

Abstract

Social interactions provide some of the most influential experiences in a social animal's life. The basolateral amygdala (BLA) and ventral hippocampus (vHPC) are two brain regions implicated in fear, anxiety and social behaviors. Lesions to the BLA have been shown to decrease anxiety and increase social behaviors in novel environments (Wang et al., 2014). In social defeat paradigms, mice that underwent an aggressive attack exhibited increased BLA activity, and decreased vHPC activity (Qi et al., 2018). Finally, work by Ortiz and Tye (2014) has demonstrated that excitatory projections from the BLA to vHPC mediate changes in social behaviors.

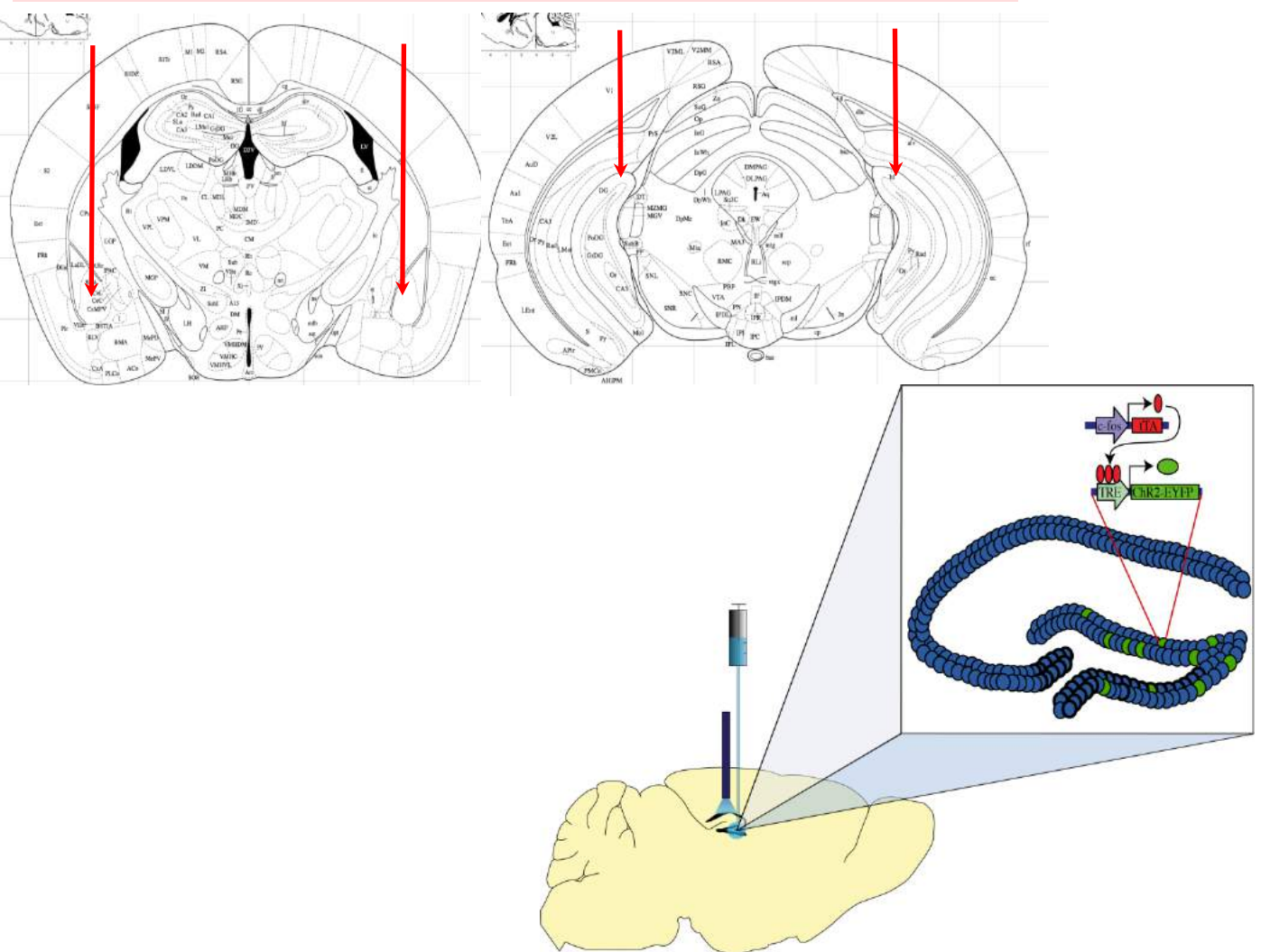
Collectively, these studies highlight the complementary and important role that the BLA and vHPC play in mediating anxiety and social behaviors. Here, we show that social interaction with a mouse that has received a foot shock induces non-generalized reinstatement of an extinguished fear memory in a portion of cagemates. Optogenetic excitation of basolateral amygdala (BLA), but not dentate gyrus (DG), cells that were previously active during the social encounter causes freezing in social reinstators but not non-reinstating cagemates and in a frequency-specific manner. However, activation of this ensemble is not necessary for reinstatement, as optogenetic silencing does not prevent reinstatement. Preliminary results show that chemogenetic inhibition of the fear memory during the social encounter prevents reinstatement, indicating the necessity of activating the fear memory during the encounter. We explore a potential circuit by which auditory social cues induce reinstatement; chemogenetically inhibiting projections from medial geniculate nucleus (MGN) to the BLA attenuates reinstatement.

