

Introduction

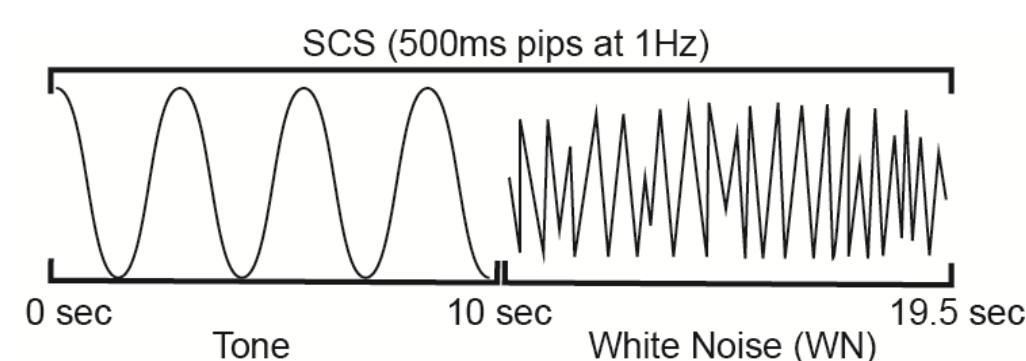
- Fear extinction is the formation of new memories that inhibit traumatic responses. In individuals with Post-Traumatic Stress Disorder (PTSD), this fear extinction process may be impaired, leading to the persistence of fear responses long after the traumatic event has ended.
- The ventral hippocampus (vHPC) has roles in stress and fear memory. The vHPC projects to the central amygdala (CEA) and has been shown to