatment groups had the same mean score (SD) at baseline with 1.9 (± 1.1). At study end, the mean changes (SD) from baseline were -0.5 (± 1.2) for placebo and -1.1 (± 1.3) for pramipexole. The difference in the treatment effect was highly statistically significant in favor of pramipexole, P<.0001.

**Conclusion :** Pramipexole (0.125-0.75 mg/d for 6 weeks) does not produce daytime sleepiness in patients with RLS and, in fact, significantly reduces daytime sleepiness compared with placebo.

**Support (optional):**

0841

**VALIDATION OF A PHONE INTERVIEW FOR THE DIAGNOSIS OF RESTLESS LEGS SYNDROME**

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**Introduction :** The "gold standard" for diagnosis remains the expert diagnostic clinical interview (CI). Because diagnosis of the restless legs syndrome (RLS) is based almost exclusively on subjective perceptions, we have been developing a structured telephone diagnostic interview (TDI) that can be used by someone familiar with RLS to make a diagnosis without face to face contact. We have now tested the validity of the TDI in a blinded fashion on a non-patient population.

**Methods :** Subjects were family members (FM) participating in a case-control family study of RLS. Family members (FM) who were not patients were diagnosed with the TDI by one RLS expert (WAH) who was blind to proband status and FM relationship to the proband. All locally resident FMs were then requested to have blinded CIs by 2 of a panel of experts (RPA, CJE, SL). We determined the inter-rater agreement for the two clinical interviews and, in cases of clinical agreement, the agreement between the TDI and the CIs. Subjects receiving a diagnosis of possible RLS or diagnosis unknown were considered uncertain and not further analyzed (N=4 FM interviews).

**Results :** Inter-rater agreement for the CIs was 96% (49 of 51 interviews). In the case of these 49 FM diagnoses by TDI, 18 of 20 TDI diagnoses of RLS were confirmed by CI, 27 of the 29 diagnoses of Not RLS were confirmed. Overall correct assignment was 92%; sensitivity of the TDI was 90% and specificity 93%. Positive predictive value was 90% and negative predictive value 93%.

**Conclusion :** The TDI successfully diagnosed family members who were not patients. Agreement between the TDI and clinical interview approached the agreement between clinical interviewers, indicating that the TDI functioned at nearly the same level of accuracy as the clinical interviews themselves. The TDI, therefore, offers a tool for diagnosing RLS in individuals within the general population and may also be useful both for clinical diagnosis and screening for therapeutic trials.

**Support (optional):** This study was supported by NIH grant RO1 AG16362 awarded to Dr CJ Earley and by M01-RR02719 to the Johns Hopkins GCRC.

0842

### ROTIGOTINE TRANSDERMAL SYSTEM IMPROVES QUALITY OF LIFE IN PATIENTS WITH MODERATE TO SEVERE IDIOPATHIC RESTLESS LEGS SYNDROME - RESULTS FROM A MULTI-NATIONAL, LONG-TERM, OPEN-LABEL MULTI-CENTER TRIAL

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**Introduction :** Rotigotine, a non-ergolinic D3/D2/D1 dopamine agonist formulated as a once-daily transdermal delivery system, is being developed for the treatment of Parkinson's disease and RLS. The patch technology releases the drug continuously and provides stable plasma levels over 24 hours. Resulting continuous dopamine receptor stimulation was shown in preclinical studies.

**Methods :** The aim of this multi-center, long-term, open-label trial is to determine safety and tolerability of long-term transdermal application of rotigotine in subjects with idiopathic RLS. The study with rotigotine is ongoing in 34 centers in Europe. It is an extension of a six-arm, placebo-controlled, dose-finding study of 7 weeks. Once the individually adjusted optimal dose is reached in a titration period, rotigotine is administered with dose-adjustments allowed at anytime to maintain optimal treatment. Data presented here were assessed for the first 12 months follow-up since the titration period.

**Results :** On average, severely affected patients were treated in the trial. The safety of rotigotine was evaluated by monitoring AEs. Efficacy variables included IRLS total score, CGI, QoL-RLS score, and RLS-6 scales. 295 patients entered the open-label extension trial. The baseline IRLS score was  $27.8 \pm 5.9$  and treatment with an optimal dose of rotigotine showed a reduction of  $18.8 \pm 8.8$  points to  $8.7 \pm 8.0$  (month 12). The baseline value on the Quality of Life total score was  $30.2 \pm 10.4$ . Treatment with rotigotine improved this score by  $19.1 \pm 12.2$  to  $10.2 \pm 10.2$  (month 12). The most common adverse events were reaction at application site, nasopharyngitis, nausea, erythema, back pain, and fatigue.

**Conclusion :** In this open-label extension trial, rotigotine was well-tolerated and safe. Patients with moderate to very severe RLS receiving rotigotine showed clinically relevant improvement in the IRLS score, the RLS-6 scales, and QoL-RLS. All improvements were observed immediately after the titration period and were sustained during 12 months follow-up.

**Support (optional):**

0843

### ACUPUNCTURE IN THE TREATMENT OF RESTLESS LEGS SYNDROME, A PROMISSORY THERAPY

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**Introduction :** The Restless Legs Syndrome (RLS) is a sleep disorder that causes great discomfort, and that acupuncture presents to be a useful option. The main goal of this study is to verify the therapeutic effects of acupuncture in the treatment of RLS patients.

**Methods :** Five subjects, diagnosed with RLS for an average of 5 years and worsening in the last six months, received acupuncture treatment for 10 times, twice a week. The main acupoints (CV4, CV12, St26, Sp10, St36, GV20, Liv3, Ki3, GB34, GB39 and Yintang) were selected for

every subject. The discomfort of the legs were assessed before and after treatment through a visual analogical scale, and the quality of life was also assessed before and after treatment through the Restless Legs Syndrome Quality of Life Instrument (RLSQLI). Any other possible complaint of the subjects, direct or indirectly related to RLS were also assessed.

**Results :** All the five subjects presented an important improvement of the quality of life in all domains of the RLSQLI. The before and after results of each domain of RLSQLI were, respectively: Social function = 63,75 - 81,25 (p=0,14); Daily function = 60,13 - 82,79 (p=0,05); Sleep quality = 31,12 - 74,44 (p=0,006); Emotional well-being = 23,37 - 68,33 (p=0,002). And they have shown an expressive reduction in their legs discomfort through the visual analogical scale from 0 to 10 (average before = 8,2; average after 5 treatments p=0,003; average after 10 treatments = 1,0; p<0,0001)

**Conclusion :** Ten sessions of acupuncture have presented good results in subjects with RLS, and further studies, with more rigorous methodologies and with a greater number of subjects are recommended.

**Support (optional):**

0844

### PRAMIPEXOLE PRODUCES SUSTAINED IMPROVEMENTS IN QUALITY OF LIFE IN PATIENTS WITH RESTLESS LEGS SYNDROME

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**Introduction :** Patients with restless legs syndrome (RLS) experience reduced quality of life (QOL) relative to the general population, and the impact of RLS is comparable to that of other major diseases when evaluated with the 36-item short form health survey (SF-36) QOL scale. Pramipexole (PPX), a D2/D3 dopamine agonist, has been shown to improve QOL in patients with RLS, but studies have not exceeded 12 weeks. The purpose of this analysis was to explore QOL, as measured with a disease-specific instrument, namely, the Johns Hopkins Restless Legs Syndrome Quality of Life questionnaire (RLS-QOL), over a period of 9 months. The RLS-QOL scores range from 0-100, with higher numbers indicating better QOL.

**Methods :** Data were collected during a 6-month open-label study (N = 224) of individualized doses (0.125-0.75 mg/d) of pramipexole followed by a 3-month, double-blind, placebo-controlled, study period (ie, half the qualifying patients randomized to pramipexole and half to placebo; N = 150). Only patients who met predefined response criteria during open-label treatment were entered into the double-blind phase.

**Results :** Data from the RLS-QOL were not normally distributed and, therefore, median values are reported here. Median changes from baseline to the end of Period 1 ranged from 16.3 (0.125 mg PPX) to 22.5 (0.50 mg PPX), indicating improvements in QOL (P<.05, except at the 0.125-mg dose). At the end of the open-label phase, median scores ranged from 85-90. At the conclusion of the double-blind period, scores in the pramipexole group were unchanged, while scores in the placebo group had worsened by 10 points. The median difference between the treatment groups (-12.5) was statistically significant (P<.0001).

**Conclusion :** Patients maintained on pramipexole over the 9-month study period experienced significant and sustained improvements in QOL; whereas, patients switched to placebo after 6 months experienced significant worsening.

Support (optional):

0845

**ROPINIROLE TREATMENT EFFECTIVELY RELIEVES SUBJECTIVE AND MOTOR SYMPTOMS OF RESTLESS LEGS SYNDROME (RLS), PROVIDING SLEEP BENEFITS**

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**Introduction :** Patients with RLS often experience sleep disturbance. This may result from the sensory symptoms of RLS, such as the characteristic irresistible urge to move the legs and the unpleasant sensations in the legs that often accompany or cause the urge to move, and also from motor symptoms such as periodic limb movements during sleep (PLMS), which occur in approximately 80% of RLS patients. This analysis examines the effect of treatment on PLMS, RLS symptoms and sleep problems using data from a pivotal trial of ropinirole in patients with moderate-to-severe primary RLS.

**Methods :** TREAT RLS US (protocol 101468/249) was a US-based, 12-week, multi-center, randomized, double-blind, flexible-dose, placebo-controlled study. Patients received ropinirole (n=187), 0.25-4.0 mg/day titrated as needed and tolerated, or placebo (n=194), once daily 1-3 hours before bedtime. Patients with an average of  $\geq 10$  PLM/h at baseline (PLM when supine throughout the night; PLMS; actigraphy measured over 3 nights; n=223) were included in analyses of changes from baseline in PLMS/h and, post hoc, for International Restless Legs Scale (IRLS) total score and Medical Outcomes Study (MOS) Sleep Scale Sleep Problems Index II.

**Results :** At Week 6 observed case, improvements from baseline in PLMS/h and IRLS total score were statistically significantly greater in the ropinirole group compared with the placebo group: PLMS/h adjusted mean treatment difference (AMTD)=-14.5 (95%CI: -20.3,-8.7; p<0.001); IRLS total score AMTD=-4.3 (95%CI: -6.3,-2.3; p<0.001). At Week 12 last observation carried forward, IRLS total score and MOS Sleep Problems Index II improvements were also statistically significantly greater for ropinirole: IRLS total score AMTD=-3.8: (95%CI: -6.0,-1.7; p<0.001); Sleep Problems Index II AMTD=-8.1 (95%CI: -12.7, -3.5; p<0.001).

**Conclusion :** Ropinirole improved measures of objective motor and subjective RLS and sleep symptoms in RLS patients with PLMS.

**Support (optional):** GlaxoSmithKline Research & Development

0846

**RESTLESS LEGS SYNDROME IS A COMMON FINDING IN MULTIPLE SCLEROSIS AND CORRELATES WITH PYRAMIDAL DISABILITY AND CERVICAL CORD DAMAGE**

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**Introduction :** Despite the spectrum of the sensory symptoms referred by multiple sclerosis (MS) patients often includes legs restlessness, no studies have been performed to correlate the restless legs syndrome (RLS) phenotype with a specific anatomic pattern of damage.

**Methods :** A prospective study, which included 156 consecutive patients (mean age=39.3 $\pm$ 10.3; M/F=59/97) with MS, was carried out to identify possible clinical and MRI differences between MS patients with and without RLS. Each patient underwent a medical history interview, a neurolog-

ical examination with the assessment of the Expanded Disability Status Scale (EDSS), a structured questionnaire to verify the presence of the standard diagnostic criteria for RLS, and standard and unconventional brain and cervical cord MRI study (cerebral hemisphere, cerebellum, brainstem dual-echo lesion load, number of cervical cord lesions, mean diffusivity (MD) and fractional anisotropy (FA) of the normal-appearing white and gray matter).

**Results :** Among the 156 patients included, 62 subjects (39.7%) (mean age 42.3 $\pm$ 11.3, M/F=16/46) met the criteria for RLS. In few patients (8.5%), the RLS preceded the clinical MS onset, while in the remaining cases the RLS followed or was simultaneous with the clinical MS onset. When comparing the RLS group with the group without RLS, no significant differences were found in MS duration, age, gender and referred sleep habits. The primary progressive MS course was more represented in the RLS group, which showed also an higher EDSS score for pyramidal impairment. Among the MRI metrics analyzed, the cervical cord average FA was significantly (p=0.01) reduced in patients with RLS compare to those without RLS.

**Conclusion :** RLS is a very common finding in MS patients and should be considered among the symptomatic RLS forms. RLS seems to be associated with a higher pyramidal disability. MRI findings demonstrated that the cervical cord damage represents a significant risk factor for RLS in MS patients.

**Support (optional):**

0847

**VALIDATION OF THE AUGMENTATION SEVERITY RATING SCALE (ASRS): RESULTS FROM A STUDY OF THE EUROPEAN RESTLESS LEGS SYNDROME GROUP (EU-RLSG)**

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**Introduction :** Augmentation is the main complication during long-term dopaminergic treatment of RLS and reflects an overall increase in Restless Legs Syndrome (RLS) severity. Despite its clinical relevance, no systematic evaluations are usually undertaken, as no specific rating instruments are available. To fill this gap, the EU-RLS-SG has developed the ASRS, which consist on 4 items that measure specific changes in severity during treatment. These changes are then summed up into an ASRS total score.

**Methods :** Sixty three mostly (85%) untreated RLS patients were included in 6 centers and treated for 6 months with L-DOPA (up to 500 mg/day, as clinically needed). Test-retest reliability was assessed by comparing two consecutive assessments at baseline. A subsample of patients underwent consecutive ASRS rating by two independent raters to evaluate inter-rater reliability. The external validation of the ASRS was performed against ratings of two independent experts. Discriminant validity was analyzed by comparing the total score in patients with and without augmentation.

**Results :** 60 patients (63% females, mean: 53 years, baseline IRLS score 24.7  $\pm$  5.2) were treated with a median daily dose of 300 mg L-DOPA (range: 50 to 500 mg). 36 patients (60%) experienced augmentation. Reliability: oTest-retest: Spearman r= .72 oInter-rater: r= .94 oThe correlations of the 4 items with the ASRS total score at maximum severity were

$r=.85$ ;  $r=.37$ ;  $r=.67$ ;  $r=.57$ , respectively.  $\alpha$  Cronbach's  $\alpha = .58$   
 Validity:  $\alpha$  Criterion expert rating (for maximal ASRS total score):  $r=.71$ .  
 $\alpha$  Discriminant: ASRS total score differed between patients without vs. with augmentation (mean: 0.31 (SD=0.32) vs. 1.30 (0.61) ( $p<.0001$ ).

**Conclusion :** These results show that the ASRS is a reliable and valid scale to measure the severity of augmentation during long-term treatment. Due to the need to systematically quantify augmentation for both long-term efficacy and tolerability, the ASRS may become a useful tool to monitor augmentation in future clinical trials.

**Support (optional):**

### 0848

#### MAGNESIUM THERAPY IN PATIENTS WITH IDIOPATHIC RESTLESS LEGS SYNDROME: A PLACEBO-CONTROLLED, RANDOMIZED, DOUBLE BLIND STUDY

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**Introduction :** Restless Legs Syndrome (RLS) is a common neurological disorder with high impact on sleep. The mainstream of therapy focuses on dopaminergic treatment. A previous pilot study of our group indicated a decrease of the PLMS-A-index (periodic leg movements in sleep associated with arousal) in RLS and PLMD (Periodic Limb Movement Disorder) patients. To prove the efficacy of magnesium treatment in RLS, we performed a randomized, placebo-controlled, double blind study in parallel design.

**Methods :** Thirty patients participated in the trial. From each group, 14 patients finished the study. Inclusion criteria were: idiopathic RLS (untreated for RLS or sleep disturbances and without use of substances influencing sleep) and a PLMS-A-index  $\geq 5$ /h sleep. Patients were treated with 15 mmol magnesium (magnesium-L-aspartate-hydrochloride) daily or with placebo. The assessments included among others PLMS monitoring at baseline (2 nights) and at the end of treatment (day 27 and day 28) and the International RLS Severity Scale (IRLS). To verify magnesium depletion, we used the magnesium loading test (MgLT) infusing 0.1 mmol Magnesium per kg bodyweight.

**Results :** We found no differences between the magnesium and placebo groups regarding the PLMS-indexes or the IRLS scores. In the ANOVA analysis, both the PLMS-A-index and the IRLS decreased with time ( $p=0.046$  and  $p=0.059$ , resp.). In the MgLT, 14 patients had high retention values indicating a (mostly slight) hypomagnesiemia. In this subgroup, we found a significant decrease of the PLMS-index ( $p=0.038$ ) in the verum group ( $n=9$ ) compared to the placebo group ( $n=5$ ) during treatment.

**Conclusion :** In our study, PLMS-indexes and the IRLS score did not differ between the Magnesium treated and the placebo group. The subgroup analysis indicated a possible benefit of Magnesium therapy in RLS patients with pre-existing hypomagnesiemia.

**Support (optional):** The study was supported by Verla-Pharm, Tutzing, Germany

### 0849

#### AUGMENTATION DURING LONG-TERM TREATMENT WITH L-DOPA: RESULTS OF A MULTICENTRE STUDY

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**Introduction :** L-DOPA has been shown to be therapeutically effective for RLS for many years. However, its main limitation is the occurrence of augmentation (AUG) during long-term treatment. Most of the evidence is based on retrospective analyses of case series without a common definition of augmentation. In order to evaluate the incidence and clinical characteristics of augmentation, the European Restless Legs Study Group has performed a multicentric, long-term study on L-DOPA.

**Methods :** The open-label study included mainly untreated patients (85%) diagnosed with RLS according to NIH criteria and was performed in 6 European countries. Treatment was started with an initial dosage of 100/25mg L-DOPA/benserazide and increased to a maximum of 500 mg/d, as clinically needed. Clinic visits were performed every week for the first month, and monthly thereafter, and involved systematic assessments on RLS severity (IRLS, RLS-6, CGI), augmentation, and safety measures. Presence of AUG was established by two independent international experts, using NIH-criteria.

**Results :** Sixty patients were treated, 35 completed the six-month trial and 25 dropped out. AUG occurred in 36 patients (60%). Among those that dropped out, AUG occurred in 68%, and was the main reason for discontinuation in 28%. Median time to dropout was 71 days. The mean dose of L-DOPA was 311 mg/d (SD: 105). However, 83% of AUG had dosages of L-DOPA of at least 300 mg/d compared to 54% without AUG ( $p=.0312$ ). The mean (SD) dosage in patients undergoing AUG was 324 (98) mg/d, against 292 (114) mg/d in Non-AUG ( $p=.2886$ ). The IRLS total score improved from 24.7 (5.2) at baseline by 6.4 (11.2) points in the AUG and from 25.7 (6.5) by 12.4 (10.7) points in the NON-AUG group at the final visit ( $p=.0386$ ).

**Conclusion :** AUG is common during treatment with L-DOPA and develops in 50% of patients. AUG was more frequent in higher doses, and developed in 50% of the cases within the first two and a half months of treatment.

**Support (optional):**

### 0850

#### INVESTIGATING RESTLESS LEGS SYNDROME BY STUDYING LEG ELECTROMYOGRAPHIC ACTIVITY IN THE FMRI SCANNER

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**Introduction :** The restless legs syndrome (RLS) is one of the most common neurological disorders. RLS is characterized by an urge to move the legs, usually accompanied by sensory leg discomfort occurring during rest and predominantly during the evening and night. Periodic leg movements, assessed by recording the tibial anterior muscles by surface electromyography (EMG), occur in 80-90 % of patients and are considered as the motor symptom of the disorder. The pathophysiology of RLS is not yet understood. For the first time we recorded tibial anterior EMG during functional magnetic resonance imaging (fMRI) in patients with restless legs syndrome.

**Methods :** Surface EMG recordings with placing the electrodes according the PLM scoring criteria were performed in 7 untreated patients with an idiopathic RLS. Patients were investigated during the afternoon ( $n=4$ ) and the evening ( $n=3$ ) over approx. 60 minutes lying awake and prone in the fMRI scanner (Siemens, 1.5 Tesla). In the signal analysis, the EMG signal was split up into tonic and phasic parts to assess slower variations in muscle tone or tension separately from muscle twitches or movements.

## Category M—Sleep Disorders-Movement Disorders

**Results :** Tonic EMG activity correlated negatively with sensory leg discomfort ( $p < 0.01$ ) in line with the clinical experience that RLS-related subjective discomfort increases during muscle relaxation at rest. The tonic EMG regressor correlated with activation of several cerebral and cerebellar areas. No significant correlation was found between phasic EMG activity and cerebral activation or sensory leg discomfort.

**Conclusion :** The methodology will be discussed. We conclude that simultaneous recording of EMG and fMRI signals appears to be a reliable method for investigating the pathophysiology of movement disorders.

**Support (optional):** This study was partly supported by Böhlinger-Ingelheim, Germany

### 0851

#### CEPHALOMETRIC EVALUATION OF PHARYNGEAL AIRWAY IN CHILDREN WITH AND WITHOUT SLEEP BRUXISM

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**Introduction :** Sleep bruxism (SB) is characterized by increased rhythmic masticatory muscle activity (RRMA), associated with tooth-grinding. The RRMA frequency is three times higher in SB patients than in non-bruxers. Based on indirect evidence that this oral motor activations possibly play a role in improving airway patency during sleep, our hypothesis is that there is a connection between increased RRMA and reduced upper airway dimensions in SB patients. The main goal of this study was to compare the upper airway dimensions of children with sleep bruxism with those of children without sleep bruxism.

**Methods :** We analyzed the upper airway dimensions on lateral cephalometric radiographs of 36 children, from 5 to 10 years of age ( $M=8.1$  yrs;  $SD=1.6$ ), clinically diagnosed with standard occlusal Angle Class II. The children were divided into 2 groups: Bruxism Group (BG) and Control Group (CG). Clinical diagnosis of sleep bruxism was done according to The International Classification of Sleep Disorders (ICSD-2). Each bruxer child was matched with a non-bruxer child according to gender and age. The PAS (pharyngeal airway space), IPAS (inferior airway space), and SPAS (superior airway space) measurements were taken by the same researcher. An independent Sample t test was carried out.

**Results :** No statistically significant differences were found between BG and CG for: SPAS (BG [ $M=5.944$ ;  $SD=1.822$ ] and CG [ $M=6.861$ ;  $SD=2.801$ ]); PAS (BG [ $M=10.305$ ;  $SD=3.606$ ] and CG [ $M=10.083$ ;  $SD=3.590$ ]) and IPAS (BG [ $M=8.750$ ;  $SD=3.154$ ] and CG [ $M=8.167$ ;  $SD=3.773$ ]).

**Conclusion :** Our data did not demonstrate statistical difference in cephalometric measurements of the upper airways when we compared children with and without bruxism even though we got different measurements in these groups, which means that RRMA did not result in increased airway space as we hypothesized. We suggest that more research be done with more subjects to clarify this issue.

**Support (optional):**

### 0852

#### PRESENCE OF SLEEP/WAKE SYMPTOMS IN PERIODIC LEG MOVEMENT DISORDER

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**Introduction :** Little research has examined Periodic Leg Movements during Sleep (PLMS) in a non-clinical population. We were interested in determining the relationship between a PLMS Index  $> 15$  and excessive daytime sleepiness and insomnia. As these two symptoms in addition to

the PLMSI  $> 15$  is needed for the diagnosis of PLMD, we sought to determine if these sleep-wake symptoms were associated with the objective criteria (PLMSI  $> 15$ ).

**Methods :** Participants ( $N=509$ ) were recruited from the tri-county Detroit area completing an overnight PSG and daytime assessment (mean age  $= 41 \pm 12.8$  yrs., 62.8% Caucasian, 30.7% African-American). A PLMS Index was created using standard criteria. We then divided participants into those with a PLMSI  $> 15$  and those with a PLMSI  $\leq 15$ . Using the Global Sleep Assessment Questionnaire, we assessed excessive sleepiness and insomnia during the previous four weeks. Comparisons of PLMSI  $> 15$  and PLMSI  $\leq 15$  and their relationship to each symptom were examined.

**Results :** The prevalence of PLMSI  $> 15$  for our sample was 7.9%. In individuals with PLMSI  $> 15$ , 55% reported symptoms, compared to only 29% with a PLMSI  $\leq 15$  ( $x^2 = 11.18$ ,  $p < .001$ ). Specifically, of individuals with PLMSI  $> 15$ , 45% reported insomnia compared to 25% with a PLMSI  $\leq 15$  ( $x^2 = 6.84$ ,  $p < .01$ ). Of those with PLMSI  $> 15$ , 12.5% reported excessive sleepiness, compared to 8.5% with a PLMSI  $\leq 15$  ( $p = n.s.$ ).

**Conclusion :** Our data shows that the prevalence of PLMSI  $> 15$  is related more closely to reports of insomnia compared with excessive daytime sleepiness. This data supports clinical observations and the diagnostic criteria of PLMD which includes complaints of sleep disturbance in addition to a PLMSI  $> 15$ . Further research may be warranted to distinguish excessive daytime sleepiness from symptoms of fatigue, which are commonly reported by patients with PLMD.

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### 0853

#### DIFFERENTIAL RISE OF BLOOD PRESSURE IN PERIODIC LEG MOVEMENTS ASSOCIATED OR NOT WITH MICRO-AROUSALS IN PATIENTS WITH RESTLESS LEG SYNDROME

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**Introduction :** Autonomic changes, namely tachycardia followed by bradycardia were found in association with periodic leg movements during sleep (PLMS) in patients with restless leg syndrome (RLS). The aim of this study was to assess blood pressure (BP) changes associated with PLMS with and without micro-arousals (MA) in these patients.

**Methods :** Seven subjects with RLS (3 females; age =  $45.6 \pm 14.4$  yrs) were included in the study. Beat-to-beat non invasive BP (Portapres) was continuously recorded during one night polysomnography. Subjects had a mean PLMS index of  $28.7 \pm 10.4$ , according to Coleman's criteria. Only movements which were separated by at least 20 seconds were selected for the analysis to avoid overlapping of the blood pressure response. A mean of 20 PLMS with and without MA were analysed in each subject. For each movement the increase of systolic BP (SBP) and diastolic BP (DBP) was calculated as a difference from the baseline (5 heart beats before the beginning of the movement) and the peak value. Mean increments associated with PLMS without and PLMS with MA were compared within subjects with a t-test with dependant sample.

**Results :** PLMS with MA, compared to PLMS alone, were associated with a higher rise of SBP ( $28.9 \pm 7.5$  versus  $23.0 \pm 10.3$  mmHg,  $p = 0.01$ ) and DBP ( $12.8 \pm 3.3$  versus  $10.7 \pm 3.7$  mmHg,  $p = 0.02$ ). The magnitude of BP



rise did not correlate with age, duration of the disease, sleep parameters or PLMS duration. No sex difference was observed.

**Conclusion :** These results show significant increase of BP in association with PLMS. PLMS associated with MA elicit a higher increase of blood pressure than PLMS without EEG signs of arousal. Epidemiological studies showed a higher risk of developing hypertension in RLS. These nocturnal BP fluctuations could be a contributing factor.

**Support (optional):** Supported by The Canadian Institutes of Health Research and Fonds de la Recherche en Sante du Quebec

## 0854

### ASSOCIATION BETWEEN RESTLESS LEGS SYNDROME AND DSM IV MAJOR DEPRESSIVE DISORDER: PRELIMINARY FINDINGS FROM THE RLS IN BALTIMORE EPIDEMIOLOGICAL CATCHMENT AREA (RIBECA) STUDY

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**Introduction :** Restless Legs Syndrome (RLS) is a common neurological sensorimotor disorder that affects 5-10 % of the general adult population. A few studies based on clinical samples have suggested an association between depression and RLS. Few studies have previously examined the potential association between RLS and Major Depressive Disorder (MDD) based on a community sample. Based on the recently completed Wave IV of the Baltimore ECA Follow-up study, we examined the association between DSM-IV MDD and RLS in the community.

**Methods :** Out of 1071 participants, 999 participants (mean age: 58.1 years + 12.2; female: 62.3%) fully completed the seven-item RLS Questionnaire (based on four diagnostic criteria established by the International RLS Study group) and the NIMH Diagnostic Interview Schedule administered by trained lay interviewers. We conducted a case-control analysis comparing RLS cases with non-RLS controls to estimate risk of 12-month and lifetime diagnosis of DSM IV-MDD based on logistic regression models with MDD as the main outcome variables and RLS as the main predictor while adjusting for relevant sociodemographic and/or health-related variables.

**Results :** 21.4% of subjects with RLS (9/42) and 8.4% of subjects without RLS (80/957) had lifetime diagnosis of MDD. Crude odds ratio (2.99, 95% confidence interval [1.38, 6.57]) and adjusted odds ratio (3.12, [1.27, 7.66]) for risk of MDD among subjects with RLS suggest a strong association between the two conditions.

**Conclusion :** Future investigations should focus on elucidating the pathophysiological mechanism underlying the linkage between the two common neuropsychiatric conditions.

**Support (optional):**

## 0855

### DOES PERIODIC LEG MOVEMENT INDEX INFLUENCE QUANTITATIVE SLEEP EEG IN MIDDLE-AGED SUBJECTS WITHOUT SLEEP COMPLAINTS?

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**Introduction :** Reports have called into question the relevance of periodic leg movements disorder (PLMD) as a specific clinical entity. We

reported that PLMS index (PLMSI) severity does not influence polysomnographic sleep parameters in middle-aged subjects without sleep complaints (Carrier et al. 2005). However, it still has to be determined whether more refined measures of sleep such as quantitative sleep EEG would provide different results.

**Methods :** The sleep of 70 healthy middle-aged subjects (40-60y) without sleep complaints was evaluated. Subjects volunteered to participate in sleep studies. All subjects were recorded for one polysomnographic sleep evaluation. Spectral analysis in N-REM sleep was performed on the C3 derivation (linked-ear, 1 Hz frequency bins from 1 to 32 Hz). Subjects were divided in 2 groups according to their PLMSI: 1) 43 subjects (28 women, 15 men, 51.5 y ±4.9) were in the low PLMSI group (index <5) and 2) 21 subjects (9 women, 12 men, 52.5 y ±4.4) were in the high PLMSI group (index >10).

**Results :** No significant effect of PLMSI was found for sleep latency, sleep duration, minutes and % of stages 1,2,3,4 and REM, number of microarousals and sleep efficiency. No frequency bins showed significant main effect of PLMSI. Significant interactions between gender and PLMSI were found only in specific beta frequencies (22-30 Hz), with women with high PLMSI showing more power than women with low PLMSI while no such effect was found in men. Men with high PLMSI showed less spectral power in 12-13 Hz frequency bin.

**Conclusion :** PLMSI severity had no effect on polysomnographic sleep variables, and only a minimal influence on quantitative sleep EEG. These results raise questions about the relevance of using PLMSI as an exclusion criterion for middle-aged subjects without sleep complaints and support the notion that an increase in PLMSI may be part of the normal process of aging.

**Support (optional):** This research was supported by scholarships and grants from the Canadian Institutes of Health Research (CIHR), the Fonds de la Recherche en Santé du Québec (FRSQ) and the Natural Sciences and Engineering Research Council of Canada (NSERC).

## 0856

### LACK OF RACIAL DISPARITY IN PREVALENCE OF RLS IN EAST BALTIMORE COMMUNITY: PRELIMINARY FINDINGS FROM THE RLS IN BALTIMORE EPIDEMIOLOGICAL CATCHMENT AREA (RIBECA) STUDY

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**Introduction :** Few published studies have previously examined the epidemiology of restless legs syndrome (RLS) among African Americans, relative to other racial groups. Due to the relative absence of African-Americans seeking treatment for RLS in specialty clinics, a lower prevalence of RLS among African-Americans than whites has been suggested. We compared the prevalence of restless legs syndrome and its associated risk factors in African Americans and whites in a biracial community sample as part of Wave IV of the Baltimore Health and Mental Health Study.

**Methods :** Of 1071 participants of Wave 4 of Baltimore ECA follow-up study, 1024 individuals (358 African-Americans (35.0%), and 633 whites (61.8%) and 33 others) fully responded to the seven-item RLS Questionnaire and composed the study sample. Diagnosis of RLS was based on endorsement of RLS symptoms by participants who responded to a seven-item RLS Questionnaire (based on four diagnostic criteria established by the International RLS Study group) during a household interview. Adjusted odds and 95% confidence intervals were calculated

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based on logistic regression models with diagnosis of RLS as the main outcome variables and black race as the main predictor while adjusting for other relevant sociodemographic and/or health-related variables.

**Results :** The point-prevalence of RLS in the total sample was 4.1% (n=42). No statistical difference was detected between the RLS prevalence rate in blacks (4.7%; n=17) and whites (3.8%; n=24). Of the 42 participants with diagnosis of RLS, 18 participants (1.8%; 9 whites and 9 blacks) reported that the symptoms occurred two or more times a week, indicating RLS severity of clinical significance.

**Conclusion :** RLS is comparably prevalent in African-Americans and in whites. Barriers affecting access to care settings for African-American RLS patients should be investigated in the future.

**Support (optional):** This research was supported by National Institute of Mental Health Grant MH47447 and MH068793 and National Institute of Aging Grant AG026331

### 0857

#### DIAGNOSING RESTLESS LEGS SYNDROME IN PERSONS WITH DEMENTIA

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**Introduction :** Restless legs syndrome (RLS), a debilitating sensorimotor sleep disorder, is highly prevalent in the elderly. Elders with dementia often have risk factors (i.e., taking dopamine antagonists) for RLS. Therefore, the syndrome probably is prevalent in this population. Diagnosis of RLS is based on self-report of symptoms from a standardized diagnostic interview. This pilot study sought to determine whether elders with mild to severe dementia could validly and reliably complete the RLS interview.

**Methods :** This sample consisted of 16 men and 9 women residing in the community and 5 men living in nursing homes. Inclusion criteria were: 1) diagnosis of dementia, and 2) 60 years of age or older. We asked 2 screening questions twice. If the elder correctly answered these questions, a registered nurse trained by a sleep specialist conducted the RLS interview, waited 15 minutes, and repeated the interview.

**Results :** Community. Mini-Mental State Examination (MMSE) scores ranged from 18-29 (mean=23.7), indicating mild to moderate cognitive impairment. While one participant (MMSE=20) did not answer the screen correctly, 24 did (MMSE mean 23.8). Of these, 5 participants (MMSE mean 22.2) did and 19 did not (MMSE mean 24.2) change their answers on the RLS interview after a 15-minute break. The nurse reported that persons with very mild dementia had difficulty describing their symptoms well enough to make a differential diagnosis. Nursing home. The MMSE scores ranged from 2-21 (mean=8.8), indicating mild to severe dementia. Three participants (MMSE 2, 2 & 7) did not correctly answer the screen. The 2 (MMSE 12 & 21) who did changed their answers on the RLS interview after the 15-minute break. The nurse reported that they did not seem to understand the interview and could not verbalize their symptoms.

**Conclusion :** Elders with dementia clearly can not respond to the current standardized RLS diagnostic interview. RLS may be a prevalent and treatable cause for nighttime sleep disturbance and exacerbation of behavioral symptoms at night in elders with dementia that burden their caregivers and lead to their institutionalization. Objective diagnostic RLS measures for this vulnerable population require development and validation.

**Support (optional):** Sleep and Behavioral Disturbance in Dementia (VA NRI 01-077-1) Effect of Activities and Exercise on Sleep in Dementia (RO1 NR 007771)

### 0858

#### PREVALENCE OF RESTLESS LEGS SYNDROME IN PATIENTS WITH RECENT STROKE

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**Introduction :** The prevalence of Restless Legs Syndrome (RLS) increases with age, yet little is known regarding the prevalence of RLS symptoms in stroke patients. Some studies have shown the prevalence of symptoms of RLS in individuals with carotid atherosclerosis is around 10%. We investigated what the prevalence of symptoms of RLS in patients with recently diagnosed stroke was.

**Methods :** Patients admitted to the UNC Stroke Center for acute stroke (31 Ischemic, 11 Hemorrhagic) were surveyed for symptoms of RLS and sleep disturbance. Patients completed the Johns Hopkins Restless Legs Syndrome Severity Scale (JHRLSS), Insomnia Severity Index, Stanford Sleepiness Scale, the Sleep Apnea component of the Sleep Disorders Questionnaire, and the Pittsburgh Sleep Quality Index Scale (PSQIS). Information of body mass index (BMI), total sleep time, age, race, and stroke type were also collected. Patients were divided into two groups (with and without symptoms of RLS) and were compared using a student t test.

**Results :** 42 patients (28 Male, 14 Female) with an average age of 66 years had overall average BMI of 28. 14 patients experienced symptoms of RLS. Their average score on the JHRLSS was 1.43. 9 noticed RLS symptoms at bedtime, 4 noticed symptoms after 6PM, and 1 noticed symptoms before 6PM. The group with RLS was more likely to be of female gender (p = 0.02) and have higher scores on the PSQIS (p<0.047). We found no significant difference in age, BMI, race, or stroke type between the two groups.

**Conclusion :** We found nearly one third of our cohort had preexisting symptoms of RLS. We were unable to identify a significant difference between patients with and without RLS symptoms for age, stroke type, or BMI. Patients with RLS symptoms were more likely to be female. Clinicians should query their stroke patients regarding RLS symptoms.

**Support (optional):**

### 0859

#### APOPTOTIC GENES INVOLVED IN IRON DEPRIVATION INDUCED SUBSTANTIA NIGRA CELL DEGENERATION AND OPIATE STABILIZATION OF THE GENE EXPRESSION: FURTHER STUDIES ON AN IN VITRO MODEL OF RESTLESS LEGS SYNDROME (RLS)

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**Introduction :** Based on new evidence, Restless Legs Syndrome (RLS) is characterized by a low opioid, dopamine (DA) and iron state. We have previously established an in vitro RLS model. Our preliminary data indicates that dopaminergic neurons undergo a cell death by apoptosis under the condition of iron deprivation (ID), and activation of delta-opioid receptors protects against Substantia Nigra (SN) dopaminergic cell damage induced by ID.

**Methods :** In this study, we investigated the effects of ID induced cell apoptosis and the effects of [D-Ala<sup>2</sup>, D-Leu<sup>5</sup>] Enkephalin (DADLE), a synthetic opioid that activates the delta-opioid receptor, on the genes responsible for the apoptosis. We did a comprehensive gene expression analysis using the array-based hybridization and serial analysis of gene expression (SAGE) in the study. Cell cultures of SN cells were estab-

lished from neonatal (2-5 day) Sprague-Dawley rats with standard protocols. Three experimental groups were established: a). 24-hour-exposure to 100 microM desferoxamine; 2). 24 hour exposure to 100 microM desferoxamine with 1 day of pre-exposure of 100 microM DADLE, and 3). control (neither desferoxamine nor DADLE exposure). At the end of exposure, cells were collected. Total RNA from each group was collected and sent to the Super Array Company in Frederick, Maryland for SAGE. Messenger RNA was then determined as a measure of gene expression.

**Results :** Gene expression activities of a total of 112 genes in 12 different apoptotic pathways were tested for each group. Of the 112 genes examined, 13 genes are activated by a short period (24 hours) of exposure to 100 microM desferoxamine including the DNA-damage induced apoptosis family gene Tp53. Pre-exposure of 100 microM DADLE prevents the activation of these genes caused by desferoxamine. The 13 genes affected by ID are distributed in 6 apoptotic gene families. Four of these genes are in a single family - the bcl-2 family (Bad, Bak1, Bax, Becn1).

**Conclusion :** The data suggests that desferoxamine causes dopaminergic cell apoptosis and that genes such as the p53 tumor suppressor gene are activated in an attempt to repair the cell. Furthermore, this process is prevented by pretreatment with opioids which supports our previous work that opioids protect against DA cell degeneration induced by ID. This also lends further strength to our hypothesis that RLS may be characterized by a low opioid, low iron and low dopamine state. An in vivo model will be necessary to verify this work.

**Support (optional):** Supported by American Sleep Medicine Foundation Career Development Award for Y. Sun.

## 0860

### DURATION OF LEG MOVEMENTS AND FERRITIN LEVELS

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**Introduction :** Routine scoring and observation of polysomnographic recordings suggests that leg movements appear to be of longer duration in patients who have a low serum ferritin level. In order to assess these differences, a retrospective study was performed on patients having a primary diagnosis of PLMD.

**Methods :** Data analysis was performed on patients who had one night of polysomnography in our sleep center. The group included pediatric (N=10), ages 1-13 years (mean 5.3 +/- 4.3) and adult (N=10), ages 27-58 (mean 44.6 +/- 9.7) patients. Baseline ferritin levels were obtained on all patients. Leg EMG was recorded from standard sites on the anterior tibialis. All polysomnographic recordings were scored for sleep stages, respiratory events, arousals, and PLM's. Arousals were differentiated by type: spontaneous, respiratory, snore, and PLM. Periodic limb movements were scored for frequency and duration. Events associated with respiratory events and PLM's during wake were rejected. Patient groups were assigned based on serum ferritin level: group I had a serum ferritin of  $\leq 50$  ng/ml; group II had a serum ferritin of  $> 50$  ng/ml.

**Results :** The duration of limb movements in Group I was significantly longer than that of Group II ( $P < .01$ ) with the mean for Group I being 4.4 ( $\pm 0.71$ ) seconds versus 1.9 ( $\pm 0.21$ ) seconds for Group II. The mean serum ferritin for Group I was 22.5 ( $\pm 10.8$ ) as opposed to 120.5 ( $\pm 54.2$ ) for Group II ( $P < .01$ ). The mean PLM Index for Group I was 20.45 ( $\pm 7.56$ ) and 30.72 ( $\pm 13.8$ ) for Group II ( $P < .05$ ).

**Conclusion :** The data suggests that there may be a relationship between low levels of serum ferritin ( $< 50$  ng/ml) and prolonged leg movements with duration greater than 3 seconds. Further research, with larger numbers, is indicated to more adequately assess the characteristics of the

PLM's in these populations.

**Support (optional):**

## 0861

### POLYSOMNOGRAPHY (PSG) STUDY OF A PATIENT WITH STIFF PERSON SYNDROME

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**Introduction :** To our knowledge, there have been no previous polysomnographic studies of Stiff-Person Syndrome (SPS). SPS is a rare neurological condition characterized by marked involuntary rigidity of the axial muscles and limbs, with intense painful muscle spasms which occur following external stimuli such as sudden noises or emotional change. Symptoms are markedly improved by sleep and by diazepam. The presence of high titers of glutamic acid decarboxylase (GAD) antibodies indicates an auto-immune etiology. Here we describe a 35 year old man who complained of bilateral hip stiffness and who was diagnosed with SPS in 2001. Currently, he is on diazepam, 15 mg daily, which has reduced his stiffness to a minimum.

**Methods :** An extended Polysomnographic montage was employed in recording (Standard PSG plus extra extremity leads, plus seizure leads). The patient filled out pre and post study questionnaires. Diazepam was held on the day of study.

**Results :** This patient is 6' 2" and 142 lbs, with a BMI of 18.2. He has an Epworth Sleepiness Scale of 4. He generally goes to bed at 1 am and gets up at 7 am during the week and 9 am on the weekends. He does not nap during the day. He does not have long periods when he is awake in the middle of the night. The patient slept 6 hours the night before the sleep study. The patient stated that he slept the same in the laboratory compared to at home. Sleep Architecture: Stage I = 2.1%, Stage II = 97.9%, Slow wave = 0.0% and REM = 0.0%. There was a significant increase in spindle density. Sleep latency was 14.5 min. Sleep efficiency was decreased to 72.4%. Total arousal index 18.4 per hour. There was mild sleep apnea. The AHI was 13.6 sleep disordered breathing event per hour of sleep (0 obstructive apneas, 1 central apnea, 0 mixed apneas and 71 hypopneas). The respiratory arousal index was 1.4/hr. The PLM index was 0.0/hr. There was no evidence suggestive of epilepsy with the full seizure montage. Video recording did not show significant behavioral changes.

**Conclusion :** The most prominent feature in this patient is the presence of excessive spindling and the loss of Slow Wave and REM sleep. Interestingly excessive spindling has been found in another movement disorder characterized by rigidity, namely Dystonia. These polysomnographic findings will have to be verified in further patients with SPS. Whether the excess spindling shared by both SPS and Dystonia has a common pathogenic basis is in further need of exploration.

**Support (optional):**

## 0862

### VALIDATION OF A SINGLE QUESTION THAT CAN SCREEN FOR THE RESTLESS LEGS SYNDROME (RLS)

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**Introduction :** With FDA approval of a medication for the restless legs syndrome (RLS) (and other approvals expected), a wider range of medical professionals will be expected to recognize and treat RLS. A single valid screening question would provide significant support to the process of reliably identifying those who suffer from RLS.

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**Methods :** A single diagnostic question was developed in interaction with members of the International RLS Study Group (IRLSSG) according to IRLSSG diagnostic criteria. This question reads: When you try to relax in the evening or sleep at night, do you ever have unpleasant, restless feelings in your legs that can be relieved by walking or movement? This question was designed to be highly sensitive (not to miss any RLS cases), but also to be reasonably specific (not to be answered positively by too many without RLS). Two populations were studied: first, individuals with a confirmed diagnosis of RLS (volunteers for the RLS Foundation brain bank) and second, individuals from a case-control family study of RLS, most of whom do not have RLS.

**Results :** 74 of 74 brain bank volunteers answered positively to the question (sensitivity 100%; one person eliminated who could not answer). In the family study, 26 of 26 diagnosed with RLS answered positively and 35 of 44 diagnosed without RLS answered negatively for a sensitivity of 100% and a specificity of 80%.

**Conclusion :** This study confirms that this single question is highly sensitive for RLS and reasonably specific. It should allow clinicians to select those who most likely have RLS and permit more specific diagnostic questioning in a restricted set of patients. This question (or its translation) has been tested in other populations; sensitivity is always near 100%, specificity varies with group being higher in clinical populations (>90% in Italy and the Czech Republic) and lower in related disorders (70% in patients with Parkinson disease in Illinois).

**Support (optional):** This study was supported by NIH grant RO1 AG16362 awarded to Dr CJ Earley and by M01-RR02719 to the Johns Hopkins GCRC. Diagnostic interview of the brain bank volunteers was supported by the RLS Foundation.

### 0863

#### SPECIFICITY AND SENSITIVITY OF THE “SINGLE QUESTION” TO SCREEN FOR RESTLESS LEGS SYNDROME (RLS) IN A SLEEP DISORDERS CENTER

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**Introduction :** RLS reported prevalence in the general population, ranges from 27%-15%. Prevalence is age, gender and ethnic dependent. A potential screening question was devised by the International Restless Legs Syndrome Study Group to be used in epidemiological studies. The question is: “When you try to relax in the evening or sleep at night, do you ever have unpleasant, restless feelings in your legs that can be relieved by walking or movement?” The purpose of this study is to determine the specificity and the sensitivity of the screening question in a sleep center setting.

**Methods :** A prospective pilot study was performed at PSMC. The patients were administered the screening question on their initial clinical evaluation. All consecutive initial visits were reviewed for responses to the screening question and were compared with clinician RLS diagnosis. Twenty records were excluded due to incomplete or inaccurate record.

**Results :** 100 patients met the criteria for entry into the analysis, 52 males (M) and 49 females (F). Ages ranged from 15-75 years old with the mean age of 44.3(SD13.3) years old. The overall sensitivity in this population was 0.91 with a negative predictive value of 97%. The overall specificity was 0.82 with a positive predictive value of 60%. The sensitivity of this screening question was higher in female population (1.0[F] vs 0.75[M]; P<0.05). However, there was no significant difference in the specificity among gender (0.76[F] vs 0.86[M]; P=NS).

**Conclusion :** It is concluded that the RLS screening question has good

sensitivity and adequate specificity in a sleep center population. The sensitivity is significantly higher in female population. We speculate that the difference in sensory perception may account for some of this disparity. Further studies are needed to elucidate this difference and provide additional information on modifications that might be considered to improve the sensitivity and specificity of this “single question”.

**Support (optional):**

0864

**SLEEP DISTURBANCES IN PATIENTS WITH KENNEDY'S DISEASE**

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**Introduction :** Kennedy's disease is a rare, X-linked neurodegenerative disorder, characterized by progressive bulbar, trunk and limb muscle weakness. Although other neuromuscular disorders, resembling Kennedy's disease, such as amyotrophic lateral sclerosis (ALS) have been associated with obstructive sleep apnea (OSA), no previous studies have evaluated the presence of sleep disturbances in Kennedy's disease.

**Methods :** Four patients presenting with Kennedy's disease were studied. All were examined by a staff neurologist and seen in the Sleep Disorders Center for consultation. Three patients were evaluated by polysomnography (PSG) and treated with continuous or bilevel positive airway pressure (CPAP or bilevel PAP). One patient received bilevel PAP empirically, followed by overnight oxymetry.

**Results :** The mean age of the patients was 69 years (range, 55-85) with average disease duration of 14 years (range, 10-19). CAG (cytosine-adenosine-guanine) expansion on the androgen receptor gene consistent with Kennedy's disease was confirmed in all patients. All patients exhibited tongue muscle weakness (Medical Research Council grade 3 and 4). Pathologic hypersomnolence was seen in 2 patients with Epworth Sleepiness Scores of 10 and 13, respectively. Two patients had excessive periodic limb movements of sleep (PLMS) with PLMS index of 26 and 44. Three patients studied by PSG showed an increased number of respiratory arousals with arousal index range of 21.8-34. Mild OSA was present in 2 patients with apnea-hypopnea indices (AHI) of 17 and 18, while the third patient had an AHI of 2.8 and evidence of upper airway resistance syndrome.

**Conclusion :** Because of bulbar muscle weakness, patients with Kennedy's disease are considered at risk for sleep-disordered breathing. Consistent with that hypothesis, all four of our patients exhibited OSA or upper airway resistance syndrome. In addition, they had sleep disruption due to PLMS. Although the sample size is small, these findings suggest that screening these patients for sleep-disordered breathing may be clinically beneficial.

**Support (optional):**

0865

**PRACTICAL TIPS FOR CONDUCTING SUCCESSFUL POLYSOMNOGRAMS IN CHILDREN WITH AUTISM SPECTRUM DISORDERS**

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**Introduction :** Sleep in children with autism spectrum disorders (ASD) is a topic of growing interest, with the performance of overnight polysomnography (PSG) an important component of the overall research. A natural concern is that obtaining quality PSGs in these developmentally delayed children would be too challenging to make this a practical goal. We highlight the potential reasons for our success to date.

**Methods :** Children ages 4 to 10 years with ASD who are seizure and medication-free were recruited into this multiphase study, which included completion of surveys on sleep and behavior by parents followed by diagnostic testing with the Autism Diagnostic Observation Schedule

(ADOS) and Peabody Picture Vocabulary Test (PPVT-III). Those children whose scores placed them on the autism spectrum with average or better cognitive skills were invited to participate in home and inpatient PSG portions of the study. The PSGs were augmented with data from sleep diaries and actigraphy, each of which was collected for 7 days.

**Results :** Each family was given desensitization games, and our staff created picture books using a "social story" approach to help prepare children for the sleep study experience. The PSG personnel had experience with children with ASD and consulted with each family for individual reinforcers. Quiet play activities, stickers and activity books promoted success for children in the inpatient PSG experience.

**Conclusion :** Presently 20 children with ASD have completed the home PSG and two nights of inpatient PSG. Eighty-three percent of children tolerated the home PSG. All children tolerating home PSG had a successful inpatient PSG study.

**Support (optional):** Vanderbilt University Interdisciplinary Discovery Award General Clinical Research Center MO1 RR00095 National Alliance of Autism Research

0866

**QUANTITATIVE ELECTROENCEPHALOGRAPH SLOWING AND NEUROPSYCHOLOGICAL IMPAIRMENT IN MALE RAPID EYE MOVEMENT SLEEP BEHAVIOR DISORDER PATIENTS**

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**Introduction :** A recent study performed in our laboratory showed a slowing of waking EEG in RBD patients compared to normal controls. The aim of the present study was to verify the functional significance of this EEG slowing in relation to the cognitive performance of these patients.

**Methods :** Eleven men (58-77 y; mean age: 67.0 ± 7.1y; mean educational level : 12.6 ± 4.3y) meeting the ASDA criteria for idiopathic RBD and eleven healthy men matched for age and education (52-74 y; mean age: 65.7 ± 7.4y; mean educational level : 13.5 ± 3.4y) underwent one night of polysomnographic recording, a 10-minute waking EEG recording and a full neuropsychological assessment. Quantitative EEG analyses were performed for frontal, central, parietal, occipital and temporal regions during wakefulness.

**Results :** Compared to controls, RBD patients had more Delta power in anterior frontal (p≤0.01), central (p≤0.02), parietal (p≤0.03) and occipital (p≤0.01) regions with a trend for more delta power in the prefrontal (p≤0.07) and temporal (p≤0.08) regions. Moreover, we found more Theta power in prefrontal region (p≤0.04) and a similar trend for the anterior frontal (p≤0.07), lateral frontal (p≤0.06) and occipital (p≤0.09) regions. These patients showed significantly poorer performance in semantic verbal fluency (p≤0.01), similarity task (p≤0.03), word memory recognition task (p≤0.03), digit coding task (p≤0.03) and Trail Making task (p≤0.006). However, correlations between quantitative EEG and neuropsychological abnormalities were not statistically significant.

**Conclusion :** The present results show that both waking EEG and cognitive performance of male RBD patients are altered compared to healthy controls. However we did not find visuospatial constructional dysfunction or altered visuospatial learning as reported previously in this patient population (Ferini-Strambi et al., 2004). Taken together, these results are congruent with the hypothesis that RBD is an early manifestation of a neurodegenerative disease.

## Category N—Sleep Disorders-Neurologic Disorders

**Support (optional):** Canadian Institute of Health Research

### 0867

#### SLEEP DISORDERS IN NONCONGENITAL CHILDHOOD-ONSET MYOTONIC DYSTROPHY TYPE 1

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**Introduction :** Slowness, fatigue, and learning difficulties are common in young patients with noncongenital myotonic dystrophy type 1 (DM1). These features might be due to poor sleep quality. The goal of our study was to search for sleep disorders in this population.

**Methods :** We included 21 consecutive patients in a prospective study involving questionnaires for daytime sleepiness and fatigue, genetic testing to determine CTG triplet repeat size, polysomnography to evaluate sleep architecture and to look for sleep apnea syndrome and periodic limb movements, and multiple sleep latency tests to evaluate objective daytime sleepiness.

**Results :** Most of the patients reported fatigue and a lesser degree of somnolence. Sleep was disturbed by numerous microarousals (mean  $16.6 \pm 7.3$ /hour of sleep) caused by abnormal respiratory events (6/21 patients) and/or periodic limb movements (8/21 patients). Mean sleep latency did not correlate with subjective symptoms or sleep disturbances.

**Conclusion :** In young patients with DM1, complaints of fatigue and/or somnolence should lead to a polysomnography to look for sleep apnea syndrome and/or periodic limb movement, which were present in 2/3 of our population.

**Support (optional):** Financial support by the French association against Myopathies (AFM)

### 0868

#### SEVERE SPASTICITY: EFFECT OF INTRATECAL BACLOFEN ON SLEEP AND VENTILATION

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**Introduction :** Severe intractable spasticity can be treated by Intrathecal baclofen (ITB) infusion which may influence sleep quality, daytime and night time ventilatory parameters.

**Methods :** Twenty consecutive adult patients were evaluated in a prospective study. Each patient underwent the week before and at least 15 days after pump implantation an evaluation of spasticity by the Ashworth and Penn spasm score, a polysomnography, pulmonary function testing and rest energy expenditure. Nearly all patients were on oral baclofen which was stopped after pump implantation and substituted by ITB. This was the only modification in the patient's treatment. Descriptive analysis is given by mean  $\pm$  SD.

**Results :** Patient's age was  $45.0 \pm 13.0$  years old. Multiple sclerosis (9 patients), spinal cord injury (8 patients), cerebral palsy, familial spastic paraparesis and Friedreich ataxia (1 patient each respectively) were present. The Ashworth score was of  $2.75 \pm 0.85$  before and  $1.15 \pm 0.36$  after ITB. The spasm score was of  $3.75 \pm 0.55$  before and of  $1.00 \pm 0.56$  after ITB. Oral baclofen dose before ITB was  $74.0 \pm 31.03$  mg/day and  $227.5$

$\pm 118.3$   $\mu$ g/day (65-500) after ITB. ITB improved total sleep time ( $p=0.05$ ) and sleep efficiency ( $p=0.01$ ) and reduced leg movements associated with micro-arousals ( $p=0.02$ ). REM sleep was increased by ITB ( $p=0.04$ ); delta sleep was not modified. Sleep related respiratory parameters and daytime respiratory function parameters were not modified by ITB nor were CO<sub>2</sub> rebreathing response and resting energy expenditure.

**Conclusion :** In relation to previous oral baclofen ITB improved sleep duration and efficiency, by reducing micro-arousals related to PLMs or spasms. Daytime and night time respiratory parameters were not modified nor respiratory response to CO<sub>2</sub> rebreathing or resting energy expenditure. These results suggest that ITB acts at a spinal level and not at a supra spinal level.

**Support (optional):** The study was supported by the Garches Institute

### 0869

#### COGNITIVE DYSFUNCTION IN OBSTRUCTIVE SLEEP APNEA SYNDROME

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**Introduction :** Obstructive sleep apnea syndrome (OSAS) is characterized by repetitive episodes of complete (apnea) or partial (hypopnea) upper airway obstruction during sleep and is highly prevalent. Cognitive deficits in patients with OSAS have been demonstrated, but the pathophysiology of these deficits is still controversial. The aim of this study is to compare the cognitive status of OSAS patients with that of normal controls and to find out the relationships between nocturnal respiratory findings and cognitive performance in OSAS patients.

**Methods :** A battery of neuropsychological tests, Beck Depression Inventory (BDI) and Epworth Sleepiness Scales (ESS) were administered to 40 patients with OSAS (age:  $42.3 \pm 11.1$ ; AHI:  $40.1 \pm 24.8$ ) and to 29 controls (age:  $37.5 \pm 10.2$ ). OSAS was diagnosed with standard full-night polysomnography.

**Results :** Compared with the controls, OSA patients had a significant impairment, in mini-mental state examination (MMSE), digit cancellation, digit symbol, phonemic and semantic verbal fluency, Stroop color word test. Between two groups, there were no significant differences in Seoul Verbal Learning Test (SVLT), Rey figure copy, forward digit span, and Wisconsin Card Sorting Test (WCST). OSA patients had a higher score of BDI, compared with controls ( $9.3 \pm 7.4$  Vs.  $6.7 \pm 5.3$ ). ESS score was significantly correlated with Trail making A, time of Stroop color word test, delayed recall of SVLT and Rey figure, conceptual response of WCST, MMSE and BDI. Apnea-Hypopnea Index (AHI) was significantly correlated with recognition of Rey figure copy. Total time slept with oxygen saturation below 90% and the lowest oxygen saturation were not correlated with any neuropsychological tests.

**Conclusion :** Patients with OSAS have cognitive deficits concerning attention, executive functions and retrieval of memory, and depressive mood. The cognitive deficits and depressive mood may not be attributed to nocturnal hypoxemia, but to subjective daytime sleepiness.

**Support (optional):**

### 0870

#### FATIGUE SEVERITY RELATED TO SLEEP DISTURBANCE IN MULTIPLE SCLEROSIS

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**Introduction :** The apparent link between fatigue in multiple sclerosis (MS) and sleep disturbances has not been widely explored. Fatigue is the most common symptom of MS, indicated in up to 92% of patients, with approximately half also reporting sleep disruption, such as difficulty initiating/maintaining sleep and frequent awakenings. Studies utilizing polysomnography indicate decreased sleep efficiency, increased awakenings and incidence of OSA and PLMs in a MS population compared to controls. The goal of the present study was to assess if MS patients with increased fatigue have more disruptive sleep compared to a non-fatigued MS group.

**Methods :** Twelve patients with clinically definite MS were divided into a fatigued (N = 7) and non-fatigued (N = 5) groups based on Fatigue Severity Scale scores. All patients received an initial screening consultation to determine eligibility. Patients underwent two consecutive nights of polysomnography (PSG), with night one serving as adaptation. Patients also wore an actigraph for the time between screening and PSG testing, and completed subjective questionnaires relating to sleep.

**Results :** The groups did not differ according to age, BMI, time since diagnosis, disease disability score, or Beck Depression Inventory scores. Results indicate that the fatigued MS group had significantly increased indices relating to sleep disturbance, such as increased awakening index and sleep stage shift index compared to the non-fatigued group. There were no significant differences in OSA or PLM indices. Sleep architecture was similar in both groups, with the exception of the fatigued group which had a significantly longer latency to persistent sleep and increased Stage 1 sleep. Differences on the ESS were approaching significance with the fatigued group reporting more daytime sleepiness.

**Conclusion :** This study demonstrates that sleep disturbances are likely one contributing factor to MS-related fatigue. Clinical interventions to detect and treat sleep problems in MS patients with fatigue are needed.

**Support (optional):**

## 0871

### THERAPEUTIC USE OF MELATONIN IN AUTISM SPECTRUM DISORDER

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**Introduction :** Sleep onset and sleep maintenance insomnia in autism spectrum disorder (ASD) cause significant morbidity in children and familial stress. Melatonin, a pineal hormone that promotes sleep and regulates circadian phase, is documented as reduced in ASD. The use of supplemental melatonin to promote sleep has gained appeal among families of children with ASD. Our objective is to describe our experience using melatonin to treat insomnia in this population.

**Methods :** One hundred and thirteen children (ages 2-18 years) with a confirmed diagnosis of ASD who received melatonin were identified by reviewing the electronic medical records of a single developmental pediatrician. Clinical response to melatonin was verified based on parental report; it was categorized as good to moderate improvement in sleep, mild improvement in sleep, no change in sleep, or worsened sleep. Sleep problems were categorized as sleep onset insomnia, sleep maintenance insomnia or both.

**Results :** Autism was diagnosed in 73% of subjects, pervasive developmental disorder-not otherwise specified (PDD-NOS) in 19%, and Asperger's disorder in 7%. The melatonin dose, including regular and extended release formulations, varied from 1-6 mg. Sleep onset insomnia was reported in 23% of children, while 8% had only sleep maintenance insomnia and 67% had both problems. 70 (62%) had good to moderate improvement in sleep, 30 (27%) had mild improvement in sleep, 10 (9%)

had no change in sleep and 1 (1%) had worse sleep. The single subject with worse sleep complained of increased early morning waking. Three children had mild side effects after starting melatonin, which included morning sleepiness, foggy and increased enuresis, but not increased seizures.

**Conclusion :** Melatonin is a safe and effective treatment for sleep onset and sleep maintenance insomnia in children with ASD. Further studies designed to determine optimal dose and formulation, as well as randomized clinical trials, appear warranted.

**Support (optional):** Vanderbilt University Interdisciplinary Discovery Award (BAM).

## 0872

### PREDICTORS OF NIGHTTIME TOTAL SLEEP IN ELDERLY WITH DEMENTIA

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**Introduction :** Nighttime sleep in elders with dementia is often of short duration and fragmented with awakenings. These sleep problems further impair daytime functioning in elders, result in their institutionalization, and burden their caregivers. The purpose of this study was to identify predictors of nighttime total sleep in elders with dementia.

**Methods :** The sample consisted of 102 elders with a diagnosis of dementia living in either a nursing home, assisted living facility, or home in the community. Sleep technicians conducted one night of attended polysomnography, using standard recording methods, in participants' usual sleep environments to obtain total sleep time (TST) and the predictors of time in bed, periodic leg movement index (PLMI), lowest oxygen saturation, and apnea-hypopnea index (AHI). Research assistants collected Mini-Mental State Examination (MMSE) scores and depression and pain status from chart review and interviews. We used multiple linear regression analyses to determine best predictors of TST.

**Results :** The mean age was 81.8 years (s.d. 7.40) and mean MMSE was 17.3 (s.d. 7.58), indicating mild to severe cognitive impairment. Mean total sleep time was only 329.7 minutes (s.d. 111.04), time in bed was 488.6 minutes (s.d. 82.48) PLMI was 17.3 (s.d. 26.80), AHI was 18.3 (s.d. 15.72) and oxygen saturation was 86.4% (s.d. 5.81). 46 (45.1%) had depression and 22 (21.6%) had at least one painful condition. A model containing time in bed, age, and PLMI explained 46.1% of the variance in TST, and each of these three variables contributed significantly to the model. After accounting for these three variables, the addition of any of the other variables considered did not significantly improve the regression model to predict total sleep time.

**Conclusion :** Longer time in bed, younger age, and a lower PLMI were associated with more sleep at night in elders with dementia. Interventions targeting time in bed and periodic leg movements may improve sleep and daytime functioning in elders with dementia.

**Support (optional):** Effect of Activities and Exercise on Sleep in Dementia (R01 NR 007771) Sleep and Behavioral Disturbance in Dementia (VA NRI 01-077-1)

## 0873

### SLEEP STAGING AND RESPIRATORY EVENTS IN EPILEPSY PATIENTS: IS THERE A FIRST NIGHT EFFECT?

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**Introduction :** Performing multiple research polysomnograms (PSGs) to account for a first night effect (FNE) and sleep apnea variability may be burdensome for both researchers and participants. We determined the extent of a FNE in patients with medically refractory epilepsy, in order to plan more effective trials. We also examined individual variations in sleep apnea ( $AHI \geq 5$ ).

**Methods :** As part of a clinical trial investigating the effects of treating sleep apnea on seizure frequency, 43 patients with medically refractory epilepsy underwent two consecutive nights of PSG. Sleep efficiency, sleep latency, REM latency, number of stage shifts, minutes and percent total sleep time for stage 1, stage 2, slow-wave sleep (NREM stages 3 and 4), REM sleep, AHI, and minimum oxygen saturation were compared for the two nights using two-tailed paired t-tests.

**Results :** Only total sleep time was significantly different between night 1/night 2 ( $363.4 \pm 59.4$  vs.  $393.8 \pm 68.6$  minutes; mean  $\pm$  standard deviation;  $p=0.03$ ). There was a non-significant trend toward increased REM sleep on night 2 ( $49.4 \pm 27.5$  minutes vs.  $60.8 \pm 30.9$  minutes for night 2;  $p=0.06$ ). Percent REM followed a similar pattern ( $12.5 \pm 5.9$  percent vs.  $15.1 \pm 6.6$  percent;  $p=0.07$ ). If only the first night of PSG had been performed, we would have missed diagnosing one patient with OSA (AHI night 1 = 3.0; AHI night 2 = 5.8). Two patients had an AHI of 5 or greater on night 1, but less than 5 on night 2. The AHI was below 5 on both nights for 7 patients and above 5 on both nights for 33 patients.

**Conclusion :** Overall sleep architecture and respiratory parameters were similar between two nights in this sample of patients with epilepsy. Performing multiple PSGs to accommodate the FNE may not be necessary in this population.

**Support (optional):** NINDS RO1 NS 042698 (BAM) and GCRC grants M01 RR00095 (Vanderbilt), RR00042 (University of Michigan) and RR00046 (University of North Carolina).

### 0874

#### STUDY OF POSTTRAUMATIC STRESS DISORDER (PTSD): CAUSES, NEURO-PSYCHIC CONSEQUENCES AND CONCOMITANT SYMPTOMS IN PATIENTS WITH SLEEP DISORDERS (SDS)

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**Introduction :** PTSD is a set of peculiar symptoms developed after a trauma of great magnitude which is witnessed or experienced. The reactions are expressed via intense fear, nightmares, intrusive ideas, disdainful behavior, increased excitability. Objective: to investigate the presence of PTSD as a causal factor in SDs. We analysed the length of time between the stressing traumatic event and several SDs, as well as other neuro-psycho disorders in patients.