Future work will clarify the role of auditory cues in social reinstatement and explore the impact of other environmental factors on memory retrieval and reinstatement.

Materials and Methods

Activity Dependent System

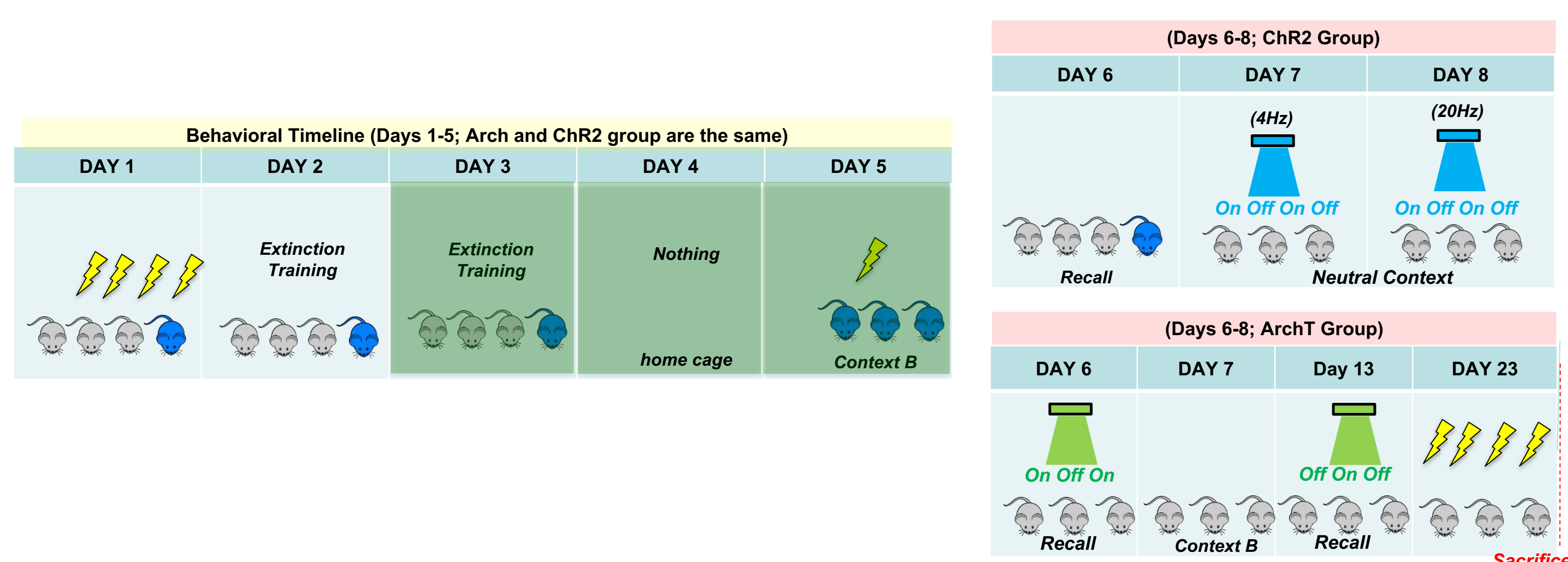
Bilateral Virus Infusions into dDG or BLA



