Conclusion: These data suggest that CSR, commonplace in millions of Americans, can negatively impact cognitive performance immediately upon awakening and have prolonged effects across dissipation for at least one hour, even in the absence of extended wakefulness. These findings are important for individuals needing to perform tasks quickly upon awakening, especially those who do not regularly obtain sufficient sleep.

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0207

NESTING OF SPIKE SEQUENCE REPLAY WITHIN SLEEP OSCILLATIONS DURING NREM SLEEP

Krishnan GP, Wei Y, Komarov M, Bazhenov M
Department of Medicine, University of California, San Diego, San Diego, CA

Introduction: Replay of spike sequences has been thought to underlie memory consolidation during sleep. Using computational models, we identified the critical mechanisms for the sequence replay during spindles (N2) and slow waves (N3) of NREM sleep.

Methods: Biophysically realistic thalamocortical network models implemented conductance based neurons and state dependent effects of neuromodulators (acetylcholine, histamine and GABA) to generate N2, N3 sleep and awake states. Spike Timing Dependent Plasticity (STDP) were implemented between cortical neurons. To simulate sequence learning, multiple trials of sequential input were presented to a group of selected cortical neurons during awake state of the model. The number of trials was varied from 10 to 100 trials. Performance was measured by the success of the sequence completion after the training, before and after the sleep.

Results: We found that learned spike sequences were reactivated spontaneously during N2 and N3 states leading to performance improvement after the sleep. In N2, the sequence replay was nested within spindle oscillations. Using spike-phase coupling analysis, we found that each neuron within a sequence fired selectively at the specific phase of the spindle oscillations. The spike-phase coupling was significantly higher for neurons involved in the sequence-learning task compared to neurons not involved in the task ($p<0.05$). In N3, replay of entire sequences occurred during the Up states of slow oscillation. Replay led to synaptic weights increase between neurons in the direction corresponding to the sequence replay while reduction in the opposite direction. Synaptic reorganization facilitated completion of the sequences learned during initial training phase. Both number of replays and change in synaptic weights were higher in trials with longer initial training.

Conclusion: We conclude that spike sequence replays are nested within sleep oscillations during NREM sleep and the nature of nesting is different between spindle and slow oscillations.

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0208

CIRCADIAN MISALIGNMENT IMPACTS ON HUMAN COGNITIVE PERFORMANCE

Chellappa SL[1], Morris CJ[1], Scheer FA[1]
[1]Harvard Medical School, Boston, MA, [2]Harvard Medical School, Boston, MA

Introduction: Shift work increases the risk for disorders of sleep and human error. Overnight operations pose a challenge because our circadian biology promotes nocturnal sleep and daytime vigilance and performance, which may underlie cognitive vulnerability at night. Here we investigated if daily circadian misalignment, typical for night shift work, adversely impacts cognition across diverse cognitive domains.

Methods: Thirteen healthy young individuals (27.8±9.5 y; 7 men) underwent two 8-day protocols including either 4 days of circadian alignment (day shifts) or misalignment (night shifts; 12-h inverted behavioral/environmental cycles). Cognitive testing included tasks of sustained attention (Psychomotor Vigilance Task; PVT), cognitive throughput (Addition Task; ADD), information processing (Digit Symbol Substitution Task; DSST) visual-spatial performance (Unstable Tracking-Task; TKT) and declarative memory (Probed Recall Memory; PRM), all of which are sensitive to increased sleep pressure and circadian phase.

Results: Circadian misalignment over successive days increased cognitive vulnerability by ~10–20% on sustained attention, cognitive throughput, information processing and visual-motor performance, as compared circadian alignment. Attention, as indexed by PVT performance, was acutely impaired during the first 2 days of misalignment with subsequent improvement after 3 days (interaction of "circadian alignment/misalignment", "day" and "time since awakening", $p=0.006$). Conversely, learning, as indexed by changes in ADD, DSST and TKT performance, significantly improved across multiple days of circadian alignment, while no improvement occurred under misalignment (interaction of "circadian alignment/misalignment" and "day", $p<0.05$). Lastly, we investigated if the effects of circadian misalignment on performance were also mediated by prior sleep-wake history. Accordingly, lower sleep efficiency in the sleep episode before cognitive testing significantly impaired performance (interaction of "sleep efficiency", "circadian alignment/misalignment" and "night"; $p<0.05$).

Conclusion: Our data indicate that daily circadian misalignment may explain cognitive vulnerabilities experienced by night workers, and provide a biological framework for the development of countermeasures against adverse cognitive effects in this vulnerable population.

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0209

OPTIMIZING SLEEP-RELATED MEMORY PROCESSES USING CLOSED-LOOP AUDITORY STIMULATION

Cellini N[1],,[2] Hernandez L[1], Shimizu R[3], Armstrong D[4], Aguilar-Simon M[3], Estrada RJ[3], Connolly PM[3], Weisend MP[4], Mednick SC[1], Simons S[3]
[1]University of California Riverside, Riverside, CA, [2]Department of General Psychology, Padova, ITALY, [3]Teledyne Scientific, LLC, Durham, NC, [4]Rio Grande Neurosciences, Dayton, OH

Introduction: Recent studies have shown that sensory stimulation can optimize memory consolidation in the sleeping brain for simple lab-based tasks. Based on these earlier results, we developed a closed-loop auditory stimulation (CLAS) system to more precisely target sensory stimulation and test whether this method can improve the more complex skill of spatial navigation in an urban environment.

