Effect of Memory Consolidation on REM P-wave Frequency

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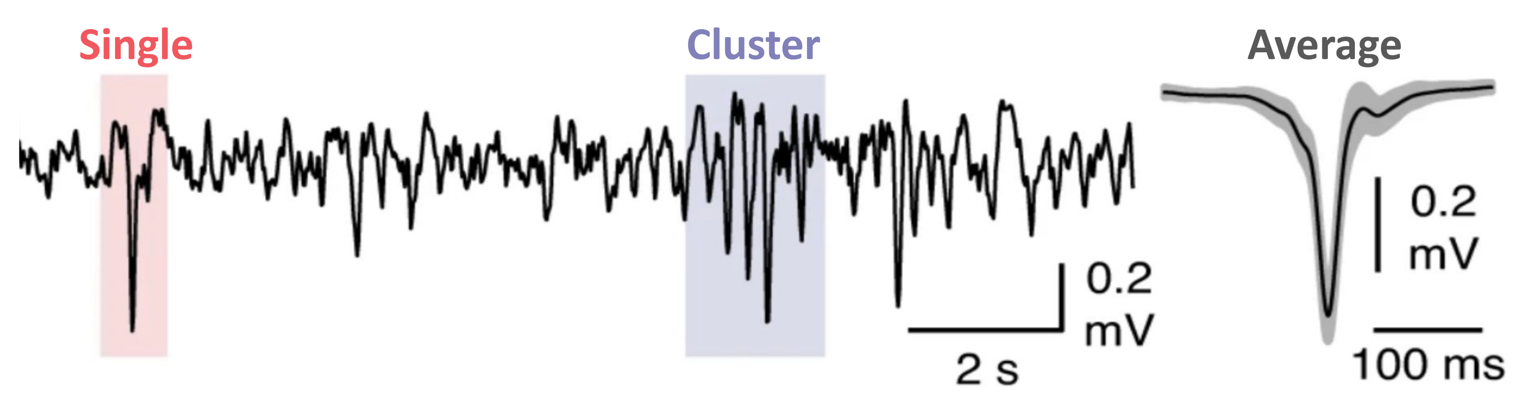
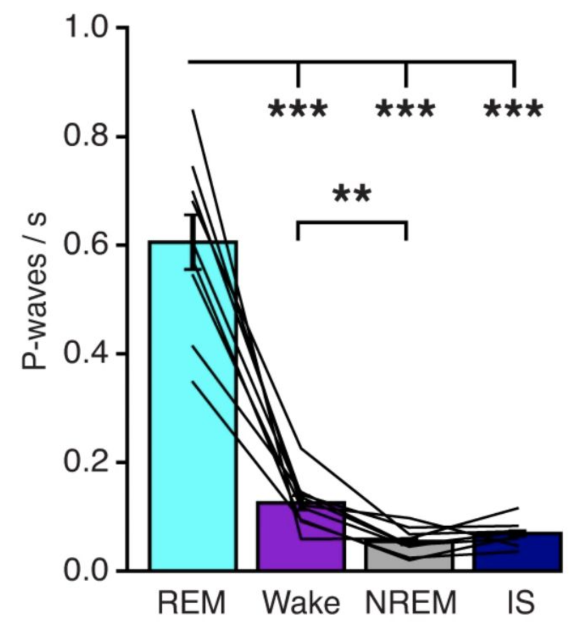
Background

- Pontine waves (P-waves) are generated by the phasic activation of glutamatergic neurons in the pons and are one of the most prominent phasic events of REM sleep.[1]
- P-waves appear most prominently in the subcoeruleus nucleus (SubC) of the pons and coincide with theta bursts that are thought to allow for synchronization of neural activity.[2,3,4]

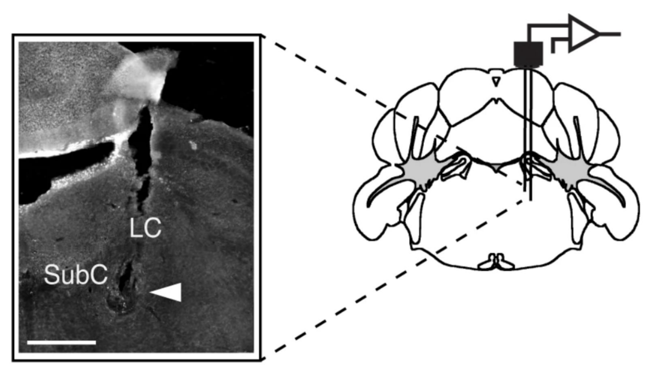
Our Previous Works [5]



