

Evaluation of PFC-MdT Circuit Deletion on Behavioral Measures of Cognition and Alcohol Consumption



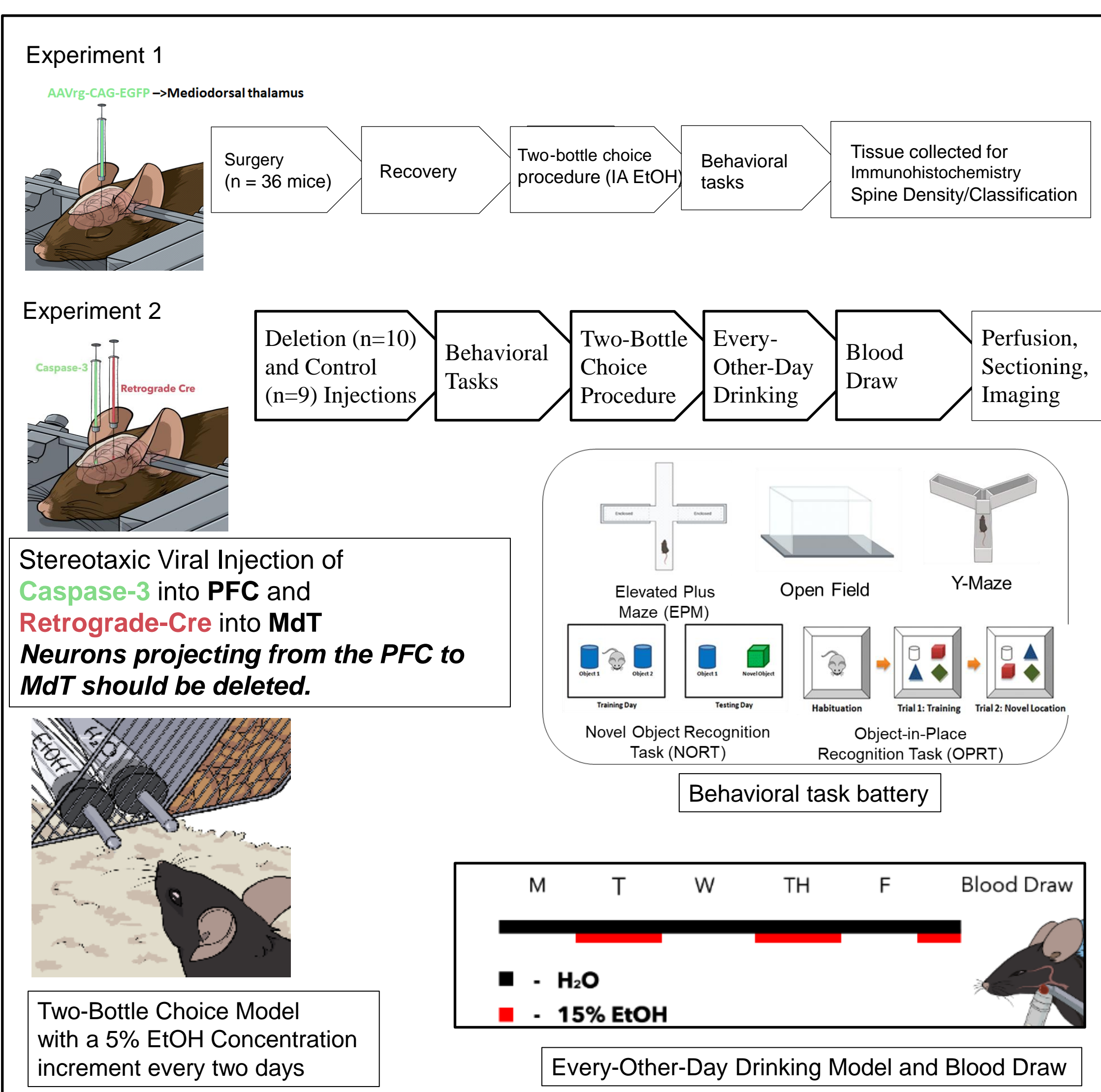
Introduction

- Excessive alcohol consumption during adolescence increases the likelihood of developing Alcohol Use Disorder (AUD) and other behavioral deficits associated with prefrontal cortex (PFC) dysfunction^{1,2}
- Our previous studies using slice electrophysiology have shown the mouse PFC to mediodorsal thalamus (MdT) circuit to be selectively vulnerable to adolescent drinking behaviors. The PFC→MdT circuit is known to mediate working memory and response inhibition^{3,4}. These behaviors have been shown to be affected by adolescent alcohol consumption in humans and rodents^{5,6}.