Inducible, activity-dependent expression of light sensitive opsins

- Removal of doxycycline (dox) from diet allows tetracycline transactivator (tTa) to bind tetracycline response element (TRE) so that active cells (cFos+) express Chr2 or ArchT
- Adding dox back into the diet closes the tagging window, limiting expression of opsins to specific ensembles.

Behavioral Schedule



Fear Conditioning: 4 shocks, 0.5mA, 2s duration, 60-75sITI) in Context A (70% EtOH)

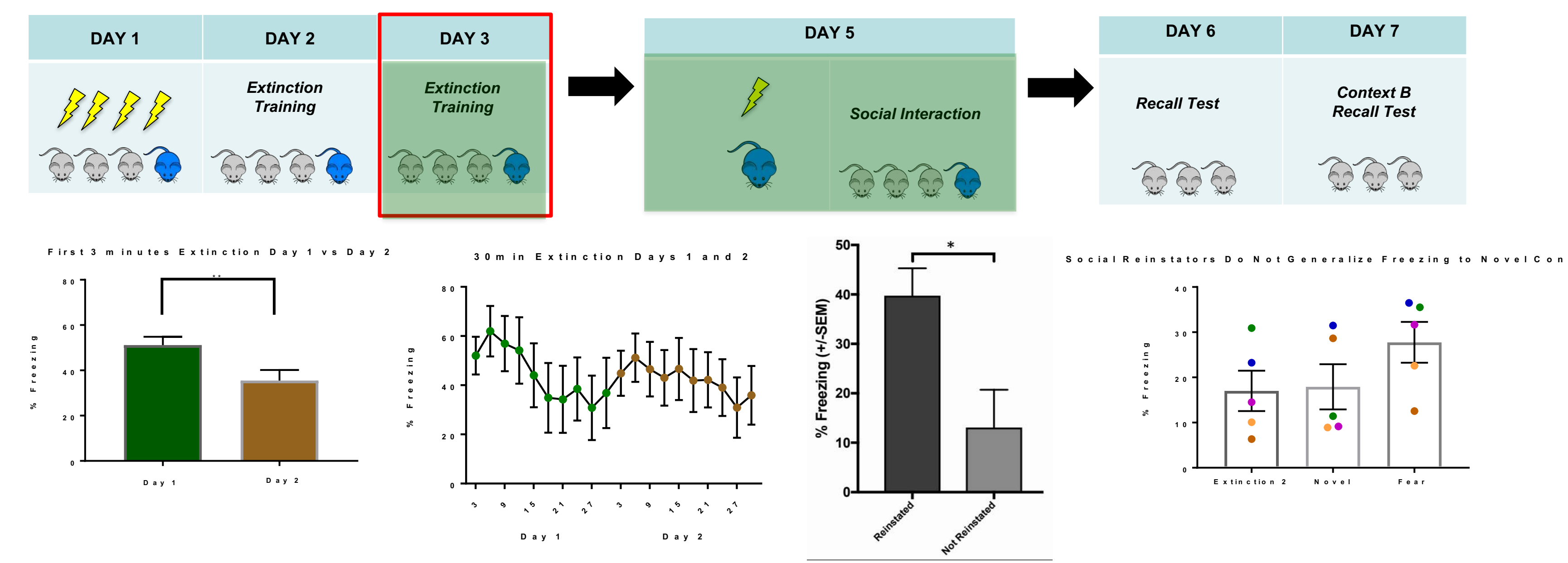
Extinction Training: 30 minutes per day, 2 days