**Methods :** 20 individuals with PTSD went to the SDDC complaining about insomnia and other sleep disorders. These patients were evaluated through clinical examination, anamnesis and submitted to the Posttraumatic Stress Diagnostic Scale (PDS) (CAPS - Clinician-Administered PTSD Scale), Impact of Event Scale (IES), Dissociative Experience Scale (DES), Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI). The three latter tests were applied according to the needs.

**Results :** from all evaluated patients with PTSD, 40% had witnessed a traumatic event and 60% had experienced a traumatic event. The SDs presented were: Psychophysiological Insomnia 15%; Sleep Respiratory

Disorders 5%; Secondary Insomnia/Depression/Anxiety 15%; Paradoxical Insomnia 5%; Secondary Insomnia/Anxiety 5%; Secondary Insomnia/Depression 15%; Periodic Movements 5%; Restless Legs Syndrome 5%; Nightmares 10%; Night Terrors 30%. The neuro-psycho symptoms were Anxiety D. 40%; Mood D. 30%, Dissociative D. 25%, ADD (Attention Deficit Disorder) 5%, IES light 20%; moderate 10% and severe 70%.

**Conclusion :** PTSD was frequently evident in patients with SDs. During clinical interview, we suggest asking whether a trauma had ever been experienced at some point in patients' lives.

**Support (optional):**

### 0875

#### SLEEP IN CHILDREN WITH AUTISM: RELATION OF PARENTAL SLEEP CONCERNS TO POLYSOMNOGRAPHY AND BEHAVIORAL MEASURES

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**Introduction :** Subjective sleep difficulties, particularly insomnia and night wakings, are common reasons why parents seek medical intervention in children with autism spectrum disorders (ASD). We characterized the relation of parental sleep concerns to polysomnography (PSG) and daytime behaviors.

**Methods :** ASD and age-matched typically developing (TD) children, 4-10 years old, with normal cognitive function and free of psychotropic medications and seizures were studied. The Parental Concerns Questionnaire (PCQ, Mc Grew et al, unpublished) was used to classify children into three groups: ASD good sleep (16 children, 9 with PSG), ASD poor sleep (14 children, 9 with PSG), and TD good sleep (26 children, 10 with PSG). Parents also completed the Child Sleep Health Questionnaire (CSHQ) and the Child Behavior Checklist (CBCL). A subset of children underwent two consecutive nights of laboratory PSG, scored by an RPSGT blinded to the child's identity, diagnosis, and PCQ/CSHQ results. One-way analyses of variance comparing the groups with adjustment for multiple comparisons were performed.

**Results :** CSHQ dimensions of bedtime resistance, sleep onset delay, sleep duration, sleep anxiety, and night wakings were worse in ASD poor sleepers compared to ASD good sleepers and TD children ( $p \leq 0.004$ ). CBCL dimensions of anxiety, attention, and aggression were worse in ASD poor sleepers than ASD good sleepers ( $p \leq 0.005$ ). PSG on night 1, but not night 2, showed increased sleep latency (SL minutes;  $p = 0.004$ ) and decreased sleep efficiency (SE;  $p = 0.004$ ) in ASD poor sleepers [SL =  $96.0 \pm 78.7$  (mean  $\pm$  standard deviation); SE =  $75.2\% \pm 10.0\%$ ] as compared to ASD good sleepers (SL =  $30.2 \pm 17.7$ ; SE =  $87.5\% \pm 9.0\%$ ) and TD children (SL =  $25.1 \pm 19.4$ ; SE =  $86.7\% \pm 4.1\%$ ).

**Conclusion :** PSG findings reflect parental sleep concerns in ASD. Poor sleep is related to problematic daytime behaviors.

**Support (optional):** Vanderbilt University Interdisciplinary Discovery Grant Vanderbilt University General Clinical Research Center MO1 RR00095 Vanderbilt Kennedy Center for Research in Human Development National Alliance for Autism Research



0876

**IMPAIRED HYPOCRETIN NEUROTRANSMISSION IN HUNTINGTON'S AND PARKINSON'S DISEASE***Fronczek R, Overeem S, Hegeman I, Roelandse F, Van Pelt J, Maat-Schieman M, Van Duinen S, Roos R, Lammers G*

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**Introduction :** The hypothalamic hypocretin system plays a central role in the regulation of various functions, including sleep/wake regulation and metabolism. There is a growing interest in hypocretin function in both Huntington's (HD) and Parkinson's (PD) disease, but studies using cerebrospinal fluid hypocretin (CSF) levels yielded contradictory results. CSF level measurement provides valuable information in narcolepsy, where hypocretin is undetectable due to a 90-95% loss of hypocretin producing neurons. However, it is limited in other disorders, where a smaller loss of hypocretin neurons might not be detectable in CSF. Measuring hypocretin content directly in brain tissue may be a more valid technique to quantify neuronal loss in these disorders and may increase sensitivity, due to higher hypocretin-1 concentrations in brain tissue compared to CSF.

**Methods :** We quantified hypocretin-1 levels directly in frozen brain tissue (prefrontal cortex) using a radioimmunoassay.

**Results :** We showed a significant decrease in hypocretin-1 concentrations in both disorders (controls:  $710.3 \pm 78.6$  pg/ml (n = 16); HD:  $510.6 \pm 60.0$  pg/ml (p = 0.048, n = 19); PD:  $448.1 \pm 82.6$  pg/ml (p = 0.043, n = 9)). Furthermore, in HD, hypocretin-1 levels decreased with disease progression indexed by Vonsattel grade (p = 0.014, r = -0.569).

**Conclusion :** The hypocretin system is impaired in Huntington's and Parkinson's disease and could form a target for future treatment.

**Support (optional):**

0877

**RELATION BETWEEN SUBTYPE OF PARKINSON DISEASE AND REM SLEEP BEHAVIOR DISORDER***Santamaria J, Kumru H, Tolosa E, Iranzo A*

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**Introduction :** Parkinson disease (PD) has been classified in two clinical subtypes (tremor-predominant and non tremor-predominant) that appear to have different patterns of progression and pathologic substrates. We have assessed in this study if REM sleep behavior disorder (RBD), a parasomnia frequently observed in PD, occurs differently in one or the other subtype of PD.

**Methods :** Sixty-one PD patients consecutively diagnosed with RBD, confirmed by video-polysomnography were evaluated. The subtype of PD and the relation between age at onset of PD and RBD were established by reviewing clinical records. The relation between age at onset of RBD and of parkinsonism was compared with that in a group of 41 multiple system atrophy (MSA) patients consecutively diagnosed with RBD.

**Results :** Fifty-four PD patients (88.5%) had the non-tremor-predominant subtype and seven (11.5%) had the tremor-predominant type. RBD preceded the onset of motor manifestations in 11 PD patients (20.4 %), all with the non tremor-predominant subtype. Age at onset of RBD and PD were negatively correlated (p<0.001), that is, the younger the age at onset of parkinsonism, the less likely it was for RBD to precede PD. In MSA this relation was not found (p:0.7). RBD only preceded parkinsonism when PD started after the age of 50 years.

**Conclusion :** This study suggests that: 1) most PD patients with RBD had the non-tremor-predominant form of PD; 2) in 20.4 % of these patients RBD preceded the onset of parkinsonism; 3) RBD never preceded parkinsonism in the tremor-predominant subtype and 4) RBD only preceded parkinsonism when the motor symptoms of the disease began after the fifth decade. A more widespread neurodegeneration in non-tremor-pre-

dominant PD may explain its preferential association with RBD.

**Support (optional):**

0878

**STRICTLY UNILATERAL RESTLESS LEGS SYNDROME. A SERIES OF THREE CASES***Valko P, Werth E, Siccoli M, Bassetti C*

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**Introduction :** Restless legs syndrome (RLS) is a clinically pleomorphic syndrome, which mostly affects the lower extremities. Although RLS complaints may show considerable asymmetry, cases with strictly unilateral long-term manifestation have not yet been reported. Our aim is to describe the characteristics of three RLS patients with exclusively unilateral symptoms.

**Methods :** The clinical histories, polysomnographic (PSG) findings and pharmacological responses are reviewed. All essential RLS criteria were fulfilled in each patient. Structural lesions were excluded by neuroimaging and electrophysiological studies.

**Results :** Patient 1 is a 68-year-old man with a 30-year history of burning sensation in his right groin, gluteal region and leg. Symptoms appeared only at rest, were initially restricted to night-time and improved by movement. Periodic limb movements in sleep (PLMS)-index was 99/h on his right and 7/h on his left. Treatment response to dopaminergics, opioids and antiepileptics was unsatisfactory. Patient 2 is a 52-year-old man with a 2-year history of painful sensations in the right lower leg, appearing only at rest in the evening, associated with an urge to move and relieved by walking. PLMS-index was 21/h on his right and 0/h on his left. With ropinirol 1.5mg daily symptoms subsided. Patient 3 is a 21-year-old man with a 5-year history of pressing pains in the right calf and sole, appearing at rest in the evening, with improvement by movement. Family history was positive for RLS. PSG shows predominantly right-sided PLMS (23/h resp. 13/h). No improvement was obtained with dopaminergics, antiepileptics, benzodiazepines and opioids.

**Conclusion :** Our observations suggest the existence of unilateral RLS with predominantly homolateral PLMS and less favourable treatment response as a (so-far unrecognized) variant of "classical" RLS.

**Support (optional):**

0879

**REM SLEEP BEHAVIOR DISORDER (RBD) AS AN EARLY MARKER FOR A NEURODEGENERATIVE DISEASE***Iranzo A, Molinuevo J, Santamaria J, Serradell M, Marti M, Valldeoriola F*

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**Introduction :** To determine the frequency and nature of the neurologic disorders developing in subjects diagnosed with RBD.

**Methods :** We systematically evaluated 44 consecutive subjects with idiopathic RBD that were diagnosed in our sleep center with a minimum clinical follow-up of two years. At the time of RBD diagnosis, patients had no waking motor or cognitive complaints and their neurologic examination was normal. Patients were assessed through a detailed clinical history and complete neurologic examination including UPDRS. Patients who were diagnosed with a neurologic disorder or reported cognitive complaints were neuropsychologically evaluated through five cognitive domains (attention, memory, language, visuospatial skills, and executive function).

**Results :** At the time of assessment, patients were 39 men and 5 women (mean age of 74 years and mean follow-up of 5 years). Nineteen patients (43.1%), 18 men and 1 woman, developed a neurologic disorder; Parkinson's disease (PD) in 8, dementia with Lewy bodies (DLB) in 6,

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and multiple system atrophy (MSA) with predominant cerebellar syndrome in 1. Four had mild cognitive impairment (MCI) with a neuropsychological pattern of prominent visuospatial and visuoconstructional impairment with relatively preserved free short-term memory recall that benefited from external cues. Interval between RBD onset and neurologic disease onset was  $10 \pm 5$  (range 3-22) years. Compared to subjects who did not develop a neurologic disorder, those who did had longer RBD duration ( $13.1 \pm 4.8$  versus  $11 \pm 7.3$  years,  $p=0.041$ ) and follow-up ( $6.7 \pm 2.9$  versus  $4.0 \pm 2.0$  years,  $p=0.001$ ).

**Conclusion :** Our findings expand previous observations by Schenck et al. indicating that RBD is often an early marker for a neurodegenerative disorder (PD, DLB, MSA and MCI). Close neurologic follow-up is necessary in idiopathic RBD subjects since early diagnosis of an evolving neurodegenerative disease may slow the rate of progression when using therapeutic strategies and when neuroprotective agents become available.

**Support (optional):**

### 0880

#### SLEEP DISORDERS QUESTIONNAIRES DO NOT CORRELATE WITH CAROTID DOPPLERS AND ECHOCARDIOGRAPHY IN STROKE PATIENTS

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**Introduction :** To investigate association between carotid dopplers, echocardiography, MRI, and MRA results with sleep apnea (SA) in stroke patients. Evidence shows that stroke patients have increased prevalence of SA (1). Comorbidities such as hypertension and cardiac disease partly explain the association. Mechanisms by which SA predisposes to stroke is unclear

**Methods :** 104 patients who were admitted to University of North Carolina's stroke center with documented ischemic strokes were screened. Age, gender, sleep apnea portion of the Sleep Disorders Questionnaire (SDQ-SA), and BMI were obtained. Carotid dopplers measured stenosis of RCC, RIC, LCC and LIC (right, left common and internal carotids); echocardiography measured ejection fraction, left ventricular hypertrophy, diastolic dysfunction, dilatation of left atrium, aortic sclerosis (AS), aortic regurgitation (AR), and aortic atherosclerosis. Presence of small and large vessel disease were indicated by MRI and MRA reports

**Results :** 104 (64 M, 40 F) patients underwent echocardiography. Of those, 78 had carotid dopplers (48 M, 38 F). The 104 patients had average age of 65 (range 26-93), SDQ-SA 33 (range 16-53); mean BMI 29 (range 8-75). A negative correlation was found between SDQ-SA score and RCC ( $r= -0.27$ ,  $r^2=0.076$ ,  $p=0.015$ ). In females, SDQ-SA negatively correlated with anterior stroke ( $r= -0.439$ ,  $r^2=0.19$ ,  $p=0.015$ ) and with AR and AS ( $r= -0.38$ ,  $r^2=0.14$ ,  $p=0.017$  and  $r= -.34$ ,  $r^2=0.12$ ,  $p=0.033$  respectively). In males, echo did not show correlation with stroke parameters (anterior, posterior) but had weak correlation between SDQ-SA and white matter disease ( $r=0.25$ ,  $r^2= 0.0.62$ ,  $p=0.0.098$ ). SDQ-SA correlated with BMI in echocardiography and carotid doppler data

**Conclusion :** These findings did not demonstrate a strong association between the risk of sleep apnea with standard echocardiography or carotid Doppler findings in patients with strokes. Possibly multiple factors are at play. Mechanisms for this relation need to be explored

**Support (optional):**

### 0881

#### DOES ACTIGRAPHY PROVIDE A VALID MEASURE OF OVERNIGHT SLEEP IN CHILDREN WITH AUTISM SPECTRUM DISORDERS?

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**Introduction :** Actigraphy, a minimally intrusive measure of disordered sleep, has promise in characterizing sleep patterns in children with autism spectrum disorders (ASD) and in following their response to treatment. We compared the performance of actigraphy to polysomnography in children with ASD to determine its usefulness in this population.

**Methods :** Two consecutive nights of polysomnographic (PSG) and actigraphic data were collected in seven children with ASD (ages 4-10 years), with one night of data collected in an additional child. Actigraphic data were recorded using the AW-64 Actiwatch (Mini-Mitter Co., Inc.), at a sampling rate of 15 seconds. "Lights off" and "lights on" were defined by the PSG technologist performing the study (PH). PSG staging was performed by a separate PSG technologist (MM) blinded to participant identity and study night, while actigraphic analyses were performed by an independent rater (CC). Total sleep time (TST), sleep latency (SL), sleep efficiency (SE), and wake time after sleep onset (WASO) for both methodologies were compared using Pearson correlation coefficients.

**Results :** As compared to night 2, night 1 PSG SL and WASO were higher, and TST and SE were lower, suggestive of first night effect. Correlation coefficients ( $r$ ) for night 1 are as follows: TST ( $r=0.89$ ,  $p=0.003$ ), SL ( $r=0.99$ ,  $p<0.0001$ ), SE ( $r=0.88$ ,  $p=0.004$ ), and WASO ( $r=0.77$ ,  $p=0.026$ ). For night 2: TST ( $r=0.87$ ,  $p=0.011$ ), SL ( $r=0.94$ ,  $p=0.002$ ), SE ( $r=0.79$ ,  $p=0.035$ ), and WASO ( $r=-0.27$ ,  $p=0.56$ ). The majority of identified WASO periods consisted of brief awakenings; only three records included periods of prolonged awakening (66.5 minutes or greater).

**Conclusion :** In children with ASD, actigraphy appears to be a valid measure of PSG-defined TST, SL, and SE, with robust correlations observed for two consecutive nights. Actigraphy did not appear as sensitive in characterizing PSG-defined nocturnal awakenings, a result described previously in other populations.

**Support (optional):** Vanderbilt University Interdisciplinary Discovery Grant. Vanderbilt University General Clinical Research Center M01 RR00095. Vanderbilt Kennedy Center for Research in Human Development. National Alliance for Autism Research.

### 0882

#### PREVALENCE OF RESTLESS LEGS SYNDROME AT A NEUROLOGY CLINIC IN KOREA

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**Introduction :** Restless legs syndrome (RLS) is a sensory-motor disorder characterized by a distressing urge to move the legs, onset or exacerbation with rest, relief with movement, and circadian pattern. Although treatment of RLS is available, this disorder has been frequently unrecognized. This study was performed to evaluate the prevalence and clinical characteristics of RLS in new patients who visited a neurology clinic.

**Methods :** New patients, who visited neurology clinic in a university affiliated hospital for various problems for one month period, were asked to complete a questionnaire including RLS diagnostic criteria and the Pittsburgh Sleep Quality Index. The responses of questionnaires by the patients were reviewed by a sleep disorder specialist. Other previous med-

ical history was recruited and laboratory study including blood test (Fe, TIBC, Ferritin, Hb), lumbosacral spine x-ray, and electrophysiologic study were performed.

**Results :** Of 231 patients (86 men and 145 women) who completed the questionnaire, 23 (10%) patients were diagnosed as RLS. The prevalence in women (15.2%) was higher than men (1.2%), and highest at patients aged 40 to 49 (13.2%). All RLS patients reported sleep disturbance: initiation disturbance (65.2%) and frequent waking (95.7%). Thirteen patients (56.5%) had low serum Ferritin (mean 33.1 ng/dl; norm > 50 ng/dl). In lumbar x-ray, 8 patients (34.8%) had intervertebral disc space narrowing. Three patients (13%) had a radiculopathy

**Conclusion :** The prevalence of RLS is not uncommon in patients who visited a clinic for other problems than RLS. The more education about RLS is needed in public.

**Support (optional):**

### 0883

#### QOLIE SCORES ARE NOT AFFECTED BY OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH INTRACTABLE EPILEPSY

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**Introduction :** Obstructive sleep apnea (OSA) is common in individuals with intractable epilepsy and appears to exacerbate seizure recurrence in some patients. While OSA typically decreases quality of life (QOL) in individuals without epilepsy, the impact on individuals with epilepsy is unknown.

**Methods :** We surveyed 35 adults undergoing polysomnography as part of a larger study evaluating OSA in patients with epilepsy. Subjects completed the Quality of Life in Epilepsy 89 (QOLIE 89) and underwent two nights of standard polysomnography including continuous nasal pressure monitoring. Recordings were scored using standard Rechtschaffen and Kales criteria and American Academy of Sleep Medicine guidelines. QOLIE parameters were correlated with results of the second night of polysomnography using Pearson correlation (significance set at  $p < 0.05$ ).

**Results :** Overall QOLIE 89 composite score did not correlate significantly with the sleep stages amounts or percents of total sleep time nor rates of apneas and hypopneas per hour (AHI). Similarly, QOLIE subscores did not correlate with polysomnographic results with one exception: health perception negatively correlated with the time and percent in stage one sleep ( $r=0.39$ ,  $p=0.024$ ,  $r=0.39$ ,  $p=0.023$ , respectively).

**Conclusion :** These findings demonstrate three possible scenarios: the QOLIE 89 lacks sensitivity to detect the impact of obstructive sleep apnea, sleep apnea has little impact on the quality of life in these patients, or our sample sizes are limited. Further impact of obstructive sleep apnea on patients with epilepsy may be judged by change in quality of life parameters following treatment of the sleep apnea. Clinicians should be aware that the QOLIE 89 may not be a sensitive tool for detecting obstructive sleep apnea in patients with epilepsy.

**Support (optional):** NINDS RO1 NS 042698 (BAM), NINDS KO2 NS2099 (BAM) and GCRC grants RR000095 (Vanderbilt), RR00042 (University of Michigan), and RRR00046 (University of North Carolina).

### 0884

#### SLEEP-WAKE DISORDERS AFTER TRAUMATIC BRAIN INJURY: RESULTS FROM A PROSPECTIVE STUDY

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**Introduction :** Sleep-wake disorders (SWD) often complicate the course of traumatic brain injury (TBI). This prospective study aims to assess the (essentially unknown) prevalence and characteristics of posttraumatic SWD.

**Methods :** Six months after TBI, 53 consecutive patients (43 males, mean age 37 years) were examined by means of sleep questionnaires, clinical examinations, computed tomography of the brain (CT), laboratory tests (including HLA typing, and cerebrospinal fluid hypocretin-1 determination), polysomnography (PSG), and multiple sleep latency tests (MSLT).

**Results :** 33 of 53 patients (62%) suffered from SWD following TBI, whereof 29 patients (55%) reported increased fatigue or excessive daytime sleepiness compared to before TBI. Epworth Sleepiness Scale (ESS) score was abnormal ( $>10$ ) in 14 patients (26%). One patient (2%) reported insomnia. Mean sleep efficiency on PSG was 92% (range 68-97), mean arousal index 8.0 (0.4-42.7). Mean sleep latencies  $<5$  minutes were found in 12 of 46 patients (26%) (mean 8.0 minutes), and were significantly lower in patients with mild TBI (mean 7.9 minutes, SD 3.3) when compared to moderate/severe TBI (mean 12.1 minutes, 4.5;  $p=0.031$ ), irrespective of apnea-hypopnea ( $>10$  in six patients) or periodic limb movement ( $>10$  in nine patients) indices. Four patients had  $\geq 2$  sleep onset REM periods on MSLT. Subjective estimation of SWD as well as PSG and MSLT findings were independent of severity or localization of TBI, gender, age, pathological neurological findings, HLA typing, or hypocretin-1 levels.

**Conclusion :** The prevalence of 62% in our consecutive study population shows that complaints of SWD are common after TBI. Excessive daytime sleepiness (as assessed by ESS and MSLT) is the most frequent posttraumatic SWD, whereas insomnia appears to be rare. Surprisingly, patients with mild TBI are more at risk for the development of posttraumatic SWD. Other risk factors such as demographic characteristics or HLA findings could not be identified, and correlations between localization of pathological CT findings, hypocretin-1 levels and outcome were not found. The pathophysiology of posttraumatic SWD, therefore, remains essentially unknown.

**Support (optional):**

### 0885

#### DAYTIME HYPOACTIVITY AND DISRUPTED SLEEP IN MIGRAINE: A PILOT ASSESSMENT VIA ACTIGRAPHY

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**Introduction :** Migraine headache is a frequent medical complaint for many. Little research has been conducted to quantify the disruption in daily activity and sleep associated with a migraine episode. This ongoing study explores the use of actigraphy as a quantitative tool for measuring migraines.

**Methods :** Migraine episodes were noted through the use of a headache calendar, and activity was continuously monitored via actigraphy for a 4-week period. Data were scored for sleep and separated into Day and Night segments. Relative changes from baseline (an average of 4 continuous non-migraine days and nights respectively) were calculated.

**Results :** Analyses ( $n=57$  episodes) found Daytime movements were less frequent, shorter in duration, and of smaller magnitude on migraine days

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compared to non-migraine days ( $F=142.160$ ,  $p<0.001$ ,  $F=92.490$ ,  $p<0.001$ , and  $F=33.123$ ,  $p<0.001$ , respectively). On Nights following migraine, decreases were seen for ZCM ( $F=12.392$ ,  $p<0.001$ ), TAT ( $F=14.036$ ,  $p<0.001$ ), and PIM ( $F=1198.941$ ,  $p<0.001$ ). Results on Nights prior to a migraine, however, showed an increase in frequency and duration of movements. No differences were found between Daytime movement for mild ( $< 7$  on 10 pt VAS) and severe headaches (7-10); however, during Nights prior to a migraine, there were more movements of longer duration for those with mild migraine ( $F=18.406$ ,  $p<0.001$ , and  $F=18.875$ ,  $p<0.001$ , respectively). Conversely, those who had severe migraines demonstrated greater magnitude of movement with longer duration on Nights following migraine ( $F=484.955$ ,  $p<0.001$  and  $F=7.127$ ,  $p<0.009$ , respectively).

**Conclusion :** Actigraphy can be useful for quantifying disruptions surrounding a migraine. Data indicated hypo-activity during the day of, and the night following an attack. More movement during the night prior to a migraine episode suggests possible pre-dromal signs or trigger of the migraine that follows. Furthermore, there is a distinct difference in the night pattern of activity between migraine episodes that are milder to those that are severe.

**Support (optional):**

### 0886

#### EVALUATION OF DAILY SLEEP DIARIES IN ALZHEIMER PATIENTS: A POLYSOMNOGRAPHIC STUDY

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**Introduction :** Alzheimer patients generally present worsening of age related sleep disturbances. Specific symptoms related to cholinergic deficit are also present. Daily sleep diaries are qualitative method that allows assessing the quality of sleep. The aim of this study was to verify the reliability of this method compared to polysomnography.

**Methods :** Fourteen Alzheimer patients aging 65-87ys, (6 males, 8 females) underwent polysomnography (PSG) and REM sleep spectral analysis with brain mapping, preceded by 2 habituation PSGs. FFT during REM sleep was performed in frontal, centro-parietal, temporal, occipital brain areas, and total averaged electrodes. After polysomnography, Alzheimer patient caregivers answered sleep diary questions for 15 consecutive days. Sleep diary scored subjective sleep quality (poor, regular, good), sleep latency ( $<30$ ,  $>30$ min), number of awakenings (0, 1,  $>1$ ), number daytime naps (0,  $\leq 2$ ,  $>2$ ). Linear correlation was performed between averaged sleep diary scores and polysomnography parameters.

**Results :** Sleep quality score inversely correlated with REM sleep latency ( $R=-0.88$ ), Number of awakenings inversely correlated with REM sleep time ( $R=-.87$ ). Number of daytime naps positively correlated with REM sleep overall delta power ( $R=0.87$ ).

**Conclusion :** All sleep diary parameters correlated with REM sleep and REM sleep EEG parameters. Sleep disturbances in Alzheimer patients mainly affect REM sleep due to cholinergic deficit. In the present study polysomnographic and qualitative parameters of REM sleep preservation were consistently correlated.

**Support (optional):** AFIP and FAPESP/CEPID

### 0887

#### ASSESSING WHOLE BRAIN PERFUSION CHANGES IN REM SLEEP BEHAVIOR DISORDER

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**Introduction :** REM behavior disorder (RBD) is a parasomnia characterized by the loss of normal atonia and abnormal motor control during REM sleep, leading to complex motor behaviors. Striatal dopaminergic abnormalities, cortical EEG slowing and cognitive deficits have also been documented, suggesting a defective cerebral network. Although the pathogenesis of RBD remains unclear, cumulative findings strongly suggest that RBD could be a prodromal feature of neurodegenerative disorders. The aim of this study was to investigate and describe voxel-based cerebral perfusion in SPECT in idiopathic RBD patients, to show the topographic networks involved in this disease.

**Methods :** Cerebral blood flow measurements using <sup>99m</sup>Tc-Ethylene Cysteinate Dimer (ECD) SPECT were performed on 8 patients with polysomnographically-confirmed RBD and 9 age-matched controls (mean age:  $69.9 \pm 8.2$  vs  $67.4 \pm 6.82$  years).

**Results :** An increased perfusion in the pons and putamen bilaterally and in the right hippocampus have been found, associated with a decreased perfusion in the frontal (Brodmann area (BA) 4, 43, 44, 6, 10, 47 bilaterally and left BA 46) and temporo-parietal (BA 7, 13, 20, 21, 22, 39, 40, 41, 42, 43, bilaterally) cortices.

**Conclusion :** Results shown perfusional abnormalities in RBD patients located in the brainstem, the striatum and in cortical areas. These abnormalities are consistent with the topographic metabolic profile of Parkinson's disease. These findings confirm the growing awareness that this disorder is much more than a mere parasomnia

**Support (optional):** This research was supported by the Canadian Institute of Health Research and The Canadian Senior Chair on Sleep Disorders.

### 0888

#### DAYTIME SLEEPINESS IN PATIENTS WITH REFRACTORY EPILEPSY

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**Introduction :** Excessive daytime sleepiness (EDS), a common complaint in epilepsy, has been attributed to antiepileptic drugs (AEDs), seizures, or comorbid obstructive sleep apnea. Whether the complaint is reflected by objective tests for EDS, and what clinical features predict sleepiness are not well known.

**Methods :** 52 adults (25F), mean age 38.6 yrs (18-63) with refractory epilepsy and symptoms suggestive of sleep apnea were enrolled in a study investigating the impact of sleep apnea on epilepsy. Subjects underwent polysomnography (PSG) for two nights, had a multiple sleep latency test (MSLT) after night 1, and completed the Epworth Sleepiness Scale (ESS) as well as a subjective self-rating of sleepiness.

**Results :** Forty of 52 subjects (76.9%) reported EDS. Mean ESS (+/-

standard deviation) was 10.9 +/- 5.8. MSLT data were available for 42 subjects. Mean sleep latency (MSL) was 8.4 minutes +/- 5.17. 21 subjects (50.0%) had abnormal MSLTs, including 14 (33.3%) with MSL < 5 minutes and 7 (16.7%) with MSL of 5-8 minutes. Four had 1 or more sleep-onset REM periods. The ESS scores were significantly higher in subjects with subjective sleepiness (12.4 +/- 5.5 vs. 6.2 +/- 4.0;  $p = 0.001$ ) but the MSLT scores were not (8.0 +/- 4.7 vs. 9.8 +/- 6.7;  $p = 0.48$ ). The only clinical variable correlating with ESS was seizure frequency ( $r=0.32$ ,  $P=0.03$ ). There was no significant correlation between MSLT and ESS ( $r=-0.11$ ,  $P=0.50$ ), age, gender, number of AEDs, seizure frequency or apnea status.

**Conclusion :** EDS is common among refractory epilepsy patients selected for sleep apnea symptoms, but seizure frequency may still be a key contributor. Subjective measures of EDS cannot replace objective measures among these patients. Patients with epilepsy and sleep complaints should be carefully screened for sleep disorders, and in some cases this should include objective testing.

**Support (optional):** NINDS RO1 NS 042698 (BAM) and GCRC grants M01 RR00095 (Vanderbilt), RR00042 (University of Michigan) and RR00046 (University of North Carolina).

### 0889

#### WAKING EEG SLOWING AND COGNITIVE IMPAIRMENT IN PARKINSON'S DISEASE ARE ASSOCIATED WITH REM SLEEP BEHAVIOUR DISORDER

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**Introduction :** Recently, a slowing of the waking EEG have been reported only in PD patients with concomitant RBD. 1 The aims of the present study was to evaluate the cognitive profile of PD patients with RBD using neuropsychological assessments and study the relation between EEG slowing and cognitive functioning in these patients.

**Methods :** Eight patients with PD and RBD (7 men, mean age: 64.0±9.5y), 8 PD patients without RBD (4 men; mean age: 65.4±4.8y), and 12 controls (9 men, mean age: 64.8±7.7y) underwent one night of polysomnography and a waking EEG recording followed by a neuropsychological evaluation.

**Results :** No between-group difference was found for age, educational level, disease severity as assessed by the UPDRS, disease duration and dosage of dopaminergic medication. A waking EEG slowing was observed in posterior brain areas, namely an increase in delta and/or theta power in temporal, parietal, and occipital regions and a decrease of dominant occipital frequency, only in PD patients with RBD. These patients also showed a significantly lower score on the Block Design compared to PD patients without RBD ( $p=0.04$ ) and controls ( $p=0.005$ ). PD patients with RBD showed poorer performances, compared to controls, on the Bells test ( $p=0.01$ ) and the Purdue Pegboard ( $p=0.005$ ). Negative correlations were found between Blocks Design performance and delta power in parietal ( $r=-0.78$ ,  $p=0.04$ ), and occipital ( $r=-0.75$ ;  $p=0.04$ ) areas.

**Conclusion :** PD patients with RBD show visuo-constructive deficits compared to both PD patients without RBD and controls. Moreover, comparatively to control subjects, PD with RBD present visuo-attentional and manual dexterity impairments. This suggests that the presence of RBD in

PD may be associated with a negative cognitive profile. Thus, a follow-up of these patients would be important in order to verify whether RBD may be an early sign of evolution toward dementia in PD patients.

**Support (optional):** 1. Gagnon et al., 2004, Neurology

### 0890

#### SLEEP AND AUTONOMIC FUNCTION IN PATIENTS WITH FAMILIAL DYSAUTONOMIA

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**Introduction :** Familial Dysautonomia (FD) is a rare genetic disorder characterized by autonomic nervous dysfunction and implicates vital systems. Although quality of life improved due to intensive treatment, sudden death at times during sleep remains an important concern. Our aim was to quantify sleep disturbance, sleep related breathing disorder and their connection to autonomic function in FD.

**Methods :** The study included 11 FD patients and 11 matched control subjects. All underwent standard sleep studies scored by an expert. Evaluation of autonomic function was based on time dependent Heart Rate Variability analysis. The LF component of the HRV spectrum represents sympathetic activity, HF mainly parasympathetic modulation and VLF stands for vasomotion, thermoregulation. Statistical analysis was performed by one tailed t-test to compare different parameters between the two groups and one way ANOVA to test the behavior of parameters across sleep-wake states within each group.

**Results :** FD patients had significantly shorter total sleep time, lower sleep efficiency, shorter sleep latency and longer REM latency than controls. The percentage of SWS and Stage II was similar in both groups; however FD patients had significantly less REM, more arousals and more movement time. Patients had significantly more desaturations, lower minimal saturation and spent more time at lower than 90% oxygen saturation. They had higher mean and maximal ETCO<sub>2</sub>. No significant difference was found between groups in VLF and LF while wake at night, whereas HF was significantly lower in FD during all sleep wake states. VLF remained similar during both NREM and REM sleep, and LF became lower in FD as compared to controls. The LF/HF ratio pointed towards sympathetic predominance in FD during all stages of sleep. The previously described behavior of LF, HF, and LF/HF ratio during sleep was reconfirmed in the control group, however it was not significantly consistent in FD.

**Conclusion :** Sleep in FD is segmented and its architecture is disturbed. The detected ventilation disturbance corroborates with results of previous studies. The autonomic function is disturbed and the wake time compensatory mechanisms are mostly lost during sleep. Understanding the compensatory mechanisms during wakefulness and why they are diminished during sleep can contribute to a more rational treatment of FD patients.

**Support (optional):**

### 0891

#### PITTSBURGH SLEEP QUALITY INDEX HAS A STRONG CORRELATION WITH VALIDATED QUESTIONNAIRES MEASURING SLEEPINESS, INSOMNIA, AND SLEEP APNEA IN PATIENTS WITH STROKES

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**Introduction :** Evidence shows that patients who suffered stroke are more likely to have pre-existing symptoms of sleep-wake disturbance.

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Sleep apnea, for example, is associated with increased risk of stroke independent of known confounding factors and that the presence of sleep apnea has been linked to recurrent strokes (1). We aim to investigate the prevalence of sleep-related symptoms in stroke patients using Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), Insomnia Severity Scale (ISI), and Sleep Apnea portion of the Sleep-Disordered Questionnaire (SA-SDQ).

**Methods :** We screened 42 patients who were admitted to University of North Carolina's stroke center with documented acute ischemic or hemorrhagic strokes. Information such as age, gender, and BMI were obtained and patients were asked to complete these questionnaires: PSQI, SDQ-SA, ISI, and ESS. Correlations were calculated using Pearson correlation ( $p < 0.05$ )

**Results :** 42 (28 M, 14 F) patients participated with total of 31 ischemic and 11 hemorrhagic strokes. Average age was 66 yo (range 31-87) and mean BMI 28 (range 20 -54). For the group, average PSQI was 13 (2-25, sd 5); ESS 7 (0-17, sd 4); ISI 8 (0-21, sd 5); and SA-SDQ 34 (20-54, sd 9). Significant correlations were found between PSQI and following questionnaires: SDQ-SA ( $r=0.54$ ,  $p < 0.0005$ ), ISI ( $r=0.77$ ,  $p < 0.0001$ ), and ESS ( $r=0.35$ ,  $p < 0.03$ ). All patients who had positive scores on ESS, ISI, and SA-SDQ had scores of 7 or greater on PSQI

**Conclusion :** These findings indicate that patients with stroke have high prevalence of sleep-related symptoms. In our cohort, all patients who had positive scores on ESS, ISI, or SA-SDQ had a positive score on PSQI. Therefore, we believe that the PSQI is a valuable screening tool for symptoms of sleep disturbance in stroke populations

**Support (optional):**

0892

### TREATING OBSTRUCTIVE SLEEP APNEA IN PATIENTS WITH COMPLEX CONGENITAL HEART DISEASE FOLLOWING THE FONTAN REPAIR

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**Introduction :** Ten percent of congenital heart disease patients have single ventricle physiology. The Fontan procedure treats this by directing systemic venous return to the pulmonary arteries. Absent right ventricular ejection, pulmonary blood flow depends on low pulmonary vascular resistance and effective systemic ventricular function. Normal inspiration with negative intrathoracic pressure enhances this flow, increasing systemic venous return. Obstructive sleep apnea (OSA) has detrimental effects on cardiac physiology. Treating OSA is challenging in Fontan patients as continuous positive airway pressure (CPAP) can interfere with systemic venous return reducing cardiac index (CI). We describe our experience establishing safe CPAP levels in 3 Fontan patients with OSA. **Methods :** Three Fontan patients diagnosed with severe OSA via polysomnography were evaluated in the cardiac catheterization lab with electroencephalographic monitoring. CPAP pressures were increased stepwise every 10 minutes while monitoring pulmonary and systemic pressures and saturations. CI and vascular resistance were calculated at each CPAP level. CPAP was increased until CI declined.

**Results :** Patient 1 had a CPAP threshold of 9 cm H<sub>2</sub>O with higher pressures decreasing CI by 0.4 L/min/M<sup>2</sup> and increasing pulmonary capillary wedge pressure (PCWP) by 4 mmHg. Patient 2 had a CPAP threshold of 12 cm H<sub>2</sub>O with higher pressures decreasing CI by 0.5-0.8 L/min/M<sup>2</sup> and increasing PCWP by 2 mmHg. Patient 3 had a CPAP threshold of 5 cm H<sub>2</sub>O with higher pressures decreasing CI by 0.5 L/min/M<sup>2</sup> and increasing PCWP by 3 mmHg. Subsequent CPAP titrations revealed subthreshold pressure requirements of 6 and 8 cm H<sub>2</sub>O for patients 1 and 2. Patient 3's OSA was not controlled at 5 cm H<sub>2</sub>O and required supplemental oxygen to maintain nocturnal saturations above 88%.

**Conclusion :** This pilot study demonstrates the safety and importance of establishing CPAP thresholds in Fontan patients with OSA ensuring maximal therapeutic benefit while avoiding potentially dangerous reductions in CI.

**Support (optional):**

0893

### DEFINING AND SCORING GASTROESOPHAGEAL REFLUX EVENTS IN OBSTRUCTIVE SLEEP APNEA PATIENTS DURING POLYSOMNOGRAPHY WITH AND WITHOUT CPAP

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**Introduction :** An increased prevalence of Gastroesophageal Reflux Disease (GERD) has been reported in Obstructive Sleep Apnea (OSA) patients using validated reflux questionnaires and by polysomnographic pH and/or Pes monitoring. Previous studies have defined a reflux event as an esophageal pH<4 for >4 seconds. Weakly acidic events (>=1 pH unit) have also been reported in association with apneas/hypopneas during polysomnography but are of unclear significance. Reflux events in OSA patients were analyzed using different scoring definitions at baseline and with CPAP.

**Methods :** Ten known apnea patients (5 male), with previous GERD

symptoms and currently receiving GERD treatment, underwent baseline polysomnography the first night and with CPAP the second study night. Patients stopped reflux therapy >7 days and CPAP >2 nights prior to testing that included pHmetry 5cm above the lower esophageal sphincter. Reflux events were scored in two ways: (1) Definition 1: pH<4 for >4 seconds (2) Definition 2: pH drop >1 unit for >4 seconds. Poisson regression, generalized estimating, and compound symmetry correlation structure were used to analyze the data based on an eight hour study.

**Results :** Average age was 51.8 (29-74); average BMI was 40.4 (29.3-50.8). Average AHI was 21.5 (10-92); average oxygen desaturation nadir was 83.5% (55-93%). pH drops >1 unit were frequently observed to mirror apnea-related oxygen desaturations, yet most did not attain a pH <4. After data from one extreme outlier was excluded, reflux events decreased significantly with CPAP using both definitions [from 25.6 (baseline) to 8.0 (CPAP) (p=0.0037) with definition 1 and from 135.6 (baseline) to 66.4 (CPAP) (p=0.0383) with definition 2].

**Conclusion :** Conventional reflux scoring requires a pH threshold of 4.0. Smaller pH drops of 1 unit have been observed in direct association with apneas/hypopneas, mirroring the "sawtooth" pattern of apnea-related oxygen desaturations. There were many more weakly acidic events (definition 2) compared to the number of severe events (definition 1). CPAP has a major positive effect on the more severe reflux events. Although the frequency of weakly acidic events was decreased with CPAP, a large number of residual weakly acidic events persisted with CPAP. The clinical significance of these residual weakly acidic events on the integrity of esophageal tissue and GER pathophysiology, symptoms, and treatment requires further investigation.

**Support (optional):** Funded by TAP Pharmaceutical Products, 11031 Birchtree Lane, Laurel, MD 20723.

0894

### ALTERATIONS IN THE SLEEP PATTERN AND ITS ASSOCIATION WITH DISEASE ACTIVITY, DEPRESSION AND FATIGUE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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**Introduction :** To assess the alterations in the sleep pattern and its association with disease activity, depression and fatigue in Mexican Patients with Systemic Lupus Erythematosus (SLE).

**Methods :** Fifty-two SLE women attending the Immunology and Rheumatology Department Outpatient Clinic from the INCMNSZ with a mean age of 38±11 years were studied by two nights of polysomnography and by a Multiple Sleep Latency Test (MSLT) and compared with nineteen healthy women (mean age 30±8 years). Validated instruments were used to measure disease activity (MEX-SLEDAI), fatigue (Fatigue Severity Scale (FSS)), and depressive symptoms (Beck Depression Inventory (BDI)).

**Results :** Polysomnographical data showed that the SLE group slept less than healthy women (390.6±27.1 vs 418.6±27.8, p<0.02) and they have a lower sleep efficiency (85.5±6.0 vs 91.0±4.0, p<0.02). SLE patients have more fragmented sleep, approximately twice the number of awakenings > 1 minute (8.7±4.9) than the healthy women (4.8±1.6, p<0.05), and also they have lighter sleep (Stage 1%; 11.3±3.8 vs 8.5±2.7, p<0.05), and they

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were more sleepy during the day than healthy women ( $7.6\pm 4.5$  vs  $13.1\pm 4.8$ ,  $p<0.0001$ ). OSAH was present in 26.9% and PLMS was present in 32.7%. Mxslsdai score was the only parameter that correlated with nocturnal sleep parameters: sleep efficiency, number of awakenings  $> 1$  minute, and stage 1%. FSS correlated with BDI score. In a multiple logistic regression model BDI score (without fatigue item) was a risk factor for fatigue with an OR of 1.2 (95% CI 1.06-1.41),  $p<0.005$ .

**Conclusion :** Alterations in sleep pattern (light sleep, sleep fragmentation and sleep deficiency) are related to disease activity in SLE, while fatigue is related to their level of depression.

**Support (optional):** This work was supported by grants from CONACYT 34937-H.

### 0895

#### SLEEP DISORDERS IN ACROMEGALIA: AN UNEXPECTEDLY HIGH PREVALENCE OF RESTLESS LEG SYNDROME (RLS)

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**Introduction :** Acromegalics suffer a high incidence of sleep related breathing disorders (SRBD) due to bone mass and soft tissue swelling in the upper airways. Sleep disorders other than SRBD have rarely been reported in acromegalia.

**Methods :** 40 acromegalics (14 M, 26 F, mean age  $52.6\pm 13.6$ ) actually under treatment (surgery and/or somatostatin analogues) referred for evaluation of possible sleep disorders, underwent a structured interview for insomnia, excessive daytime sleepiness (EDS), SRBD, sleep related movement disorders (SRMD), circadian sleep disorders and parasomnias. Epworth sleepiness scale (ESS) and RLS diagnostic interview (Allen 2003) were performed in pts reporting EDS and SRMD or specific sensory symptoms at general assessment. We selected 21 pts for video-polysomnography (vPSG), and 19 for portable SRBD monitoring.

**Results :** Grouping by symptoms, insomnia was reported in 7, EDS in 21, snoring in 28, apneas in 13, PLMS in 4, RLS in 12, bruxism in 1, recurrent nightmares in 1, delayed sleep phase in 1. So far 16 standardized PSG have been obtained in the most symptomatic pts (4 M, 12 F, mean age  $57\pm 14$ , mean BMI  $30\pm 5$ ). 5 proved positive for SAS (mean apnea index  $11\pm 19$ , mean SaO<sub>2</sub>  $96\pm 1$ ), 6 for snoring, 8 for RLS, 10 for PLMS (PLMS index  $29\pm 24$ ). Sleep efficiency (SE) was overall reduced (mean  $66\pm 13$ ), more so in pts with RLS (mean SE  $62\pm 14$ ). EDS was generally mild, (mean ESS  $6\pm 6$ ) in pts with RLS, more severe by report in SAS pts (despite mean ESS  $5\pm 4$  and mean sleep latency [SL] at MSLT  $12\pm 5$ ). Nocturnal SL was longer in RLS pts (mean  $42\pm 33$ ) than other pts (mean  $18\pm 16$ ).

**Conclusion :** Acromegalics sleep poorly, and are fatigued during daytime. Snoring is quite prevalent, SAS less, usually mild to moderate, RLS highly prevalent (30%). A role for somatostatin and GH control of dopaminergic sleep related mechanisms could be hypothesized.

**Support (optional):**

### 0896

#### SIMULTANEOUS AMBULATORY BLOOD PRESSURE MONITORING AND POLYSOMNOGRAPHY: EFFECT OF SLEEP STATE ON THE DETECTION OF NOCTURNAL DIPPING

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**Introduction :** Absent nocturnal blood pressure (BP) dipping ( $<10\%$  fall from daytime level) bears better relation to the prognosis of hypertensive disease than daytime records. BP at night does not necessarily represent BP during sleep. No study has concentrated on the effect of distinguishing between nighttime and sleep on the detection of nocturnal dipping in ambulatory blood pressure monitoring (ABPM).

**Methods :** We have recruited 36 patients, 28 male, with suspected OSAHS attending the sleep clinic for diagnostic PSG and who agreed to wear an Spacelabs 90207 ABP monitor during the PSG. Their mean age was  $45\pm 11$  years, AHI was  $35\pm 29$  AH/h, BMI was  $30.8\pm 5.4$  kg/m<sup>2</sup>, 13 had history of hypertension. A microphone attached to the ABP monitor recorded its noise when activated and allowed to classify each BP measurement in the PSG as being made in awake or sleep state. We defined nocturnal dipping as  $>10\%$  reduction in systolic (S), diastolic (D) and mean arterial pressure (M) from daytime to nighttime (DIPnight) or from daytime to sleep (DIPsleep).

**Results :** Patients were asleep during (mean $\pm$ SD)  $61\pm 24\%$  (range 0 to 100%) of the  $14\pm 1$  nighttime BP measurements. Average DIPnight-S was  $9\pm 6\%$ , DIPnight-D was  $16\pm 9\%$ , and DIPnight-M was  $13\pm 7\%$ . Dipping was significantly larger when calculated from daytime to sleep: DIPsleep-S was  $11\pm 8\%$  (paired  $t=3.1$ ,  $p=0.004$ ); DIPsleep-D was  $18\pm 10\%$  (paired  $t=2.7$ ,  $p=0.01$ ); and DIPsleep-M was  $15\pm 9\%$  (paired  $t=3.0$ ,  $p=0.005$ ). Using DIPnight we found 17 S-dippers, 27 D-dippers, 23 M-dippers. Using DIPsleep the number of dippers increased respectively to 21 S-dippers, 30 D-dippers, 26 M-dippers (respectively,  $p=0.000$ ;  $p=0.024$ ;  $p=0.000$ ).

**Conclusion :** Awakenings during ABPM can lead to inadequate dipper/non-dipper classification. This conclusion might not be confined to patients with OSAHS since AHI and other measures of disturbed sleep did not correlate with the number of awakenings during the BP measurements.

**Support (optional):**

### 0897

#### DEPRESSIVE SYMPTOMS MEDIATE THE RELATIONSHIP BETWEEN SLEEP AND FATIGUE IN BREAST CANCER

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**Introduction :** Breast cancer patients often have complaints of poor sleep, fatigue and depressed mood. We explored the relationship between self reports of sleep disturbance, fatigue, and depression symptoms in women with breast cancer.

**Methods :** 82 women with stage I-III breast cancer undergoing adjuvant anthracycline-based chemotherapy were studied. Assessments were taken before and during cycle 1 and cycle 4 chemotherapy. Sleep complaints were assessed with the Pittsburgh Sleep Quality Index (PSQI), fatigue was assessed with the short form of the Multidimensional Fatigue Symptom Inventory (MFSI-SF), and depression was assessed with the Center of Epidemiologic Studies Depression scale (CES-D). At each time point, Pearson product correlations between PSQI, MFSI-SF and CES-D were computed. In addition, partial correlations between sleep and fatigue controlling for depression were computed, as well as partial correlations between sleep and depression controlling for fatigue.

**Results :** Fatigue and depressive symptoms were significantly correlated with sleep disturbance at all time points (fatigue and sleep correlation coefficients ranged from  $r=0.40$  to  $r=0.61$ ; depressive symptoms and sleep correlation coefficients ranged from  $r=0.48$  to  $r=0.65$ ; all  $p<0.0005$ ). After controlling for depressive symptoms, the relationships



between sleep and fatigue at each time point were no longer significant. After controlling for fatigue, the relationships between sleep and depressive symptoms at each time point were still significant.

**Conclusion :** The relationship between sleep and fatigue was explained by depressive symptoms. Although cause and effect may not be concluded, the consistency of the mediation effect of depressive symptoms between sleep and fatigue across multiple time points warrants future testing of causal models. Future studies should examine the effect of treating depressive symptoms on sleep and fatigue in breast cancer.

**Support (optional):** NCI CA85264, NCI CA112035, CBCRP 11IB-0034, CBCRP 11GB-0049 and VASDHS

## 0898

### INITIAL REPORT OF SLEEP DISRUPTION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

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**Introduction :** There is an increased prevalence of gastrointestinal (GI) symptoms, peptic ulcer disease & colon CA in night shift-workers; less is known about sleep in IBD, a chronic immuno-inflammatory disorder that greatly impacts quality of life (QOL). Sleep may contribute to medical morbidity through immune and inflammatory processes. While sleep disturbances are a common extrapyramidal symptom of Irritable Bowel Syndrome (IBS), this is one of the first studies to report on sleep patterns in IBD.

**Methods :** 16 inactive IBD, 9 IBS & 7 healthy controls (C) completed the Pittsburgh Sleep Quality Index (PSQI), Epworth Sleepiness Scale (ESS), IBD-Quality of Life Scale (IBDQ), SF-12 & overnight polysomnography (PSG). Mean ages of IBD, IBS & C were 41.4(13.3), 52.7(12.1) & 34.3(9.4). C were younger & age served as a covariate in analyses. PSGs were scored manually in 30s epochs w/standard criteria. Arousals were scored according to standard criteria. Time in bed was held constant at 8h.

**Results :** IBD had poorer sleep quality and higher PSQI global scores than C but did not differ from patients w/IBS [ $F(2, 26) = 11.05, p = .00$ ]. The IBS group further differed from C on PSQI in terms of sleep efficiency (SE), duration of sleep (TST) and presence of disturbances. Numerically, across most measures, IBS reported the most sleep disruption, followed closely by IBD, followed by C. IBD did not differ from IBS or C on objective sleep parameters; IBS exhibited about 1 hour less TST [ $M = 365.65(66.4)$ ;  $F(2,26) = 5.49, p = .01$ ] & reduced SE [ $M = 78.0(13.4)$ ;  $F = 5.05, p = .01$ ] on PSG. Both IBS & IBS had less than 85% SE on PSG, more arousals [IBD = 17.89(12.1), IBS = 18.73(10.6), C = 8.70, 3.6] & %S1 [IBD = 12.38(5.2), IBS = 14.03 (9.14), C = 6.46,(5.1)]. PSQI global scores were linked to IBDQ ( $R^2 = .63, p = .00$ ), SF12-physical ( $R^2 = .25, p = .01$ ) & mental health ( $R^2 = .43, p = .00$ )QOL.

**Conclusion :** This is one of the first studies to look directly at sleep in patients with IBD. IBD & IBS both exhibit similar sleep c/o, objectively & subjectively; c/o are linked to QOL. Consistent with previous literature on IBS and sleep, IBS consistently reported the most disturbances. However, IBS did not differ from IBD on most parameters; the IBD group numerically fell between IBS and C but resembled IBS more closely. CNS hyperarousal & cognitive attributions may contribute to sleep c/o in IBS; However, sleep may affect IBD through immuno-inflammatory pathways & increased risk to flare and may be important in IBD disease management.

**Support (optional):**

## 0899

### THE EFFECTS OF NAPPING ON THE COGNITIVE PERFORMANCE OF WOMEN WITH SIGNIFICANT EMOTIONAL/BEHAVIOURAL PREMENSTRUAL SYMPTOMS

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**Introduction :** Daytime sleepiness can largely impede global functioning and lead to incidents and accidents. A population that is prone to the effects of daytime sleepiness is women with significant premenstrual symptoms, during the late-luteal phase of the menstrual cycle. Naps can help improve alertness and cognitive performance. The aim of this study was to examine the potential benefits of a short mid-afternoon nap on the cognitive performance of women with significant emotional/behavioural premenstrual symptoms.

**Methods :** Ten women with significant emotional/behavioural premenstrual symptoms (mean = 26.7 years) and nine women with minimal symptoms (mean = 26.6 years) took a mid-afternoon nap of approximately 30 minutes during the late-luteal phase of their cycle, and completed the Cognitive Performance Test (CPT) before and 30 minutes after napping. This protocol was repeated on another day of the late-luteal phase, but participants did not nap (no-nap condition). The napping and no-napping conditions were counterbalanced.

**Results :** The total number of correct responses significantly increased 30 minutes after napping compared to before napping for both groups of women,  $F(1,14) = 16.09, p < .01$ . In addition, reaction time significantly decreased 30 minutes after napping compared to before napping for both groups of women,  $F(1, 14) = 10.52, p < .01$ . This improvement was not found in the no-napping condition.

**Conclusion :** These results indicate that a short afternoon nap during the late-luteal phase improves cognitive performance among women with significant and minimal emotional/behavioural premenstrual symptoms. The possibility of using a nap to counteract declines in cognitive performance among women with significant premenstrual symptoms, during the late-luteal phase of their cycle, is therefore worth consideration.

**Support (optional):**

## 0900

### SLEEP COMPLAINTS AND QUALITY OF LIFE IN DEPRESSED VS. NON-DEPRESSED BREAST CANCER SURVIVORS

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**Introduction :** Insomnia is common in breast cancer (BRCA). We previously observed that depressed BRCA survivors reported greater insomnia than those who were not depressed. Here, we compare depressed/non-depressed survivors on specific sleep complaints, predictors of insomnia and quality of life (QOL).

**Methods :** 2959 women who had finished initial treatment for Stage I(>1cm)-IIIA BRCA <4yrs prior to enrollment completed a Thoughts and Feelings questionnaire which included the Center for Epidemiologic Studies—Depression screen (CESDsf), RAND36 QOL, and Women's Health Initiative—Insomnia Rating Scale (WHI-IRS). 17% had CESDsf scores >0.06, indicating clinically significant depressive symptoms ('depressed'). The WHI-IRS yields scores for overall insomnia (>9 indi-

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cates problematic insomnia), 9 sleep complaints (scored 0-4, higher scores indicate more frequent complaints) and sleep duration.

**Results :** Depressed survivors reported more overall insomnia (9.88 vs. 7.08), medication/alcohol use for sleep (2.20 vs. 1.63), trouble falling asleep (1.55 vs. .89), waking several times (2.69 vs. 2.4), waking up early (1.69 vs. 1.17), trouble resuming sleep (1.55, vs. 1.01), napping (1.13 vs. .92) and worse sleep quality (2.38 vs. 1.76) (all  $p < 0.001$ ). Differences were not significant for snoring, daytime sleepiness and sleep duration. In hierarchical regression, cancer stage, treatment and time since diagnosis, demographics, and health behaviors did not predict insomnia. However, in depressed survivors, more vasomotor symptoms and pain, and less optimism predicted insomnia. In non-depressed survivors, predictors were more vasomotor, gastrointestinal and psychological symptoms and worse emotional well-being. In multivariate analyses of variance, depressed women who reported the most medication/alcohol use, waking several times, snoring, or worst sleep quality had worse mental components of QOL; however, links to physical components of QOL were weaker.

**Conclusion :** Compared with non-depressed BRCA survivors, those who were depressed reported problematic insomnia and 11-74% greater frequency for 7 out of 10 specific sleep complaints. Predictors of insomnia varied by depression status, but cancer-specific variables were not significant risk factors. Insomnia in non-depressed survivors was associated with more psychological symptoms, suggesting that even subthreshold levels of distress are linked with worse sleep. Comorbid depression and sleep complaints particularly portend poorer functioning in survivors of early-stage BRCA.

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### 0901

#### DAYTIME SLEEPINESS AND SYMPTOMS ARE IMPORTANT CORRELATES OF FUNCTIONAL STATUS 3 MONTHS AFTER IMPLANTABLE CARDIOVERTER DEFIBRILLATOR (ICD) INSERTION IN VENTRICULAR ARRHYTHMIA PATIENTS

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**Introduction :** Implantable cardioverter defibrillators (ICD) have emerged as the standard treatment for life threatening cardiac arrhythmias. Greater understanding of factors influencing early postoperative recovery after ICD insertion is needed to develop interventions to improve outcomes. The purpose of the study was to examine associations among demographic, clinical variables, daytime sleepiness, sleep quality, psychological states, and illness appraisal on functional outcomes 3 months after ICD placement.

**Methods :** Demographic and clinical data including age, gender, and left ventricular ejection fraction (LVEF) were collected prior to hospital discharge following ICD insertion. Functional status, psychological and symptom measures were obtained 3 months later. The sample comprised 240 patients (75% men), ages 23-79 (mean 58.5) years who received their initial ICDs. Variables and measures: functional status (Duke Activity Scale Index [DASI]), sleep quality (Pittsburgh Sleep Quality Inventory [PSQI]), daytime sleepiness (Epworth Sleepiness Scale [ESS]), pain severity (Brief Pain Inventory [BPI]), depressive symptoms (Beck depression Inventory II [BDI-II]), illness appraisal (Meaning in Illness Questionnaire [MIQ]). Univariate correlations and multiple regression were used to predict functional status at 3 months.

**Results :** Poor sleep quality (PSQI>5) was reported by 52.6% of participants; 29.5% reported excessive daytime sleepiness (ESS>=10). Mean

ESS was 7.94 + 4.46. Multiple regression analysis demonstrated scores on ESS ( $p=0.021$ ), BPI ( $p < 0.001$ ), BDI-II ( $p=0.003$ ), MIQ ( $p=0.001$ ) significantly explained an additional 26.9% of variance in functional status above that explained by demographic (age [ $p=0.05$ ], gender [ $p=0.014$ ]) and clinical variables (ejection fraction [ $p=0.001$ ]).

**Conclusion :** Greater daytime sleepiness, higher pain severity, greater depressive symptoms and higher threat of illness appraisals were associated with reduced functional status 3 months after ICD insertion in ventricular arrhythmia patients. Daytime sleepiness, pain severity, mood and illness appraisal are modifiable factors in the recovery process that contribute to functional outcomes. Interventions aimed at decreasing symptoms and altering patient's illness appraisals need to be tested to optimize functional outcomes in the early recovery process.

**Support (optional):**

### 0902

#### RELATIONSHIP OF MENOPAUSAL STATUS TO SLEEP IN WOMEN UNDERGOING CHEMOTHERAPY

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**Introduction :** Chemotherapy induces menopause in a large percent of women with breast cancer. Evidence has shown that natural menopause may affect sleep quality, but less is known about the effect of medical menopause with breast cancer patients.

**Methods :** 44 women (mean age=50.1 yrs, SD=9.3, range:34-79 yrs) diagnosed with stage I-III breast cancer, scheduled to receive at least 4 cycles of adjuvant anthracycline-based chemotherapy participated. Sleep was estimated with actigraphy (Ambulatory Monitoring, Inc.). Menopausal status was assessed with the Greene Climacteric Scale before chemotherapy (Time 1) and at the end of cycle 4 chemotherapy (Time 2). Women were divided into three groups: premenopausal throughout treatment (n=10), menopause occurring during treatment (n=13), or postmenopausal throughout treatment (n=21).

**Results :** ANOVA and paired t-tests revealed a significant interaction for wake time after sleep onset (WASO;  $F [2,42] = 4.65, p=.015$ ) and percent wake time at night (%Wake;  $F [2,41] = 3.31, p=.047$ ) between Time (Time 1 and Time 2) and Menopausal Status ( $p=.015$ ), with those women premenopausal throughout treatment having increased WASO ( $t = -3.40, df = 9, p=.008$ ) and more %Wake ( $t = 2.55, df = 9, p=.031$ ) after chemotherapy than before. There were no significant differences in WASO or %Wake between women who underwent medically induced menopause vs. postmenopausal women. There were no significant differences in sleep duration or other sleep variables.

**Conclusion :** Women with breast cancer who remain premenopausal spend more time awake during the night after chemotherapy than before the start of treatment. Women who are premenopausal pre-chemotherapy but postmenopausal after, or who are postmenopausal before the start of treatment showed no change in their sleep and were not different in their sleep characteristics. Further analyses of the climacteric variables may help explain these changes and if other similarities exist between these two groups prior to chemotherapy.

**Support (optional):** Supported by NCI CA85264, NCI CA112035, CBCRP 11IB-0034 CBCRP 11GB0049 and the research service of the VASDHS

**0903****PRE-TREATMENT SUBJECTIVE SLEEP QUALITY PREDICTS FATIGUE, MOOD, AND QUALITY OF LIFE IN BREAST CANCER PATIENTS DURING CHEMOTHERAPY**Liu L,<sup>1,2</sup> Parke B,<sup>3,4</sup> Dimsdale J,<sup>1,3</sup> Fiorentino L,<sup>5</sup> Johnson S,<sup>1,2</sup> Ancoli-Israel S<sup>1,2,3</sup>

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**Introduction :** Fatigue, sleep and mood problems are common, distressing symptoms in breast cancer patients undergoing chemotherapy, and adversely affect quality of life (QOL). As a part of larger study on sleep in breast cancer, we examined whether pre-treatment sleep predicted fatigue, mood, and QOL.**Methods :** Eighty women (mean age=50.2 yrs, SD=9.6, range: 34-79 yrs) diagnosed with stage I-IIIa breast cancer, scheduled to receive at least 4 cycles of adjuvant or neoadjuvant anthracycline-based chemotherapy were included. Subjective sleep, fatigue, mood and QOL were assessed using Pittsburgh Sleep Quality Index (PSQI), Multidimensional Fatigue Symptom Inventory (MFSI), Center for Epidemiologic Studies-Depression (CES-D), and Functional Assessment of Cancer Therapy - Breast (FACT-B). All questionnaires were administered before and during weeks 1-3 of both cycle 1 and cycle 4 chemotherapy. Patients were divided into two groups according to the pre-treatment PSQI: good sleepers (GS with PSQI<5) and poor sleepers (PS with PSQI≥5).**Results :** PS reported significantly more total fatigue before (p=0.024) and during cycle 1 week 2 (p=0.039) than GS. PS also had significant higher total CES-D scores and significant lower total FACT-B scores before and during weeks 1-3 of cycle 1 chemotherapy than GS (CES-D: p-values ranged from 0.0024 to 0.0053; FACT-B: p-values ranged from 0.0019 to 0.044). By cycle 4, scores of the GS group reached levels of the PS group with no significant differences between them.**Conclusion :** The results indicate that breast cancer patients with poor sleep quality before chemotherapy suffer from more fatigue, more depression, and poor QOL before and during cycle 1 chemotherapy than those starting out with better sleep. By cycle 4 however, fatigue, mood and QOL of all patients were similar. Improving sleep in breast cancer patients before the start of treatment might decrease fatigue and depression symptoms, at least during the first cycle of chemotherapy.**Support (optional):** Supported by: NCI CA85264, NCI CA112035, CBCRP 11IB0034, CBCRP 11GB0049, the UCSD General Clinical Research Center (NIH MO1-RR00827), the Rebecca and John Moores UCSD Cancer Center (NCI P30 CA-23100), and the Research Service of the Veterans Affairs San Diego Healthcare System.**0904****PRE-TREATMENT DEPRESSION PREDICTS FATIGUE, SLEEP, AND QUALITY OF LIFE IN BREAST CANCER PATIENTS DURING CHEMOTHERAPY**Liu L,<sup>1,2</sup> Fiorentino L,<sup>5</sup> Dimsdale J,<sup>1,3</sup> Parke B,<sup>3,4</sup> Ancoli-Israel S<sup>1,2,3</sup>

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**Introduction :** Depression is a common symptom in breast cancer patients, often associated with poor sleep, fatigue, and decreased quality of life (QOL). As a part of larger study on fatigue/sleep in breast cancer,

we examined whether pre-treatment depressive symptoms predicted poor sleep, fatigue, and poor QOL.

**Methods :** Eighty-four women (mean age=50.1 yrs, SD=9.6, range: 34-79 yrs) diagnosed with stage I-IIIa breast cancer, scheduled to receive at least 4 cycles of adjuvant or neoadjuvant anthracycline-based chemotherapy were included in this study. Depression, sleep, fatigue, and QOL were assessed using Center for Epidemiologic Studies - Depression (CES-D), Pittsburgh Sleep Quality Index (PSQI), Multidimensional Fatigue Symptom Inventory (MFSI), and Functional Assessment of Cancer Therapy - Breast (FACT-B), respectively. All questionnaires were administered before and during weeks 1-3 of both cycle 1 and cycle 4 chemotherapy. Patients were divided into two groups according to the pre-treatment CES-D scores: few depressive symptoms (CES-D<16) and depressive symptoms (CES-D≥16).**Results :** Patients with depressive symptoms before chemotherapy reported: significantly worse sleep on PSQI from pre-treatment through cycle 4 week 1 of chemotherapy (p values ranged from <0.0001 to 0.041), with a trend during weeks 2-3 of cycle 4 (both p=0.08); significantly more total fatigue at almost all assessment points (p values ranged from <0.0001 to 0.029), except for cycle 4 week 2 (p=0.32); and significantly lower QOL on FACT-B at all eight assessment points (p values ranged from <0.0001 to 0.039).**Conclusion :** The results indicate that breast cancer patients with depressive symptoms before chemotherapy suffer from more poor sleep, more fatigue, and poorer QOL during cycle 1 and cycle 4 chemotherapy than those starting out with fewer depressive symptoms. Improving depression in breast cancer patients before the start of chemotherapy, might decrease patients' fatigue, and improve their sleep quality and QOL through the chemotherapy.**Support (optional):** Supported by: NCI CA85264, NCI CA112035, CBCRP 11IB0034, CBCRP 11GB0049, the UCSD General Clinical Research Center (NIH MO1-RR00827), the Rebecca and John Moores UCSD Cancer Center (NCI P30 CA-23100), and the Research Service of the Veterans Affairs San Diego Healthcare System.**0905****CPAP DIFFERENTIALLY IMPROVES METABOLIC SYNDROME TREATED BY PIOGLITAZONE OR METFORMIN**Perdikis DA,<sup>4,1,2,3</sup> Siddique MI,<sup>1,3</sup> Bowers-Pepe J<sup>4,3</sup>

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**Introduction :** Metabolic syndrome and its attendant insulin resistance are thought to be mechanistically involved in obstructive sleep apnea (OSA). Pioglitazone and metformin are targeted to improving insulin sensitivity but they exhibit differential effects on such characteristics of the metabolic syndrome as hypertension, inflammation and dyslipidemia. Since CPAP for OSA is thought to influence such neuroendocrine pathways operative in metabolic syndrome as sympathetic regulation and the renin-angiotensin-aldosterone-system, we theorized that CPAP might affect metabolic syndrome characteristics differentially with pioglitazone or metformin.**Methods :** We studied 51 patients with OSA with an apnea/hypopnea index (AHI) >11 (age 48.4±/5.65 years, AHI 19.1±/7.44, mean±/SD) and metabolic syndrome, diagnosed according to National Cholesterol Education Program and Endocrine Society criteria, but not frank diabetes mellitus. Of these patients, 25 were treated with pioglitazone (mean 30mg daily; mean 7.2 months), 16 were treated with metformin (mean 900mg daily; mean 9.3 months), and 10 were treated with diet therapy alone (mean 26% carbohydrate/day, mean 8.8 months) prior to a diagnosis of

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OSA and CPAP therapy. None of these subjects had congestive heart failure, parenchymal renal disease or coronary artery disease. We quantitated insulin resistance as a function of the insulin response area under the curve (AUC) constructed by four time-points during a 3-hr oral glucose tolerance test (OGTT) before and 4 months (4.55±1.2, mean±SD) after initiation and compliance to CPAP. We measured cardiac index and systemic vascular resistance by transthoracic impedance.

