Late Breaking Abstracts

LBA 1

GALANINERGIC NEURONS IN THE VENTROLATERAL PREOPTIC AREA PROMOTE NON-RAPID EYE MOVEMENT (NREM) SLEEP IN MICE

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Introduction: Ventrolateral preoptic area (VLPO) has been shown to be a critical region for sleep regulation in mammals. Because the galaninergic (GAL) neurons in the VLPO express cFos following periods of increased sleep and project to key wake-promoting regions in the posterior hypothalamus and brainstem, we proposed that the GAL neurons in the VLPO may be able to drive sleep behavior. To address this question, we selectively activated VLPO GAL neurons using chemogenetic tools and studied the consequent changes in sleep-wake in free moving mice.
Methods: Under anesthesia, adult male GAL-Cre mice (transgenic mice expressing cre-recombinase under GAL promoter) were stereotaxically injected with adeno-associated viral vectors (AAV) containing the Cre-dependent gene for the excitatory DREADD, hM3Dq and a red fluorescent tag, mCherry (AAV8-DIO-hM3Dq-mcherry) or AAV containing the gene for Cre-dependent mCherry alone (AAV8-DIO-mCherry; sham control) into the VLPO. All mice were then implanted with miniature transmitter for recording the electroencephalogram (EEG), electromyogram (EMG) and body temperature (Tb). Four weeks after the surgical procedure, we intraperitoneally (i.p.) injected clozapine-N-oxide (CNO; ligand for hM3Dq to activate GAL neurons) or saline (vehicle) and studied the changes in sleep-wake and Tb.
Results: Activation of preoptic GAL neurons by i.p. CNO during the light and dark periods resulted in significant increase in NREM sleep (up to 100%) and complete suppression of REM sleep for 6-8 hours in mice. Increase in NREM sleep was brought about by a decrease in sleep latency and increases in number and durations of NREM bouts. Preoptic GAL neuronal activation also caused a significant fall in Tb (up to 5°C) lasting for 6-12 hrs.

Conclusion: Activation of VLPO GAL neurons dramatically increased NREM sleep. Either VLPO or nearby median preoptic GAL neurons play an important role in maintaining Tb in a warm environment.
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LBA 2

CATECHOL-*O*-METHYLTRANSFERASE (COMT) GENOTYPE AFFECTS DYNAMIC DECISION MAKING DURING SLEEP DEPRIVATION

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Introduction: Decision making that requires flexible updating of decision-relevant information is profoundly degraded by total sleep deprivation (TSD). Dopamine is a key neurotransmitter in neural pathways involved in attentional control during such dynamic decision making. Dopamine is metabolized by the catechol-*O*-methyltransferase (COMT) enzyme, and COMT activity is influenced by a polymorphism, Val158Met. We investigated whether dynamic decision making during TSD is affected by COMT genotype.
Methods: N=41 healthy adults (26.3±4.7y; 17 females) participated in a laboratory study. After a baseline day (10h TIB), subjects were randomized to 38h TSD (n=20) or well-rested control (10h TIB; n=21). Subjects performed a *go*/*no-go* reversal learning task (GNGr) at baseline (6h awake) and again 24h later during TSD or well-rested control. The GNGr task required subjects to learn the *go*/*no-go* stimulus-response relationships from feedback. Halfway through the task, these relationships were reversed unexpectedly, which subjects were to discover from feedback. GNGr performance was quantified by discriminability (d') between *go* and *no-go* stimuli before and after the stimulus-response reversal. Subjects' genomic DNA was extracted from whole blood samples and assayed using real-time PCR. COMT genotype frequencies were in Hardy-Weinberg equilibrium ($\chi^2_2 = 0.21$).
Results: Mixed-effects ANOVA showed no significant main effect of COMT genotype on GNGr performance (F=1.50, p=0.22). However, there was a significant interaction between genotype and experimental condition (F=3.98, p=0.019). Compared to subjects heterozygous or homozygous for the Met allele, subjects homozygous for the Val allele had significantly worse GNGr performance during TSD. In fact, their GNGr performance during TSD after stimulus-response reversal was no better than chance.
Conclusion: TSD exposed effects of the COMT Val158Met polymorphism on a task requiring updating of information and dynamic attentional control. With TSD the Val/Val genotype impaired overall performance and was especially disadvantageous for utilization of dynamic attentional control.
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LBA 3

SLEEP RESTRICTION SLOWS METABOLISM AND IMPAIRS PERFORMANCE IN ELITE CYCLISTS

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Introduction: The effects of sleep restriction on physiology and impact on exercise performance in healthy fit adults are not well elucidated. Chronic sleep restriction is widespread and few studies have investigated the impact on metabolism and heart rate in fit adults. The aim of the study was to examine the effects of 3 days of sleep restriction (SR) on exercise physiology and performance in healthy athletes.
Methods: In a randomized crossover design, 12 healthy elite male cyclists (29.2 ± 5.3 years) restricted sleep to 4 hours for three days or extended sleep to 10 hours for two weeks. Cyclists completed a baseline week of habitual sleep and a 2-week washout period in between interventions. Outcome measures pre and post intervention included: a 20-minute submaximal test, a 1-minute incremental maximal exercise test, and a maximal time to exhaustion test on a bicycle ergometer and metabolic collection system as well as the Psychomotor Vigilance Task.
Results: Following sleep restriction, energy expenditure during submaximal exercise decreased 3.9% (13.74 ± 0.60 vs. 13.20 ± 0.64 Kcal/min, $p<0.001$). Submaximal heart rate decreased after SR (135.7 ± 13.8 vs 128.6 ± 12.1 bpm, $p<0.01$) as well as peak heart rate (184.3 ± 7.6 vs 179.3 ± 7.9 bpm, $p<0.01$). Following SR, maximal aerobic power decreased 2.9% (430 ± 40 vs. 417 ± 39 watts, $p<0.05$) and time to exhaustion decreased by 10.7% (37 seconds) (353 ± 108 vs 315 ± 92 seconds, $p<0.05$). Psychomotor Vigilance Task response speed decreased following SR (3.86 ± 0.39 vs 3.51 ± 0.36, $p<0.05$).
Conclusions: 3 days of sleep restriction decreased energy expenditure and heart rate during exercise. Findings suggest that sleep loss results in performance impairments including decreased peak power and endurance performance, as well as decreased response speed in fit adults.
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LBA 4

TRANSVENOUS STIMULATION OF THE PHRENIC NERVE TO TREAT CENTRAL SLEEP APNEA: RESULTS OF A RANDOMIZED TRIAL

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Introduction: Central Sleep Apnea (CSA) is associated with multiple co-morbidities and increases the risk for adverse consequences. An implantable neurostimulation system (the remedē® System, Respicardia, Inc., MN) has been designed to be implanted by a cardiologist to transvenously stimulate a phrenic nerve to restore normal breathing patterns in patients with CSA. A randomized trial evaluated stimulation of the phrenic nerve in patients with moderate to severe CSA.

Methods: Following polysomnography (PSG), 151 patients with apnea-hypopnea index (AHI) ≥20 events/hour and predominantly CSA were implanted and randomized (1:1) to stimulation (treatment) or no stimulation (control) for 6 months. The primary effectiveness endpoint was a comparison of the proportions of patients in treatment versus control achieving a ≥50% AHI reduction. If the primary effectiveness endpoint was met, seven secondary endpoints also were tested hierarchically. Following the 6 month effectiveness assessment, control subjects had stimulation turned on. The primary safety evaluation was freedom from related serious adverse events through 12 months. PSGs were scored by a blinded core laboratory.

Results: The average baseline AHI was 46 ± 18 and central apnea index (CAI) was 28 ± 17. A statistically significantly higher proportion of patients in the treatment group achieved an AHI reduction ≥50% at 6 months compared to control (P<0.001). Freedom from related serious adverse events was 91%. All 7 hierarchical secondary endpoints were statistically significant, with treatment being superior to control for each endpoint CAI (p<0.001), AHI (p<0.001), arousal index (p<0.001), REM sleep (p=0.024), patient global assessment (p<0.001), oxygen desaturation index 4% (p<0.001) and Epworth Sleepiness Scale (p<0.001).

Conclusion: Unilateral transvenous stimulation of the phrenic nerve effectively treats CSA as demonstrated by reductions in the AHI and other sleep indices, increases REM, and improved sleepiness and quality of life.