modulate fear response (Xu et al., 2016). Thus, we are investigating this pathway's role in fear extinction.
- We also used a modified Pavlovian fear conditioning paradigm to investigate dynamic defensive behaviors that change during and after extinction.

Research Questions

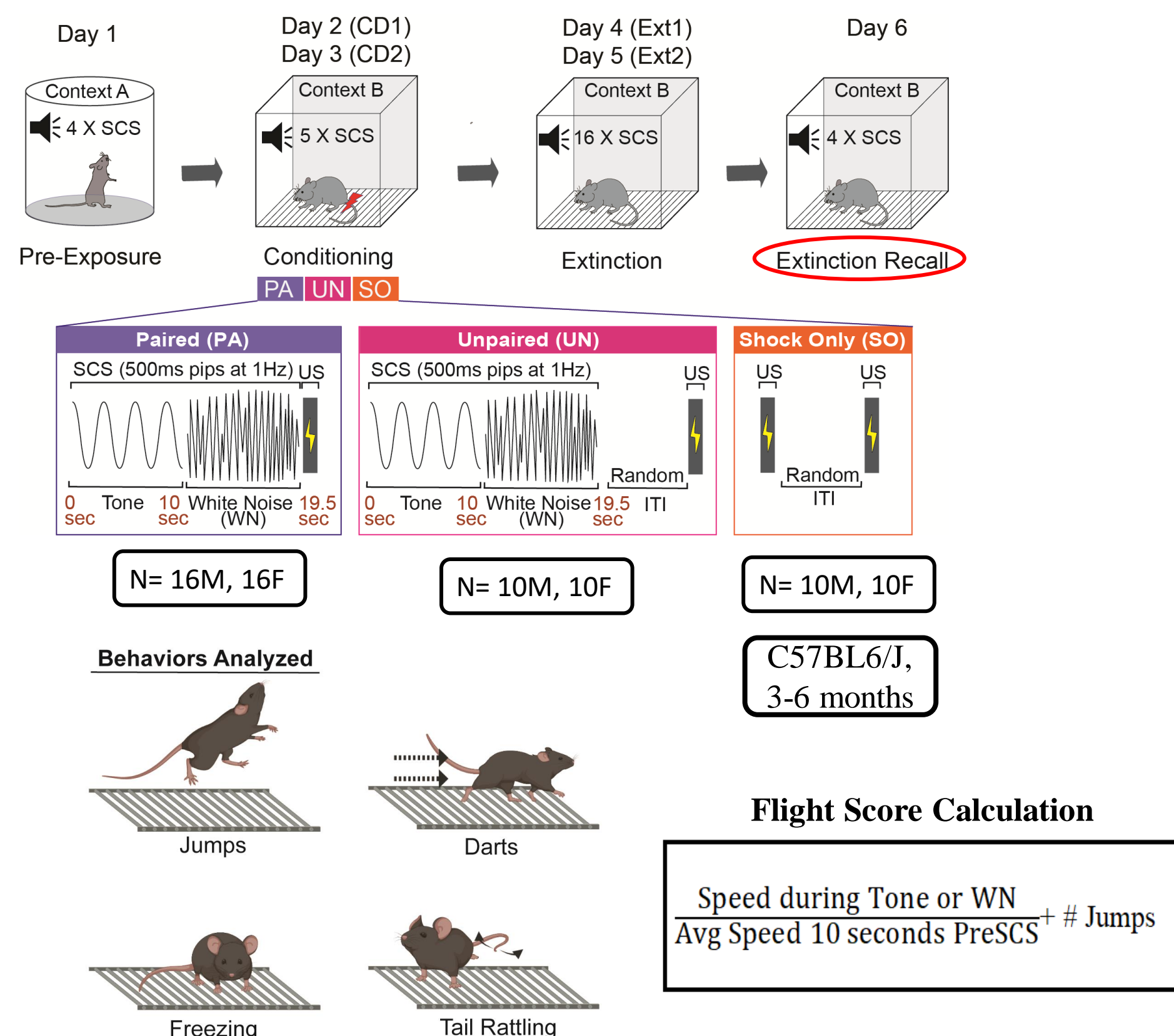
1. How do dynamic defensive behaviors change after extinction?
2. How does the vHPC-CEA pathway influence defensive behavior selection during fear extinction?

