

Structural Assessment of Adolescent Alcohol's Impact on a Prefrontal Corticothalamic Circuit Using Expansion Microscopy

Introduction

- Heavy alcohol use during adolescence is associated with an increased risk of developing alcohol use disorders later in life, as well as deficits in behaviors mediated by the prefrontal cortex (PFC).
- The PFC → mediodorsal thalamus (MDT) circuit is specifically associated with behaviors known to be impacted by adolescent alcohol: working memory and response inhibition.
- In our previous studies, we found this circuit is uniquely vulnerable to the effects of adolescent alcohol consumption as indicated by long term reductions in glutamatergic neurotransmission.

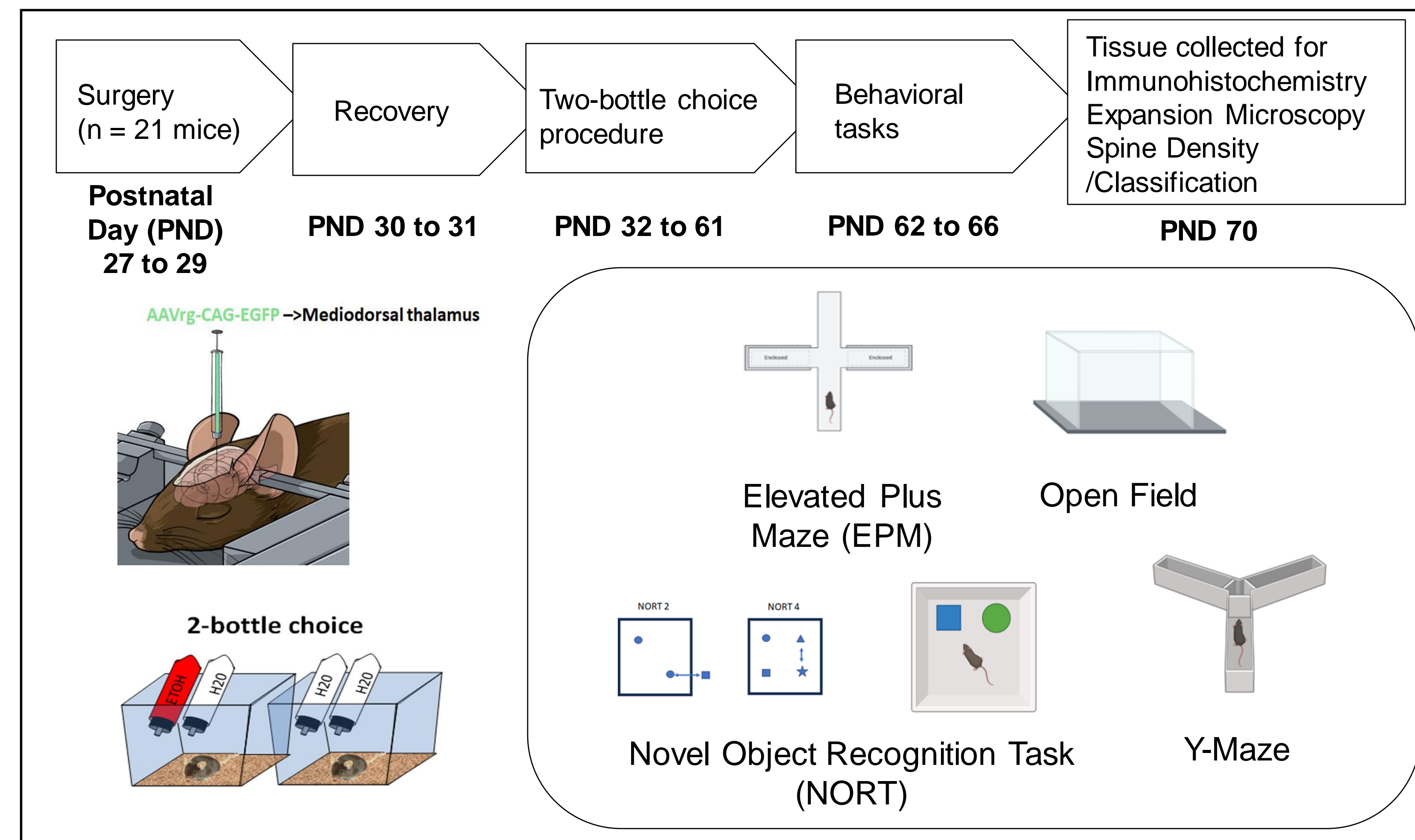
Objective

Use a mouse model of binge-like alcohol consumption during adolescence to assess if there are structural changes in neurons projecting from the PFC to the MDT that are associated with behavioral deficits

