DISENTANGLING NATURE VS NURTURE IN A MOUSE MODEL OF ALCOHOL USE

Laura Bauer, Allison R. Bechard Ph.D.
Department of Psychology and Neuroscience, SUNY Geneseo

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INTRODUCTION

- Alcohol use disorder (AUD) is a significant issue with a lifetime prevalence of 29.1% in the U.S. (Grant et al., 2015), so understanding how it develops is a crucial point of research. This research investigates the role of parenting on the development of AUD in mice.
- Two strains of mice, one genetically predisposed to drink alcohol (B6) and the other not genetically predisposed (FVB), were cross-fostered.
- It was hypothesized that pups not predisposed to drink reared with dams predisposed to drink would drink more alcohol. It was also hypothesized that mice predisposed to drink reared with dams not predisposed to drink would drink less alcohol.

METHODS

- Mice were set up with 2 females and 1 male of the same strain for both the B6 strain and FVB strain. Coinciding litters from each strain were then cross-fostered. Any pups born in litters that were not within 3 days of each other were non-fostered and kept as controls.
- Maternal observations were recorded on days 1, 3, and 5 based on an ethogram.
- When pups were 42 days old, they were run in a Light Dark Box (LDB) to measure anxiety.
- Then pups were run in a Drinking in the Dark paradigm (DiD). Mice were put in separate cages with 10% ethanol and were left to drink in the dark for 2-hour sessions for 20 total sessions. Total alcohol consumption was recorded.

FIGURES

Maternal Care Day 5 for Resting with Pups

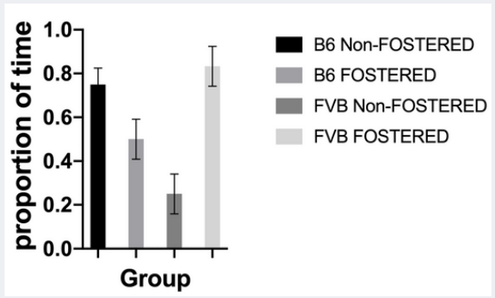

Figure 1: The amount of time spent resting with the pups resulted in a strain by group interaction ($F(1, 5) = 22.72$, $p = 0.005$).

Total Time in Light in Control and Fostered Mice

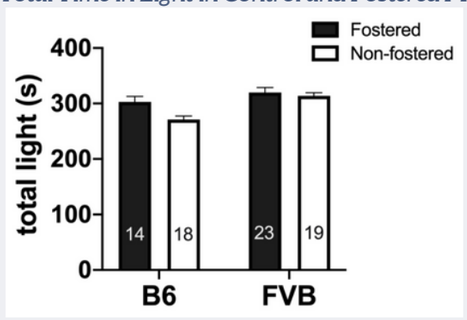

Figure 2: Fostered mice spent more time in the light side than non-fostered mice (Fostered: $F(1, 97) = 5.75$, $p = 0.018$) and FVB mice spent more time in the light side than B6 mice (Strain: $F(1, 97) = 14.35$, $p < 0.0001$). No effect of Sex or interactions.

Total Alcohol Consumption in Control and Fostered Mice

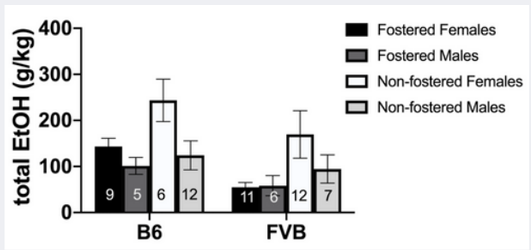

Figure 3: B6 mice drank more than FVB mice (Strain: $F(1, 60) = 4.92$, $p = 0.03$). Non-Fostered mice drank more than fostered mice (Fostered: $F(1, 60) = 6.71$, $p = 0.012$). Females drank more than males (Sex: $F(1, 60) = 4.84$, $p = 0.032$). No interactions were significant.

RESULTS

- **Maternal Care:** On day 5, FVB mothers with non-fostered pups rested with pups the least, while FVB and B6 dams with B6 pups rested with pups the most. The amount of time spent resting with pups resulted in a strain by group interaction (see *Figure 1*).
- **LDB:** Fostered mice and FVB mice spent more time in the light than control mice and B6 mice overall (see *Figure 2*).
- **DiD:** B6 mice, females, and non-fostered mice consumed more alcohol than FVB mice, male mice, and fostered mice (see *Figure 3*).

KEY TAKEAWAYS

- Any dams rearing FVB pups spent less time resting with them, and dams rearing B6 pups rested with them the most.
- FVB mice were less anxious than B6 mice, and cross-fostered mice were less anxious than non-fostered mice, which was unexpected.
- Rather than finding B6 mice reared by FVB dams drank less (or FVB reared with B6 drink more), we found a main effect of fostering.
- Females drank more than males, and B6 mice drank more than FVB mice; both of these results were expected.
- Cross-fostering influenced pup anxiety and drinking behaviors and acted as a protective agent, which was also unexpected.

LIMITATIONS/ FUTURE DIRECTIONS

- Due to COVID-19 restrictions, maternal care observations for fostered and non-fostered mice were completed using two different methods (live and recorded), and only day 5 data were comparable across all groups.
- For future studies, we are looking to complete maternal observations for mice that are cross-fostered within strains to strengthen our study's findings. Also, we will be pursuing the effects of early trauma on AUD. Specifically, how early life trauma may act as a protective agent for anxiety and AUD.