Off Dox: From end of second extinction session until 1 hour after social interaction (shaded green)

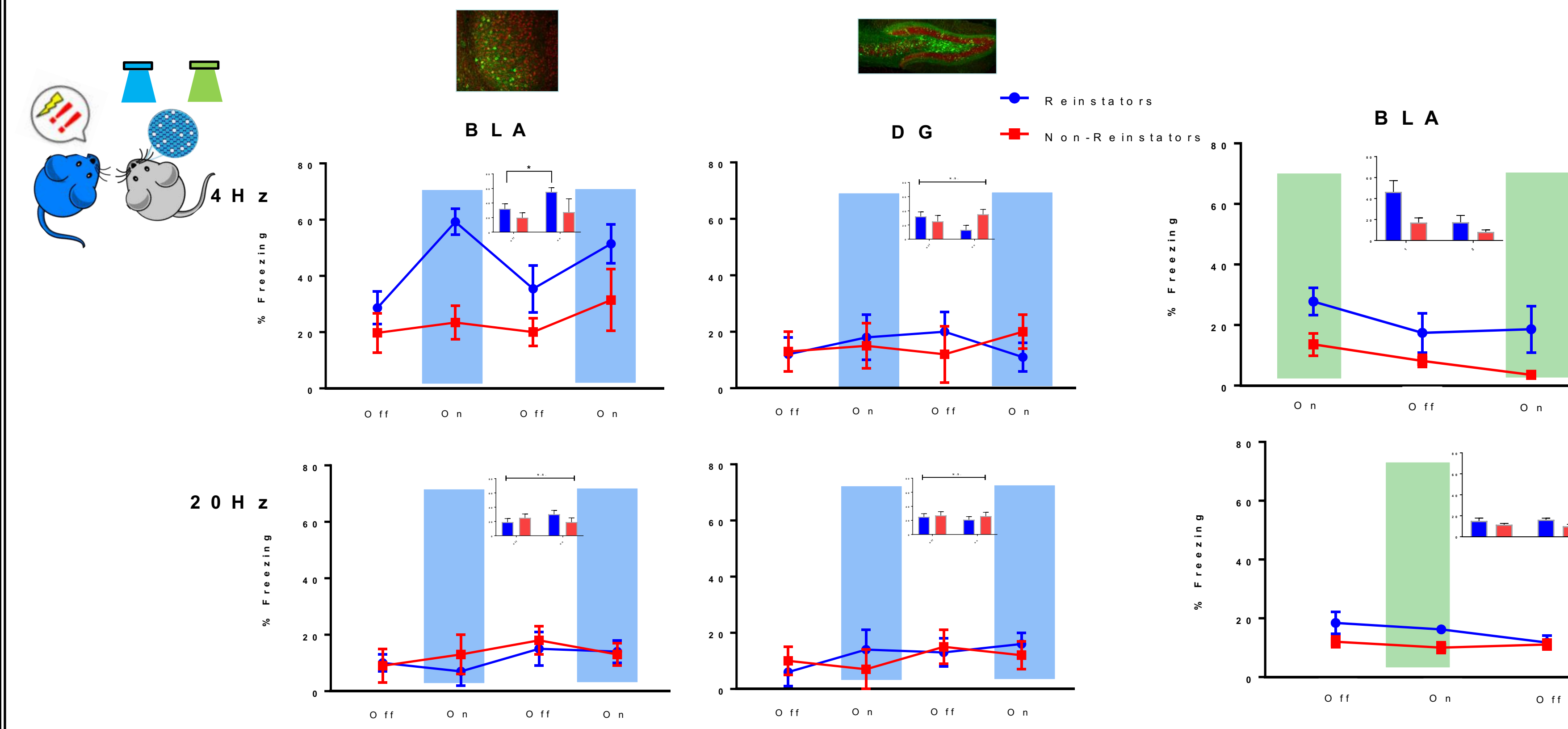
Immediate Shock: "Jeff" mouse (indicated in blue) received single immediate shock followed by 58 seconds undisturbed in Context B (black and white walls, almond extract).

