Co-morbidity of PSTD and AUD: Using an Animal Model of the Single Prolonged Stress to Examine Stress-induced Reinstatement of Alcohol-Seeking Behavior

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Background

- Alcohol use disorder (AUD) is a chronic relapsing brain disease characterized by an impaired ability to control alcohol use
- AUD is frequently comorbid with posttraumatic stress disorder (PTSD)
- A history of stressful life events increases one's susceptibility of AUD and risk of relapse
- The single prolonged stress (SPS) animal model is effective in producing PTSD pathophysiology in rodents
- King & Becker (2019) exhibited that the pharmacological stressor yohimbine induced alcohol-seeking behavior in mice after a period of extinction and systemic oxytocin (OXT) administration attenuated the effects of stress-induced reinstatement
- Investigation of pharmacological treatments need to take place to mitigate relapse initiated by stress
- The **aim** of this study was to evaluate the effects of a prior stress experience on alcohol seeking and drinking behavior induced by acute stress exposure after a period of extinction

Methods

Subjects

- 48 adult male and female C57BL/6J mice were obtained from Jackson Laboratories (Bar Harbor, ME) at 9 weeks of age (24/sex)
- Females and males were group housed (4 per cage) but separated by sex

Procedures

- Mice were trained to lever press for alcohol (12% *v/v* ethanol) in operant conditioning chambers until a stable baseline was achieved
- Half of these mice underwent a single prolonged stress (SPS) protocol [restraint (2-hr), forced swim (10 min), and exposure to anesthesia (to effect)]
- Immediately after exposure mice resumed alcohol self-administration
- The dependent variables analyzed were number of lever responses and alcohol intake before and after SPS

Results

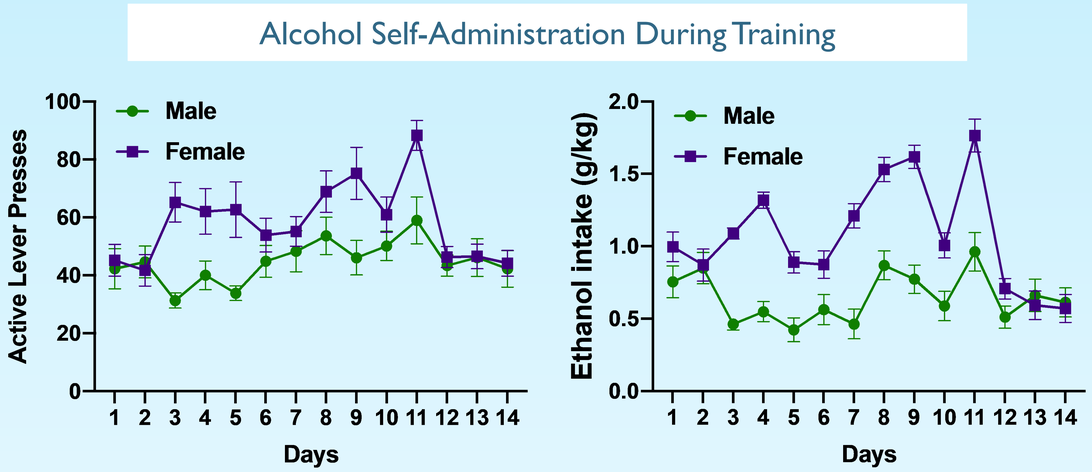

Figure 1. Alcohol intake in female and male mice during early baseline training. Females had a higher rate of alcohol consumption. Values are mean ± s.e.m.

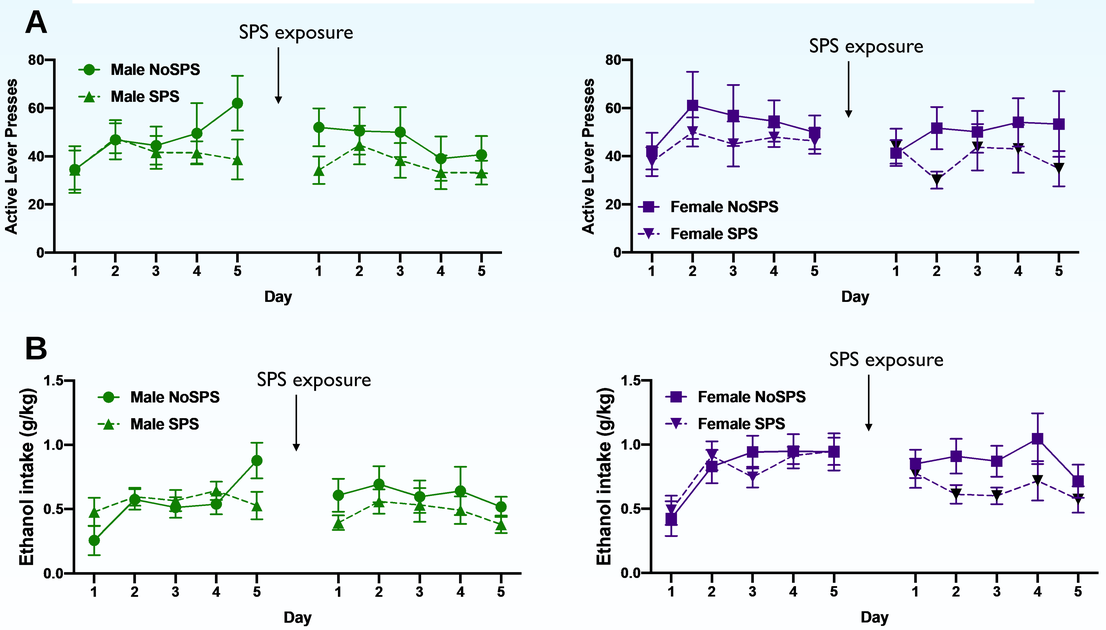

Figure 2. Average lever presses did not significantly differ in responding between male and female mice. However, average alcohol intake on average was higher in females (B). Responding for alcohol (A) and alcohol intake (B) was not significantly affected by SPS exposure in both male and female mice. Values are mean ± s.e.m. (SPS: mice that underwent single prolonged stress exposure)

Conclusions

- **Average alcohol intake (g/kg) was significantly higher in females compare to males**
- **Exposure to SPS did not affect levels of alcohol seeking and drinking behavior**
- **This study is still ongoing**
- **Mice will later be evaluated for alcohol intake under extinction conditions before stress-induced reinstatement with yohimbine**
- **Blood alcohol concentrations will be assessed to examine the extent of intoxication in mice**
- **It is predicted that there will be an increase in alcohol seeking and drinking behavior during reinstatement in animals that have a history of stress exposure (i.e. SPS)**
- Previous studies have demonstrated that OXT has been utilized to attenuate stress-induced reinstatement in mice
- These studies have elicited sex-related differences in sensitivity to the effects of OXT
- The low availability of pharmacological interventions for the treatment of comorbid PTSD and AUD urges future studies to evaluate the effect of OXT and other drugs using this animal model of SPS and alcohol relapse
- Other studies could analyze gender differences present in drug responses and relapse
- Understanding the co-occurrence of PTSD and AUD is especially important because of the negative implications' previous trauma-exposure presents in triggering alcohol relapse

Acknowledgements

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