Rebecca K. Yoon
T4
Tulane University School of Medicine, New Orleans, LA

Dr. Tiffany Wills
LSUHSC, Department of Cell Biology and Anatomy

Sex Differences in the Effects of Adolescent Alcohol Exposure

Adolescent alcohol exposure is one of the strongest risk factors for the development of alcohol use disorder. Notably, affective disorders tend to emerge during this period of development as well. There is a growing body of evidence that suggests adolescent alcohol use in females is outpacing males, and that there are sex differences in various aspects of alcohol use. Women are more likely to use alcohol to blunt emotions of negative affective disorders such as anxiety and depression, while men are more likely to drink alcohol for the positive reward effects. To understand the underlying mechanism, it is necessary to understand the sexually dimorphic brain circuitry impacted by adolescent alcohol use.

In part, emotional behaviors are regulated by the bed nucleus of the stria terminalis (BNST). The BNST is a sexually dimorphic region of the brain that modulates negative affect and stress. Alcohol-induced changes in BNST plasticity may explain the mechanism of sex differences in negative affect phenotypes that develop during adolescence in people that consume alcohol.

Previous behavior experiments in the Wills Lab have revealed that glutamatergic signaling in the BNST is disrupted by adolescent alcohol use, however the mechanisms are distinct between males and females. Male and female C57Bl/6J mice underwent two 4-day cycles of alcohol vapor exposure (16 hours/day) with a 3-day period of rest between cycles from PND 30-41 (adolescent intermittent alcohol exposure: AIE). The control groups were in chambers with vaporized water. During acute withdrawal, brains were collected for RNAscope, We identified BNST cell populations activated during acute withdrawal from AIE by labeling RNA transcripts for the immediate early gene, cfos. RNAscope was used to quantify co-localization of cfos expression with corticotropin releasing factor (CRF) and corticotropin releasing factor receptor 1 (CRFR1). CRF-CRFR1 signaling in the BNST is activated in times of stress and anxiety. Our goal is to identify whether CRF and/or CRFR1 signaling is activated during the withdrawal from AIE and if there are sex differences in this activation between male and female mice.

Overall, RNAscope data reveals several non-significant, but trending results. In the BNST, female mice have higher overall cellular activation and CRF/CRFR1 colocalization, but these levels are not impacted by AIE treatment. In male mice, AIE enhances CFOS/CRF/CRFR1 co-expression demonstrating a greater sensitivity of BNST CFOS/CRF/CRFR1 signaling from alcohol withdrawn male mice, and this expression is almost significant in terms of sex differences ($p=0.0580$). These results suggest sex differences in CRF-CRFR1 signaling and the regulation of this signaling by AIE. Future studies will increase the animal number in each to group to see if these trends will become significant.