Generalization Test: 5 minute test session in Context B

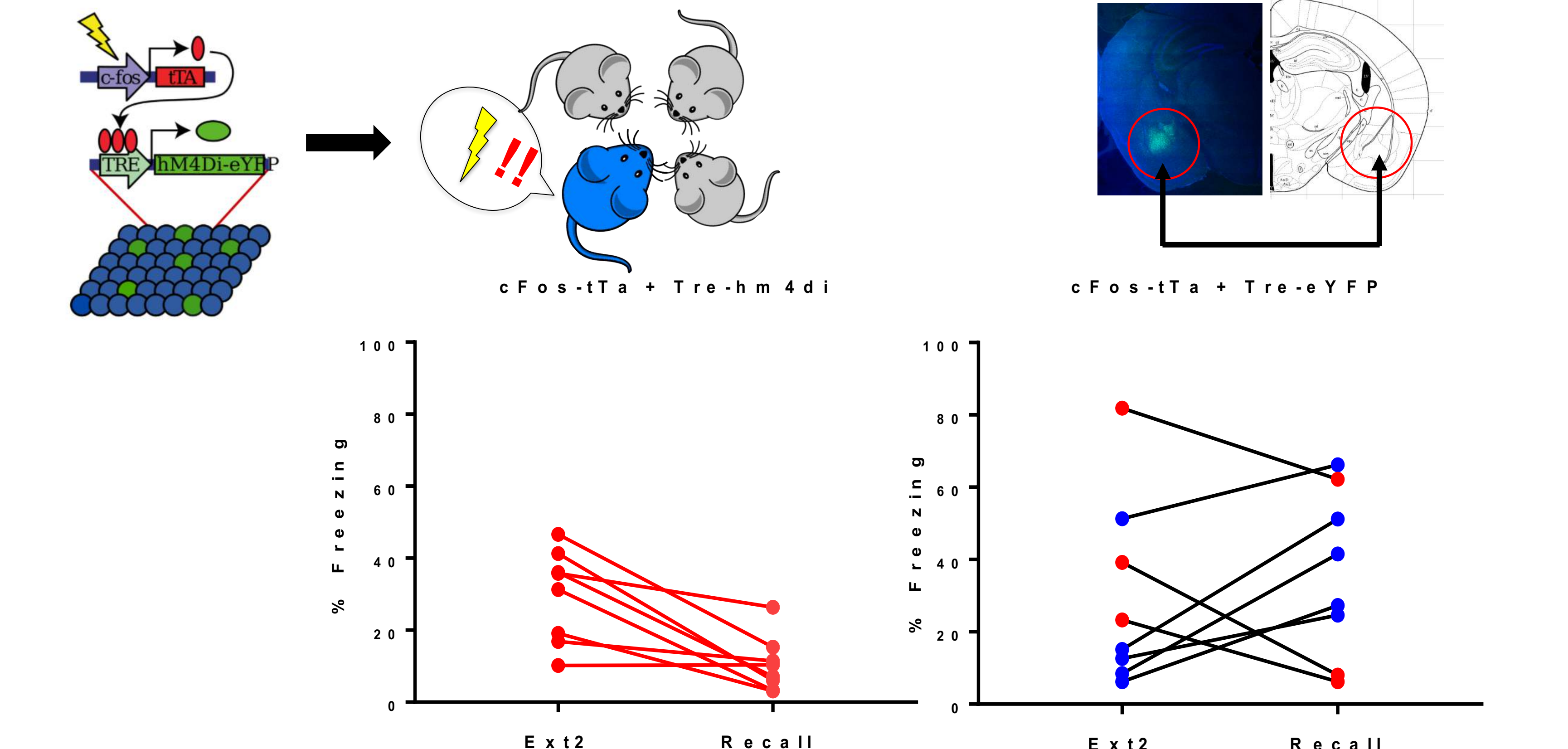
Validation of Social Reinstatement