**Results :** Patients treated with CPAP/pioglitazone exhibited a marked improvement in insulin response, vascular resistance and LDL:HDL ratio compared to both CPAP/metformin and CPAP/diet. Interestingly, there was no statistical significance between the CPAP/metformin and CPAP/diet groups in any of the measured parameters other than insulin response ( $p<0.01$ ).

**Conclusion :** These data support the notion that insulin sensitivity alone may not independently affect OSA. Since the diverse intranuclear gene interactions of peroxisome proliferator-activated receptor ligands underlie the observed physiological effects related to both OSA and metabolic syndrome, it may be important to study the gene product set influenced by these agents in the setting of OSA.

**Support (optional):**

### 0906

#### WHAT PREDICTS SLEEP DURATION IN PATIENTS WITH ASTHMA?

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**Introduction :** Patients with asthma report reduced sleep quality and excessive daytime sleepiness. We assessed potential contributors to sleep duration in asthmatics.

**Methods :** Patients returning for routine follow-up at a tertiary Asthma Clinic completed the Epworth Sleepiness Scale (ESS) and question-items about 24-hour average sleep duration, perceived daytime sleepiness, and asthma symptom frequency (National Asthma Education and Prevention Program guidelines). Medical records were reviewed to help determine asthma severity (step 1 to 4) and search for established comorbid diagnoses such as psychopathology (depression, anxiety, bipolar disorder, and panic disorder) and current medications.

**Results :** Among 87 subjects, who were not on treatment for sleep-disordered breathing and did not have other lung conditions, age (mean±sd.) was 45±13 yrs; 66 (76%) were women; body mass index (BMI) was 31±8.5; forced expiratory volume in one second as percent of predicted value (FEV1%) was 85.09±21.41; 21 subjects (24%) were in asthma severity step 1, 6 (7%) in step 2, 31 (36%) in step 3, and 29 (33%) in step 4. The mean self-reported sleep duration was 7.05±1.74 hours (range 3.5-12). Twenty (23%) subjects had an established diagnosis of depression and 4 (4.6%) of other psychiatric conditions. Sleep duration correlated only with coexistent psychopathology (Spearman  $\rho=0.233$ ,  $p=0.03$ ) and trended toward associations with the use of inhaled corticosteroids ( $\rho=-0.199$ ,  $p=0.06$ ) and psychoactive medications ( $\rho=0.194$ ,  $p=0.07$ ). No correlations were observed between sleep duration and asthma severity step ( $\rho=-0.148$ ,  $p=0.17$ ), FEV1%, ESS score, perceived daytime sleepiness, age, gender, BMI, history of allergic rhinitis, gastro-esophageal reflux, inhaled long-acting bronchodilator use, anticholinergic use, or theophylline use. Among the psychiatric diagnoses, only a diagnosis of depression correlated with sleep duration ( $\rho=0.266$ ,  $p=0.01$ ). In a final regression model which included depression, inhaled steroid use, and psychoactive medication use as covariates, only comorbid depression was independently associated with sleep duration (general linear model, R-

square =0.121,  $p=0.05$ ).

**Conclusion :** In this sample of asthmatics, longer sleep duration was predicted by coexistent psychopathology, in particular depression. Severity of asthma showed no clear correlation with shorter sleep duration. Asthmatics who complain about sleep-related problems should be screened for comorbid psychiatric conditions.

**Support (optional):** M01-RR00042, 5T32NS007222 (MT)

### 0907

#### A RANDOMIZED, DOUBLE BLIND, PLACEBO-CONTROLLED, MULTI-CENTER STUDY OF THE BENEFICIAL EFFECTS OF SODIUM OXYBATE ON PAIN AND SLEEP IN PATIENTS WITH FIBROMYALGIA

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**Introduction :** We describe a randomized, double-blind, placebo-controlled, 3 parallel-group, multi-center trial comparing the effects of orally administered Xyrem [sodium oxybate (SO)] 4.5 and 6 Gms with placebo for the treatment of fibromyalgia syndrome (FMS). Because recent studies of EEG cyclical alternating patterns (CAP) in FMS indicated sleep instability, we hypothesized that SO would reduce pain and improve sleep EEG CAP indices of sleep stability.

**Methods :** After screening 320 subjects, 195 with FMS were randomized after washout and 147 completed per protocol (mean age 47.1 yr, 93.9% female). At wk 6, 10 and 14, 52 received placebo, 51 and 44 received SO 4.5 and 6.0 Gm/day respectively in divided doses at bedtime and 4 hours later. Sleep studies excluded sleep apnea and RLS/PLMS. Daily electronic diary pain and fatigue VAS ratings were recorded. The Tender point Count (TC), Tender point Index (TI), Jenkins Scale (JS), the Fibromyalgia Impact Questionnaire (FIQ), Functional Outcome of Sleep Questionnaire (FOSQ), SF36 Questionnaire, Epworth Sleepiness Scale (ESS), Patient's Global Impression of Change (PGIC), and Clinical Global Impression of Change (CGI-C) were assessed.

**Results :** FMS symptoms were reduced in the 6.0 Gm SO group: pain VAS ( $p=0.004$ ), fatigue VAS ( $p=0.005$ ), TC ( $p=0.01$ ), JS ( $p<0.001$ ), FIQ ( $p=0.001$ ), FOSQ ( $p=0.05$ ), ESS ( $p<0.001$ ), PGI-C ( $p=0.05$ ), and CGI-C ( $p=0.001$ ). Among those with EEG measurements (Placebo: N=18, 4.5 Gm SO: N=13, 6.0 Gm SO: N=11), sleep stability improved in the 6.0 Gm SO group: the mean phase A1 CAP rate was increased ( $p=0.01$ ), the mean Phases A2 and A3 CAP after the second night-time dose were decreased ( $p=0.004$ ,  $p=0.04$ ), and the increase in Phase A1 CAP rate correlated with sleep quality ( $p=0.02$ ) at wk 14.

**Conclusion :** SO shows promise as an effective drug for restorative sleep and reducing the severity of symptoms of fibromyalgia.

**Support (optional):** The study from which these results were abstracted was funded by Orphan Medical, Inc, Minnetonka, MN and Jazz Pharmaceuticals, Inc, Palo Alto, CA. All of the authors were funded by Orphan Medical and Jazz Pharmaceuticals during the conduct of this study.

### 0908

#### INFLUENZA VIRUS RAPIDLY ENTERS THE MOUSE BRAIN AFTER INTRANASAL INOCULATION PRIOR TO ONSET OF SYMPTOMS

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**Introduction :** Primary human influenza viral infections cause severe

systemic symptoms, including greatly increased sleep time, though virus is thought to be restricted to the upper respiratory tract. These symptoms are assumed to be mediated by circulating cytokines. We have investigated an alternative hypothesis, i.e., whether virus enters the brain before or at the time of symptom onset (13-15 h) and induces cytokines in situ.

**Methods :** Mature C57BL/6 male mice were infected intranasally (IN) with PR8 human influenza and euthanized at 4, 7, and 15 h post-infection (PI). Viral nucleoprotein RNA (minus strand genomic RNA and plus strand replication intermediates) was detected with nested RT-PCR and cytokine mRNA levels in the OB were measured with quantitative RT-PCR. Immunohistochemistry was also used to detect H1N1 antigen and glial cell markers.

**Results :** Both viral RNA strands were readily detected in OB as early as 4 hr PI by nested RT-PCR, indicating at least partial replication in this brain region. Cytokine mRNAs were also significantly elevated in the OB at 7 and 15 hr PI, specifically TNF- $\alpha$  and type I interferon-induced enzymes (Mx1, 2',5'-oligoadenylate synthetase). Controls receiving inactivated (boiled) virus expressed only input viral RNA and that only in lung. Immunohistochemistry demonstrated localization of H1N1 antigen in the glomerular layer (GL) of the OB in cells with microglial characteristics. No viral antigen was seen in the OB when mice were inoculated IN with boiled virus. The antigen in the GL appeared to be associated with microglia-like cells that stain with F4/80 antibody.

**Conclusion :** A non-neurovirulent strain of influenza virus invades the OB within a few hours PI, undergoes at least partial replication, and induces cytokine mRNAs in the OB. If these observations apply to humans, they might explain the unique severity of influenza viral symptoms as well as influenza-associated encephalopathy.

**Support (optional):** NIH Grant HD36520

## 0909

### INDEPENDENT CONTRIBUTIONS OF OBSTRUCTIVE SLEEP APNEA AND OBESITY IN CARDIOVASCULAR DISEASE: A CROSS-SECTIONAL STUDY

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**Introduction :** Obesity is set to overtake smoking as the most common preventable cause of illness and premature death in the United States. While it has been established that obstructive sleep apnea (OSA) is a risk factor for cardiovascular disease independent of obesity, the mechanisms behind the cardiovascular risk of obesity vs. OSA remain to be elucidated. We hypothesize that OSA independently contributes to the development of abnormal cardiovascular function in obese individuals.

**Methods :** Obese subjects with and without OSA, based on in laboratory polysomnography, were studied. Co-morbidities known to affect endothelial function or sleep other than OSA were excluded. To evaluate the effect of severity of OSA on cardiovascular abnormalities, we measured traditional cardiovascular biomarkers: heart rate variability, sympathetic tone (pre-ejection period, urine catecholamines), arterial stiffness (radial arterial tonometry to measure aortic augmentation index), brachial artery response to flow mediated dilation (FMD) and nitroglycerin, as well as, fibrinolytic factors, inflammatory mediators and adipokines. In addition, we assessed microvascular function using laser doppler flowmetry with iontophoresis of acetylcholine and nitroprusside to evaluate endothelium dependent and independent vasodilatation. Furthermore, to assess platelet function at baseline and with ADP activation, we assayed by flow cytometry: 1) leukocyte platelet aggregates and 2) expression of platelet surface

P-selectin (granule release), fibrinogen, and vWF receptors.

**Results :** 7 subjects, 3 subject with OSA (AHI >15 events per hour) and 4 without (AHI < 10) have been studied to date. For the first 7 subjects, platelet analysis, laser doppler flowmetry and available results for brachial FMD were within the normal range. Platelet flow cytometry at baseline demonstrated %p-selectin positivity varying from 2.1-5.5% and increased to 67.6-97.4% with ADP activation. Monocyte-platelet aggregates increased from baseline 6.1-12.5% to 34.4-63.6% with ADP activation. Laser doppler flowmetry with iontophoresis of acetylcholine and nitroprusside demonstrated increase in blood flux of 24-50% and 20-77% respectively. The aortic augmentation index, normalized to a heart rate of 75 bpm, ranged from -4% to 28%. Enrollment is ongoing, with formal data analysis planned after 15 subjects have been studied.

**Conclusion :** Further assessment of cardiac biomarkers and how they are influenced by OSA will be required to plan larger scale clinical trials.

**Support (optional):** Funded by HL73146 and an unrestricted research grant from Respironics Inc.

## 0910

### SLEEP-DISORDERED BREATHING AND HEART RATE VARIABILITY IN HEMODIALYSIS PATIENT

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**Introduction :** Sleep disturbance manifesting as insomnia, daytime sleepiness, fatigue, and other symptoms is frequently found in patients with end-stage renal disease treated with dialysis. Many of factor including neurosis factor, uremia symptom, dialysis drag and sleep-wake rhythm and so on is guessed, however this realities also is not clarified. We tested sleep apnea/hypopnea and heart rate variability reflecting autonomic activity in hemodialysis patient.

**Methods :** Eight hemodialysis patient (age 48.7 $\pm$ 11.4 years, mean $\pm$ SD) and 7 healthy adults (controls) (age 42.7 $\pm$ 12.2 years) were enrolled in this study. We performed screening test for sleep-disordered breathing using the home medical care device (morpheus C set, TEIJIN, Tokyo) in all subjects. The number of apnea/hypopnea episodes per hour (apnea/hypopnea index; AHI) and the heart rate variability (HRV) [low frequency: LF (0.04-0.15Hz), high frequency: HF (0.15-0.4Hz), very low frequency: VLF (0.033-0.04Hz), and LF/HF] were measured.

**Results :** There was no significant difference between hemodialysis day and non-hemodialysis day in AHI (10.1 $\pm$ 9.0 vs 14.0 $\pm$ 15.6/hr). HF, VLF, and LF/HF did not differ significantly between hemodialysis day and non-hemodialysis day (HF: 81.4 $\pm$ 84.8 vs 98.4 $\pm$ 98.5ms<sup>2</sup>, VLF: 945.9 $\pm$ 767.2 vs 829.3 $\pm$ 705.6 ms<sup>2</sup>, LF/HF: 5.7 $\pm$ 3.8 vs 4.4 $\pm$ 4.4). HF and VLF significantly decreased in the hemodialysis patients than in controls (HF: 105.3 $\pm$ 74.1 vs 352.1 $\pm$ 211.6ms<sup>2</sup>, VLF: 1140.7 $\pm$ 767.2 vs 2483.4 $\pm$ 1272.8ms<sup>2</sup>, p<0.05), but there was no significant difference in LF/HF. Heart rate tended to increase in the hemodialysis patients compared with controls (84.1 $\pm$ 18.9 vs 60.9 $\pm$ 4.0 bpm).

**Conclusion :** Our findings suggest that hemodialysis itself might not be the important contributing factor to sleep-disordered breathing, furthermore the analysis of HRV would provide valuable information on the balance of autonomic activities in hemodialysis patients.

**Support (optional):**

0911

**INFLUENCE OF SLEEP IN CIRCADIAN DISTRIBUTION OF VENTRICULAR ARRHYTHMIA IN PATIENTS WITH CHAGAS DISEASE**

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**Introduction :** There is a circadian distribution in ventricular arrhythmias in patients with coronary disease. The autonomic nervous system plays an important role in triggering these events. However, the 24-h distribution of arrhythmias has not been described in patients with Chagas disease. The aim of this study is to evaluate the wake-sleep cycle distribution of ventricular arrhythmias (VA) in patients with Chagas disease.

**Methods :** Twenty chagasic patients underwent a clinical evaluation, Holter monitoring, and polysomnography (PSG). Sleep-disordered breathing were excluded from analysis. Patients were allocated in two groups according to day or night pattern of occurrence of VAs: Group 1: Daytime VA (13 patients) (defined as more than 50% of events occurring during daytime), and Night-time VA (7 patients) (defined as more than 50% of events during night time). We analyzed the PSG parameters and the time domain heart rate variability (HRV) variables for 24 hours.

**Results :** There were no differences between groups in age, gender, body mass index, ejection fraction of left ventricle, and use of amiodarone or beta-blockers. Arousal index was significantly higher in the Daytime VA group compared to Night-time ( $p < 0.05$ ). The mean RR interval was also significantly shorter in the Daytime VA group ( $p < 0.05$ ). The other PSG parameters and HRV results were not different in both groups.

**Conclusion :** The increase in arousal index was associated with preferential daytime distribution of VAs in Chagas patients. The arousal system may change the autonomic regulation, thus influencing VAs occurrence. A possible limitation was the absence of recording of esophageal pressure.

**Support (optional):** Supported by FAPESP-CEPID (98/14303-3), FAPESP (2003/12208-3), and AFIP, FCT-BSAB (373).

0912

**DESCRIPTION OF SLEEP QUALITY USING THE PITTSBURGH SLEEP QUALITY INDEX IN SARCOIDOSIS**

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**Introduction :** Excessive daytime sleepiness and fatigue are common in sarcoidosis, however sleep quality has not been described. Sarcoidosis is associated with increased prevalence of obstructive sleep apnea (OSA), with upper airway involvement as a specific risk factor. We report a cross-sectional survey describing sleep quality in sarcoidosis using the Pittsburgh Sleep Quality Index (PSQI).

**Methods :** Sarcoidosis patients were recruited from pulmonary and sarcoidosis clinics at Mount Sinai Hospital from November- December 2005. Patients completed the PSQI. Charts were reviewed to ascertain upper airway involvement of sarcoidosis, glucocorticoid use, and diagnosed OSA. Mean and standard deviation or median and range are reported depending on normality.

**Results :** All twenty-four patients approached for the study participated. Eleven (46%) were male, mean age 51.4 +/-SD 10.28. Median BMI = 28.5 Kg/m<sup>2</sup> (range 21-53). Median PSQI global score was 7.5 (range 1-18), eighteen (75%) demonstrated poor sleep quality, as indicated by PSQI global score >5. Five subjects (21%) had confirmed OSA, one receiving treatment. All subjects with OSA had PSQI >5. This did not differ signif-

icantly from subjects without a diagnosis of OSA ( $p = 0.1$ ), although our power to detect a difference was limited. Five subjects (21%) had upper airway sarcoidosis, four (80%) had PSQI >5; this was not significantly different from subjects without upper airway involvement ( $p = 0.77$ ). Five subjects (21%) were receiving systemic glucocorticoids. Four (80%) had PSQI >5; this was not significantly different from those not receiving systemic glucocorticoids ( $p = 0.77$ ).

**Conclusion :** Our study demonstrates a high prevalence of poor sleep quality in sarcoidosis, indicated by PSQI >5. In this patient population, neither upper airway sarcoidosis nor glucocorticoid use predicted poor sleep quality. A larger study is ongoing to confirm these findings and to determine whether PSQI >5 in sarcoidosis is dependent upon OSA.

**Support (optional):**

0913

**CHRONIC ALCOHOL TREATMENT DISRUPTS CIRCADIAN PATTERNS OF SLEEP IN RATS**

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**Introduction :** Most alcoholics have sleep disturbances, including prolonged sleep latency, decreased total sleep time, increased SWS%, decreased REM%, and increased REM sleep latency that can persist even after abstinence and can predict relapse. However, the physiological mechanisms that underlie these disturbances remain unknown. The current study was designed to define more precisely the nature of sleep disturbances induced by chronic alcohol in an animal model.

**Methods :** Sprague-Dawley rats (males, ~ 250 g) were used. Alcoholic rats were fed 6% grain alcohol in liquid diet (Bio-serv) for 6 weeks. Weight matched pair-fed rats had iso-caloric liquid diet. Rats were instrumented for EEG recordings in the fifth week of treatment and after recovery from surgery (one week) adapted to the environmental chambers for three days prior to continuous sleep recordings for two days.

**Results :** The alcohol treatment caused disruption of circadian variations of a number of sleep parameters including time spent in NREMS, REMS, and wake, and loss of the peak of slow wave amplitude (SWA) during NREMS in the first 2 hours of the light period. These disturbances were due in part to the fragmentation of long duration sleep bouts in the light period, and the appearance of more frequent sleep periods in the dark period. Interestingly, the loss of circadian variation in SWA was due to an enhanced EEG power spectrum in the dark period in the alcoholic rats. Alcoholic rats also exhibited enhanced theta power in REMS.

**Conclusion :** The current work reveals that 6-week alcohol treatment leads to a profound disruption of circadian variations in a number sleep related parameters. The disruption of long sleep bouts in the light period in rats is consistent with the complaint in human alcoholics of frequent awakening and fragmentation of normal sleep.

**Support (optional):** NIAAA Grant No. R01-AA013248.

0914

**PRENATAL ETHANOL EXPOSURE ALTERS TNF-INDUCED SLEEP RESPONSES IN FEMALE RATS**

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**Introduction :** Rats and humans exposed to alcohol during fetal life have alterations in sleep patterns including reductions of REMS. The cytokine tumor necrosis factor  $\cdot$ (TNF $\cdot$ ) is both an important sleep regulatory substance and plays a role in brain development. Further, it has been shown that chronic ethanol exposure increases cytokine levels in rat cerebral cortex and in cultured astrocytes. Because alcohol exposure may alter the expression of this important developmental and sleep regulatory signal,

we hypothesize that fetal alcohol exposure (FAE)-induced alterations in sleep may be related to changes in cytokine function that persist into adulthood.

**Methods :** On gestational day 8, pregnant Sprague-Dawley rats were randomly assigned to two groups. Group I rats (FAE) had free access to a liquid diet with 6% ethanol added. Group II rats were weight matched to group I rats and pair-fed iso-caloric amounts of liquid diet without alcohol. Alcohol administration was halted on gestational day 20. After birth, offspring were culled to 8 pups per mother, weaned at 21 days of age, and then raised on standard lab chow. At 8 months of age FAE and pair-fed rats were instrumented with EEG and EMG electrodes and an i.c.v. cannula. After recovery from surgery, baseline sleep values and sleep responses to TNF were determined. Hypothalamic RNA was isolated and TNF mRNA was measured using real time PCR.

**Results :** Female FAE rats had less REMS after challenge with TNF compared to pair-fed controls. In contrast, no changes were observed in non-REMS between the groups after TNF. A significant increase in hypothalamic TNF mRNA levels was observed in female offspring from alcoholic mothers.

**Conclusion :** The sleep responses to a sleep regulatory substance, TNF, appear to be altered by fetal alcohol exposure in female rats.

**Support (optional):** Supported by NIH NS31453, AA13248 and Washington State Alcohol and Drug Abuse Program

## 0915

### SLEEP DURATION AND OBESITY: THE ROLE OF STRESS AND SLEEP COMPLAINTS

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**Introduction :** Several epidemiological studies have reported that obesity is associated with short sleep duration. The goal of this study was to assess the contribution of stress and sleep complaints in this association.

**Methods :** A random sample of 1,741 men and women of a wide-age range (Penn State Cohort) were evaluated in the sleep laboratory as part of a project for the assessment of sleep apnea in the general population. Thirteen hundred (1,300) completed the Minnesota Multiphasic Personality Inventory (MMPI). The sample was not different from the overall sample of 1,741 in terms of age, gender, body mass index (BMI), or sleep complaint. All subjects were interviewed for the presence of sleep disorders.

**Results :** Comparison of obese subjects with “insomnia” and/or “sleep difficulty” and/or “excessive daytime sleepiness” with obese subjects free of any sleep complaint showed that obese with sleep complaints had significantly higher mean values in the eight clinical scales of the MMPI ( $P < 0.05$ ) and reported significantly shorter sleep time. In contrast, there was no difference in terms of sleep time or MMPI scales between obese and lean subjects without sleep complaints. In a multivariate analysis, MMPI clinical scales were strong and independent predictors of short sleep duration after controlling for the confounding effects of age, gender, BMI, smoking, and sleep disordered breathing ( $P < 0.05$ ).

**Conclusion :** Emotional stress and sleep complaints are strong and independent predictors of short sleep duration in obese individuals. Sleep duration may be a marker of emotional stress and sleep complaints commonly reported by obese, and they should be part of our preventative and therapeutic strategies for obesity.

**Support (optional):** R01 Grants: HL 40916 HL 51931

## 0916

### IDENTIFYING THE EFFECT OF DAYTIME SLEEPINESS ON DIABETES MANAGEMENT

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**Introduction :** To achieve good glucose control, persons with type 2 diabetes mellitus (T2DM) need to engage in exercise and carefully manage their diet. Although it is known that excessive daytime sleepiness negatively affects activities sensitive to sleep disruption such as vigilance and general productivity, it is unknown how sleepiness affects diabetic management. The purpose of this study was to ask persons with T2DM to identify how daytime sleepiness affects them.

**Methods :** This study had a qualitative design where the participants of a focus group are considered the experts in what it is like to have T2DM and be excessively sleepy. Nominal Group Technique (NGT) was used to obtain information on two questions: 1) what does sleepiness mean to you? and 2) how does daytime sleepiness affect how you deal with your diabetes? Inclusion criteria for participants was adults over age 21 with Type 2 DM, English speaking, and with a screening Epworth Sleepiness Score (ESS)  $\geq 11$ . Two focus groups each lasting no longer than 2 hours were held. The steps to NGT include silent individual generation of ideas in writing, group recording of ideas, discussion and clarification of each idea, a preliminary vote on the priority of each idea, discussion of the preliminary vote, and a final vote on priorities.

**Results :** A total of 12 persons participated in the two focus groups (42% male, 75% white, mean age  $55.5 \pm 7.8$ , mean repeat ESS at focus group =  $11.25 \pm 3.51$ ). Significant problems identified by the participants included impaired mood and decreased motivation for engaging in health promoting activities important for diabetic management including cooking healthy meals or exercising.

**Conclusion :** Although participants voiced they performed structured tasks such as taking their medications and testing their blood sugar, they reported that sleepiness impaired motivation to perform more complex or unstructured activities that are also important in managing T2DM.

**Support (optional):**

## 0917

### USING A HOME-MONITORING SYSTEM TO IMPROVE SLEEP IN DEMENTIA CAREGIVERS

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**Introduction :** As a result of the disease process, persons with dementia frequently awaken and get up during the night. This is problematic because judgmental errors may endanger the individual either through injuries in the home (e.g. burns) or exiting unattended from the home. Caregivers respond by sleeping lightly and frequently awakening to ensure the safety of the person with dementia every night even when that individual is sleeping soundly. Technology needs to be developed that will accurately inform the caregiver about bed exits of the person with dementia. This will allow the caregiver to be notified when needed, but sleep soundly when it is safe

**Methods :** The purpose of this study was to develop and test a novel home monitoring system that can be used by caregivers of persons with dementia. The system, called CareWatch, was developed using STTR Phase I and II awards. The purpose of the study was to test the feasibility of the system when installed in homes of caregivers. Sixty caregivers were recruited and 30 of those were randomly assigned to receive and use the

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system for one year.

**Results :** The system was successfully installed in 30 homes. All proofs of feasibility were met in each home indicating that the monitoring system reliably identified exits from the bed, bedroom, motion through the home and exits from the home. All caregivers were able to independently operate the system after approximately 3 training sessions. During the study, there were no unattended exits from the home. Caregivers reported significantly less worry about nighttime activity and improved sleep.

**Conclusion :** A home monitoring system can significantly improve the safety of the home during the night for persons with dementia. Caregivers are able to correctly operate the system and report reduced levels of worry and improved sleep.

**Support (optional):** National Institute of Nursing Research(1R41NR004952, 2R42NR4952-02A2, 5R42NR004952-03, 3R42NR004952-03s1)

### 0918

#### FATIGUE AND SLEEP AT BASELINE AND AFTER THE FIRST ADJUVANT BREAST CANCER CHEMOTHERAPY TREATMENT WITHIN A RANDOMIZED CONTROL TRIAL

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**Introduction :** This study evaluates the impact of a tailored behavioral sleep intervention (BSI) delivered two days before the first chemotherapy treatment on women's sleep time as well as subjective perceptions of sleep quality and fatigue.

**Methods :** Subjects (N=93) were randomized to BSI or a healthy eating control group. They were post-operative for Stage I/II/IIIA breast cancer, receiving four or more chemotherapy treatments; mean age 50.9 yrs (35-74). Most were married, employed, and had some college education. Instruments included Piper Fatigue Scale (PFS) and Pittsburgh Sleep Quality Index (PSQI). Wrist actigraphy data were also collected for 2 days at baseline and 7 days after chemotherapy.

**Results :** At baseline, there were no group differences on age, stage of disease, menstrual and performance status; nor were there differences on PFS [ $\mu=2.44(1.92)$ ] or PSQI [ $\mu=6.66(3.39)$ ]. PSQI score was  $>5$  in 57% and  $>8$  in 26% of subjects. Actigraphy data showed total sleep time minutes [ $\mu=413.6(80.4)$ ], awake% [ $\mu=11.77(11.1)$ ], number of night awakenings [ $\mu=10.1(5.68)$ ] and minutes awake after sleep onset (WASO) minutes [ $\mu=55.4(52.5)$ ]. After chemotherapy, mean PFS rose to 4.76(2.53). Actigraphy data showed non-significant increases in total sleep time minutes [ $\mu=438.6(97.7)$ ], awake% [ $\mu=14.88(14.4)$ ], number of night awakenings [ $\mu=10.6(4.86)$ ] and WASO [ $\mu=74.9(70.1)$ ] minutes. At baseline, PFS was related to PSQI ( $r = .34, p<.001$ ) and 4 PSQI subscales (sleep quality, latency, sleep disturbance, daytime dysfunction).

**Conclusion :** Fatigue and sleep results were not different between groups at baseline and after chemotherapy. Increases in fatigue and all actigraphic sleep parameters were noted after chemotherapy. Higher fatigue was associated with poorer subjective sleep quality, but not objective sleep, regardless of group assignment. Areas for continued focus include reducing awake percent and WASO minutes. These short-term results will be compared to long-term results to test the effects of BSI on reducing cancer-related fatigue and maintaining quality sleep during long-term chemotherapy.

**Support (optional):** Funded by NIH, 5R01NR007762-04

### 0919

#### EFFECTS OF CHRONIC ALCOHOL INTAKE ON ELEVATION IN DAYTIME BLOOD PRESSURE AND REDUCTIONS OF NOCTURNAL HEART RATE VARIABILITY

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**Introduction :** Regular use of ethanol is associated with elevation of blood pressure but the underlying mechanism is not known. This study was conducted to investigate the relationship of chronic alcohol intake, blood pressure, and nocturnal heart rate variability.

**Methods :** Thirty-seven subjects (age  $41.4\pm 12.7$  years) included 11 hypertensives were enrolled in the study. The measurement was performed for 24 hours from the midday. Power spectral analysis of heart rate variability was performed by maximum entropy method(using MemCalc/Chiram® , Suwa Trust, Tokyo ), and the ultra low frequency (ULF:  $\leq 0.0003$ Hz), the very low frequency (VLF: 0.0003 - 0.004Hz), the low frequency (LF: 0.04 - 0.15Hz) , high-frequency (HF: 0.15 - 0.4Hz) components power and LF to HF ratio(LF/HF) were calculated. Simultaneously ambulatory blood pressure monitoring and nocturnal pulse oximeter monitoring were performed.

**Results :** The amount of habitual ethanol consumption (EC) was positively correlated with mean daytime systolic blood pressure (SBP) (Pearson's correlation coefficient ( $r$ )  $r=0.559$  ( $P<0.001$ )). Significant negative correlations were observed between EC and all nocturnal heart rate variability spectral components power (ULF  $r=-0.363$  ( $P=0.028$ ), VLF  $r=-0.347$  ( $P=0.035$ ), LF  $r=-0.415$  ( $P=0.011$ ), HF  $r=-0.461$  ( $P=0.004$ )). Significant positive correlations was observed between EC and LF/HF ( $r=0.466$  ( $P=0.004$ )). Significant negative correlations were observed between SBP and LF power as well as HF power (LF  $r=-0.363$  ( $P=0.032$ ), HF  $r=-0.425$  ( $P=0.011$ )). Significant positive correlations was observed between SBP and LF/HF ( $r=0.379$  ( $P=0.025$ )). Multiple linear regression was performed to explore determinants of SBP. Age, EC, ODI and all nocturnal heart rate variability spectral components power were included in this model. The final regression model included ODI ( $B=2.599$ , 95%Confidence interval (CI) : 1.602 - 3.596,  $P<0.001$ ), HF power( $B=-0.015$ , 95%CI : -0.005 - -0.025,  $P=0.004$ ) and VLF power ( $B=0.002$ , 95%CI : 0.001 - 0.003,  $P=0.009$ ) as significant variables influencing SBP.

**Conclusion :** The results of this study suggested that chronic ethanol intake inhibited nocturnal autonomic function dose-dependently and, together with sleep apnea, attributed to elevation of daytime blood pressure.

**Support (optional):**

### 0920

#### 24-HOUR SLEEP PATTERNS MAY BE A USEFUL MARKER IN PHENOTYPIC SUBTYPING OF OBESITY

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**Introduction :** Recent epidemiological studies, based on subjective reports, have reported U-shaped curvilinear association between sleep duration and body mass index (BMI), i.e., some obese report short sleep duration, whereas others do not. What distinguishes the two groups is not known. The goal of this study was to characterize the profile of these two groups, based on polysomnographic, psychometric, and hormonal data.

**Methods :** Seventy three obese patients without sleep apnea and 45 nor-



mal-weight controls were monitored in the sleep laboratory for one night (8 hours) followed by two daytime naps and completed the Minnesota Multiphasic Personality Inventory (MMPI). Another group of 13 obese non-apneic, non-depressed men and 16 normal-weight controls were monitored in the sleep laboratory for four consecutive nights, and during the fourth day, serial 24-h plasma measures of cortisol were obtained.

**Results :** Analysis of nighttime and daytime sleep data indicated that there is a bimodal distribution of sleep in obese. Those obese that slept (percent sleep time [%ST]) better at night were sleepier (sleep latency) during the day, whereas those that slept poorer at night were less sleepy during the day. Furthermore, the short sleepers (based on %ST of both nighttime and daytime recording), after adjusting for age and BMI, exhibited significantly higher mean values in three MMPI scales, i.e., hypochondriasis, depression, and hysteria ( $P < 0.05$ ). Finally, obese, normal sleepers showed significantly lower 24-h mean values of cortisol compared to lean controls ( $P < 0.05$ ).

**Conclusion :** These data provide the basis for a meaningful phenotypic subtyping of obesity. One subtype is associated with depression, poor sleep, lack of true sleepiness (fatigue), plus HPA axis hyperactivity, and the other with normothymia, better sleep/sleepiness, and HPA axis hypoactivity. The first may be more responsive to psychological/behavioral methods, whereas the second may be more responsive to biological/medical approaches.

**Support (optional):**

## 0921

### SLEEP ARCHITECTURE AND WAKING EEG SPECTRAL ANALYSIS IN ATHLETES FOLLOWING A CONCUSSION

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**Introduction :** As many as 300 000 sport-related concussions occur each year in the USA and approximately 40% of concussed athletes will develop post-concussion symptoms such as headaches, drowsiness, dizziness, irritability, sleep disorders, as well as neuropsychological deficits. The aim of the present study was to investigate the effects of sport-related concussions on sleep architecture and on waking quantitative EEG.

**Methods :** Ten athletes who sustained a concussion during the last year and ten normal athletes (age:  $24.3 \pm 6.1$  and  $22.6 \pm 2.4$  years respectively) were included. Athletes had a past history of  $4.5 \pm 2.1$  concussions. All athletes completed the Pittsburgh Sleep Quality Index (PSQI) and were recorded for two nights (the first night served as adaptation only) in the sleep laboratory and during a 10-min period of wakefulness (eyes closed) the next morning. A total of 120 sec of artifact-free EEG were selected for spectral analysis using FFT on 4 sec epochs with a resolution of 0.25 Hz and cosine tapering during wakefulness. Group differences on PSG data were assessed by t-tests and differences on quantitative EEG in frontal, central, temporal, parietal and occipital regions were assessed by a two-way ANOVA (Group x Region).

**Results :** Concussed athletes reported worse sleep quality on PSQI ( $p=0.01$ ) than control athletes. No between-group difference was found on PSG sleep variables. A Group effect was observed for the relative delta power during wakefulness ( $F(1,12)=13.9$ ,  $p<0.01$ ); concussed athletes showed more delta activity than control athletes. Inversely, a reduction in relative alpha power was found in concussed athletes in comparison with control athletes ( $F(1,12)=10.4$ ,  $p<0.01$ ).

**Conclusion :** Concussions in athletes were associated with an increase in relative delta and a reduction in relative alpha power. In spite of the subjective complaints in sleep quality of concussed athletes, no change was

observed in sleep characteristics.

**Support (optional):**

## 0922

### SLEEP PARAMETERS CORRELATED WITH NEUROCOGNITIVE FUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) PATIENTS

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**Introduction :** It has been well known that cognitive dysfunction frequently occurs in hypoxemic COPD patients. However, there is a debate on the cognitive decline in non-hypoxemic COPD patients, and it has been suggested that sleep disorders including nocturnal hypoxemia could affect this. Previous studies on the relationship of sleep and cognitive function is limited. We aimed to examine the relationship of sleep parameters with the neurocognitive function in elderly COPD patients who have the cognitive impairment.

**Methods :** Epworth Sleepiness Scale (ESS) was administered to COPD patients above 60 yr., who visited to Kangwon National University Hospital. For 23 subjects, CERAD-K (the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet) neuropsychological battery (Lee, J Gerontol: Psych Sci 2002; 57B: P47-53) and Stroop test were done. Nocturnal polysomnography (NPSG) was done for 10 patients (Age:  $70.8 \pm 7.3$ ) among 13 COPD patients who had the score below 1.5 standard deviation in at least one test of CERAD-K neuropsychological battery. P value below 0.05 had a statistical significance.

**Results :** The NPSG result showed lower sleep efficiency ( $70.3 \pm 14.9\%$ ), higher respiratory disturbance index ( $13.4 \pm 12.5$ ), and higher limb movement index (LMI) ( $28.6 \pm 23.5$ ). Verbal Fluency score was correlated with stage 2 sleep amount ( $r=0.73$ ). Central apnea index (CAI) was negatively correlated with the scores of Word List Memory and Word List Recall tests ( $r=-0.84$ ,  $-0.81$ ), and obstructive apnea index was correlated with Stroop Interference score (SI) ( $r=0.71$ ). LMI was correlated with Stroop Color-Word and SI scores ( $r=0.73$ ,  $0.82$ ) Forced expiratory volume at one second (FEV1) had no correlation with sleep parameters.

**Conclusion :** In COPD patients with impaired neurocognitive function, decreased stage 2 sleep amount was associated with decreased language ability. And, increased sleep disordered breathing without respiratory effort was associated with verbal memory impairment.

**Support (optional):**

## 0923

### SUBJECTIVE SLEEP DISTURBANCES IN TINNITUS PATIENTS ARE RELATED TO THEIR SUBCLINICAL DEPRESSIVE SYMPTOMS

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**Introduction :** Tinnitus is the sensation of sound that is perceived in the ears or head without any external sound source. It is experienced by about 20% of the population over 50 of age. Diagnosis relies on subjective self-reports of symptoms, and there is no treatment available. Most people habituate to tinnitus after some time, but a small proportion experiences important psychological distress. Sleep disturbance is one of the most frequent complaints associated to tinnitus, but supporting data in well screened groups of patients are scarce and the relationship between sleep

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disturbances and depressive symptoms is unclear.

**Methods :** Data were obtained from 51 tinnitus patients (67.8 y., 21 females, 30 males) and 49 controls without tinnitus (67.0 y., 26 females, 23 males) matched in age, education level, and general health condition, on the Pittsburgh Sleep Quality Index, BDI-II, and auditory sensitivity. Hearing thresholds were also assessed. Tinnitus patients also completed the Tinnitus Reaction Questionnaire.

**Results :** Compared to the control group, tinnitus patients showed greater subjective sleep disturbances (PSQI: 6.7 vs. 4.7), more depressive symptoms (BDI-II: 8.9 vs. 4.8), greater auditory sensitivity (19.9 vs. 14.2), and greater hearing loss (29.2 vs. 17.7). In the Tinnitus group, higher tinnitus-related distress (TRQ) was associated with greater sleep disturbances (PSQI). When BDI scores were put as a covariate, tinnitus patients still showed greater auditory sensitivity and hearing loss than control subjects, but did not differ on subjective sleep quality. The relationship between TRQ and PSQI scores was no longer significant when BDI-II scores were controlled for.

**Conclusion :** Tinnitus patients have greater self-reported sleep difficulties compared to control subjects and high tinnitus-related distress is associated with greater sleep disturbances. Sleep complaints in this population are mostly explained by subclinical depressive symptoms, a plausible consequence of tinnitus.

**Support (optional):** This research was supported by Fondation Caroline-Durand.

### 0924

#### FATIGUE SEVERITY IN HIV DISEASE IS ASSOCIATED WITH SLEEP DISTURBANCES: A POLYSOMNOGRAPHIC STUDY

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**Introduction :** Fatigue and sleep disturbances are common complaints of individuals affected with HIV disease. These two complaints present early in the disease and severity worsens with disease progression. Earlier studies have described fatigue or sleep disturbances in HIV, but the contribution of sleeping difficulties to fatigue severity in HIV is unknown. The aim of this study was to explore whether fatigue severity and specific polysomnographic parameters are correlated.

**Methods :** 17 HIV positive subjects (15 men, 2 women) were studied by overnight polysomnography (2 nights) and Multiple Sleep Latency Test (MSLT). Fatigue severity was assessed with the Global Fatigue Index (GFI) scale. Sleep disturbances were evaluated with the Pittsburgh Sleep Quality Index scale (PSQI) and daytime sleepiness with the Epworth Sleepiness Scale (ESS). Statistical correlates for polysomnography parameters (total sleep time, TST; time awake, TA; percentage REM sleep, PREM; sleep latency, SL) were obtained.

**Results :** Scores in the GFI scale were positively correlated with sleep quality (PSQI)( $p < 0.03$ ;  $r = 0.51$ ). In addition, severity of daytime sleepiness (ESS) also positively correlated with the number of spontaneous arousals from sleep ( $p < 0.03$ ;  $r = 0.52$ ). TST correlated with sleep efficiency ( $p < 0.00003$ ). PREM was decreased in all subjects with HIV when compared to age/gender matched controls. Total REM time decreased as a function of TA ( $p < 0.0004$ ;  $r = 0.76$ ). MSLT scores did not correlate with fatigue severity. The frequency of sleep stage shifts did not differ in HIV positive individuals when compared to controls.

**Conclusion :** Fatigue severity in HIV disease correlated with specific polysomnographic changes. Disruption of sleep continuity by frequent arousals, and decreased REM significantly correlated with daytime fatigue severity. These results suggest that fatigue severity in HIV infec-

tion is partially explained by a sleep disorder intrinsic to disease progression. Further studies into the role of decreased REM sleep and spontaneous arousals during sleep in the genesis of fatigue in HIV disease are warranted.

**Support (optional):**

### 0925

#### SLEEP CONTINUITY AND SLEEP ARCHITECTURE IN CANCER PATIENTS PRIOR TO CHEMOTHERAPY

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**Introduction :** Fatigue is a commonly reported complaint of cancer patients. The cause(s) of this fatigue are unknown. It is often assumed that this symptom is iatrogenic and potentially the result of treatment-related factors such as anemia. Whether abnormal sleep continuity and/or sleep architecture mediates or moderates the association between cancer and fatigue has only been explored in a preliminary way and there are no studies that assess PSG sleep prior to treatment. The present analysis addresses the latter issue.

**Methods :** The data presented here are drawn from an ongoing longitudinal study evaluating sleep and fatigue prior to, during, and after treatment. 13 cancer patients (1 lymphoma, 8 breast, & 4 colorectal [3 men, age range 45-63]) were evaluated polysomnographically immediately prior to the commencement of chemotherapy. The PSG data from these patients (SL, WASO, TST, NOA, SE%, STG1%, STG2%, STG3%, STG4%, SWS%, REM%, Wake% and REM Latency) were compared to age and gender matched archival good-sleeper data. In addition, the cancer patient group was subdivided into two groups, those taking ( $n = 6$ ), and not taking ( $n = 7$ ) CNS active medications (SSRIs and/or benzodiazepines and/or carbamazepine).

**Results :** One-Way ANOVAs for each of the 13 variables revealed significant differences or trends ( $p < 0.20$ ) for 5 parameters. Post hoc t-tests revealed that the 2 cancer groups significantly ( $p < 0.05$ ) differed only with respect to REM Latency; patients taking CNS medications had longer REM latencies. In contrast, both cancer groups significantly differed from the controls on TST, STG2%, STG4%, and SWS%; the cancer patients had greater TST and STG2% and less STG4% and SWS%. TST was greater by about 1 hour and SWS% was approximately 50% less than that of the good sleeper controls.

**Conclusion :** These data suggest that cancer itself (disease or life stress associated with the disease) effects sleep architecture and sleep continuity. Whether these effects are progressive and/or systematically related to fatigue remains to be determined.

**Support (optional):** Support for this project comes from the American Cancer Society & NIH R01 MH59392

### 0926

#### THE EFFECTS OF VALERIAN EXTRACT ON SLEEP DISTURBANCES IN PERSONS WITH ARTHRITIS

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**Introduction :** Among the most troublesome symptoms of arthritis is fragmented sleep. The purpose of this study was to investigate whether or not valerian, a commercially available and commonly-used herb with sedative properties, reduces sleep disturbances in persons with arthritis.

**Methods :** The study used a double-blind, randomized, placebo-con-

trolled design. Participants received either valerian extract (600 mg) or a placebo (600 mg vegetable oil) one hour before bedtime. Sleep outcomes were measured for 3 nights of baseline and 5 nights using the assigned intervention. Outcomes included sleep efficiency, number of awakenings, and sleep latency measured by wrist actigraphy, as well as subjective sleep quality (rated on 0-10 Likert-type scale) and estimated sleep latency reported by daily diaries. Daytime sleepiness was measured (rated 0-10) as a secondary outcome. Group differences were tested using repeated-measures ANOVA comparing baseline (nights 1 and 2 averaged) to the intervention (nights 7 and 8 averaged).

**Results :** Participants were found to have mildly disrupted sleep at baseline. The intervention groups differed only in objective sleep latency ( $F=6.49$ ,  $p=.03$ ), but latency was longer in the valerian group, and the group difference was not clinically meaningful. Subjective sleep quality increased slightly over time ( $F=6.57$ ,  $p=.02$ ), but the groups did not differ, indicating a small placebo effect. There were no significant differences in objective sleep efficiency, number of awakenings, or in subjective sleep latency. No significant group difference was found in daytime sleepiness, indicating that valerian did not cause residual sedation.

**Conclusion :** In the current sample, valerian did not reduce sleep disturbances. However, valerian did not appear to cause daytime sleepiness, which is a side effect of certain sedatives. Because of study limitations, which include a small sample with only mild sleep disturbances, further investigation is needed to determine whether or not valerian is useful as a sleep aid.

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## 0927

### ADULT GROWTH HORMONE DEFICIENCY IS ASSOCIATED WITH MAJOR OBJECTIVE ALTERATIONS OF SLEEP ARCHITECTURE

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**Introduction :** Adults with growth hormone deficiency (GHD) frequently complain of impaired sleep quality. The aim of the present study was to examine the sleep quality of patients with untreated GHD in comparison to that of age, gender, and body mass index matched (BMI) healthy subjects.

**Methods :** Thirty GHD patients ages 19-74yr and thirty age- and BMI-matched controls spent two consecutive nights (one habituation and one assessment night) with their usual bedtimes in the sleep laboratory. Polygraphic sleep records were obtained, using a portable EEG acquisition system (DigiTrace Care Services, Boston, MA), and scored according to standard clinical procedures. The EEG signal was submitted to spectral analysis using a software package (PRANA, PhiTools, Strasbourg, France). Delta activity was calculated as the absolute spectral power in the frequency band 0.5-4 Hz.

**Results :** Total sleep time ( $433 \pm 11$  vs.  $450 \pm 9$  min; mean  $\pm$  SEM) and REM sleep ( $91 \pm 6$  vs.  $101 \pm 5$  min) were similar in GHD subjects and matched controls, respectively ( $p \geq 0.18$ ). In contrast, GHD patients had a significant increase in slow-wave sleep (SWS;  $118 \pm 8$  vs.  $82 \pm 7$  min;

$p < 0.0001$ ) and a decrease in light non-REM sleep (Stages I+II;  $219 \pm 10$  vs.  $267 \pm 13$  min;  $p = 0.004$ ). Sleep maintenance was slightly lower in GHD patients than in controls ( $88 \pm 2\%$  versus  $93 \pm 1\%$ ;  $p=0.03$ ). This reflected a significant increase in wake in GHD patients in the later part of the night. The sum of absolute delta activity in stages III+IV sleep was significantly increased in GHD group ( $471360 \pm 83391$  vs.  $270868 \pm 39457 \mu V2$ ;  $p = 0.02$ ) during the first 6h of sleep. Mean delta activity per min of SWS was similar in both groups. Thus, GHD appears associated with an increase in the prevalence, but not the intensity, of delta activity.

**Conclusion :** In summary, our results indicate that GHD is associated with major objective alterations in sleep architecture with increased duration of delta activity in early sleep and increased sleep fragmentation in late sleep.

**Support (optional):**

## 0928

### INTRAOCULAR PRESSURES IN AFRICAN AMERICAN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA (OSA)

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**Introduction :** Glaucoma is a progressive optic neuropathy that is often but not always associated with chronically elevated intraocular pressure (IOP). The etiology of optic nerve damage is not clear and may be multifactorial. Many patients with IOP>21 mmHg do not develop glaucoma. 1/3-1/2 of glaucoma patients do not have IOP>21 mmHg. In normal-tension glaucoma, IOP is not elevated; optic nerve damage is attributed to vascular causes. OSA is associated with cardiovascular disorders and has been associated with glaucoma in several studies. African Americans (AA) with OSA appear at increased risk (4.2%) for glaucoma. Study objectives were: (1) To determine if apnea severity is associated with IOP (2) To determine if oxygen saturation nadir or time SaO2 <90% are associated with increased IOP.

**Methods :** African Americans (AA) with OSA from the Penn Presbyterian Sleep Center were consecutively invited to participate in glaucoma screening that included complete ophthalmologic exams including FDT perimetry, applanation tonometry, pachymetry and dilated fundus exams performed by Penn Presbyterian glaucoma specialists. If patients were evaluated within 3 years, this data was included.

**Results :** 79 patients (100% AA, 67% female, age:57, BMI:40, apnea hypopnea index (AHI):35, SaO2 nadir:80%, time with SaO2 <90%:13%) were classified as no glaucoma (70%), glaucoma suspect (14%), or definite glaucoma (16%) based on findings. Of glaucoma suspects, 64% had normal IOP. Of definite glaucoma patients, 62% had normal IOP. There was no correlation ( $0.03$ ,  $95\%CI=(-.19, .25)$   $p=0.77$ ) between AHI and IOP. There was no correlation ( $-0.15$ ,  $95\%CI=(-.36, .07)$   $p=0.18$ ) between SaO2 nadir and IOP. There was little correlation ( $0.20$ ,  $95\%CI=(-.02, .41)$   $p=0.07$ ) between hypoxia time and IOP. There was no correlation ( $p=.92$  for Chi-square test) between AHI classes (mild:5-15, moderate:15-30, severe:>30) and the 3 glaucoma groups.

**Conclusion :** The prevalence of glaucoma was increased in this group of AA apnea patients (16%) compared to general AA population (4.2%). Although the majority of glaucoma patients have increased IOP, the majority of these AA apneic glaucoma suspects and definite glaucoma patients did not have increased IOP. As well, IOP was not correlated with AHI severity, SaO2 nadir, or time with SaO2<90%. Other genetics, comorbidity, or other vascular pathophysiology may contribute to this increased glaucoma prevalence and lower than expected IOP in this group of AA with OSA.

**Support (optional):**

**0929**

**SELF-REPORTED SLEEP AND ILLICIT DRUG USE IN HIV-POSITIVE ADULTS**

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**Introduction :** Medical conditions associated with HIV and illicit drug use is well studied, yet few studies report the effects of HIV and drug use on sleep. The purpose of this study is to describe self-reported sleep and depression in this population.

**Methods :** As part of a descriptive study of sleep in HIV-infected adults, data were collected on 124 who indicated no current illicit drug use. Of 112 with complete sleep questionnaires, 58 tested positive for illicit drugs (amphetamine, cocaine, marijuana, opiates) during sleep monitoring. Self-report measures included: Pittsburgh Sleep Quality Index (PSQI) about the past month, General Sleep Disturbance Scale (GSDS) about the past week, Center for Epidemiological Studies-Depression (CES-D) for depressive symptoms during the past week, and demographic information on age, CD4 cell count, ethnicity, income, and psychiatric history.

**Results :** Results to date are presented for 33 men and 25 women, primarily African American (45%) and Caucasian (31%) with mean age 44±7 years. CD4 cell count ranged from 2 to 1088. The PSQI mean score was 7.7±4.1; 66% (n= 38) exceeded the cut off score of 5. The GSDS mean was 54±25. CES-D was 21.2±9.8, with 74% (n= 43) depressed and exceeding the cut off score of 16 or higher. CES-D scores were correlated with PSQI ( $r=.44$ ,  $p=.001$ ) and GSDS ( $r=.53$ ,  $p<.001$ ). There were no gender differences on sleep or depression measures. While those using illicit substances had similar CES-D and PSQI scores as those not using illicit substances, illicit substance users reported significantly more sleep disturbance on the GSDS ( $t[110] = 3.20$ ,  $p=.002$ ).

**Conclusion :** Preliminary findings suggest HIV-positive adults using illicit drugs have a high degree of self-reported sleep disturbance. Findings support the need for health care providers to further assess factors that contribute to impaired sleep when developing effective care for this population.

**Support (optional):** NIH Grant# R01 MH074358, KA Lee, P.I.

**0930**

**GASTROESOPHAGEAL REFLUX AND OBSTRUCTIVE SLEEP APNEA: CAN REFLUX ALTER OBSTRUCTIVE SLEEP APNEA AND SLEEP PATTERNS IN MILD OSA?**

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**Introduction :** Previous studies have revealed conflicting data, but it has been speculated that GER may alter the upper airway in a way which would facilitate the occurrence of OSA. In this investigation we have tested the hypothesis that significant acid suppression and reduction of GER would significantly reduce the rate of OSA in patients with mild OSA.

**Methods :** All subjects underwent a sleep evaluation as well as a 24-hour esophageal pH evaluation. To qualify subjects had to have an AHI of <15,

and esophageal acid contact time in the supine position of >6% total or 3% supine. Qualifying subjects underwent 8 weeks of treatment with 20mg bid of rabeprazole. The Epworth Sleepiness Scale (ESS) and the Pittsburg Sleep Quality Index (PSQI) were completed before and after treatment. At the end of 8 weeks all subjects repeated the sleep and 24-hour esophageal pH evaluations.

**Results :** Subjects had significantly ( $p<.05$ ) less reflux events in both upright and supine positions and significantly less ( $p<.05$ ) % acid contact time post treatment. Subjects also had significantly shorter reflux events post treatment compared to baseline. Sleep onset latency was significantly ( $p<.05$ ) shorter post treatment compared to baseline, however total sleep time and stages 3+4 sleep were not significantly different post treatment. There was no difference in the AHI index at baseline compared to post treatment. Subjects reported significantly ( $p=.02$ ) less daytime sleepiness after treatment (ESS = 10) compared to the pre-treatment condition (ESS=12). The PSQI score was also significantly improved after treatment (pre=8, post=6,  $p=.02$ ).

**Conclusion :** 1. Rabeprazole improved heartburn symptoms and subjective reports of daytime sleepiness and sleep quality in patients with mild OSA. 2. Reduction of GER in patients with OSA does improve sleep quality and daytime sleepiness and should be an important consideration in treatment.

**Support (optional):** Janssen Pharmaceutica, Inc.

**0931**

**SLEEP-RELATED BREATHING DISORDER IN ADVANCED LUNG CANCER PATIENTS**

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**Introduction :** Patients with lung cancer commonly report disturbed sleep. Because a sleep-related breathing disorder (SRBD) may be an underlying factor, we performed an analysis of polysomnographic (PSG) measures of sleep and nocturnal pulse oximetry (SaO<sub>2</sub>) to examine nocturnal hypoxic burden and its relationship to sleep variables.

**Methods :** The sample included 23 outpatients (19 male, 4 female; mean age 58.74±8.13 years) with primary or secondary lung cancer who were part of a larger study of pain, opioids and sleep. All patients underwent 48-hour ambulatory PSG including pulse oximetry (sampling rate 1 Hz). Subjects with high nocturnal hypoxic burden (>20% of total sleep time [TST] with SaO<sub>2</sub> <90%) were compared to those with low burden relative to sleep and demographic/clinical characteristics using Mann-Whitney U tests.

**Results :** Thirty percent of the subjects (n=7) had a high nocturnal hypoxic burden. While this group was younger ( $p<.05$ ), had a lower BMI ( $p<.01$ ), and tended to have lower functional status ( $p=.09$ ), there were no other demographic (gender, race), clinical (hematology, blood chemistry, smoking or pain status), or treatment (chemotherapy, radiotherapy, opioid equivalents received) differences between groups. The high burden group had a lower mean nocturnal SaO<sub>2</sub> (91.80±1.11% vs. 94.11±1.94%;  $p=.02$ ) and averaged 101.79±59.95 minutes with an oxygen saturation < 90% vs. 21.97±22.94 minutes ( $p<.001$ ) in the low burden group. Sleep in the high burden group was characterized by a significantly lower TST ( $p<.01$ ), lower sleep efficiency ( $p<.01$ ) and more time awake after sleep onset ( $p<.001$ ).

**Conclusion :** These preliminary data suggest that a substantial number of lung cancer patients may have a high nocturnal hypoxic burden that adversely affects sleep. Further investigation of the prevalence and type(s) of SRBD in this population is warranted to establish effective interventions to decrease the adverse effects of both disturbed sleep and hypoxia.

**Support (optional):** National Institute of Nursing Research, RO1 NR008124

### 0932

#### LARYNGEAL CHANGES AFTER SUPPRESSION OF GASTROESOPHAGEAL REFLUX IN MILD OSA

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**Introduction :** Gastroesophageal reflux (GER) has been proposed as a factor in the pathogenesis of OSA. No studies to date have evaluated GER and laryngeal function in a group of patients pre selected with both significant GER and OSA.

**Methods :** Fifteen subjects underwent a sleep evaluation, a 24-hour esophageal pH evaluation and laryngopharyngeal function evaluations. To qualify subjects had to have an AHI of < 15 and esophageal acid contact time in the supine position of >6% total or 3% supine. Qualifying subjects underwent 8 weeks of treatment with 20mg bid of rabeprazole. At the end of treatment all subjects repeated all evaluations. The Reflux Finding Score is a composite of laryngeal measures used to quantify laryngopharyngeal function. Voice evaluation was also conducted before and after treatment.

**Results :** Subjects had significantly ( $p<.05$ ) less ( $p<.05$ ) % acid contact time post treatment. There was no change in the AHI post treatment. The Reflux Finding Score was reduced ( $p=.07$ ) and there was significantly ( $p=.04$ ) reduced posterior commissure hypertrophy (mean=1.26 vs.73, scale 0-4) and vocal fold edema (mean= 1.50 vs .30,  $p=.03$ ) (scale 1-4). Subglottic pressures were not significantly different post treatment.

**Conclusion :** 1) Reduction of esophageal acid contact time can substantially improve upper airway abnormalities noted in mild OSA; 2) The identification of GER is an important element in the appropriate treatment of patients with OSA.

**Support (optional):** Janssen Pharmaceutica, Inc.

### 0933

#### RISK FACTOR FOR PRE-ECLAMPSIA AND NASAL CPAP

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**Introduction :** Pre-eclampsia occurs in 10% of snorers compared to 4% in non-snorers, and CPAP administered at time of pre-eclampsia reduced hypertension.

**Methods :** Women with known factors for pre-eclampsia, ie: prior pre-eclampsia, hypertension, diabetes, thrombophilic disorders, obesity, were prospectively recruited between 6 and 9 weeks of GA. Subjects underwent nocturnal polysomnography to evaluate breathing during sleep and were offered to undergo nasal CPAP treatment titrated during sleep to eliminate presence of snoring and flow limitation.

**Results :** 12 women 7 with hypertension, 2 with prior pre-eclampsia, 3 with obesity (BMI>30kg/m<sup>2</sup>) mean age 29 (SD:3) years, had polysomnography at a mean of 7.5 weeks GA. All snored, had flow limitation at nasal cannula (mean 47minutes of TST 28-79 minutes) without apnea or hypopneas. Nasal CPAP pressure was initially 5 to 6 and increased to 6 to 9 cm/H<sub>2</sub>O with compliance check at mask in 8/12 women between 5 and 6 months GA Women with hypertension maintain

diastolic BP below 90 mmHg without change in medication and delivered full term infants (n=7), 1 obese woman had a miscarriage near 14 weeks GA; another had delivery of a 34 weeks GA premature infant without pre-eclampsia, while the 3rd presented clinical features of pre-eclampsia and had cesarean section at 7 ½ months as did one of the 2 women with history of prior pre-eclampsia.

**Conclusion :** Systematic treatment with nasal CPAP, started before 9 weeks GA did not avoid pre-eclampsia in 2 women, but women with history of hypertension, snoring and flow limitation during sleep had stable BP and normal pregnancy with combine medical and CPAP treatment.

**Support (optional):**

### 0934

#### NOCTURNAL SYNCOPE AMONG SUBJECTS WITH DIURNAL VASO-VAGAL SYNCOPE

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**Introduction :** Syncope refers to sudden transient loss of consciousness and postural tone due to cerebral hypoperfusion. Vaso-vagal refers to the activation of pathological neuro-cardio-vascular reflexes that lead to sudden marked peripheral vasodilation and/or bradycardia. While patients typically experience syncope during the day, there is evidence to suggest that syncope may also occur during the night, thereby interrupting sleep. In the current study we explored the prevalence of self-reported nocturnal syncope and associated sleep complaints in subjects prone to daytime syncope of suspected vaso-vagal origin.

**Methods :** 29 women and 16 men (age 17-59 years) with suspected diurnal vaso-vagal syncope were questioned about the presence and characteristics of nocturnal syncope, sleep quality, presence of insomnia as well as psychological distress.

**Results :** Eight subjects (17.7 %) reported having experienced nocturnal syncope or pre-syncope. Five (11%) reported awakening with nausea, tachycardia and diaphoresis, prior to losing consciousness. In three subjects, symptoms occurred after getting up from bed during the night. Subjects with nocturnal syncope had more frequent episodes of diurnal syncope (5 ± 6) versus those without (1.8 ± 2.7) ( $p<0.001$ ). No differences were observed in age, BMI, sex, sleep complaints, hypertension, use of medications, and level of distress between the two groups.

**Conclusion :** Nocturnal syncope is not infrequent in subjects prone to diurnal syncope, especially in those with frequent episodes. Investigations are required to clarify the mechanism underlying the genesis of syncope experienced during sleep in subjects prone to vaso-vagal syncope.

**Support (optional):**

### 0935

#### SYMPTOMS OF RESTLESS LEGS SYNDROME AMONG ADULTS WITH HIV INFECTION

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**Introduction :** HIV-infected adults often report pain and abnormal sensa-

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tions in their extremities. These symptoms are typically attributed to neuropathic pain and treatment is prescribed accordingly. However, these symptoms could also be indicative of restless legs syndrome (RLS). This study describes RLS symptoms and incidence of RLS-related symptoms in a sample of HIV-infected adults.

**Methods :** As part of a study of sleep in HIV-infected adults, those diagnosed with RLS or other sleep disorders were excluded from participation. Neuropathic pain was not an exclusion criterion. To date, 120 participants have completed wrist actigraphy, sleep questionnaires, and the Memorial Symptom Assessment Scale (MSAS) modified to include 4 RLS items experienced during the past week.

**Results :** The sample was ethnically diverse (43% African American, 35% Caucasian, 13% Latino, and 9% mixed/other) and consisted of 70 men, 43 women, and 7 transgender adults with a mean age of  $43\pm 7$  years and mean CD4 cell count of  $458\pm 286$ . On the MSAS, 39% reported numbness/tingling in their hands/feet; 18 (38%) of those went on to indicate an abnormal sensation in their legs, while 9 (12%) of the remaining 61% also went on to indicate an abnormal sensation in their legs. Despite their response to the numbness/tingling item, 27 (22.5%) reported an abnormal sensation or urge to move their legs (23% of males, 19% of females, and 43% of transgender adults). Of those 27, 52% indicated it was worse at night, 56% indicated it came on at rest, and 56% indicated it was relieved with movement. Only 6% endorsed all 4 RLS criteria. RLS symptoms were more common among those with CD4 counts  $< 500$  (30% vs 12%,  $\chi^2[1]=4.95$ ,  $p=.026$ ).

**Conclusion :** Findings support the need for health care providers to distinguish symptoms of RLS from neuropathic pain prior to initiating opiates or other drug therapy in this patient population.

**Support (optional):** NIH Grant# R01 MH074358, KA Lee, P.I.

### 0936

#### SECONDARY INSOMNIA, DEPRESSIVE SYMPTOMS, AND SLEEP SELF-EFFICACY IN CARDIOVASCULAR DISEASE PATIENTS

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**Introduction :** Sleep disturbance and depressive symptoms are frequently secondary or comorbid with cardiovascular disease, the leading cause of death in the United States. Previous research has examined relations among sleep and depression in cardiovascular patients; however, no research has compared various subgroups of cardiovascular disease patients on indices of sleep. We investigated relations among sleep quality, depressive symptoms, and sleep self-efficacy in cardiac patients with coronary artery disease (CAD), congestive heart failure (CHF), cardiac arrhythmias (CA), and those undergoing implantable cardioverter defibrillator (ICD) therapy.

**Methods :** Twelve participants (CAD,  $n=4$ ; CHF,  $n=2$ ; CA,  $n=4$ ; ICD,  $n=3$ ) were recruited as part of a larger investigation of sleep and depression in cardiovascular patients. Participants completed the following psychometric questionnaires: Pittsburgh Sleep Quality Index (PSQI); Center for Epidemiological Studies Depression Scale (CESD), and Lacks' Sleep Self-Efficacy Scale (SSES).

**Results :** Mean overall sleep quality score on the PSQI was 7.75 (SD =4.90) with 75% of the sample above the clinically significant cut-off score of five. (Higher PSQI scores are associated with poorer sleep.) Correlations revealed somatic depressive symptoms were highly positive-

ly associated with overall sleep quality ( $r=.83$ ,  $p<.001$ ), subjective sleep quality ( $r=.87$ ,  $p<.01$ ), total sleep time ( $r=.85$ ,  $p<.001$ ), sleep efficiency ( $r=.70$ ,  $p<.05$ ), and daytime dysfunction ( $r=.71$ ,  $p<.01$ ). Sleep self-efficacy was highly negatively correlated with overall sleep quality ( $r=-.84$ ,  $p<.001$ ), subjective sleep quality ( $r=-.86$ ,  $p<.001$ ), daytime dysfunction ( $r=-.77$ ,  $p<.01$ ), overall depressive symptoms ( $r=-.68$ ,  $p<.05$ ), and somatic depressive symptoms ( $r=-.89$ ,  $p<.001$ ).

**Conclusion :** Preliminary data converges with previous findings that sleep in cardiovascular patients is associated with sleep disturbance, depressive symptoms and patient confidence in their ability to sleep well. Cardiovascular patients may benefit from psychosocial interventions designed to improve cognitions and beliefs that pertain to sleep. A more detailed discussion of results by cardiac patient subgroup from a larger sample size will be presented by the conference date.

