Support (If Any): Supported by the Force Health Protection Program of the Office of Naval Research (SAA2402925-1, Contract Award no. N0001418IP00050) and the NASA Airspace Operations and Safety Program, System-Wide Safety.

0300

EARLY LIFE SLEEP FRAGMENTATION IMPAIRS HIPPOCAMPAL-DEPENDENT LEARNING AND SLEEP-DEPENDENCY IN HIPPOCAMPAL CALCIUM TRANSIENTS

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Introduction: Sleep deprivation impairs hippocampal-dependent memory, and hippocampal-dependent memory impairments occur in some dementias, including Alzheimer's disease. As our population continues to age, understanding the molecular basis for memory impairments is increasingly important. We hypothesized that early life sleep fragmentation would result in lasting increases in hippocampal calcium transient activity.
Methods: B6 mice were randomized to 12wk of sleep fragmentation or rested control conditions at age 8wk. Mice were microinjected with AAV9-CamKII-GCamp6F into the hippocampus and later implanted with a GRIN Lens into CA1 secured to a baseplate along with chronic EEG/EMG electrodes and recording connector. Calcium recordings were obtained two to three months after injection and recordings were obtained across sleep-wake cycles>4mins of wake and NREM sleep. Individual cells across animal were combined into sleep fragmented (n = 521 cells) or rested (n = 443 cells) groups during wake or sleep. Average FFx was analyzed by group and condition by T-tests, paired for within and unpaired across groups. A spatial object recognition assay was also performed on all mice (n=16 for both groups) and performance across group was analyzed by paired T-tests.
Results: Rested mice showed normal spatial object recognition (n = 16, $p<0.05$). In contrast, SF mice showed impaired spatial object recognition (n = 16, N.S.). There were no differences across sleep conditions in calcium transient FFx for waking ($p>0.05$). However, in sleep, cells in SF mice had significantly higher average FFx values than cells in rested mice ($p<0.0001$).
Conclusion: Early-life sleep fragmentation has long-lasting impacts on memory. Since spatial memory is dependent on hippocampal function, the calcium transient FFx data suggests that a driver of this hippocampal memory impairment may be higher firing rates in sleep and/or greater calcium exposure in hippocampal CamKII neurons in sleep, both of which may perturb microglial maintenance of synapses. Understanding the molecular drivers behind this calcium dysfunction will be essential in our understanding of neurodegeneration, dementia, and Alzheimer's disease.
Support (If Any): NIH AG054104; AG064231

0301

DOES OREXIN INFLUENCE SLEEP FRAGMENTED BRAIN INFLAMMATION? A PILOT STUDY

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Introduction: Fragmented sleep occurs when there are repetitive, short interruptions of sleep, resulting in less than six hours of sleep per day. Overall, however, in the United States, sleep fragmentation is reported by 30% of employed adults. Sleep fragmentation may be a risk factor for Alzheimer's disease, and orexin reduction appears effective in reducing amyloid plaque formation in mice with transgenic Alzheimer's disease. Orexin is a neuropeptide that regulates arousal, wakefulness, and appetite. Thus we hypothesized that loss of orexin might also be protective against sleep disruption injury in non-Alzheimer's mice. This study aims to combine sleep fragmentation with orexin loss to see if brain health is severely reduced.
Methods: The 24 mice in this study were split into four groups: B6 rested, B6 sleep fragmented, orexin knockout rested, orexin knockout sleep fragmented. The sleep fragmented mice were placed on a shaker table for 10½ weeks to initiate chronic sleep loss. The mice were all perfused within five to eight months of birth, and then the brains were cryopreserved and sliced. These sections were immunolabeled with different protein antibodies using immunohistochemistry techniques. The stained brains were either analyzed through microscope stereology counts or computer image analysis.
Results: Two-way ANOVA analysis for tyrosine hydroxylase, ionized calcium binding adaptor, and vesicular acetylcholine transporter had $p<0.05$ for the sleep fragmentation variable, showing differences in these antibodies for rested and sleep loss mice. ANOVA for cluster of differentiation 68, cofilin, postsynaptic density protein, and RanBP had $p<0.05$ for the genotype variable, showing differences in these antibodies for knockout and normal orexin mice. ANOVA for glial fibrillary acidic protein and amyloid-beta had $p<0.05$ for both variables, showing differences for sleep and orexin levels. There was no ANOVA significance for synapsin.
Conclusion: Our results show that knocking out orexinergic neurons causes hippocampal tissue damage, dampens the functioning of synapses, and diminishes the ability of the brain to adapt through plasticity and memory. Sleep fragmentation, however, increases phagocytic activity, and harms the acetylcholine and norepinepherine neurotransmitter pathways. When combined, cell communication worsens and the blood brain barrier loses function, resemblant of neurodegenerative diseases.
Support (If Any): NIH AG054104; AG064231