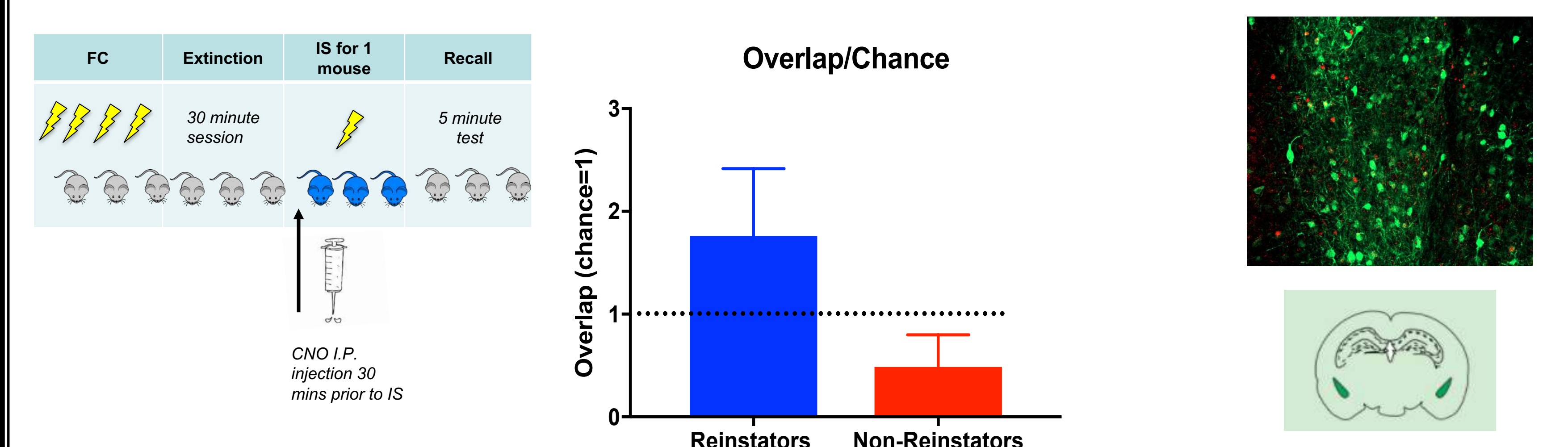
Activating the social ensemble induces freezing in a novel context