**Support (optional):**

### 0937

#### CHALLENGES TO SLEEP IN ASTHMA STUDIED UNDER BASELINE CONDITIONS, REDUCED HOMEOSTATIC SLEEP DRIVE, AND ADVERSE CIRCADIAN PHASE FOR SLEEP

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**Introduction :** Nocturnal worsening of asthma is common and reported to disrupt sleep. We hypothesized that subjects with asthma will have disrupted sleep at baseline and exaggerated sleep disruption in response to reduced homeostatic sleep drive (i.e., later in the sleep opportunity), and particularly when sleep opportunity occurs at an adverse circadian phase (i.e., during the biological day).

**Methods :** 15 subjects (10 asthma, 5 controls) were studied polysomnographically throughout a 10-day protocol in dim light. After an habituation and a baseline night, sleep opportunities were scheduled across all circadian phases with a recurring artificial day length of 28 h. Each 10.33-h sleep episode was split into three equally parts interspersed by brief awakenings (for pulmonary function measurements). Core body temperature (CBT) was used as the circadian phase marker. Data were subjected to 3-way ANOVA (asthma vs. control; 6 circadian-phase bins; thirds of sleep opportunity). The only medication was symptom-based bronchodilator rescue medication (beta2-adrenergic agonist inhaler).

**Results :** On the baseline night following habituation, there was no significant difference between groups in the amount of sleep or in the proportions of any of the sleep stages. Average sleep efficiency was 89% in asthma and 94% in control subjects. Both groups had a significant: (i) circadian rhythm in sleep efficiency, peaking around minimum CBT (peak-trough = 26%;  $p<0.0001$ ); (ii) effect of time-into-sleep, with sleep efficiency declining across each sleep opportunity ( $p<0.0001$ ); (iii) interaction between circadian and homeostatic influences on sleep efficiency, with the strongest circadian influence in the last third of sleep opportunity (peak-trough = 56%;  $p<0.0001$ ). The combined challenges of reduced homeostatic sleep drive (last third of the sleep opportunity) and adverse circadian phase (biological day) resulted in worse sleep efficiency in the control group than in the asthma group (12% vs. 59%;  $p<0.01$ )

**Conclusion :** In studying the interaction of a disease and sleep, we found no difference in either baseline sleep quantity or quality between control and asthma subjects. More surprisingly, asthma did not result in an exaggerated sleep disruption in response to a combined homeostatic and circadian challenge to sleep continuity.

**Support (optional):** NIH RO1 HL064815; K24 HL076446 in support of SAS; Pickwick Fellowship in support of FAJLS; NCRR GCRC M01 RR02635

## 0938

## SLEEP-DISORDERED BREATHING TREATMENT OUTCOMES IN ACROMEGALY SUBJECTS

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**Introduction :** Obstructive sleep apnea-hypopnea, central apnea-hypopnea syndromes and hypoventilation are highly prevalent in acromegaly and they correlate with acromegaly symptoms severity. Yet, UAW soft and bony tissue overgrowth correlates with OSAHS severity. Treatment with octreotide decreases UAW tongue volume and RDI. The objectives of this investigation is to determine the effect of acromegaly treatment over the RDI.

**Methods :** 11 severe acromegaly subjects (6 male, 5 female, mean age 49.9 years, range 32-71; BMI=32.9(3.1); IGF-1=1312.2 (SD±640.9) microg/l; GH=22.1 (SD±21.8) (median GH =25 microg/l) underwent in-hospital sleep studies at baseline, 1 month and 4 months after treatment. Treatment consisted of octreotide acetate (Sandostatin LAR 20-30 mg / 4 weeks I.M.) or neurosurgery. GH and IGF-1 levels were assessed 1 and 4 months later.

**Results :** Baseline: all subjects presented RDI>5 events/hr (range 19-60.2; mean=36.60/hr). Four months post-treatment RDI was not statistically different (RDI=33.0(22.3) (mean [SD]) at (surgery or octreotide). However, a significant reduction in GH (7.0(11.0) median 2.3, p<0.05) and IGF-1 (714.1(485.3) p<0.05) levels were recorded and IGF-1 became normal within the age-adjusted range in 45% of the subjects.

**Conclusion :** A high prevalence rate (100%) of sleep-disordered breathing was confirmed in this sample of severe acromegaly subjects with 63% of the sample with RDI>30. Treatment with octreotide or surgery produced no RDI difference even after four months validating the 1 month poor treatment outcome as previously documented by the authors. The current 4-month data challenges studies with 6-month octreotide treatment showing a clinically significant RDI improvement.

**Support (optional):**

## 0939

## REGULATION OF PLASMA RENIN ACTIVITY BY AHI SEVERITY IN HYPERTENSION

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**Introduction :** Compensatory cardiovascular mechanisms in obstructive sleep apnea (OSA) have been reported to affect comorbid hypertension and the severity of sleep disordered breathing is known to influence the operative neurohormonal axes. We theorized that plasma renin activity (PRA) is affected by the degree of respiratory disturbance.

**Methods :** We, therefore, measured PRA in 36 hypertensive patients (age 64±7.9 years, mean±SD) with OSA organized in quartiles by apnea/hypopnea index (AHI) as AHI 5-15, AHI 16-25, AHI 26-40, AHI>41. None of the studied patients had renal artery stenosis, parenchymal renal disease or emphysema. PRA was measured by radioimmunoassay of angiotensin I appearance per second following measurement of renin kinetics. Blood for PRA assay was obtained after each patient had been seated for five minutes. After preparation at ambient temperature each plasma sample was quickly frozen and handled per usual for PRA. All patients followed a restricted sodium diet and were advised to maintain their usual dietary routine around the time of urine collection for 24-hour urinary sodium excretion measurement. Creatinine clearance was

calculated from direct urinary and serum measurement. Serum aldosterone and cortisol were measured by enzyme immunoassay. Vascular resistance index was quantified by transthoracic impedance.

**Results :** PRA, blood pressure and urine sodium are shown to be directly proportional to AHI across all quartiles of AHI (n=36, 95% CI, p<0.001). By contrast, serum aldosterone and serum cortisol were unrelated to AHI (p>0.20) while body mass index and systemic vascular resistance index appear to be correlated with AHI (Pearson, r=0.64, n=36).

**Conclusion :** These data imply a direct interaction between sleep-associated respiratory disturbance and renal peptide hormone induction in secondary hypertension. Elucidating the distal neurovascular effects of OSA at the level of the glomerular complex may improve our understanding of the pathophysiology associated with sleep disorders.

**Support (optional):**

0940

ATTENTION DEFICIT AND HYPERACTIVITY DISORDER (ADHD) IN CHILDREN AND SLEEP DISORDERED BREATHING

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**Introduction :** ADHD is a common childhood disorder with implications on the growth and development of children. Sleep disordered breathing and accompanying sleep disruption also has implications on the behavior and learning in children. Several studies have suggested an association between symptoms of ADHD and sleep disordered breathing in children while others have refuted this etiologic association. To evaluate if there is an association between these two disorders is of immense clinical importance in the management of these children. The purpose of this study is to evaluate the link between sleep disordered breathing and symptoms of ADHD in children between the age of 2 and 18 years.

**Methods :** 1. All children (age: 2 to 18 years) who had polysomnography at our sleep laboratory between June 26, 2005 and Dec 02, 2005 are analyzed. 2. After medical chart review, children with clinical diagnosis of ADHD based on DSM-IV criteria are included in the analysis. 3. Demographic characteristics, polysomnographic characteristics (sleep latency, REM latency, sleep efficiency, % of each sleep stage) and apnea-hypopnea indices (AHIs) are described in children with ADHD and compared with children with and without sleep disordered breathing. These parameters are also compared with children who have no evidence of ADHD and sleep disordered breathing. 4. We are also analyzing the effects of tonsillectomy and adenoidectomy on the symptoms of ADHD in children with co morbid diagnosis of ADHD and sleep disordered breathing.

**Results :** 289 children underwent polysomnography between June 26, 2005 and December 02, 2005. We identified 10 children with clinical diagnosis of ADHD based on DSM-IV criteria. Increased REM latency and decreased REM percentage was seen in children with clinical diagnosis of ADHD. There were no significant differences in the polysomnographic characteristics of children with clinical diagnosis of ADHD with and without polysomnographic evidence of sleep-disordered breathing.

**Conclusion :** This study of small sample size does not point towards an association between ADHD in children and sleep disordered breathing in the study population. The polysomnographic characteristics of children with ADHD in this study are comparable to other studies.

**Support (optional):**

0941

DOES AMYGDALAR PERFUSION CORRELATE WITH ANTIDEPRESSANT RESPONSE TO PARTIAL SLEEP DEPRIVATION IN MAJOR DEPRESSION?

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**Introduction :** This study used functional MRI (fMRI) to investigate mechanisms of antidepressant effect of 1 night's late-night (awake beginning at 3 am) partial sleep deprivation (PSD) in major depression. We hypothesized: 1) baseline perfusion in right and left amygdalae will be greater in responders than in nonresponders; following partial sleep deprivation (PSD), perfusion in responders' right and left amygdalae would decrease.

**Methods :** 17 unmedicated unipolar outpatients (baseline 17-item Hamilton Depression Rating Scale (HDRS17) > 16, M/F 5/12, 42.8 + 9.7 years) and 8 controls (M/F 4/4, 35.0 + 9.5 years) received 3 nights polysomnography (adaptation, baseline, and PSD) in the sleep laboratory.

Approximately noon after the baseline and PSD nights, subjects received anatomical and perfusion magnetic resonance imaging (MRI) using pulsed arterial spin labeling, with baseline and PSD blocks in randomized counterbalanced order. Responders were defined by a decrease of 40% or greater in the modified HDRS17 (omitting sleep and weight loss items.) Data were analyzed using Analysis of Functional NeuroImages (AFNI) 2.56b. Each subject's amygdalae were hand traced blindly according to anatomic criteria.

**Results :** Baseline bilateral amygdalar perfusion was greater in responders than nonresponders ( $P < 0.048$  left,  $P < 0.001$  right). Clusters involving both amygdalae decreased from baseline to PSD specifically in responders. Right amygdala change scores (baseline minus PSD) significantly differed between nonresponders and responders ( $P < 0.033$ ), with perfusion increasing in nonresponders and decreasing in responders with PSD.

**Conclusion :** These novel amygdalar findings are consistent with the overarousal hypothesis of SD as well as other functional imaging studies showing increased baseline amygdalar activity in depression and decreases in amygdalar activity with remission or antidepressant medications.

**Support (optional):** 5K08MH01642, RR00827, Laboratory of Sleep and Chronobiology, Laboratory of Cognitive Imaging, VA MIRECC, Human Brain Morphometry BIRN

0942

ACTIGRAPHY AND POLYSOMNOGRAPHIC SLEEP IN JUVENILE BIPOLAR DISORDER

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**Introduction :** Juvenile bipolar disorder (JBD) is characterized by abrupt swings of mood and activity that occur multiple times per day ("ultra-ultra rapid cycling")<sup>1</sup>. Parents commonly report a consistent diurnal pattern with increased evening activity and difficulty initiating nighttime sleep plus extreme lethargy for several hours upon awakening. We studied actigraphy and polysomnography in children with JBD to obtain objective evidence for such a diurnal pattern.

**Methods :** Six children with JBD (using modified DSM-IV criteria) wore a wrist actigraph for 3-8 days, during which 2 night sleep (PSG) recordings were obtained. PSG results were compared with age-matched normal values<sup>2,3</sup> to detect any measure that was >2 SDs from the norms. Due to first night effects, only N2 PSG data were used for norms comparison. Diurnal actigraphy patterns were assessed using 30-minute activity bins anchored to actigraphy-derived wake times. Each subject's binned values were averaged across days.

**Results :** All patients showed abnormal (as defined above) PSG sleep on at least 1, and often several, measures. The most consistent differences were long sleep onset latency (5/6 Ss), short REM latency (4/6), and increased minutes (5/6) and % (4/6) REM. Actigraphy data revealed bursts of evening activity in all 6 Ss, while absolute activity levels were significantly lower in the first 3 bins after wake time than in any other bin during the day in 5/6 Ss (using one-way repeated measures ANOVA with planned comparisons). One 13 y.o. patient's actigraphy strongly suggested non-24h sleep wake syndrome: her sleep offset/wakeup time progressed from 1139h to 1529h across 5 days, delaying by an average of 58 min/day (x2 periodogram  $\tau = 25.3h$ ), concurrent with maternal reports of circa 1-month cycles for past 3 years of gradually delaying sleep times until sleep occurred during the day, followed by a gradual return to nighttime sleep.



**Conclusion :** This pilot study of actigraphy and PSG sleep in children with JBD generally supports the ubiquitous parental and clinical assessments of sleep difficulties in this population. Most of these children had late bedtimes for their ages, even at home, difficulty initiating sleep, clear morning lethargy, and bursts of high activity in the evening hours prior to bedtime. A larger sample with additional measures (temperature, melatonin) is needed to characterize putative abnormalities in the circadian and/or homeostatic regulation of sleep in children with JBD.

**Support (optional):** This research was supported by the Juvenile Bipolar Research Foundation, NIH R01 AG12112, and NIH R01 AG15370.

### 0943

#### EFFECTS OF LONGITUDINAL HALOPERIDOL-WITHDRAWAL ON REM SLEEP EEG SPECTRAL ANALYSIS IN CLINICALLY STABLE PATIENTS WITH SCHIZOPHRENIA

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**Introduction :** It have been shown that sleep architecture continues to change following neuroleptic-withdrawal in clinically stable patients with schizophrenia (Nofzinger et al.,1993). The present study aim to verify if this applies to REM sleep EEG spectral analysis.

**Methods :** Ten male inpatients (age: 39.4 +/- 4.4 years) diagnosed with schizophrenia slept three nights in a sleep laboratory for each of these treatment conditions: at baseline treated with haloperidol, after two-weeks and after six-weeks of neuroleptic withdrawal. Spectral analysis was performed on the C3 EEG channel of each conditions. For each 60-sec epoch over the whole sleep period, absolute and relative EEG spectral power were extracted using FFT for Delta (0.75-3.75 Hz), Theta (4.00-7.75 Hz), Alpha (8.00-12.75 Hz), Beta1 (13.00-19.75 Hz) and Beta2 (20.00-30.00 Hz) frequency bands. Ten epochs without artefact were selected from each of the three first REM sleep periods (previously visually identified using standard criteria). The mean spectral power for each frequency band was then calculated. Comparisons between separated REM sleep periods (REM1 Vs REM2 Vs REM3) and treatment conditions (Baseline Vs two-weeks Vs six-weeks) were performed using 3X3 ANOVAs and Tukey tests.

**Results :** Treatment effects were observed for absolute Theta [ $F(2, 40) = 5.09, p < .01$ ] and Beta1 [ $F(2,40) = 4.47, p < .02$ ] frequency bands. Post-hoc comparisons shown higher absolute spectral power during the third REM sleep period for Theta ( $p < .04$ ) and Beta1 ( $p < .02$ ) frequency bands during the two-weeks neuroleptic-free condition compared to baseline. There was no difference between baseline and the six-weeks neuroleptic-withdrawal condition.

**Conclusion :** REM sleep EEG absolute spectral power increased during the third REM sleep period for Theta and Beta1 frequency bands after 2-weeks, but returned to baseline after 6-weeks of haloperidol-withdrawal. This suggest that the increase of Theta and Beta1 REM sleep EEG spectral power is mediated by the dopaminergic effect of neuroleptic-withdrawal.

**Support (optional):**

### 0944

#### ASSOCIATIONS BETWEEN MOOD AND MELATONIN - SLEEP PHASE ANGLES IN HEALTHY AND DEPRESSED PREGNANT AND POSTPARTUM WOMEN

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**Introduction :** The study aim was to test the hypothesis that depressed mood is associated with altered timing of melatonin (MLT) onset/offset with respect to sleep onset/offset (phase angles), in pregnant and postpartum women. It was expected that patients who met Diagnostic and Statistical Manual (DSM-IV-TR) criteria for Major Depressive Disorder (DP) would exhibit altered phase angles between sleep and MLT, relative to normal control (NC) subjects.

**Methods :** In 16 pregnant women (6 NC, 10 DP) and 16 postpartum women (5 NC, 11 DP), age range 21.4 - 34.4 years, baseline polysomnography (PSG) was recorded after an adaptation night in the sleep laboratory. Plasma MLT was sampled at 30-minute intervals from 18:00 - 11:00 h. MLT onset and offset were estimated by visual inspection of the ascending and descending slopes (dy/dt) of individual melatonin concentration curves. The Hamilton Depression Rating Scale (HDRS), including atypical items, and the Beck Depression Inventory (BDI) were correlated (by Pearson tests) with sleep and MLT measures.

**Results :** In pregnant women, MLT offset - sleep onset phase angle was positively correlated with HDRS ( $r = .612, p = .026$ ) and BDI ( $r = .670, p = .024$ ) score, for NC + DP combined. In postpartum women, MLT onset - sleep onset phase angle was positively associated with HDRS score ( $r = .558, p = .031$ ) and with atypical items ( $r = .583, p = .022$ ), for NC + DP combined. Pregnant and Postpartum DP versus NC women did not differ with respect to phase angles by Multivariate Analyses of Variance (MANOVA).

**Conclusion :** These findings support the hypothesis that depressed mood in pregnant and postpartum women is associated with an increased time interval between melatonin (MLT) onset/offset and sleep onset/offset (phase angles), although the differences did not distinguish DP versus NC women or pregnant versus postpartum women in this sample.

**Support (optional):**

### 0945

#### LONG TERM SUBJECTIVE STRESS AND REPEATED SLEEP POLYSOMNOGRAPHY

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**Introduction :** Long-term exposure to stress is usually seen as the major cause of primary (psychophysiological) insomnia. However, very few studies have tried to relate real life stress to polysomnography. The present study sought to do that, using several recorded sleep episodes and several weeks of stress ratings.

**Methods :** 33 subjects kept a sleep/wake diary across 6 weeks. Subjective stress was rated on a scale from 1-9 (totally relaxed to maximum imaginable stress) every 3 hours each day. Polysomnography was carried out in the home of each participant 4 times (different weeks) using standard derivations. Subjects went to bed and rose at their normal hours. Means were computed across the 6 weeks for subjective stress and across the 4 sleep episodes (for each standard sleep variable, including latency to stages 1,2,3 and REM). The obtained data was subjected to a stepwise multiple regression analysis with subjective stress as the dependent variable and the sleep parameters as predictors. Age and gender were forced into the regression as controls.

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**Results :** Mean stress was  $2.3 \pm 1$  (SD) ranging between 1 and 4.6. The results showed that the significant predictors were Latency to Stage 1 sleep ( $\beta = .37$ ,  $R^2 = .17$ ) and Stage 1 sleep (minutes) ( $\beta = .44$ ,  $R^2 = .12$ ) with  $F = 5.2$ ,  $p < .01$ ) and total  $R^2 = .35$  (including forced variables). To study the role of other predictors, Stage 1 was removed. This resulted in TST entering the regression ( $\beta = .39$ ,  $R^2 = .10$ ), without affecting the beta weight of Latency to Stage 1. Note that stress is associated with longer TST.

**Conclusion :** The results show that subjective stress across 6 weeks is related to a long sleep latency and high amounts of Stage 1 across several sleep episodes.

**Support (optional):** The Swedish Council of Research Councils.

### 0946

#### SLEEP QUALITY AND PSYCHOSOCIAL PARAMETERS OF PTSD PATIENTS TREATED BY EYE MOVEMENT DESENSITIZATION REPROCESSING (EMDR®) BECOME SIMILAR TO THOSE OF HEALTHY CONTROLS

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**Introduction :** The impact of PTSD on the sleep of patients is widely reported. However, the parameters that can be altered are not the same for all patients. Some studies report an impairment of sleep maintenance and recurrent nightmares, whilst others failed to find such alterations. Among the many treatments, the EMDR® is a therapy used specifically to treat PTSD and general trauma. The purpose of this study was to examine whether EMDR® treatment can improve PTSD symptoms, such as disrupted sleep, depression, anxiety and poor quality of life.

**Methods :** Seven patients (both genders, aged 24 to 36 years), victims of assault or kidnapping underwent psychiatric evaluation, according to SCID-DSM-IV to confirm the diagnosis of PTSD and to determine possible co-morbidities. They were submitted to psychological evaluation and polysomnography at the time of inclusion. Treatment ended when the patient reported not having the typical PTSD symptoms on his/her daily life. After the end of treatment the patients were again evaluated exactly in the same way as the first time. The PTSD group was compared to a group of healthy subjects (gender and age matched,  $N = 5$ ) who have never experienced trauma, which was submitted to the exact same protocol.

**Results :** The average number of EMDR therapy sessions was 5, occurring once a week. The results showed an increase in sleep efficiency and reduced time of waking after sleep onset, reduction of depression, anxiety, fatigue, impact of the event, and stress symptoms scores, and an improvement of quality of life, of sleep quality and general well-being in the PTSD patients. All psychosocial indices were similar in post-therapy PTSD and control groups.

**Conclusion :** Our preliminary results indicate that this type of therapy is effective to treat many of the PTSD symptoms that can impair people's daily life activities.

**Support (optional):** AFIP and FAPESP/CEPID # 98/14303-3. Deborah Suchecki and Sergio Tufik are fellows from CNPq.

### 0947

#### EFFECTS OF A BRIEF BEHAVIORAL TREATMENT FOR PTSD-RELATED SLEEP DISTURBANCES: A PILOT STUDY

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**Introduction :** Sleep disturbances are core features of posttraumatic stress disorder (PTSD), and are often resistant to first-line PTSD treatments. This pilot study explored the effects of a brief intervention for PTSD-related nightmares and insomnia.

**Methods :** Participants were seven adult victims of violent crimes (3 men, 4 women,  $M$  age =  $33.93 \pm 5.67$  years) with a current diagnosis of PTSD, as determined on the Clinician-Administered PTSD Scale. All received a single, individual 90-minute intervention session that combined imagery rehearsal, stimulus control, and sleep restriction. Sleep diary measures, and self-report and clinician-administered measures of sleep quality and emotional dream valence, intensity, and PTSD symptoms severity were completed at baseline and six weeks post-intervention. Cohen's  $d$  effect sizes were computed to assess the magnitude of pre- to post-treatment changes. Cohen's  $d$  coefficients of 0.20, 0.50, and 0.80 were taken to indicate small, medium, and large effect sizes, respectively.

**Results :** Sleep diary measures indicated a mean reduction of 20.2 minutes ( $SD = 36.4$ ) in sleep latency ( $d = .28$ ), a mean increase of 45 minutes ( $SD = 179$ ) in total sleep time ( $d = .37$ ), and a mean reduction of 15.5 minutes ( $SD = 27$ ) in wake time after sleep onset ( $d = .66$ ). Reductions in dream frequency ( $d = .67$ ), dream intensity ( $d = .32$ ), negative emotions ( $d = .45$ ) were also reported. Improvements in sleep were accompanied by improvements in overall daytime PTSD symptom severity ( $d = .67$ ), daytime intrusions ( $d = .89$ ), hyperarousal ( $d = .78$ ), and avoidance symptoms ( $d = .39$ ).

**Conclusion :** A very brief behavioral intervention targeting posttraumatic nightmares and insomnia was associated with significant improvements in sleep and daytime PTSD symptom severity. Brief sleep-focused behavioral interventions may be helpful adjuncts to first-line PTSD treatments. The present results warrant further evaluation in a controlled trial.

**Support (optional):** This work was supported by the Pittsburgh Mind-Body Center funded through NIH grants HL65111 and HL65112, the Canadian Institutes of Health Research, the National Institute of Health (AG00972, RR00056; MH01554; MH66227, MH61566 MH24652, MH60783).

### 0948

#### MEDICATIONS, PSYCHOLOGICAL WELL-BEING, AND SLEEP DISORDERS

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**Introduction :** Sleep disorders (SDs) compromise cognition, emotional well-being, and general health. Prior research indicates sleep disturbances may increase the risk of being formally diagnosed with a psychological disorder (PD). Some researchers argue that sleep disturbances may be clinical indicators of PDs. Others argue that chronic, treatable SDs remain unrecognized as PDs are diagnosed without thoroughly assessing sleep complaints. These issues are further complicated because pharmacological treatment of PDs may disrupt sleep. To examine these concerns, we compared data from people who were referred for sleep studies and had a diagnosis of a PD with those who did not. Further, we investigated the relationship shared by PD (e.g., anxiolytics, antidepressants etc) medications and sleep.

**Methods :** We assembled a team comprised of professionals from a broad spectrum of specialty areas and constructed questionnaires to use in conjunction with nocturnal polysomnography (NP) studies, multiple sleep latency tests (MSLT), and medical chart reviews of people with SDs.

**Results :** Our study includes 604 participants, of which 235 (39%) (137 females, 98 males, age range: 8-83; : 46.83) had been diagnosed and treated for PDs and 369 (132 females, 237 males, age range: 2.75-89.17, : 52.34) had not been diagnosed with a PD. Examples of findings include: people with PDs had significantly more health problems, reported sleepiness having more deleterious effects on daily activities, and were more likely to have abnormal sleep architecture. There were no differences between groups in rates of diagnoses of obstructive sleep apnea. With

respect to medications, people who used antidepressants were significantly more likely to drink alcohol, report arm/leg jerks during sleep, sleep walk, and sleep talk.

**Conclusion :** PD diagnoses are rapidly increasing in the U.S.A while SDs remain vastly under diagnosed. The use of PD medications is also on the rise. Investigations are needed to understand the relationships shared by these complex myriads of intervening variables.

**Support (optional):**

## 0949

### PARADOXES AND PROMISES: THE EFFECTS OF MINDFULNESS MEDITATION ON SLEEP IN DEPRESSION

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**Introduction :** Although mindfulness-based interventions have been associated with improvement in subjectively-rated sleep quality in a range of clinical populations, these findings have yet to be confirmed with objectively measured sleep in a laboratory. This study is a randomized controlled trial (RCT) that investigated the effects of Mindfulness-Based Cognitive Therapy (MBCT) on both objectively and subjectively measured sleep.

**Methods :** Individuals with partially remitted depression (n=52) underwent overnight polysomnographic (PSG) sleep studies before and after 8 weeks of MBCT or a waitlist control condition. All participants completed sleep diaries and depression inventories before and after the program.

**Results :** Significant 3-way interactions were found for awakenings (p=.038), arousals (p=.005), and stage 1 minutes (p=.006). The medicated MBCT group showed a pattern of decreases (awakenings, p=.11, arousals, p=.04, and stage 1 min, p=.03), while the non-medicated MBCT group showed significant increases in awakenings, p=.04, arousals, p=.02, and stage 1 min, p=.02). Neither control group exhibited any change in these variables across time. According to sleep diary data, there was a significant main effect for time on sleep efficiency, (p=.00001), WASO, (p=.0004), awakenings (p=.0001), and sleep onset latency (p=.01) with the greatest improvement in the non-medicated MBCT group. BDI scores decreased significantly in the MBCT group only, (p<.005), with the greatest improvement in the non-medicated MBCT group. Changes in self-reported sleep efficiency predicted improvement in depression scores (r=.51, p=.001) and were associated with meditation practice (p<.05). In the non-medicated MBCT group, BDI scores were negatively correlated with awakenings (r=-.57, p=.054) at time 2.

**Conclusion :** MBCT is associated with sedating effects in medicated individuals and arousing effects in non-medicated individuals. Arousing effects were associated with improvements in depression scores, which suggests that meditation may have a similar outcome profile to antidepressant medications. Possible mediators, such as monoamine changes, meditation practice, and baseline characteristics, will be discussed.

**Support (optional):** NCAM/NIH T32-AT001287

## 0950

### MANAGEMENT OF COMORBID INSOMNIA IN PSYCHIATRIC PATIENTS: A SURVEY CONDUCTED ON ITALIAN PSYCHIATRISTS

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**Introduction :** Chronic insomnia is usually comorbid with psychiatric and physical disorders. Two epidemiological surveys (Studio Morfeo 1 and Studio Morfeo 2) conducted in Italy provided information on the frequency and management of insomnia in the primary care setting. In the case of comorbidity, the risk of insomnia was higher in the patients who suffered from depressive symptoms. To evaluate the approach to psychiatric patients with sleep problems, a questionnaire was proposed to 5,000 Italian psychiatrists covering homogeneously the national territory in the period between July and December 2005.

**Methods :** A specifically designed questionnaire was prepared by a panel of six specialists indicated by the Italian Association of Sleep Medicine and the Italian Society of Psychopathology. A total of 48 items were submitted to the Italian psychiatrists to investigate their general knowledge of sleep and their opinion on the diagnostic and therapeutic management of insomnia in patients with sleep disorders concomitant with psychiatric diseases (subdivided into anxiety disorders, mood disorders and schizophrenia).

**Results :** Available results derived so far from 510 completed questionnaires indicate that: I) 82.2% of the interviewed psychiatrists addresses the patient to a sleep specialist only if insomnia is associated with another sleep disorder; II) psychiatrists consider benzodiazepines as the drugs that more often cause EEG alterations (68.8% vs. 8.4% for non-benzodiazepine hypnotics); III) anxiety generalized disorder is considered as the anxiety disorder most frequently associated with sleep disorders (67.7%); IV) psychiatrist consider insomnia as the most frequent symptom preceding depression (45.5%) and the most frequent residual symptom after depression improvement (28%); V) 53% expect insomnia to remain after an manic episode.

**Conclusion :** For Italian psychiatrists insomnia is difficult to manage only when associated with other sleep disorders. Italian psychiatrists indicate anxiety generalized disorder as frequently comorbid with sleep disorders and consider insomnia as a pivotal symptom in the evolution of depression and manic episodes.

**Support (optional):** The survey is supported by an educational grant provided by sanofi-aventis

## 0951

### MAJOR DEPRESSIVE DISORDER, SLEEP EEG AND AGOMELATINE

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**Introduction :** Evaluation of the effect of agomelatine, a melatonergic receptor agonist (MT1 and MT2) and 5-HT<sub>2C</sub> antagonist antidepressant, on sleep architecture in outpatients suffering from Major Depressive Disorder.

**Methods :** Open study of 15 outpatients (20 to 56 years old, 8 women), with a Major Depressive episode, with a baseline Hamilton depression (HAM-D) score > 20, and receiving agomelatine 25 mg a day for 42 days. Polysomnographic and subjective evaluations were performed at D-1, D0, D7, D14, D41 and D42 with sleep/wake staging and calculation of the delta ratio (ie: delta power first NREM sleep period / delta power second NREM sleep period). The evolution compared to baseline was studied by the 95% confidence interval of the median and by the two tailed Wilcoxon tests.

**Results :** After 28 days of treatment the HAM-D score decreased below 50 percent the value of baseline (9.2±5.5 versus 21.8±1.5). Sleep efficien-

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cy and wake after sleep onset improved progressively from day 7 and the difference from baseline was significant at last evaluation for both parameters ( $p < 0.05$ ), with a significant increase in amount of slow wave sleep (SWS) ( $p < 0.005$ ). The SWS increase was predominant during the first sleep cycle from day 14 on. Delta ratio increased at day 14 ( $p = 0.007$ ). Subjectively, sleep quality improved from day 7 with subsequent improvement of daytime alertness. No effect was seen in different REM sleep indexes, but there was normalization of SWS and REM sleep distribution from 1st to last sleep cycle. No serious adverse events occurred during the study.

**Conclusion :** Agomelatine 25 mg at night time, in addition to its antidepressant activity, improved sleep continuity and quality in depressed patients. It normalized the distribution of SWS, REM sleep and delta power over sleep cycles. The improvement of sleep quality was already evident on day 7 followed by improved daytime alertness.

**Support (optional):** The study was supported by the Institut de Recherches Internationales Servier, Courbevoie, France

### 0952

#### OUTPATIENT HEALTHCARE UTILIZATION AMONG VETERANS WITH SLEEP DISORDERS

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**Introduction :** Sleep disorders such as insomnia and sleep apnea are widespread health problems that enhance healthcare utilization and costs among affected individuals. The present study compared outpatient healthcare utilization among veterans with specific sleep disorder diagnoses.

**Methods :** 224 veterans (MAge =  $57.0 \pm 12.2$  yrs.) with sleep complaints were administered the Duke Structured Interview for Sleep Disorders and assigned to one of three diagnostic categories: primary insomnia ( $N = 63$ ); comorbid insomnia ( $N = 60$ ); or other (e.g., apnea, RLS) primary sleep disorder ( $N = 101$ ). Healthcare utilization for six months prior to diagnosis was obtained from the VA Outpatient Clinic File. Outcome variables were number of mental health, medical, and total outpatient VA clinic visits. Covariates included body mass index (BMI), age, service connection, and number of self-reported medical and psychiatric comorbidities. Negative binomial regression models were used to examine the association between sleep disorder categories and outpatient utilization.

**Results :** The median number (first and third quartiles) of mental health, medical, and total visits were 0 (0, 2), 7 (3, 12), and 8 (4, 16), respectively. In bivariate analyses, sleep disorder diagnosis was statistically associated with outpatient mental health utilization ( $p = 0.02$ ), but not with medical utilization ( $p = 0.99$ ) nor with total number of outpatient visits ( $p = 0.37$ ). In adjusted analyses, younger age ( $p = 0.05$ ), service connection ( $p = 0.05$ ), and having more psychiatric comorbidities ( $p = 0.005$ ) was statistically associated with more mental health visits, and psychiatric comorbidities ( $p = 0.04$ ) was related to having more total outpatient visits. Sleep disorder diagnosis was not statistically associated with increased outpatient utilization in any of the adjusted models.

**Conclusion :** Among veterans with sleep complaints, healthcare utilization is not associated with specific sleep disorder diagnosis but with number of comorbidities, particularly those related to mental and emotional disorders.

**Support (optional):** Department of Veterans Affairs Health Services Research and Development Grant # IIR 00-091

### 0953

#### EFFECTS OF VENLAFAXINE ON SLEEP EEG OF MAJOR DEPRESSED PATIENTS

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**Introduction :** Acute effects of antidepressants with mainly noradrenaline reuptake inhibition on sleep EEG consist of a suppression of REM sleep together with an increase of stage 2 sleep, where as antidepressants with mainly serotonergic uptake inhibition increase wakefulness in combination with REM sleep suppression. However, relatively few studies have examined the persistence of these sleep EEG changes. We studied the effects of 9 week treatment with venlafaxine (SR) on sleep EEG of depressed patients.

**Methods :** Six outpatients with Major Depression (DSM III R), a score  $\geq 18$  on the Hamilton Depression Rating Scale and a drug free period of two weeks were included. Following a 7 day placebo washout period, all patients received venlafaxine 75 mg at first night. During the following 21 days, doses were titrated upward until reaching 150 mg. Single night polysomnograms (PSG) were conducted at baseline, day 1 (75 mg), 35 (150 mg) and 63 (mean dose 160 mg). We performed Friedman's analysis to estimate differences in clinical and PSG variables.

**Results :** Venlafaxine (75 mg) produced a significant increase of total time (TT) awake ( $37.7 \pm 40.5$  vs  $144.8 \pm 115.9$ ), percentage (%) of stage 1 ( $10.4 \pm 12.7$  vs  $16.9 \pm 8.7$ ), and REM latency ( $79.9 \pm 34.5$  vs  $268.3 \pm 144.6$ ), and a decrease of % ( $24.9 \pm 6.9$  vs  $2.4 \pm 4.3$ ) and TT ( $120.1 \pm 35.9$  vs  $11.3 \pm 20.8$ ) of REM sleep. In the second PSG assessment there was only an increase in % ( $37.0 \pm 6.5$  vs  $54.3 \pm 7.8$ ) and TT ( $177.2 \pm 29.7$  vs  $258.9 \pm 38.1$ ) of stage 2, which persisted in the last PSG evaluation. The increase in REM latency and decrease of REM sleep persisted but they did not differ significantly from baseline values.

**Conclusion :** Acute but not persistent suppression of REM sleep produced by venlafaxine suggests the development of tolerance this sleep effect.

**Support (optional):**

### 0954

#### THE RELATIONSHIP BETWEEN REM LATENCY AND SWS IN HEALTHY AND DEPRESSED CHILDREN AND ADOLESCENTS

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**Introduction :** Most current views of sleep regulation assume that there is a reciprocal relationship between REM and SWS such that a shorter latency to the first REM period results in a shorter SWS duration, reduced Stages 3 and 4 and less slow-wave activity SWA in the first NREM period. Sleep findings in major depressive disorders (MDD) are often interpreted in this context, although this assumption is rarely evaluated empirically. The present study evaluated the relationship among SWS and SWA in the 1st NREM period and REM latency in a sample of 170 children and adolescents, healthy controls ( $n=74$ ) and symptomatic but unmedicated MDD ( $n=96$ ).

**Methods :** Each participant spent two consecutive weekend nights in the lab after a 5-day regularized sleep schedule. Standard visual stage scoring quantified REM and NREM sleep characteristics and power spectral analysis was used to compute SWA. Data were coded for diagnostic group (HC vs MDD), sex and age. Regression analysis and correlations evaluated the relationship between REM and NREM variables by group.

**Results :** The overall regression analysis, predicting REM latency from SW measures, was not significant for healthy controls ( $F < 1.0$ ) with an  $r$ -square=.02). For those with MDD, the overall regression was significant ( $F=2.9$ ,  $df=4,91$ ,  $p < .05$ ) with an  $r$ -square=.11). REM latency was significantly correlated with the duration of the first NREM period in both controls ( $r=.93$ ,  $p < .001$ ) and MDD ( $r=.94$ ,  $p < .001$ ) groups. REM latency was not correlated with the first NREM period variables including SWA power, % SWA, nor did REM latency correlate with average all-night SWA in either group. Restricting the analysis to those with short REM latency did not improve the regression solution or the amount of variance explained.

**Conclusion :** REM latency does not correlate with SWS or SWA in the first NREM period in either MDD or healthy control children and adolescents

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## 0955

### THE TIME COURSE OF SLOW-WAVE ACTIVITY IN DEPRESSED AND HEALTHY CHILDREN AND ADOLESCENTS

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**Introduction :** There has been substantial interest in the temporal dynamics of slow-wave activity (SWA) in healthy individuals and in those with major depressive disorders (MDD). The accumulation and dissipation of SWA appears to be compromised in adults MDD, but is strongly sex-dependent. Contrary to findings in adults, preliminary studies suggested that adolescent girls with MDD had a lower accumulation and slower dissipation than healthy controls (HC). It is not clear whether boys with MDD also show SWA abnormalities. The present study evaluated the temporal dynamics of SWA in a large-scale sample of depressed and healthy children.

**Methods :** 172 participants 8-17 years of age were included (75 HC and 97 MDD). Those with MDD were symptomatic and unmedicated at the time of study. Each participant spent 2 consecutive nights in the lab after a week-long regular sleep schedule. EEG data were digitized and SWA power was assessed in each NREM period in each subject, and expressed relative to total SWA. Data were coded for diagnostic group, sex and age (chronological and maturational age). Exponential regression analyses evaluated the accumulation and dissipation of SWA.

**Results :** Overall, HC showed a significantly higher accumulation of SWA with a faster dissipation than those with MDD, regardless of age. Females had a significantly faster dissipation of SWA than males in both HC and MDD groups. With regard to age-related differences, the accumulation of SWA did not show a systematic change across groups. The dissipation of SWA was, however, faster in adolescents than in children in both HC and MDD groups.

**Conclusion :** The time course of SWA is abnormal in early onset MDD, with lower accumulation and slower dissipation than that observed in healthy controls. Dissipation in SWA was faster in adolescents than in children in both groups

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## 0956

### SLEEP DISTURBANCE FOLLOWING STRESS INDUCTION IN CHRONICALLY DEPRESSED INDIVIDUALS

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**Introduction :** Anxiety is typically associated with sleep disturbance, although research in clinical populations has yielded mixed results. The current study sought to investigate the effect of a standardized acute stress paradigm on objective sleep in a chronically depressed population. It was predicted that the degree of the subjective anxiety would be positively correlated with sleep disturbance.

**Methods :** Fifty-two partially remitted depressed individuals (44% on antidepressants) underwent the Trier Social Stress Test (TSST), a standardized laboratory stressor that involves a simulated public speech task. Following stress induction, participants reported their subjective anxiety using the Spielberger State-Trait Anxiety Inventory (STAI) and then underwent an overnight polysomnographic (PSG) sleep study.

**Results :** Total minutes of NREM sleep was negatively correlated with post-stress anxiety levels, ( $r = -.327$ ,  $p < .05$ ). Within NREM sleep, SWS minutes, showed a trend toward a significant correlation with post-stress anxiety ( $r = -.268$ ,  $p = .062$ ). Contrary to predictions, but consistent with other clinical populations, microarousals were negatively correlated with subjective anxiety ( $r = -.306$ ,  $p < .05$ ). When groups were separated according to antidepressant medication status, the non-medicated individuals showed the expected relationship, but the medicated participants showed a paradoxical relationship between sleep and anxiety. There was no effect of medication on anxiety, but the medicated group had significantly more arousals ( $p = .008$ ). In addition to arousals, the medicated group's post-stress anxiety levels were also negatively correlated with sleep onset latency ( $r = -.504$ ,  $p = .014$ ).

**Conclusion :** The impact of the stress induction on sleep depends on antidepressant medication status. Non-medicated individuals show the intuitive positive relationship between anxiety and sleep disturbance, while the medicated individuals showed an inverse relationship. Antidepressant medication is often associated with decreased levels of anxiety and increased sleep disturbance, and therefore may account for the counterintuitive results. Alternatively, these results may be due to higher arousal thresholds in highly anxious individuals (as seen in PTSD), or a bell curve in which too much and too little stress are both detrimental to sleep maintenance while a moderate amount keeps sleep stabilized.

**Support (optional):**

## 0957

### SLEEP, SYMPTOM SEVERITY, AND SUICIDALITY IN DEPRESSED ADOLESCENTS

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**Introduction :** Sleep disturbances are key features of depressive disorders. Although polysomnographic data may not always differentiate depressed patients from healthy controls, subjective sleep disturbances are pervasive in both depressed adults and children. Moreover, persistent sleep complaint is associated with a poor course of illness and increased risk of suicide in adults. The present study evaluated the relationship between sleep disturbance, suicidality and symptom severity in adolescents with depressive disorders.

**Methods :** Youths, ages 12-17 years, seeking services at the University of Michigan Depression Center, were screened using a semi-structured diagnostic interview (KSADS-P/L) for study eligibility of current depressive disorder. Exclusion criteria included significant mental impairment (e.g. Autism, mental retardation). A standard clinical interview was conducted

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on 70 adolescents (23 males, 47 females) with a mean age of 14.7 years (SD=1.6), assessing depressive symptom severity from the Children's Depression Rating Scale (CDRS) and suicidality from the Suicidal Ideation Questionnaire (SIQ). A cutpoint of 2 on the Sleep Disturbance item of the CDRS defined group membership and a total CDRS score was computed minus the sleep item. ANOVA evaluated group differences in symptom severity and suicidality. Correlations were also computed by sleep disturbance categories.

**Results :** Significant sleep disturbance by gender interactions were obtained for both CDRS and SIQ ( $p<.05$ ) with more severe depressive symptoms and more suicidal ideation in those with more severe sleep disturbance. With regard to the relationship between suicidality and symptom severity, those with less disturbed sleep showed weaker correlations between these two variables. The strongest correlations between the CDRS and SIQ were evident in depressed boys with the most disturbed sleep ( $r=.91$ ,  $p<.0001$ ).

**Conclusion :** The degree of sleep disturbance in adolescent depression strongly moderates the relationship between depression severity and suicidality. Sleep disturbance may be an important factor in identifying those at high risk for suicide.

**Support (optional):**

### 0958

#### NON-REM SLEEP EEG ACTIVITY IN ADOLESCENTS WITH ANXIETY DISORDERS

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**Introduction :** We reported last year that adolescents with anxiety disorders show polysomnographically recorded sleep disorders, particularly in REM sleep but not nonREM sleep. The purpose of the present study was to further investigate nonREM sleep in anxious adolescents by using EEG spectral analysis.

**Methods :** Participants were recorded for two nights. Twelve adolescents (5 W, 7 M, mean age = 13.9) diagnosed with anxiety disorders using DSM-IV criteria were compared to nine controls (6 W, 3 M, mean age = 15.3). NonREM sleep (stages 2, 3, 4) EEG spectral power amplitude was computed for the first seven hours of the second night for the electrodes C3, C4, O1 and O2 referenced to linked earlobes. Delta (0.05-3.75Hz), Theta (4-7.75Hz), Alpha 1 (8-10Hz), Alpha 2 (10.25-12.75Hz), Total Alpha (8-12.75Hz), Sigma (11.5-14.5Hz) and Beta (13-30Hz) was extracted. Groups were compared using t-tests.

**Results :** Sleep disorders were absent from nonREM sleep, including disordered breathing and periodic leg movements. Theta, Alpha 1, Total Alpha and Sigma activity during nonREM sleep was significantly reduced at C4 electrode in anxious patients compared to controls (all  $p<.04$ ). No differences were found for any other electrodes.

**Conclusion :** These results show that right central midrange frequency EEG activity is reduced during nonREM sleep in adolescents with anxiety disorders. Even though more analyses need to be performed, including hourly time course and more electrodes, the present results point toward physiopathological processes at the level of the thalamo-cortical loop.

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### 0959

#### SLEEP DISTURBANCE FOLLOWING A STRESSOR PREDICTS LATER POSTTRAUMATIC STRESS SYMPTOMS: EVIDENCE FROM THE TERRORIST ATTACKS OF SEPTEMBER 11, 2001

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**Introduction :** Sleep disturbances are among the most common reactions to trauma, so much so that they can be considered "normal" responses to a stressor. For example, many Americans experienced difficulty falling and staying asleep following the terrorist attacks of September 11, 2001. Disturbed sleep is also one of the hallmarks of the extreme reaction to trauma known as posttraumatic stress (PTS). This study examines the extent to which initial sleep disturbance following a stressful event predicts the later development of PTS symptoms.

**Methods :** Questionnaires were distributed via Knowledge Networks, a survey research firm that has created a web-based panel whose demographic distribution (age, sex, race, geographical region, etc.) closely matches current U.S. census counts. Prior to 9/11/01, participants completed a health questionnaire that asked whether they had ever been professionally diagnosed with anxiety, depression, and insomnia. Two weeks following the terrorist attacks, participants answered a question about 9/11-related difficulty falling or staying asleep. They later completed a PTS symptom questionnaire at 2 months and 6 months post-9/11. A total of 745 participants (50.3% female; mean age=48.6 years) responded.

**Results :** Separate hierarchical regression analyses predicting non-sleep-related PTS symptoms at 2 months and 6 months post-9/11 were performed. Sleep disturbance measured 2 weeks post-9/11 accounted for a significant amount of variance in non-sleep-related PTS symptoms both at 2 months ( $R\text{-square}=0.071$ ,  $p<.001$ ) and 6 months ( $R\text{-square}=0.064$ ,  $p<.001$ ) post-9/11 above and beyond demographics (age and sex) and pre-9/11 psychiatric diagnoses.

**Conclusion :** Sleep disturbance experienced in the weeks immediately following the 9/11 terror attacks had a small, but significant, predictive value on the development of later PTS symptoms. This is true even after controlling for the contribution of pre-existing anxiety, depression, and insomnia. These findings raise the possibility (among others) that initial disturbed sleep directly contributes to the exacerbation and eventual development of PTS symptoms.

**Support (optional):**

### 0960

#### DISCREPANCY BETWEEN OBJECTIVE AND SUBJECTIVE SLEEP VARIABLES IN PATIENTS WITH POST-TRAUMATIC STRESS DISORDER: AN ACTIGRAPHIC STUDY

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**Introduction :** Sleep disturbances are common and core clinical features in posttraumatic stress disorder (PTSD) patients. Nonetheless, sleep studies with PTSD patients have reported inconsistent findings. This may be caused by not controlling for comorbidity and heterogeneity of the subjects. Strict selection of subjects without any other psychiatric, medical disorder or medication usage and within the same traumatic event is very important. Taegu subway fire in Korea, on February 18, 2003 resulted in 192 loss and hundreds injured. We, in this study, attempted to assess dif-

ferences between objective and subjective sleep variables in a very homogeneous, single event-related PTSD subjects and controls based on actigraphic monitoring and self-rating questionnaires.

**Methods :** We examined 14 survivors of Taegu subway fire (7 males, 7 females,  $26.4 \pm 6.7$  years of age) and 15 age- and sex-matched controls (6 males, 9 females,  $28.7 \pm 6.6$  years of age). Wrist-actigraph (Actiwatch®, Mini Mitter Co., U.S.A.) was worn on their non-dominant hand for more than 3 days with 1 minute data acquisition interval. Simultaneously, sleep diary and PSQI (Pittsburgh Sleep Quality Index) were administered. The 3-day actigraphic data were averaged. We, using Actiware®-Sleep (Mini Mitter Co., U.S.A.), analyzed total sleep time, sleep latency, sleep efficiency and other variables of actigraphic data to assess objective sleep and also obtained self-reported total sleep time, sleep latency, sleep efficiency and others from PSQI to assess subjective sleep. And then, we compared objective and subjective sleep variables between PTSD patients and controls.

**Results :** No significant differences of sleep variables measured with the actigraph were found between the two groups. However, subjective sleep scores obtained from PSQI showed poor sleep in PTSD patients vs. controls (global PSQI score:  $10.9 \pm 3.1$  vs.  $5.1 \pm 2.6$ ,  $p < 0.001$ ; sleep efficiency:  $84.2 \pm 9.5$  vs.  $95.7 \pm 6.2$ ,  $p < 0.05$ ; sleep latency:  $46.4 \pm 36.7$  vs.  $20.7 \pm 15.4$ ,  $p < 0.05$ ).

**Conclusion :** PTSD patients strictly selected from a single event of subway fire compared with age- and sex-matched normal controls showed no significant differences in objective sleep quality but rather significant differences in subjective sleep quality. This finding supports previous studies which report and interpret poor sleep quality in PTSD patients as sleep state misperception.

**Support (optional):**

## 0961

### THE SUBJECTIVE SYMPTOMATOLOGY IN PATIENTS WITH DIFFERENT SLEEP DISORDERS

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**Introduction :** There are few studies comparing the self-reported symptoms in patients with different sleep disorders. The objective of this study was to investigate differences between groups of patients attending a sleep disorder's center depending on the primary diagnosis given during the initial consultation.

**Methods :** 891 consecutive patients consulting Bergen Sleep Disorders Center from 1997 to 2003 due to sleep complaints. Patients received a questionnaire (adapted from the Insomnia Interview Schedule by C. Morin) before the consultation. The sleep specialist gathered additional information while interviewing the patient during the initial consultation. Based on this, the sleep specialist gave a tentative diagnosis. In this study, 8 separate diagnostic groups were formed, based on the patient's main complaint: Primary insomnia (PI,  $n=353$ ), insomnia due to depression (D,  $n=207$ ), circadian rhythm sleep disorders (CRSD,  $n=163$ ), hypersomnia/narcolepsy (H,  $n=46$ ), restless legs/PLMS (RLS,  $n=40$ ), sleep apnea (OSAS,  $n=34$ ), parasomnias (P,  $n=10$ ) and other ( $n=38$ ). The latter group comprised diagnosis like bipolar disorder, hypothyroid disease, seasonal affective disorder, head trauma, and anxiety. Statistical analysis was performed using one-way ANOVA and chi-square test.

**Results :** Mean age was 41.2 years; CRSD/H patients being younger, and OSAS/RLS older. D scored highest on many subjective complaints (scale

1-5), such as sleep onset problems (4.0, CI 3.8-4.1), dissatisfaction with sleep pattern (4.7, CI 4.7-4.8), and daytime impairment (4.5, CI 4.4-4.6). H scored highest on daytime sleepiness (3.8, CI 3.4-4.2), and PI lowest (1.6, CI 1.5-1.7). Sleep onset latency was more than 90 min for CRSD, D, RLS and PI. Sleep lengths varied extensively; RLS reported shortest (253 min), D 258 min, PI 272 min, OSAS 344 min, CRSD 362 min, P 423 min, H 512 min. 63% in PI and D used hypnotics, whereas none in P.

**Conclusion :** Major differences in self-reported sleep-wake variables were found in the different diagnostic groups.

**Support (optional):**

## 0962

### SLEEP DISTURBANCES IN PTSD: PUBLIC HEALTH ISSUES

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**Introduction :** PTSD is a common problem after significant wide-spread traumas. The consequences of these traumatic events have an important impact on the community and the aim is to clarify the relationship between trauma, PTSD, sleep disturbances and public health.

**Methods :** A literature search yielded 300 articles about PTSD and sleep difficulties and 120 of them were related to public health. They were evaluated for the impact of sleep disturbances in PTSD on public health.

**Results :** The results were grouped into several categories: epidemiology (types of trauma), consequences of traumatic events in the community, relationship between PTSD, sleep disturbances and public health, solutions. War, natural disasters and terrorist attacks are some of the wide-spread traumatic events studied. Most of the community members experience a traumatic event during their lifetime. The impact of traumas on society varies from social or occupational impairment to medical or psychiatric illnesses. PTSD can last from months to years (50% becoming chronic) affecting a large number of people from direct victims to community residents (family, responders, mass-media consumers) and is often underreported. Sleep disturbances (insomnia, nightmares) are key symptoms in PTSD no matter the type of trauma and they can cause major distress in functioning. When these affect a large number of people, it becomes a public health matter because of costs and disruption. The quality of life improves when the sleep disturbances are corrected. Solutions were suggested to anticipate and treat the sleep problems in PTSD in order to lessen their consequences on society (prevention, education, national programs of response in case of emergency, psychopharmacology, psychotherapy).

**Conclusion :** PTSD has an impact on public health and sleep disturbances are central in PTSD. Treating the sleep problems may alleviate the burden of PTSD on the community. The focus in future research should be on efficacy of sleep disturbance management in PTSD in relationship to public health.

**Support (optional):**

## 0963

### THE EFFECTS OF NEUROFEEDBACK TRAINING ON SLEEP CHARACTERISTICS OF CHRONIC SCHIZOPHRENIA PATIENTS: A PRELIMINARY STUDY BASED ON MULTIPLE CASE STUDIES

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**Introduction :** Research indicates that insomnia and psychiatric disorders are characterised by specific sleep and wake EEG characteristics. As such, the treatment of these disorders at the level of the Central Nervous

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System might be an interesting perspective for future research. Neurofeedback, a relatively new treatment modality in the field of applied neuroscience, makes use of operant conditioning, and aims at facilitating self regulation and normalising brain functioning.

**Methods :** Four chronic schizophrenia/schizoaffective inpatients received a combination of sensorimotor rhythm (SMR: 12-15 Hz) and alpha (8-12 Hz) training and five inpatients served as a control group. No major changes were made in medication. They received five sessions a week of approximately 30 minutes for a total of eight weeks. To achieve optimum effect this standard protocol was adjusted to the individual EEG characteristics of every participant after two weeks. Sleep was measured using Biosomnia Plus (Oxford Biosignals Ltd. Oxford) pre and post treatment. Latency to Persistent Sleep (LPS), Wake After Sleep Onset (WASO), Total Sleep Time (TST), Sleep efficiency (SE) were our primary outcome variables .

**Results :** Concentration problems resulted in a lack of attention for the presented feedback halfway every session. One patient of the experimental group ended the study after 26 sessions. In the experimental group, two patients improved on TST and WASO, two improved on LPS and one showed an enhancement of SE. In the control group, two patients deteriorated on TST and WASO, two patients improved on WASO. One patient deteriorated on SE and one patient showed the same impairment in TST and SE at both measurements.

**Conclusion :** Schizophrenia inpatients showed enough motivation to follow neurofeedback therapy, but attentional problems indicate that the sessions need to be shortened. The observed positive effects in the sleep variables studied warrant further research of this treatment modality.

**Support (optional):**

### 0964

#### CORRELATION OF POLYSOMNOGRAM TEST RESULTS AND PRE-TEST QUESTIONNAIRES

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**Introduction :** Obstructive sleep apnea (OSA) is the most common form of sleep-disordered breathing (SDB), frequently coexisting with depression and sleepiness. Our practice is to administer a series of questionnaires assessing the patient's depression symptoms through the Beck's Depression Inventory (BDI) and sleepiness through the Epworth Sleepiness scale one to two weeks prior to polysomnographic (PSG) testing. We tested correlations between these questionnaires and the results of the PSG to examine the relationships between depression, sleepiness, and SDB.

**Methods :** We pursued linear regression modeling of age, gender, Epworth score, BDI, RDI totals, mean SaO<sub>2</sub> levels, # of desaturations, mean SaO<sub>2</sub> levels with desaturations, and minimum SaO<sub>2</sub> levels desaturations in 92 men and 29 women diagnosed with moderate to severe OSA.

**Results :** Higher levels of depressive symptoms in the BDI were reported by women (15.4+ 10.5) vs. men (8.1+ 6.6) ( $p < 0.01$ ). Using a BDI cut off of 10 for mild depression, 44.6% of all patients had mild depressive symptoms, with 62% of women and 39% of men ( $p < 0.05$ ). Using a BDI cut off of 19 for moderate depression, 11.6% of the sample had at least moderate depressive symptoms, with 28% of women, and 6% of men ( $p < 0.01$ ). The Beck's Depression Inventory was inversely related ( $p < .001$ ) to the desaturation nadir. The degree of daytime sleepiness was unrelated to depression severity.

**Conclusion :** As has been shown in other clinical settings, depressive symptoms are more common and more severe in women with SDB than in men. Also, the degree of arterial desaturation may play a role in depressive severity.

**Support (optional):**

### 0965

#### CORTICAL TOPOGRAPHY OF WIDE-RANGE SLEEP EEG ACTIVITY IN DRUG-NAIVE PATIENTS WITH SCHIZOPHRENIA

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**Introduction :** We have previously reported low delta EEG activity during slow-wave sleep (SWS) in centro-temporal areas of drug-naive patients with schizophrenia (Dubuc et al., APSS 2005). In the present study, analyses were extended to faster EEG frequencies in order to test the specificity of these previous findings.

**Methods :** Nine acute patients never exposed to neuroleptics (4 women, 5 men, 30.2 +/-16.2 years old) were recorded for two consecutive nights the first week of their hospitalization. The final diagnosis was confirmed within six months. Patients were compared to six healthy controls (3 women, 3 men, 23.3 +/- 9.3 years old). All participants had a 10-electrodes EEG montage (C3, C4, Fp1, Fp2, F7, F8, T3, T4, O1, O2) referenced to linked ear-lobes. Non-REM sleep (Stages 2, 3, 4) EEG spectral power amplitude was computed for the first seven hours of the night. Theta (4.00-7.75 Hz), Alpha (8.00-12.75 Hz), Sigma (11.75-14.75 Hz), Beta (13.00-30.00 Hz) and Total Activity (0.75-30.00 Hz) was extracted. Groups were compared using t-tests.

**Results :** In addition to decreased centro-temporal delta activity, the most consistent finding was that drug-naive patients with schizophrenia displayed a parallel increase in Stage 4 total Beta activity for frontal (F7-F8) and occipital (O1-O2) electrodes compared to controls (all  $p < .05$ ).

**Conclusion :** Increased fast (Beta) and decreased slow (Delta) EEG activity during SWS in drug-naive patients with schizophrenia suggests that both ends of the thalamo-cortical loop are involved in the physiopathology of this disease. Together with our previous finding of increased Beta activity during REM sleep, the present results further indicate that both SWS and REM sleep mechanisms are involved. Given the specific topography of the observed differences, further research should aim at identifying specific generator system.

**Support (optional):**

### 0966

#### DELAYED SLEEP PHASE SYNDROME AND DEPRESSION

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**Introduction :** Studies of depressed patients have often indicated a tendency towards low Horne-Ostberg morningness-eveningness scores, that is, a tendency towards eveningness. This result has been somewhat surprising, in view of clinical teachings relating depression to early awakening. In this study, we examine the prevalence of depression in a sample recruited for delayed sleep phase.

**Methods :** As part of an ongoing study of genetic polymorphisms related to circadian rhythm sleep disorders, we have recruited over 100 participants over age 25 with chronic delayed sleep phase syndrome. We attempted to recruit DSPS subjects where the onset of DSPS preceded depression, though this was often difficult for subjects to recollect, and where DSPS was present even when mood symptoms were absent. An additional 60 participants with normal sleep phases have been recruited. Participants completed a health history form with numerous questions



about sleep, general health, and emotional history and the QIDS self-rating scale for depression.

**Results :** DSPS and control participants were well matched in age,  $41.9 \pm SD 13.3$  and  $40.4 \pm SD 16.0$  respectively, and had no significant differences in racial distribution or Hispanic percentage. However, mean Horne-Ostberg scores were 29 and 57 respectively ( $P < 0.001$ ). Further, the DSPS subjects had a mean QIDS of 5.3 versus 2.3 for the controls ( $P < 0.001$ ) and reported a much higher percentage of lifetime usage of antidepressants (4% vs 0.4%, NS). On a lifetime basis, 49% of DSPS subjects but only 17% of controls reported symptoms of a major depression ( $P < 0.001$ )

**Conclusion :** These observations provide further evidence for comorbidity of DSPS and depression. It may be difficult to determine which illness is primary. Perhaps DSPS and depressive phenotypes share genetic susceptibility factors. Our limited experience suggests that both DSPS and depressive symptoms should be treated, e.g., with bright morning light.

**Support (optional):** Supported by HL071123.

## 0967

### SLEEP EEG ABNORMALITIES IN SUBJECTS WITH SCHIZOPHRENIA

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**Introduction :** Sleep electroencephalographic (EEG) abnormalities consistently occur in patients with schizophrenia (Kupfer 1990). The recent development of high-density (hd)-EEG holds promise for an accurate mapping of potential sleep EEG rhythm abnormalities in schizophrenia as well as in other psychiatric patients. We present an ongoing investigation of sleep patterns in schizophrenia using a 256-channel hd-EEG (EGI, OR).

**Methods :** We recorded the first sleep episode in subjects with schizophrenia ( $n=17$ , all taking antipsychotics), subjects with major depression ( $n=15$ ), and age-matched controls ( $n=17$ ). Subjects were allowed to sleep at their customary bedtime. EEG signals were digitized at 500 Hz together with electromyogram and electrooculogram, filtered (0.5-50 Hz), artifact-rejected, average-referenced, and sleep-staged. Recordings were analyzed by power spectral analysis and topographic mapping of signal strength at frequencies of interest, in particular the spindle frequency range (12-15 Hz). We also detected individual sleep spindles and analyzed several spindle parameters: duration, amplitude, density and time integrated spindle amplitude (ISA).

**Results :** Schizophrenia patients had reduced power in the 12-15 Hz frequency band compared to controls and depression subjects. This reduction peaked in the 14-15 Hz and was localized in the centro-parietal region ( $p < 0.01$ , statistical nonparametric mapping, suprathreshold test controlling for multiple comparison). Consistently, all spindle parameters investigated were significantly reduced in schizophrenics in the same general area that showed decreased power.

**Conclusion :** These spindle abnormalities may reflect dysfunction in the thalamocortical network involving the reticular nucleus, a system thought to be implicated in the biological vulnerability to schizophrenia. Further studies are needed to determine whether such changes represent potential trait or state markers of schizophrenia and to rule out possible confounding factors.

**Support (optional):** Supported by NARSAD Grant #133GG22

## 0968

### PSYCHOMOTOR VIGILANCE PERFORMANCE DECREMENTS AND REDUCED P300 EVENT-RELATED AMPLITUDE IN WOMEN WITH PREMENSTRUAL DYSPHORIC DISORDER

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**Introduction :** 3-8% of women of reproductive age suffer from premenstrual dysphoric disorder (PMDD) characterized by disabling psychological and physical symptoms, including complaints of fatigue/sleepiness and cognitive impairment in the week preceding menstruation. The aim of this study was to evaluate sleepiness/fatigue, psychomotor performance, and event related potentials (ERPs), thought to be related to cognitive function, in women with PMDD and healthy controls.

**Methods :** Six women meeting DSM-IV criteria for PMDD and four screened controls (age range: 24-39 y) participated at two phases of their menstrual cycles: 1-5 days premenstrually (late luteal phase, LLP) and 6-12 days after menstruation onset (follicular phase, FP). Four times across the day, at 2-h intervals, women completed the 10-min psychomotor vigilance task (PVT) and were presented with a 10-min auditory oddball task to elicit ERPs. Results from the four sessions were averaged. EEG was recorded from 5 scalp electrodes. Subjects also completed the Stanford sleepiness scale (SSS), Chalder Fatigue Questionnaire (FQ), and the Beck Depression Inventory (BDI).

**Results :** In women with PMDD, the LLP was associated with elevated BDI and fatigue scores ( $P < 0.01$ ), a tendency for higher sleepiness scores ( $P = 0.08$ ), and more lapses, slower 90th percentile (slowest) reaction times, and greater variance in reaction times (SD) on the PVT ( $P < 0.05$ ). There was no menstrual phase effect for these variables in controls but they had overall lower scores on the BDI ( $P < 0.02$ ), fewer lapses and less variance on the PVT ( $P < 0.05$ ) than women with PMDD. P300 amplitude displayed no menstrual phase effect in either group but was significantly reduced in women with PMDD ( $P < 0.05$ ).

**Conclusion :** Women with PMDD are more depressed and fatigued and show performance decrements during the LLP. They also have reduced P300 amplitude, regardless of the presence of symptoms. There are, therefore, underlying differences between women with PMDD and asymptomatic women that are not all specific to the LLP.

**Support (optional):** Study supported by a developmental grant from SRI International (Dr F Baker)

## 0969

### MARKOV ANALYSIS OF EYE MOVEMENT DENSITY IN NORMAL CONTROLS UNDER TRYPTOPHAN DEPLETION AND ACUTE FLUVOXAMINE TREATMENT

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**Introduction :** Sleep was measured in 10 normal subjects who slept under 4 conditions, repeated measures: (A) Placebo / sham diet, (B) tryptophan depletion / placebo, (C) fluvoxamine / sham diet, (D) tryptophan depletion and fluvoxamine. Fluvoxamine alone altered tonic REM (RL increased, RT reduced); the effect was antagonized by addition of tryptophan depletion. Tryptophan depletion alone decreased RL and increased RT. Phasic REM (REM density, RD) did not differ significantly. This study examined RD with a different method.

**Methods :** Markov analysis (Douglass 1992, Biol. Psychiatry) was done

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on the time intervals between successive eye movements (EM's). Markov states: "Burst" ( $< 4.2$  s), and "Isolated" ( $> 4.2$  s). A 2 x 2 Markov transition probability matrix was calculated from EM's in all REM periods by subject by condition. Log-Linear analysis was performed on the 4 conditions, with Markov matrix as a repeated measure.

**Results :** The Markov "Isolated-to-Isolated" transition probability differed significantly between all pairs of the 4 conditions ( $p < 0.05$ , A-D comparison  $p < 0.0001$ ). Probabilities by condition (95% C.I.) were: A=0.483 (0.464-0.501); B=0.572 (.0544-0.600); C=0.536 (0.515-0.558); D=0.639 (0.592-0.683). Markovian "Burst-to-Burst" transition probability was higher ( $p < 0.05$ ) on night "A" than in the other 3 conditions, which did not differ among themselves: A=0.600 (0.584-0.616); B=0.539 (0.510-0.568); C=0.561 (0.540-0.581); D= 0.533 (0.479-0.585).

**Conclusion :** Under greater 5HT tone, "Isolated" EM's predominated and fewer "Burst" EM's were seen. Tryptophan depletion antagonized fluvoxamine's effect on tonic REM parameters but was synergistic for Markov phasic REM. Possible explanation: tryptophan depletion is known to increase noradrenergic (NA) neuron firing via reduced serotonin tone at the 5HT<sub>2a</sub> receptors on NA neurons. Our results suggest that both 5HT and NA inputs are important in the control of phasic REM sleep parameters (Markov transition probability), whereas 5HT input is the major influence on tonic REM parameters.

