Selective disruption of hippocampal sharp-wave ripples leads to impaired object-place recognition memory

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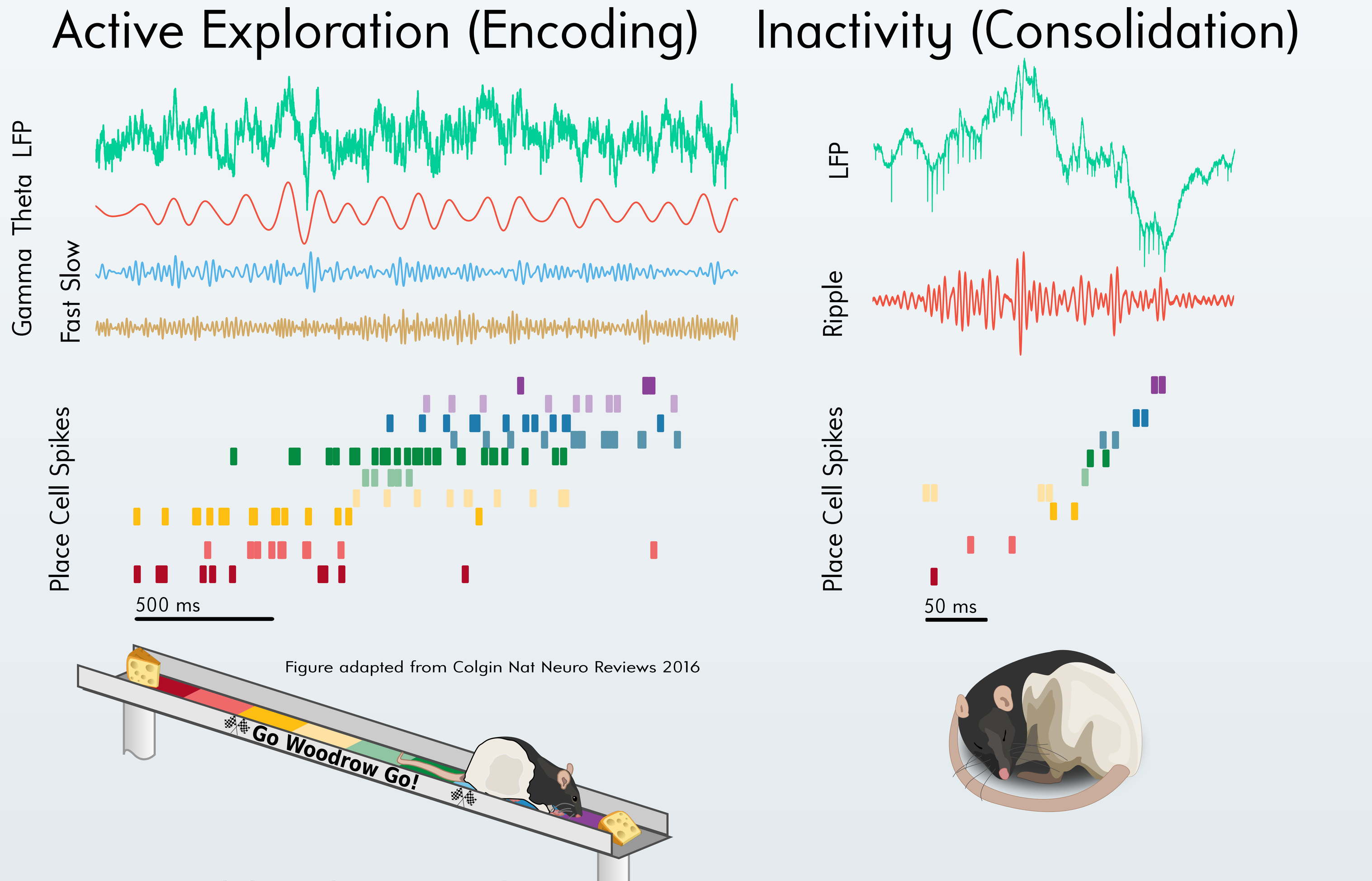
Introduction

Rodents have an innate curiousity to explore both novel locations and objects. This preference has long been studied behaviorally through various paradigms of a novel object test (NOT). Lesion studies have established that the hippocampus is necessary for this behavior. More recently, studies have been done to find correlative neural substrates to this discrimination. However,we still lack a robust understanding of hippocampal activity that promotes this behavior.