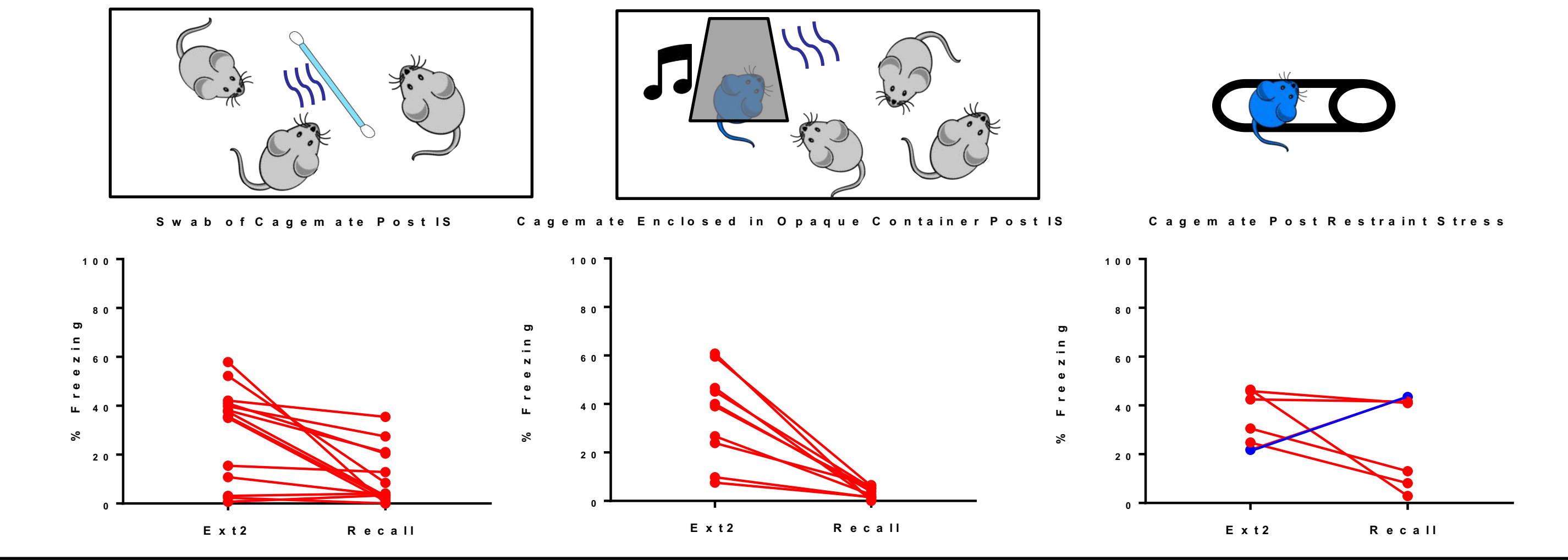
Necessity of Fear Memory Activation in BLA During Social Encounter



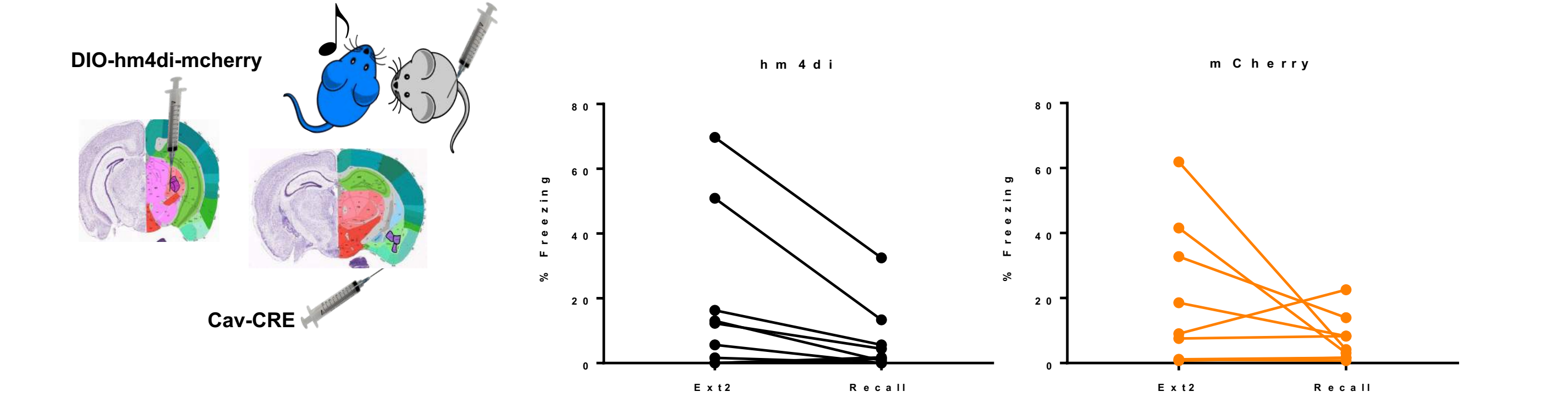
Fear Ensemble Reactivation During Recall



