

# SLEEP

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## Late Breaking Abstracts

### LBA 1

Sleep characteristics are associated with white matter microstructure in middle-aged and older adults: Findings from the Wisconsin Sleep Cohort Study

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**Introduction:** Sleep promotes myelination and oligodendrocyte precursor cells proliferation. Sleep-disordered breathing and self-reported sleep quality have been associated with neuroimaging-assessed white matter microstructure. In particular, sleep-disordered breathing and poor sleep quality are associated with decreases in fractional anisotropy (FA) and increases in mean diffusivity (MD) in varying areas of the brain indicating less organized myelin and/or axonal structures. However, there is a paucity of research investigating associations of sleep characteristics with white matter microstructure assessed by diffusion tensor imaging (DTI). The objective of this study is to explore associations between sleep characteristics and DTI assessed white matter microstructure.

**Methods:** This cross-sectional analysis used 145 middle- to older-age adults' DTI and polysomnography data from the Wisconsin Sleep Cohort Study (mean [SD] age = 68 [8] years; 51% male). Sleep-disordered breathing severity was measured by overnight in-laboratory sleep studies (polysomnography) and quantified by the apnea-hypopnea index (AHI, events per hour). Following polysomnography, to assess white matter microstructure integrity, a region of interest analysis was performed on fractional anisotropy maps and mean diffusivity maps using the John Hopkins (JHU) white-matter labels atlas transformed to each individual's native space. Linear regression models estimated associations between sleep and DTI measures adjusting for age, sex, continuous positive airway pressure use, white matter hyperintensities, and time interval between neuroimaging and polysomnography.

**Results:** Sleep-disordered breathing severity (higher AHI) was statistically significantly associated with lower FA of the right superior fronto-occipital fasciculus and higher MD of the left medial lemniscus, and lower MD of the left sagittal stratum and left fornix/stria terminalis. Greater total sleep time (min) was associated with lower FA and higher MD in the right superior cerebellar peduncle. Greater sleep latency was associated with higher FA in the right sagittal stratum as well as reduced MD in the left posterior and the bilateral anterior limb of the internal

capsule, the bilateral superior longitudinal fasciculus, the left uncinate fasciculus, and the right posterior corona radiata.

**Conclusion:** In middle-aged and older adults, sleep-disordered breathing and lower total sleep time may be associated with attenuated white matter microstructure integrity contributing to compromised functional connectivity.

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## LBA 2

### Tasimelteon Demonstrates Efficacy to Treat Jet Lag Disorder in an 8 Hour Phase Advance Clinical Study

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**Introduction:** Jet lag disorder is a circadian rhythm disorder that commonly affects millions of travelers per year who cross multiple time zones. Tasimelteon, a MT1 and MT2 melatonin receptor agonist, demonstrated significant and clinically meaningful benefits in nighttime and daytime sleep parameters in the JET8 eight hour phase advance study. The JET8 study design induced the circadian challenge experienced by travelers who cross 8 time zones, which leads to jet lag disorder. The JET8 study was a randomized, double-blind, placebo-controlled, multicenter phase III study that randomized 318 healthy subjects.

**Methods:** Subjects received 20 mg of tasimelteon or placebo orally prior to their 8 hour phase advance bedtime and were assessed on nighttime sleep parameters including total sleep time (TST), latency to persistent sleep (LPS), and wake after sleep onset (WASO), as measured by polysomnography (PSG). Next Day Alertness was determined from the Karolinska Sleepiness Scale (KSS) and the Visual Analog Scale (VAS).

**Results:** Subjects receiving tasimelteon compared to placebo had a significant improvement in TST in the first two thirds of the night (tasimelteon=216.4 min., placebo=156.1 min., p<0.0001), TST in the full night (tasimelteon=315.8 min., placebo=230.3 min., p<0.0001), LPS (tasimelteon=21.8 min., placebo=36.8 min., p<0.01), and WASO (tasimelteon=144.6 min., placebo=219.1 min., p<0.0001). Tasimelteon demonstrated improvement in Total Sleep Time by 85 minutes. Additionally, significant improvement in Next Day Alertness were observed as measured by average KSS (tasimelteon=4.0, placebo=4.5, p<0.01) and average VAS (tasimelteon=60.8, placebo=54.2, p<0.01).

**Conclusions:** The JET8 study demonstrated clinically meaningful and statistically significant improvement of TST, LPS, WASO, and Next Day Alertness (KSS and VAS). These results

suggest that tasimelteon can be an effective therapeutic tool in the treatment of individuals that experience symptoms of jet lag disorder.