Serial Compound Stimulus (SCS) Paradigm

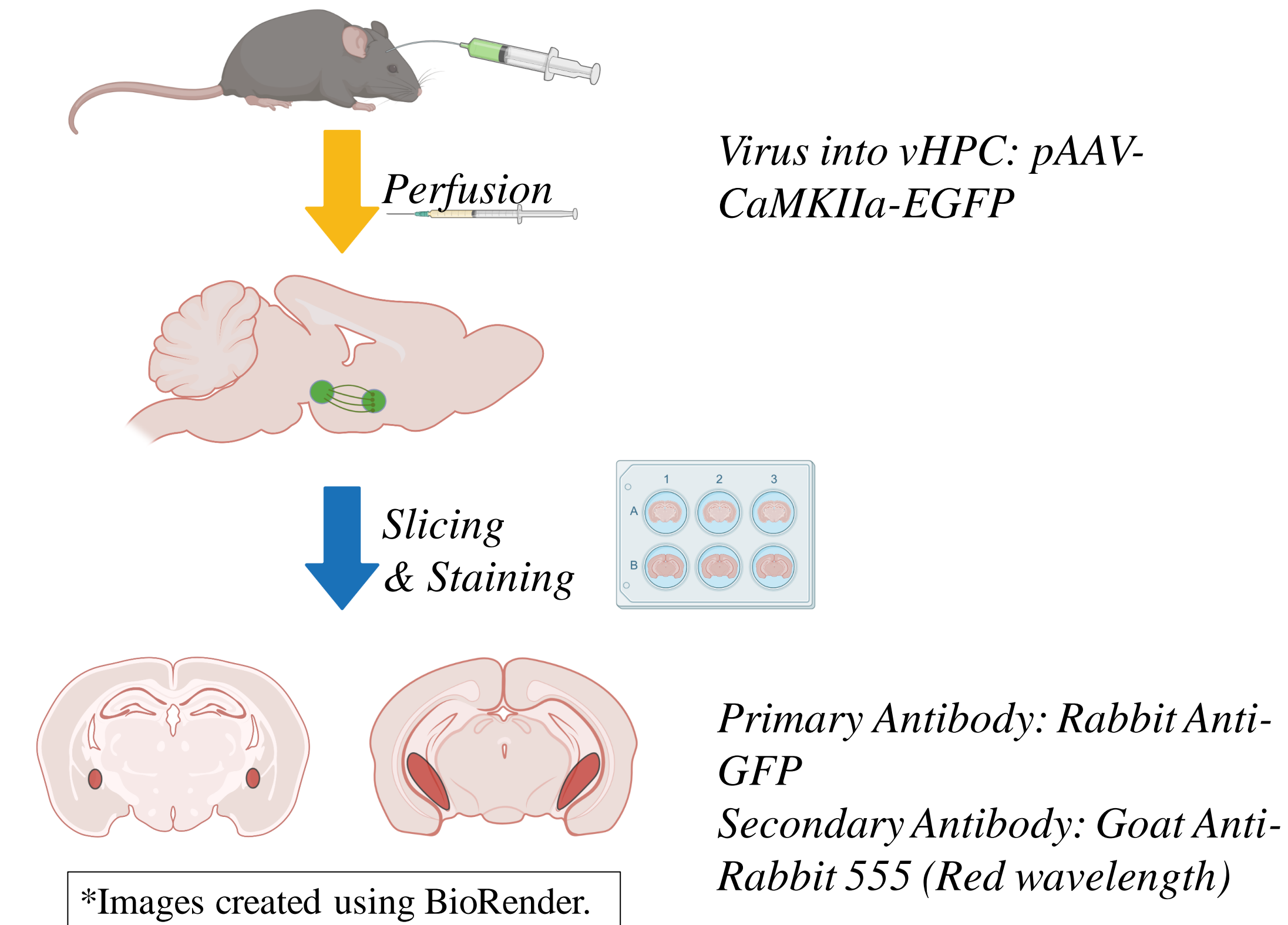
- Fear conditioning involves associating a conditioned stimulus, such as white noise, to signal threat due to the subsequent shock that follows it.
- The SCS paradigm involves playing a tone segment followed by a white noise segment and then a shock. This allows us to gauge different fear responses to a series of fear-signaling stimuli.



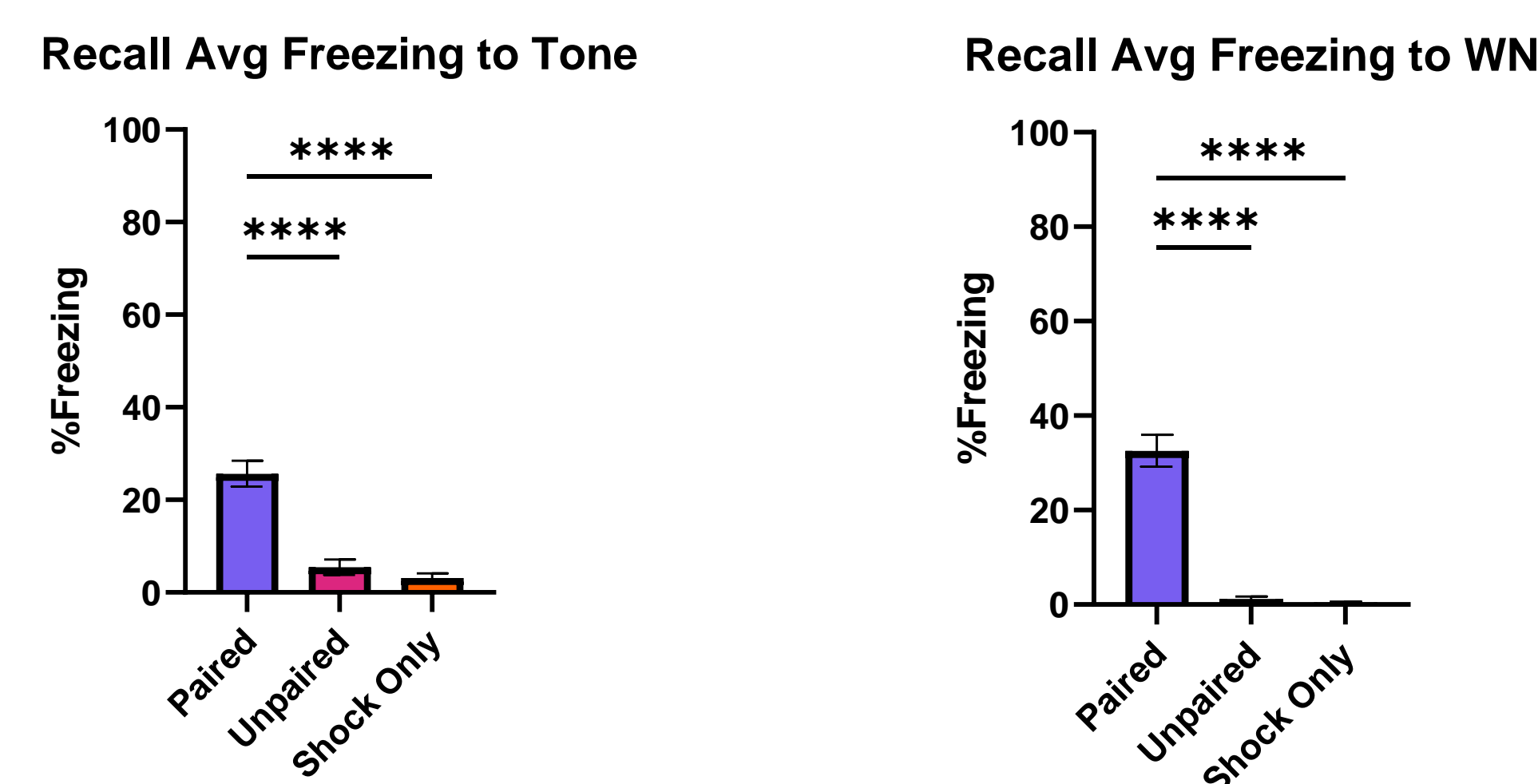
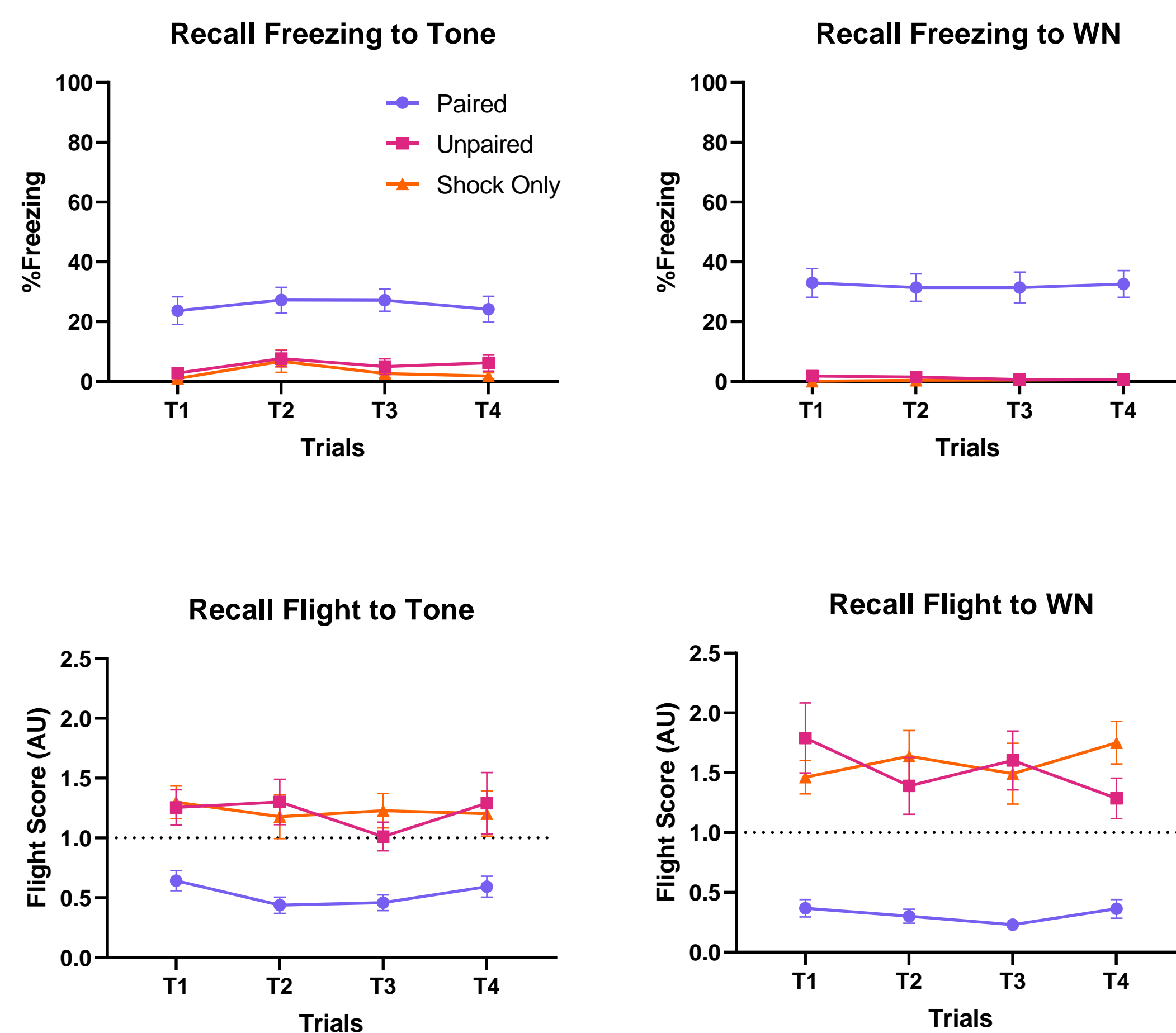
Project 1: Behavioral Analysis of Extinction Recall