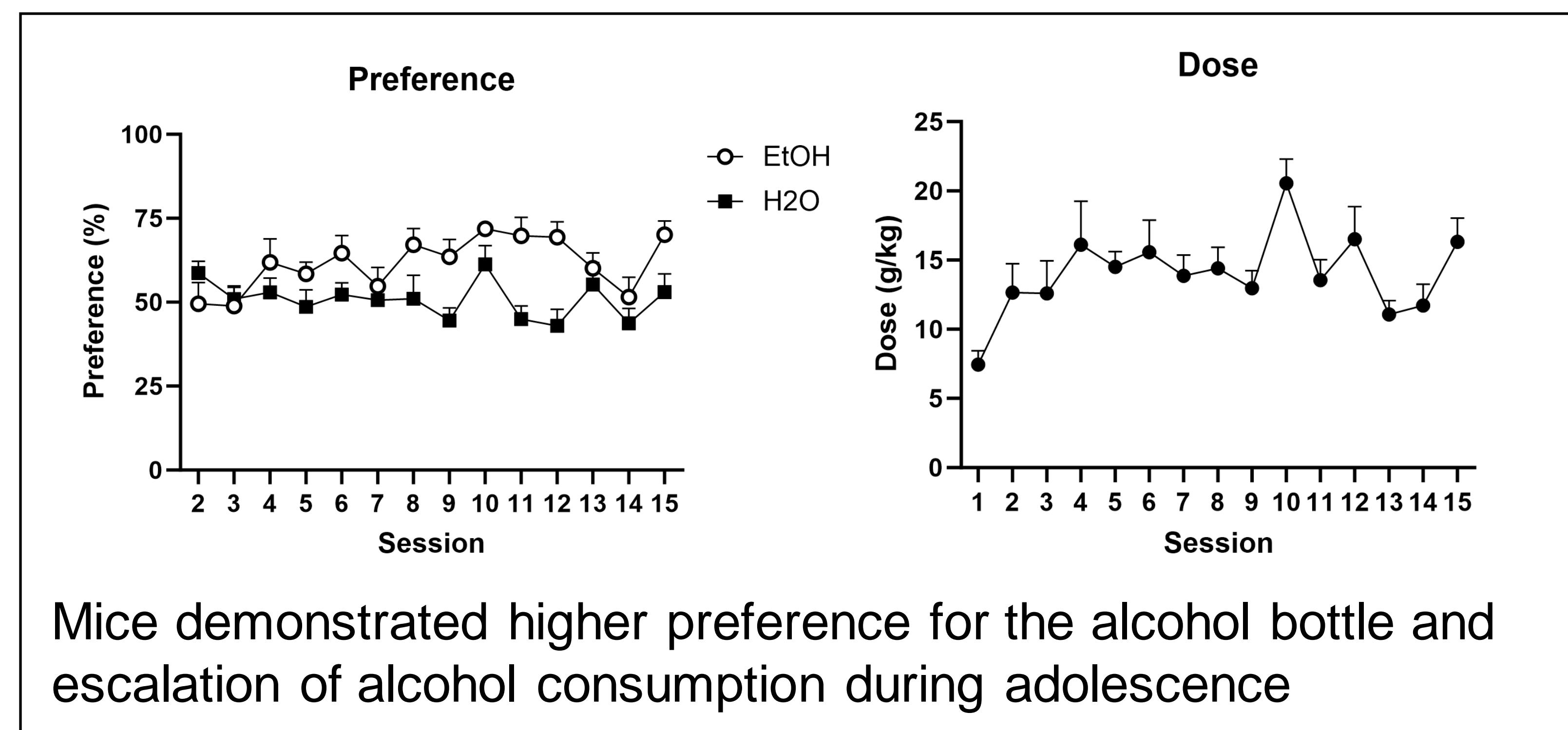
Hypothesis

We hypothesized that mice given access to alcohol during adolescence will show a reduction in spine density of PFC to MDT neurons that is associated with impaired performance on working memory and on a version of the novel object recognition task (NORT4) that is sensitive to PFC and MDT lesions.

