Late Breaking Abstracts

LBA 1

BLUNTED EMOTIONAL INTENSITY FOLLOWING REPEATED EXPOSURE TO SLEEP RESTRICTION

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Introduction: While acute sleep loss (up to three days) has shown adverse effects on emotional functioning, it is unknown whether such effects acclimate following chronic insufficient sleep. We investigated changes of affective responses to emotional photographs using a 3-week long in-laboratory model mimicking a pattern of sleep restriction during workweeks and recovery sleep during weekends.

Methods: Fourteen healthy participants (ages 18-55, 7 female) completed two 25-day stays in the Clinical Research Center. Participants completed a control stay, with 8-hour sleep opportunity every night, and a sleep restriction stay, with three cycles including 5 nights of 4-hour sleep opportunity and 2 nights of 8-hour sleep opportunity. Emotion testing involved presentation of 30 photographs (11 positive, 14 neutral, 5 negative; International Affective Picture System validated), during baseline and the 4th day of each week. Participants rated their affective valence (how positive or negative) and emotional intensity (strength of emotion) for each photograph using the Self-Assessment Manikin.

Results: A repeated measures mixed model analysis was used to examine effects of repeated sleep restriction compared to control sleep on ratings of valence and intensity. Participants reported less intense reactions to photographs throughout the sleep restriction stay compared to control ($P < 0.10$ for interaction effect), reaching significance during the third week of sleep restriction ($p < 0.05$). This effect resulted from decreased intensity to negative photographs ($p < 0.05$). No significant effect was found for valence.

Conclusion: These findings indicate prolonged exposure to sleep restriction adversely affects emotional functioning by decreasing intensity of emotions. Blunted emotional intensity is a risk factor for anhedonia, a symptom in psychiatric diseases. This is consistent with literature showing blunted emotional reactivity, but conflicts with disinhibition models predicting greater reactivity with sleep deprivation. This study provides first insight into how chronic insufficient sleep may increase risk of mental illness.

LBA 2

GENETIC ASSOCIATION OF DAT1 GENETIC VARIANTS WITH SLEEP DURATION

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Introduction: Short sleep duration has been linked to negative health effects, but is a complex phenotype with many contributing factors, including genetic factors. Methods: Twenty-seven single nucleotide polymorphisms (SNPs) from 20 candidate genes were chosen from the literature for testing for association with sleep duration in the public UK Biobank sleep duration GWAS. Association analyses were performed between genetic variability in the selected genes and measurements of sleep duration, adjusted for age, sex and principal components of ancestry, in 111,975 individuals of European ancestry.

Results: A genomic region within DAT1, represented by lead SNP rs464049, was significantly associated with sleep duration ($p=4.00*10-5$) and another in DRD2 (rs17601612) showed some evidence of association ($p=0.0014$). The DAT1 association signal has never before been described in humans.

Conclusion: Overall, SNPs in two dopamine-related genes were significantly associated with sleep duration, highlighting the important link of the dopamine system with sleep duration in humans.

LBA 3

α_2-ADRENERGIC BLOCKADE AS A NOVEL PHARMACOTHERAPY FOR OBSTRUCTIVE SLEEP APNEA

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Introduction: Previous drug candidates for obstructive sleep apnea (OSA) aiming to restore hypoglossal nerve activity and resultant pharyngeal dilator muscle tone during sleep have proved largely ineffective in preclinical and clinical studies. Episodic airway obstruction is known to induce a long-lasting noradrenergic-dependent increase in hypoglossal activity called hypoglossal long-term facilitation (hLTF) in animal models. We hypothesized that: (1) impairment of hLTF as a second-line motor defense against pharyngeal collapse during sleep may contribute to the pathogenesis of OSA; and (2) pharmacologic targeting of central

noradrenergic neurons to restore not only hypoglossal activity but also hLTF may provide an effective drug treatment of OSA.

Methods: hLTF was induced by episodic airway obstruction and by optogenetic stimulation of A7 and A5 noradrenergic neurons in rats during spontaneous or cholinergic-induced REM sleep. Central noradrenergic drive was modulated by a clinically well-tested α_2-adrenoceptor antagonist (yohimbine, a dietary supplement available over-the-counter in the USA) administered either systematically or focally at bilateral A7 and A5 neurons.

Results: (1) hLTF was robustly induced by episodic optogenetic stimulation of A7 or A5 neurons, as indicated by significant increase of hypoglossal activity (>30% above baseline, $p<0.05$, n=5) lasting >20 min post-stimulation. (2) REM sleep significantly decreased not only baseline hypoglossal activity but also hLTF induced by episodic airway obstruction ($p<0.05$, n=11). (3) The depressant effects of REM sleep on these first- and second-line motor defenses against pharyngeal collapse were promptly reversed by systemic administration of yohimbine (0.25-1.0 mg/kg i.v.). (4) Focal injection of yohimbine into bilateral A7 and A5 regions (n=5) produced similar beneficial effects on baseline hypoglossal activity and hLTF. (5) Systemic yohimbine also significantly enhanced phrenic activity during REM sleep (>30% above baseline, $p<0.05$, n=7).

Conclusion: Disinhibition of A7 and A5 neurons by α_2-adrenergic blockade with yohimbine constitutes a potentially effective and relatively safe pharmacotherapy for OSA.

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LBA 4

UPPER AIRWAY STIMULATION THERAPY UTILIZED AS A RESCUE PROCEDURE FOR FAILED SLEEP SURGERY

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Introduction: Many patients with obstructive sleep apnea (OSA) are unable to tolerate CPAP and alternative strategies are necessary. Upper airway stimulation (UAS) is a new addition to the surgical armamentarium which has shown success in initial outcome studies. We hypothesize that UAS is a successful rescue procedure for those patients who have failed sleep surgery.

Methods: We reviewed our series of patients undergoing UAS and selected those patients having undergone unsuccessful prior sleep surgery. We defined prior sleep surgery as unsuccessful if there was a residual AHI greater than 20. We reviewed demographic data including gender, age, BMI, and pre and postoperative Epworth Sleepiness Scale (ESS) score results. We also assessed pre and postoperative polysomnographic (PSG) data including AHI and O_2 nadir. We also calculated rate of surgical success, defined as a decline in postoperative AHI by 50% and to a value less than 20. Lastly, we compared the outcome data to the cohort of patients who received

UAS implantation, but did not undergo other types of sleep surgery.

Results: We have performed 66 UAS implantations at our institution. Of these patients, 12 received prior surgery for OSA. This included 8 UPPP, 3 MMA, and 1 tongue base resection. The patients undergoing prior sleep surgery consisted of 7 men and 5 women. The average age, BMI, and preoperative ESS scores were 53.2, 29.1, and 9, with standard deviations of 13.1, 3.3, and 3.9 respectively. The mean preoperative AHI and O_2 nadir were 34.3 and 80.4 with standard deviations of 8.9 and 4.8 respectively. The mean postoperative AHI, O_2 nadir, and ESS scores were 7.8, 87.8, and 6.7 with standard deviations of 11.4, 3.2, and 3.6 respectively. Postoperative AHI was significantly improved from preoperative. The surgical success rate was 91.7%. Compared to outcome measures of a cohort of patients undergoing UAS, but not other types of sleep surgery, there was not a significant difference in postoperative AHI, O_2 nadir, ESS, or success rate.

Conclusion: UAS is a successful method of treating OSA and can be used to treat patients who have failed other types of sleep surgery.