Ashai K. Williams
Undergraduate
Xavier University of Louisiana, New Orleans, Louisiana

Tiffany Wills, PhD
Louisiana State University Health Sciences Center, Department of Cell Biology and Anatomy

"Activation of CRF- and CRFR1-expressing Neurons in the Central Nucleus of the Amygdala Following Stress in Adult Mice with Adolescent Alcohol History"

Abstract

Adolescent alcohol exposure is a strong predictor for the onset of mental health issues and alcohol use disorder (AUD) during adulthood.[1] The three-stage framework of alcohol addiction involves binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation. Motivations and behaviors that are associated with each of the three stages vary greatly between men and women. In general, men tend to consume alcohol in more social situations, making alcohol a positive reinforcer. Women, however, are more likely to drink to alleviate anxiety or other psychological distress, suggesting that females are more likely to seek alcohol for its acute anxiolytic properties.[2] After several instances of binge-drinking, individuals may begin to experience a negative affect state during alcohol withdrawal. The negative affect state can lead an individual into a cycle of negative reinforcement, eventually leading to AUD. The central nucleus of the amygdala (CeA) is a key modulator of anxiety and alcohol withdrawal. Neurons in the CeA are primarily inhibitory and project to regions such as the bed nucleus of the stria terminalis (BNST), which integrates stress- and alcohol-related stimuli. The CeA has numerous stress-related neuropeptides, such as the corticotropin-releasing factor (CRF). CRF is the primary pro-stress modulator in the CeA and contributes largely to withdrawal-associated anxiety. By activating CRF receptors type 1 (CRFR1) in the CeA, CRF contributes to alcohol withdrawal-related behaviors.[1] The aim of this study was to assess the changes in the activation of CRF- and CRFR1-expressing cells in the CeA following restraint stress in adult mice with a history of adolescent alcohol. A key parameter in evaluating activation of CRF- and CRFR1-positive neurons is c-Fos mRNA expression. C-Fos indicates overall neuronal activation and increases in c-Fos mRNA expression are rapidly induced by stress. Male and female C57BL/6 mice were given either adolescent intermittent ethanol (AIE) vapor exposure or air exposure. Mice underwent two cycles of AIE. This involved four 16-hour periods of vapor exposure separated by 8-hour periods of withdrawal separated by 3 days starting on postnatal day (PND) 30 and ending on PND41. Mice were then left undisturbed until adulthood (PND 70+), when they were exposed to 1-hour restraint stress and euthanized 1-hour later. The brains were extracted, sliced, and used for RNA in situ hybridization, which allowed for quantification of c-Fos, CRF, and CRFR1 expression in the CeA. