A TRAPPED & DREADD-ED MEMORY: CONTEXTUAL FEAR MEMORY & DPAT

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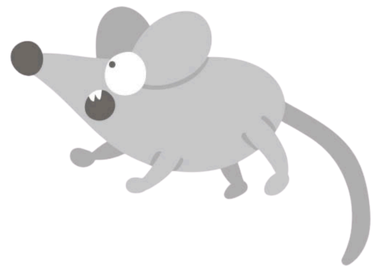


Background

- PTSD and other fear conditions are explored through neurobiological manipulations with forms of fear conditioning
- Certain brain regions and neurotransmitter systems have been implicated in such fear conditions
- Modulation of these systems could offer treatment of these conditions

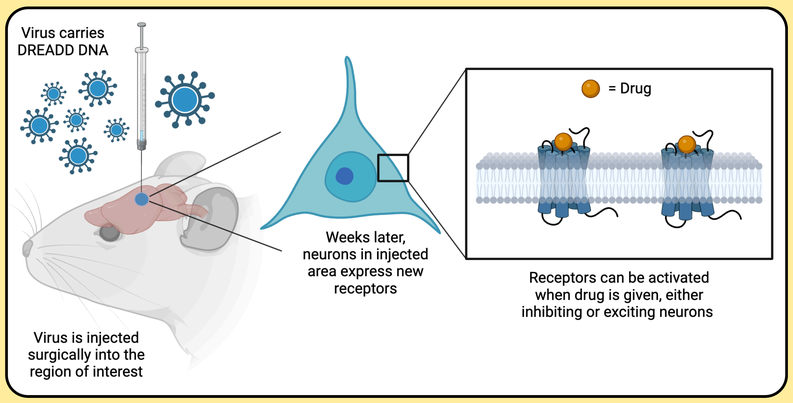
My tools and targets:

- **Dorsal Hippocampus** - region of the brain implicated in contextual fear
- **5-HT1A receptors** - inhibitory serotonin receptor activated by **DPAT**, an agonist of the receptor
- **DREADDs** - injection of a viral vector in an area of interest that can later be activated through **CNO** injection
- **TRAP2** - a transgenic mouse model that expresses cre following brain activation, which allows cre-dependent DREADDs to be expressed in specific neurons
- **Contextual Fear Conditioning (CFC)** - mice are placed into a novel context (black box) and shocked, so they associate that context with a negative, fearful feeling

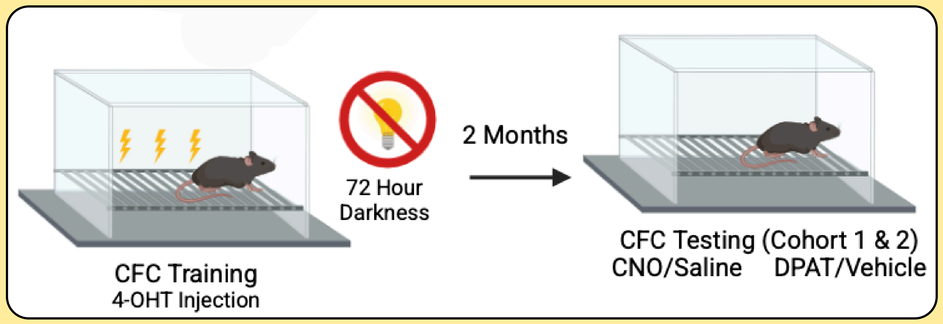
Methods

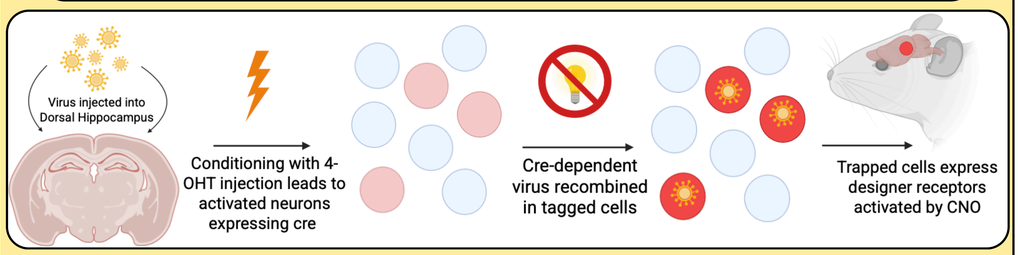
- Cre-dependent DREADDs that can later **excite the dorsal hippocampus**
- DPAT to systemically **inhibit the serotonin system**
- CFC to mimic fear conditions like **PTSD**
- Freezing behavior as a **measure of fear memory**

Stereotaxic DREADDs Surgery

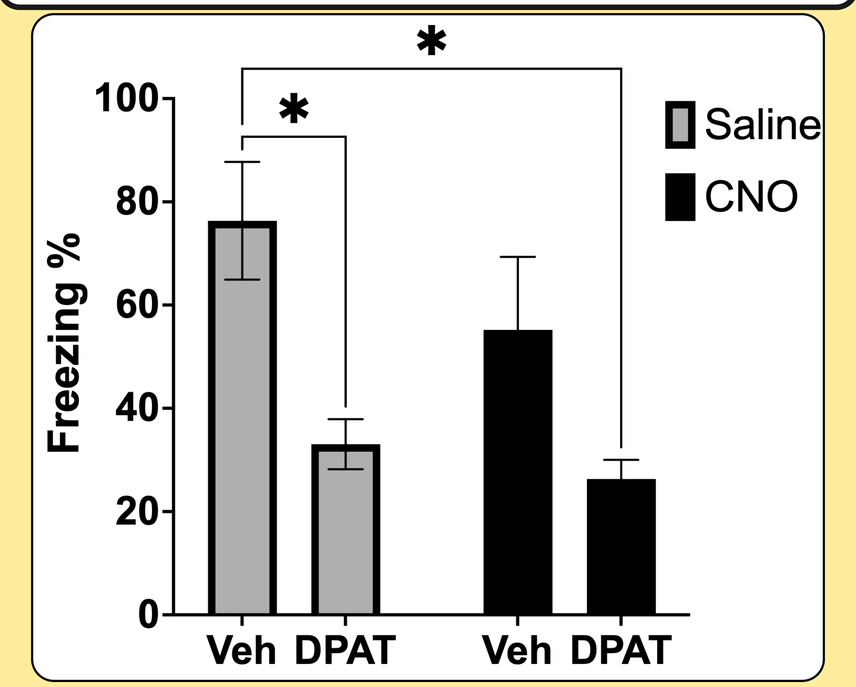


Timeline for Training, Testing, and Tagging



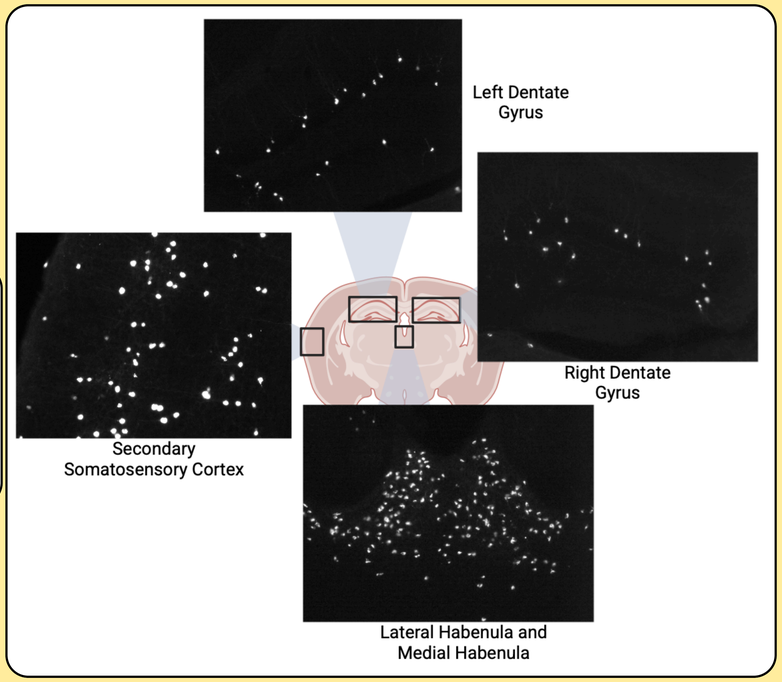


DPAT Reduces Fear Behavior while CNO has a Stabilizing Effect



A significant effect of DPAT was found following a two-way ANOVA; there was no effect found for CNO and no interaction. A post-hoc analysis was done to further understand group differences; there was a significant difference in the groups depicted above.

Highest Concentration of Tagged Neurons not in Hippocampus



No HA tag was detected, indicating no detectable viral expression. However, FzGreen was visible and concentrated in the above areas, indicating successful neuronal tagging.

Conclusions

- DPAT offers promise in **treating fear conditions**
- Some of the fear memory engram lies in dorsal hippocampus, which was activated by CNO
  - However, a lot of it is seen in other regions involving sensation and negative emotions
- **Modulating fear versus modulating memory**

Future Directions

- Larger sample sizes
- Targeting other modulated areas
- Redoing IHC protocol, testing cre-inducing stimuli length or power
- Different ways of testing memory versus emotion