**Support (optional):**

### 0970

#### SLEEP TREATMENT LEADS TO DIFFERENT OUTCOMES IN MALES AND FEMALES FOR PSYCHOLOGICAL DISTRESS AND DRUG PROBLEMS IN ADOLESCENTS WITH A HISTORY OF SUBSTANCE ABUSE

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**Introduction :** Adolescent males and females were found to have different substance abuse patterns. As part of a larger study to develop and evaluate a treatment for sleep and daytime sleepiness for adolescents with substance abuse problems, the present analysis examines sex differences in outcomes for psychological distress and drug problems in response to a multi-component sleep and sleepiness treatment.

**Methods :** Participants were fifty-five adolescents (20 females) aged 13 to 19, who completed an outpatient substance abuse treatment program and reported problems with sleep. Completers of the sleep treatment (10 females and 13 males) attended at least four of the six sleep therapy sessions. The psychological assessment instrument was the Global Appraisal of Individual Needs: Initial (GAIN-I) and Monitoring (GAIN-M90). Internal psychological distress, external psychological distress and severity of drug problems were assessed using the General Mental Distress Index (GMDI), the Behavior Complexity Index (BCI) and the Substance Problem Index (SPI), of the GAIN, respectively.

**Results :** Both males and females significantly improved on levels of internal psychological distress (GMDI), ( $p = .003$ ). Compared to males, females expressed greater severity of internal distress at baseline ( $p = .001$ ) and three months post-treatment ( $p = .006$ ). Female Completers significantly reduced scores on levels of external psychological distress (BCI), from baseline to post-treatment ( $p = .007$ ). The SPI, in which higher scores represent greater severity of drug problems, males significantly increased scores and females decreased scores over time ( $p = .015$ ).

**Conclusion :** Although the sleep treatment resulted in reduced emotional distress for both males and females, only females reported reduced substance related problems through the 3-mo follow-up. The mixed results on substance related problems suggest it may be beneficial to have a treatment strategy that combines treatment for substance abuse and sleep in a single, integrated therapy.

**Support (optional):** This project was supported by the Office of National Drug Control Policy, "Reducing Adolescent Substance Abuse through the Treatment of Sleep Disturbances and Daytime Sleepiness" PIs: Richard R. Bootzin and Sally J. Stevens

### 0971

#### CORRELATES OF LONG SLEEP DURATION

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**Introduction :** Sleep durations greater than 7-8 hours per day have been consistently associated with increased mortality. Whether this association is causal and what factors may explain this association are unknown. We sought to identify factors correlated with long sleep duration that could potentially explain the association between long sleep and mortality risk.

**Methods :** A cross-sectional questionnaire-based survey was performed in 85,700 middle-aged women participating in the Nurses Health Study II who provided information about sleep habits on the 2001 questionnaire.

**Results :** Multiple sclerosis (OR=3.7, 95% CI [3.0-4.5]), use of antidepressants (OR=3.1, [2.9-3.3]), use of benzodiazepines (OR=3.0, [2.6-3.3]), and systemic lupus erythematosus (OR=2.9, [2.3-3.6]) were the factors most strongly associated with prolonged sleep. Combining these odds ratios with prevalence data and a range of plausible associations with mortality for each factor, the degree of confounding that each factor could produce on the long sleep - mortality association was estimated with the confounding rate ratio (CRR). Based on this parameter, the variables with the greatest potential to inflate the relationship between long sleep and mortality were psychiatric and socioeconomic factors. In particular, assuming each factor doubles the risk of mortality, the CRRs for depression, antidepressant use, and unemployment were 1.10, 1.18, and 1.12. Other potentially important factors were benzodiazepine use, low household income, low perceived social status, and obesity.

**Conclusion :** These data suggest depression and low socioeconomic status are strong candidates as mediators of the long sleep - mortality association. The potential for most lifestyle habits as well as medical, gynecological, and sleep disorders to distort the long sleep - mortality association is of lesser magnitude. Future research on the health effects of sleep should more closely assess differences in psychiatric disease and socioeconomic status. In particular, a better understanding of the causal relationships between long sleep and depression is needed.

**Support (optional):** NIH CA50385, HL081385 and the AHA.

### 0972

#### ADAPTATION EFFECTS TO SLEEP STUDIES IN PARTICIPANTS WITH AND WITHOUT CHRONIC POSTTRAUMATIC STRESS DISORDER

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**Introduction :** Variability in sleep parameters during the first night of polysomnographic (PSG) testing, known as the "first night effect" (FNE), has been observed in many clinical populations. Few studies have assessed whether those with chronic post-traumatic stress disorder (PTSD) demonstrate significant FNE. Moreover, no study has systematically examined whether the FNE represents adaptation to recording equipment, environment, or both. We examined FNE in subjects with chronic PTSD and controls with PSG studies in both home and hospital settings. We hypothesized that (a) participants with PTSD would have greater FNE compared to controls in night 1 versus night 2 of the study

in both settings; and that (b) PTSD and control participants would have greater FNE in the hospital than at home.

**Methods :** Forty-two men and women with PTSD and 34 age-matched controls completed four nights of ambulatory PSG, two in participants' homes and two in a hospital research unit. Participants were medically healthy without sleep apnea and free of psychotropic medication. The order of "home first" versus "hospital first" conditions was counterbalanced.

**Results :** The PTSD group demonstrated no first-night changes in sleep architecture in either location. The control group assigned to the "hospital first" condition showed adaptation changes in total sleep time in the hospital ( $F[1, 33.0] = 5.019, p < .032$ ), but not in the subsequent nights of the study at home. The control group assigned to the "home first" condition did not have any FNE, at home or in the hospital.

**Conclusion :** Contrary to our expectations, the PTSD group showed no adaptation effects in either setting. Only the control group assigned to the "hospital first" condition showed significant decreases in total sleep time on night 1 versus night 2 of the study, suggesting that the "first night effect" may be due to adaptation to the combination of both the recording equipment and sleeping environment. Subjects who were previously studied at home did not show an adaptation response to laboratory setting. It is possible that the lack of adaptation response of PTSD subjects to admission to the hospital was driven by their perception that the hospital was a safe sleeping environment.

**Support (optional):**

### 0973

#### EFFECTS OF REM SLEEP ON AFFECTIVE MEMORY CONSOLIDATION IN PATIENTS WITH DEPRESSION

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**Introduction :** REM sleep has been posited to have both memory consolidation and mood regulatory functions. REM sleep in depression (as compared to normal controls) tends to show signs of disinhibition, as evidenced by earlier onset (shorter REM latency), increased duration, and increased density of eye movements. Depressed individuals also tend to have negative memory biases, that is, tend to recall more negative and less neutral stimuli. In combination, these findings support the hypothesis that REM sleep may be associated with affective memory biases in individuals with depression.

**Methods :** Subjects with partially remitted Major Depressive Disorder ( $n=52$ ) were shown 30 slides from the International Affective Picture System (with equal numbers of positive, negative, and neutral valences) and asked to recall them approximately 45 minutes following their presentation. Following recall, sleep was assessed by overnight polysomnography, and subjects were asked to recall the pictures again the following morning. Bivariate correlations were run to assess the relationship between REM sleep and affective picture recall.

**Results :** REM latency was positively correlated with the proportion of neutral pictures recalled both before ( $r=0.375, p < .05$ ) and after ( $r=0.425, p < .05$ ) sleep. REM latency also showed a trend towards a negative correlation with the proportion of negative pictures recalled after sleep ( $r=-0.29, p=.059$ ). The proportion of neutral pictures recalled after sleep showed a trend towards a negative correlation with REM percent ( $r=-.278, p=.07$ ).

**Conclusion :** As REM latency decreased (as is associated with depression), negatively valenced picture recall increased. Conversely, as REM suppression increased (as manifested by longer REM latency and reduced REM percentage), neutral picture recall increased. These findings suggest that disinhibited REM sleep may be related to the preferential consolidation of affect-laden memory, and may contribute to daytime memory bias-

es in depressed individuals.

**Support (optional):**

### 0974

#### PREVALENCE OF SLEEP DISTURBANCES AMONG CHILDREN AND ADOLESCENTS WITH COMORBID PSYCHIATRIC DISORDERS

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**Introduction :** There is growing evidence that children with psychiatric disorders have an increased risk of having disrupted sleep or a sleep disorder. The mechanisms linking sleep and psychiatric disorders are not yet fully understood. The direction of the causal relationship is likely to differ between individuals and is likely to include a host of moderating factors. This study, a follow-up to a prior report of a smaller psychiatric sample, provides estimates of the prevalence of sleep problems in children diagnosed with psychiatric disorders.

**Methods :** A sleep questionnaire was completed by parents of children participating in a study of psychiatric disorders ( $n=57$ , age range 6-18). Psychiatric diagnoses were confirmed with the K-SADS, CDI, Conner's, and SCARED. Seventy five percent of subjects had comorbid psychiatric diagnoses. The group was divided into children ( $n=31$ , 6-11 years) and adolescents ( $n=26$ , 12-18 years).

**Results :** Children's total sleep time ( $M=8.9$ hrs,  $SD=1.1$ hrs) was significantly higher than adolescents' ( $M=7.8$ hrs,  $SD=1.5$ hrs),  $p < .05$ . Napping was reported to occur more than once a week in 16% of children and 46% of adolescents. Additionally, 29% of children and 23% of adolescents had a high likelihood of falling asleep in various settings throughout the day. Results yielded four key findings: 1) 77% with insomnia symptoms were diagnosed with an anxiety disorder; 2) 84% with symptoms of sleep disordered breathing were diagnosed with ADHD; 3) 14% reported parasomnias; and 4) 5% had nightmares more than once a week. Overall, 79% endorsed symptoms suggestive of a diagnosable sleep disorder.

**Conclusion :** This study found a high rate of sleep disturbances in youngsters diagnosed with co-morbid psychiatric disorders. It is recommended that clinicians routinely ask about the presence of sleep problems when conducting psychiatric evaluations. Furthermore, treatment of sleep disorders may be a priority in populations with complex psychiatric disorders.

**Support (optional):**

### 0975

#### WEB SURVEY OF SLEEP PROBLEMS ASSOCIATED WITH EARLY-ONSET BIPOLAR SPECTRUM DISORDERS (EOBPSD)

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**Introduction :** Although a reduced need for sleep and insomnia/hypersomnia are listed as DSM-IV symptoms of mania or depression, respectively, only two publications exist on EOBPSD-related sleep problems. Building on our initial research, we report findings from a web-based survey of sleep problems in 4-to-12 year-olds reported to have EOBPSD.

**Methods :** Participants were 254 parent-members of the Child and Adolescent Bipolar Foundation (CABF), who reported their children had been diagnosed with EOBPSD. The Children's Sleep Habit Questionnaire and six additional items were administered in a web-based survey to explore the occurrence of ICSD sleep problems and associated severity, mood episode, and impairment during the child's "worst mood episode:"

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sleep difficulties with other mood episodes; and current mood-related sleep problems.

**Results :** The majority of parents recalled a “worst mood episode” involving mixed manic-depressive symptoms (79%) during which the following occurred “2-5 times per week”: Bedtime Resistance (56-70%); Sleep Onset Delay (76%); Sleep Duration (73-82%); Sleep Anxiety (55-74%); Night Wakings (57-73%); Parasomnias (63-95%); and Daytime Sleepiness (52%-93%). Most parents rated associated mild-to-severe impairments at home (94%), school (86%) and with peers (71%). Similarly, the majority of parents reported additional sleep difficulties occurring during other mood episodes (75%) and over the last month (63%).

**Conclusion :** Overall, most parents of children previously identified with EOBPSD reported past and current mood-related sleep difficulties; several frequent ICSD sleep problems within a mixed manic-depressive “worst mood episode;” and related psychosocial impairments. Rates compare to our previous clinic-based study of children diagnosed with EOBPSD most of whom experienced manic (60%) or depressive (80%) related sleep difficulties. Limitations of the web-based methodology, clinical and research implications and additional data on the effectiveness of pharmacological and nonpharmacological sleep interventions will be discussed at APSS.

**Support (optional):**

### 0976

#### SLEEP DYSREGULATION IN COCAINE DEPENDENT MEN DURING ACUTE ABSTINENCE

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**Introduction :** Sleep disturbance is one of the most prominent complaints of cocaine dependent patients with over 70% of subjects reporting disordered sleep during recovery. However, few polysomnography studies have been conducted in cocaine dependent individuals and conclusions are limited by small sample sizes, clinical heterogeneity, and failure to include controls who are matched on potentially confounding variables.

**Methods :** This study evaluated 17 males with cocaine dependence and 14 matched controls. The groups did not differ in: age, body mass index, ethnicity, marital status, or the time elapsed since their last alcohol consumption. Cocaine dependent men were acutely abstinent having actively used cocaine within the last 2.5 days prior to sleep assessment. Continuous polysomnography data was acquired for three consecutive nights at the UCLA General Clinical Research Center. EEG sleep was scored in accordance to Rechtschaffen and Kales criteria. Data are presented for the third night.

**Results :** As compared to controls, cocaine dependent men showed increases of stage 1 sleep (34.0 ± 18.0 min vs. 22.7 ± 10.9 min; p<0.05), loss of stage 3 (0.4 ± 0.8 min vs. 18.9 ± 18.8 min; p<0.05) and of stage 4 sleep (0.0 ± 0.0 min vs. 1.9 ± 2.8 min; p<0.05), and decreases in REM latency (34.5 ± 23.8 min vs. 69.2 ± 56.1 min; p<0.05). Differences in sleep continuity measures were not found between the two groups.

**Conclusion :** These data are among the first to show that chronic cocaine dependence is associated with a loss of slow wave sleep and increases in REM pressure in men. Given the important role of sleep in the homeostatic regulation of the immune and autonomic systems, these data have important implications for understanding the health risks in persons who chronically use cocaine.

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### 0977

#### TOBACCO SMOKING, SLEEP AND CLINICAL SYMPTOMS IN NEUROLEPTIC-TREATED SCHIZOPHRENIA

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**Introduction :** Tobacco smoking is highly prevalent in schizophrenia. It is considered a self-treatment since it is often associated with less cognitive deficits. The aim of the present study was to investigate the relationship between smoking habits, sleep and clinical scales in chronic schizophrenia.

**Methods :** Twenty-two persons diagnosed with schizophrenia and clinically stable under chronic neuroleptic treatment spent two consecutive nights in a sleep laboratory. All patients were treated with atypical neuroleptics except one. Sleep stages were determined for night two. The Positive and Negative Syndrome Scale (PANSS) and the Fagerstrom scale for nicotine dependence were administered on the morning following night two. Fifteen patients with chronic smoking habits (12 M, 3 W, mean age: 27.5 +/- 6.1) were compared to eight non-smokers (4 M, 2 W, mean age: 32.5 ± 10.3) using t-tests. Spearman's rho assessed the relationship between sleep variables, smoking habits, and PANSS scores. Cognitive performance was evaluated with the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).

**Results :** Smokers showed less SWS (Stages 3+4: 6.8% +/- 9.0 versus 17.7% +/- 14.8; p<.05), more REM sleep (20.3% +/- 5.4 versus 13.0% +/- 5.2; p<.01) and more REM sleep efficiency (85.7% ± 8.0 versus 69.7% ± 8.4; p<.0007) than non smokers. Smokers also had more positive symptoms (20.5 ± 2.8 versus 17.1 ± 3.8; p<.04) and a higher total PANSS score (77.9 ± 8.2 versus 70.2 ± 7.8; p<.06) than non-smokers while they performed better than non-smokers on the RBANS.

**Conclusion :** Chronic tobacco use by persons with schizophrenia is associated with an amplification of sleep characteristics known to be typical of this condition as well as with more severe psychotic signs despite superior cognitive performance. These results suggest a dissociation between the effect of chronic tobacco use on cognitive deficits versus its effect on sleep and psychotic symptoms.

**Support (optional):**

### 0978

#### ADHD AND MILD OBSTRUCTIVE SLEEP APNEA: A TREATMENT OUTCOME STUDY

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**Introduction :** Children diagnosed with ADHD, based on DSM-IV criteria may also have mild obstructive sleep apnea OSA, but it is unclear if treating OSA has similar results as methylphenidate, a commonly used treatment for ADHD.

**Methods :** This study enrolled 66 school-age children, referred for and diagnosed with ADHD and 20 healthy control. Polysomnography performed after ADHD diagnosis, showed presence of mild OSA. After otolaryngological evaluation, parents and referring physicians of these children could select treatment of ADHD with methylphenidate (MPH), treatment of OSA with adenotonsillectomy or no treatment. Systematic follow-up was performed 6 months after initiation of treatment, or diagnosis

if no treatment. All children had pre- and post-clinical interviews; pediatric, neurologic, psychiatric and neurocognitive evaluation; polysomnography; child behavior checklist (CBCL) filled by parents and teacher; TOVA attention test; and quality of life with questionnaire (OSA-18).

**Results :** ADHD children had an AHI > 1 < 5; Twenty seven were treated with MPH, 25 had adenotonsillectomy, and 14 had no treatment. The surgical and MPH groups improved more than the non treatment group. When comparing MPH to post-surgery, the polysomnographic and questionnaire sleep variables, some daytime symptoms (including attention span) and TOVA subscales (impulse control, response time and total ADHD score) were more improved in the surgical group than the MPH group. The surgical group had TOVA ADHD score lower than 1.8 and close to normal controls.

**Conclusion :** Low AHI score is detrimental to children with ADHD. Recognition and surgical treatment of underlying mild SDB in children with ADHD, avoid unnecessary long-term drug usage.

**Support (optional):**

### 0979

#### QUETIAPINE IMPROVES SLEEP IN NON-PSYCHOTIC UNIPOLAR DEPRESSION WITH RESIDUAL SYMPTOMS. A DOUBLE BLIND, RANDOMIZED PLACEBO CONTROLLED STUDY

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**Introduction :** New studies indicate the benefit of quetiapine on measures of subjective sleep in patients with mental illness and objective sleep in healthy controls. The effects on subjective sleep quality were investigated as a secondary endpoint in a recent study of adjunctive quetiapine treatment in non-psychotic depression.

**Methods :** 16 patients with residual symptoms of a current major non-psychotic depressive episode (after at least 6 weeks of an adequate dose of antidepressant) were randomized into placebo and flexibly dosed (100-600mg given at night) quetiapine groups for 8 weeks. Sleep variables were defined as the individual sleep items on the clinician rated Hamilton Anxiety Scale (HAMA), Montgomery-Asberg Depression Scale (MADRS), the 3 sleep items on the Hamilton Depression Scale (HAMD17) and the self rated 7 component items of the Pittsburgh Sleep Quality index (PSQI).

**Results :** A last observation carried forward (LOCF) analysis (n=15) using independent samples t-tests demonstrated significantly greater (p < .05) mean improvements for the quetiapine group (n=8) versus the placebo (n=7) group in: HAMD17 total sleep score, HAMD17 item 5 (middle insomnia), MADRS and HAM-A sleep disturbance items, PSQI components 3 (hours of sleep), and 7 (alertness + enthusiasm). Trends towards significance were seen in the total PSQI and the PSQI component 4 (sleep efficiency). The average dose of quetiapine in the treatment group was 350mg.

**Conclusion :** This study demonstrated the benefit of quetiapine on sleep when used as an adjunctive treatment for depression with residual symptoms. Improvements were seen in clinician rated overall sleep quality, middle insomnia, self reported sleep amount, and potentially sleep efficiency. Limitations of this study include the small sample size and no objective determination of sleep quality. Larger scale controlled trials in this area are needed.

**Support (optional):** Research supported in part by the Investigator initiated trials program from Astra Zeneca

### 0980

#### PATIENTS WITH MAJOR DEPRESSION SHOW SEVERE DAYTIME SLEEPINESS USING A 15-MINUTE, OFFICE-BASED, NEURO-BEHAVIORAL TEST

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**Introduction :** Depression not only impairs mood and sense of wellbeing, but also affects sleep and is associated with daytime fatigue and sleepiness. A convenient and accurate assessment of sleepiness would provide valuable supplemental information for the diagnosis and confirmation of the depression as well as for quantification of the impact of antidepressants. Current clinical objective methods, such as multiple sleep latency test (MSLT), are not practical for applications outside specialized sleep clinics. In this study, a portable neuro-behavioral evaluation device (NeuroCAP) was utilized in an outpatient setting to quantify sleepiness in patients with major depression. We have reported previously that this test showed strong correlation with MSLT in patients with primary sleep disorders.

**Methods :** Fifteen patients, who were diagnosed with major depression (DSM-IV criteria) at the psychiatric offices of the NorthCoast Clinical Trials (NCCT), were recruited. In a patient evaluation room within NCCT facilities, a 15-minute sleepiness assessment test was administered prior to initiation of antidepressant treatment. In three patients, a second test was obtained one month after antidepressant treatment. The test is based on simultaneous acquisition/analysis of EEG and behavioral response in a protocol that challenged the patient to maintain their vigilance and accurately respond to auditory target cues in a sleep promoting environment. In addition to the alertness test, patients were evaluated by subjective measures such as Epworth Sleepiness Scale (ESS).

**Results :** The Sleepiness index (output of the test) was significantly (p < .02) larger in unmediated depressed patients (mean=1.65 ± 2.5) compared with the results of 12 normal alert volunteers tested in other protocols (mean= 0.037 ± 0.04). In the three patients who were tested both before and after treatment, sleepiness index improved (decreased) from a mean of 0.47 ± 0.31 to a normal range of 0.06 ± 0.08 after antidepressant treatment (average improvement of 88%). This improvement in alertness is also confirmed by ESS score which shows a reduction in all of the three patients (before treatment: 9.33, after treatment 6.33).

**Conclusion :** The ambulatory, neuro-behavioral test shows the presence of severe sleepiness in depressed patients using a relatively fast protocol. The results demonstrate the potential of this method for assessing the degree of sleepiness/alertness in depression as well as for gauging the impact of treatment with psychotropic medications.

**Support (optional):**

### 0981

#### SLEEPINESS, CATAPLEXY AND HLA IN CHINESE TAIWANESE

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**Introduction :** There is little data on HLA typing and MSLT results in Chinese with daytime sleepiness and results of nocturnal polysomnography followed by MSLT (5naps).

**Methods :** Successively seen patients free of treatment, with cataplexy and/or isolated daytime sleepiness had clinical evaluation, sleepiness scale, cataplexy questionnaire and 2 polysomnography with MSLT repeated within 3 months to affirm findings. Blood was drawn from subject and family members for HLA typing.

**Results :** 32 patients (mean age 19.75 years, 11 women) were collected

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without any associated cause of sleepiness at clinical evaluation and polysomnography, and sleep latency below 8 minutes at 2 different MSLT. 16 patients had clinically determined cataplexy and 28 subjects had two or more SOREMP at repeat MSLT. HLA typing indicated that 15/16 cataplectic patients were DQB1-0602 (one homozygote) All non adopted children had at least one parent with same haplotype. 2 Cataplectic-DQB1-0602 had only 1 SOREMP at both MSLT, but 14/16 non cataplectic non DQB1-0602 patients had 2 or more SOREMP. Mean sleep latency at MSLT dissociate better narcoleptic-cataplectic with a mean of 1.64 vs 4.96 minutes ( $p=0.001$ ) than SOREMP (2.6 vs 3.1) that had no diagnostic value in this group of subjects with daytime sleepiness complaint.

**Conclusion :** Chinese Taiwanese with EDS and cataplexy present same results as Caucasian at HLA typing:94% of patients with Cataplexy were HLA DQB1-0602. Investigation of SOREMP at MSLT had no diagnostic value to dissociate narcoleptic from non narcoleptic subjects. Mean sleep latency was more helpful indicating much shorter mean SL in cataplectic subjects independently of presence-absence of 2 or more SOREMP.

**Support (optional):**

### 0982

#### ANXIETY AND DEPRESSION ON THE TOLERANCE OF A CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) MASK IN SPLIT-NIGHT SLEEP STUDIES

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**Introduction :** Obstructive sleep apnea (OSA) is a common and important medical condition. Standard of care treatment involves CPAP. A split-night study involves the first portion of the night study as diagnostic, followed by a treatment titration. Split-night studies are a tool to meet the high demand for overnight diagnostic and treatment assessment of OSA. Many patients do not adhere to treatment, and compliance with treatment is often considered poor. Various correlates of compliance have been studied, with inconsistent results. Some point to anxiety and depression as decreasing CPAP tolerance. There are not studies in the literature about tolerance of split-night studies.

**Methods :** 200 consecutive charts from the Veterans Hospital sleep lab subjects were reviewed. The 68 of those who had split night studies were further evaluated to collect objective polysomnography data and subjective information from a sleep questionnaire filled out by all participants.

**Results :** 76% of the total subjects tolerated the attempted CPAP titration. Those endorsing depression did not have a statistically different rate of tolerance (81%). Contrary to expected, anxiety overall was correlated with increased tolerance ( $COR=0.2829$ ,  $p=0.0543$ ) of CPAP. Those endorsing post-traumatic stress disorder tolerated CPAP better than those without (88%). 22 of the 68 subjects (32%) were on psychotropic medications (antidepressants, anti-anxiety, or antipsychotic medication). Of people on psychotropic medications, 3 did not tolerate the CPAP titration (13.6%), compared to 13 of 46 (28%) not tolerating it in the group not on psychotropic medications, (Likelihood Ratio= 1.899 ( $p=0.1682$ )), which was not statistically significant.

**Conclusion :** Subjects with depression did not tolerate CPAP in the split-study worse than those without. Subjects with anxiety may tolerate CPAP better, potentially due to some beneficial effect on the anxiety. Psychotropic medications may improve the tolerance of a CPAP trial, or may be an indication of an underlying condition that increases CPAP tolerance.

**Support (optional):**

### 0983

#### DECREASED REM SLEEP IN POSTTRAUMATIC STRESS DISORDER VA PATIENTS

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**Introduction :** Rapid Eye Movement(REM) Sleep has been postulated to play a role in Posttraumatic Stress Disorder (PTSD). We observed alterations in the sleep architecture of PTSD patients seen at the James A. Haley VA Hospital in Tampa, FL. REM sleep was markedly suppressed and in many cases, completely absent, which is at variance with published data, that typically shows no decrease in REM sleep in PTSD patients.

**Methods :** The sleep studies of all patients diagnosed with PTSD and referred to the sleep lab in 2004 were reviewed. Patients referred for CPAP titration were excluded. 77 patients, 71 males, 20-84 years of age, mean 56 years, 6 females 32-52 years of age, mean 42 years, met criteria. Their polysomnographic studies (PSGs) were analyzed with respect to total sleep time (TS), total REM time (TREM), REM latency (REM Lat), and percent REM sleep (%REM). Study data was compared to published data for PTSD and nonPTSD patients.

**Results :** In this study the mean TS was 225 min., compared to published data on PTSD patients, 329 min, and controls 364 min. Mean TREM was 20 min. in this study, vs. 66 min. and 72 min. for published PTSD and controls, respectively. Mean REM Lat was 164 min. for this study, vs. 64 min. and 79 min. for published PTSD and controls, respectively. Mean %REM was 0.07% in this study vs. 21.4% and 19.4% in published PTSD and controls, respectively.

**Conclusion :** The patient population had markedly impaired REM sleep compared to published data. We noted that almost all of these patients were on two antidepressants and one other psychotropic medication. We hypothesize that this medical regimen is a major factor in the decreased REM found in the study population.

**Support (optional):**

0984

### SLEPMED INSOMNIA INDEX (SMI) AND EPWORTH SLEEPINESS SCALE (ESS) AS OUTCOME MEASURES IN SODIUM OXYBATE TREATED PATIENTS

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**Introduction :** This is a retrospective study to examine the Epworth Sleepiness Scale (ESS) and SleepMed Insomnia Index (SMI) as treatment outcome measures in 86 patients currently taking sodium oxybate. Outcome measures assist the clinician in the initial quantitative assessment of illness and clinical progress as well as response to drug therapy. ESS and SMI are validated tools to measure excessive daytime sleepiness and sleep continuity respectively. The SMI is a 10 item questionnaire developed to assess and manage patients with an insomnia component. However, it discriminates individuals with sleep disorders from normals. Patients with sleep fragmentation score much higher than patients with excessive daytime sleepiness. The purpose of this study is to evaluate outcome measures as tools to examine a broad range of variables including sleep quality, daytime function, mood, and quality of life.

**Methods :** A total of 86 patients at one sleep clinic in S.C. currently taking sodium oxybate were studied. A chart audit was conducted to retrieve their ESS and SMI scores at 2 different time intervals for comparison: at baseline prior to drug therapy and at first office visit post-therapy initiation. There were no changes in concomitant medications during the evaluation period or other treatment variables.

**Results :** There were 22 males (ages 20-76) and 64 females (ages 16-76). Dates for initiation of drug ranged from 2002-2005. All patients on drug therapy were included at the time of the audit. Drug dose ranged from 3.0-10.8 grams. Diagnoses included: 40-narcolepsy; 22-idiopathic hypersomnia; 8-insomnia; 10-fibromyalgia; 4-REM behavior disorder; 2- chronic fatigue syndrome. Off label use was done with informed consent. Mean scores with standard deviations for ESS were: pre 14(6) and post 9(5). T-tests on ESS results were significant  $p < 0.00003$ . Mean scores for SMI were: pre 22(10) and post 12(8). T-tests on SMI results were significant  $p < 0.0000001$ .

**Conclusion :** The SMI as a measure of sleep fragmentation is significantly elevated in narcolepsy patients. Sodium oxybate improved excessive daytime sleepiness as measured by the ESS. Sodium oxybate improved sleep continuity as measured by the SMI. The ESS and SMI can be useful to quantify disease impact and response to therapy.

**Support (optional):**

0985

### AUTOMATED FUNDAMENTAL FREQUENCY MEASURES WITH MORPHEUS OF HUMAN ELECTROENCEPHALOGRAPHY (EEG) IN PATIENTS TREATED WITH SODIUM OXYBATE

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**Introduction :** Advanced automated EEG signal processing with Morpheus uses multidimensional mathematical analyses of digitized biological signals applying adaptive segmentation with fuzzy logic. Sodium oxybate is used to treat narcolepsy with cataplexy and is known to increase stage 3,4 (slow wave) sleep. This study applies advanced signal processing in patients treated with sodium oxybate.

**Methods :** Ten polysomnography (PSG) studies were analyzed by Morpheus. Five patients who had their initial dose of sodium oxybate administered in the sleep lab were compared with their baseline PSG

results. Morpheus fundamental frequency changes were quantified as an outcome measure of improvement in sleep state with drug therapy. Fundamental frequency is the modal frequency of quasi-stationary states represented as adaptive segments. Adaptive segments include mixed frequency 1, mixed frequency 2, low frequency, and high frequency segments. Fundamental frequency values below 4 Hz are believed to represent EEG synchrony. The percentage of fundamental frequency below 4 Hz as a function of total sleep time was calculated during the baseline PSG and compared with the treatment night. T-tests were performed to assess statistical significance.

**Results :** Of the five patients included there were 3 women ages (15- 58 years) and 2 men ages (70-75 years). All five had baseline PSG studies prior to their treatment with sodium oxybate occurring between 9/04 and 7/05. Mean and standard deviation for the percentage of time under 4 Hz in the baseline period was 15%(13); treated with sodium oxybate was 36%(13). The range of percentage in the baseline period under 4 Hz was 0-32%; while the range when treated with first dose of sodium oxybate in the sleep lab was 19-56%. A T-test comparing the percentage of 4 Hz at baseline compared with first night of sodium oxybate treatment in the sleep lab was statistically significant  $p < 0.02$ .

**Conclusion :** Morpheus automated analysis differentiated baseline and treatment PSGs as to an increase in the percentage of time at modal frequency below 4Hz. Sodium oxybate enhances fundamental frequency below 4 Hz demonstrating EEG synchrony. Enhanced resolution by automated analysis may offer improved efficiencies, reproducibility, and insights into sleep states and processes.

**Support (optional):**

0986

### QUANTITATIVE EEG (QEEG) POWER CHARACTERISTICS OF CHILDREN WITH OSA IN A PEDIATRIC AD/HD POPULATION

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**Introduction :** QEEG differences in theta/beta EEG power ratios can identify individuals with pediatric AD/HD with >86% sensitivity and >94% specificity. The authors' hypothesize that pediatric obstructive sleep apnea (OSA) also induces identifiable changes in physiologic EEG rhythms.

**Methods :** Outpatient pediatric psychiatry clinic clients with AD/HD as based on evaluation by a Board Certified Pediatric Psychiatrist and at least one positive psychological test (N=50, Age: mean 12.3, range 6-17). Obstructive apnea-hypopnea index (oahi) based on full night nocturnal polysomnography used to divide total group into groupings with oahi < 2.5 (N=12), 2.5-5 (N=16), and > 5.0 (N=22). QEEG analysis of EEG data sampled from waking, eyes open and closed. Delta, theta, alpha, and beta EEG frequencies analyzed as to absolute and relative power at the CZ, C3 and C4 sites.

**Results :** 1) Values by group for delta absolute power at Cz with eyes closed: oahi < 2.5 (mean 66.0, stdev 31.1), oahi 2.5-5.0 (mean 53.5, stdev 22.7), and oahi > 5.0 (mean 49.8, stdev 26.1). Group differences between relative and absolute delta power at Cz, C3, and C4 were not statistically significant. 2) Values by group for theta absolute power at Cz with eyes closed: oahi < 2.5 (mean 70.2, stdev 50.5), oahi 2.5-5.0 (mean 45.9, stdev 28.5) and oahi > 5.0 (mean 44.3, stdev 36.0). Group differences between relative and absolute theta power at CZ, C3, and C4 were not statistically significant. 3) Statistically significant group differences were found for alpha absolute power with eyes closed at Cz, C3, and C4, and eyes open

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at Cz and C3. Values by group for alpha absolute power at Cz with eyes closed were as follows: oahi < 2.5 (mean 55.5, stdev 37.9), oahi 2.5-5.0 (mean 41.3, stdev 25.2), and oahi > 5.0 (mean 28.7, stdev 19.9). Post hoc analysis demonstrates a significant difference between oahi < 2.5 and oahi > 5.0, supporting a decrease in alpha absolute power with an increase in oahi. A logistic regression model using age and alpha absolute power at Cz with eyes closed predicts the probability of having oahi > 5.0 with a specificity of 88.9%, a sensitivity of 63.2%, and an overall accuracy of 78.3%. 4) No consistent trend was found between groups for beta frequency.

**Conclusion :** Pediatric OSA is associated with changes in background physiologic EEG rhythms in AD/HD children with OSA. Absolute alpha power is significantly lower in children with oahi > 5.0 with that finding potentially predictive of OSA in this population.

**Support (optional):**

### 0987

#### DAILY VARIABILITY IN WRIST ACTIGRAPHY IN BREAST CANCER SURVIVORS EXPERIENCING HOT FLASHES

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**Introduction :** Sleep disturbances are common in menopausal breast cancer survivors. Previous research has found that a majority of breast cancer survivors (BCS) have hot flashes and report poor sleep quality and high sleep disturbance using subjective reports and objective wrist actigraphy. However, daily variability of actigraphy findings such as wake after sleep onset (WASO) and actual sleep time (AST) has not been fully examined. We examined daily variability in WASO and AST in this population in order to determine the number of days needed for adequate measurement of sleep activity.

**Methods :** One week baseline data BCS participating in hot flash intervention studies. Data were analyzed from 7 consecutive days of wrist actigraphy (objective sleep) using WASO and AST. Days of the week (Mon-Sun) were examined.

**Results :** The sample consisted of 55 BCS who were a mean age of 54 years (SD=9), Caucasian (80%), employed (75%), postmenopausal (93%), with a mean of 16 years education, and at least one concurrent medical problem (64%). Women were a generally stage I-II at diagnosis (69%) and taking endocrine therapy (51%). The majority of the sample slept less than 6 hrs (+ 1.7) with 15% of sleep time spent awake. Significant bivariate correlations were found between WASO and day of week ( $r=0.39$  to  $0.84$ ,  $p=.01$ ) and AST and day of week ( $r=0.36$  to  $0.72$ ,  $p=.01$ ). WASO on Saturday was related to every day except Monday whereas the AST was related based on specific groupings of days excluding Saturday.

**Conclusion :** Results suggest to obtain an accurate measurement of WASO could be collected on any weekday except Monday while accurate measurement of AST depends on 7 days of data. Further investigation is warranted to determine more accurate recommendations for daily recording.

**Support (optional):** Supported by NINR/NIH grant #R01 NR05261 (Carpenter), the Mary Margaret Walther Program of the Walther Cancer Institute (Carpenter) and an American Cancer Society Doctoral Scholarship in Cancer Nursing (Elam)

### 0988

#### UPPER AIRWAY RESISTANCE BASED ON COMPUTATIONAL FLUID DYNAMICS (CFD) ANALYSIS OF VOLUME-GATED MRI

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**Introduction :** To develop a technique based on volume-gated MRI of the upper airway and a mask flow measurement using CFD to produce continuous pressure and flow fields and to calculate resistance between any points in the upper airway.

**Methods :** Volume-gated MR images were obtained during tidal breathing. Resistances from the choanae to epiglottis spanning 10 points in the tidal breathing cycle were computed using flow measurements and CFD analysis of the reconstructed upper airway of a 5.5 years old child with OSAS and a matched 5.1 years old control. Minimum pressures along the airway segment axis were selected after CFD computation (Fluent Inc.) and resistance values were calculated for both subjects.

**Results :** Using CFD modeling we found that the tidal flow waveform exhibits significant inspiratory flow limitation in the OSAS subject. In addition, mean cross-sectional area is decreased throughout inspiration with an increase on expiration. Pmin for the cycle decreases progressively in inspiration with a pronounced minimum in late inspiration. These are in contrast to a constant cross-sectional area and pressures in the control. Finally, the OSAS subject's resistance is increased to a peak value during inspiration and is minimal over expiration, concomitant to the increased cross-sectional area.

**Conclusion :** The combination of imaging and flow measurement with CFD analysis allows us to evaluate the interactions between airway deformations, flow, resistance, and compliance along any region of interest then that the upper airway, over the breathing cycle.

**Support (optional):** NIH HL-62408

### 0989

#### VALIDATING THE GENERAL SLEEP DISTURBANCE SCALE AMONG PARENTS WITH AN INFANT IN THE ICU

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**Introduction :** Sleep disturbance is prevalent in childbearing parents with a healthy newborn baby. Yet, studies focused on sleep disturbances in parents with a hospitalized infant are rare, and there are no published reports on psychometric properties of sleep measures for parents with a sick infant. The aim of this study was to determine the construct equivalence and other psychometric features of the General Sleep Disturbance Scale (GSDS).

**Methods :** This cross-sectional descriptive study included 22 mothers and 17 fathers who had an infant hospitalized in three San Francisco ICU settings. Three sets of data were collected: 1) infant's medical records and parent's demographic data, 2) General Sleep Disturbance Scale, Lee Fatigue Scale, and 3) total sleep time (TST) and sleep efficiency (SE) from two nights of wrist actigraphy monitoring.

**Results :** The possible range of GSDS scores is 0 to 147, with higher scores indicating a greater amount of sleep disturbances. The mean score of GSDS for the participants was 44.5 (SD= 20.1). The Cronbach alpha coefficients were .82 for the GSDS. Concurrent validity of the GSDS was demonstrated through correlations with higher sleep problem perception from sleep diary ( $r= .71$ ,  $p< .001$ ), and less TST ( $r= -.35$ ,  $p= .03$ ) and less SE ( $r= -.33$ ,  $p< .05$ ) from wrist actigraphy. The less TST was correlated with higher sleep quantity disturbance from the GSDS subscale ( $r= -.40$ ,  $p= .01$ ). Parents who scored higher GSDS reported a severe morning fatigue level ( $r= .51$ ,  $p= .001$ ).

**Conclusion :** The GSDS is a valid method to evaluate a parent's quality and quantity of sleep. The GSDS can be completed in less than five min-



utes and is a non-invasive method for measuring sleep disturbances consistent with the DSM-IV insomnia criteria. Since wearing a wrist actigraphy may be burdensome to participants, equipment failure is common, and actigraphy is not generally available in most clinical settings, it was reassuring that the GSDS provided a valid and reliable way to assess sleep disturbance among this population of parents.

**Support (optional):** This study was supported by NINR T32NR 07088, and the Graduate Division, University of California, San Francisco.

## 0990

### PSYCHOMOTOR VIGILANCE TASK PERFORMANCE IN 6-11 YEAR OLD CHILDREN--THE TUCSON CHILDREN'S ASSESSMENT OF SLEEP APNEA STUDY (TUCASA)

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**Introduction :** Although the psychomotor vigilance task (PVT) is commonly used in sleep and other research settings, normative data for PVT performance in children have not been published. Using data from the Tucson Children's Assessment of Sleep Apnea (TuCASA) study, this report presents normative PVT performance data and relationships with age, gender, and ethnicity.

**Methods :** A community-based sample of 367 Caucasian and Hispanic children completed cognitive evaluations for TuCASA, including a standard 10-minute PVT trial. PVT performance data were processed using REACT software. Children with respiratory disturbance index (RDI)  $\geq$  1 event/hour based on unattended home polysomnograms were excluded, as were those with parent-reported insomnia, snoring, or excessive daytime sleepiness. All others ( $n = 162$ ) were included in the analysis.

**Results :** Participants were 51% female and 35% Hispanic; mean age was 8.9 years. Average mean and median reaction times (RTs) decreased with increasing age ( $p$  for trend  $< 0.001$ ). Children 6 years of age had average mean and median RTs of 721.15 ms and 528.50 ms, respectively; those 11 years of age had average mean and median RTs of 396.35 ms and 325.70 ms, respectively. Average standard deviations in RTs also decreased with increasing age ( $p$  for trend = 0.001), as did average number of lapses ( $p$  for trend  $< 0.001$ ), but no trend was apparent in average number of total errors. There were statistically significant ( $p = 0.005$ ) differences in the performance of boys and girls. Gender differences were greatest at age 6, where boys had shorter mean and median RTs, and decreased with age until performance was approximately equal at age 11. No ethnic differences were detected.

**Conclusion :** Children's PVT performance changes with age and gender. These differences in performance must be considered when the PVT is utilized in pediatric populations.

**Support (optional):** Supported by HL62373

## 0991

### PSYCHOMETRIC PROPERTIES OF TWO NEW SCALES FOR MEASURING DAYTIME FUNCTIONING FOR INSOMNIA

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**Introduction :** Much of the research focus on insomnia has been on poor night-time sleep. Simple measures are needed to assess the reported poor daytime experiences of insomnia sufferers, especially the common feeling of fatigue (physical and mental tiredness/exhaustion as distinct from sleepiness). This study presents the psychometric properties of two new

scales: The Flinders Fatigue Scale (FFS) and the Daytime Feelings and Functioning Scale (DFFS).

**Methods :** The FFS is a 7-item scale that measures characteristics of fatigue (e.g. frequency, severity) experienced in the past 2 weeks. The DFFS is a 12-item scale that measures the frequency of various daytime feelings (e.g. lethargy, poor concentration, irritability) experienced over the past 2 weeks. These daytime scales were administered to three samples. Sample 1 consisted of 87 insomniacs enrolled in a 3-month insomnia treatment program with scales administered at baseline, 5 weeks and 3 months after treatment. Samples 2 (183 volunteer psychology students) and 3 (1039 subjects from the general population) were administered the DFFS, FFS and the Pittsburgh Sleep Quality Index to assess poor sleep.

**Results :** For the three samples, the internal consistency of the FFS was 0.86, 0.89, and 0.91, respectively; and 0.92, 0.89, and 0.94 for the DFFS. Both scales were unrelated to sleepiness (ESS) (FFS:  $r(79) = -.14$ ,  $p = .23$ ; DFFS:  $r(79) = -.06$ ,  $p = .58$ ). For the insomniacs who had undergone 5 weeks of treatment, there was a significant decrease in the mean FFS and DFFS scores (FFS:  $t(58) = 5.67$ ,  $p < .0001$ ; DFFS:  $t(58) = 7.19$ ,  $p < .0001$ ), that continued to decline at 3 months ( $p < .02$ ). For samples 2 and 3, poor sleepers reported significantly greater fatigue and worse daytime functioning (both  $p < .0001$ ).

**Conclusion :** The Flinders Fatigue Scale and the Daytime Feelings and Functioning Scale are brief and reliable scales that distinguish between good and poor sleepers, and are sensitive to the effects of insomnia treatment.

**Support (optional):**

## 0992

### COMPARISON OF SLEEP ASSESSMENT DEVICES IN SLEEP APNEA AND INSOMNIA - FINAL REPORT

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**Introduction :** There is a paucity of data comparing alternative sleep methodologies such as actigraphy (ACT), sleep log (SL), and REMView™ (RV; Respironics, Inc.) with the "gold standard" of polysomnography (PSG). We compared the performance of these alternative devices against PSG for estimating common sleep parameters in sleep apnea and insomnia patients. This report updates our 2005 APSS abstract.

**Methods :** Participants were 98 (90 male) VA primary care outpatients undergoing screening procedures for an insomnia treatment study. They underwent one night of unattended ambulatory PSG, including an Actiwatch-64 actigraph (Mini-Mitter Co., Inc.) and the RV device. A sleep log was completed the following morning. These devices yielded estimates of time in bed (TIB), total sleep time (TST), total wake time (TWT), sleep onset latency (SOL), sleep efficiency (SE), and wake after sleep onset (WASO) that were subsequently compared to corresponding PSG-derived values.

**Results :** Pearson correlations between sleep devices and PSG showed moderate to high correlations for all sleep variables. Participants were divided into 3 groups based on their sleep diagnoses (34 sleep apnea, 35 primary insomnia, 29 insomnia comorbid with another active medical or psychiatric disorder). Group differences between PSG and the other devices were investigated using repeated-measures ANOVA with Dunnett's adjustment. In all 3 groups, SL and RV overestimated SOL while RV and AW underestimated WASO. AW overestimated TST and underestimated TWT. SL underestimated TST. In the apnea and comorbid

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insomnia groups, TIB was underestimated on SL. SE was overestimated by AW in the apnea and primary insomnia groups, but underestimated by SL in the primary and comorbid insomnia groups.

**Conclusion :** These data enhance our previous findings that alternative sleep devices provide reliable estimates compared to PSG, but the accuracy varies depending on the sleep parameter of interest and the diagnosis. Although for most sleep parameters the devices performed similarly among the three diagnostic groups, the accuracy of some sleep parameters, particularly TIB, varied by group.

**Support (optional):** Department of Veterans Affairs Health Services Research and Development Grant # IIR 00-091

### 0993

#### QUANTIFICATION OF INSPIRATORY AIRFLOW OBSTRUCTION USING A NOVEL LIGHT-WEIGHT FLOWMETER

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**Introduction :** Assessing degree of inspiratory airway obstruction is based on detection of airflow reductions during sleep. However, direct quantification of airflow during sleep is difficult because of the bulky, uncomfortable nature of current instrumentation (eg pneumotachograph). We tested the response characteristics for a prototype, light weight (1.5 grams), low dead space (~10cm<sup>3</sup>) flowmeter (Keytech, Baltimore USA) designed for polysomnography.

**Methods :** A polyester human face model, with patent nasal orifices, was instrumented with a nasal mask and flowmeter. Steady state, graded inspiratory airflows were generated through the model's nasal passages using: 1) an airflow generator and rotameter (0.05-0.4 L/sec, 6 runs); and 2) a human subject breathing through a mask and pneumotachograph (Fleisch #2) attached to the posterior nasal openings of the model (graded peak airflows of 0.02 to 0.5 L/sec). For subject generated breaths, sensitivity and specificity of the flowmeter signal for detection of a 50% reduction in airflow was determined.

**Results :** There was a highly significant ( $r^2 > 0.99$ ,  $P < 0.001$ ) linear correlation between flowmeter and rotameter values ( $0.44 \pm 0.10$  volts/L/sec, mean  $\pm$  SD for repeated runs). The flowmeter signal detected all reductions in peak inspiratory airflow with no false positives or negatives (ie sensitivity = specificity = 100%).

**Conclusion :** When tested in a model, the flowmeter exhibited linear response characteristics in relation to airflow, and high accuracy in the detection of reduced inspiratory airflow. The light weight flowmeter may facilitate breath-by-breath quantification of the level of inspiratory airway obstruction during polysomnographic studies. This novel approach will smooth the progress of phenotyping individuals based on the degree of inspiratory airflow obstruction.

**Support (optional):** NIH - HL72126, NHMRC - 353705

### 0994

#### A RETROSPECTIVE STUDY OF THE EFFICACY OF HOME OXIMETRY FOR SCREENING FOR OBSTRUCTIVE SLEEP APNEA IN BARIATRIC PATIENTS

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**Introduction :** There is a high prevalence of obstructive sleep apnea (OSA) in those undergoing bariatric surgery. Patients undergoing bariatric surgery with untreated OSA have high morbidity and mortality. The optimal method for screening for obstructive sleep apnea in pre-operative bariatric surgery patients is not known. Home oximetry is less sensitive and less specific than polysomnography for detecting obstructive sleep apnea, but is relatively cheap and is usually more convenient for the patient than polysomnography.

**Methods :** One of the authors (MJR), in his role as sleep consultant for the UMC bariatric surgery program, ordered preoperative home oximetry examinations (using Respironics 920M oximeters with PROFOX software version PFW 02/99) on a number of pre-operative bariatric surgery patients with the symptom of snoring and a low to moderate likelihood of OSA. The 14 adult patients who had home oximetry and bariatric surgery performed before 5/15/05 were included in this retrospective analysis. Home oximetry reports, sleep study reports, and surgery discharge summaries were utilized. Respiratory Disturbance Index (RDI), defined as the hourly rate of desaturation events of at least 4% severity and lasting at least 10 seconds, was determined for home oximetry.

**Results :** Six of the fourteen patients had oximetry examinations suggestive of OSA and therefore had baseline polysomnograms performed. Polysomnography confirmed the diagnosis of OSA in all six patients. There was a high correlation ( $R = 0.97$ ) between RDI and polysomnographically-determined AHI. These six patients underwent CPAP titrations prior to surgery, and CPAP was utilized during the perioperative period. The eight patients with relatively normal home oximetry examinations did not have further sleep evaluation prior to surgery. There were no major perioperative complications in any of the fourteen patients.

**Conclusion :** In a small group of preoperative bariatric surgery patients, overnight home oximetry was a safe and effective screening method for OSA.

**Support (optional):**

### 0995

#### DO AROUSALS DEMONSTRATE A FIRST NIGHT EFFECT?

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**Introduction :** The first night of laboratory sleep adversely affects sleep stages in what is known as the "first night effect". However, whether there is a first night effect on arousals in normal sleepers has never been examined. This study compared the number and frequency of arousals from the first three laboratory nights in normal sleepers.

**Methods :** Forty-nine normal young adults without sleep apnea or PLMS, ages 18-39, slept in the sleep laboratory for three baseline nights. Sleep and arousal data were scored by the same scorer for each night (comparable to clinical polysomnograms) and summarized by night.

**Results :** ANOVAs were performed on the data. On the first night there was a significant increase in wake and decrease in total sleep time compared to the second two nights, ( $p < 0.05$ ). This resulted in a significant decrease in sleep efficiency for the first night compared to the subsequent nights ( $p < 0.01$ ). On the first night there was also an increase in stage 1 ( $p < 0.1$ ), a decrease in REM ( $p < 0.05$ ), and more stage changes ( $p < 0.05$ ) compared to the next two nights. There was no difference in slow wave sleep or EEG arousals across the three nights. The mean number of EEG arousals for nights 1, 2 and 3 was 65, 68, and 64 respectively. Mean arousal index for each night was 8.8, 8.8, and 8.3 respectively.

**Conclusion :** This study replicated the first night effect typically report-

ed for sleep staging in normal subjects. As expected there was an increase in wake, stage 1, and number of stage changes with a decrease in REM. However, neither the number of EEG arousals, nor the arousal index showed significant differences between the first night and subsequent nights. This indicates that arousals, like SWS, are a very stable measure in normal subjects and do not demonstrate a first night effect.

**Support (optional):** Supported by the Department of the Army and the Sleep-Wake Disorders Research Institute.

## 0996

### THE CLAYTON DAYTIME FUNCTIONING SCALE: A NEW MEASURE OF FATIGUE AND SLEEPINESS

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**Introduction :** Daytime impairments are a common consequence of patients evaluated at a sleep center. Both hypersomnolence and fatigue are often reported, but can manifest from different causes. Unfortunately, there is no quick measure to evaluate both of these factors in a clinical sleep population. This is a preliminary report in the development of the Clayton Daytime Functioning Scale (CDFS) to assess these factors of daytime functioning.

**Methods :** From September-November 2005, 143 patients undergoing polysomnography completed the CDFS, the Epworth Sleepiness Scale (ESS) and the Fatigue Severity Scale (FSS). Demographic, PSG, and questionnaire data were maintained in a database. Patients were placed into one of the following groups: OSA (AHI > 15), EDS (AHI < 10, ESS > 10), and history of depression with no diagnosed sleep disorder. Patients not fitting the criteria for a given group were excluded. Thirteen healthy age-matched controls, who had no sleep complaints per a screening questionnaire, were used for comparison.

**Results :** A total of 86 patients were used for analysis: OSA = 28, EDS = 41, and Depression = 17. Using a one-way ANOVA, the CDFS global score, as well as the fatigue and sleepiness subscales, were able to discriminate between a normal and clinical group ( $p < .001$ ). Validity assessment was significant, correlating the fatigue subscale to the FSS ( $r = .77$ ,  $p < .01$ ) and the sleepiness subscale to the ESS ( $r = .72$ ,  $p < .01$ ). Reliability analysis was performed on 13 patients who returned for subsequent testing, resulting in a significant correlation for CDFS global score ( $r = .87$ ,  $p < .001$ ), fatigue subscale ( $r = .84$ ,  $p < .001$ ), and the sleepiness subscale ( $r = .88$ ,  $p < .001$ ).

**Conclusion :** Although further validation is needed, the CDFS may prove to be a valuable assessment tool for daytime functioning.

**Support (optional):**

## 0997

### TOTAL SLEEP TIME AND SLEEP LATENCY DERIVED FROM A SINGLE EEG CHANNEL COMPARED TO A FULL SLEEP MONTAGE

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**Introduction :** For accurate sleep staging at least 5 channels (2 x EEG, 2 x EOG, and EMG) are used, but with limited or ambulatory polysomnography it is uncommon for all 5 channels to be available. In the measurement of sleep disordered breathing, sleep onset and total sleep time are important measurements as they form the denominator in the calculation of the AHI. This study aimed to compare the total sleep time and sleep latency measured using a standard montage (C3-A2, C4-A1, LOC-A2, ROC-A1 and chin EMG) to using a single EEG lead (C3-A2).

**Methods :** 60 diagnostic studies (recorded using Compumedics E-Series) were selected randomly. To ensure that a range of severity of sleep disordered breathing was assessed, there were 20 studies with an AHI <5, 20 with AHI >5 and <30, and 20 with AHI >30. Each study was staged using both the standard montage and single EEG by the same sleep scientist. Studies were presented in random order and identifying information removed.

**Results :** Although in a small proportion of studies, signal quality was not optimal, all 60 studies were included in the analysis to best reflect clinical practice. The total sleep time was 3.21 (95% CI -0.53 to 6.94,  $p=0.09$ ) minutes longer, and sleep latency was 0.11 (95% CI -0.95 to 1.12,  $p=0.84$ ) longer when staged using a single EEG lead compared to standard montage. Overall there was  $93.5 \pm 3.8\%$  concordance in the ability to correctly identify sleep or wake across all studies.

**Conclusion :** Staging with a single EEG can be used to accurately determine wake versus sleep, total sleep time and sleep latency, and returns similar results to staging using a standard montage. The TST measured from a single EEG lead could then be used in the calculation of AHI when limited polysomnography devices utilising less than a standard sleep staging montage are used.

**Support (optional):**

## 0998

### NON LINEAR EEG FREQUENCY DYNAMICS DURING SLEEP ONSET

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**Introduction :** Inter-individual cognitive processes during sleep may influence sleep onset differently in individual sleepers. Therefore the dynamics of EEG during the sleep onset process were analyzed, while experimentally standardizing the cognitive processes during the sleep onset period. As the duration of the wake-sleep transition differs widely between individuals the analyses were normalized over time.

**Methods :** Twenty subjects (mean age = 22.1, SD = 3.6) were recorded with full PSG during the sleep onset process. An auditory oddball task was presented during the session where subjects had to respond to the deviant tones by pressing a button, strapped to the subjects' preferred hand. Sleep onset was defined as onset of the first sleep spindle. Spectral analysis was performed from Lights Off to 3 minutes after the first sleep spindle. The duration between Lights Off and the point of sleep onset were normalized over time to take the individual variance in duration of the sleep onset process into account.

**Results :** Power in the alpha- and theta band increased from Lights Off ( $p < 0.001$  and  $p < 0.0001$  respectively), whereas the power in the beta band showed a trend to decrease ( $p < 0.07$ ) until the point of Sleep Onset. The power in the delta band started to rise shortly before Sleep Onset. MANOVA analysis of the relative contribution of the various frequency bands to the changes around the point of Sleep Onset revealed that at that point the relative contribution of the frequency bands became different ( $p=0.00$ ). This was mainly caused by a difference in contribution of the lower and higher frequency bands, where the power in the theta band remained high and the power in the alpha band decreased.

**Conclusion :** The data from the spectral analysis showed that the sleep onset process is continuous until the onset of sleep. In addition, alpha and theta band showed a synchronous asymptotical increase from 3 bins before Sleep Onset, The power in theta band showed a plateau after Sleep Onset and the power in the alpha band decreased, indicating an increasing synchronization of EEG activity.

**Support (optional):**

0999

**EFFECT OF EXHALATION UNLOADING ON SHORT-TERM COMPLIANCE ON CPAP PRESSURES +10 CMH2O OR GREATER A RANDOMIZED, CROSSOVER, SINGLE-BLINDED, DUAL-CENTER TRIAL**

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**Introduction :** SoftX (PolarisEX CPAP - Invacare, Elyria, OH) is a form of exhalation unloading (EU) that may allow more comfortable transition to exhalation during CPAP. This study was conducted to determine the effect EU has on CPAP compliance for pressures of  $\geq +10\text{cmH}_2\text{O}$ .

**Methods :** Two patient groups were provided CPAP with standard and EU conditions in a single-blinded, simple crossover design. Group-1 utilized therapy for 2-weeks in standard mode followed by 2-weeks with EU. Group-2 utilized therapy for 2-weeks with EU followed by 2-weeks in standard CPAP mode. All participants were CPAP naïve and utilized a heated humidifier. The study measured average minutes of use per night. Of the 55 patients recruited, 44 completed both phases of the study. 7 patients required interface changes, 2 requested EU be re-engaged during the standard trial and 2 patients could not be located for follow up.

**Results :** Analysis was conducted using 2-tail t-statistic. CPAP initiated with EU demonstrated, average nightly usage increased by an average 44 minutes per night compared to therapy in the standard mode ( $p=0.028$ ). When EU was utilized following a two-week trial of standard CPAP the average nightly use increased by 11.5% ( $p < 0.01$ ). When EU was replaced by standard CPAP the average use decreased by 4.1% ( $p=0.011$ ), however the duration of use remained, on average, 30 minutes (~10%) higher than when standard CPAP was the initial form of therapy.

**Conclusion :** Many patients find CPAP uncomfortable, particularly at higher pressures, which may adversely effect compliance. This study suggests that EU results in improved therapy compliance. Additional investigation may prove beneficial to validate these preliminary findings on EU.

**Support (optional):**

1000

**A PRELIMINARY ASSESSMENT OF THE UTILITY OF FMRI TO DIFFERENTIATE EARLY AND LATE STAGE-1 SLEEP**

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**Introduction :** Sleep onset is a heterogeneous process. Several areas of the brain exhibit a decrease in activity while others exhibit an increase and these changes are not stable across time. These processes cannot be properly characterized by a single sleep stage. This research examined the possibility that Functional Magnetic Resonance Imaging (fMRI) could identify differences in brain activity during epochs of Stage-1 at different time points within the sleep cycle.

**Methods :** Data for this research were obtained across two runs from 02:00-05:00 in a single participant without any prior sleep deprivation. EEG data were obtained using MRI-compatible equipment (BrainAmpMR, Brain Products, Munich) and fMRI data were obtained using a 3-Tesla scanner (Signa Excite HDx, GE Healthcare, Milwaukee). fMRI data were collected using a repetition time of 3s and sleep was scored from the EEG alone using standard criteria with 12-s epochs. Periods were identified that began with >30s of continuous Wake, were followed by >3 minutes of continuous Stage-1, and ended with >30s of continuous Stage-2. The fMRI analysis then contrasted the volumes during the first 90s of Stage-1 and last 90s of Stage-1 with volumes obtained

during continuous Wake.

**Results :** When comparing early to late Stage-1, increased activity ( $p<8.3E-7$ ) that was evident in the anterior and posterior lobe of the cerebellum shifted inferiorly to the nodule. Decreases in the posterior lobe of the cerebellum became more pronounced. Thalamic activity showed differences related to early and late Stage-1. Increases in the left hippocampus became less pronounced. Increases and decreases in the occipital lobe were no longer present.

**Conclusion :** While the interpretation of the specific changes in activity are difficult to generalize from a single participant, the changes themselves highlight the utility of fMRI to differentiate and further subdivide stages of sleep that would otherwise be grouped together based on standard EEG criteria.

**Support (optional):** DP is supported by the National Academy of Sciences-National Research Council Postdoctoral Research Associateship Program.

1001

**RELATIONSHIP BETWEEN MSLT-MWT AND DRIVING SIMULATOR PERFORMANCE IN OSAS PATIENTS**

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**Introduction :** There is an increasing interest in evaluating OSAS patients' driving ability because of the medico-legal implications concerning driver licensing. We previously designed a monotonous Driving Simulation Task (DST) (STISIM 300) able to evaluate sleepiness in healthy subjects (1,2). Aim of this study was to correlate our DST with standard vigilance test (MSLT, MWT) in OSAS patients.

**Methods :** We studied 12 OSAS pts, (11 m, 1 f), age=51.8±8 yrs, RDI=52.6±16.5, ESS score =10±2.7. The patients underwent, during 2 days randomly assigned, four 20-minute MSLT trials and four 40-minute MWT trials, each one followed by 30-minute DST. Subjects were instructed to drive in the right-hand lane respecting the speed limits and to attend to a secondary task (Divided Attention, DA). DST data included: mean and standard deviation (SD) of midline, mean and SD of Reaction Time (RT) at DA, incorrect response to DA (DA index), speeding and crash frequency. These data were analysed with one-way ANOVA and related to the sleep latencies (SL) at each trial of MSLT and MWT with Pearson's correlations ( $p<0.05$ ).

**Results :** The SL at the MSLT trials correlated with crashes ( $\hat{U}=-0.337$ ) and SD midline ( $\hat{U}=-0.458$ ) while the SL at the MWT trials correlated with crashes ( $\hat{U}=-0.389$ ), SD midline ( $\hat{U}=-0.594$ ), DA index ( $\hat{U}=-0.549$ ) and mean RT ( $\hat{U}=-0.577$ ). We appreciated a small learning effect between the two days for DA and speeding, but any significant difference across the day.

**Conclusion :** Our DST correlates with standard objective tests of vigilance, mainly with MWT, and may be useful in evaluating driving performance decrements related to sleepiness in OSAS patients.

**Support (optional):**

1002

**THE "BASIS" QUESTIONNAIRE, A NEW OUTCOMES MEASUREMENT TOOL**

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**Introduction :** The BASIS (Behaviors and Symptoms Impacting Sleep) Questionnaire is a 95 item instrument developed for the purpose of measuring clinical outcomes in sleep medicine. Each item is a proposition representing symptoms or situations that may be encountered by patients in

a sleep disorders clinic (e.g., "difficulty getting up in the morning", "sleepiness makes it difficult to drive"). Answers are rated categorically in the frequency domain (N=never, S=seldom, O=occasionally, F=frequently, D=daily, NS=not sure). Each frequency choice has a corresponding numerical value (N=0, S=1, O=2, F=4, D=8). "Not sure" answers are excluded from analysis. Answers are clustered into domains of function (Sleepiness, fatigue, depression, anxiety, irritability, motor function, breathing, environmental factors, sleep hygiene, somatic factors, pain, global impression of sleep quality). Each domain is then normalized to a score between 0 (worst) and 100 (best).

**Methods :** We administered the BASIS as part of a health screening at a Seattle, WA shopping mall. A total of 780 responses were obtained. Participants were offered a small stipend to complete the questionnaire. They were not informed about the content or subject of the questionnaire in advance to avoid selection bias. Questionnaires took on average 10 - 20 minutes to complete. Scoring was computer aided, taking 2 - 3 minutes per questionnaire.

**Results :** Domain scores had excellent internal consistency (Cronbach's alpha values ranged from 0.88 to 0.92). Domain score frequency distributions were primarily exponential in shape except for the sleepiness domain, which was best fit by a log normal distribution. Population norms were derived from the subset of respondents in the top 20% of the global impression of sleep quality domain and are presented.

**Conclusion :** The BASIS questionnaire is a useful alternative to currently available sleep outcomes instruments such as the FOSQ. It is rapidly completed, easily scored, has excellent internal consistency and encompasses a wide range of human function pertaining to sleep and wakefulness.

**Support (optional):**

### 1003

#### NOCTURNAL 12-CHANNEL DIAGNOSTIC ECG TO DETECT MORPHOLOGICAL CHANGES IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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**Introduction :** Cyclical variability of heart rate is a specific pattern occurring with obstructive sleep apnea. This pattern is so characteristic that it has been used for the early recognition of obstructive sleep apnea by ambulatory recording systems which aim to detect sleep apnea with a reduced set of signals. Several studies could show that advanced methods to analyze heart rate variability can detect sleep apnea with a high degree of confidence. Whether heart rate variability analysis is still valid in patients with autonomic dysfunction and in patients with central sleep apnea remains to be unclear.

**Methods :** We investigated 95 consecutive patients with obstructive sleep apnea with cardiorespiratory polysomnography and a parallel diagnostic 12-channel ECG. The validated ECG system was modified in such a way that it could record continuously 12 channels. After the recording a full ECG analysis with 250 ECG parameters per heart beat was undertaken. For subsequent correlation with the respiratory PSG signals only five parameters were chosen. These were heart rate, normalized R-wave amplitude, QRS-wave amplitude, area under the QRS wave, and QRS vector angle.

**Results :** For 56 patients valid ECG and parallel recordings were obtained. Mean AHI was 23 events per hour. The five parameters did show periodic variations in parallel with apnea and hypopnea events as detected by the polysomnography. To quantify further these periodic variations a Fast Fourier analysis was applied to all five signals. Thereafter a threshold was applied in order to classify minutes of normal breathing and

minutes with disordered breathing. The derived minutes with disordered breathing were correlated with the total number of apnea events. The heart rate based comparison resulted in a correlation of  $r=0.64$  ( $p<0.01$ ) and the area under the QRS wave resulted in a correlation of  $r=0.61$  ( $p<0.01$ ) being the two best parameters.

**Conclusion :** During sleep apnea not only heart rate shows characteristic changes with obstructive sleep apnea but also the ECG waveform changes with sleep apnea. This was confirmed by the cyclic variations in the ECG morphology parameters. The ECG waveform changes detected here persist in patients with autonomic dysfunction and possibly in central sleep apnea. The waveform changes may be attributed to intrathoracic pressure changes during obstructive sleep apnea.

**Support (optional):** This study was supported by a grant from the Bavarian States Foundation project entitled "Sleep-Home-Monitoring"

### 1004

#### PICKING REM FROM THE FINGER - FURTHER IMPROVEMENT OF THE ALGORITHM USING AN ADVANCED PREDICTING FUNCTION

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**Introduction :** REM sleep is associated with a tonic attenuation of the peripheral arterial tone (PAT) with superimposed phasic vasoconstrictory events. This unique pattern coupled with actigraphy sleep-wake detection was the base for a REM detection algorithm previously described. The present study further improved %REM, REM periods and epoch-by-epoch total agreement.