- The behavioral effects of adolescent alcohol consumption may be also captured by related tasks including the elevated plus maze (EPM), open field task novel object recognition task (NORT), switched object recognition task (SORT), and Y-Maze. The SORT has been previously associated with PFC and MdT function via lesion studies⁷.
- Deficits in behaviors related to cognitive function and PFC integrity are risk factors for developing AUDs⁸
- A fuller understanding of how PFC circuitry is impacted by adolescent alcohol in preclinical models may open the door for new treatment strategies.

Hypothesis

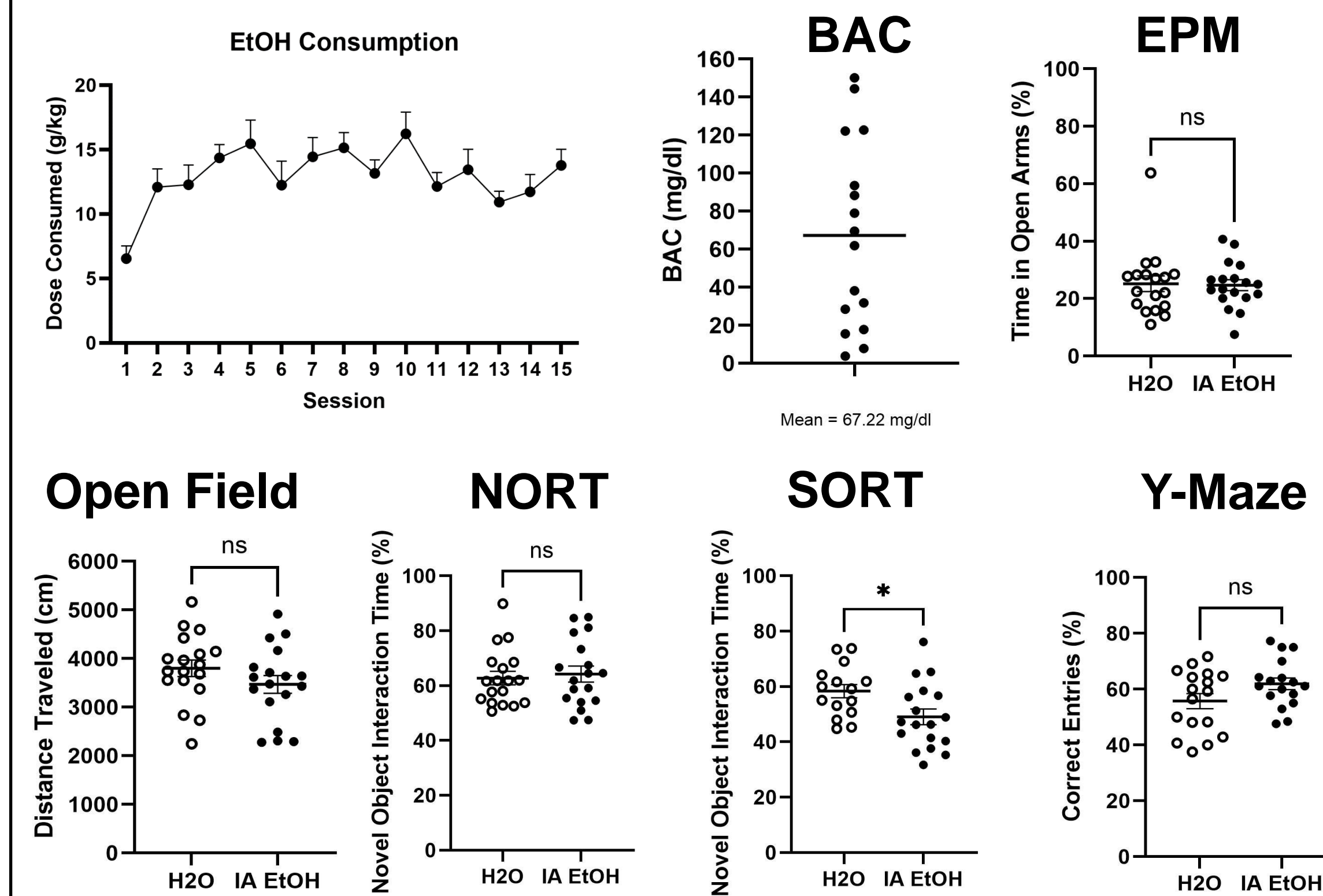
Deletion of the PFC→MdT circuit during adolescence will produce a similar behavior profile to adolescent alcohol drinking and result in increased alcohol consumption in adulthood.

Timeline and Methods



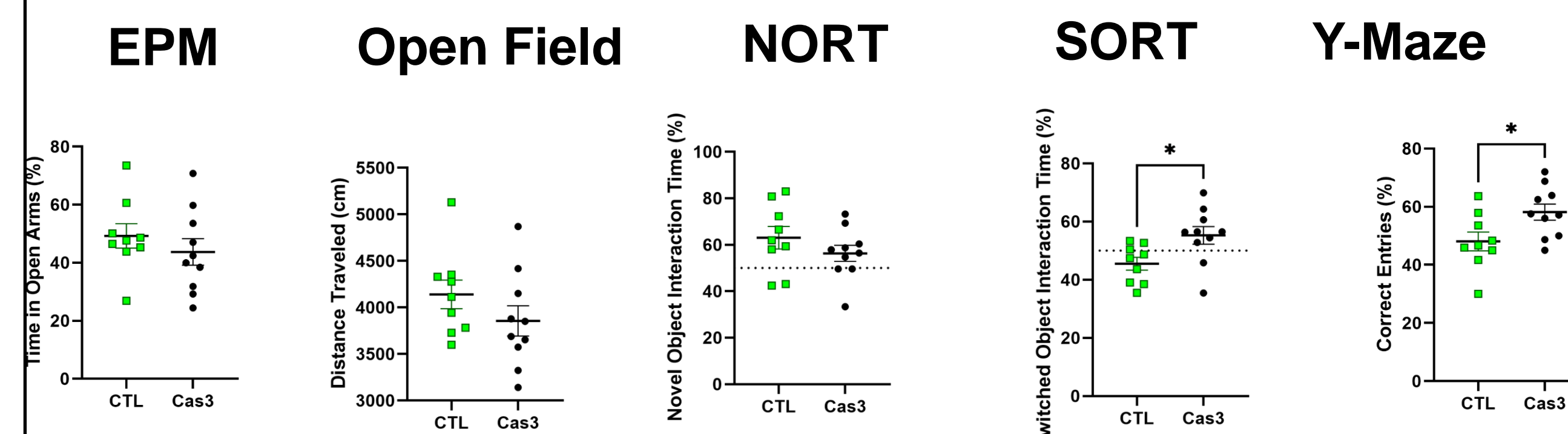
Results

Experiment 1: Behavioral task findings after adolescent alcohol



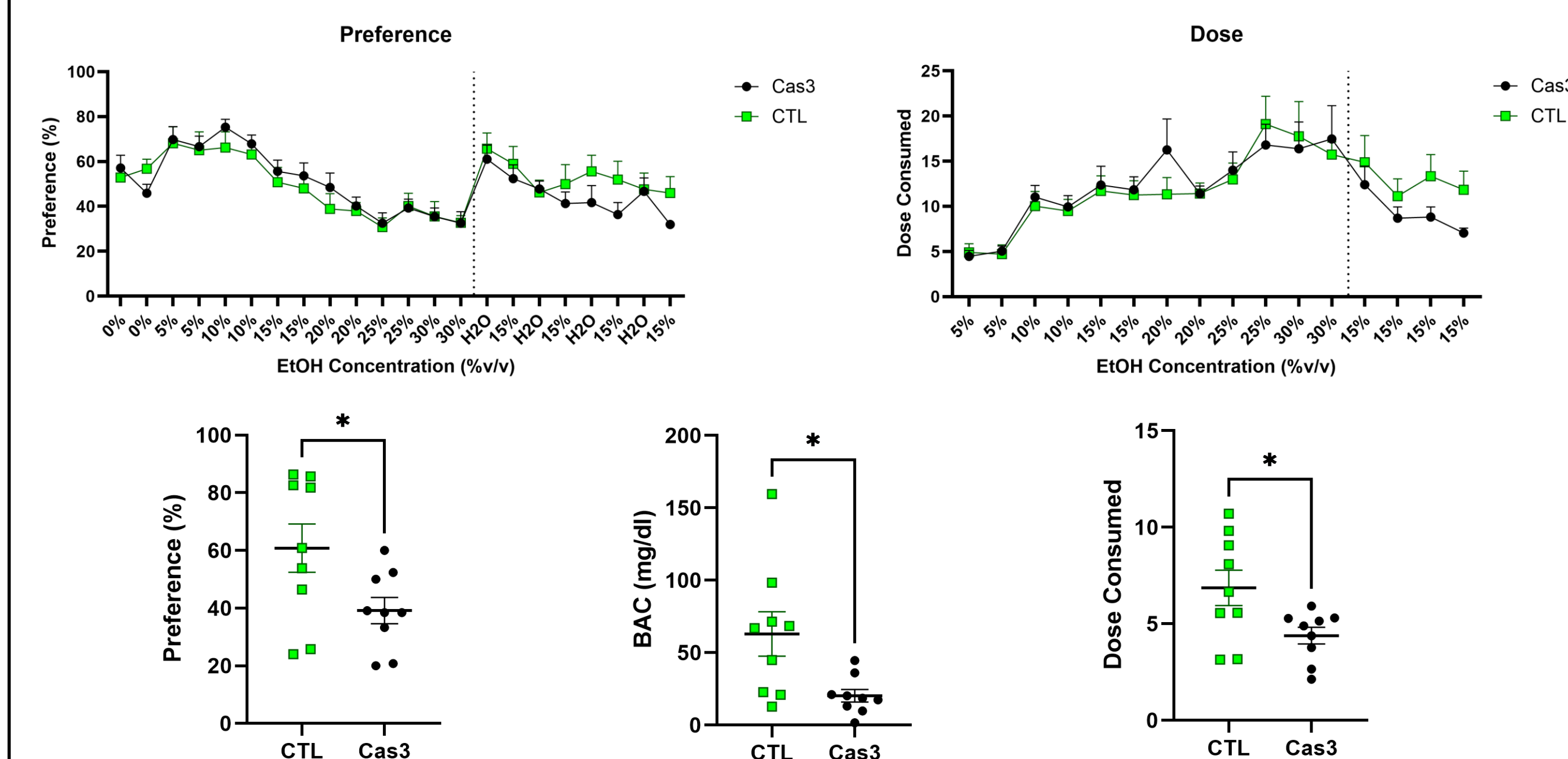
Previously our lab, mice drinking alcohol during adolescence have previously shown behavior deficits on the SORT but not other tasks (unpublished).

Experiment 2.1: Behavioral task analyses after PFC → MdT deletion



Against our hypothesis, mice with the PFC→MdT deletion show improved function on the SORT (Figures 3.1 and 3.2) and Y-Maze Task (Figure 4)