Social Mechanisms

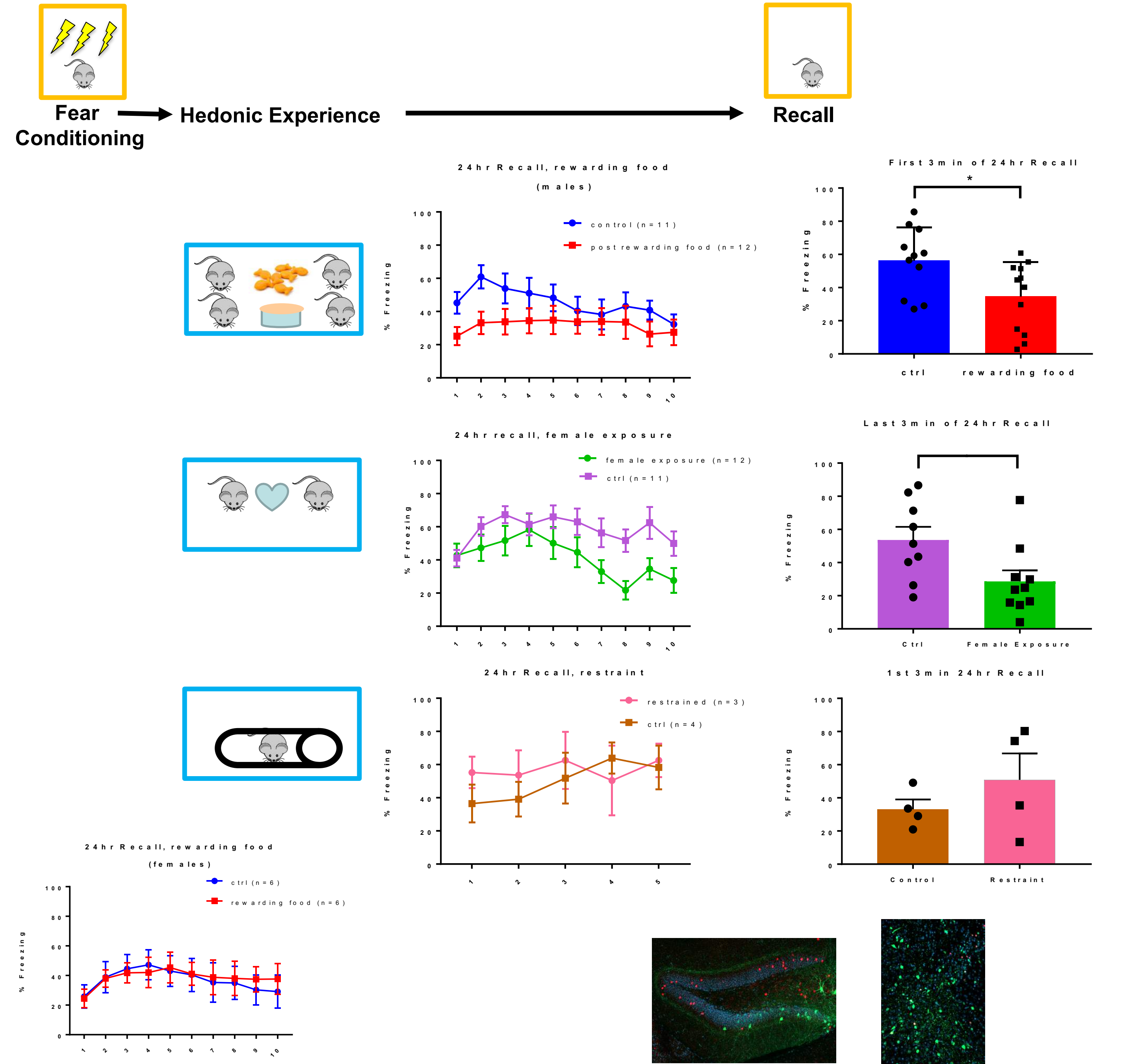


Necessity of Auditory Input MGN→BLA



Future Directions:

Affective State Impacts Retrieval, Extinction, and Beyond



References

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