- P-waves appear most prominently during the transition from slow-wave sleep (SWS) to REM sleep, as well as throughout REM sleep.[1]
- An increase in P-wave density during REM after training in certain learning tasks is positively correlated with the effective consolidation and recall of the task.[1]
- Evidence suggests that P-waves may play an important role in successful formation of extinction memory in contextual learning.[6]



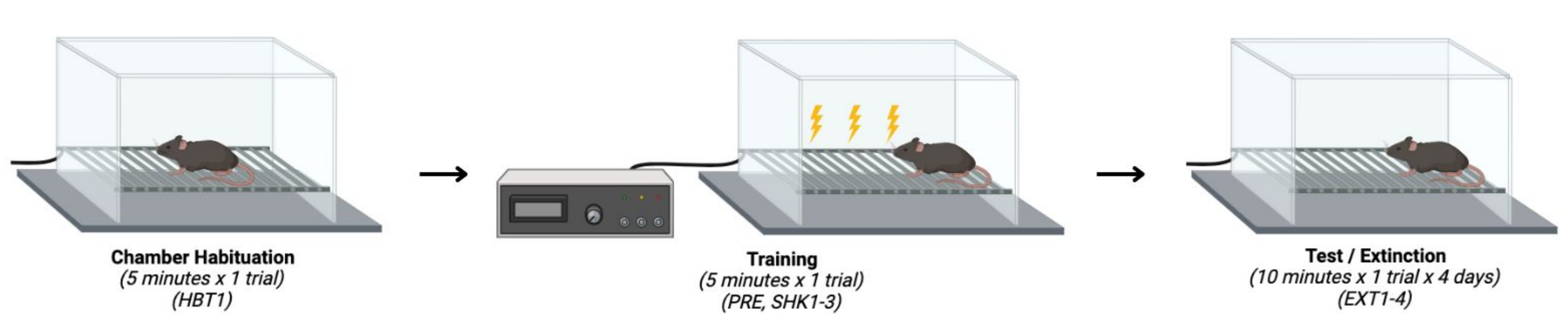
Experimental Design/Methods



Coronal brain scheme adapted from Allen Reference Atlas

- Mice: 10-15 week old male C57-B6 wild type mice (n=4)
- Two LFP electrodes surgically implanted in the subcoeruleus nucleus (SubC) of the dorsal pons in n=4 mice to record P-waves
- Arrowhead indicates tip of electrode