Through closed-loop perturbation we aim to *(1) uncover uncover a causal link to this object-place discrimination between hippocampal oscillatory patterns* and *(2) shed further light upon the intricacies of object-place memory consolidation.*

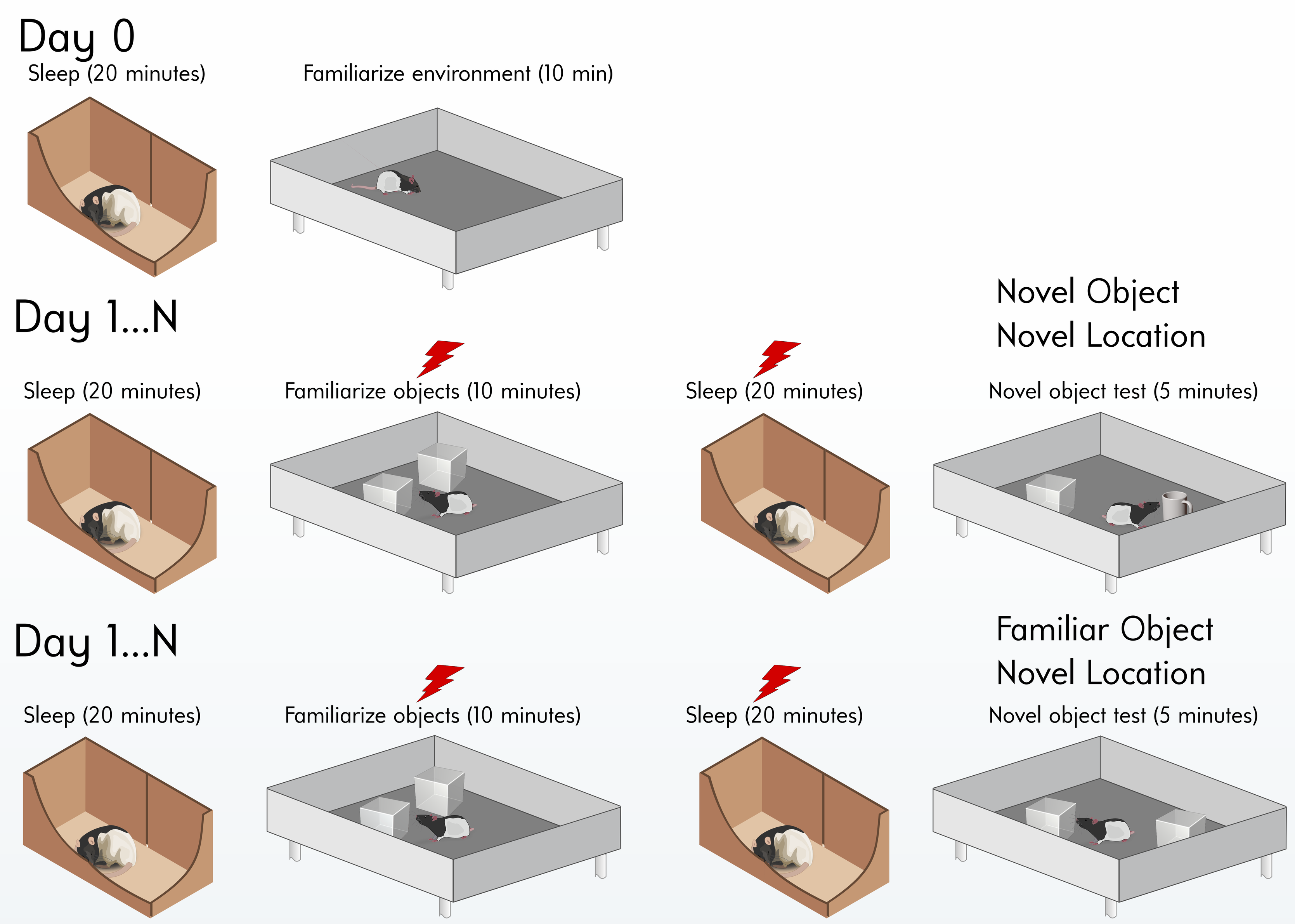
Background



Hippocampal background:
In vivo extracellular recordings from the rodent hippocampus exhibits transient osscilations associated with different processes:
- theta & gamma for encoding, retrospection, perspection, decision making
- sharp-wave ripple (SWR) complexes for memory retreival, consolidation, decision making.