**Support:** This work was supported by Vanda Pharmaceuticals Inc.

### LBA 3

#### Sleep Duration Mediates the Relationship Between Health Behavior Patterns and Obesity

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**Introduction:** Recent evidence suggests there is a reciprocal relationship between obesity-related health behaviors and sleep, with sleep influencing obesity risk independent of changes in health behaviors. There is an urgent need to better understand the pathways by which modifiable health behaviors influence risk for obesity, as well as potential mediators of this pathway. In understanding the pathway by which sleep mediates the association between health behaviors and obesity, it is important to capture health behaviors as they co-occur in the real world. Therefore, our objective was to examine associations between health behavior patterns and childhood obesity, and the mediating effect of sleep duration.

**Methods:** This secondary analysis used year 6 follow-up data from the Infant Feeding Practices Study II (n=1073). Mothers self-reported their child's health behaviors and current heights and weights. Latent class analysis determined the child's health behavior patterns based on diet, physical activity, and screen time variables. Child sleep (in hours) was examined as a mediator between the categorical class membership variable and %BMI<sub>p95</sub>.

**Results:** A 3-class model fit the data best, with classes labeled as "Poorest eaters," "Healthy," and "Active, super-eaters, highest screen time." "Poorest eaters" had an increased %BMI<sub>p95</sub> ( $\beta=4.11$ ,  $p=0.006$ ) vs the "Healthy" class. Both the "Poorest eaters" and "Active, super-eaters, highest screen time" classes had significantly shorter sleep duration ( $\beta = -0.51$ ,  $p<0.001$ ;  $\beta = -0.38$ ,  $p<0.001$ ; respectively) vs. the "Healthy" class. Independent of class membership, each additional hour of sleep was associated with a %BMI<sub>p95</sub> that was 2.93 units lower ( $p<0.001$ ).

**Conclusions:** Children with health behavior patterns consisting of low fruit and vegetable intake and high fast food consumption had higher %BMI<sub>p95</sub> compared to children with healthy patterns. These children classified as "Active, super-eaters, highest screen time" also had significantly reduced sleep duration compared to children classified with having "healthy" patterns. We found

that sleep duration mediated the association of health behavior patterns and a child's %BMI<sub>p95</sub>. These results suggest that diet and activity behaviors influence obesity risk through sleep duration suggesting that interventions may want to explore whether improving diet and activity behaviors in turn can improve sleep to improve a child's weight.

**Support:** This research was funded by the American Heart Association, through a scientist development grant award (16SDG29170007).

#### LBA 4

Long-term continuous positive airway pressure treatment does not induce weight change in obstructive sleep apnea: a sub-study of the SAVE trial

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**Introduction:** To determine the impact of long-term continuous positive airway pressure (CPAP) treatment on the weight of adults with obstructive sleep apnea (OSA).

**Methods:** Participants in the Sleep Apnea Cardiovascular Endpoints (SAVE) study, a multicenter, randomized controlled trial were randomized to receive either CPAP treatment plus usual care (CPAP group) or usual care alone (control group) and had their weight, and neck and waist circumferences measured at regular intervals during follow-up. Participants were excluded from analysis if they had a missing baseline value or an outlier measurement being  $\geq 4$  SDs from the mean. Linear mixed modelling was used to test separately in men and women for differences

between baseline and follow-up measurements. A sensitivity analysis was also conducted to compare CPAP participants who adhered to therapy  $\geq$  4 hours per day with propensity matched control patients.

**Results:** 2,483 adults (1,248 CPAP group and 1,235 control group) were included in the analyses. They had an average of  $6.10 \pm 1.48$  (range 1 to 8) measures of weight including baseline. Males and females in the CPAP group used CPAP for a daily average of  $3.33 \pm 2.29$  and  $3.15 \pm 2.19$  hours respectively. After a mean follow-up of 3.5 years, there was no difference in the change in weight from baseline between the CPAP and control groups in either men (mean [95% CI] between-group difference: 0.07 [-0.40 to 0.54] kg,  $p = 0.773$ ) or women (-0.14 [-0.37 to 0.09] kg,  $p = 0.233$ ). There were also no significant differences in body mass index, neck circumference, waist circumference, and waist-hip ratio. Male CPAP patients who used CPAP  $\geq$  4 hours per day gained more weight than men in the control group (mean difference [95% CI]: 0.383 [0.035 to 0.730] kg,  $p = 0.031$ ), but there were no between-group differences in women, and no between-group differences in other anthropometric variables.

**Conclusions:** There was no evidence of a clinically significant weight change in patients with co-morbid OSA and cardiovascular disease following long-term CPAP treatment.

**Support:** This study was supported by the SSAVE trial.