Influence of Early Life Stress on a Mouse Model of Binge Alcohol Drinking

Behavioral Neuroscience Group

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Introduction

- Exposure to foot shock in infancy significantly increases the fear response to later fear conditioning, suggesting that early life stress (ELS) can have a significant negative impact on well-being later in life, even without the memory of the traumatic event [1].
- Compulsive alcohol drinking is a hallmark of alcohol use disorder. The "drinking in the dark" (DID) paradigm is often used to model binge-drinking and compulsive behaviors in animals [2].
- **The current study examined whether exposure to ELS in mice increases compulsive alcohol drinking in adulthood.**

Methods

Subjects: C57BL/6J male and female mice were generated from breeding pairs purchased from The Jackson Laboratory, Bar Harbor, ME.

Early life stress (ELS): On postnatal day (PND) 17, mice were exposed to 15 foot shocks (1 mA) in 1 h (ELS groups). Control animals (non-ELS) were placed in the conditioning chamber but were not shocked. A 3 h maternal separation followed the conditioning session.

Adult fear conditioning: In adulthood (PND60-90), the mice underwent fear conditioning in a novel context. Mice received 1 or 0 foot shocks (1mA) 180 seconds after being placed in the chamber.

Drinking in the Dark Paradigm: After fear conditioning, mice began the DID paradigm. Each mouse was housed individually. Three hours into the dark cycle, water bottles were replaced with one bottle containing 15% ethanol (EtOH) and another containing drinking water. Each session, the side of the EtOH bottle was switched to avoid the mice developing a side preference. Two hours later, the alcohol bottles were removed, and the water bottles were returned. This process was repeated for 10 sessions over 2 weeks, 5 days per week.

Quinine Addition: For sessions 11-14, 100uM of quinine was added to the EtOH bottles on day 11 and 13 while only 15% EtOH was in the bottles on days 12 and 14.

Experimental Design

Timeline

Early Life Stress Exposure
PND 17

↓

Fear Conditioning
Adulthood

↓

DID Sessions 1-10

↓

Quinine Day 1, 100 µM

↓

Quinine Day 2, 0 µM

↓

Quinine Day 3, 100 µM

↓

Quinine Day 4, 0 µM

Alcohol consumption

Effects of early life stress in drinking

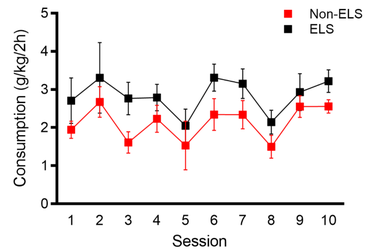

Fig. 1. Mice that were exposed to ELS show an increased consumption over mice that did not. A 2 Way ANOVA revealed significant main effects of session ($F(9, 218) = 2.012$, $P = 0.0392$) and ELS ($F(1, 218) = 13.22$, $P = 0.0003$).

Addition of quinine

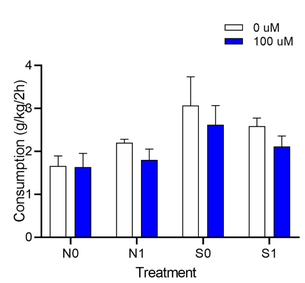

Fig. 2. Within each of the four treatment groups, quinine did not decrease consumption. This suggests aversion-resistant drinking regardless of ELS exposure

Effects of consumption in each of the four treatments

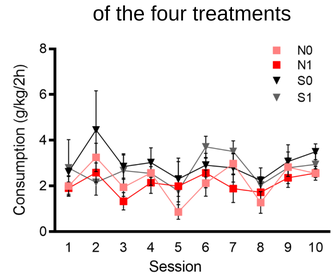

Fig. 3. Effects on ethanol consumption were present between groups that solely received ELS and those that did not as well as groups that received only adult fear conditioning and groups that only received ELS. Post-hoc comparison tests revealed significant differences between N0 vs. S0 ($P = 0.0434$) and N1 vs. S0 ($P = 0.0113$).

Fear learning

Freezing during retrieval test

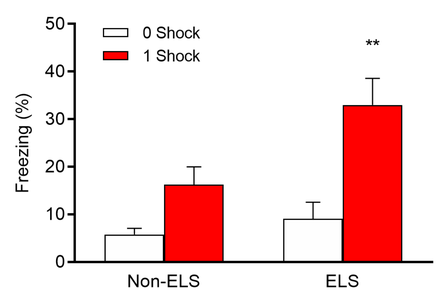

Fig. 1. Mice exposed to ELS exhibited greater fear learning during adulthood. A RM ANOVA revealed a significant main effect of early life stress exposure ($F(1, 55) = 5.98$, $P = 0.018$) and a significant main effect of adult fear conditioning ($F(1, 55) = 17.64$, $P < 0.0001$). A post hoc Holms-Sidak multiple comparisons test revealed a significant difference between Non-ELS/1 Shock and ELS/ 1 Shock, **$P = 0.009$.

Conclusions

- Both male and female mice that received early life stress showed higher overall consumption of EtOH than mice that did not.
- The addition of quinine modeled aversion-resistant drinking since mice continued to consume EtOH with quinine.
- The model described in this study can be used to effectively measure the effects of a stress-related traumatic event occurring in early development on alcohol consumption and addictive behavior.
- **EtOH consumption in mice was increased by ELS but not adult fear conditioning, suggesting that effects of stress on alcohol consumption can have varying effects depending on age.**

References

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