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SLEEP TRAITS AND INCIDENT DELIRIUM DURING A DECADE OF FOLLOW-UP IN 173,000 PARTICIPANTS.

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Introduction: Delirium is an acute decline in attention and cognition that is with associated long-term cognitive dysfunction in elderly patients. Accumulating evidence points to strong associations between sleep health and disorders of the brain. We tested whether baseline sleep duration, chronotype, daytime dozing, insomnia or sleep apnea predict incident delirium during hospitalization.
Methods: We studied participants from the UK Biobank who have been followed for up to 10 years until 2017. We included 173,221 participants (mean age 60±5; range 50-71 at baseline) who had at least one episode of hospitalization/surgery and were free from prior episodes of delirium. Delirium diagnosis, hospitalization and surgical events were derived using ICD-10 coding. Multivariate logistic regression models were performed to examine the associations of self-reported baseline sleep duration (<6hrs/6-9h/>9h), daytime dozing (often/rarely), insomnia (often/rarely) and presence of sleep apnea (ICD-10 and self-report) with incident delirium during follow-up. Models were adjusted for demographics, education, Townsend deprivation index, and major confounders (number of hospitalizations/surgical procedures, BMI, diabetes, major cardiovascular diseases and risk factors, major neurological diseases, major respiratory diseases, cancer, alcohol, depression/anxiety, sedatives/sleep aides, antipsychotics, steroids and opioids).
Results: In total, 1,023 (5.7 per 1,000 subjects) developed delirium. A prior diagnosis of sleep apnea (n=1,294) saw almost a two-fold increased odds (OR 1.96, 95% CI: 1.30-2.30 p=0.001) while those who often had daytime dozing were also at increased risk (OR 1.35, 95% CI: 1.02-1.80, p=0.025). Both these effects were independent of each other. No independent effects on incident delirium were observed from sleep duration, insomnia, or chronotype.
Conclusion: Certain sleep disturbances, in particular sleep apnea and daytime dozing, are independently associated with an increased risk for developing delirium. Further work is warranted to examine underlying mechanisms and to test whether optimizing sleep health can reduce the risk of developing delirium.
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IMPROVED DAYTIME SLEEPINESS FOLLOWING DAILY MORNING BLUE LIGHT THERAPY IS ASSOCIATED WITH ALTERED RESTING-STATE NETWORK CONNECTIVITY

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Introduction: Light exposure, particularly blue wavelength light, has consistent positive effects on daytime sleepiness following mild traumatic brain injuries (mTBIs). While self-perceived improvements in daytime sleepiness are well-documented, the neurobiological underpinnings are not well understood. The purpose of this study was to localize changes in functional connectivity after daily morning blue light therapy (BLT) and to associate these changes with improvements in post-mTBI daytime sleepiness.
Methods: 29 individuals with a history of mTBI were randomized to receive either BLT (n=13) or placebo amber light (ALT; n=16). All participants self-reported daytime sleepiness (Epworth Sleepiness Scale (ESS); lower is better) and underwent resting-state functional magnetic resonance imaging at pre- and post-treatment. Whole-brain functional connectivity (FC) was estimated as the correlations between 400 cortical regions of interest (ROIs) assigned to 7 resting-state networks. A two-sample T-test for post-treatment ROI-to-ROI FC identified target connections (FDR corrected p<0.01). Post-treatment ESS scores and FC for these connections were correlated for treatment-related brain-behavior associations (uncorrected p<0.05).
Results: Lower FC after BLT in 4 ROI-to-ROI connections linking the default mode and visual networks was associated with lower ESS scores. Higher FC after BLT in 9 ROI-to-ROI connections linking attention, cognitive control, and visual networks was also associated with lower ESS scores.
Conclusion: BLT resulted in decreased self-reported daytime sleepiness, which was associated with decoupling of the default mode and visual networks as well as increased connectivity between and within attention and cognitive control networks, suggesting potentially improved attention to relevant stimuli and cognitive processes and less internal mentation. These associations may contribute to improved alertness, attention, and cognitive performance following a mTBI. Further work is needed to identify the optimal timing and dosage of BLT to maximize these outcomes.
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TASIMELTEON SHOWS PERSISTENCE OF EFFICACY IN IMPROVING SLEEP DISTURBANCES IN PATIENTS WITH SMITH-MAGENIS SYNDROME (SMS) IN OPEN-LABEL EXTENSION STUDY

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Introduction: Smith-Magenis Syndrome (SMS) is a rare (1/15,000 - 25,000 births) neurodevelopmental disorder resulting from an interstitial deletion of chromosome 17p11.2, or from a point mutation in the *RAI1* gene. Severe sleep disorder is almost universal in patients with SMS and poses a significant challenge to patients and their families. Tasimelteon improved sleep symptoms in a randomized, double-blind, two-period, crossover study; and here we show that this effect persists for up to four years in an open-label extension. To our knowledge, this is the largest interventional study of SMS patients to date.
Methods: Following the 4-week crossover study, all eligible participants had the option to enroll in an open-label extension. 31/39 (79.4%) of all individuals who participated in the efficacy study have continued on tasimelteon treatment. Participants in the open-label extension provided daily diary sleep quality (DDSQ), and

daily diary total sleep time (DDTST) measures via parental post sleep questionnaire and characterized behavior using the Aberrant Behavior Checklist (ABC).

Results: In the open-label extension, tasimelteon continued to show improvement in the primary endpoints of 50% worst sleep quality (mean = 0.7, SD = 0.94) and 50% worst total nighttime sleep duration (mean = 53.3, SD = 59.01) when compared to baseline. Tasimelteon also improved overall sleep quality (mean=0.7, SD=0.83) and overall total nighttime sleep duration (mean = 51.9, SD=53.03). ABC scores also improved with tasimelteon (mean= -16.3, SD = 15.82).

Conclusion: Tasimelteon continues to demonstrate persistence in efficacy (longest approximately 4 years) with similar magnitudes observed in the 4-week crossover study for sleep quality and total sleep time. Interestingly, daytime behavior also demonstrates long-term improvement in patients with SMS treated with tasimelteon. These results further confirm tasimelteon as a novel therapy for the treatment of sleep disorders in patients with SMS and may provide benefit for behavioral symptoms.

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