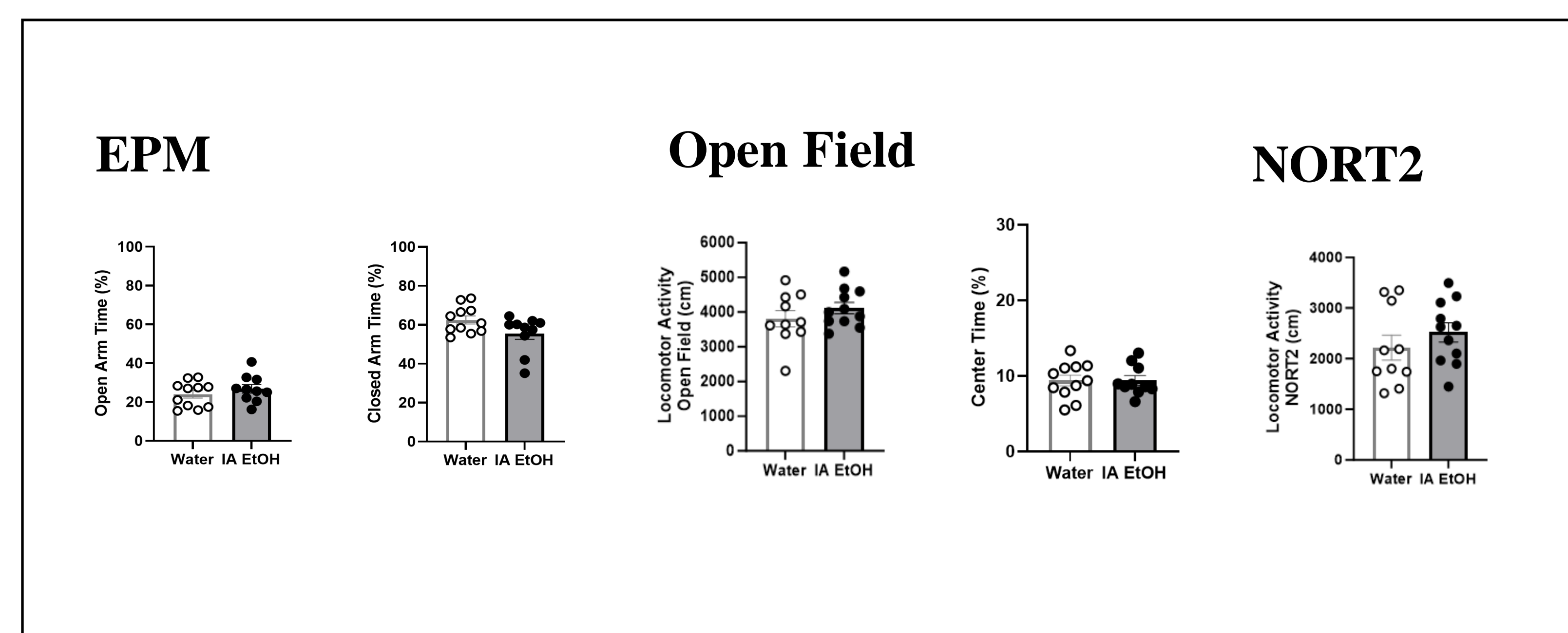
Methods



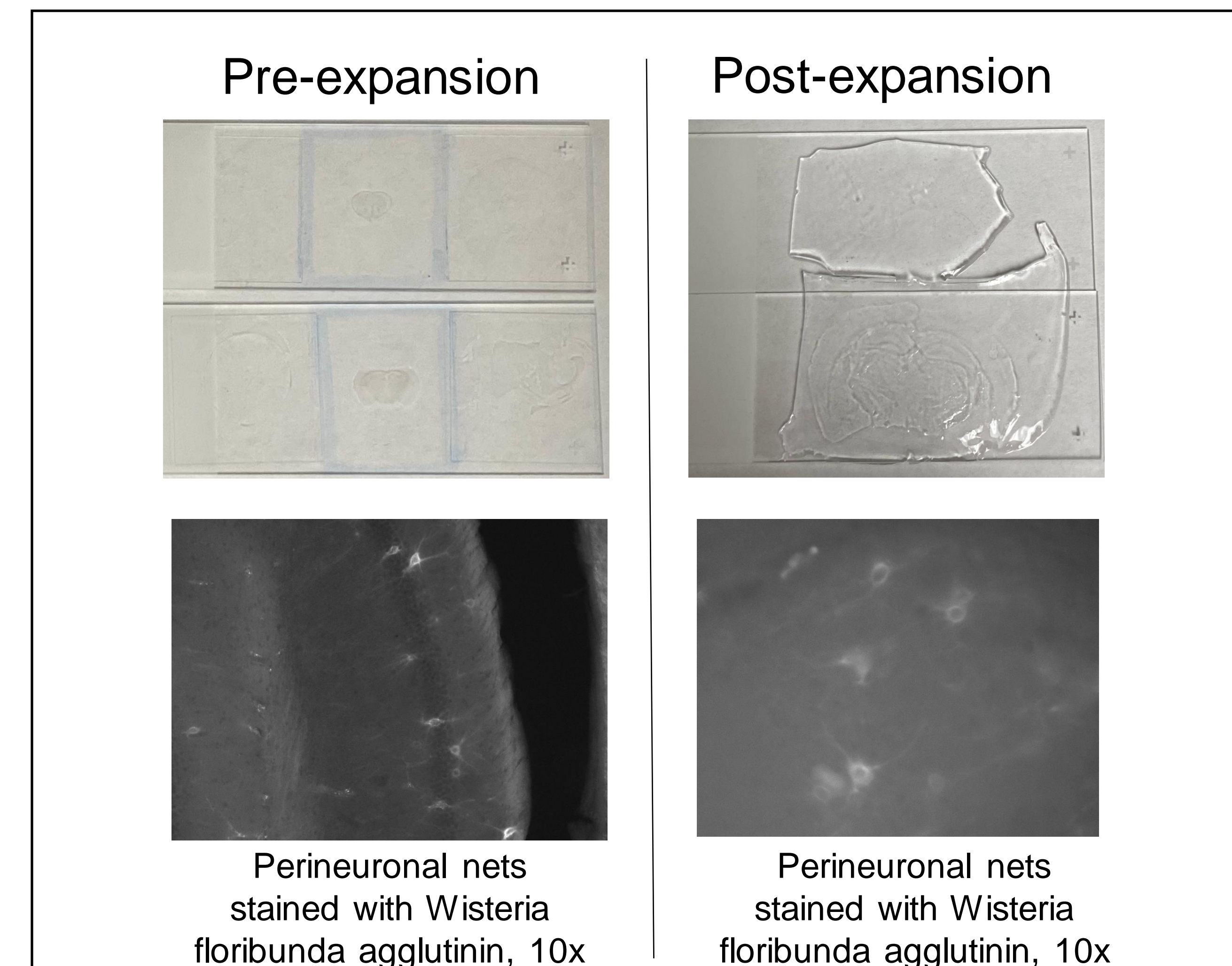
Results: Adolescent Alcohol Consumption



Results: Behavioral Analyses



Results: Expansion Microscopy



Conclusions

- Adolescent mice consumed alcohol similar to previous experiments (Salling et al. 2018).
- Following IA EtOH, mice did not demonstrate changes in locomotor activity in EPM, open field, or NORT. We did not detect differences in anxiety measures (Center Time, EPM Open Arms).
- NORT2/4 and Y-maze experiments are complete, but not fully analyzed.
- We successfully expanded brain tissue using the Magnify protocol and were able to observe perineuronal nets. Immunohistochemistry and morphological analyses of expanded tissue are currently being tested.

Future Directions

- Collect brain tissue and perform immunohistochemical and structural analyses of GFP-positive neurons from both groups
- Expand a subset of the tissue sections using the Magnify expansion microscopy protocol
- Findings from these studies will improve our understanding of the impact of adolescent alcohol consumption on the highly relevant PFC-MDT circuit