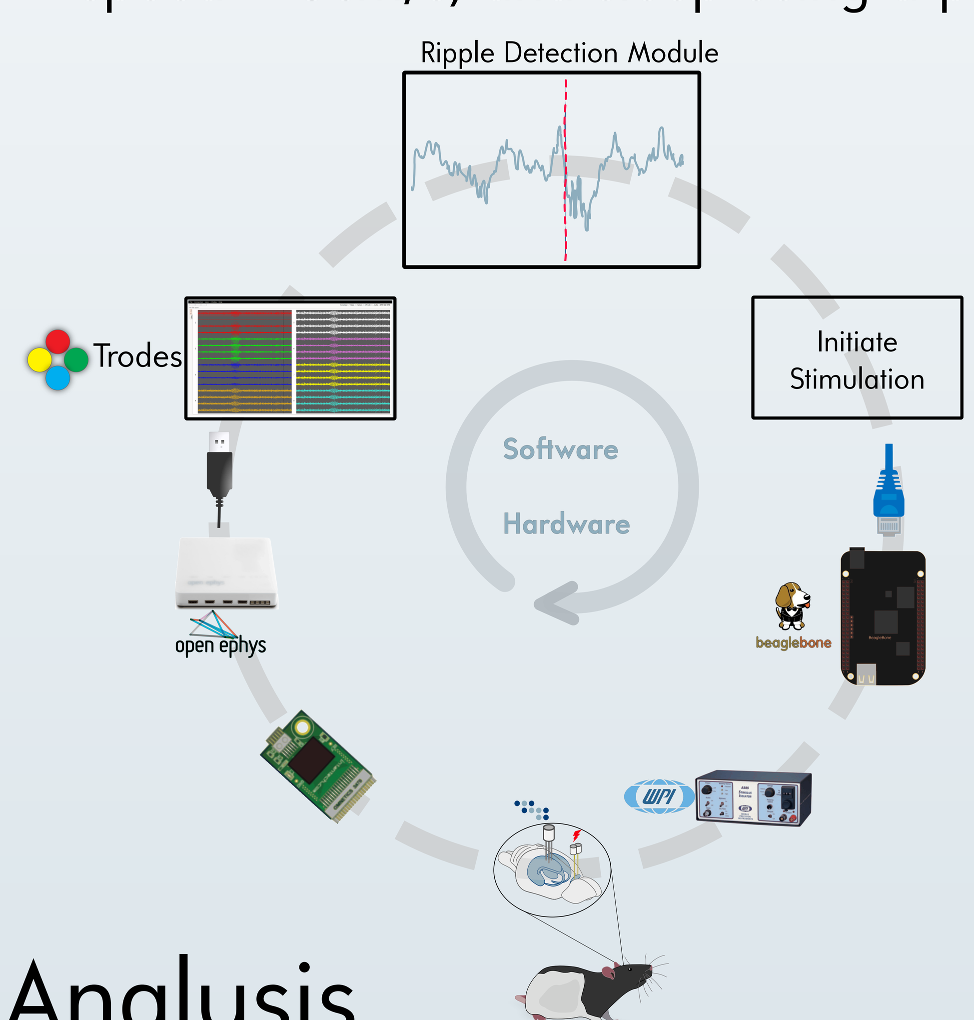
Novel Object Test Background:
- Hippocampal lesions prevent re-exploration of familiar objects in novel locations[A]
- Fast gamma power increases during exploration of novelty[B]
- SWRs increase after NOT but ripple content is not reflective of spatial regions of change[C]