0302

RECOVERY SLEEP IN UNIVERSITY STUDENTS

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Introduction: Poor sleep hygiene is common in American college students, with the majority reporting insufficient sleep. Previous studies suggest that many students extend sleep during the weekend to recover sleep debt accrued during the week. In the current study we objectively measured sleep to determine if weekend catch-up sleep was practiced. We also provided students with a 9h sleep opportunity in order to observe how an extended sleep period affected sleep architecture.
Methods: Students (N=36, 20 women, 19.9±1.7 years) participated in the study from September 2019-March 2020. Sleep-wake behavior was assessed for two weeks using wrist actigraphy and a twice-daily diary. During this two-week period, participants wore at-home polysomnography (PSG) on two non-consecutive nights. For these two nights, in counterbalanced order, participants were instructed to follow their typical sleep pattern or to extend their sleep opportunity to 9h. Within-subjects ANOVA were used to compare sleep between week (Sunday-Thursday) and weekend (Friday and Saturday) nights as well as between typical and 9h PSG nights.

Results: Compared to week nights, participants went to bed 35 minutes later and woke up 58 minutes later on weekend nights (ps<0.01). Measures of sleep duration and sleep continuity were comparable (ps>0.10) between week and weekend nights and indicated that students averaged less than 7h of sleep per night (6.3±1.0h on week nights and 6.7±1.1h on weekend nights). Self-report measures of sleep quality and daytime sleepiness were also comparable between week and weekend nights (ps>0.05). When instructed to extend their sleep opportunity to 9h, participants exhibited high adherence and increased total sleep time by 88 minutes compared to the typical night (p<0.05). This increase in sleep was due to significant increases in time spent in all four stages of sleep (NREM S1-3 and REM sleep, ps<0.05).
Conclusion: In this study, students did not utilize weekend nights to extend sleep in order to recover accumulated sleep debt from the week. When provided with a 9h sleep opportunity, participants were physically able to extend sleep and exhibited high quality sleep, suggesting that the primary driver of insufficient sleep in this population is a lack of sleep opportunity rather than impaired sleep ability.
Support (If Any):

0303

THE EFFECTS OF LATITUDE ON SLEEP AT 4300M

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Introduction: Worldwide, 140-million people live above 2400m and even more visit high altitudes (HA) annually. Exposure to HA is associated with hypoxia-related cognitive impairments and sleep disruptions. Additionally, both planetary axial tilt, solar gravity, and planetary spin distort the earth's atmosphere pulling the equator's atmosphere further from the earth's surface when compared to the poles. These forces may have additional impacts on physiology at HA. There has yet to be a study to determine these effects of latitude on physiology at HA. Therefore, the aim of the current study was to determine if latitude exacerbates the effects of HA on sleep.
Methods: Similar testing protocols were utilized at 4,300m at Camp-14 on Denali at a latitude of ~63° and in the village of Dingboche on the route to Mount Everest at a latitude of ~28°. Exclusion criteria included 18-65 years, self-reported drug use, cigarette-smoking, sleep disorders, abnormal body mass index (BMI), falling asleep more than one hour or awakened more than an hour during the night. Wireless sleep recording devices recorded the sleep architecture of qualified participants. Twenty-two climbers (3 females) participated in the Denali study (age 34.0±9.7 mean±SD) and twenty-five climbers (6 females) participated in the Everest study (age 28.0±9.7 mean±SD). Participants were instructed to go to bed and wake up at their habitual bedtimes and wake times.
Results: Independent t-tests revealed a statistically significant decrease in total sleep (p<0.05) on Denali when compared to Mt. Everest. There were nonsignificant trends for a decrease in rapid eye movement (REM) and sleep onset latency on Denali. Other sleep stages appear relatively unaffected by latitude.
Conclusion: Our findings indicate that a decrease in total sleep time occurs at higher latitude with comparable altitude. Prior research has linked a decrease in total sleep time to decreased cognitive impairments and physiologic disruptions. Our findings suggest that latitude should be considered when venturing into HA environments, designing research protocols, analyzing results, and clinical applications or military operations.
Support (If Any):