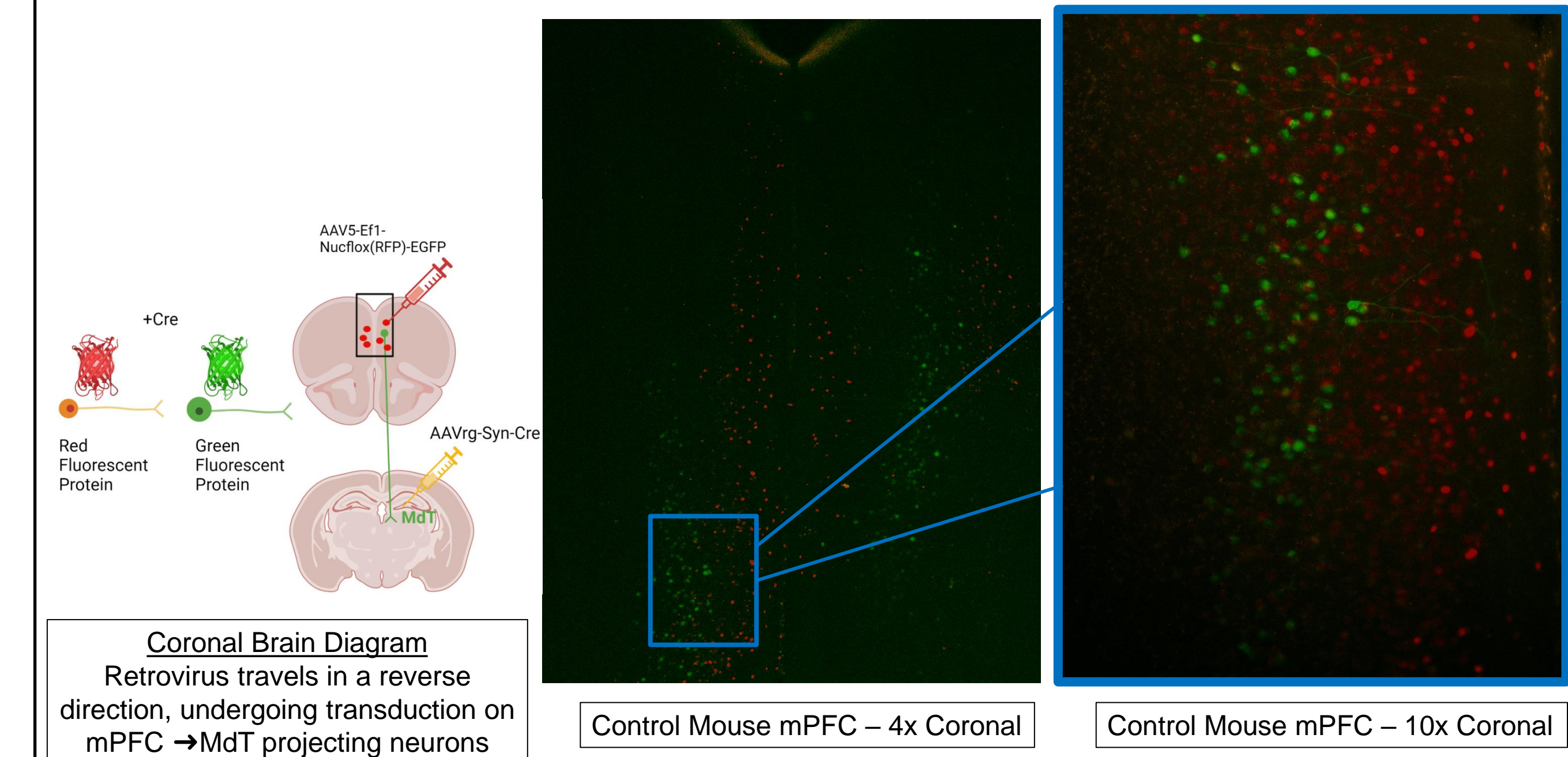
Experiment 2.2: Alcohol consumption after PFC → MdT deletion



Against our hypothesis, mice with the PFC→MdT deletion did not demonstrate differences in alcohol escalation with controls, and showed decreased alcohol consumption, preference and Blood Alcohol Concentrations at 6 hours into IA EtOH session

Results

Confirmation of control viral injections



Green Fluorescent Protein displays PFC → MdT neurons that would have been deleted in the experimental mice

Conclusions

- Adolescent alcohol impaired SORT task recognition memory consistent with PFC and MdT lesion studies.
- Deleting the PFC→MdT circuit did not affect anxiety, locomotor or NORT task performance.
- However, deleting the PFC→MdT circuit also show improved performance on SORT and Y-maze tasks.
- Deleting the PFC→MdT circuit did not increase alcohol consumption in adulthood during escalated alcohol consumption. It did decrease alcohol consumption, preference, and BACs at 6 hours into an intermittent alcohol session.

Future Directions

- Additional characterization of PFC →MdT circuitry deletion
- In vivo recording of PFC →MdT using fiber photometry following adolescent alcohol drinking

References

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