Experimental Protocol



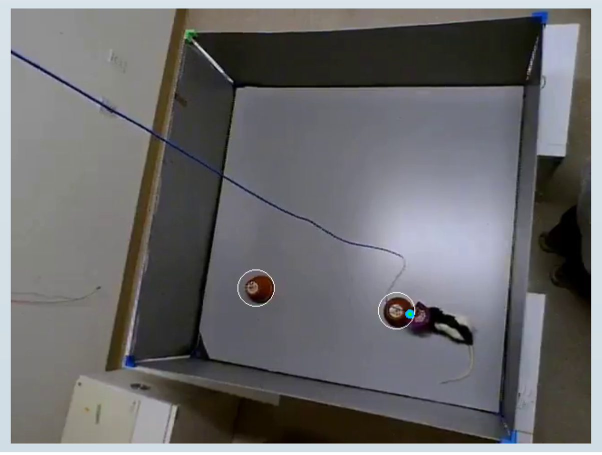
Closed-loop disruption

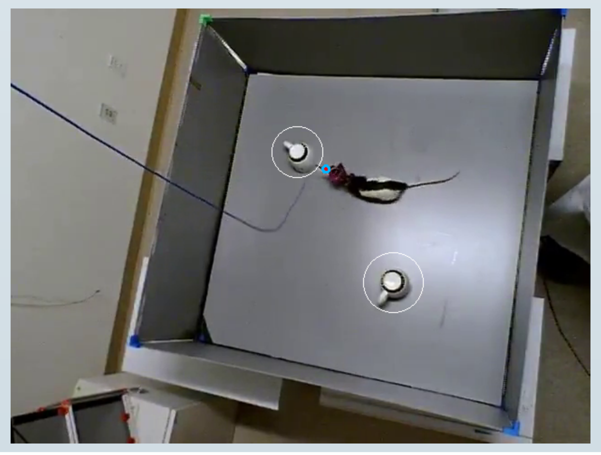
- Disruption of sharp-wave ripples during both awake behavior (animal speed < 3cm/s) and sleep using a previously engineered system[D]



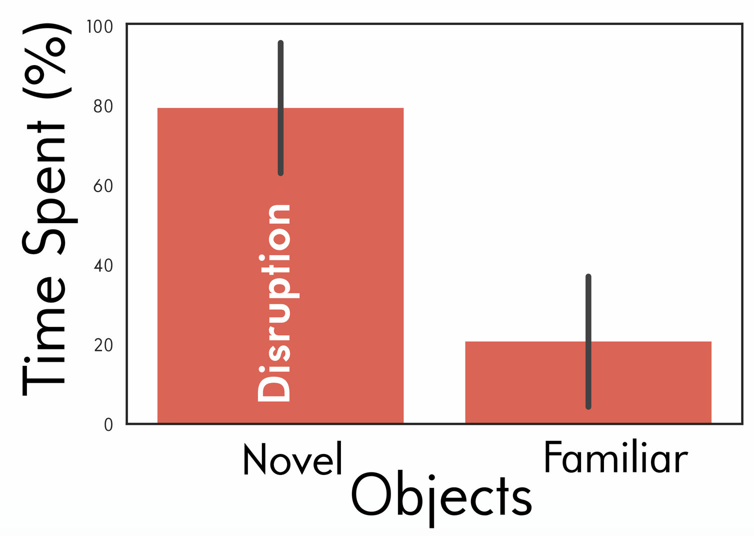
Analysis

- Object interaction and exploration defined by rat's head within 5-10 cm of object center depending on object size
- Head tracking performed via DeepLabCut[E]

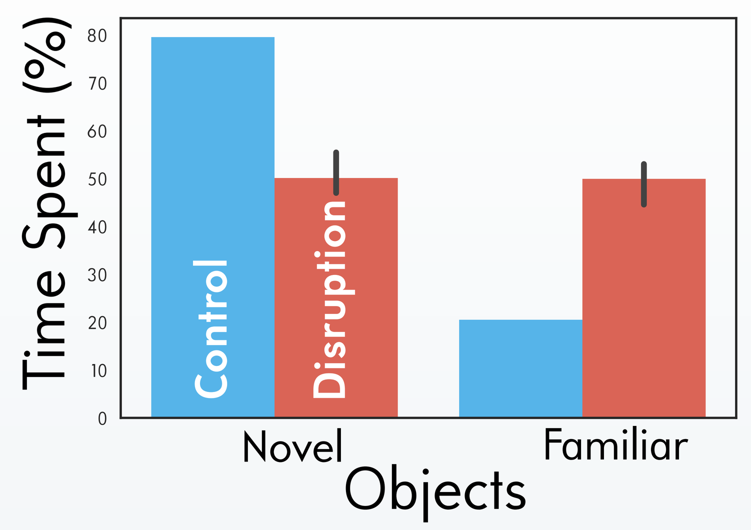




Preliminary Results



- Disruption during the novel object novel location paradigm does not affect behavior



- Disruption during familiar object novel location impairs novelty preference
- Novelty preference is restored under a control disruption paradigm

Discussions & Future Works

Previous closed-loop disruption studies have shown that SWR are imperitive for learning and consolidation of sequential memory dependent tasks[F,G], whereas, blocking SWRs during open-field exploration without any sequential requirement or memory guided behavior does not seem to alter behavior or place cell stability[H]. However, disrupting ripples within an open-field with a goal related task does indeed affect behavior as well as place cell stability[J].

Given the necessity for a sequential memory and goal dependence, we look to answer *why SWR disruption has impairs object-place preference discrimination.* As the co-occuring spiking activity with SWRs is not spatially restricted to regions of objects or environmental change[C] nor affected by place cell stability[H], our results suggest *a more vital role for SWRs in object-place recognition than broadcasting the presence of novelty.*

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