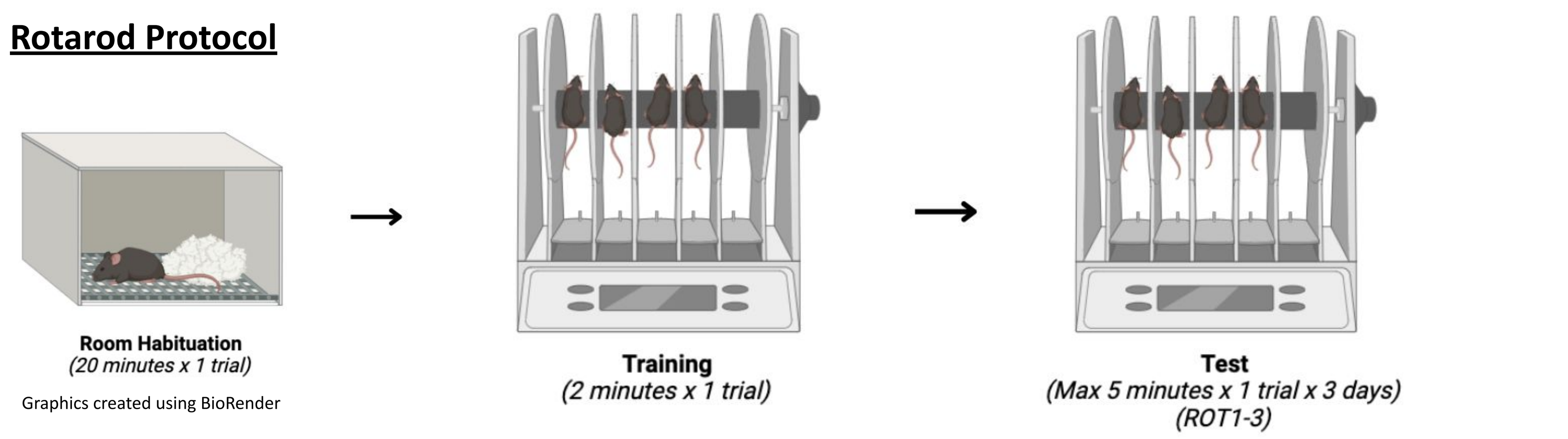
CFC Protocol



Graphics created using BioRender

- In contextual fear conditioning (CFC), mice learn to associate a neutral context with an aversive stimulus and display fear responses to a context.[7]
- Fear extinction in CFC does not erase conditioned fear, but rather creates new memories that coexist / compete with the fearful memory.[6]
- Training: A 0.75 mA shock was administered for 1 second every minute over a 3-minute period (SHK1-3) following a 2-minute delay (PRE)
- Freezing behavior was measured by direct observation, scoring time spent freezing (sec) with a stopwatch.[9]

Rotarod Protocol

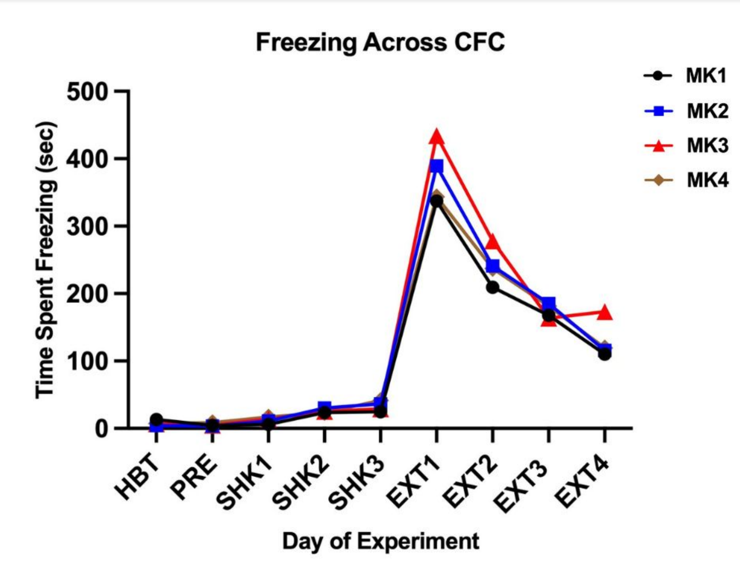


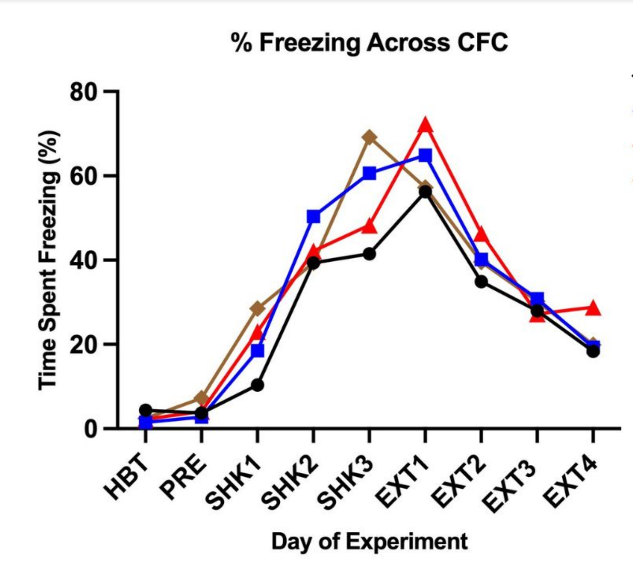
- Rotarod test involves mice running on a bar that rotates at a constant acceleration; performance over time is improved, which demonstrates consolidation of motor responses.[8]
- Mice were able to run for a maximum of 5 min (300 sec) during testing; bar remained stationary during training.
- Room habituation / training occurred on same day as initial test day (ROT1)

Aim

- To determine the effect that learning and subsequent memory consolidation from CFC and rotarod has on p-wave frequency in mice during REM sleep.