**Methods :** The PAT signal measured by the Watch\_PAT 100 (Itamar-Medical Ltd, Caesarea, Israel) and PSG were simultaneously recorded in 30 patients (training set) stratified into 3 groups of mild (M/F: 5/5, age:  $39.1\pm 15.3$ ), moderate (M/F: 8/2, age:  $47.9\pm 14.7$ ), and severe (M/F: 8/2, age:  $53.3\pm 11.5$ ) obstructive sleep apnea (OSA). Each sleep record was divided into 5-minute intervals where two time-series were constructed from the PAT signal amplitudes and inter-pulses periods. A set of variables was derived from these time series: PAT amplitude, pulse rate, fractal exponent of the PAT amplitudes and pulse rate, various spectral components of the PAT amplitude and pulse rate and their ratios. Based on these variables, a REM predicting equation was calculated every 30-sec epoch. The prediction was optimized in the training set using Genetic algorithms and then tested on an independent validation sample of 30 patients with similar characteristics.

**Results :** The sensitivity/specificity and overall agreement of the algorithm in identifying epochs of PSG defined REM in no-mild, moderate and severe OSA were 67%/93%/88%, 76%/95%/92% and 65%/95%/91%, respectively. The algorithm slightly over estimated %REM by  $5.0\pm 6.7\%$  and number of REM periods by  $0.7\pm 1.2$ .

**Conclusion :** This REM prediction in OSA patients enhances the diagnostic capability of an unattended hand-mounted device, by providing the physician in addition to the OSA severity its effect on gross sleep architecture.

**Support (optional):** This is an industrial supported study financed by itamar-Medical Caesarea Ltd, Israel.

### 1005

#### VALIDATION OF A SELF-APPLIED UNATTENDED MONITOR FOR SLEEP DISORDERED BREATHING (SDB)

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**Introduction :** Increasing appreciation of SDB has prompted evaluation of unattended monitoring to help with the large numbers of undiagnosed patients. Prior work found good agreement between an unattended ARES Unicorder (ABM, Carlsbad CA) with automated scoring (using saturation plus behavioral indices of arousal) and in-lab NPSG. An airflow signal (nasal cannula) has recently been added to the analysis. The present study evaluates validity of this in-home monitor and algorithm for assessing AHI.

**Methods :** 47 subjects were enrolled. 40 completed both in-lab and in-home evaluations: 13 asymptomatic volunteers (8M/5F, age 19-73, BMI 19.5-27.1kg/m<sup>2</sup>); 27 patients with symptoms of EDS and/or snoring (22M/5F, age 27-74 yr, BMI 23.4-43.6 kg/m<sup>2</sup>). The ARES Unicorder was used 2 nights at home with only written instructions to guide application. Within 2 weeks, a simultaneous in-lab NPSG and in-lab ARES recording were performed. NPSGs were scored manually for sleep and respiratory events, using the AASM criteria, which include apnea, hypopnea and RERAs (Sleep 1999). ARES studies were autoscored to calculate an equivalent index. For both, AHI>15 events/hr defined significant SDB.

**Results :** For simultaneous recordings, the sensitivity of the ARES compared to NPSG was 100% (25/25 patients) and specificity 67% (10/15 subjects). For the 5 false-positives, AHIARES was 7.2±2.7/hr greater than AHINPSG. Sensitivity for the in-home ARES study compared to the NPSG was 96%; specificity was 80%. Across all subjects AHIARES in-home averaged 8.4/hr lower than AHIARES in-lab, with ICC 0.68.

**Conclusion :** In-home monitoring with the new ARES Unicorder provided similar information about SDB as the in-lab NPSG. The addition of a flow signal led to detection of events without desaturation that might have been missed by the previous version, allowing closer approximation to standards proposed by AASM. Thus, if AHI is the metric used for triage of SDB, in-home monitoring with the ARES Unicorder may be an appropriate substitute for full in-lab NPSG.

**Support (optional):** NCRR M01RR00096, Advanced Brain Monitoring, Foundation for Research in Sleep Disorders

### 1006

#### NOVEL SCALE MEASURING BOTH SLEEPINESS AND FATIGUE

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**Introduction :** Fatigue and sleepiness are easily confounded symptoms. Fatigue is gradually being recognized as a significant complaint whereas, excessive daytime sleepiness is a well-known symptom of many sleep disorders. It is desirable to differentiate between the two symptoms. Current scales assessing sleepiness and fatigue do not permit a simultaneous comparison due to differences in the measurement properties.

**Methods :** We devised a 31-item Likert scale with 2 sets of separate yet simultaneous assessments for fatigue and sleepiness. 26 controls and 114 sleep-disordered patients completed the scale. Subsequently, the scale was reduced to 10 questions by eliminating questions unanswered by more than 25% of respondents and items with item-total correlations > 0.8 or < 0.2. The Epworth Sleepiness Scale (ESS) was compared to the sleepiness subscale of this questionnaire and the Fatigue Severity Scale (FSS) to the fatigue subscale. Cronbach's alpha was computed for scale reliability.

**Results :** Fatigue and sleepiness symptoms correlated highly ( $r = 0.65$ ,  $p = 0.001$ ) on the scale for the controls, and the patient group ( $r = 0.75$ ,  $p < 0.001$ ). Correlation for the fatigue component was moderate with FSS ( $r = 0.54$ ,  $p = 0.010$ ) and low with ESS for the sleep component ( $r = 0.30$ ,  $p$

$= 0.163$ ) for the controls, but moderate ( $r = 0.54$ ,  $p < 0.001$ ;  $r = 0.61$ ,  $p < 0.001$ , respectively) for the patient group with FSS and ESS. Cronbach's alpha was 0.81 for the sleepiness subscale in the controls and 0.73 for the fatigue subscale, and  $r = 0.80$  and  $r = 0.81$  for the patient group for the sleepiness and fatigue subscales, respectively.

**Conclusion :** Fatigue and sleepiness may have partial overlap but are not identical phenomena and thus require independent assessments. Distinguishing these symptoms is important as their etiology and treatment may differ. This novel scale will provide insight into the relationship between sleepiness and fatigue.

**Support (optional):**

### 1007

#### ACTIGRAPHY EVALUATION OF SLEEP PRECEDING MULTIPLE SLEEP LATENCY TESTING

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**Introduction :** Evaluation of excessive daytime sleepiness (EDS) relies on obtaining an accurate sleep history and may require formal laboratory studies, including multiple sleep latency testing (MSLT). Sleep latency is influenced by prior sleep quality, quantity and timing, as well as clinical disorders such as obstructive sleep apnea. Current AASM guidelines mandate an overnight polysomnogram (PSG) prior to the MSLT in order to rule out sleep disorders and ensure at least 6 hours of sleep. Unfortunately, this does not preclude the possibility of accumulated sleep debt. For this reason, we use actigraphy in addition to a sleep diary to better assess sleep patterns and quantity 14 days prior to performing an MSLT.

**Methods :** We retrospectively reviewed the records of 54 patients who had undergone actigraphy monitoring prior to laboratory evaluation (PSG and MSLT) in the past two years. Actigraphy data were compared with patient diary entries and sleep data collected during the PSG.

**Results :** Demographic data was as follows: age 30.7 +/- 10.3, gender (45 M, 9 F), ESS 16.2 +/- 4.7. Average sleep time measured by actigraphy during the two weeks prior to the PSG/MSLT was 333 +/- 89 min. This was considerably less than patient diary recorded sleep (419 +/- 50 min,  $p < 0.001$ ) for the same period. It was also significantly less than sleep time in the laboratory measured by either actigraphy (425 +/- 84 minutes,  $p < 0.001$ ) or PSG (442 +/- 39 minutes,  $p < 0.001$ ).

**Conclusion :** Our findings suggest that chronic partial sleep deprivation is common in patients referred for an MSLT. Although history and sleep diary entries are important parts of the evaluation for EDS, they are insufficient for some patients. Actigraphy may provide a clinically useful measure of pre-MSLT sleep that reduces the likelihood of misdiagnosing accumulated sleep debt as a sleep disorder.

**Support (optional):**

### 1008

#### DEVELOPMENT OF A BRIEFER VERSION OF THE PSYCHOMOTOR VIGILANCE TASK

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**Introduction :** The 10-minute psychomotor vigilance task (PVT) was developed by Dinges and Powell (1985) and extensively validated to be

sensitive to alertness from sleep loss. We developed a special 3-min. PVT based on analyses of the effects of varying inter-stimulus intervals (ISI) on PVT performance, and performed an experiment to determine the relationship between the two.

**Methods :** N=12 healthy adults completed a 10-min. PVT every 2h during a 38h period of wakefulness. A 3-min. PVT (with unique ISI) was completed 5 min. before each 10-min. PVT. The following variables were analyzed from each PVT test: speed (1/RT); number of lapses; fastest RTs; slowest responses (1/RT); median RT; and post-PVT visual analog scales (VAS) for fatigue. Pearson correlations were calculated within each of the 12 subjects across the 38-hour period of wakefulness to evaluate the concordance of the 3-min. and 10-min. PVTs.

**Results :** Average correlation coefficients (across subjects for each outcome variable) between the 3-min. and 10-min. PVT tasks were 0.79 (mean speed [1/RT]), 0.66 (number of lapses), 0.68 (mean slowest 1/RT), 0.56 (median RT), 0.46 (mean fastest RTs), and 0.58 (mean post-test VAS). In 8 of the 12 subjects (75%) the average coefficient between the two PVT versions was between 0.81 and 0.93.

**Conclusion :** These results provide evidence that response speed on the 3-min. PVT tracked variations in alertness over time nearly as well as the standard 10-min. PVT. Further improvements in sensitivity of the 3-min. PVT are underway.

**Support (optional):** Federal Aviation Administration, grant # 04-G-010

## 1009

### DESIGN AND ANALYSIS FOR THE SIMULTANEOUS ESTIMATION OF INTRA- AND INTER-SCORER AGREEMENT OF SLEEP STAGING

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**Introduction :** Quality control for large sleep studies requires on-going monitoring of scoring agreement. Current approaches for assessing agreement are limited by only assessing inter-scorer agreement with no consideration for intra-scorer agreement. By chance alone a scorer can have measures of agreement with themselves less than agreement with other scorers. By restricting inter-scorer by intra-scorer agreement, agreement estimates for sleep staging are more accurate. Our objectives were to develop an approach for measuring agreement across multiple scorers and examine staging score shift in the quasi-ordinal sleep staging scale that overcome these limitations.

**Methods :** Twenty studies were selected at random from the Outcomes of Sleep Disorders in Older Men (MrOS Sleep Study) Study. Five sleep technologists scored each study twice, separated by  $\geq 1$ -2 weeks. The Kappa statistics and transformations of the odds ratio (OR) are used to describe agreement of 5 epoch-by-epoch comparisons; (1) wake vs. sleep, (2) Stage (S) 1 vs. S2/Delta/REM, (3), S1-2 vs. Delta/REM, (4) S1-2 vs. Delta, (5) S1-2 vs. REM. For each comparison intra-scorer agreement is bounded below by inter-scorer agreement. The order-restricted global OR measures are estimated using generalized log-linear models. Since the 30-second epochs are not independent intervals, a subset was systematically chosen.

**Results :** Technologists demonstrated an overall high agreement with themselves, with poorest agreement for differentiating S1 from deeper stages. Similar results were observed for pairwise inter-scorer agreement. Examining scorer shift provided further evidence for differentiating S1 from S2. One bounding violations occurred in the comparison of S1-2 vs. Delta.

**Conclusion :** These methods of simultaneously estimating intra- and inter-scorer agreement provide conservative estimate for quantifying scorer agreement and identifying specific sources of scorer variability.

Implementing such scoring agreement assessments are useful for directing retraining efforts and for understanding which indices are most reliable for epidemiological analyses and clinical assessments.

**Support (optional):** MrOS Sleep Study is supported by the NHLBI (R01 HL071194, R01 HL070848, R01 HL070847, R01 HL070842, R01 HL070441, R01 HL070837, R01 HL070838, and R01 HL070839).

## 1010

### PHARYNGOMETRY AND THE DEVELOPMENT OF A CLINICAL ASSESSMENT TOOL TO PREDICT SLEEP DISORDERED BREATHING

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**Introduction :** Upper airway anatomy influences susceptibility to sleep disordered breathing (SDB). However, the role of simple assessments of pharyngeal dimensions, such as pharyngometry, in the assessment of SDB has not been defined. Our objectives were to assess the association between pharyngometry measures and SDB and develop a clinical tool for determining the likelihood of SDB.

**Methods :** Analyses were based on 210 European American participants ages > 14 yrs from the Cleveland Family Study with  $\geq 2$  reproducible pharyngometry curves. Acoustic pharyngometry was performed sitting, awake. Pharyngometry measures included minimum (minCSA) and maximum cross-sectional area, and fractional distance along the airway at which maxCSA occurred (FrcmaxCSA). SDB was defined as a respiratory disturbance index  $\geq 5$  events/hour. Logistic regression and receiver operating characteristic (ROC) models included adjustments for traditional risk factors (age, sex, body mass index (BMI), snoring), with and without inclusion of pharyngometry measures. The final model was expressed as a nomogram, a graphical tool that can be used in a clinical setting.

**Results :** Subjects were 44( $\pm 19$ ) years, 45% male, 58% snorers, 32 kg/m<sup>2</sup>( $\pm 8.3$ ) and 46% had SDB. BMI (odds ratio(OR)=1.12 per kg/m<sup>2</sup>) and age (OR=1.06 per yr) were significantly associated with SDB, and male snorers (OR=4.5) were significantly at increased likelihood of SDB compared to female non-snorers. The addition of pharyngometry measures increased the area under the ROC curve (0.839 vs. 0.864, p=0.05), implying that they contributed to the correct classification of SDB. At minCSAs < 1.4 cm<sup>2</sup>, a linear increase in likelihood of SDB was observed with decreasing minCSA (p<0.0001). FrcmaxCSA was also significantly associated with SDB (OR=1.6 per 0.2 units).

**Conclusion :** Consideration of pharyngometry improved prediction of SDB over common clinical data. Specifically, pharyngometry improved classification in individuals with small minCSA or large FrcmaxCSA, many of whom would have been classified as unaffected by routinely available data.

**Support (optional):** NIH HL 46380 and GCRC M01RR00080

## 1011

### PATIENT-REPORTED OUTCOMES FOR SLEEP/WAKE FUNCTIONING IN THE NIH ROADMAP PROMIS INITIATIVE: ITEM BANKING AND PRELIMINARY PROGRESS

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**Introduction :** The PROMIS (Patient-Reported Outcome Measurement Information System) Network is an NIH Roadmap initiative. It is a multi-institution collaborative effort to develop outcome measures for computerized testing that will integrate the assessment of physical, emotional,

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and social functioning in future NIH-funded clinical trials. We report here on initial progress with the sleep/wake functioning component of PROMIS, which is a Pittsburgh site-specific project.

**Methods :** A comprehensive set of literature search terms were developed by a professional librarian. An electronic system of voting on these terms by psychiatric and sleep professionals helped to refine these terms. With them, 535 potential citations that contained sleep-related questionnaires were identified as potentially containing psychometric data. In parallel, collaborative discussions were organized to specify all relevant sleep/wake functioning domains.

**Results :** After review, 126 literature citations were examined, with 71 retained, with additional questionnaires added from other sources. A total of 2,529 questionnaire items were item-banked, but reduced to 1660 after redundancies were removed. Consensus emerged for 17 domains of interest (quality, onset, duration, continuity, offset, rhythms, causes, beliefs, habits, sleepiness, consequences, dreams, breathing, movements, parasomnias, energy, and insomnia). After classification of the questionnaire items into these 17 domains, the collection was initially winnowed to 310 items, and rewritten to conform to network specifications for sentence form (first person, past tense) and 5th-grade vocabulary level.

**Conclusion :** Further winnowing is planned before planned focus group testing, cognitive interviews and item-response testing can proceed. However, this effort demonstrates the utility of using item-banking and winnowing methods for sleep/wake functioning items. This effort will make it possible to study item functioning against non-sleep domains using integrated item-response theory (IRT) methods, and enable the clarification of the role sleep/wake functioning has in other domains of functioning.

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### 1012

#### AUTOMATED & MANUAL POLYSOMNOGRAPHY FROM REDUCED SENSOR SET

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**Introduction :** Standard PSG is typically performed by analyzing EEG, EOG, EMG, ECG, SpO<sub>2</sub> and respiration. Acquiring these signals in a regular hospital bed is cumbersome and difficult. Therefore, a new manual and automatic analysis of a reduced signal set including respiration, ECG and SpO<sub>2</sub> was assessed.

**Methods :** 50 SDB patients were simultaneously monitored with: 1.) ALICE-5 PSG system with a full standard montage, and 2.) DASH-4000 bed side monitor (BSM), acquiring respiration, ECG and SpO<sub>2</sub>. The data were partitioned into: 1.) a training set of 20 patients and 2.) a validation set of 30 patients. Manual scoring of PSG studies (M\_PSG), performed by PSG technologist, included R&K sleep staging, arousal and PLMS scoring according to ASDA criteria and respiratory event scoring according to Medicare criteria. Manual and automatic scoring of BSM studies using NOGA system, denoted by (M\_NOGA) and (A\_NOGA), respectively, included classification of wake/sleep and respiratory event scoring. Automatic analysis is based on respiration and heart rate complexity analysis and respiration signal envelope estimation and segmentation.

**Results :** Since the validation set is not complete, only training set is presented. Agreement and Cohen's Kappa are tabulated using: (a) sleep stages epoch by epoch agreement matrix (2x2: Wake, Sleep), (b) respiratory event epoch by epoch agreement matrix (3x3: 0, 1, 2 events/epoch) for M\_NOGA-M\_PSG and A\_NOGA-M\_PSG pairs. Measurements of M\_PSG, M\_NOGA and A\_NOGA included (mean±standard deviation): total sleep time (min) 299.8±88.9, 318.6±92.2, and 329.1±98.3, sleep latency (min) 23.5±21.7, 17.3±18.2, and 13±18.6, and RDI 22±31.1,

22.7±29.9, and 20.4±28.2, respectively. The agreement and Cohen's Kappa between M\_NOGA-M\_PSG and between A\_NOGA-M\_PSG were 89%&0.67, 82%&0.48 for the sleep stage agreement matrix and 96%&0.86, 94%&0.76 for the respiratory agreement matrix, respectively.

**Conclusion :** Results prove the feasibility of automatic and manual screening of respiration and sleep using a reduced sensor set that is practical in the hospitalized patient. Performance analysis of the validation will follow.

**Support (optional):** This research was sponsored by WideMed Ltd., Herzliya, Israel and by GE-HealthCare Milwaukee, WI, USA.

### 1013

#### THE PREVIOUS NIGHT SLEEP INVENTORY (PNSI): A USEFUL AND COST-EFFECTIVE SELF-RATING TOOL IN RELATION TO DAYTIME SOMNOLENCE AND PERFORMANCE TESTING

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**Introduction :** To measure the validity of the PNSI questionnaire as an effective quantitative subjective scale assessing previous night's sleep by examining its relationship to subjective and objective measures of sleepiness during a driving simulation task.

**Methods :** 45 subjects (25 M, 20 F) participated; 21 healthy ("Normals"), 24 patients diagnosed with excessive daytime sleepiness ("Drowsers"). Subjects were administered PNSI questionnaire and Stanford Sleepiness Scale (SSS) before a 30-minute simulated driving test with continuous EEG recording. Five reliable measures: crash frequency, reaction time, SSS, and microsleep episodes were recorded. Scores were rated as mildly (6-10), moderately (11-14), or severely (15-20) disturbed sleep.

**Results :** Pearson correlation tests showed a significant correlation between the PNSI and mean number of crashes ( $r=0.316$ ,  $p=0.034$ ), mean reaction time (RT) ( $r=0.262$ ,  $p=0.082$ ), mean SSS ( $r=0.320$ ,  $p=0.032$ ), and mean Microsleeps ( $r=0.342$ ,  $p=0.035$ ). This indicates an association between elevated scores on the PNSI and multiple driving performance measures as well as EEG evidence of sleep intrusion. In comparing PNSI results between normal subjects and Drowsers gave an expected lower mean PNSI score for normals ( $3.09\pm 2.51$ , SD error mean= 0.55) than Drowsers ( $7.66\pm 3.03$ , SD error mean=0.62). This demonstrates that the PNSI adequately measures differing sleep quality of healthy patients and Drowsers.

**Conclusion :** The PNSI appears to be a useful quantitative scale to assess sleep duration and quality on the night prior to driving performance testing. While we continue to recommend overnight polysomnography prior to daytime and performance tests as a gold standard, for research purposes the PNSI seems to be an effective and cost-effective screening tool in assessing the pathology/normalcy of previous night's sleep.

**Support (optional):**

### 1014

#### USE OF THE SF36V2™ IN A CLINICAL SLEEP PRACTICE

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**Introduction :** Our Sleep Disorders Center began utilizing the SF36v2™ in a clinical setting to ascertain if we were having an impact on our patient's lives. All patients were given the questionnaire, regardless of their sleep complaint. The SF36v2™ is divided into 8 subscales and 2 composite scales. It has been standardized with a rating in each subscale or composite of 50 being the norm. A deviation of 10 points in either



direction is approximately equal to 1 standard deviation.

**Methods :** The questionnaire was given to all patients prior to seeing the Sleep Physician (RDS). The same questionnaire was repeated at least 3 months later. This is an initial report on 161 patients with baseline and follow-up surveys with a separation of at least 90 days between questionnaires.

**Results :** Initially, on average, our patients scored below the norm in all subscales and composites. The follow-up surveys indicated many of our patients improved in some subscales and composites, although the ratings remained below the 50th percentile. Statistically significant improvements were noted in the following scales: Role Physical, Bodily Pain, Vitality, Role Emotional, Mental Health, and Mental Component Summary. For this group of patients, the percentage of those showing improvement varied from a low of 35% in Social Functioning, to a high of 68% in Vitality. Overall, 60% of the patients improved in the Physical Composite Scale, and 65% improved in the Mental Composite Score.

**Conclusion :** The SF36v2™ is useful in a clinical sleep medicine practice. We are able to track changes in the individual patient's quality of life as we diagnose and treat their various sleep disorders. This approach may help tailor treatment plans based tracking changes in this survey instrument.

**Support (optional):**

## 1015

### ALTERNATIVE NON-INVASIVE METHOD TO MONITOR RESPIRATION DURING SLEEP

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**Introduction :** Standard and partial sleep studies include recording of respiration signals essential for diagnosis of breathing disorders. Noninvasive methods for respiratory evaluation include measurement of oronasal flow, nasal pressure, abdominal and chest effort. These methods are cumbersome and their reliability is limited. Additional non-invasive, cost effective, reliable methods are required to evaluate respiration during sleep. We aimed at evaluating respiration by deriving it from the robust ECG signal.

**Methods :** Data from 36 standard whole night sleep studies with ECG digitized at 200Hz, nasal-flow, chest and abdomen effort at 10 Hz were analyzed. ECG derived respiration (EDR) was based on 3 methods based on: (i) R-Wave Amplitude (RWA), (ii) R-Wave Duration (RWD), (iii) QRS-Area. The extracted series resulted in time series proportional to the standard respiration signals. Fourier transform for unevenly sampled data was used to extract EDR frequency from these series and compared to the frequencies calculated from the recorded respiratory signals. Spline interpolation was used for EDR frequencies obtained from the three used methods, and the results were correlated to the respiratory signals and averaged over all subjects. Next, changes in EDR during apnea events were checked. To characterize respiration in different states, the dispersion of breathing rate was calculated for wake, Non-REM and REM.

**Results :** The averaged correlation between the extracted EDR frequency and the respiratory frequency calculated from Flow-Air was:  $0.88 \pm 0.07$ ,  $0.87 \pm 0.07$ ,  $0.88 \pm 0.07$  for RWA, RWD, and QRS-Area respectively, with Thorax frequency was:  $0.87 \pm 0.07$ ,  $0.84 \pm 0.07$ ,  $0.85 \pm 0.08$  for RWA, RWD, and QRS-Area, and with Abdomen:  $0.91 \pm 0.07$ ,  $0.90 \pm 0.06$ ,  $0.91 \pm 0.06$  for RWA, RWD, and QRS-Area. During Obstructive Sleep Apnea (552 events) the peak-to-peak amplitude of the breathing signal decrease by 58% in RWD, 57% in RWA, and 59% in QRS-Area. During central apnea (351 events) it decrease by 57% in RWD, 63% in RWA, and 68% in QRS-Area. The respiration-rate dispersion was calculated based on STD. The averaged ratio of REM/Non-REM shows a 30% increase, and the ration of Wake/Non-REM a 60% increase.

**Conclusion :** EDR can be used to extract respiratory frequency during sleep. Apneas can be detected by means of EDR. The respiratory instability during REM can be detected by EDR. Thus ECG can supply an inexpensive diagnostic tool for sleep analysis.

**Support (optional):**

## 1016

### REPEATED ADMINISTRATION OF THE EPWORTH SLEEPINESS SCALE INCREASES THE SCORE

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**Introduction :** The Epworth sleepiness scale (ESS) is a validated questionnaire for estimating daytime sleepiness. Episodic autobiographical memory may take time to be recalled. Repeated administration of a questionnaire may yield a different answer on the second time. We tested the hypothesis that a better correlation of the ESS with polysomnography (PSG) will emerge if a trained professional helps the patient to repeat and explore the meaning of the questions.

**Methods :** We studied 115 consecutive patients with suspected sleep disorder referred to the sleep laboratory for PSG in whom the ESS was self-administered and reviewed either one hour after or in the next morning with the help of a nurse. 78 patients were male, 37 female, mean( $\pm$ SD) age  $46 \pm 13$  years, BMI  $27.4 \pm 4.7$  kg/m<sup>2</sup>, AHI  $25 \pm 22$  AHI/hour; periodic limb movement (PLM) index  $9 \pm 16$  PLMs/hour. Educational level was ranked from 1 to 4 according with the number of years of education.

**Results :** Revisions took 1 to 10 minutes. After revision by a nurse 94% of the patients increased their ESS scores from  $9 \pm 5$  to  $12 \pm 5$  points (paired  $t=12.9$ ,  $p=0.000$ ), ranging from 0 to 10 points, with mean, mode and median increase of 3 units. Seven questions had scores significantly increased, the largest being  $0.8 \pm 0.9$  point (paired  $t=7.7$ ;  $p=0.000$ ) in question "Lying down to rest in the afternoon...". The smallest and only non-significant change occurred in question "In a car, while stopped..."  $0.05 \pm 0.5$  point. The difference between scores did not correlate with age, gender, AHI, or educational level. Comparing results of ESS before and after revision, the Pearson's correlation with the AHI increased from 0.170 to 0.241. Other measurements of sleep quality, as percentage of slow wave sleep, increased correlation from  $-0.199$  to  $-0.314$  after revision. In the initial assessment, 20 of 46 (43%) patients with severe OSAHS (IAH>30) had ESS>10; after revision, 32 of 46 (70%) had ESS>10 ( $p=0.01$ ).

**Conclusion :** Patients with sleep disorders tend to underestimate their sleepiness regardless of age, gender, educational level or sleep disorder; a trained interviewer helps patients to answer the ESS questionnaire to obtain more reliable results.

**Support (optional):**

## 1017

### A NOVEL EEG-BASED DROWSINESS TRACKING VARIABLE SHOWS STRONG CORRELATION WITH BEHAVIORAL LAPSES IN VIGILANCE

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**Introduction :** Real-time EEG-based tracking of subjects' drowsiness has a number of important research and clinical applications ranging from clinical quantification of daytime sleepiness to a potential drowsiness warning device. A highly sensitive test of sleepiness based on simultaneous acquisition of EEG and behavioral response (reaction time to auditory target stimulus) has been reported previously. This test has been evaluated with normal sleep-restricted volunteers and medical resident on call, as well as patients with excessive daytime sleepiness. For this study,

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the data from these tests of sleepiness was used to formulate a novel EEG-based quantity for dynamic tracking of drowsiness.

**Methods :** Drowsiness Tracking Index (DTI) is developed based on an innovative combination of several signal processing methods for quantifying EEG, including traditional Short-Term Fourier Transform and Wavelet analysis. DTI is thus a time-varying quantity (computed every second) whose value is indicative of the level of the subject's drowsiness at that instance of time. For the algorithm formulation of DTI, the test data from 10 normal volunteers with varying levels of sleepiness were utilized. The developed DTI was then evaluated using a separate set of data from 5 normal volunteers each tested twice under alert and sleep-restricted conditions. These evaluations were based on cross-correlation analysis between DTI and behavioral parameters (profile of reaction times).

**Results :** Overlay time plots and cross correlation analysis revealed that DTI had a strong correlation with the behavioral parameters for all the individual subjects (normalized cross correlation was as high as 0.9). Furthermore, an increase in DTI usually preceded the prolongation of reaction times during the alert to drowsy transitions (DTI changed 10 seconds or more before a prolonged response/non-response episode). However, DTI and behavioral parameters became highly synchronized around the time of severe drowsiness/micro-sleep when the subjects failed to respond to the target cues for several consecutive seconds. Finally, the averaged DTI was strongly correlated with behavioral parameters (Corr. Coeff. 92%) for the 5 subjects used in the evaluation phase.

**Conclusion :** The novel EEG-based drowsiness tracking index precedes and strongly correlates with behavioral lapses of vigilance. DTI can potentially be used for a real-time drowsiness warning device.

**Support (optional):** 5R44 HL070327-03 and 1R43 HL078442-01

### 1018

#### EVALUATION OF AN AUTOMATED SYSTEM FOR IN-HOME BEHAVIORAL TREATMENT OF CHRONIC INSOMNIA: PART I

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**Introduction :** A multi-year effort has been dedicated to the development of a single-channel EEG-based system to facilitate in-home use of CBT with stimulus control rules. This system uses a real-time detection algorithm, operating on the differential-mastoid EEG channel, to determine sleep state (awake or asleep) every 30 seconds throughout the night. The system is self-tuning in that the detection algorithm parameters are refined with each night of use. System functions include: alerts to get out of bed in accordance with stimulus control rules, automatic sleep diary entries, and daily feedback to enable users to review their progress. In this study, the system was tuned and tested on the same night of data. Sleep onset alert times were determined by the sleep state detection algorithm and compared with those based on a consensus of human sleep scorers.

**Methods :** 100 paid volunteers underwent an overnight laboratory PSG. 3 subjects were excluded from analysis (1 dropout, 1 equipment malfunction, 1 procedural error). 52F/45M, 18-60 years (median 32.7). Each PSG was independently scored by 3-4 certified polysomnographic technologists.

**Results :** 100% of primary system alert times coincided with time periods that were scored as awake by the majority of human scorers. For 85.6% of primary alert times generated by the system, the majority of human scorers also generated an alert within  $\pm 1$  minute, and 96.9% within  $\pm 3$  minutes. For 84.5% of primary alert times generated by a majority of human scorers, the system also generated an alert within  $\pm 1$  minute, and 93.8% within  $\pm 3$  minutes.

**Conclusion :** The automated system has the ability to accurately classify

sleep/wake in the context of CBT implementation using stimulus control rules based on the same night of data. Current research is directed at evaluating the efficacy of the automated system in helping treat chronic insomnia.

**Support (optional):**

### 1019

#### A WATERMARKING ALGORITHM FOR POLYSOMNOGRAPHY DATA

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**Introduction :** The value of standardized research data sets such as the Sleep Heart Health Study (SHHS) may be maximized through collaborative analyses with the scientific community. To facilitate collaborations, a web-based data dissemination system for electronic distribution of polysomnograms (PSG) has been developed that allows researchers to query for studies that meet their criteria and download studies in EDF format for visual and quantitative analysis. Wide-spread data sharing requires implementation of procedures that permit appropriate attribution of the data source.

**Methods :** Watermarking refers to a set of approaches where information is included into a file for copyright protection, integrity verification, and source attribution. We identified a need to incorporate a watermark into the PSG time series that did not alter the data in ways that would limit its intended research use. Our approach is based on hiding a unique identifier in the phase spectrum of each PSG epoch. An undisclosed key is used so that a third party cannot retrieve the watermark without knowledge of the key. A pattern discovery algorithm is developed to find the watermark pattern even though the data has been altered.

**Results :** 25 PSGs were watermarked. The integrity of the signal data was interrogated by computing the Power Spectral Density, Correlation Dimension, Approximate and Sample Entropies, Activity, Mobility, Complexity, Spectral Entropy and Spectral Variance of both the original and watermarked signals. The Power Spectral Density, Mobility, Complexity, Spectral Entropy and Spectral Variance of signals from the original and watermarked studies are statistically equivalent. Correlation Dimension, Approximate and Sample Entropies from each set of studies are slightly different (with 95% confidence intervals for % variations of (-.4263, -.0449), (-5.8062, .5094), (-.6202, -.0369), respectively).

**Conclusion :** The watermarking algorithm provides a means for attributing a given epoch of data with the SHHS data set; the small variations in spectral parameters introduced are unlikely to impact most research applications of physiological signals.

**Support (optional):** HL94092

### 1020

#### AN INVESTIGATION OF THE ACCURACY OF THE LIFESHIRT IN COMPARISON TO STANDARD POLYSOMNOGRAPHY

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**Introduction :** Due to the cost of traditional sleep studies, there is great interest in finding less expensive alternatives for the diagnosis of sleep disorders, particularly sleep apnea. Several alternatives exist, one of which is the Lifeshirt, manufactured by Vivometrics. As part of a separate

investigation, our laboratory utilized the Lifeshirt and compared its accuracy to that of traditional polysomnography (PSG).

**Methods :** On 1-2 occasions across 48 different people, PSG was performed with simultaneous utilization of the Lifeshirt (68 total PSGs were analyzed). Participants came to the sleep lab approximately 2 hours before their normal bedtime. A sleep technician set each participant up for combined PSG and Lifeshirt monitoring. "Lights Out" occurred when the participant was ready for bed, and time in bed was standardized to approximately 7 hours. PSGs were scored by trained personnel in our laboratory, while Lifeshirt data were scored via automated analysis.

**Results :** The Lifeshirt had a sensitivity of .83 and a specificity of .87 when an AHI of  $\geq 10$  was used as a cutoff score. Sensitivity ranged from .82 (with an AHI of  $\geq 15$ ) to 1.00 (with an AHI of  $\geq 25$ ). Specificity ranged from .81 (with an AHI of  $\geq 5$ ) to 1.00 (with an AHI of  $\geq 30$ ). Using the Bland Altman technique of determining agreement, the mean difference between the Lifeshirt and PSG was .79 (+/- 14.46). When these values are plotted, it is clear that every case falls within the limits of agreement, with the exception of one outlier.

**Conclusion :** The Lifeshirt had excellent agreement with traditional PSG. The sensitivity and specificity of this tool were quite high, making it an acceptable alternative to PSG.

**Support (optional):**

## 1021

### EVALUATION OF AN AUTOMATED SYSTEM FOR IN-HOME BEHAVIORAL TREATMENT OF CHRONIC INSOMNIA: PART II

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**Introduction :** A multi-year effort has been dedicated to the development of a single-channel EEG-based system to facilitate in-home use of CBT with stimulus control rules. This system uses a real-time detection algorithm, operating on the differential-mastoid EEG channel, to determine sleep state (awake or asleep) every 30 seconds throughout the night. The system is self-tuning in that the detection algorithm parameters are refined with each night of use. System functions include: alerts to get out of bed in accordance with stimulus control rules, automatic sleep diary entries, and daily feedback to enable users to review their progress. In this study, subjects spent two nights in the sleep laboratory. The system self-tuned on the first night of data and was tested on the second night of data. Sleep onset alert times for the second night were determined by the sleep state detection algorithm and compared with those based on a consensus of human sleep scorers.

**Methods :** 24 paid volunteers underwent two overnight laboratory PSGs. The time interval between these two PSGs ranged from 20-334 days (median 186). 16F/8M, 20-60 years (Median 36). Each PSG was independently scored by 2-3 certified polysomnographic technologists.

**Results :** For the second night of real time testing, 100% of primary system alert times coincided with time periods that were scored as awake by the majority of human scorers. For 83.3% of primary alert times generated by the system, the majority of human scorers also generated an alert within  $\pm 1$  minute, and 95.8% within  $\pm 3$  minutes. For 95.8% of primary alert times generated by a majority of human scorers, the system also generated an alert within  $\pm 1$  minute, and 100% within  $\pm 3$  minutes.

**Conclusion :** The automated system has the ability to accurately classify sleep/wake in the context of CBT implementation using stimulus control rules by self-tuning and testing on different nights.

**Support (optional):**

## 1022

### THE EFFECT OF MASK SELECTION ON SLEEP PARAMETERS DURING SPLIT POLYSOMNOGRAPHY

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**Introduction :** The duration of NCPAP titration is truncated by the process of split polysomnography. Previous reports have suggested patient gender, BMI, AHI, and neck circumference are all useful predictive factors of the optimal pressure level. The authors chose to evaluate the effect of interface category on the parameters of split polysomnography. The concept of interface efficiency is introduced.

**Methods :** We evaluated variables of the titration response between differing categories of interface. Data was gathered by modification of the software such that parameters of interest were tabulated during report generation by the Sandman Elite sleep system. All split polysomnography studies performed between April of 2004 and June of 2005 were evaluated retrospectively for the purpose of this abstract. Exclusion criteria included a pre-titration AHI of less than 5 and patient age less than 16. Patient interfaces included full face, nasal mask, and nasal prong based. Interface selection was a cooperative decision between the patient and recording technician. Statistical evaluation utilized ANOVA and Mann-Whitney rank sum tests for data comparison. Only significant results are presented in the format - mean(s.d.).

**Results :** Data was available from 2850 studies: age = 47.7 (12.5), BMI = 35.73 (9.03) and Pre-titration AHI = 43.65 (34.39). The change in the average value of sleep efficiency was -0.47% (18.17) for full face, 3.18% (20.06) for nasal prong and 6.54% (17.54) for nasal mask interfaces. The change in WASO was -1.25% (17.31) for full face, -2.98% (18.35) for nasal prong and -5.24% (16.35) for nasal masks. The average pressure utilized was 12.89 cm (4.36) for full face, 11.73 cm (2.98) for nasal prong devices and 11.36 cm (3.26) for nasal masks. The relative change in AHI was -54.51% for full face masks, -54.06% for nasal prong devices and -67.03% for nasal masks.

**Conclusion :** We conclude efficiency of nasal masks exceeds that of full face and nasal prong devices during the initial split titration studies. Efficiency factors could certainly be overcome by pressure increments for nasal prong devices, however, full face devices may be sleep disruptive per se. Given the brevity of split night titrations, maximizing the interface efficiency would seem a reasonable option to enhance selection of the optimal pressure.

**Support (optional):**

## 1023

### PASSIVE BALLISTOCARDIOGRAPHY SYSTEM COMPARED TO EKG: PRELIMINARY VALIDATION

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**Introduction :** Heart rate and regularity are important parameters that have been used to assist in assessing sleep staging without electroencephalogram data. The NAPS (Non-invasive Analysis of Physiological Signals) System is designed to obtain physiological measurements passively while the subject is in bed. It consists of two pressure sensitive pads which are connected to a base unit that converts minute movements from heart and lungs into electrical signals. The pads and sensors can be placed on any bed in order to measure pulse from the test subject.

**Methods :** The study was approved by the University of Virginia's

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Institutional Review Board and the General Clinical Research Center (GCRC). Forty generally healthy adult subjects who had signed an informed consent underwent an overnight sleep study with conventional polysomnography, while simultaneously monitored by the passive system, at the University of Virginia's GCRC. Preliminary analysis scored two three-minute blocks of data from each subject selected at random from an entire night's study. One data set contained no apneas or arousals and the other data set contained at least one apnea. Heart rate data from EKG waveforms was manually scored while data from the passive system was automatically scored using our algorithm. They were compared by averaging the data over 30 second epochs.

**Results :** The average heart rate data obtained over a total of 480 30-second epochs by the passive system correlated very significantly with similar data from EKG ( $r = 0.972$ ). Standard errors were within 2.54 beats per minute of the EKG data. The passive system heart rate measurements exhibited an 89.4% detection rate limited by movement artifacts.

**Conclusion :** The preliminary results of this study demonstrate the validity of the passive system's ability to provide clinically meaningful heart rate data. Further validation will be performed on data collected from the full nights of sleep.

**Support (optional):** This work was supported in part by a grant to the University of Virginia's General Clinical Research Center, 5 M01 RR00847.

### 1024

#### PUPILLARY UNREST AS AN OBJECTIVE MEASURE OF TREATMENT RESPONSE IN SLEEP DISORDERS

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**Introduction :** Pupillary unrest index (PUI), a measure of pupil size instability associated with daytime sleepiness, is objective, relatively quick, and non-invasive. We compared PUI with the Multiple Sleep Latency Test (SL) and with self-reported sleep and mood measures in subjects with narcolepsy ( $n = 20$ ) and obstructive sleep apnea ( $n = 9$ ).

**Methods :** Subjects were assessed in a sleep laboratory while off- and later on-treatment. For each condition, following overnight PSG, SL testing was conducted at 1000, 1200, 1400, and 1600 hours and PUI testing at 900, 1100, 1300, and 1500 hours with the AMTech GmbH pupillometer. During PUI testing (11 min.), subjects were seated comfortably in a quiet, dark room with instructions to stay awake and keep eyes open. Subjects were also assessed with a number of subjective measures, including Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), Functional Outcomes of Sleep Questionnaire (FOSQ), and the Profile of Mood States (POMS) Vigor and Fatigue subscales.

**Results :** Mean off-treatment SL was 5.4 minutes. We log transformed the PUI (lnPUI) to normalize its distribution. Comparing sleepiness measures off- and on-treatment, paired t-tests showed statistically significant differences (in expected directions) for the lnPUI [ $t(28)=4.504$ ,  $p<.001$ ] and scores on the ESS [ $t(27)=3.954$ ,  $p<.001$ ], PSQI Daytime Dysfunction subscale [ $t(28)=2.117$ ,  $p<.05$ ], most subscales of the FOSQ, as well as FOSQ Total Scale [ $t(28)=-2.876$ ,  $p<.01$ ], POMS Vigor [ $t(28)=-3.237$ ,  $p<.005$ ], and POMS Fatigue [ $t(28)=4.565$ ,  $p<.001$ ]. However, the MSLT did not show a significant change [ $t(27)=-1.433$ , n.s.].

**Conclusion :** The PUI provided an objective measure, comparable in power to questionnaires or self-reports in detecting improvements in daytime sleepiness following treatment for sleep-related conditions. In con-

trast, the MSLT seemed less sensitive in detecting improvement due to treatment.

**Support (optional):** Funded by the National Institute of Nursing Research, NIH, RO1 NR04959 and by Mr. J.A. Piscopo.

### 1025

#### FIELD STUDY PILOT TEST OF FATIGUE MANAGEMENT TECHNOLOGIES IN COMMERCIAL TRUCKING

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**Introduction :** Fatigue due to sleepiness/drowsiness is a risk factor for commercial truck drivers. A large-scale field experiment was conducted to assess whether fatigue management technologies (FMT) deployed during regular work operations would improve truck driver alertness, especially during night driving, and/or increase sleep time on workdays and/or non-workdays.

**Methods :** Over-the-road testing of a set of four technologies was undertaken in  $N=38$  volunteer CMV operators in Canada and the US. FMT included monitoring driver sleep need (by actigraph algorithm), driver drowsiness (by PERCLOS), and lane tracking (by video system), as well as increased control of vehicle stability while driving (by special steering system). A within-subjects cross-over design was used to compare the effects of FMT feedback to no-feedback—each driver underwent 2-weeks of no feedback (control) followed by 2-weeks of FMT feedback (intervention). PVT testing was undertaken before, midway and after each duty day, as an independent evaluation of driver fatigue.

**Results :** Data from the FMT devices and other driving variables were recorded by a black box every second the trucks were driven over the road, resulting in 8.7 million data records. FMT feedback significantly reduced drivers' drowsiness ( $p=0.004$ ) and lane tracking variability ( $p=0.007$ ) during night driving. Mean sleep duration was significantly less on work days than on non-workdays for both U.S. and Canadian drivers ( $p=0.011$ ). FMT feedback had no effect on workday sleep durations, but it increased sleep time on non-workdays in both Canadian ( $p=0.023$ ) and U.S. drivers ( $p=0.018$ ). PVT performance results suggested there was a fatiguing effect induced by FMT feedback, probably through compensatory effort to drive more alertly.

**Conclusion :** FMT feedback can improve CMV driver alertness on workdays, and increase sleep time on non-workdays, but it has little influence on sleep taken during workdays. More work is needed to understand what factors determine sleep durations of drivers on workdays.

**Support (optional):** U.S. DOT Federal Motor Carrier Safety Administration

### 1026

#### INNOVATIVE WIRELESS SLEEP DISORDERS DIAGNOSIS SYSTEM

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**Introduction :** Over 10 million patients in the U.S. with obstructive sleep apnea (OSA) remain undiagnosed and untreated. The need to expedite sleep diagnosis is further highlighted by significant comorbidity between

OSA and other diseases, which often complicates standard patient care. To that end, a new easily deployable wireless PSG system, Crystal 20-S, that allows attended sleep studies to be conducted in any hospital or clinic room was developed and tested.

**Methods :** A side-by-side comparison of the Crystal 20-S and a commercial system was conducted at Cleveland Clinic Sleep Disorders Center in 6 subjects undergoing routine polysomnography. Most of the channels were connected to both systems via a “Y” connection between head boxes. A separate pulse oximetry sensor was worn for each system. The wireless system includes a patient unit, computer unit and sleep software. The system uses the 900 MHz wireless band, provides real-time acquisition and scoring, and generates flexible reports. The patient unit weighs 210g and measures 5.25” x 2.5” x 1”. The system acquires fourteen PSG channels. A pressure transducer inside the patient unit detects airflow. Algorithms derive snore from the airflow cannula. A single registered technologist scored recordings acquired from the laboratory and the wireless system independently.

**Results :** The difference in sleep staging between both systems was within intrascorer variability indicating similar sleep architecture results. Both devices generated identical OSA diagnoses in all subjects (2 normal (AHI < 5), 1 moderate (5 < AHI < 30), 3 severe (AHI > 30)). 100% of the epochs were scored in the wireless system indicating excellent immunity to radio interference.

**Conclusion :** The two systems gave comparable results in sleep architecture and respiratory events detection. Overall, this study shows the potential viability of a wireless system as an accurate and convenient way to extend PSG testing to new settings. One potential application is for hospitalized patients.

**Support (optional):** This work was funded by NIH SBIR grant: 2R44NS42451-02A1

## 1027

### EVALUATION OF PRESSURE ADJUSTMENTS WITH THREE AUTO-TITRATION CPAP MACHINES

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**Introduction :** The introduction of auto-titrating CPAP machines has brought a new treatment option for people with obstructive sleep apnea. Individual machines vary in the method used to adjust pressure. Three machines were tested with the Hans Rudolph Breathing Simulator (HR 1101) set to mimic an obstructive sleep apnea/hypopnea breathing pattern.

**Methods :** Three auto-adjust CPAP machines were tested: Resironics REM Star Auto, ResMed AutoSet Spirit, and DeVilbiss RPM AutoAdjust. Each machine was connected to the HR 1101. HR 1101 settings: resistance (RAW) 5, 10, 20, 30 and 50 cm H<sub>2</sub>O/L/sec; compliance (CST) 40 mL/cm H<sub>2</sub>O. The machines were set at the minimum and maximum range. PEEP was the average of a minimum of five breaths, while RAW was changed.

**Results :** At a set RAW of 5 cm H<sub>2</sub>O/L/sec: measured PEEP (cm H<sub>2</sub>O) was 7.75 with the Autoset; 3.81 with the REM Star; 4.64 with the AutoAdjust. At RAW of 10 cm H<sub>2</sub>O/L/sec: measured PEEP was 8.89 with the Autoset; 8.83 with the REM Star; 4.67 with the AutoAdjust. At RAW of 20 cm H<sub>2</sub>O/L/sec: measured PEEP was 8.89 with the Autoset; 8.13 with the REM Star; 4.67 with the AutoAdjust. At RAW of 30 cm H<sub>2</sub>O/L/sec: measured PEEP was 8.87 with the Autoset; 8.11 with the REM Star; 4.70 with the AutoAdjust. At RAW of 50 cm H<sub>2</sub>O/L/sec: measured PEEP was 8.81 with the Autoset; 8.09 with the REM Star; 4.70 with the AutoAdjust.

**Conclusion :** The ability of auto-titrating CPAP machines to maintain adequate positive end-expiratory pressure during increased airway resist-

ance varies depending upon the machine. Positive end-expiratory pressure should be carefully monitored while ventilating patients with an auto-titrating machine.

**Support (optional):**

## 1028

### PRELIMINARY VALIDATION OF NEW DEVICE FOR STUDYING SLEEP

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**Introduction :** This study examined the validity of the BodyMedia's SenseWear™ armband as new tool to assess sleep and wakefulness, using polysomnography (PSG) as the gold standard. SenseWear measures body movement, like actigraphy, but also acquires other physiological signals, including surface body temperature, galvanic skin response, and heat flux, that may permit distinctions between NREM and REM sleep.

**Methods :** Twenty-seven participants (Mean age = 28.7 years, 16 women) underwent PSG recordings while wearing the armband. PSG and armband data were scored in 20-second epochs. BodyMedia's sleep algorithm was developed using techniques from statistical machine learning. Relevant features that distinguish characteristics of NREM and REM were first identified, including length of inactivity and rate of change in heat-flux. These features were then combined using a method that incorporates the probability of the feature for each sleep state, of each sleep state at each time point, and of different sequences of sleep states. Performance was evaluated using the method of "leave one out" cross-validation, which repeatedly trains the model on all but one of the subjects and tests on the remaining subject. Monte Carlo simulations were used to evaluate the rate of correct sleep stage detection attributable to chance.

**Results :** The algorithm correctly identified 93% of all sleep epochs, and 83% of all wakefulness epochs, for an overall epoch-by-epoch accuracy of 89%. The algorithm correctly identified 65% of all NREM sleep epochs (vs. 43.9% by chance), and 45.6% of all REM sleep epochs (vs. 13.9% by chance), for an epoch-by-epoch accuracy of 70% (vs. 39% by chance).

**Conclusion :** BodyMedia's algorithm identified sleep and wakefulness with moderate to high sensitivity, specificity, and accuracy. Detection of NREM and REM substantially exceeds chance levels. Although further improvement is needed, SenseWear appears to be a promising, unobtrusive means for measuring NREM and REM as well as overall sleep and wakefulness.

**Support (optional):** The present work was supported by the Mental Health Research and Intervention Center of the University of Pittsburgh through an NIMH funded grant (MH30195), the Fonds de la recherche en Santé du Québec, and the Canadian Institutes of Health Research.

## 1029

### BEHAVIOURAL TREATMENT FOR INSOMNIA: MEASURING COMPLIANCE OBJECTIVELY USING ACTIGRAPHY

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**Introduction :** Behavioural treatments for insomnia (e.g. stimulus control, sleep restriction) generally reduce sleep difficulties, although not all individuals improve or they improve at different rate or to different degrees. Because such interventions rely upon home implementation of behavioural instructions, compliance might be critical. Notwithstanding, perhaps due to its elusive nature, compliance is seldom measured. This study aimed at developing a measure of home compliance using objective

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data obtained via actigraphy (movement and light sensors).

**Methods :** Data were gathered from a sample of volunteers (N=45, f=30, m=15, age= 20 to 70 years) in a randomised clinical trial. Treated participants were asked to 'switch on the light and read if not asleep within a quarter of an hour' (QHR). They wore actigraphs during this treatment phase (three weeks). Cambridge Neurotechnology Actiwatch-L (ACTW-L) devices monitor both movement and light intensity and were used to objectively assess whether the behavioural treatment was implemented. Participants' compliance with the QHR was also measured subjectively (daily compliance diary).

**Results :** Based on the data gathered during home implementation of the QHR via the ACTW-L, a rule based algorithm relating movement and light was developed and tested. The algorithm employs binary logic, for each sixty seconds epoch of the night, on i) movement, ii) light and iii) a combination of the two values. A compliance score was then produced and this value linked to treatment outcome. Results are summarised and illustrated using case material and highlight that this available technology can be successfully employed to discretely monitor home implementation of behavioural insomnia instructions.

**Conclusion :** This exploratory study proposes a simple and unobtrusive way to monitor compliance objectively and suggests that further systematic research using actigraphy, as a measure of compliance, would be worthwhile. The investigation of the relationship between rate of compliance and treatment outcome is especially important. For example to explore the minimum and the optimum amount of instruction implementation needed to produce effective treatment outcome.

**Support (optional):**

### 1030

#### HOME MONITORING SLEEP AND CRYING IN INFANTS

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**Introduction :** Crying is an important communication between infants and their parents. Crying is also a major signal for parents to intervene during the night when the infant wakes up. The aim of this study was to assess the use of a miniature sound sensor for detection of crying in infants during the sleep period.

**Methods :** Twenty-six infants (16 boys, 10 girls) were monitored at home for 3 consecutive nights. Their sleep was monitored by actigraphs attached to their non-dominant ankle. In addition, two methods were used to record sound. Digital voice operated recorder (Sony ICD-ST10) was used to record sound above threshold including crying. The MicroMini Sound Sensor (Ambulatory Monitoring Inc.) was used to record sound level continuously. This sensor is a miniature device with a capacity to monitor sound levels continuously for extended period. The recorder and the sound sensor were mounted on little board placed 50 cm from the center of the crib. Data obtained from the recorder were coded minute-by-minute for crying behavior. Data collected by these three methods (actigraphy, voice recorder, and sound sensor) were aligned on a minute-by-minute basis for data analysis.

**Results :** Discriminant analysis was used to develop an algorithm for identifying crying minutes using data obtained from actigraphy and the sound sensor. The algorithm was developed with data derived from the first night, and the minute-by-minute agreement between the crying detection based on voice activated recorder and the sound sensor and actigraphy was 95.2%. Validation on the second and third nights led to 94.9% and 96.6%, respectively. Night-to-night stability of the crying time ranged between .58 and .85.

**Conclusion :** Our results suggest that crying during the sleep period could be reliably detected using an actigraph and a miniature sound monitor placed near the crib. This methodology could be instrumental for the

study of sleep-wake behavior in infants.

**Support (optional):** Micromini sound sensors were provided for testing by Ambulatory Monitoring Inc.

### 1031

#### EFFECT OF MASK CATEGORY EFFICIENCY ON TITRATION OUTCOME

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**Introduction :** Split polysomnography is a truncated procedure by nature. The rate of unsatisfactory titrations has been reported to be 10% when final pressure is used as a parameter in comparison with full night studies. In another abstract the authors reported that the efficiency of nasal prong based devices, as well as full face masks is less than that of nasal masks. It was suggested that this finding might be insignificant with regard to long term therapy, but could result in a higher rate of unsatisfactory titrations when time is limited.

**Methods :** Data was reviewed from 2850 sequential split polysomnograms between April of 2004 and June of 2005. Nasal pressure interfaces were categorized as full face, prong based and nasal mask. We looked at the ratio of procedures in which the final average AHI was less than 50% of the diagnostic AHI (a figure which would indicate resolution of events based on the average value of a function). A Chi square was used to assess significance of proportions.

**Results :** Of 546 studies performed using a prong based device, 401 achieved an average AHI during the titration of 50% or less of the baseline AHI. Of 2207 studies performed with a mask device, 1847 achieved the 50% or less target. For full face masks, 67 of 96 studies reached the 50% or less target. Ratios were 0.719 for full face devices, 0.734 for nasal prong interfaces, and 0.837 for nasal masks. The difference for nasal masks was statistically significant.

**Conclusion :** We conclude that the suggested higher efficiency of nasal masks in comparison with full face and nasal prong devices does result in a greater proportion (83.7% v. 71.9% and 73.4% respectively) of studies with a lower AHI during the therapeutic portion of the split diagnostic/therapeutic study. The authors are not surprised by the lower efficiency of full face devices, but do find the result provocative with regard to nasal prong based interfaces.

**Support (optional):**

### 1032

#### CYCLIC ALTERNATING PATTERN SLEEP AND CENTRAL SLEEP APNEA IN STABLE METHADONE MAINTENANCE PATIENTS

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**Introduction :** Stable methadone maintenance patients (MMPs) have increased rates of central sleep apnoea, report poor sleep and increased daytime fatigue. However, using conventional sleep analysis techniques the changes in sleep architecture compared to control groups are relatively small. Visual EEG analysis may not give an accurate measure of sleep architecture, particularly in the presence of persistent alpha activity in NREM. Therefore we aimed to measure cyclic alternating pattern (CAP) sleep using the electrocardiogram-based cardio-pulmonary coupling

(CPC) technique in a group of MMPs.

**Methods :** MMPs and controls matched for age and BMI participated in the study. All subjects had overnight polysomnography as well as waking measurements of hypoxic and hypercapnic ventilatory response, quality of life and toxicology. Sleep studies were staged and scored according to standard criteria, and using the CPC technique to categorise sleep as CAP, non-CAP, wake/REM or other.

**Results :** 45 patients (10 controls, 35 methadone) aged  $36\pm 9$  years, BMI  $27\pm 5$  kg/m<sup>2</sup>, participated in the study. MMPs had a higher central apnoea index ( $8.8\pm 16.6$  vs  $0.4\pm 0.4$ ,  $p<0.001$ ) but similar obstructive apnea ( $0.06\pm 0.14$  vs  $0.25\pm 0.8$ ,  $p=0.17$ ) and hypopnea ( $11.1\pm 10.6$  vs  $8.6\pm 7.1$ ,  $p=0.47$ ) indexes. MMPs reported higher Epworth sleepiness scores  $6.8\pm 4.9$  vs  $1.5\pm 1.4$  ( $p<0.001$ ) but had a similar mean arousal index ( $13.5\pm 4.5$  vs  $14.7\pm 6.1$ ,  $p=0.48$ ) to controls. The proportion of CAP sleep accounted for 16% ( $p=0.02$ ) of the variance of the central apnea index in MMPs, and 13/14 (93%) of subjects with the highest proportion of CAP ( $>0.5$ ) were MMPs ( $p=0.10$ ). A CPC derived measure of central sleep disordered breathing was elevated in 7/35 (20%) of MMPs, but none of the controls ( $p=0.12$ ).

**Conclusion :** In this study, the proportion of CAP sleep was related to the degree of central sleep apnea and MMPs were more likely to have a high proportion of CAP sleep than controls. These relationships between sleep architecture and sleep disordered breathing in MMPs were not found in a previous study using standard measures of sleep architecture. Alternative measures of sleep architecture such as CAP, and novel techniques for analysis of sleep such as the CPC technique offer complementary information to standard sleep staging and scoring. However, further work across a range of disease states as well as in normal controls is needed to better define the clinical role of CAP scoring and CPC analysis.

**Support (optional):**

1033

A PILOT SURVEY AND EVALUATION OF A JETLAG MANAGEMENT COURSE FOR THE CANADIAN NATIONAL SPEED SKATING TEAM

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**Introduction :** Sleep problems and jetlag have been identified as contributing factors in poor performance of elite athletes (Postalache et al. 2005). In response to the results of a general sleep survey of 82 Canadian National Speed Skating Team athletes and coaches, the team initiated a sleep education program. A segment of the program focused on jetlag and travel fatigue. We report the results of a structured evaluation of this segment of the sleep education program.

**Methods :** Eighteen athletes, based in Calgary, Alberta, Canada, participated in a 3 hour course on the basic science of sleep, jetlag and travel fatigue prior to competition in Asia and Europe. The athletes filled out a Pre-Trip survey, Post-Trip survey and Post-Course Evaluation. The surveys were designed to evaluate sleep habits, jetlag symptoms and jetlag coping strategies. Questions were rated on a 5-point Likert scale and reported as frequencies. Symptoms and events were reported as frequencies. The "n" for the surveys were as follows: Pre-trip questionnaire: n=18, Post-trip questionnaire: n=17, Course evaluation: n=19.

**Results :** The pre-trip survey revealed that 13/18 athletes "occasionally"(6) or "rarely"(7) travel well. All athletes (18/18) report being "fatigued" as a result of travel. The Post-trip survey did not show a significant improvement in jetlag symptoms. However 13/17 athletes agreed that the course improved their ability to cope with travel. Napping was used by 12/17 athletes and bright light therapy was used by 13/17 athletes for management of jetlag. Questions addressing the impact of direction of travel confirmed that regardless of location, travel east is more difficult to adjust to than travel west. The course evaluation revealed that 16/19 athletes found the program "very valuable" and 3/19 athletes found the program "valuable". The jetlag management section of the course was reported as "very useful" by 14/19 athletes. The travel management section of the course was reported as "very useful" by 12/19 athletes.

**Conclusion :** The results of the surveys confirm that athletes do suffer the ill effects of jetlag and travel, and that direction of travel is a contributing factor. The athletes do use jetlag management strategies and interventions. Most athletes found the course valuable. The results of this pilot project indicate that a jetlag and travel management course would be a valuable resource to the team. Further work needs to be done to standardize the course and evaluate the impact of the course.

**Support (optional):**

1034

SLEEP AND SLEEP DISORDER KNOWLEDGE AMONG PHYSICIANS AND PHYSICIANS-IN-TRAINING

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**Introduction :** Over 75% of adult Americans surveyed in an NSF Poll reported having a sleep problem, with 34% identified as being at risk for a major sleep disorder. Despite the prevalence of sleep disorders, sleep medicine has only recently become a regular part of the medical school curriculum. With the inception of the Sleep Academic Awards program in 1996 by the NHLBI National Center of Sleep Disorders Research, there has been a focus on implementation of such programs at medical schools,

and subsequent measures of outcomes. Our study aimed to assess this initiative, by evaluating the difference in knowledge amongst physicians and physicians-in-training. By studying physicians at different levels of experience, we hoped to determine whether initiatives to increase the education about sleep medicine have had a positive effect on the knowledge level of physicians.

**Methods :** An electronic version of the Dartmouth Sleep Knowledge and Attitude Survey was created, using QuestionPro software. The survey was modified to include feedback following each response. This survey was distributed by e-mail to all medical students and practicing physicians in the Champaign-Urbana area. Responses were collected anonymously, categorized based on years since graduating from medical school, and scored for correct answers.

**Results :** Of 652 subjects polled, 80 responded to our survey. Physicians 6-10 yrs out of medical school performed significantly better than medical students ( $p < 0.05$ , ANOVA). While not significant, physicians 6-10 yrs out of school also showed a trend towards performing better than physicians >10 yrs out. A significant difference ( $p < 0.05$ , ANOVA) was observed between third and fourth year medical students, who had completed the curriculum, when compared to first and second year medical students, who were still taking courses.

**Conclusion :** Our results suggest that reforms in sleep education may be effective in improving knowledge of sleep disorders. Medical students exposed to a curriculum with information about sleep and sleep disorders performed better than entering students. In addition, physicians who graduated from medical school following the inception of the Sleep Academic Awards program performed better than current students, and showed a trend towards performing better than physicians who graduated before the implementation of these programs. However, our study represented a small population, with a low response rate, so we intend to expand our survey to include a larger group of physicians.

**Support (optional):** GM07143 (SMA)

1035

EFFECTS OF TELEVISION VIEWING ON SLEEP HABITS AND DREAM CONTENTS IN CHILDREN AT AGES 3-8

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**Introduction :** Television plays an important role in the lives of children and different studies has shown both positive and negative effects. This paper presents the results of an extensive study on the effects of the television viewing on the sleep habits and on dreaming of children 3-8 years-old of center-north Italy.

**Methods :** Data were collected through a questionnaires compiled by parents. 1148 questionnaires were distributed to parents in several Italian schools. 652 returned to the experimenter (return rate = 57%), 565 were usable (usability rate = 49%) (255 female / 310 male, aged 3 to 8). In 325 questionnaires (57%), the parents wrote down the last dream reports of their children.

**Results :** Sleep. Children who view more television have less total sleep [ $F(3, 510) = 3,396$ ;  $p = 0,018$ ], later awakenings in the morning when they don't go to school ( $p = 0,036$ ), shorter naps ( $p = 0,005$ ], longer wake ( $p = 0,003$ ), more time in bed, ( $p = 0,017$ ), and they spent more time in bed after the morning awakening ( $p = 0,042$ ); No significant effects were observed for other sleep variables such as time to go to bed, number and duration of awakenings, frequency of naps, sleep efficiency index. Dreaming. The 21% (66/317) of the children's dreams have TV contents. This parents' evaluation generally accord whit judgement's score of (agreement 87%). Children who see the TV longer report more often TV



characters in their dreams and they interact with them with an intense emotional involvement (negative / positive) (Kruskal Wallis Test,  $p = .012$ ).

**Conclusion :** The results most agreement with previous classical studies furthermore for its brief time of compilation and reduced costs the questionnaire show certain utility for the study of large sample of children (i.e., screening for a prevention in the exposure risks TV).

**Support (optional):**

### 1036

#### DO PRIMARY CARE PHYSICIANS SCREEN FOR SLEEP COMPLAINTS?

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**Introduction :** Sleep complaints are common in the general populations and have significant impact on their quality of life. Primary care physicians (PCPs) usually perform systematic review of systems during their first encounter with their patients. The aim of this study is to investigate whether PCPs inquire about sleep complaints during the first encounter with their patients and if patients routinely inform their PCPs about their sleeping habits.

**Methods :** A questionnaire (14 questions) of the most common sleep complaints was distributed to patients after their first encounter with PCPs in outpatient clinics of two university affiliated hospitals. Patients also were asked if their PCPs inquired if they have any sleep complaints, and if they told their PCPs about their sleeping habits.

**Results :** 78 adult patients (age between 22 to 83) were interviewed (37 M, 41F). Only 9 patients (11.5%) had no sleep complaints, whereas 69 patients (88.5%) had one or more sleep complaints. Only 11 patients (14.1%) were asked by their PCPs whether they have any sleep complaints. Of the 67 patients who were not asked, 59 patients (88.1) had one of more sleep complaints. Only 11 patients (14.1%) told their PCPs about their sleeping habits. Of the 67 patients who did not tell about their sleeping habits, 58 patients (86.6%) had one or more sleep complaints.

**Conclusion :** Sleep complaints are common in the general population and are not routinely investigated by primary care physicians. Patients do not routinely inform their primary care physicians about their sleeping habits, therefore primary care physicians should consider routine screening for sleep complaints.

**Support (optional):**

### 1037

#### ASSESSMENT OF SLEEP KNOWLEDGE IN PHYSICIANS CARING FOR PREGNANT PATIENTS

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**Introduction :** This study was designed to assess sleep disorders knowledge in those physicians that are caring for pregnant women.

**Methods :** We modified the ASKME (assessing sleep knowledge in medical education) survey to include 9 sleep knowledge questions specific to sleep disorders in pregnancy with permission from the original authors. The questionnaire was administered anonymously to 28 Obstetrician/Gynecologists (Ob/Gyn) and 66 Family Practitioners (FP). Twelve general Neurologists were also surveyed and used as a comparative reference. The survey consists of 30 true/false sleep knowledge ques-

tions, practice type, years in practice (<2, >2 but <5, and >5) and dedicated sleep education in hours (0,<3,>3).

**Results :** Statistics were run using the multiple analysis of variance (MANOVA). Ob/Gyn and FP were compared to Neurologists by sleep category. Both FPs and Ob/Gyns had significantly less correct answers in Narcolepsy (Mean % correct for FP, OB/Gyn, and Neuro: 50, 35.7, and 86.1 respectively), Parasomnias (Means: 36.4, 34.5, and 66.7), and Effects of Drugs/Alcohol on Sleep (Means: 45.5, 35.7, and 72.2) while OB/Gyn scored significantly lower in Sleep Disorders in Pregnancy (Mean 34.8 vs. 55.2) and Basic Sleep Principles (Mean 38.4 vs. 72.9) when compared to Neurologists. Physician experience (years in practice) positively impacted on test scores in Sleep Disordered Breathing (60.7% for <2 years in practice vs. 74.6% for >5 years in practice). Physicians who self reported dedicated sleep education of >3 hours scored significantly better in Basic Sleep Principles (46% vs. 67.9%), Parasomnias (35.1% vs. 73.8%), Effects of Drugs/Alcohol on Sleep (40.9% vs. 66.7%), and Sleep Disorders in Pregnancy (36.8% vs. 54.5%).