Methods: Forty participants (Mean age = 26.2 years, F = 18) were trained to navigate within a large and detailed urban environment in virtual reality. Participants first learned the environment by freely navigating to specific points of interest (24 unique landmarks) in a virtual city. As participants navigated, they encountered different auditory cues (e.g., the barking of a dog near a park) associated with areas in the environment. Following learning, all participants underwent a

90-min polysomnographically-recorded nap, with half the participants receiving CLAS. CLAS detects slow oscillations during non-rapid eye movement (NREM) sleep using a minimum negative threshold criterion coupled with online automated sleep staging, to trigger delivery of short (700 ms) auditory cues during the down-state to up-state transition (DUPT). After sleeping, participants were tested in 6 of the previously trained routes.
Results: Compared with controls, the CLAS treated group was significantly faster in post-nap navigation ($p<0.01$). Additionally, CLAS participants showed an increase in DUPT phase-locked spindle activity in both the slow (9–12 Hz) and fast (12–16 Hz) frequency bands. No effect of the CLAS on sleep architecture was observed.
Conclusion: CLAS successfully improves the complex task of navigation in a virtual environment without any negative effects on sleep architecture.
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0210

INHIBITION OF PROTEASOME ACTIVITY MITIGATES THE EFFECTS OF SLEEP DEPRIVATION ON OPERANT MEMORY IN APLYSIA

Lyons LC, Krishnan HC, Noakes EJ
Department of Biological Science, Program in Neuroscience, Florida State University, Tallahassee, FL

Introduction: Technological advances, societal changes and increased emphasis on longer working hours for individuals have resulted in rising incidences of sleep deprivation for adolescents and adults. Consequently, sleep deprivation represents a growing public health and economic concern due to adverse effects on individual health, cognition and productivity. Recent research in rodents suggests that sleep deprivation inhibits hippocampal dependent memory through suppression of protein synthesis; however, it remains unknown whether these interactions are conserved across learning paradigms or phylogeny. The marine mollusk Aplysia californica with a relatively simple nervous system and well-established learning paradigms has recently emerged as an excellent model system for studies of sleep deprivation and memory. Recently, we found that maintenance of steady state protein levels through concurrent inhibition of protein synthesis and protein degradation permitted the induction of long-term memory. To test the hypothesis that sleep deprivation impacts memory formation through regulation of protein levels, we investigated whether the inhibition of proteasome activity ameliorated the effects of sleep deprivation on memory.
Methods: Animals were sleep deprived for 9 hours using context changes and tactile stimulation. Three hours prior to the end of sleep deprivation, animals were injected with either the proteasome inhibitor MG-132 or vehicle. Animals were trained following sleep deprivation using the learning that food is inedible paradigm, wherein animals form an association between a specific seaweed and failure of the swallowing attempts.
Results: We found that pharmacological inhibition of proteasome activity during sleep deprivation permitted the induction of associative memory. Sleep deprived animals treated with MG-132 exhibited robust short-term memory whereas vehicle injected animals failed to exhibit memory. Experiments on long-term memory are ongoing.
Conclusion: Inhibition of proteasome activity ameliorates memory decrements caused by sleep deprivation suggesting that sleep deprivation may inhibit the induction of memory through increased protein degradation or limitations on protein synthesis.
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0211

ENHANCING MEMORY CONSOLIDATION WITH TARGETED MEMORY REACTIVATION DURING SLEEP

Chappel-Farley MG, Madala KS, Jones BJ, Spencer RM
University of Massachusetts Amherst, Amherst, MA

Introduction: In young adults, memories can be strengthened during sleep through cued memory reactivation, a process whereby a sensory cue associated with prior learning is introduced again during sleep. It is unknown whether this procedure could be effective in older adults who typically exhibit memory decline. Thus, the purpose of this study is to replicate previous findings in young adults in order to develop a paradigm to test healthy older adults in the future.
Methods: Young adults (N=24, M=20.72 years) completed both an experimental and control condition. In both conditions, participants learned 30 picture-location pairs while wearing a nasal cannula. Two odors were administered during learning, Odor A (rose) and Odor B (mint), with half of the pairs being associated with each odor. Immediately after encoding, participants wore a polysomnography cap and nasal cannula during overnight sleep. One of the two odors was presented during sleep in the experimental condition, and a vehicle was administered during sleep in the control condition. The following morning, participants were tested on recall of all picture-location pairs without any odors.
Results: In both conditions, there was no significant difference in memory at the end of the learning session between cards associated with Odor A and those associated with Odor B ($p's>0.39$). In the experimental condition, memory accuracy improved between learning and recall for pairs associated with the odor presented during sleep ($p=0.003$) but not for the other pairs ($p=0.47$). Overall, memory accuracy was equivalent in the experimental and control conditions ($p=0.44$).
Conclusion: Results indicate that this cuing procedure does not enhance sleep dependent consolidation in general but rather in a stimuli-specific fashion. Future work will determine whether this procedure can enhance memory consolidation in older adults.
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0212

CRITICAL WINDOWS OF WAKING: SLEEP-DEPENDENT MEMORY CONSOLIDATION REQUIRES A WAKING PERIOD PRIOR TO SLEEP

Stepan M, Fenn K
Michigan State University, Lansing, MI

Introduction: Sleep has consistently been shown to be beneficial for hippocampal-dependent declarative memory, such as memory for word pairs. Prior research has found that sleeping within 3 hours after learning is more beneficial for memory than delaying sleep for 15 hours. However, the ideal relationship between waking and subsequent sleep is unclear. The purpose of the current research was to investigate how information learned at various intervals prior to sleep was later affected by sleep.
Methods: During Encoding, participants learned 24 pairs of non-semantically related words and completed a cued recall test without feedback to assess learning. That night, participants recorded when they went to bed using a smartphone app. Twenty-four hours after Encoding, participants returned to the lab and completed a final cued recall test.