Enhancing Sleep Stability to Facilitate Memory Function

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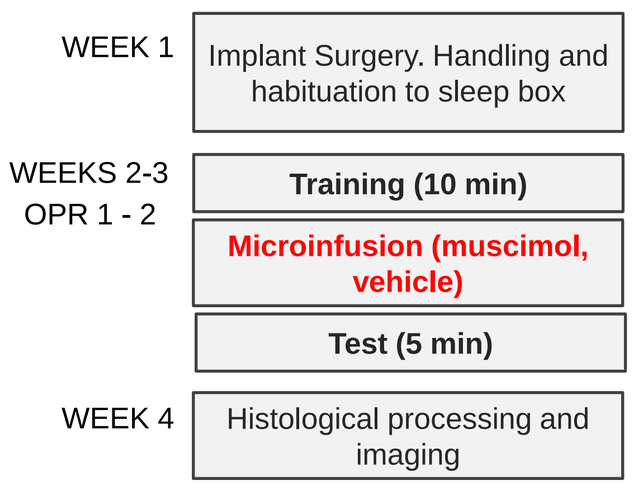
Background and Goals

- Sleep fragmentation impairs cognitive functions like memory and is linked to cognitive decline in Alzheimer's disease.
- Our goal is to understand the basic cellular mechanisms that facilitate sleep stability and the consolidation of memory during sleep.
- During non-rapid eye movement (NREM) sleep, neurons in the thalamus, a brain region critical for sleep, are inhibited. A key question is whether pharmacological induction of thalamic inhibition can facilitate sleep stability and enhance cognitive functions, such as sleep-dependent memory consolidation.
- Answering this question can guide the development of new pharmacological interventions for sleep-related cognitive issues.

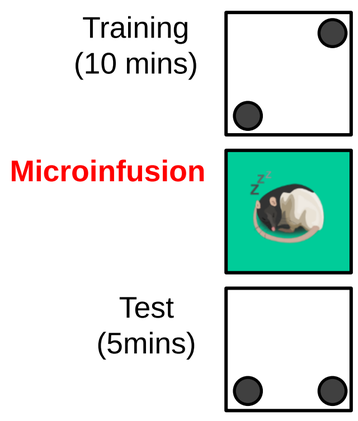
Research Approach

- We used pharmacology, electrophysiology, and behavioral neuroscience methods in rats.
- We investigated the hypothesis that promoting inhibition of neurons within the thalamus (using muscimol) is sufficient to enhance sleep. We tested two predictions:
  - Sleep bouts will be longer after microinfusion of muscimol compared to vehicle microinfusions.
  - Memory will be enhanced following microinfusion of muscimol in thalamus compared to vehicle.

A Timeline for each rat

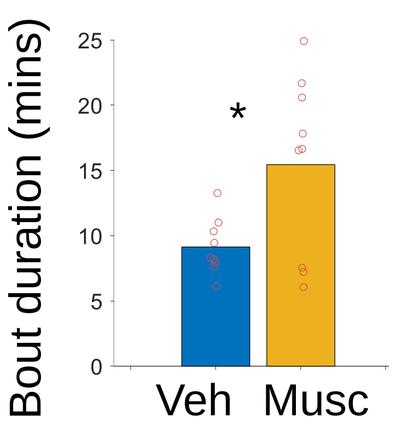


B Object- Place Recognition

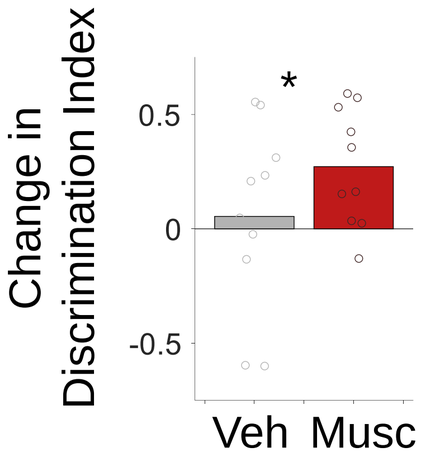


Results

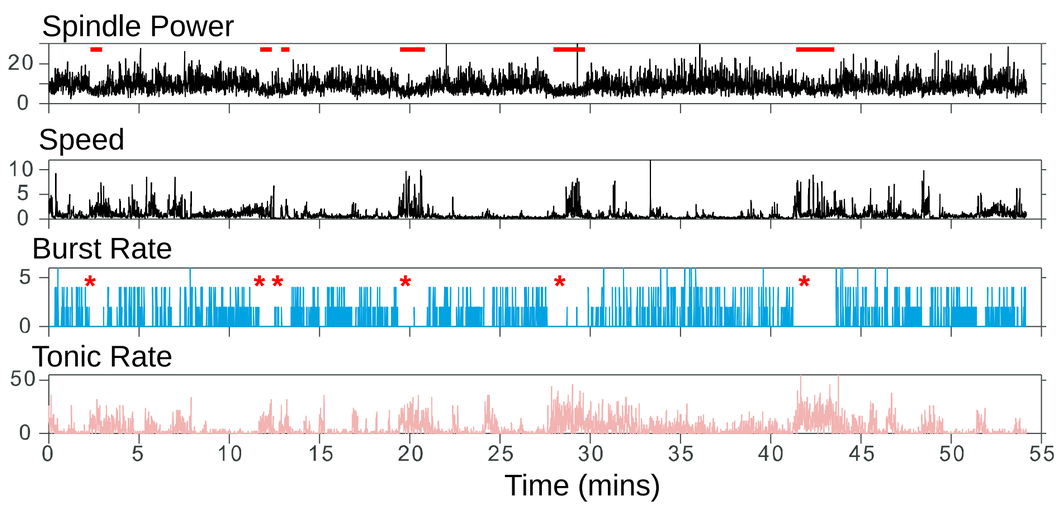
A Increased Sleep Stability Following Muscimol



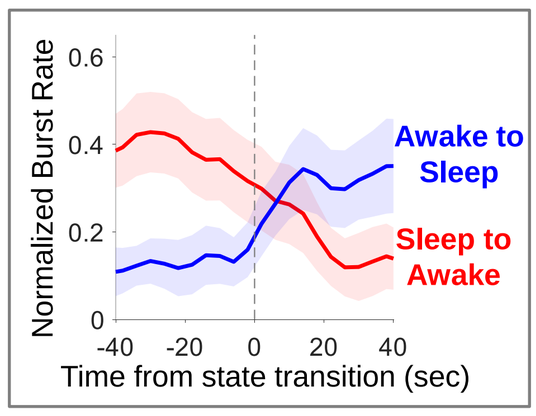
B Memory Recall Increases after Muscimol



C Sleep-to-wake transitions are associated with large drops in burst firing rate.



D Transitions between Wakefulness and Sleep Correlate with Changes in Firing Mode in Thalamic Neurons



Outcomes and Future Goals

- Microinfusion of the GABA agonist muscimol in the thalamic nucleus reuniens promotes sleep stability and memory consolidation.
- Sleep is associated with higher rates of burst firing in the thalamus, which drop dramatically during transitions to wakefulness.
- To continue this work, I have used these results in an R03 application to the NIA program to promote the Next Generation of Researchers in AD/ADRD Research.
- In future work, we aim to use optogenetics to regulate the rate of thalamic bursts and determine their causal contribution to sleep stability and memory consolidation.

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