**Conclusion :** This study suggests sleep disorders knowledge is lacking in physicians caring for pregnant patients. Obstetricians scored much lower in this category than expected and practical experience did not improve these scores. Dedicated sleep medicine education for practicing physicians caring for pregnant women may improve sleep disorders recognition and impact positively on patient care.

**Support (optional):**

### 1038

#### COST-BENEFIT ANALYSIS OF E-LEARNING VS. FACE-TO-FACE FORMAT FOR SLEEP MEDICINE EDUCATION FOR MEDICAL STUDENTS

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**Introduction :** Previous studies have documented the limited inclusion of sleep medicine education in medical school curriculum. However, as clinical RVU demands escalate and compete with time to provide core instruction, it is imperative to use cost-effective instructional delivery methods in sleep medicine.

**Methods :** Costs associated with the design and on-going delivery of sleep medicine instruction using e-learning and face-to-face (F2F) interactive lectures for Year One of a two year project were tracked. The number of hours/individual associated with the development of instructional units (content, tests, evaluation) for F2F and e-learning for four sleep medicine domains were recorded. Personnel costs were calculated based on average salaries using a 50-hour work week (2600/hrs year). Supplies and expenses were tracked using institution's purchasing order system (CD ROMS, duplication, video production) during the study period.

**Results :** Core Module and Exam development (80 MD hours, 40 educator hours) cost \$7,000 and module related supplies 6500, used for both methods. F2F design and delivery (110 MD hours) cost \$7,900. Additional development e-learning and delivery and maintenance (40 MD hours, 196 educator hours) cost \$8,252. Total development and delivery costs for the implementation phase/first year of instruction for F2F \$21,640 and e-learning \$21,752 are equivalent.

**Conclusion :** E-learning delivery requires a high start up cost comparable to traditional F2F during the implementation year but will certainly yield a better return on investment instruction over time as frequency/longevity of the delivery increases. On going benefits of e-learning including improved quality of face-to-face instructor time and flexibility for learn-

## Category R—Sleep Education

ers and instructors cannot be truly measured with this cost formula.

**Support (optional):** American Sleep Medicine Foundation Educational Research Grant

### 1039

#### EQUIVALENCE OF SELF-PACED ELECTRONIC LEARNING AND TRADITIONAL FACE-TO-FACE FORMAT FOR SLEEP MEDICINE EDUCATION IN MEDICAL SCHOOL

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**Introduction :** To address the gap between the prevalence of sleep disorders and poor performance by medical students on sleep related knowledge and/or skills assessments, we developed a series of modules highlighting four core clinical areas of sleep medicine. Modules were delivered either face-to-face (F2F) or via a self-paced, asynchronous e-learning format and included pre-post test assessment of knowledge and post-test learner reaction surveys.

**Methods :** Medical students rotating through the required third year pediatric clerkship were randomized to the e-learning or F2F format. At the beginning of each rotation, students completed a 20-item multiple-choice question (MCQ) examination developed based on test blueprint matched with the four sleep medicine competencies. MCQ testing was re-administered at end rotation along with a learner satisfaction form focused on clarity of objectives, organization, effectiveness of instruction, and impact on learning. Repeated Measures ANOVA (RMANOVA) was performed on MCQ test and descriptive statistics on learner reaction form data.

**Results :** In this preliminary analysis of ongoing educational research, 68 students have completed either the e-learning or F2F and the pre-post MCQ test. RMANOVA revealed a significant difference in pre-post MCQ scores (Mean % Correct: F2F pre 52.7 vs. post 76.3; e-learning pre 53.7 vs. post 80.7)  $p < 0.001$ , with no significant difference between the online and the F2F. Learner satisfaction surveys for e-learning and F2F were comparable based on value and ease of format but students reported too heavy a time commitment required for both.

**Conclusion :** E-learning and F2F instruction in sleep medicine are equally effective in improving student knowledge of sleep medicine. Learner perception regarding the amount of instructional time is problematic. However, given the relative prevalence of sleep related disorders across all age groups, the value of this education will be realized in time by the learners.

**Support (optional):** American Sleep Medicine Foundation Educational Research Award

### 1040

#### CONSTRUCTING ENDURING ELECTRONIC SLEEP MEDICINE EDUCATION FOR MEDICAL STUDENTS

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**Introduction :** Enduring electronic teaching resources are becoming an attractive adjunct for the education of trainees and continuing education of practicing physicians. Electronic formats allow students access to educational materials at their convenience while freeing the physician-educator

for other activities. Academic sleep medicine clinicians are in short supply and there is a large unmet need for sleep education. We undertook to create enduring electronic based education in 4 key areas of sleep medicine.

**Methods :** We developed curriculum spanning four key domains of sleep medicine: Sleep Process and Circadian Rhythms, Sleep Disordered Breathing, Parasomnias, and Hypersomnia. We scripted 40-minute modules using Powerpoint and Windows Microsoft Producer to allow the student to listen while viewing the slides. We purchased videotaping equipment to film patients undergoing an office visit and a polysomnographic study from setup to cpap application and obtained videos from colleagues to enhance the concepts of REM behavior disorder, Night terrors, Cataplexy, and drowsy driving. A Learning Management System allowing accessibility for students and instructors already in place at our institution was used for online access for viewing all module materials and test/survey administration.

**Results :** The core modules required 60 physician hours and 160 educator hours to produce and pilot. These modules were then serially piloted online along with their companion questions to fourth year medical students and edited to 30 minutes based on feedback that the time commitment was too great. Companion case based learning was also produced and made available online to students for review. Forty-seven MCQs were developed and piloted to a naive group of 4th year medical students (n=134) with 20 questions retained based on discriminatory power. The development and production of the MCQ test required 20 physician hours and 40 educator hours. The online learning management system allowed rapid assessment of learner utilization of materials and mass/individual communications between learners and instructors.

**Conclusion :** Electronic based learning for sleep medicine required a large upfront commitment in physician and educator time as well as money for production materials and an online depository. Once completed this media provides facilitated accessibility to sleep medicine education. The impact on practice patterns and long-term knowledge retention remains to be determined.

**Support (optional):** American Sleep Medicine Foundation Educational Research Grant

**1041****BRIEF SLEEP DEPRIVATION PRODUCES SELECTIVE DEFICITS IN LATE-PHASE LONG-TERM POTENTIATION IN AREA CA1 OF MOUSE HIPPOCAMPAL SLICES**Vecsey CG,<sup>1</sup> Abel T<sup>1,2</sup>

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**Introduction :** Previous work from our lab demonstrated that physiologically brief sleep deprivation (SD; 5 hrs) produces impairments in hippocampus-dependent memory consolidation, but the mechanisms by which SD impairs memory remain unknown. Long-term potentiation (LTP) in the hippocampus has been shown to rely on molecular mechanisms that are also important for long-term memory. In order to dissect the cellular and molecular mechanisms that are targeted by brief SD, we studied the effects of brief SD on multiple forms of hippocampal LTP with different sets of molecular requirements.

**Methods :** LTP studies were performed in hippocampal slices from young adult C57BL/6J mice that were either sleep deprived by gentle handling for 5 hrs or left undisturbed in their home cages. CA1 field excitatory post-synaptic potentials (fEPSPs) were evoked by Schaffer collateral stimulation. 1-train LTP was induced by a single 100 Hz, 1-s duration train of stimuli. 4-train LTP consisted of 4 such trains applied with a 5-minute inter-train interval. Paired-pulse facilitation was measured in response to closely timed stimuli, and input-output curves recorded the fEPSP slope in response to increasing stimulation.

**Results :** We found that transcription- and translation-dependent maintenance of 4-train LTP was greatly impaired in hippocampal slices from sleep-deprived mice at 150 minutes post-tetanus ( $185.8 \pm 32.8\%$  in control mice (n=4),  $100.8 \pm 3.5\%$  in SD mice (n=5),  $p < 0.05$ , whereas transcription- and translation-independent 1-train LTP was unaffected at 120 minutes post-tetanus. No impairments in initial potentiation or basal synaptic properties were observed in slices from sleep-deprived mice.

**Conclusion :** These findings demonstrate that brief sleep deprivation, in contrast with longer periods of deprivation, has selective effects on late-phase LTP without affecting basal synaptic properties or early-phase LTP. This suggests that brief SD specifically targets mechanisms underlying long-lasting forms of hippocampal LTP, many of which are also required for hippocampus-dependent memory consolidation.

**Support (optional):****1042****SCATTERBRAIN: A NEW MUTANT AFFECTING HYPOTHALAMUS FORMATION AND HYPOCRETIN CELL LOCATION IN ZEBRAFISH**

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**Introduction :** Hypocretin (hcr) is an important modulator of sleep and wakefulness; disruption of the hcr system causes narcolepsy. We are employing a forward genetic approach to discover novel functional regulators of hcr and other sleep-related neurochemical systems. Our model, zebrafish (*Danio rerio*), is ideally suited for developmental and genetic research; it expresses hcr ligands and receptor mRNA in a pattern and location similar to that observed in mammals.

**Methods :** From a pilot wholemount in situ hybridization screen of approximately 200 F2 families from a three-generation ENU mutagenesis, we isolated a family with aberrant hcr expression, and began to characterize this mutation.

**Results :** This new mutant, scatterbrain (F2W315), displays displaced hcr-expressing cells, scattered laterally and dorsoventrally. The pheno-

type is fully penetrant and due to a recessive mutation. At 24 hours post-fertilization (hpf), overall body morphology is normal and the hindbrain and forebrain are well-formed, but the midbrain-hindbrain boundary is partially affected, and the tectal ventricle appears filled with tissue. Lens deterioration generally begins around 48 hpf. Expression of several neurotransmitters, including histamine and melanin-concentrating hormone, appears normal, but expression of others is abnormal: hcr and isotocin (the fish homolog of oxytocin) appear laterally scattered. Interestingly, this suggests that the gene underlying the scatterbrain phenotype is necessary for the organization of a particular subregion of the hypothalamus. Because scatterbrain resembles mutants of the N-cadherin gene (*cdh2*, parachute, *ml17*), we performed complementation tests with the *ml17* (glass onion) allele. Intercrosses had normal phenotypes, indicating complementation. This shows that scatterbrain is a new mutant, corresponding to another - hopefully novel - gene. Genetic mapping and further phenotype characterization is ongoing.

**Conclusion :** The zebrafish can be used as a genetic model to study hypocretin cell development. The existence of this scattered-pattern mutation indicates hcr cells do not need to be organized in clusters: hcr expression is likely cell-autonomous. Cloning of this novel mutation will shed light on the development of the hypocretin system as well as on the development of other brain/vision systems in zebrafish. This approach has potential applications to human disorders, including complex syndromes in which narcolepsy is associated with other defects.

**Support (optional):** NIH NS23724 and HHMI**1043****PRIOR WAKING EXPERIENCE MODIFIES THE SLEEP HOMEOSTAT**Ganguly I,<sup>1</sup> Greenspan R,<sup>1</sup> Shaw P<sup>2</sup>

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**Introduction :** Mounting evidence suggests that sleep may be required for the consolidation of waking memories. However, the molecular link between sleep and memory remains uncharted. This study explores the molecular-genetic basis for the effect of prior waking experience on subsequent sleep in *Drosophila*.

**Methods :** All strains were reared under identical controlled environments to reduce spurious variability in measurements. In addition to standard wild-type strains, EMS-induced point mutations and 50 single P-element insertional mutants and transgenic stocks were screened. The Gal4-UAS enhancer-trap technique was employed for the functional analyses of specific neuronal groups. HPLC was conducted to assay for neurotransmitter content in adult brains. Activity in the fly was assessed using the *Drosophila* Activity Monitoring System (DAMS) developed by Trikinetics (Waltham, MA).

**Results :** Prior waking experience stably modifies the sleep homeostat. Hence, individuals that are socially-stimulated, or trained for an associative learning task, sleep significantly longer than controls. Experience-dependant plasticity in the sleep homeostat is correlated with changes in dopamine levels in the brain and persists beyond a critical period of behavioral development. Increasing the intensity of social interactions during prior waking is linearly correlated with increases in subsequent sleep. The modifiability of the sleep homeostat by prior waking experience is abolished by blocking olfactory and visual input; dopaminergic transmission; by interfering with cAMP signaling and ablating genes that are specifically involved in the formation of long-term memories.

**Conclusion :** This study demonstrates that sleep requirement is dependant on the complexity of social interaction and/or information gleaned during prior waking. Furthermore, this relationship is modulated by dopamine, cAMP signaling and subserved by a genes involved in memo-

ry consolidation.

**Support (optional):** The Neurosciences Support Corps.

### 1044

#### INHIBITION OF THE ENZYME THIOETHER S-METHYLTRANSFERASE MODULATES SLEEP IN MICE

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**Introduction :** Our previous data indicate that mRNA of the gene thioether S-methyltransferase (Temt) varies as function of mouse strain, brain region, time of day, and health status. To evaluate the impact of the enzyme TEMT on sleep, we treated C57BL/6J and BALB/cByJ mice with the TEMT inhibitor sinefungin. These two strains of mice respectively develop dark phase sleep enhancement and light phase sleep fragmentation after influenza infection.

**Methods :** On day 1 of the study, baseline patterns of sleep, activity and temperature were recorded. Immediately after light onset on day 2, mice received an intraperitoneal injection of sinefungin (4 or 8 mg/kg) or saline. C57BL/6J mice were also inoculated intranasally with influenza virus (5 X 10<sup>4</sup> PFU, strain A/HKX31). Recording then continued for 72 hours. Sinefungin or saline injections were repeated on days 3 and 4. Mice were euthanized on day 5, and tissues were collection for subsequent analysis.

**Results :** C57BL/6J mice that were treated with saline (n=6) developed enhanced sleep during the post-inoculation period (paired t-test, p=0.03). This enhancement of sleep was significantly attenuated in mice treated with sinefungin (4 mg/kg/day, n=9) (p=0.038). Administration of sinefungin (4 or 8 mg/kg/day; n=6 and 9, respectively) to uninfected BALB/cByJ mice induced a modest and marginally significant reduction in time spent in SWS as compared to saline-treated mice (n=5) (ANOVA: F=3.521, p=0.053). Sinefungin also significantly reduced Temt mRNA in basal forebrain (ANOVA: F=6.812, p=0.012). Sinefungin treatment did not significantly alter core temperature or locomotor activity.

**Conclusion :** These data suggest that inhibition of the enzyme TEMT reduces sleep in mice. This finding is consistent with our hypothesis that TEMT may regulate sleep by influencing prostaglandin metabolism.

**Support (optional):** Supported by NIH grants HL70522 and RR17543

### 1045

#### INTRACELLULAR cAMP-PKA SIGNALING SYSTEM IN THE PEDUNCULOPONTINE TEGMENTUM (PPT) AND MEDIAL PONTINE RETICULAR FORMATION (MPRF) PLAY OPPOSING ROLES IN THE REGULATION OF REM SLEEP IN FREELY MOVING RATS

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**Introduction :** Our recent studies have demonstrated that the physiological activation of kainate and GABA-B receptors and adenylyl cyclase (AC) within the cholinergic cell compartment of the PPT are involved in regulation of physiological REM sleep (Datta and Prutzman, 2005. *J. Neurophysiol.* 94:1928-1937). These receptors and AC may also directly and/or indirectly involve intracellular cAMP-PKA signaling pathway. Therefore, we hypothesized that this signaling pathway may be involved in the PPT to regulate spontaneous REM sleep. To test this hypothesis, the expression of PKA catalytic (CS-PKA) and regulatory subunits were measured in the PPT and three other parts of the brain at three different conditions of REM sleep.

**Methods :** Experiments were performed on 53 adult male Wister rats. Rats were chronically instrumented with sleep-wake recording electrodes

and guide tubes for the microinjections into the PPT. Following surgical recovery and adaptation to the recording conditions, PKA subunits were measured in the PPT, mPRF, medial prefrontal cortex (mPFC), and anterior hypothalamus (AHTh) of rats with normal level, 77% less, and 84% more REM sleep conditions. In 35 rats, sleep-wake activities were measured for 6-hours (10:00h - 16:00h) following a single microinjection of control vehicle or one of the four different doses (0.28, 0.55, 1.1, and 2.2 nmol/100 nl) of cAMP-PKA activation inhibitor (Rp-CAMPS).

**Results :** The results demonstrated that the amount of CS-PKA in the condition with less REM sleep is reduced in the PPT and mPFC but increased in the mPRF. With higher amount of REM sleep, CS-PKA level increased in the PPT and decreased in the mPRF and mPFC. In addition, the results show that the local inhibition of cAMP-PKA activation in the PPT suppressed REM sleep in a dose-dependent manner.

**Conclusion :** These findings suggest that the activation of the cAMP-PKA signaling pathway in the PPT is an intracellular biochemical/molecular step for generating physiological REM sleep in the freely moving rat. These results also suggest that increased REM sleep suppresses CS-PKA subunit expression in the mPRF.

**Support (optional):** This research was supported by NIH grants: MH59839 and NS34004.

### 1046

#### MICROARRAY EXPRESSION ANALYSIS OF HYPOTHALAMUS MRNA AFTER INTERLEUKIN 1 BETA

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**Introduction :** Interleukin 1 beta (IL1<sub>β</sub>) is well established as a sleep regulatory substance. Low doses of IL1<sub>β</sub>, given intraventricularly (icv) increase NREMS in rats; higher doses decrease NREMS. We analyzed hypothalamic mRNA gene expression after IL1<sub>β</sub> injection using microarrays to identify gene changes associated with low and high dose injection of IL1<sub>β</sub>.

**Methods :** Sterile PBS or IL1<sub>β</sub> was injected icv into rats. Rats were sacrificed two hours later and hypothalami snap-frozen in liquid nitrogen. RNA was extracted, cDNA synthesized and hybridized to U34A rat arrays at Washington State University's Laboratory for Bioanalysis and Biotechnology. Data was uploaded onto the GeneSifter® website and analyzed with GeneSifter® software. Gene expression after low or high doses were compared to that observed after PBS samples. Gene ratios greater than 2.0 (up or down) were tabulated.

**Results :** Low dose IL1<sub>β</sub> altered expression of 36 genes (8 up and 28 down). High dose IL1<sub>β</sub> altered expression of 69 genes (44 up and 25 down). VCAM-1 and ELAM-1 were both up-regulated in both treatment groups. Down-regulated genes in both treatment groups included MIP1alpha, MIP1beta and interleukin 1 alpha. Low dose injection also down-regulated interleukin 6, MX1, IL1<sub>β</sub>, pituitary glycoprotein hormone alpha-subunit and heat shock protein 70. High dose IL1<sub>β</sub> injection up-regulated genes like GADD45a, regulator of G-protein signaling and s100 calcium binding protein. Some genes down-regulated by the high dose include heat shock protein 4, syntaxin 5, and dynamin 2.

**Conclusion :** Comparing results between low and high dose IL1<sub>β</sub> does not obviously identify which genes are responsible for induced sleep or wakefulness since those that promote sleep could be up- or down-regulated after both doses. Further, IL1<sub>β</sub> may act directly upon neurons at the protein level to stimulate a sleep response that doesn't manifest in RNA expression analysis.

**Support (optional):** Supported by NIH NS25378.

## 1047

**REM SLEEP LOSS AFFECTS PLASTICITY-LINKED EARLY IMMEDIATE GENE HOMER1 ISOFORMS IN THE RAT HIPPOCAMPUS**

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**Introduction :** Homer1 is an activity-dependent immediate early gene involved with regulating synaptic plasticity germane to learning via scaffolding glutamate receptor-activated calcium signaling mechanisms. The isoforms of Homer1 carry out contrasting functions. For instance, Homer1a initiates anti-scaffolding events, while Homer1b and 1c execute pro-scaffolding processes.

**Methods :** Male Sprague-Dawley rats (4-6 weeks) were REMS deprived (RD) for 48 hrs by the inverted flowerpot method. Large pedestal control (PC) and cage control (CC) rats were also employed for comparison. Animals were euthanized at 0 and 12 hrs after pedestal removal (1900 and 0700 hrs, respectively). The hippocampus was extracted, flash-frozen, and stored at -70°C for quantitative PCR analyses.

**Results :** At 0 hrs more hippocampal Homer1bc mRNA was detected in the PC group than the CC group. This increase could result from the exposure of the rats to the deprivation chambers. A novel environment affords exploration opportunities that may instigate plasticity events in select neural structures. Such changes appear to be impeded by sleep loss as the RD group did not differ from CCs. There were no group differences in Homer1bc mRNA at the 12 hr timepoint. However, Homer1a mRNA was elevated in RD animals at 12 hrs compared with CC and PC rats, while there were no statistical differences among groups at the 0 hr timepoint.

**Conclusion :** These findings are consistent with a previous report from our laboratory showing cortical Homer1a mRNA to be up-regulated with total sleep deprivation by gentle handling. This increase of the anti-scaffold signal, Homer1a, may trigger a dissociation of glutamate receptor complexes thereby disrupting neural communication. Moreover, the attenuated Homer1bc response incurred by REMS loss could hamper glutamate receptor synchronization of calcium signaling. Such signaling deficits would ultimately suppress synaptic efficacy. Thus, the observed changes in Homer1 appear to be an important mechanism underlying REMS deprivation-induced cognitive deficits.

**Support (optional):** Supported by NSF IBN-0091337 and NIH NS25378.

## 1048

**ISOFORMS OF GHRH RECEPTOR MRNA AND GHRH MRNA IN RAT CORTEX**

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**Introduction :** Hypothalamic GHRH is a sleep regulatory substance. Cerebral cortical GHRH may also play a role in EEG delta wave power since local application of GHRH to the cortex enhances EEG delta power during non-REM sleep thereby suggesting that the GHRH-GHRH-receptor complex is functional in the cortex. Recently we also showed that GHRH receptor protein is present in the rat cortex by Western blot and immunohistochemical methods. However, the isoforms of the GHRH receptor and GHRH expressed in rat cortex are unknown.

**Methods :** Total RNA was obtained from rat cortex, hypothalamus and pituitary tissue. cDNA was synthesized and combined with a variety of gene specific primers for PCR amplification of GHRH receptor and GHRH isoforms. Synthesized products were separated and size estimated

by agarose gel electrophoresis. The GHRH product was sequenced. mRNA levels were estimated by real-time (RT) PCR.

**Results :** The rat cortex contained measurable amounts of GHRH receptor mRNA and GHRH mRNA. Cortical GHRH receptor mRNA included the M-alpha and Z-beta isoforms. The sequence of cortical GHRH exactly matched the pituitary, but not the placental form, of GHRH.

**Conclusion :** Significant expression levels of both genes suggest an important function for GHRH receptor and GHRH in the cortex. Their presence in the rat cortex is consistent with the idea that regulation of sleep is in part, a localized process of the cortex. The identification of alpha and beta isoforms of the GHRH receptor and the pituitary form of GHRH is important for further investigations into the roles these genes play in the cortex and sleep.

**Support (optional):** Supported by NIH NS27250.

## 1049

**QUANTITATIVE VARIATION IN PULMONARY CYTOKINE RESPONSES IN INBRED MICE WITH DIFFERENT SLEEP PHENOTYPES**

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**Introduction :** After intranasal inoculation with influenza virus, C57BL/6J mice demonstrate increased SWS during the dark phase, while BALB/cByJ mice show no sleep enhancement. This time course indicates that sleep-promoting stimuli are generated during the early nonspecific immune response in C57BL/6J mice. In the current study, we assessed whether facets of the early immune response to influenza infection differ in BALB/cByJ and C57BL/6 mice.

**Methods :** C57BL/6J and BALB/cByJ mice (10 per strain) were infected intranasally with A/HKx31 influenza virus immediately after light onset, and were killed 30 hours later (i.e., mid-point of the light phase). Half of the lung was frozen for viral culture and measurement of cytokine levels, and half was fixed in buffered 10% formalin for histopathologic analysis. IL-1-, IL-2, IL-4, IL-5, IL-6, IL-10, IL-12 (p70), and GM-CSF levels were analyzed using Luminex multiplex technology. MIP-1-, TNF- and IFN $\alpha$  were analyzed using commercially available ELISA kits. Cytokine levels were compared between strains using a Student's t-test. Histologic data were evaluated using Mann-Whiney rank sum and Spearman rank order correlation tests.

**Results :** Pulmonary inflammation, as quantified by the percentage of bronchioles and alveoli containing inflammatory cell infiltrates, did not differ significantly between strains (median score of 3 in C57BL/6J mice and 2 in BALB/cByJ mice). BALB/cByJ mice had significantly higher levels of MIP-1- and TNF- in lung homogenates than did C57BL/6J mice ( $1564 \pm 104$  vs.  $716 \pm 138$  pg/mL, and  $4286 \pm 266$  vs.  $2027 \pm 432$  pg/mL, respectively;  $p < 0.0001$ ). IL-1-, IL-2, IL-4, IL-5, IL-10, IL-12, IFN $\alpha$  and GM-CSF did not differ significantly different between strains.

**Conclusion :** BALB/cByJ and C57BL/6J mice differ quantitatively in their early immune responses to influenza infection. These differences may contribute to the generation of the divergent sleep phenotypes observed in these strains.

**Support (optional):** Supported by NIH Grants HL-70522 and RR-17543

## 1050

**ANALYSIS OF A VARIABLE NUMBER OF TANDEM REPEATS (VNTR) OF PER3 GENE IN PRIMATES**

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**Introduction :** Clock genes are usually known to be very well conserved across animal species. Despite these similarities among different species and mainly among mammals, a variable number of tandem repeat (VNTR) localized in exon 18 of Per3 gene seems to be present only in primates. Rodents and dogs show only one copy of the repeat while humans present four or five copies of the repeat. Analysis of this VNTR in different primate species have shown that this repeat also exists but the repetition number is different between species. Curiously a polymorphism in this VNTR, as found in humans, was only found in Gorilla from all studied primates. It is of interest to verify the existence of polymorphisms in this VNTR in other primate species, since it is associated with Sleep Phase Delayed Syndrome and Morning/Evening preferences in humans and may contribute to variability in circadian phenotypes in other primate species as well. In the present study we have analyzed 24 marmosets (*Calithrix jacchus*) and four capuchin monkey (*Cebus apella*) for the VNTR and start to characterize the whole Per3 gene in the marmoset.

**Methods :** We used Clustal W software (MEGALIN, DNA star, Madison, WI) to align human, chimp and mouse Per3 sequences, where we found sequence similarities among the three species, we have designed primers to start to clone the marmoset Per3 gene. Total RNA extracted from liver was reverse transcribed and the designed primers were used to amplify the coding region of the Per3 gene for further sequencing. Genomic DNA was extracted from blood of marmoset and capuchin monkey and the VNTR region was amplified using primers designed from white-tufted-year marmoset deposited sequence (AY827153).

**Results :** From the 24 marmosets studied we have confirmed a former report from one animal that shows this specie contain a longer VNTR expansion with seven repeated copies while the capuchin monkey carries only two copies. Any polymorphism in this region was found in both species.

**Conclusion :** These results suggest that the Per3 VNTR polymorphism, that in humans is associated with circadian phenotypes, is not present in the new old monkeys and may be present only in the primates closest to *Homo sapiens* in the phylogenetic scale. This polymorphism may confer special features to the human circadian system.

**Support (optional):** AFIP FAPESP (CEPID)

## 1051

### LOCAL APPLICATION OF SHORT INTERFERING RNA TARGETING TUMOR NECROSIS FACTOR · (TNF·) INDUCES STATE-SPECIFIC ASYMMETRIES IN EEG SLOW WAVE ACTIVITY

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**Introduction :** TNF· is one of the sleep regulatory substances (SRSs) responsible for locally enhanced EEG slow wave activity (SWA). TNF· mRNA and TNF· protein levels vary in the cerebral cortex with highest levels occurring in rat at light onset, the rats sleep period. The purpose of the current experiment was to identify the effects of locally knocked down TNF· mRNA on the sleep EEG.

**Methods :** Male Sprague-Dawley rats (n=6) with EEG electrodes and micro injection cannula over the somatosensory cortex on both sides of the brain were used. On day 1, the EEG baseline was recorded. On day 2, one side of the brain received 2µl of TNF·-siRNA(50nM) while the opposite side received the same volume of control-siRNA. After injection, EEG and EMG were recorded for 4 additional days.

**Results :** On experimental day 3, there was a small, non-significant, decrease in EEG SWA on the side receiving the TNF· siRNA during daylight hours. On day 4, the side receiving TNF· siRNA had significantly

lower EEG SWA than the side receiving the control siRNA during the daylight as compared to baseline. The reduced EEG SWA occurred only during non-REM sleep. On day 5, the deficit in EEG SWA had returned to control values and was not different from the side of the brain receiving the control siRNA.

**Conclusion :** The deficits in EEG SWA after TNF siRNA occurred at the time of day that deficits in non-REM sleep occurred in TNF-receptor knockout mice. Results suggest that local transcription of TNF· mRNA has a role in sleep regulation.

**Support (optional):** Supported by NIH NS31453

## 1052

### SHORT INTERFERING RNA TARGETING TUMOR NECROSIS FACTOR ·(TNF·) INHIBITS EXPRESSION OF TNF· MESSENGER RNA AND IMMUNOREACTIVITY IN VITRO AND IN VIVO

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**Introduction :** Tumor necrosis factor · (TNF·) is a sleep regulatory substance. RNA interference is the process of silencing genes after transcription using nucleotide specific sequences. The aim of the current experiments was to silence cortical TNF· mRNA in vivo and in vitro and to evaluate the expression of TNF· mRNA using real-time reverse transcription-polymerase chain reaction (PCR) and protein using immunohistochemistry.

**Methods :** For the in vivo experiment, Group I and II male rats were implanted with bilateral guide cannula in the somatosensory cortex (Bregma: -2.5mm AP, 5.5 mm ML). One side received 2µl of si-TNF· (50 nM) while the opposite side received si-Control RNA. Half of the rats were injected with the siTNF on the left, while the other half, were injected on the right. These injections were made at light onset (9am). In Group I after 24 h, the rats (n=8) were killed to analyze mRNA levels. In Group II rats, 48 h after siRNA and 6 h of sleep deprivation, rats (n=6) were perfused for immunohistochemistry. For the in vitro experiment, primary cultures of somatosensory cortical neurons were prepared from 19-21 day fetuses. The cultures were treated with siRNA transfections with Lipofectamine 2000 for 24 h. Total RNA was extracted using Trizol reagent and analyzed for TNF· mRNAs using real-time PCR.

**Results :** Silencing of TNF· mRNA in Group I resulted in a 50% (p<0.0001) decrease in somatosensory cortex TNF· mRNA in vivo. In Group II the number of TNF·-immunoreactive cells in layer V of the somatosensory cortex relative to the opposite side injected with the control siRNA was reduced. In vitro transfection with TNF· siRNA also resulted in a significant 45% suppression of TNF· mRNA as compared with control siRNA transfection.

**Conclusion :** Results suggest that silencing of TNF· mRNA reduces both mRNA and protein in the rat cortex.

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

## 1053

### ZEBRAFISH IS A VALUABLE MODEL FOR PHARMACOLOGY OF SLEEP STUDIES

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**Introduction :** The zebrafish is an emerging model organism in pharmacological and behavioral research. Neurochemical modulators of sleep have been identified and appear to anatomically interconnect similarly as in mammals. Zebrafish proteins typically display high levels of identity

with their human orthologs in functional domains, approaching 100% in substrate binding regions, explaining why many drugs elicit comparable effects in zebrafish and humans. Here we investigated the effects of commonly used hypnotics on zebrafish locomotor activity using an automated behavioral analysis system.

**Methods :** Locomotor behavior was monitored in 5-8 dpf zebrafish larvae in response to single exposures (1.10<sup>-6</sup> M to 1.10<sup>-3</sup> M) to conventional hypnotics. Video images of the treatment and control groups (n=20 larvae/group; n=6 groups/treatment/dose) were recorded in constant darkness for 5 hours, and locomotor activity was measured using the movement quantization version of Videotrack (Viewpoint). Classical drug reversal experiments were performed to verify specificity. Zebrafish homologs of histamine receptor H1, GABA A (alpha subunit) and GABA B (1 and 2) receptors were identified through translating queries of the zebrafish Ensembl database using human sequences as queries. Multiple alignments and phylogenetic trees were performed using ClustalW.

**Results :** Of 23 compounds tested, 14 significantly altered the swimming behavior of zebrafish larvae. Dose/response experiments showed that pentobarbital, flurazepam, baclofen (both R and S) and mepyramine induced significant dose-dependent decreases in spontaneous locomotor activity. The maximal effect (Emax) for Baclofen S was about 3 times lower than Emax for Baclofen R, suggestive of partial agonism. At high dose, larvae were clearly sedated and no spontaneous movement was detected, except for baclofen R, for which residual activity was present. Pretreatment with baclofen S or specific GABA B Receptor antagonists, blocked the behavioral effects induced by baclofen R at EC50, indicating this effect is mediated through a specific receptor.

**Conclusion :** Genomic analysis of the targeted receptors together with pharmacological data provide evidence for the functional conservation of neuropharmacologic pathways in zebrafish. We believe that forward genetics in zebrafish through pharmaco-behavioral screens may become an important step toward discovery of new hypnotic drugs and their targets

**Support (optional):** NIH NS23724 and HHMI

## 1054

### APPLICATION AND VALIDATION OF RNA INTERFERENCE IN SLEEP RESEARCH: TARGETING OREXIN SYSTEM IN RATS

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**Introduction :** RNA interference is a sequence-specific gene suppression mechanism induced by a double-stranded short interfering RNA (siRNA). However, to our knowledge, in vivo siRNA application has never been used in sleep research. To investigate the broad applicability of siRNA in spontaneously behaving rats, we have used siRNA targeted against selective components of the orexin/hypocretin system, namely, preproorexin (P-orexin) in the perifornical hypothalamus (PFH) and orexin type I receptor (OR1) in the locus coeruleus (LC), and studied their effects on sleep-wakefulness

**Methods :** Effect of siRNAs on sleep-wakefulness. Adult male rats were housed under 12:12 h light-dark cycle. The siRNAs (targeting either P-orexin or OR1) were microinjected bilaterally into the target regions (PFH or LC) and their EEG and behavior were monitored light-dark cycle. The siRNAs (targeting either P-orexin or OR1) were microinjected bilaterally into the target regions (PFH or LC) and their EEG and behavior were monitored. Validation of specific knockdown. The siRNAs were ipsilaterally microinjected into the target regions and scrambled siRNA into the contralateral side. Rats were sacrificed at different time points, brains removed and processed for immunohistochemistry and/or in situ

hybridization to demonstrate the knockdown of the targeted mRNA and protein. Selectivity (“on target effects”) of siRNAs was determined by detection of melanin-concentrating hormone (MCH) and dynorphin B (Dyn-B) (colocalized with orexin) (PFH) and tyrosine hydroxylase (TH) immunoreactivity (LC).

**Results :** Our initial data indicates that siRNA against P-orexin specifically reduced the target mRNA and peptide. MCH neurons were unaffected. Behavioral/EEG data (N=6) showed a persistent increase in REM, only during the dark period, for 4 days following siRNA injection. In the rats treated with siRNA against LC OR1, an increase in REM sleep (for 2 days, only in dark period) was observed. Immunohistochemical detection of Dyn-B in orexin neurons and OR1 on TH neurons is pending.

**Conclusion :** Our results indicate that siRNA is a powerful tool to selectively knockdown target gene expression in naturally sleeping rats. Furthermore, our data suggest the orexin system may be involved in diurnal gating of REM sleep.

**Support (optional):** NIMH grants 062522, 01798 and Dept. Vet. Aff.

## 1055

### MUTATIONS IN HYPERKINETIC (HK) REDUCE SLEEP IN DROSOPHILA MELANOGASTER

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**Introduction :** The Shaker (Sh) gene encodes the alpha subunit of a tetrameric potassium channel that passes a fast inactivating voltage-dependent current (IA). Here we tested whether other genes that affect IA also affect sleep. Hk encodes a beta regulatory subunit that, when bound to the alpha subunit, changes the kinetics and increases the peak and sustained current. We studied two loss-of-function Hk mutants (HkY and Hk1) and a wild-type Hk+ transgene to determine if Hk affects daily sleep amount in flies.

**Methods :** Locomotor activity, sleep intensity, and performance were measured as previously (Huber et al., 2004; Cirelli et al., 2005). The HkY and Hk1 alleles were tested in three different genetic backgrounds: w1118, wCS10 and Canton-S. A wild-type Hk+ transgene (Hk17K-X194) inserted on chromosome 2 was crossed with HkY and Hk1 mutants to determine its ability to complement the sleep phenotype

**Results :** Daily sleep amount in HkY and Hk1 male mutants was reduced by one-third to one-half compared to their wild-type siblings in all three genetic backgrounds. After inheriting the wild-type Hk+ transgene mutant Hk- male flies slept as much as their wild-type sibling (Hk is on the X chromosome). Also, homozygous (Hk- /Hk-) females slept less than heterozygous (Hk- /Hk+) females in the w1118 background (female have only been tested in the w1118 background thus far).

**Conclusion :** Hk- loss-of-function mutations consistently reduce sleep in both female and male flies in all the genetic backgrounds tested so far. The ability of the wild-type Hk+ transgene to complement the sleep phenotype confirms that the Hk locus is responsible for the sleep phenotype. Hk- mutations produce a weaker sleep phenotype than Sh- loss-of-function mutations, which can reduce sleep by two-thirds. This weak phenotype is expected, since Hk- mutations only reduce current amplitude and intensity while Sh- mutations can completely abolish pore function.

**Support (optional):** United States Defense Advanced Research Project Agency

## 1056

### RARB GENE AFFECTS CORTICAL SYNCHRONY DURING SLEEP

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**Introduction :** In contrast to most inbred strains, DBA/2J (D2) mice show reduced delta activity during SWS, and the EEG is dominated by theta activity instead. Using a genetic approach we identified the molecular cause of this EEG trait.

**Methods :** The contribution of delta oscillations to SWS power spectra was determined in >10 inbred strains. 25 BXD-RI lines were used to map the gene responsible for the difference in delta power between D2 and C57BL/6J (B6) mice. Retinoic acid receptor beta (Rarb) subtype knockout lines and their D2 hemizygotes were recorded. Effects of the Rarb polymorphisms on in vivo transcription level were assessed by Taqman.

**Results :** QTL analysis indicated the presence of an autosomal recessive gene in the centromeric region of chromosome 14 tightly linked to delta activity. Fine mapping revealed a single nucleotide polymorphism in the second untranslated exon of the Rarb gene. Delta activity was increased in Rarb KO mice, while a significant 'recovery' of delta power was observed in Rarb/D2 hemizygotes confirming the implication of this gene in delta activity. All four Rarb transcripts are expressed at higher levels in D2 mice compared to B6 but only Rarb1 expression varied with delta activity in 8 other strains. Preliminary findings indicate that in D2 mice, but not in B6 mice, injections of all-trans retinoic acid (10mg/kg) enhance delta activity specifically.

**Conclusion :** Changes in the relative contribution of delta oscillations to the SWS EEG are linked to Rarb gene and more specifically to Rarb1. Retinoic acid, the active derivative of vitamin A plays a major role during ontogenesis and particularly during the development of the brain through dopaminergic pathways. Sleep and the sleep EEG are also developmentally regulated. Whether it is through brain development and plasticity or through dopaminergic pathways that Rarb regulates the contribution of delta activity during SWS remains to be documented.

**Support (optional):** Research supported by Swiss National Science Foundation, CNRS, and INSERM

## 1057

### LEPTIN GENE VARIATION IS ASSOCIATED WITH SLEEP DISTURBANCE IN HIV-INFECTED ADULTS

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**Introduction :** A combination of genetic and environmental factors impact sleep in HIV-infected adults. This study examines the relationship between genetic variation of two adipokines, leptin and adiponectin, as predictors of variations in total sleep time (TST), body mass index (BMI), and lipoprotein profiles.

**Methods :** Fasting bloods were collected from 105 HIV-infected men and women (ages 23 to 60) for genetic and metabolic analyses. The adiponectin c.45T>G and leptin c.-2548G>A genotypes were collected by restriction fragment polymorphism assay. Wrist actigraphy (Ambulatory Monitoring, Inc.) was used to monitor their sleep for 72 consecutive

weekday hours. Data were also collected from a 3-day Sleep Log during the 72-hour collection period. The sample was dichotomized as those having less than 7 hours TST and those with 7+ hours of nighttime TST.

**Results :** This sample had a leptin c.-2548G>A minor allele frequency of 0.338 with the following genotype frequencies: AA:0.152, AG:0.372, and GG:0.476. The minor A allele carriers were more likely to have increased plasma triglycerides (p = 0.017), increased very low density lipoprotein-triglyceride (p = 0.031), and increased high density lipoprotein-cholesterol (p=0.007) as well as actigraphy recorded TST of 7 hours or more at night (42% vs. 23%, p = 0.049). Adiponectin c.45T>G had a G minor allele frequency of 0.15 and genotype frequencies: TT:0.717, GT:0.264, and GG:0.019. The TT genotype carriers were less likely to sleep 9 hours or more at night (3% vs. 14%, p = 0.040). There was no relationship between these two adipokine gene variations and BMI or time spent awake after sleep onset (WASO).

**Conclusion :** These results provide preliminary evidence in a sample of HIV-infected subjects of a genetic association between two adipokine gene variations and sleep parameters that include TST. Analyses are currently in process to examine associations with circadian rhythm parameters as well.

**Support (optional):** NIH Grant# R01 MH074358, KA Lee, P.I.

## 1058

### THE <Lc>MA RECEPTOR ,1 SUBUNIT IS REDUCED BY STIMULATION OF HYPOTHALAMIC GABAA RECEPTORS IN VITRO

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**Introduction :** Posterior hypothalamic GABA release is increased during sleep (Nitz & Siegel, 1996). We found that the rat ,1 subunit (r,1) of GABAA receptor (GABAAR) mRNA level is reduced in the perifornical region of hypothalamic slices in vitro following stimulation of GABAARs, and that the same mRNA is also decreased following sleep when compared to short-term sleep deprivation at the same circadian time (Volgin & Kubin, APSS2003; 2005). GABA suppresses human ,1 subunit (h,1) promoter activity and ,1 subunit mRNA expression in vitro, with a 72-bp construct containing a tripled initiator element (3xInr) being sufficient to mediate this response (Russek et al., 2000). Our computational analysis revealed the presence of a common binding site for the nuclear DEAF-1 related transcriptional regulator (NUDR) on the sequence of both h,1 3xInr and a homologous region of the predicted r,1 promoter. We now investigated whether hypothalamic NUDR mRNA levels in rat hypothalamic slices in vitro are sensitive to stimulation of GABAARs.

**Methods :** Posterior hypothalamic half-slices from 12 rats were incubated for 1.5 h in artificial cerebrospinal fluid (ACSF), or a GABA reuptake blocker (NO-711; 20 μM), or NO-711 with the GABAAR antagonist, gabazine (20 μM). mRNA levels of NUDR and c-fos were then quantified in 700 μm tissue punches from the perifornical region using RT-PCR. The data are expressed in cDNA copy numbers per 1 ng of total RNA in the sample ±SE.

**Results :** The NUDR mRNA levels were 990±140 (n=8) following incubation with ACSF; 540±140 (n=6) in NO-711 (p<0.05 vs. ACSF), and 930±85 (n=6) in NO-711 with gabazine (p<0.04 vs. NO-711 only). In contrast, c-fos mRNA levels were not altered.

**Conclusion :** Stimulation of perifornical GABAARs decreases the mRNA level of NUDR, a factor that may stimulate transcription of r,1. This mechanism may be also responsible for transcriptional downregulation of r,1 that occurs during sleep.

**Support (optional):** HL-071097 and ASMF # 26-CA-04.



1059

**SLEEP-WAKE ARCHITECTURE EXHIBITS A GENETIC RELATIONSHIP TO DAILY FLUCTUATIONS OF LOCOMOTOR ACTIVITY***Paul KN, Losee MW, Simkin D, Turek FW, Shelton J*

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**Introduction :** Empirical relationships between daily fluctuations of locomotor activity and the corresponding amount, distribution, and intensity of sleep have been examined however the physiological and genetic mechanisms linking activity and sleep-wake architecture remain largely undefined. In the current study, we have investigated potential genetic links that may associate sleep and wakefulness with total activity.

**Methods :** At four months of age, male mice from eight different inbred strains were implanted with EEG/EMG electrodes for the polysomnographic determination of sleep-wake states. Following recovery, 48 hrs of baseline recordings were collected. In addition, a grid array of infrared beams was used to measure spontaneous locomotor activity simultaneously. For correlative analysis, a Pearson's test was used to detect the association between activity and sleep-wake parameters. To determine significance, means of correlation coefficients for each strain were compared using an ANOVA.

**Results :** One-way ANOVA revealed significant differences ( $p < .05$ ) in the linear correlations between total activity and amounts of sleep and wakefulness across the eight strains. The strain with the greatest correlation had a mean coefficient of  $(-0.91 \pm 0.02)$  for total sleep and activity while the strain with the least correlation had a coefficient of  $(-0.42 \pm 0.09)$  for sleep and activity. The mean intrastrain variance for these measures was relatively low while interstrain variance was relatively high. By contrast, NREM delta power, a measure of sleep intensity during NREM sleep, did not exhibit a high degree of correlation with activity in any strain and exhibited a relatively high intrastrain variance and a relatively low interstrain variance.

**Conclusion :** These data suggest that the relationship between locomotor activity and daily amounts of sleep and wakefulness is at least partially genetically encoded, while the relationship between activity level and sleep intensity is not.

**Support (optional):** This research was supported by NIH AG18200 and AG11412.

1060

**SEASONALITY ASSOCIATED WITH THE SEROTONIN 2A RECEPTOR POLYMORPHISM***Lee H, Sung S, Lim S, Paik J, Kim L*

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**Introduction :** This study investigated the relationship between the serotonin 2A receptor -1438 A/G polymorphism and seasonal variation in a Korean young population.

**Methods :** 297 young Korean medical students were recruited in this study. All subjects were free of major medical and psychiatric problems. They were genotyped for the 5HTR2A -1438 A/G SNP and evaluated the seasonal variation in mood and behavior by Seasonality Pattern Assessment Questionnaire (SPAQ).

**Results :** Global Seasonality Score (GSS) of SPAQ between three genotypes were not different. However, the comparison between seasonals (syndromal plus subsyndromal SAD according to Kasper's criteria) and normal subjects showed significant difference in the genotype distribution between seasonal and normal subjects. Winter type seasonals showed significantly higher frequency of 5HTR2A -1438 A allele compared with other subjects ( $\chi^2 = 6.80$ ,  $p = 0.009$ ; odds ratio [OR] = 1.79; 95% confidence

interval [CI], 1.15 - 2.78).

**Conclusion :** These results suggest that the 5HTR2A -1438 A/G polymorphism is related to seasonality in the Korean population.

**Support (optional):**

1061

**ADOLESCENT SLEEP DISTURBANCE AND SCHOOL PERFORMANCE: THE COFOUNDING VARIABLE OF SOCIOECONOMICS**

Forister N,<sup>2</sup> Pagel JF<sup>1</sup>

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**Introduction :** Sleep disturbances occur at high frequency in adolescents. This study assesses the association of reported adolescent sleep disturbance with school performance while controlling for socioeconomic variables.

**Methods :** An IRB approved questionnaire was distributed in science and health classes at two associated middle and high schools in Pueblo Colorado near the end of the 2005 school year (#500). This questionnaire included questionnaires on sleep disturbance for completion by students, and socioeconomic for completion by parents. School performance was assessed by student report of grade point average (GPA).

**Results :** Of 279 completed questionnaires 55.8% (165) included complete demographic data (33%). Questionnaires assessed 18 sleep variables and 6 socioeconomic indices. Variables significantly affecting reported GPA are described below: 1)GPA of less than 2.0 was significantly correlated with total household income (THI) < \$50,000 (50K)(p<.01), higher avg. weight(p<.01), and increased student reports of difficulty focusing(p<.01), falling asleep in class(p<.01), restless legs(p<.02), hard to wake in the morning(p<.02) and student report of not getting enough sleep(p<.05). GPA > 3.5 was significantly correlated with total household income > \$75,000 (75 K)(p<.02) and lower frequency of daytime sleepiness(p<.05). 2)Because of the significant contribution of socioeconomic status as defined by household income, data was reanalyzed controlling for this variable. Note that no students with THI > 75K had a GPA of less than 2.0. For the grouping with THI < 50K, GPA < 2.0 was significantly correlated with higher average weight(p<.01) and student reports of sleep onset insomnia(p<.02) and falling asleep in class(p<.01). A reported GPA > 3.0 was significantly correlated with less reported snoring more than ½ the time(p<.02). For the grouping with total household income > 75 K; GPA < 3.0 was significantly correlated with increased student reports of daytime sleepiness(p<.02); and GPA > 3.5 was significantly correlated with higher avg. weight(p<.02) and increased reports of snoring more than ½ the time(p<.01).

**Conclusion :** The socioeconomic variable of total household income significantly impacts the effects of disordered sleep on school performance. After controlling for that variable, student reports of sleep onset insomnia, daytime sleepiness and falling asleep in class persist in their significant correlation with lower levels of school performance.

**Support (optional):**

1062

**SLOW WAVE SLEEP ENHANCEMENT PROMOTES SUSTAINED ATTENTION INDEPENDENTLY FROM ALERTNESS**

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**Introduction :** Slow wave sleep (SWS) has been hypothesized to be a time of heightened restoration. We explored the value of enhanced SWS, by administering tiagabine during a period of sleep restriction.

**Methods :** After baseline PSG, performance, sleepiness and mood assessment, 38 subjects received either tiagabine 8mg (T8; 8m, 11f; 26.7+8.1

y/o) or placebo (PBO; 9m, 10f; 26.0+6.1 y/o) on four consecutive nights (N3-N6) with sleep restricted (SR) to 5 hours (0100-0600). PSGs were performed nightly and daytime assessments were repeated after SR N5 and N6.

**Results :** Baseline PSG and MSLT did not differ between groups. On SR N3-N6 sleep was identical between groups with the exception that T8 averaged 29.1 more minutes of SWS as compared to baseline; whereas SWS for PBO averaged 5.4 minutes less. Mean MSLT latencies on SR days 5 and 6 were 5.2 (+/- 3.4) and 4.3 (+/- 3.6) minutes for T8 and 5.4 (+/- 3.3) and 5.0 (+/- 3.4) minutes for PBO (ns). Mean PVT reaction time (p<.042), number of lapses (square root transformation; p<.018), and slowest 10% of responses (p<.029) were significantly lower in T8 than PBO. T8 Ss reported greater restorative nature of sleep than did PBO (p<.006). On the Wisconsin Cart Sorting Task T8 Ss took fewer trials to complete the first category (p=.007) and the entire task (p=.036), committed fewer total (p=.047) and perseverative errors (p=.044), and had a higher correct trial response rate (p=.049) than did PBO. No group differences were seen on the POMS, KSS, TTCT-Verbal, PASAT or N-Back tasks.

**Conclusion :** During the four-night SR period T8 increased SWS, and the impact of SR on PVT and WCST performance and ratings of the restorative nature of sleep were significantly reduced. MSLT and KSS did not differ between groups. These findings are consistent with the hypothesis that SWS enhancement is protective against some consequences of sleep restriction.

**Support (optional):**

1063

**IN THE DROWSY STATE, ERRORS OF OMISSION IN A VISUAL REACTION-TIME TEST OCCUR WITH EYES OPEN OR CLOSED**

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**Introduction :** In a previous pilot study (Johns MW. Sleep 2003;26:A52) it was reported that errors of omission (EOO) in a visual reaction-time test while in the drowsy state can occur with eyes open or closed. Our aim was to replicate that study with new subjects and many more EOOs.

**Methods :** Twenty seven volunteers (M/F=15/12, ages 17-29 yr) performed a 10-20 min visual reaction-time test (the Johns Test of Vigilance or JTV) when alert, and after being awake for 20-40 hr. They made a push-button response to a 400 msec change of shapes on a computer screen at intervals of 5 to 15 sec. The position of their eyelids, recorded continuously by a system of infrared oculography (Optalert™) and confirmed by video-camera, was noted whenever an EOO occurred (no response within 2 sec).

**Results :** There were 507 EOOs when sleep-derived (9.6% of 5280 stimuli presented) but only 11 EOOs (0.2% of 6971 stimuli) when alert. When drowsy, the eyes were closed throughout the stimulus for 46.2% of EOOs, partially closed throughout the stimulus for 27.8 %, fully open for some of the stimulus for 11.2%, and fully open throughout the stimulus for 14.8%. ie. a total of 26.0% of EOOs occurred with eyes wide open for long enough to see the stimulus. Occasional EOOs of this type also occurred when alert.

**Conclusion :** Eyelid closure prevents visual input and can cause an EOO to a brief (400 msec) stimulus whether the subject is alert or drowsy. EOOs are much more common after sleep deprivation, but not simply because of more frequent and prolonged eyelid closures with blinks etc. Many EOOs occurred here in the drowsy state with eyes wide open, implying a failure of visual attention which may be centrally mediated and which occurs much more frequently when drowsy. Eyelid closure alone cannot characterize drowsiness.

**Support (optional):**

**1064****RELATIONSHIP BETWEEN REPORTED AND MEASURED SLEEP TIMES. THE SLEEP HEART HEALTH STUDY (SHHS)**

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**Introduction :** Subjective and objective assessments of sleep may be discrepant due to sleep misperception and measurement, which may change the quality and quantity of a person's usual sleep. This report compares actual sleep times from polysomnography (PSG) with self-reports of habitual sleep times and sleep times estimated on the morning after PSG in adults.

**Methods :** Unattended PSGs were performed as part of the 2nd examination of the SHHS in the subject's home. PSG total sleep time (PSG-TST) and sleep onset latency (PSG-SOL) were obtained. Habitual total sleep time (HAB-TST) and sleep onset latency (HAB-SOL) were obtained from participants who completed a Sleep Habits Questionnaire. Estimated total sleep times (EST-TST) and sleep onset latency (EST-SOL) were obtained from subjects who completed a Morning Survey the day after the PSG. Differences were evaluated according to gender, ethnicity, body mass index (BMI), and the time-zone of their residency.

**Results :** Subjects were 55.2% female, 75% Caucasian, and 38.4% were obese. 51.2% of the subjects resided within the Pacific/Eastern time-zones and 48.8% within the Mountain/Central time-zones. The mean HAB, EST, and PSG, TST were 426, 384, and 364 minutes respectively ( $p < 0.001$ ). The mean HAB, EST, and PSG, SOL were 16, 21, and 16 minutes respectively ( $p < 0.001$ ). PSG-TST was higher for females (371 min.) than males (355 min.  $p < 0.001$ ), and lower for obese (358 min.) than non-obese subjects (367 min.  $p < 0.001$ ). Although subjects in the Mountain/Central time-zone reported higher HAB and EST, TST (432 and 393 min. respectively) than those in the Pacific/Eastern time-zone (420 and 375 min. respectively  $p < 0.001$  for both), there were no significant differences in the PSG-TST.

**Conclusion :** Self-reported total sleep times are overestimated even on the morning after a night of sleep. There is less overestimation of sleep latency. Subjects in the Mountain/Central time-zones reported more sleep time than those in the Pacific/Eastern time-zones.

**Support (optional):** HL062373-05A2S1 HL53940, HL53941, HL53938, HL53916, HL53934, HL53931, HL53937, HL64360, HL63463, HL63429.

**1065****A NEW SCALE OF DROWSINESS BASED ON MULTIPLE CHARACTERISTICS OF BLINKS: THE JOHNS DROWSINESS SCALE**

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**Introduction :** Drowsiness is the intermediate state between alert wakefulness and sleep, to be distinguished from fatigue. We describe here a new scale, the Johns Drowsiness Scale (JDS), that measures different levels of drowsiness continuously, particularly in people who should remain alert, e.g. while driving.

**Methods :** Volunteers performed a 10-20 min visual reaction-time test (the Johns Test of Vigilance or JTV) when alert, and after being awake for

20-40 hr, while their eye and eyelid movements were monitored by infrared reflectance oculography (Optalert™). The mean and SD for each min (after logn transformation where appropriate) for many variables, such as the velocity and duration of saccades and of each component of blinks, were generated automatically. Backward stepwise multiple regression analysis was performed on data for 542 min from 41 alert Ss, who responded normally in the JTV (coded 1), and for 326 min from 25 sleep-deprived Ss, who made errors of omission in JTVs, with no response within 2 sec (coded 8).

**Results :** Multiple  $R=0.72$  ( $R^2=0.52$ ) ( $p < 0.0001$ ). The JDS (range 0-10) was based on regression weights for significant predictors of JTV errors, many newly described, such as the velocities of eyelid closure and reopening during blinks, the duration of each component of eyelid movements during blinks (eg duration of eyelids remaining closed), and total blink duration (not pupil size or blink frequency) The mean JDS when alert was  $2.3 \pm 1.2$ , and when drowsy was  $5.9 \pm 2.3$  ( $p < 0.001$ , t-test). The sensitivity of the JDS was 91.3% and specificity 81.6% for detecting drowsiness that caused significant performance impairment.

**Conclusion :** The JDS measures drowsiness continuously, based on a combination of ocular measures, many of which are new. The JDS does not require individual calibration. It can be used to monitor drivers' drowsiness and warn them before they fall asleep at the wheel and crash.

**Support (optional):**

**1066****INDICATIONS OF EFFORT REGULATION: HEART RATE VARIABILITY, SLEEPINESS, AND PERFORMANCE IN OLDER DRIVERS**

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**Introduction :** Heart rate variability (HRV) decreases with increasing age and workload. Heart rate (HR) increases with increasing workload and decreases with time on task. This study's objective was to investigate the relationship between HRV and extended driving simulator performance. Given that older drivers already have decreased HRV, we expected fatigue effects to result in increased HRV and decreased HR.

**Methods :** Twenty older participants (72 + 5 y/o) drove for 60-minutes on a monotonous highway simulation (STISIM). We analyzed HRV using the normalized low frequency (LF) power band (0.04-0.15 Hz), HR, and driving performance over six consecutive 10-minute driving segments. Participants were divided into those with increasing (N=8) and decreasing (N=12) HRV power over time. Subjective sleepiness was assessed using a visual analog scale.

**Results :** Consistent with fatigue and workload effects, driving performance measured by lane position variability ( $p=.004$ ) and HR ( $p < .001$ ) decreased over time but did not differ between the increasing and decreasing HRV groups. An interaction between HRV group and subjective sleepiness indicated that the increasing HRV group had more subjective sleepiness before and after the drive as compared to the decreasing HRV group ( $p=.044$ ). However, there was no change for decreasing HRV group in subjective sleepiness before and after the drive. In sum, performance and HR was consistent between the two HRV groups but sleepiness differed.

**Conclusion :** The driving task becomes more difficult as arousal decreases and sleepiness increases. As expected, those with increased HRV had increased sleepiness and decreased HR indicating a decrease in workload over the drive. However, those with decreasing HRV had no increase in sleepiness. This suggests that those with decreasing HRV were aware of

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their sleepiness, adjusted their arousal level by increasing their effort, and consequently increased workload. Regulation of effort may help maintain arousal and performance in older drivers.

**Support (optional):** Research was supported by the EVMS Glennan Center for Geriatrics and the Division of Sleep Medicine. Technical support and analysis of HRV was performed using the Kubios HRV Analysis software from the Biomedical Signal Analysis and Medical Imaging Group, University of Kuopio, Finland.

### 1067

#### COMPARING THE BENEFITS OF A NAP, CAFFEINE, MODAFINIL AND PLACEBO ON MULTIPLE MEMORY PROCESSES

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**Introduction :** Naps enhance a wide range of learning, including visual perceptual, motor and declarative memory. However, napping is not as common a sleepiness-countermeasure as caffeine and modafinil. The extent to which these wakefulness promoters produce benefits equal to napping is unknown. In a double-blind study, we compared the effects of a 60-90min nap to 200mg of caffeine, 100mg of modafinil, and placebo on three different memory processes.

**Methods :** 16 healthy volunteers were tested on three different types of learning: 1) perceptual: Texture Discrimination Task (TDT), 2) motor: Finger Tapping Task (FTT), 3) declarative: Hopkins Verbal Learning Task-revised (HVLT). The first test session was at 9:30AM. At 12:30, all subjects were fitted with polysomnography monitors. Starting at 1PM, nappers slept up to 90 minutes but stayed in bed no later than 3PM, while non-nappers listened to a book on tape. Pills were administered at 2:30PM. Vitals signs were measured every half hour. At 3:30PM, all subjects retested. Task order was randomized across subjects, and each test session lasted 1.5 hours.

**Results :** Group differences were found on the three memory tasks. TDT: nappers showed improvement, there was no change in either drug group, and performance deteriorated in the placebo group. FTT: The caffeine group showed faster response times, whereas the modafinil group showed impaired accuracy. HVLT: the modafinil group showed increased delayed recall, whereas the caffeine group showed decreases in most measures of declarative memory; nappers and placebo showed no change.

**Conclusion :** We found differential memory enhancement and deterioration with the administration of a nap, caffeine and modafinil. In these preliminary results, napping enhanced perceptual learning; caffeine improved motor learning, but impaired declarative memory; modafinil improved declarative memory but impaired motor learning. These results have important implications for sustained performance applications in civilian and military operations.

**Support (optional):** Research supported by F32 EY015564

### 1068

#### THE EFFECT OF EXPERIMENTALLY INDUCED SLEEP FRAGMENTATION ON TWO TESTS OF ATTENTION IN RATS

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**Introduction :** Sleep fragmentation, a symptom in many clinical disorders leads to sleepiness, deficits in attention, and cognitive impairment.

The effect of experimental sleep interruption (SI) on rats' performance in operant tasks of attention was studied.

**Methods :** Forced locomotion on either a treadmill (with a rubber belt) or a rotating disk (with standard bedding material) was used to awaken male Fischer-Norway rats every 2 min using a schedule of 30s on: 90s off. An exercise control used a forced locomotion schedule of 10min on: 30 min off. In the rodent sustained attention test (RSAT) rats were required to monitor a light and respond on one lever if the light had flashed (500ms), or the other lever if no light was seen. Rats were water restricted and received 100ul water for a correct response.

**Results :** 10, 24, or 72h of SI on the treadmill prior to RSAT performance led to a significant increase in the number of errors of omission, an effect that was not dose dependent. Video observation revealed that these omissions occurred during protracted grooming episodes. Next, after 24h treadmill-induced SI rats were allowed to groom (but not sleep) in their home cage prior to RSAT testing; subsequently rats neither groomed nor made any omissions during task performance. Similarly, SI induced by the rotating disk produced neither grooming nor omissions in RSAT performance. Finally, initial findings indicate that 24h SI on the rotating disk did not produce grooming, but did increase omissions in the 5 Choice Serial Reaction Time test (5CSRT), supporting our published findings with this test.

**Conclusion :** We conclude that the RSAT, when using a fixed stimulus duration, is less sensitive than the 5CSRT to SI-induced disruption. Ongoing studies will use variable stimulus durations in the RSAT, and complete the 5CSRT study using both treadmill and rotating disk methods of inducing SI.

**Support (optional):**

### 1069

#### RESPONSE SURFACE MAP ANALYSIS OF PVT PERFORMANCE IN A CHRONIC SLEEP RESTRICTION DOSE RESPONSE EXPERIMENT WITH AND WITHOUT NAPS

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**Introduction :** This study investigated the effect of a range of restricted nocturnal sleep schedules with and without diurnal naps on psychomotor vigilance test (PVT) performance. The objective was to determine whether split sleep schedules with reduced sleep time could serve to increase total wake time while preventing cumulative reductions in alertness.

**Methods :** N=93 healthy adults (aged 21-49y; 39 females) participated in a 10-night sleep restriction protocol where they were assigned to one of 18 sleep regimens. These conditions involved restricted nocturnal anchor sleep (4.2h, 5.2h, 6.2h or 8.2h TIB) and a diurnal nap (0.4h, 0.8h, 1.2h, 1.6h, 2.0h or 2.4h TIB) or no nap. Neurobehavioral performance was tested at 2h intervals during scheduled wakefulness. PVT performance lapses (sleep inertia bouts excluded) were averaged by day for each subject. Response surface maps were constructed to examine cumulative impairment across days as a function of anchor sleep and nap sleep durations.

**Results :** The rate of degradation in PVT performance across the 10 restriction days was found to be accurately described by a linear function of daily total TIB (i.e., anchor + nap), with greater total TIB per 24h resulting in fewer PVT lapses ( $\chi^2[1]=4.9$ ,  $p=0.03$ ). Differentiating between anchor and nap sleep durations did not result in significantly improved goodness-of-fit ( $\chi^2[1]=0.3$ ,  $p=0.58$ ); nor did differentiating between each of the 18 different conditions separately ( $\chi^2[16]=18.3$ ,

p=0.31).

**Conclusion :** Across a range of chronic nocturnal sleep restriction conditions (4.2h to 8.2h TIB) with and without diurnal nap (0h to 2.4h TIB), neurobehavioral performance as measured by PVT lapses was primarily a function of total TIB per 24h—regardless of how sleep was divided among nocturnal anchor sleep and diurnal nap sleep periods. This suggests that split sleep schedules offer no clear advantage over monophasic sleep patterns with regard to preventing cumulative impairment from chronic sleep restriction.

**Support (optional):** Supported by NASA cooperative agreement NCC 9-58-159 with the National Space Biomedical Research Institute.

## 1070

### RECOVERY FROM SLEEP DEBT: THE EFFECT OF VARYING TIB SLEEP DOSE ON MWT

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**Introduction :** Little is known about the sensitivity of the Maintenance of Wakefulness Test (MWT) to differing amounts of recovery sleep in normal healthy subjects after sleep loss. The aim of this study was to investigate the effect of varying TIB sleep doses on 2 consecutive nights of recovery sleep following sleep restriction.

**Methods :** 54 healthy subjects (age=30.1±6.7yr, 32f) participated in a controlled laboratory protocol. Subjects underwent 2 nights of baseline sleep (TIB=10h) followed by 5 nights of sleep restriction (TIB=4h) and 2 nights of recovery sleep (R1 & R2). On R1 subjects were randomized to one of six TIBs (0h, 2h, 4h, 6h, 8h, 10h TIB). All received a fixed TIB of 8h on R2. Modified single trial (30min) MWTs were conducted between 1430h-1600h on the day after the second baseline night, after the fifth sleep restriction night and after both recovery nights. Sleep latency was defined as time to the first appearance of a brief sleep (10sec microsleep).

**Results :** MWT sleep latency (±SD) after 5 nights of chronic sleep restriction was 11.2±8.6min, which differed significantly from baseline (21.8±9.9min; p<0.001). All R1 TIB doses (0h, 2h, 4h, 6h, 8h, 10h) yielded MWT sleep latencies significantly below those at baseline (all p<0.05). R1 0h and 2h TIB decreased alertness below that on the last day of sleep restriction (p<0.05). R1 TIB ≥ 6h did not improve alertness above the final restriction day (p>0.05). The R2 recovery sleep (8h TIB) improved alertness most when subjects had <6h TIB on R1 (p<0.05).

**Conclusion :** A single MWT was sensitive to sleep restriction to 4h TIB a night for 5 nights, and to the dose of subsequent recovery sleep. However, MWT did not show dramatic recovery after the 1st recovery sleep, suggesting that alertness remains compromised following a single recovery, post restriction sleep episode.