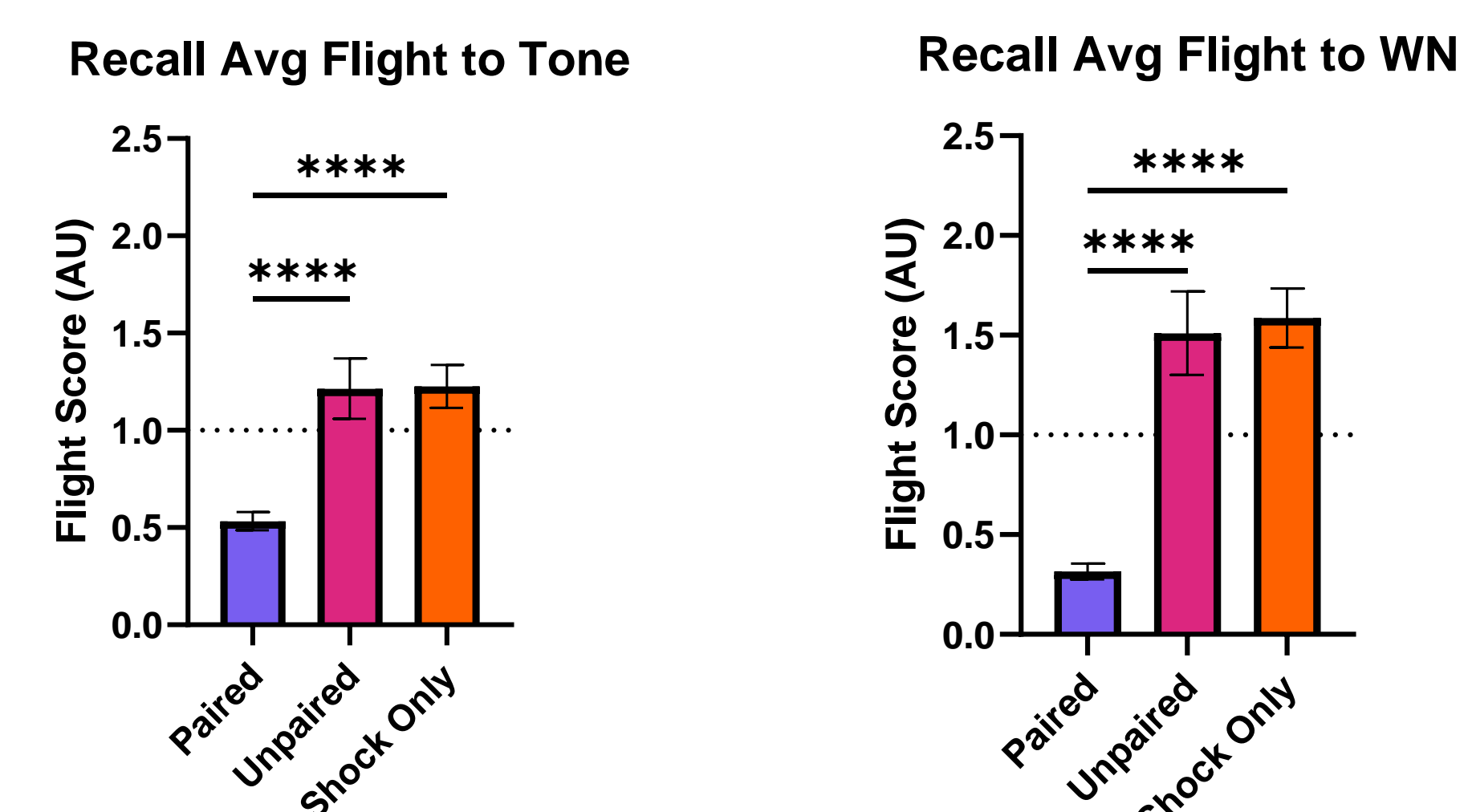
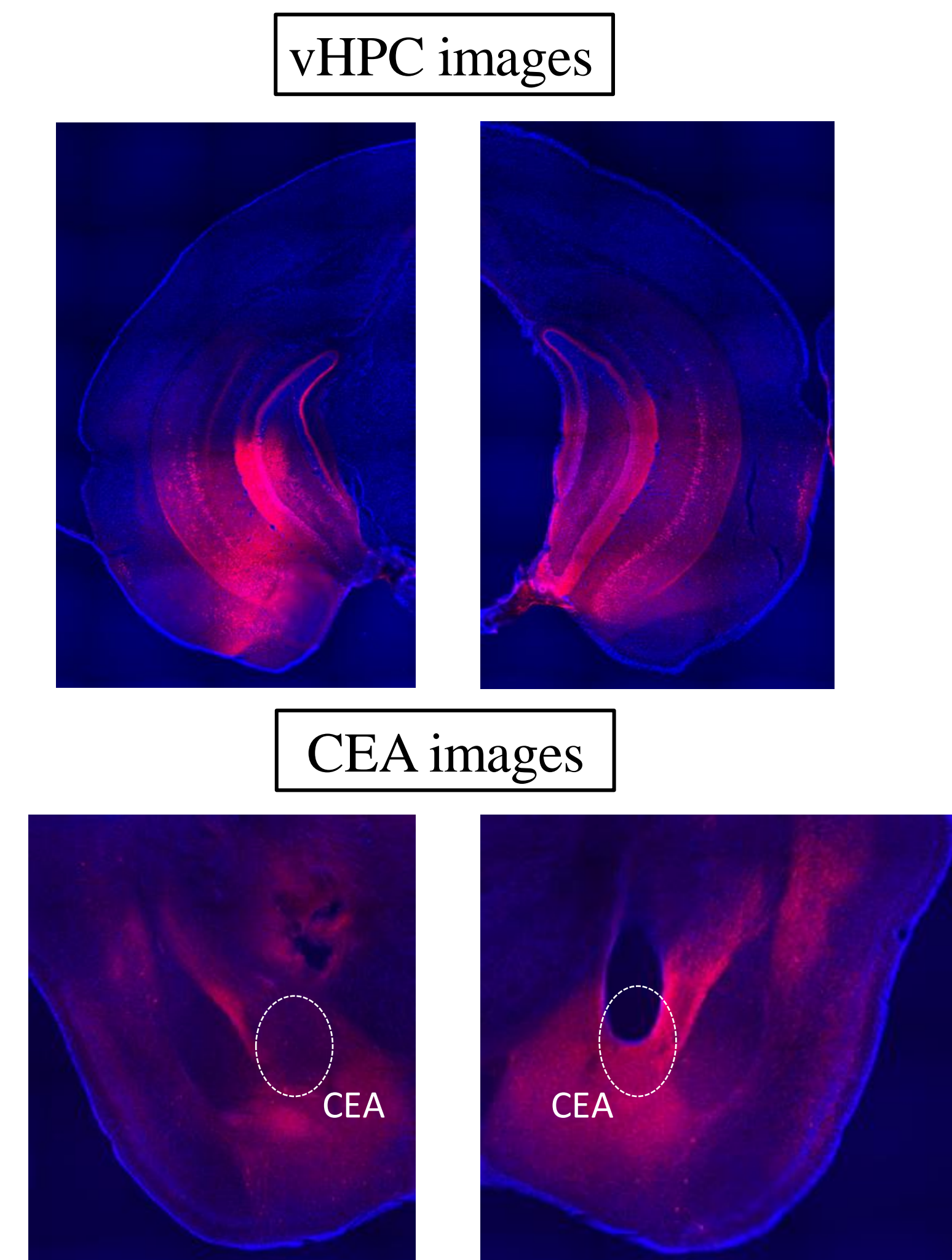
Project 2: Brain Perfusion & Immunohistochemistry



Paired group significantly differs from control groups in defensive response post-extinction



vHPC projects to CEA (preliminary data for optogenetics experiment)



Results

- Paired group showed greater freezing and less movement during tone and white noise compared to unpaired and shock only (**** $p < 0.0001$, Tukey's multiple comparisons test). This indicates that only the paired group showed spontaneous recovery of fear response post-extinction.
- This shows that the behaviors elicited through the SCS paradigm can be used to study mechanisms of fear extinction modulation.
- In the paired and unpaired cohorts, <15% of cohorts showed tail rattling during SCS. No jumps or darts were observed from any group during recall.
- We observed expression of fluorescent virus injected into the vHPC and expression in CEA, indicating that the vHPC projects to the CEA.

Future Directions

- We plan to use optogenetics to investigate the vHPC-CEA pathway's role in fear extinction.
- Also, we plan to use optogenetics to investigate the role of corticotrophin-releasing-factor-positive and somatostatin-positive cells in the CEA in fear extinction.

Citations

Xu C, Krabbe S, Grundemann J, et al. Distinct Hippocampal Pathways Mediate Dissociable Roles of Context in Memory Retrieval. *Cell*. 167(2016): 961-972. <https://doi.org/10.1016/j.cell.2016.09.051>

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