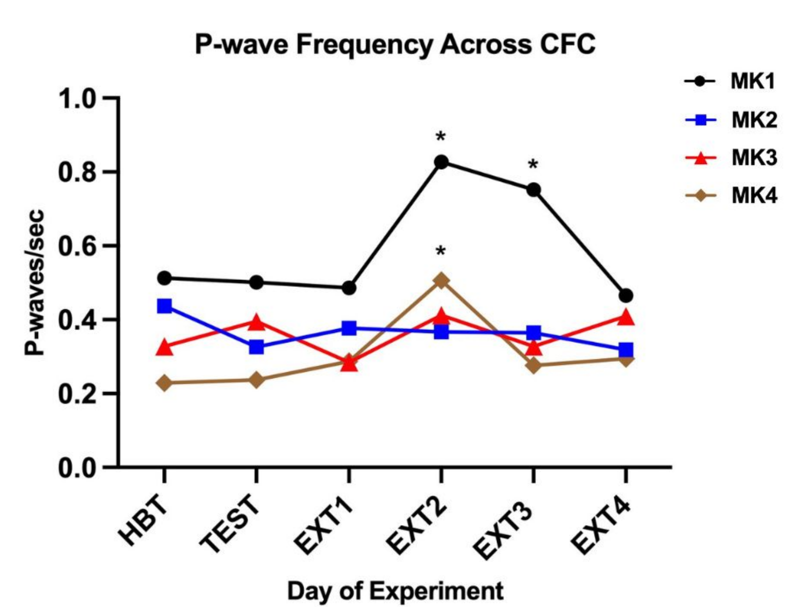
Results





PRE, SHK1, SHK2, and SHK3 all took place on the same day, within a total duration of 5 minutes.

All tested mice (n=4) demonstrated successful fear conditioning/extinction. The first day of extinction testing (EXT1) showed a significant increase in freezing time for all mice compared to the previous day when shocks were administered at 1-minute intervals. Subsequent days of extinction yielded a continuous decline in freezing time.

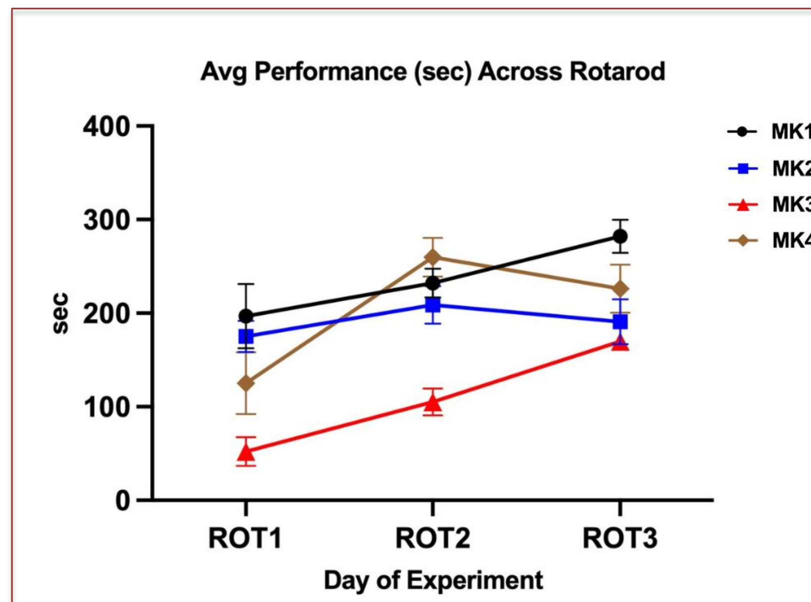


(mean − 3.0 * std) P-wave detection threshold for all recordings; processed using LFP2

P-wave Frequency Analysis Range: Initial 3 hrs of each 6 hr sleep recording

Mice MK1 and MK4 showed a significant increase in P-wave frequency on EXT2, reaching approximately 0.9 and 0.5 p-waves/sec respectively, followed by a decline on subsequent days.