**Support (optional):** Supported by NIH NR 004281 and RR00040

## 1071

### ATTITUDE RELATED PREDICTORS OF SLEEP AND SLEEP BEHAVIOR IN COLLEGE STUDENTS

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**Introduction :** Attitudes toward specific health behaviors have been studied in many domains such as smoking, nutrition, and STD prevention. Though biological and clinical advances in sleep abound, little empirical research has been done on the role of attitudes in predicting sleep. Sleep is a rather unique domain in which to examine attitude processes because it is presumably affected by both biological components (which constrain

controllability) as well intentional processes. In addition, predictors of sleep length in young adults between age 19 and 24 are particularly important because of the high risk of fall-asleep car collisions in this age group.

**Methods :** Students (N=143) at the University of Connecticut answered survey questions about their sleep habits and attitudes. Attitude questions were partly based on the Theory of Reasoned Action/Planned Behavior of Fishbein and/or Ajzen. The survey explored subjective norms, self-efficacy, enjoyment of sleep, beliefs about the importance and health benefits of sleep, and attitudes toward specifically sleeping eight hours per night every night.

**Results :** Students reported getting close to the amount of sleep recommended by health professionals (M=8.02 hours per night), yet they reported surprisingly high levels of daytime sleepiness on the Epworth Sleepiness scale (M=9.70, SD=3.03). Regression analyses reveal that self-efficacy (β=.0425) and beliefs about the health benefits and importance of sleep (β=.197) were the primary predictors of sleep obtained per night, ps < .05. However, sleep obtained was not predicted by target-specific attitudes.

**Conclusion :** These results indicate that sleep may be driven more by perceived controllability, and by general pragmatic issues rather than by overtly expressed attitudes toward sleeping 8 hours per night. Such social psychological issues could play an important role in creating interventions to decrease sleep deprivation, and in turn decrease the risk of fall-asleep collisions in this population.

**Support (optional):**

## 1072

### A LEARNING TASK SENSITIVE TO SLEEP DEPRIVATION IN DROSOPHILA

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**Introduction :** A single night of sleep deprivation is sufficient to reduce performance on many cognitive tasks. Surprisingly the reasons why sleep loss should have such an immediate and large negative impact on normal brain functioning remains ill understood. To address this issue we have validated an associative learning paradigm that is sensitive to sleep deprivation and, more importantly, is amenable to genetic dissection using the model organism *Drosophila melanogaster*.

**Methods :** We have selected an associative learning paradigm that requires flies to inhibit a potent attraction towards light. Flies are individually placed in a T-maze and allowed to choose between a lighted and a darkened chamber. When an aversive stimulus (quinine) is placed in the lighted chamber, flies learn to choose the darkened chamber in the course of 16 trials. Sleep was monitored throughout the experiments and Sleep Deprivations (SD) were performed during the primary sleep period using a previously described device that disrupts sleep without eliciting a stress response.

**Results :** Learning was significantly reduced following 6 h and 12 h of sleep deprivation. It was impaired during the biological day as the amount of waking cumulated and was disrupted in wild-type flies that are unable to sustain consolidated sleep at night. Control experiments excluded non-specific effects of the stimulation used to keep flies awake and the intrusion of sleep into periods of waking. Importantly, learning is restored in SD flies following a short nap or increased incentive. Moreover, mutants resistant to SD maintain learning.

**Conclusion :** The deficits we observed following sleep deprivation are remarkably similar to those identified in mammals and are correlated with both wake time and sleep quality. Thus the flexibility and power of *Drosophila* genetic tools can now be used to investigate mechanisms

whereby sleep deprivation disrupts normal brain function in flies and possibly mammals.

**Support (optional):**

### 1073

#### LEARNING-RELATED CHANGES IN SLEEP SPINDLE ACTIVITY DEPEND ON THE NATURE OF WORD-PAIR ASSOCIATES

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**Introduction :** Learning-dependent increases in sleep spindle density have been reported during nocturnal sleep immediately following the learning session. Here, we investigated experience-dependent changes in daytime sleep EEG activity after declarative learning of word-pairs differing in encoding difficulty.

**Methods :** At weekly intervals, thirteen male volunteers (21-28y) spent 3x24h in the chronobiology facility (<8 lux) under constant routine conditions in bed. Around midday, subjects carried out one of two word-pair learning tasks or a non-learning control task in counterbalanced order (all similar in visual input and cognitive effort). The two learning lists differed in the abstraction level of the associations between word pairs, resulting in an easy and a difficult encoding condition. After immediate cued recall, subjects were allowed to sleep for 4 hours. Delayed cued recall was tested 30 min after awakening. Polysomnographical data were collected and subjected to spectral analysis and a sleep spindle detecting algorithm.

**Results :** All volunteers performed better in the easy than in the difficult encoding condition (66% vs. 48%;  $p < 0.05$ ). Performance remained stable between immediate and delayed recall in both the easy and difficult encoding condition ( $p > 0.1$ ). In comparison to the control condition, sleep EEG activity in the low sigma range (11.5-13.25 Hz) was significantly increased after the more difficult encoding condition, particularly left frontal (F3;  $p < 0.05$ ). Furthermore, the incidence of low frequency sleep spindles was significantly enhanced in the fronto-central areas (F3, F4 and C4;  $p < 0.05$ ). After the easy word list no such modification in the low sigma range was observed.

**Conclusion :** Our results suggest that changes in daytime sleep EEG oscillations after declarative word-pair learning depend upon the nature of the word-pair associations. Frontal sleep spindles in the lower sigma range are predominantly increased after learning, which supports the hypothesis of a specific functional implication of fronto-central located spindles in memory processing.

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### 1074

#### RELATIONSHIP OF SLEEP PARAMETERS WITH THE NEUROCOGNITIVE FUNCTION IN NORMAL ELDERLY SUBJECTS AND MILD COGNITIVE IMPAIRMENT (MCI) PATIENTS

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**Introduction :** In the elderly, excessive daytime sleepiness and sleep disordered breathing (SDB) are relatively common, and these could be associated with neurocognitive dysfunction. There have been limited studies on the relationship of sleep disorders and neurocognitive dysfunction, especially for specific cognitive domains in MCI patients. We aimed to illustrate the relationship of sleep parameters with the neurocognitive function in community-dwelling normal elderly subjects and MCI patients.

**Methods :** Epworth Sleepiness Scale (ESS) was administered to elderly subjects above 60 yr., who visited to the Public Health Center in Chuncheon City. CERAD-K (the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet) neuropsychological battery and Stroop test were done for each subject. Nocturnal polysomnography was done for 8 normal controls (NC) (Age:  $68.1 \pm 3.4$ ) and 12 MCI patients (Age:  $68.2 \pm 3.9$ ). P value below 0.05 had a statistical significance.

**Results :** There was no difference in sleep parameters between NC and MCI patients. In NC, Verbal Fluency (VF) score was correlated with sleep efficiency (SE) and REM sleep amount (REMS) ( $r = 0.71, 0.79, 0.71$ ), Stroop Color-Word score was negatively correlated with respiratory disturbance index (RDI) ( $r = -0.74$ ), and Stroop Interference (SI) score was correlated with SE and REMS ( $r = 0.74, 0.81$ ). In MCI patients, VF score was negatively correlated with RDI ( $r = -0.63$ ), Boston Naming Test score was correlated with slow wave sleep (SWS) ( $r = 0.75$ ), and SI score was negatively correlated with limb movement arousal index ( $r = -0.61$ ).

**Conclusion :** In NC, poor sleep quality and decreased REMS were associated with impaired language and executive functions. In MCI patients, decreased SWS and increased SDB were associated with impaired language ability, and increased limb movements during sleep with impaired executive function. That is, the findings on the relationship of REMS with neurocognitive function were different in two groups.

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### 1075

#### THE IMPACT OF ONE WEEK OF SLEEP EXTENSION ON EATING BEHAVIOR AND FEELINGS OF HUNGER IN HEALTHY YOUNG ADULTS

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**Introduction :** Research suggests sleep deprivation may be related to obesity. Although a number of variables are positively correlated with eating (time since last meal, pleasantness of available food, number of others present), it is not clear that food intake is related to prior sleep time or sleepiness. Our objective was to examine whether short-term sleep extension produces declines in eating or hunger.

**Methods :** Nineteen healthy university students (19-23 yrs) trained by a registered dietician kept daily food and sleep diaries for three weeks during summer break. Participants recorded intake for each meal/snack, pre and post meal sleepiness and hunger on a 7-point scale, and number of people present. Participants slept and ate normally for weeks 1 and 3 and remained in bed at night 2 additional hours during week 2.

**Results :** During week 2, participants significantly extended sleep from 7 to 8 hours per night ( $F(2,30) = 40.776$ ;  $p < 0.05$ ) but showed no significant declines in calories, fat, carbohydrates, protein, pre or post meal hunger. Correlation coefficients for each participant between prior night's sleep, premeal sleepiness, number of others present, caloric consumption, and

hunger were converted to z-scores using Fisher's transformations and average correlations compared to 0 using t-tests. Replicating previous findings, eating was positively correlated with number of people present (mean correlation=.28,  $t(15)=4.605$ ;  $p<.05$ ). However, no significant correlations between sleep time or sleepiness with eating or hunger were found.

**Conclusion :** This study, although powerful enough to detect relationships between social variables and eating, revealed no significant change in eating or hunger with a week of sleep extension, nor any significant correlations between sleep time or sleepiness with eating or hunger. Although significant sleep deprivation may lead to increased eating/hunger, healthy adults may tolerate modest sleep changes with no significant effect. Future research should include longer in-lab sleep extensions and direct food measures.

**Support (optional):**

## 1076

### GENDER DIFFERENCES IN THE EFFECTS OF STIMULANT MEDICATIONS ON THE ABILITY TO ESTIMATE UNKNOWN QUANTITIES WHEN SLEEP DEPRIVED

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**Introduction :** Previous research has suggested that the ability to make quantitative estimations in the face of limited information may be impaired by sleep deprivation. We examined the effects of three psychostimulants on cognitive estimation performance after 46 hours of sleep deprivation using the Biber Cognitive Estimation Test (BCET), which presents a series of questions requiring exact numeric answers, but for which no exact answers really exist. Questions were asked regarding estimates of length, time, quantity, and weight (e.g., how many seed are in a watermelon?).

**Methods :** Fifty-three participants (28 males) received 8 hours time in bed followed by 66 hours of continuous wakefulness. After 44 hours awake, participants ingested either modafanil 400 mg, dextroamphetamine 20 mg, caffeine 600 mg or a placebo in a double-blind administration. After 46.5 hours of wakefulness, participants completed the BCET. Performance was scored according to published norms.

**Results :** Total scores on the BCET in this sleep deprived group were significantly lower than published norms ( $p<.00001$ ). Analysis of covariance (adjusted for weight) yielded a significant sex by drug interaction. For females dextroamphetamine was associated with significantly better BCET performance than placebo ( $p=.012$ ) or caffeine ( $p=.038$ ). In contrast, the performance of males was not significantly affected by any of the stimulants, although males tended to outperform females on the BCET overall.

**Conclusion :** Sleep loss significantly impaired cognitive estimation ability. Dextroamphetamine was significantly more effective than caffeine or placebo at improving the cognitive estimation ability of females after two nights of sleep deprivation, while the performance of males was relatively unaffected. Furthermore, males significantly outperformed females when taking only a placebo, a finding not observed in rested samples, suggesting that males' cognitive estimation ability may be less affected by sleep loss. Psychostimulants may have different sex-related effects on some aspects of higher cognitive function.

**Support (optional):**

## 1077

### INDIVIDUAL DIFFERENCES IN COGNITIVE PERFORMANCE DURING SLEEP INERTIA

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**Introduction :** Sleep inertia in the morning following an 8-h sleep episode has been reported to produce significant performance impairments that can be worse than the impairments seen during total sleep deprivation. Stable and large individual differences in performance have been reported in response to repeated episodes of sleep deprivation. Whether stable individual differences in performance occur in response to repeated episodes of sleep inertia was examined.

**Methods :** Nine healthy men and women, aged  $29.3\pm 6.6$  (Mean $\pm$ SD), participated. Participants were scheduled to sleep 8-h per night for 3 baseline weeks at home, verified by sleep diaries, call-ins to a time stamped recorder and by at least one week of actigraphy. Subjects lived in the laboratory for seven days with sleep-wake times scheduled at subjects' habitual times. We analyzed data from two mornings. Cognitive performance was assessed with a computerized mathematical addition test ~1, 21, 41, and 61 min after EEG verified awakening. Intraclass correlation coefficients (ICC) were computed to quantify individual variability in performance across repeated bouts of sleep inertia.

**Results :** On the first morning, six subjects were awakened from stage 2, two subjects from REM, and one from stage 1; whereas, on the second morning, three subjects were awakened from stage 2, five subjects from REM and one from stage 1. In the 30 min prior to scheduled waketime, average time awake was  $1.5\pm 1.8$  min and  $0.55\pm 0.60$  min for the first and second mornings respectively. We observed an ICC value of 0.876 for performance at ~1 min following awakening. ICC values of 0.600, 0.849 and 0.873 were observed at ~21, 41 and 61 min, respectively. Large individual differences in performance were observed immediately upon awakening such that the best two subjects performed 3-6 times better than the worst two subjects.

**Conclusion :** Individual differences in cognitive performance are large and are stable across repeated episodes of sleep inertia.

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## 1078

### VISUOSPATIAL PERCEPTION OF LINE ORIENTATION IS RESISTANT TO ONE NIGHT OF SLEEP LOSS

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**Introduction :** Sleep deprivation impairs performance across a spectrum of cognitive abilities including vigilance, attention, and executive function. Although some studies have reported deficits on tasks requiring visual attention and spatial awareness, it is not clear if these impairments are due to altered visuospatial perception or due to reduced attention and vigilance. To clarify this issue, we examined visuospatial and vigilance performance in the same subjects at rested baseline and again following one night of sleep deprivation.

**Methods :** Fifty-four healthy participants (29 male) participated. Visuospatial performance was assessed at rested baseline and again after

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22.5 hours of wakefulness using the Judgment of Line Orientation Test (JLO). Alternate forms of the JLO were counterbalanced across the two sessions. Speed (1/Reaction Time x 1000) from a Psychomotor Vigilance Test (PVT) was used to assess alertness and vigilance.

**Results :** Total scores on the JLO were not found to differ significantly between baseline and sleep deprivation [ $t(53) = -1.412, p = .164$ ]. Items were also separated by difficulty for further analysis. Similarly, there was no significant difference between baseline and sleep deprived performance for easy [ $t(53) = .000, p = 1.000$ ] or hard test items [ $t(53) = .207, p = .837$ ]. In contrast, PVT declined significantly from baseline to sleep deprived performance [ $t(53) = 5.97, p < .001$ ], indicating that participants were showing decreases in alertness and psychomotor vigilance.

**Conclusion :** Despite significant declines in a measure of alertness and vigilance, sleep deprivation was not associated with significant changes on a task of visuospatial perception requiring the ability to distinguish subtle differences in line angles. This suggests that performance deficits associated with sleep loss are unlikely to be due to dysfunction within systems of the brain responsible for simple visuospatial perception and processing of line angles.

**Support (optional):**

### 1079

#### THE RELATIONSHIP BETWEEN SLEEP QUALITY AND PERCEPTIONS OF MEMORY AMONG A COMMUNITY SAMPLE OF PERIMENOPAUSAL WOMEN

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**Introduction :** The transition from pre- to post- menopausal status, namely perimenopause, is often fraught with a number of physiological and psychological changes. Common complaints among perimenopausal women include the onset of hot flashes and/or night sweats, sleep disturbances, mood symptoms, and cognitive impairments. While memory decline and concentration difficulties may be accounted for by decreases in estrogen, recent studies indicate that memory changes may be independent of stage of menopausal transition or age. Perceived memory functioning has been found to strongly correlate with perceived health, depressed mood, and perceived stress among women during perimenopause. Given the interrelationships between sleep quality, cognitive compromise, and depression, we sought to examine the contribution of sleep quality, independent of depression, which has been shown to predict perceptions of memory among perimenopausal women.

**Methods :** Based on a prior, comprehensive survey of a community sample of perimenopausal women ( $N = 168$ ), we examined a subset of variables that specifically ascertained reports of sleep quality, depressed mood, and perceptions of memory. A linear regression analysis was conducted on the Pittsburgh Sleep Quality Index-Global Score (PSQI-G), Beck Depression Inventory-Second Edition (BDI-II), and the Memory Scale of the Women's Health Questionnaire (WHQ).

**Results :** Ratings of sleep quality and estimates of memory function were significantly correlated,  $r = .36, p < .001$ . Preliminary analyses also suggests that the PSQI-G and the BDI-II uniquely predict perceptions of memory among our sample of perimenopausal women ( $R^2 = .20, F(2,124) = 15.79, p < .001$ ).

**Conclusion :** The findings suggest that sleep quality and depression distinctively predict perceptions of memory among perimenopausal women. Further studies are needed to better understand the connection between menopausal status, sleep quality, depression, and memory among perimenopausal women.

**Support (optional):**

### 1080

#### SHORT-TERM VS. LONG-TERM PLANNING ABILITIES: DIFFERENTIAL EFFECTS OF STIMULANTS ON EXECUTIVE FUNCTION IN SLEEP DEPRIVED INDIVIDUALS

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**Introduction :** Sleep deprivation produces a range of detrimental effects on cognitive functions. As little as one night of total sleep deprivation has been found to reduce performance on tasks that reflect prefrontal cortex functioning. Although stimulant medications have been found to improve the general alertness, vigilance, attention, and concentration of sleep deprived individuals, it is not clear whether these compounds are equally effective at restoring higher order complex cognitive capacities such as planning and decision making. This study compared 3 different stimulant drugs, dextroamphetamine 20 mg, modafinil 400 mg, and caffeine 600 mg, with a placebo to determine the effects on executive function in individuals who have been sleep deprived for 2 days.

**Methods :** Fifty-four healthy volunteers (29 males, 25 females) were deprived of sleep for 61 hours. In a double-blind design, participants received a single dose of one of the study medications or placebo at 44 hours awake. After 48-50 hours of wakefulness, participants completed computerized versions of the 5-Ring Tower of Hanoi (TOH) and the Tower of London (TOL) tests.

**Results :** On the TOL, performance was significantly better for modafinil ( $p = 0.015$ ) and dextroamphetamine ( $p = 0.038$ ) relative to the placebo group. Conversely, caffeine did not significantly improve performance on the TOL in comparison to placebo. On the TOH, however, drug groups did not differ significantly in performance (all  $p > .05$ ).

**Conclusion :** Although the TOL and TOH are both tasks of executive function, each assesses slightly different facets. The TOL measures the ability to plan multiple steps ahead and maintain this plan in working memory. The TOH, in contrast, requires less working memory load, but places greater emphasis on the ability to inhibit propotent responses and apply a long-term strategy. These findings suggest that modafinil and dextroamphetamine improve working memory and immediate planning, but not long-term strategic planning.

**Support (optional):**

### 1081

#### INDIVIDUAL DIFFERENCES IN STRESS MANAGEMENT CAPACITY PREDICT RESPONSIVENESS TO CAFFEINE DURING SLEEP DEPRIVATION

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**Introduction :** It is generally accepted that some individuals are more resistant to sleep loss than others, but the factors that lead to such resistance are poorly understood. One potential factor may involve individual differences in emotional intelligence, which can be defined as the non-cognitive capabilities and skills that influence an individual's ability to cope successfully with environmental pressures and demands. In the present study, baseline scores on the Bar-On Emotional Quotient Inventory (EQ-i) were used to predict sustained vigilance and alertness performance, as measured by the psychomotor vigilance test (PVT), during three successive nights of sleep loss.

**Methods :** Twenty-three subjects (19 male) were sleep deprived for 77 hours. The EQ-i and PVT were administered at rested baseline. In a dou-



ble-blind administration, subjects received either caffeine (n=12; 200 mg every 2 hours from 0100 to 0700) or placebo (n=11) for the three nights they remained awake. The PVT was then administered 39 times each night from 0015 to 0845.

**Results :** For caffeine, multiple stepwise regression analyses indicated that scores on the Stress Management scale significantly predicted PVT performance during the first night of sleep loss ( $r=-0.85$ ,  $p=0.001$ ), with poorer stress management scores associated with faster speed on the PVT relative to baseline. After the first night, none of the EQ-i scales were predictive of PVT performance for either drug group.

**Conclusion :** During the first night of sleep loss, caffeine's alerting capacity appears to be amplified in individuals with limited stress management capacities. When administered caffeine, individuals with poor stress management scores demonstrated relatively greater alertness and vigilance performances than individuals with strong in stress management capacities. We interpret these data as suggesting that individuals with poor stress management skills were more likely to experience heightened emotional/autonomic arousal when trying to perform under the influence of caffeine, thus amplifying its alerting effects.

**Support (optional):**

## 1082

### EFFECTS OF SLEEP INERTIA ON EXECUTIVE FUNCTION

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**Introduction :** Sleep inertia has been reported to impair performance including vigilance and working memory; however, little is known about how sleep inertia influences executive function. The frontal cortex is implicated in executive function tasks including inhibition of responses. It has been reported that it takes longer for the frontal cortex to show increased activation than brain areas important for arousal upon awakening from sleep, which suggests that sleep inertia may impair frontal cortex tasks. The aim of the current study was to test the hypothesis that executive function would be significantly impaired upon awakening from an afternoon nap.

**Methods :** Eight healthy, drug free individuals (5 females, 3 males) aged  $23.13 \pm 2.70$  (mean  $\pm$  SD) participated. Performance was assessed following a 2-h afternoon nap opportunity with a computerized Stroop color word test at ~1, 9, 17, 25, and 60 min after EEG verified awakening. We also assessed a standard measure of mathematical addition/working memory performance previously used to assess effects of sleep inertia. Participants practiced the tests prior to the nap until the steep portion of the learning curve was removed.

**Results :** Five participants were awakened from stage 2, two from stage 1, and one from stage 4. In the 30 min prior to scheduled waketime, average time awake was  $2.3 \pm 2.5$  min. Repeated measures ANOVA showed significant impairments on both tests immediately upon awakening ( $P < 0.05$ ) versus the last practice trial before the nap. Specifically, there was on average an ~49 msec slower median reaction time in response to inhibition stimuli on the Stroop test, and an ~16% decrease in the number correct on the mathematical addition test. Performance was not different than pre-nap values at ~9, 17, 25, and 60 min following awakening.

**Conclusion :** Sleep inertia impaired executive function and working memory immediately upon awakening from a 2-h afternoon nap, suggesting that sleep inertia impairs complex cognitive tasks.

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## 1083

### REPLICABILITY OF THE TIME-ON-TASK EFFECT DURING SLEEP DEPRIVATION

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**Introduction :** For cognitive tasks practiced to asymptotic performance, sustained task performance leads to progressive performance degradation across the task duration. This "time-on-task" (ToT) effect is known to be intensified by sleep deprivation. However, sleep deprivation also leads to increased moment-to-moment performance variability. This would suggest that, at least in data not averaged over subjects and time, the ToT effect may not be highly replicable. We tested this hypothesis in a repeated sleep deprivation paradigm.

**Methods :** As part of a larger study, 21 healthy subjects (age  $28.5 \pm 5.5$ ; 11 females) each underwent two sessions of 36h total sleep deprivation (TSD) in a strictly controlled laboratory environment. During TSD, performance on a 10min psychomotor vigilance task (PVT) was measured every 2h (i.e., 18 test bouts per session). For every test bout in each individual subject, the number of performance lapses ( $RT \geq 500$ ms) was assessed. In addition, the ToT effect was estimated as the linear slope of change in RTs (transformed to  $1/RT$ ) across the 10min bout. These data were analyzed using mixed-effects ANOVA with test bouts as repeated measures. The intraclass correlation coefficient (ICC) was computed to quantify replicability across TSD sessions. The ICC can range from 0 (no replicability) to 1 (perfect replicability).

**Results :** PVT performance lapses exhibited significant replicability:  $ICC=0.51$  (95% CI: 0.37-0.68). Replicability of the ToT effect was much lower:  $ICC=0.04$  (95% CI: 0.03-0.10).

**Conclusion :** At the level of test bouts, performance impairment measured by PVT lapses showed replicability across two identical TSD sessions. However, the replicability of the ToT effect was poor. While the ToT effect is seen in aggregate data, it does not appear to be observed robustly across individual test bouts. To characterize PVT response changes over task duration, it may be more suitable to consider measures of RT variability or instability.

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## 1084

### TRADE-OFFS IN DISCRETIONARY TIME: LEISURE VS. SLEEP

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**Introduction :** Previous studies have shown that pressures of modern society often force people to make a decision between the biological imperative for sleep, and the societal requirement for wakefulness. While much research has been devoted to studying sleep time versus work time trade-offs, little attention has been paid to pleasurable discretionary activities, which are dominated by leisure time and time for sleep. As study was performed to evaluate how leisure time and sleep time co-vary in the American Time Use Survey database (ATUS).

**Methods :** The 2003 ATUS database is a random national telephone survey of men and women over 15 years of age, conducted by the US Census Bureau for the Bureau of Labor Statistics. ATUS respondents are interviewed about how they spent their time on the previous 24-h period.  $N=19689$  respondents reported some time spent sleeping and in leisure activities. Data are codified into 17 separate categories, which included sleep time and time spent in socializing, relaxing and leisure. The latter

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was further subcategorized into: socializing and communicating; social events; relaxing and leisure (includes television watching); and arts and entertainment. ANOVA and regression were used to evaluate sleep time relative to leisure time.

**Results :** Total sleep time varied as a function of total leisure time ( $P<0.001$ )—a similar relationship was found between sleep time and certain subcategories of leisure (e.g., television watching). In general, subjects in both short and long sleep categories had more leisure time than those in 7-8h sleep category. Among weekday working adults ( $N=4363$ ) leisure was higher only for those who slept less than 7h.

**Conclusion :** It is particularly interesting that the greatest difference in leisure time was explained by the leisure category dominated by activities such as television watching. Further analyses will determine what aspects of leisure are most associated with reduced sleep time.

**Support (optional):** NIH NR04281.

### 1085

#### PREMORBID INTELLIGENCE CORRELATES WITH DURATION AND QUALITY OF RECOVERY SLEEP FOLLOWING SLEEP DEPRIVATION

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**Introduction :** Sleep is believed to be important for memory consolidation and learning, although the specific stages of sleep that are most important to these cognitive abilities remain uncertain. Rapid Eye Movement (REM) increases following acquisition of new learning, and the magnitude of the increase appears to correlate with intelligence. However, it is not clear to what extent pre-existing intellectual ability is associated with the subsequent architecture of recovery sleep following a cognitively demanding period of prolonged wakefulness. Therefore, we examined the relationship between premorbid intelligence and polysomnographic indices of sleep following sleep deprivation.

**Methods :** Thirty-four (18 men) healthy volunteers were the Wechsler Abbreviated Scale of Intelligence (WASI) to determine Full Scale (FSIQ). Following 8 hours time in bed, participants then remained awake for 61 hours, followed by 12 hours of recovery sleep monitored with polysomnography. Sleep records were manually scored for Total Sleep Time, Sleep Efficiency, percent of time in Stages 1, 2, Slow Wave Sleep, and REM, and latency to onset of these stages. Pearson correlations were calculated between FSIQ and these indices.

**Results :** FSIQ correlated significantly with Total Sleep Time ( $r=.37$ ,  $p=.03$ ), Sleep Efficiency ( $r=.37$ ,  $p=.03$ ), percent of total sleep that was REM ( $r=.36$ ,  $p=.04$ ), and actual time spent in REM sleep ( $r=.40$ ,  $p=.02$ ). Other indices were not significantly correlated with intelligence.

**Conclusion :** Stable indices of intellectual ability are positively related to the quality and duration of recovery sleep following a cognitively demanding period of continuous wakefulness. This was particularly true for measures of REM sleep, indicating that individuals with higher intellectual abilities spent more of their recovery sleep time in REM sleep than those with lower levels of IQ. Findings suggest a relationship between intellectual ability and the quality and quantity of sleep, although the direction of causation will require further research.

**Support (optional):**

### 1086

#### SUBJECTIVE SLEEPINESS AND SIMULATED ACCIDENT RISK AVOIDING THE ECOLOGICAL FALLACY

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**Introduction :** In the presence of individual differences, group average estimates of Relative Risks (RR) may not relate to any subject in the population (i.e. the ecological fallacy if used to infer effects in individual subjects). The present study aimed to provide conditional RRs of sleepiness related accident risk for inference in individual subjects.

**Methods :** Five male and five female shiftworkers, mean age 37 years, participated with a 2 hour drive (08:00-10:00h) in a dynamic high fidelity moving base driving simulator, after a night of work and after a night of sleep. Ratings of subjective sleepiness were obtained at five minutes intervals during the drive using the Karolinska Sleepiness Scale (KSS), 1=very alert, 9=very sleepy, fighting sleep, an effort staying awake. Accidents (2 wheels outside the road edge or 4 wheels in opposite lane) were recorded for each segment during the drive. The probability of an event the subsequent five-minute segment was modelled with a Generalized Linear Mixed Model (GLMM) approach.

**Results :** The result showed that time and condition was related to accident risk ( $p<.001$ ). However, adding sleepiness to the model substantially increased model fit ( $\chi^2=151$ ,  $df=1$ ,  $p<.001$ ) and reduced time and condition to non-significant effects. A quadratic component of KSS further increased model fit ( $p=.001$ ). Two different ICC estimates suggest that 79% of the individual differences were stable across conditions and that the reliability across all observations was 51%. Relative risk estimates, adjusted for instability across conditions, showed that an increase from KSS=5 to 8 was associated with  $RR=30.1$  (95% CI  $RR=7.29-124$ ). Between KSS=5 and KSS=9, the risk increase was  $RR=145.9$  (95% CI  $RR=23.4 - 911$ ).

**Conclusion :** The results have shown that subjective sleepiness (KSS) was strongly related to accident risk. Large individual differences were also observed and the conditional RRs was substantially higher than can be inferred from earlier studies of group averages. These estimates should be used to infer effects in individual subjects to avoid the ecological fallacy.

**Support (optional):**

### 1087

#### SLEEP DEBT OR A DESIRE FOR MORE 'TIME OUT' ?

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**Introduction :** When asked if they would like more daily sleep, many people say 'yes', which could be taken as evidence of a 'sleep debt'. We explored this further in a more general sleep survey of 10,616 20-65y adults, by asking respondents with and without 'sleep debt' what they would do if given an extra hour of free time in the day, when sleeping was one of several attractive alternatives.

**Methods :** Questions included: good/poor sleeper, perceived TST, actual sleep need (from which was calculated apparent sleep deficit - ASD), Epworth sleepiness scores (ESS), and 'If you had an extra hour in the day, how would you prefer to spend it? (playing sport/exercising; socialising; reading/relaxing; watching tv/film or listening to radio; working; sleeping; other),and stressful lifestyle?

**Results :** As expected, TSTs were normally distributed, women slept longer than men and TST declined with age. Perceived sleep need was similar for good and poor sleepers, with men generally having smaller ASDs. Interestingly 30.76% of good sleepers thought they needed less sleep. Poor sleepers showed greater ASDs, with no age or sex differences, here. The extent of ASDs was not associated with ESS for any age/sex

group for either good or bad sleepers. Only a minority of those with ASDs chose to spend the extra times sleeping (22.4% Vs 31.5% for male good and poor sleepers respectively, and 33.8% Vs 35.5% for female good and poor sleepers respectively). Of those respondents with ASD's  $\geq 1$ h who would spend an extra hour sleeping, only 10.83% good sleepers, and 6.65% poor sleepers considered their lifestyles non-stressful.

**Conclusion :** For many, a desire for more sleep is synonymous with having more free-time for pleasurable activities often within a stressful lifestyle.

**Support (optional):**

## 1088

### THE RELATIONSHIP BETWEEN SLEEP QUALITY, MOOD, AND STRESS IN COLLEGE WOMEN

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**Introduction :** Traditional measures of sleep quality fail to include stress and mood in their assessments. In college students, women are more vulnerable to stress, and report lower sleep quality and more mood changes than men (Tsai & Li, 2004; Édell-Gustafsson, 2001). To explore the relationship between these factors in college women, we administered a survey of stress, mood, and sleep quality and assessed self-reported consequences of these interactions on college life.

**Methods :** The Pittsburgh Sleep Quality Inventory (PSQI), Profile of Mood States (POMS), and the Subjective Units of Disturbance Scale (SUDS) was administered to a random sample of college women (N=263). Participants were classified as either good ( $\leq 5$ ), medium (6-7), or poor ( $\geq 8$ ) quality sleepers based on the PSQI score; differences between these groups were analyzed with a one-way ANOVA.

**Results :** Poor quality sleepers reported higher levels of stress on week and weekend days [ $F(2,258) = 13.79, 9.28, p < .001$ ], and attributed their poor sleep quality to stress more so than good sleepers [ $F(2,258) = 47.23, p < .001$ ]. Poor quality sleepers also reported higher rates of negative mood states, including tension, depression, anger, fatigue, lack of vigor, and confusion [in all cases  $F(2,258) > 8, p < .001$ ]. Poor quality sleepers also had lower GPAs [ $F(2,255) = 4.01, p < .05$ ], and reported more often that the stress led to physical illness and feelings of "giving up" [ $F(2,256) = 6.46, 19.81, p < .05$ ].

**Conclusion :** Our study demonstrates that there is a strong relationship between poor sleep quality, problematic mood states, and increased stress in college women. Women report poorer academic performance, more frequent physical illness, and increased feelings of defeat as consequences of these problems. Future studies will examine the longitudinal impact of menstrual cycle on sleep quality and stress.

**Support (optional):**

## 1089

### SLEEPINESS INCREASES 'NON-MICROSLEEP' DRIVER DISTRACTIONS

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**Introduction :** Sleepy people are more liable to self-generate non-microsleep distractions ostensibly to provide stimulation during boring and monotonous tasks, with the occurrence being exacerbated in busy, distractive environments. Here, we address the impact of sleepiness on visual signs of distractions during a simulated 2h drive.

**Methods :** Eight healthy, young (20-26y) male, good sleepers ( $8 \pm 1$ h), without daytime sleepiness ( $< 2$ naps/month and ESS  $\leq 10$ ), underwent a 2h simulated drive at 14:00h following a night of normal ('alert'), or restrict-

ed sleep (02:00-07:00h - 'sleepy'), counterbalanced a week apart. Infra-red video recordings of participants' faces (measuring distraction) and vehicle positioning on the road (for lane drifting 'incidents') were recorded throughout the drive. Continuous EEGs and subjective sleepiness ratings (KSS, every 200sec) were obtained. Distractions (directing gaze away from the road, without droopy eyes or EEG signs of microsleeps) were assessed by an independent experimenter, blind to the condition, and logged as 'short' ( $< 3$ sec) and 'long' ( $> 3$ sec) distractions.

**Results :** Distractions increased under sleepy conditions ( $p < 0.002$ ), for both short ( $p < 0.004$ ) and more importantly, long distractions ( $p < 0.01$ ). As expected, lane drifting increased when sleepy ( $p < 0.0005$ ). These incidents were positively related to distractions for both alert ( $r = 0.95, p < 0.00005$ ) and sleepy conditions ( $r = 0.83, p < 0.01$ ). However, of greater concern was that longer distractions linked to an incident markedly increased with sleepy vs alert ( $p < 0.03$ ). KSS data indicated drivers were aware of sleepiness as impairment increased. Microsleep-related incidents also increased.

**Conclusion :** Moderate sleepiness increased non-microsleep distractions (and microsleeps) linked to lane drifting, during a simulated 2h drive. Drivers were aware of the increased sleepiness as distraction worsened. Sleepiness-related distraction in drivers remains a poorly investigated, albeit important area in road safety.

**Support (optional):**

## 1090

### SLEEP INCREASES FALSE RECALL OF SEMANTICALLY RELATED WORDS IN THE DEESE-ROEDIGER-MCDERMOTT MEMORY TASK

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**Introduction :** The role of sleep in the consolidation of declarative memory has become an issue of considerable theoretical and practical importance. Several recent studies of verbal memory strongly suggest that sleep plays a beneficial role in the consolidation of declarative memories. However, these studies tested memory for words after 3 hours of early-night sleep, or after 3 hours of late-night sleep. Few, if any, verbal memory studies have shown that declarative memory is facilitated across an entire night of sleep. Here we studied the impact of a night of sleep on the ability to accurately recall semantically-related word-lists using the Deese, Roediger-McDermott "DRM" technique.

**Methods :** Participants studied eight 12-word lists at 9AM or 9PM. They recalled these words (1) after 12 daytime hours spent awake, (2) after 12 nighttime hours containing sleep, (3) after just 20 minutes in the morning, or (4) after 20 minutes later in the evening. These last two conditions were included as circadian controls.

**Results :** A 12-hour nighttime period containing sleep significantly increased participants' ability to remember these words compared to an equivalent 12-hour daytime period spent awake. Moreover, we found that participants in the "sleep" group were significantly more likely than those in the "wake" group to falsely recall "critical lure" words that were semantically associated to the theme or gist of the list but never presented for study.

**Conclusion :** In addition to producing enhanced recall across a full night of sleep, we have shown that a period of time containing sleep elevated incorrect recall of semantically related words compared to time spent awake. These findings support the hypothesis that sleep enhances the integration of episodic memories into neocortically based semantic networks.

**Support (optional):**

1091

CHANGES IN MOOD AND PERFORMANCE DURING SLEEP EXTENSION IN YOUNGER AND OLDER PEOPLE

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**Introduction :** Many people self-select habitual bedrest durations that lead to a sleep debt as assayed by sleep propensity. Sleep “need” may have many dimensions, and whether self-selected bedrest durations cause impairments in mood and performance remains unknown. We studied changes in mood and performance during a sleep extension protocol in younger and older people.

**Methods :** Thirty-five younger (17 males; 18-32 years) and 18 older (12 males; 60-76 years) healthy volunteers slept at their habitual time and duration during the first inpatient night (BL). Thereafter, subjects were scheduled to three days (5 younger, 4 older) or four or more days (13 younger, 14 older) of 12 hours bedrest centered at mid-habitual nocturnal sleep episode and 4 hours bedrest centered 12 hours opposite this. Sleep was recorded. During all wake episodes, subjects completed visual analog scales (VAS) several times per hour, and KSS, Calculation, Digit Symbol Substitution Task (DSST), Probed Recall Memory (PRM) and Psychomotor Vigilance Task (PVT) tests once every two hours. Calculation, DSST and PRM tests have practice effects. PROC SAS NLMixed with random effects and T-tests were used.

**Results :** Younger subjects habitual bedrest duration (HBD) was 6.1-10.3 hours; older subjects' HBD was 7.0-9.0 hours. TST increased significantly from BL to the first extended sleep opportunity (ED1), with younger subjects increasing their TST more than older subjects. All mood and performance measures improved from BL to after ED1 with age-related differences in Calculation, DSST and PRM. Across days after extended sleep opportunity, there were significant ED effects for Alert, KSS, Calculation, DSST, and PVT median reaction times, and significant age effects for Calculation, DSST and PVT median reaction times.

**Conclusion :** With increased TST during extended bedrest opportunities, there are initial improvements in all and sustained improvement in some mood and objective performance measures in both younger and older people.

**Support (optional):** NIH grants P01-AG09975, K02-HD045459 (EBK) and NCRR-GCRC M01 RR02635, Research Fund of the University of Surrey (DJD) and grant BBS/B/08523 (DJD).

1091

EFFECTS OF ALCOHOL CONGENERS ON SLEEP DISTURBANCE

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**Introduction :** It is widely known that acute alcohol ingestion disrupts sleep, but no study has assessed whether beverage congeners moderate these effects. Congeners are the components of alcohol beverages, exclusive of alcohol and water. We hypothesized that objective sleep disturbance would be greater following a high congener (bourbon) compared to a low congener (vodka) beverage.

**Methods :** Using a placebo-controlled, crossover, randomized design, seventy-six (47 women) healthy young adult volunteers (mean age 24.6 ± 2.8 years) participated. After an 8-hour sleep schedule (confirmed by actigraphy and sleep diary) for three days prior to test sessions and a baseline screening night, they participated in two experimental nights one week apart: alcohol (mean BrAC 0.11g% ± 0.01) and placebo. At each session, participants consumed either high (bourbon) or low (vodka) congener beverages or matching placebo between 2045 and 2200. Sleep was monitored using polysomnography between 2300 and 0700 hours.

**Results :** Repeated measures ANOVA indicated that, relative to placebo, alcohol increased wake after sleep onset (35.3 ± 22.8 vs. 28.0 ± 22.2 min, p <0.01), percent time in slow wave sleep (26.9 ± 7.2 vs. 25.3 ± 6.9 percent, p <0.05), and latency to REM sleep (136.3 ± 60.6 vs. 101.2 ± 42.6 min, p <0.0001) and decreased percent time in stage REM (19.6 ± 6.0 vs. 23.4 ± 6.5 percent, p <0.0001) and latency to slow wave sleep (13.4 ± 7.6 vs. 17.7 ± 8.9 min, p <0.001). There were no differences for sleep latency, total sleep time, or any respiratory measures. Sleep continuity, architecture, and respiration also did not differ by congener content.

**Conclusion :** As expected, this high dose of alcohol disrupted sleep continuity and altered sleep architecture, however, no change in respiratory parameters was evident. Moreover, congener content does not appear to moderate these effects. Ongoing recruitment will provide more power to detect congener effects.

**Support (optional):** National Institute on Alcohol Abuse and Alcoholism (R01 AA12087-04A1)

1092

SLEEP FACILITATES CONSOLIDATION OF EMOTIONALLY AROUSING DECLARATIVE MEMORY

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**Introduction :** Both sleep and emotion are known to modulate processes of memory consolidation, yet their interaction is poorly understood. Here we examine the influence of sleep on consolidation of emotionally arousing and neutral declarative memory, evaluating both recognition accuracy and also memory bias (selection criterion) using the remember/know paradigm.

**Methods :** Subjects (n=14) performed an initial “study” session containing standardized arousing and neutral pictures, either in the evening or morning. Twelve hours later, after sleep or wake, subjects performed a recognition “test”, discriminating between these original and novel pictures using a response of Remember (R), Know (K), or new.

**Results :** Selective overnight sleep effects were observed for consolidation of arousing, but not neutral stimuli, with recognition accuracy for K judgments improving by 42% relative to the waking period (p=0.006). In addition, sleep enhanced recognition bias by 58%, resulting in less indiscriminate responding for R judgments (p=0.007), potentially by strengthening confidence judgments for remembered stimuli.

**Conclusion :** These data indicate the selective facilitation of emotional memory consolidation across sleep, resulting in the specific enhancement of both recognition accuracy and bias overnight. Indeed we propose that the previously reported benefit of affect on long-term memory consolidation (hours/days), in both animals and humans, is an enhancement that preferentially develops during sleep rather than time per se. Such findings may be especially important in affective clinical disorders exhibiting abnormalities of sleep and memory processing (e.g. dementia, PTSD, depression), which instead of being viewed as co-occurring factors, may now be considered as more causally related.

**Support (optional):** NIH; NIMH NIDA

## 1093

**SLEEP AND MEMORY CONSOLIDATION FOR SEMANTICALLY-RELATED VERSUS UNRELATED WORDS IN A PAIRED-ASSOCIATES MEMORY TASK**

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**Introduction :** Whether sleep influences the consolidation of declarative memory is of interest to both the sleep- and memory-research communities. Recent studies suggest that sleep plays a beneficial role in the consolidation of verbal declarative memories. However, these studies tested memory for words after 3 hours of early-night sleep, or after 3 hours of late-night sleep. Few, if any, verbal memory studies have shown that declarative memory is facilitated across an entire night of sleep. Some have used a paired-associate list-learning task in which the word-pairs were semantically related to one another. Here, we used the word lists of Gais and Born, translated into English, and compared performance on the original, semantically-related word-pairs to performance on a matched list of unrelated word-pairs after either 12 daytime hours spent awake or after 12 nighttime hours containing sleep.

**Methods :** Participants studied semantically-related or unrelated word-pairs at 9AM or 9PM. They then recalled these words (1) after 12 daytime hours spent awake, (2) after 12 nighttime hours containing sleep, or (3) after 24 hours as a circadian control.

**Results :** Participants recalled significantly more unrelated words after a period of sleep than after an equivalent period of wake. Semantically related words, on the other hand, did not benefit from a night of sleep - and in fact showed a marked reduction after sleep relative to wake.

**Conclusion :** We found that verbal declarative memories benefit from a full night of sleep. However, it was the semantically unrelated words that showed the greatest enhancement. In contrast to the findings of Plihal and Born (using the early-night/late-night procedure), semantically-related words did not benefit from an entire night of sleep, and in fact showed a decrease in our study. Our results suggest that sleep might benefit new semantic relationships, and the consolidation and integration of these relationships into pre-existing neocortical memory stores.

**Support (optional):**

## 1094

**SLEEP SPINDLES AND MOTOR ADAPTATION LEARNING: THE ROLE OF INITIAL SKILL LEVEL**

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**Introduction :** The present study examined the role that initial skill level has on the relationship between sleep states and motor adaptation learning. We tested the hypothesis that post-acquisition spindle density would increase in individuals that demonstrated an initially high level of skill on the task.

**Methods :** In-home sleep recordings were performed on 24 subjects across three consecutive nights. Subjects also completed thirty 30-second trials on the pursuit rotor task, once between the second ('baseline') and third ('post-acquisition') nights and once again after a one-week delay. Spindle density (number of spindles per minute of Stage 2 sleep) was determined for the baseline and post-acquisition nights. A median-split was used to divide the sample into a low-skill group (n=12) and a high-skill (n=12) group based upon the total time on target for the first three trials of the first pursuit rotor session.

**Results :** A 2 (group: low-skill, high skill) x 2 (night: baseline, post-acquisition) mixed ANOVA was performed to assess whether performing the motor adaptation task was associated with changes in spindle density in the two skill-level groups. There was a significant interaction between

group and night indicating that the increase in spindle density across the two nights was greater in the high-skill group than the low-skill group,  $F(1,22) = 9.45, p = .006$ . Spindle density on the post-acquisition night was significantly correlated with performance on the pursuit rotor during session 2 for the high-skill group ( $r = .64, p = .026$ ) but not the low-skill group ( $r = -.18, p = .597$ ).

**Conclusion :** Our hypothesis was supported. Spindle density increased following acquisition of the pursuit rotor task but only in those individuals that demonstrated a high level of initial skill. In addition, there was a positive correlation between post-acquisition spindle density and pursuit rotor performance one week later.

**Support (optional):**

## 1095

**DECLARATIVE LEARNING-DEPENDENT CHANGES IN THETA POWER DURING REM SLEEP**Fogel SM,<sup>1</sup> Smith CT<sup>2</sup>

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**Introduction :** There is now considerable support for a role of sleep in memory consolidation. However, it is not clear what role, if any, sleep plays in declarative memory consolidation. We investigated declarative learning-dependent changes in sleep. Theta has been implicated in hippocampal-dependent memory acquisition and long-term potentiation. It was hypothesized that a period of declarative learning would increase theta power during REM sleep following learning compared to baseline sleep. The data reported here are part of a larger multi-learning task study.

**Methods :** Twenty participants (Mean age=19) spent three consecutive nights in the sleep laboratory. Baseline polysomnographic recordings were collected on night 2. Participants were assigned to one of two conditions: either Paired-Associates (PA) or control (C). The PA group was instructed to memorize 168 word-pairs and recall them from memory. The C group spent an equivalent amount of time completing demographic questionnaires. PA training occurred on night 3 followed by polysomnographic recording. PA re-testing occurred one-week following training. FFT and statistical analyses were carried out for Delta(0.5-4Hz), Theta(4-8Hz), Alpha(8-12Hz), Sigma(12-14Hz;14-16Hz), and Beta(16-35Hz) from 16 sites: Fp1,Fp2,F3,Fz,F4,C3,Cz,C4,P3,Pz,P4,O1,Oz,O2.

**Results :** The PA group improved from test to re-test one-week later ( $t(8)=4.19, p=.003$ ). Following PA learning, there was an increase in theta power at Cz ( $t(8)=4.52, p<.01$ ) and an increase in sigma(12-14Hz) power at Cz ( $t(8)=4.17, p<.01$ ). In those that learned, there was a relationship between the increase in theta and the increase in PA recall ( $r(6)=.74, p=.03$ ), but not between sigma and PA recall.

**Conclusion :** It was found that there was a declarative learning-dependent change in sleep theta and sigma power, and that the increase in theta was correlated with the improvement in word recall. This is consistent with previous findings that suggest theta is involved in declarative memory acquisition. The current data suggest that theta may also be involved memory consolidation during REM sleep.

**Support (optional):** Support provided by Natural Sciences and Engineering Research Council (NSERC) of Canada

1096

SEASONALITY, ANXIETY AND DEPRESSION

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**Introduction :** Change in mood and behaviour across seasons is termed seasonality, a phenomenon observed among most people. Winter depression encompasses recurrent depressions every winter. In this study, we explored the relationships between depression, anxiety and seasonality in a population study.

**Methods :** All persons aged 40-45 years in Hordaland County, Norway, were invited to participate in a health survey in 1997-99. Totally, 4299 men and 9983 women were offered questionnaires measuring seasonality, anxiety and depression. Of these, 2980 men (68.9%) and 8074 women (80.9%) agreed to participate and completed the questionnaires correctly. Seasonality was assessed by the Global Seasonality Score (GSS), and the Hospital Anxiety and Depression Scale (HADS) was used for measuring depression and anxiety. Based upon their scores on the GSS subjects were divided into three groups, low (GSS<8), moderate (GSS=8-10) and high (GSS≥11) seasonality. On HADS, a cut-off score of eight was used for both anxiety and depression.

**Results :** Anxiety was significantly more prevalent in the high (21.9%[men]; 26.0%[women]) and moderate (19.6%[men]; 20.4%[women]) seasonality groups compared to the low (7.1%[men]; 10.2%[women]) seasonality group. The relatively high level of anxiety in the high/moderate seasonality groups persisted through all seasons. Seasonality was also related to depression. Subjects with high (7.7%[men]; 6.6%[women]) or moderate (8.8%[men]; 2.8%[women]) seasonality reported more depression than subjects with low seasonality (4.2%[men]; 2.1%[women]). Depression was more prevalent throughout the whole year among subjects with high/moderate seasonality than among those with low seasonality. Subjects with high/moderate seasonality reported depression more frequent during winter than summer months, while there was no summer/winter difference in the low seasonality group. When using high seasonality as a dependent variable, both anxiety (OR=2.7, 95%CI=2.1-3.5[men]; OR=2.5, 95%CI=2.2-2.9 [women]) and depression (OR=1.6, 95%CI=1.1-2.4[men]; OR=3.3, 95%CI=2.4-4.4 [women]) were significant predictors.

**Conclusion :** High/moderate seasonality is linked to higher prevalence of both depression and anxiety during all seasons.

**Support (optional):**

1097

AUDITORY STIMULATION INCREASES PHASIC EMG ACTIVITY DURING REM SLEEP

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**Introduction :** We tested the hypothesis that auditory stimulation and/or learning would increase the number of REM phasic events. It has been shown that auditory stimulation increases PGO waves during REM sleep and REM duration. In our hands, auditory stimulation did not increase REM duration. We wondered whether auditory stimulation would

increase phasic events, which have themselves been correlated with learning by others.

**Methods :** Male Fisher 344 rats were implanted with screw electrodes and nuchal EMG electrodes for sleep/waking analysis. After one week recovery, animals were acclimated for 2 days to the recording apparatus and baseline sleep recorded for 2 more days. Six animals received auditory stimulation across a 4 hour sleep period for 3 days. The numbers of REM phasic EMG twitches, defined as the number of spikes above one standard deviation of the mean, were compared between the same 4 hour periods during baseline and stimulation days. Six animals were trained on the 8-box choice spatial learning task 30 minutes per day for 7 days. Three rats received auditory stimulation (multiple bouts lasting 20-160 s of 80 dB, 12 ms long clicks every 10 s) in the 4 hours after spatial training, whereas three others did not. T-tests were conducted to determine if the number of twitches at baseline, auditory stimulation, and training were different.

**Results :** Auditory stimulation increased the number of REM phasic events by 85.5% (p>0.01), whether given only in REM or across states. Learning itself without auditory stimulation did not significantly increase the number of REM phasic events (p=0.24), although learning combined with auditory stimulation did increase REM phasic events (105.6% +/- y, 52.3<0.05).

**Conclusion :** Auditory stimulation increased phasic EMG twitches during REM sleep regardless of state stimulated or learning condition. The relationship between these evoked increases in REM phasic activity and learning remains to be determined.

**Support (optional):** NIMH MH60670

1098

FACTORS INFLUENCING SELF-REPORTS OF SLEEP

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**Introduction :** Traditional self-reports of sleep behavior require respondents to provide a single numerical value (ex: 'I slept seven hours') and these estimates are often inaccurate compared to PSG. Self-reports of sleep can also be collected using a fuzzy set format, requiring respondents to provide a range of values (ex: 'I slept between 6 and 8 hours'). This study compared self-report data in traditional and fuzzy response formats to PSG data.

**Methods :** Data was taken from a study of sleep in pregnancy. Twenty-six women (mean(SD) age=28.1(7.7) years) completed post-sleep questionnaires following a night in the sleep laboratory in either their first or third trimester. On the questionnaire subjects provided estimates of the preceding night's sleep for sleep latency (SOL), total sleep time (TST), wake after sleep onset (WASO) and sleep quality in both traditional and fuzzy formats. Current level of sleepiness was rated on the Karolinska Sleepiness Scale. Correlations between subjective and PSG estimates were computed. Regression analyses computed the contribution of sleepiness and sleep quality ratings to subjective estimates controlling for PSG values.

**Results :** For TST, PSG values were closer to the lower range of fuzzy estimates than traditional estimates. PSG values of SOL were very similar to traditional self-report estimates. Subjects were least accurate for WASO estimates, with PSG values falling outside of the fuzzy range of estimates. Correlations between subjective estimates and PSG were similar across response formats. Sleepiness significantly predicted SOL estimates (p=.038) over and above PSG values. Sleep quality ratings tended to predict TST estimates (p=.086) in a similar manner.

**Conclusion :** Accuracy of self-reports of sleep varied across sleep vari-

ables. Using a non-traditional fuzzy response format improved accuracy for some variables. Interestingly, estimates of sleep were influenced by subjective perceptions of sleepiness and sleep quality, suggesting that these factors may contribute to discrepancies between self-report and PSG estimates of sleep.

**Support (optional):**

### 1099

#### PREDICTING LANGUAGE PERFORMANCE UNDER SUSTAINED OPERATIONS CONDITIONS

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**Introduction :** Past research has indicated that performance is negatively affected under sustained operations conditions; however, few studies have attempted to predict performance decrements or provide models that predict performance decrements. The purpose of this study was to examine whether relatively short “predictor” tasks could predict performance decrements in language tasks across a 30-hour work period at night.

**Methods :** Thirty-eight non-native English speaking students (mean age:  $24.3 \pm 2.5$ ) were paid to train on and complete numerous tasks over a 30-hour period. The participants completed several potential predictor tasks. Three predictor tasks were simple memory tasks: AX task (participants looked for an A at the start of a string of letters followed by an X at the end), Sternberg memory task, and continuous performance task (CPT, a 1-back task). A fourth predictor task was the psychomotor vigilance task (PVT). Two language tasks were completed: the GRE verbal test and the logical reasoning portion of the LSAT. Each task was administered four times during the night, once in each testing session (6:30 - 10:30PM, 11:00PM - 3:00AM, 3:30 - 7:30AM, and 8:00 - 12:00PM). All tasks were counter-balanced across the testing sessions.

**Results :** Mixed model analyses were conducted to determine how well the predictor tasks predicted performance on the GRE verbal and LSAT tasks. The results indicated that accuracy on the AX task predicted performance on the GRE and LSAT task ( $p=.000$ ) and accuracy on the Sternberg memory predicted performance on the LSAT task ( $p=.005$ ). Rate of responding on the PVT (inverse RT) predicted performance on the GRE ( $p=.001$ ) and LSAT task ( $p=.000$ ).

**Conclusion :** These findings indicate that it is possible to predict performance on language tasks. This result is relevant in many work settings where language performance needs to be maximized and would benefit from a model that could be used to predict performance decrements.

**Support (optional):** This research was funded by the Department of Defense and the Center for Advance Study of Language at the University of Maryland.

### 1100

#### BRAIN ACTIVATION PATTERNS DURING COGNITIVE FMRI TESTING BEFORE AND AFTER CPAP TREATMENT FOR OSA

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**Introduction :** Patients with obstructive sleep apnea (OSA) show improvement in cognitive functions after treatment with continuous positive airway pressure (CPAP) therapy. Very little is known about functional brain activation patterns during cognitive testing in OSA and following treatment with CPAP. The purpose of this study was to identify brain activation patterns during cognitive testing before and after initiation of CPAP treatment for OSA.

**Methods :** Subjects were eight men (age  $45.6 \pm 7.2$  years) with OSA (mean AHI  $30.1 \pm 20.3$ , mean min O2 saturation  $92.3 \pm 5.4\%$ , mean 3% desat index  $13.8 \pm 22.8$ , mean BMI  $27.4 \pm 2.6$ ) who had no contraindications to MRI, significant medical, neurological or psychiatric co-morbidities. Subjects were tested with a paced auditory serial addition test (PASAT) in a GE 1.5 T MRI scanner before and after a minimum three months of treatment for OSA. CPAP use was measured objectively by chart review or by subjective report at time 2 testing period. Significant fMRI activations were identified by contrasting experimental (PASAT) and control (7's) conditions of echo-planar imaging blood oxygen level-dependent (EPI-BOLD) signal patterns with MedX software and pairwise t-tests (significance threshold of  $Z=3.0$ ).

**Results :** Group PASAT task performance was 99.2 % accurate at both pre- and post-treatment measurements. Nightly CPAP use was reported by 6 of the 8 subjects. Compared to pre-treatment, subjects with 360 minutes or more of nightly CPAP (mean,  $365.2 \pm 29.2$  minutes) use showed the strongest pattern of decreased EPI-BOLD signal in frontal, parietal and cerebellar brain regions during PASAT task performance.

**Conclusion :** Subjects who used CPAP an average of 6 hours at night showed decreased EPI-BOLD signal levels of activation during cognitive testing. This observation could reflect more efficient use of neuronal resources following treatment for OSA. Further analyses are underway to quantify these changes and explore potential mechanisms.

**Support (optional):** University of Washington Royalty Research Fund (RRF) to CAL.

### 1101

#### BOTH AROUSAL AND SLOW-WAVE SLEEP FACILITATE SLEEP-RELATED MEMORY

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**Introduction :** Both arousals and slow-wave sleep have been positively implicated in facilitating sleep-related memory consolidation. According to the cognitive theories of insomnia literature, poor sleepers tend to have better memory than good sleepers for information presented prior to sleep. According to the memory consolidation literature, slow wave sleep may be especially important for consolidation of explicit memory.

**Methods :** Participants with partially remitted Major Depressive Disorder were presented with 4 series of 22 words, each containing 6 positive, 6 negative and 6 neutral, counterbalanced for emotionality, arousal and frequency. All sets started and ended with the two extra neutral words to control for primacy and recency effects. Lists were presented in the evening, with the last list being presented at bedtime. In this study, we investigated morning recall.

**Results :** Participants who successfully recalled one or more of the 18 valenced words presented just before sleep had a longer sleep-onset latency ( $t = -3.3$ ,  $p = 0.002$ ), more WASO ( $t = 2.33$ ,  $p = 0.024$ ) and more slow-wave sleep than participants who did not ( $t = 2.202$ ,  $p = 0.040$ ). In addition, participants who recalled more than 7 words out of 54 that were presented earlier in the evening also had longer SOLs ( $t = -2.861$ ,  $p = 0.007$ ).

**Conclusion :** Participants who had greater levels of arousal (as measured by SOL and WASO) and more SWS recalled more words from a list read aloud before sleep. This suggests that both increased arousal and time spent in slow wave sleep contribute to memory processing. Since increased SOL predicted recall of lists presented several hours before bed, this may indicate that participants who had long SOL were more aroused throughout the experimental evening, not just at sleep onset.

**Support (optional):** T32-AT001287 (W. Britton, P.I.)

## 1102

### WAKING ACTIVITIES ASSOCIATED WITH REDUCED SLEEP TIME

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**Introduction :** Reduced sleep time has been associated with increased risk of obesity, mortality, and accidents, yet little is known about which waking activities are most associated with reduced sleep time. We evaluated this question using the American Time Use Survey (ATUS) database.

**Methods :** Cross sectional survey data from the 2003 ATUS database (a random national telephone survey of men and women over 15y of age, conducted by the US Census Bureau for the Bureau of Labor Statistics) were used to determine which of 16 different waking activity categories had relationships to sleep time in N=4749 adults (25-64y) who had worked on weekdays.

**Results :** Sleep time declined with age, to a low at 45-54 years, when work time and pay were highest. Waking activities reciprocally related to sleep time were (1) work time; (2) time for traveling; (3) leisure time; (4) household activity time; (5) time spent caring for household members. As these activities increased, sleep time decreased in working adults (adjusted  $R^2=0.464$ ,  $p=0.0001$ ). The largest reciprocal relationships to sleep (most variance) were for work time and travel time—increases in either activity were associated with near-linear decreases in sleep time. When commute time to work was analyzed separately, the same robust effect was observed. Age showed a very modest reciprocal relationship to sleep time. These relationships were found for both women and men, despite substantial sex differences in time spent at work, on household activities and care of household members, in leisure time, and weekly pay.

**Conclusion :** Work time and travel time, and to a lesser extent, domestic chores and leisure time, are the primary activities working adults appear to exchange for sleep time. While work time had an expected negative effect on sleep time, the finding that travel time had as robust an effect as work was unexpectedly provocative.

**Support (optional):** NIH NR04281.

## 1103

### EFFECT OF INTROVERSION-EXTROVERSION ON MOOD DURING CHRONIC SLEEP RESTRICTION

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**Introduction :** It has been reported that introverts report more anger and hostility. The aim of this study was to investigate the effects of introversion-extroversion on mood during 5 nights of sleep restriction.

**Methods :** Analyses were conducted on 33 healthy adults (17m; 16f; aged 22-45y), who participated in a 5-night sleep restriction protocol (4h TIB) following 2 baseline nights (10h TIB). The Millon Index of Personality Styles (MIPS) was used to identify extroverts (n=25) and introverts (n=8). Throughout the study, subjects completed the POMS and the psychomotor vigilance test (PVT) every 2 hours during wakefulness. POMS total mood disturbance (TMD) scores were used as the primary outcomes, but analyses were also run on POMS subscales.

**Results :** Sleep restriction significantly increased PVT lapses in both introverts and extroverts (both  $p<0.001$ ), with no differences between them. On the first 3 days of the study (baseline days 1 and 2, and sleep restriction day 1), introverted subjects reported significantly greater total mood disturbance compared to extroverts ( $p=0.006$ ). A repeated measures general linear model with baseline day 1 differences in TMD as a covariate, revealed that TMD increased steadily across days of sleep restriction

( $p=0.006$ ), but there was no interaction with introversion-extroversion ( $p=0.798$ ). Thus, by the final day of sleep restriction, initial mood differences between introverts and extroverts were no longer significant ( $p=0.404$ ). Analyses of POMS subscales generally fit the results for TMD, except for anger/hostility ratings, which remained higher for introverts throughout the study ( $p=0.017$ ).

**Conclusion :** These data suggest that sleep loss affects mood states and PVT performance similarly in introverts and extroverts, despite the former showing higher mood disturbance when not sleep deprived.

**Support (optional):** Supported by NASA cooperative agreement NCC 9-58-159 with the National Space Biomedical Research Institute, NIH NR04281 and RR00040

## 1104

### SLEEP DURATION PREDICTS PERFORMANCE ON THE PSYCHOMOTOR VIGILANCE TASK IN A HEALTHY SAMPLE OF POLICE ACADEMY RECRUITS

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**Introduction :** This study examines the relationship between sleep duration, perceived stress, and performance on the psychomotor vigilance task in a healthy sample of police academy recruits without current psychopathology. Our hypothesis was that short sleep duration was associated with increased perceived stress and worse performance on vigilance testing.

**Methods :** The study data are derived from the baseline assessment of a large prospective study of risk and resiliency for stress-related disorders in police academy recruits who were studied during police academy training prior to exposure to duty-related critical incidents. Subjects (N= 177; mean age= 26.5, SD = 4.3, range 21-43; 87% male) were medically and psychiatrically healthy with no current Axis I psychiatric disorder as assessed by a SCID interview. Subjective stress was assessed with the Perceived Stress Scale. Sleep wake activity was assessed with wrist actigraphy for 7 days. Subjects performed the Psychomotor Vigilance Task (PVT) for 5 minutes on a personal digital assistant (PDA) device morning and evening during the 7 days. Repeated measures logistic regression was used to estimate the probability of having 1 or more lapse (> 500msec reaction time) on the PVT as a function of previous night sleep duration.

**Results :** Valid estimates of sleep duration were obtained in 1095 nights of sleep. Mean sleep duration was 6.3 hours, SD = 1.7. Morning lapses were predicted by previous night sleep time, OR = 1.145, 95% C.I. = 1.05 to 1.24,  $p = .0014$ . There was a 14.5 percent (C.I. 5.3% to 24.4%) decrease in the odds of having at least one lapse for each hour of sleep obtained the previous night. Evening lapses were not significantly related to sleep duration. Perceived stress was not associated with sleep duration or probability of performance lapse.

**Conclusion :** In a sample with a relatively short mean sleep duration, performance on the PVT in the morning was significantly associated with the length of the previous night of sleep. Performance on the PVT during the evening, when the circadian alerting signal is presumed to be greater, was not associated with duration of the previous night of sleep. Perceived stress in a sample of healthy young adults without current psychopathology was not associated with sleep duration or performance on the PVT.

**Support (optional):**



1105

**SLEEP AND DAYTIME FUNCTIONING IN ADOLESCENTS WITH ADHD OR A LEARNING DISABILITY***O'Brien E,<sup>1</sup> Mindell JA<sup>2,3</sup>*

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**Introduction :** Adolescents who are diagnosed with Attention-Deficit/Hyperactivity Disorder (ADHD) and adolescents with learning disabilities have been noted to experience increased sleep disturbances. Sleep disturbances among adolescents with ADHD may be further exacerbated by the use of medications that are often used to treat this condition.

**Methods :** The present study examined the sleep patterns and daytime behaviors of a group of 388 adolescents between the age of 14 and 19 years old. Approximately 9% of this sample ( $N = 35$ ) indicated that they had ADHD or a learning disability, which is consistent with the prevalence of these disorders among the general adolescent population. All participants completed the School Sleep Habits Survey and a modified version of the Youth Risk Behavior Survey as part of this study.

**Results :** Independent-samples *t*-tests indicated significant differences between groups for weekend bedtime ( $t(38.62) = -2.54, p < .05$ ), weekend delay of bedtime ( $t(378) = -2.35, p < .05$ ), and overall risk-taking behavior ( $t(36.41) = -2.93, p < .05$ ); a trend for differences in sleep latency on school-nights between groups was also noted ( $t(37.60) = -1.93, p = .06$ ).

**Conclusion :** The adolescents reporting a diagnosis of ADHD or a learning disability indicated shorter sleep latency on school nights, later weekend-night bedtimes, and longer weekend delays, compared to a group of control adolescents. These findings are consistent with previous literature. Although adolescents with ADHD or a learning disability reported higher levels of overall risk-taking behaviors, no additional significant differences were found between the groups on any of the other daytime behavior variables measured (daytime sleepiness, sleep problems, depressed mood). Overall, these results support previous research demonstrating sleep disturbances in adolescents with ADHD and learning disabilities, and also indicate increased risky behaviors in this group. These findings suggest a need to address sleep disturbances in this vulnerable population in order to enable these children to achieve an optimal state of functioning.

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