severe consequences for the affected individual and their families. Although mouse models can be used to investigate the mechanistic basis for social deficits and other symptoms of NDDs, recapitulating sleep phenotypes in mice has proven to be difficult. In this study, we determined whether a sleep-disruption challenge could reveal or exacerbate sex and strain differences in sleep patterns, using two well-validated mouse models of autism-like behavior; the BALB/cByJ and C58/J inbred strains.

Methods: Mice were placed in a piezoelectric sleep system for 3 days to evaluate baseline sleep rhythms. Mice were then exposed to a series of novel environments, including open field boxes and activity wheel cages, for 3 hours during the morning period of the light cycle. Sleep rebound was determined by comparing percent time spent sleeping and average sleep bout length in the three 6-hr intervals before and after the sleep disruption. Subjects were males and females of the C57BL/6J, BALB/cByJ and C58/J strains.

Results: At baseline, the C57BL/6J and BALB/cByJ females showed significantly reduced percent sleep, in comparison to males. During rebound from sleep disruption, BALB/cByJ mice had higher percent time and longer sleep bouts than C57BL/6J, suggesting a greater vulnerability to the effects of sleep disruption. Additionally, female C58/J mice lacked the highly robust increase in percent sleep seen in C57BL/6J in the early night interval after sleep disruption.

Conclusion: Overall, the data provide evidence that this sleep disturbance procedure can induce a sleep rebound effect, which could be helpful in revealing strain and sex differences in NDD mouse models.

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0298

KYNURENIC ACID SYNTHESIS INHIBITOR PROMOTES ENHANCED SLEEP RECOVERY FOLLOWING ACUTE SLEEP DEPRIVATION IN ADULT WISTAR RATS

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Introduction: Sleep disorders and cognitive dysfunction often afflict the general population and are common amongst patients with neuropsychiatric disorders like schizophrenia. Sleep deprivation (SD) disrupts cognitive function, yet little is known about underlying mechanisms. The tryptophan metabolite kynurenic acid (KYNA), an endogenous a7nACh and NMDA receptor antagonist, is synthesized by kynurenine aminotransferase II (KAT II). KYNA is increased in the brain of patients with schizophrenia and our translational studies demonstrate that elevated KYNA disrupts hippocampal learning and sleep architecture in rodents (Pocivavsek et al. 2017 Sleep). We hypothesize a mechanistic link between KYNA, sleep, and cognitive dysfunction.

Methods: In vivo microdialysis in the dorsal hippocampus and simultaneous EEG/EMG telemetry was conducted in adult male Wistar rats (N=3-5 per group). Using a within-subjects experimental design, rats underwent a control and SD day. Animals received either vehicle or KAT II inhibitor PF-04859989 (PF), 30mg/kg s.c., on both days at zeitgeber time (ZT) 0 or ZT6. SD occurred from ZT0-6 by gentle handling. KYNA levels were evaluated in the microdialysate.

Results: SD effectively eliminated REM sleep (100%) and significantly reduced NREM (94%) during ZT0-6. Extracellular KYNA levels in the hippocampus significantly increased with SD (2-way ANOVA, time x SD: **P<0.0001) and PF readily prevented this accumulation. Initial sleep recovery (ZT6-12) did not significantly differ between treatment groups. During the dark phase (ZT12-24), PF treatment of SD animals promoted REM sleep parameters, including total REM duration (2-way ANOVA, SD x treatment ZT: P<0.05). PF treatment enhanced theta spectral power determined by Discrete Fourier transform during REM sleep recovery (ZT12-24). PF alone during the control day enhanced NREM delta power (P<0.05) during the late light phase (ZT6-12).

Conclusion: Importantly, the KAT II inhibitor PF promoted sleep recovery following acute SD, supporting our hypothesis that the accumulation of KYNA may exacerbate sleep disruptions. Changes in sleep parameters elicited by PF, a potential therapeutic avenue, may be indicative of mild somnolence. The present and future complementary experiments with cognitive behavioral tasks in rodents support our understanding of the role of KYNA in modulating sleep and cognition.

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0299

THE EFFECTS OF CHRONIC SLEEP RESTRICTION ON CALORIE AND MACRONUTRIENT INTAKE

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Introduction: Chronic sleep restriction (CSR) has been associated with increased calorie intake and increased consumption of fats and carbohydrates, with inconsistent changes in protein. However, the majority of studies have either been observational field studies with no sleep intervention, or laboratory-based studies where food availability may not have reflected participants' real-world choices. We hypothesized that calorie, fat, and carbohydrate intake would increase during a week of imposed CSR compared to a week of sleep satiation (SS) among individuals living in their home environment.

Methods: Twelve healthy participants (6 females) kept a fixed sleep-wake schedule, with a constant waketime, at home for four weeks (actigraphy confirmed compliance). During weeks one and three, participants maintained 9 hours in bed. During weeks two and four, participants were randomly assigned to experimental weeks of 5 and 9 hours of time-in-bed in a crossover design. Participants documented their food consumption during both experimental weeks using a picture-based meal logging application (MealLogger). Intake of calories and macronutrients were classified by two blinded evaluators. Descriptive statistics were calculated in SAS (Cary, NC).

Results: Participants averaged 4.43 ± 0.33 (SD) hours of sleep per night during CSR compared to 7.42 ± 0.42 hours during SS. Participants consumed a daily average of 1812 ± 672 kilocalories, 71 ± 31 grams of total fat, 217 ± 69 grams of carbohydrates, and 84 ± 40 grams of protein during CSR, compared to 1682 ± 514 kilocalories, 68 ± 23 grams of total fat, 198 ± 61 grams of carbohydrates, and 77 ± 32 grams of protein during SS.

Conclusion: Preliminary descriptive findings suggest that, on average, participants consumed more calories, from an increase in consumption of each macronutrient group, during a week of sleep restriction compared to a week of sleep satiation. Further analysis is needed to determine whether these differences are statistically different and to identify when calories were consumed in each of the experimental conditions.

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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.
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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.
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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.