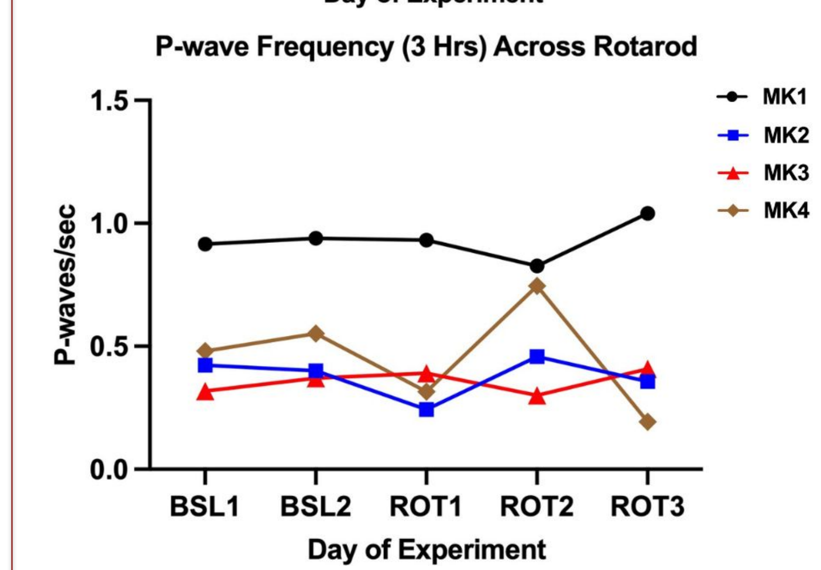
Mice MK2 and MK3 maintained relatively consistent P-wave frequencies throughout the experiment, with minor fluctuations but no significant peaks.

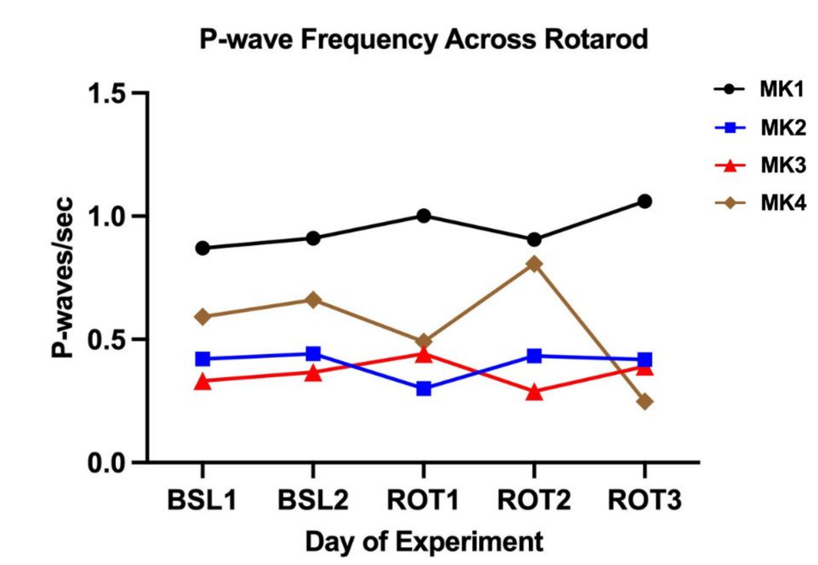


All tested mice (n=4) showed improved performance on the second day of testing (ROT2) compared to the first day (ROT1).

Mice MK1 and MK3 continued to improve from day 2 (ROT2) to day 3 (ROT3), while the performance of mice MK2 and MK4 plateaued after day 2 (ROT2).

P-wave Frequency Analysis Range: 3 hrs starting from first REM period (left); entire 6 hr recording (right)





(mean − 3.0 * std) P-wave detection threshold for all recordings; processed using LFP2

Mouse MK4 displayed the most variation in P-wave frequency across all days, with a peak close to 0.8 P-waves/sec after day 2 of testing (ROT2) and a sharp drop on the following day of testing (ROT3). Mouse MK1 experienced a slight increase in frequency on the third day of testing (ROT3).

Data yields no significant effect of memory consolidation on P-wave frequency for the rotarod test.

Conclusions / Future Directions

Conclusions

- CFC: For certain subjects, there is a significant increase in P-wave frequency during the second day of extinction (EXT2). This may indicate a heightened neural response associated with extinction learning on this day.
- Rotarod: Different groups respond differently across the experimental days; no concrete effect of motor response consolidation on P-wave frequency.

Future Directions

- Can results be replicated with higher power and lower variance utilizing larger cohorts of mice?
- How would optogenetic stimulation of the subcoeruleus nucleus (SubC) affect P-wave frequency and performance of mice in rotarod and extinction in CFC?
- Does ablation of the subcoeruleus nucleus (SubC) or corresponding regions affect performance of mice in rotarod and extinction in CFC?

Funding & References

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- Key References:

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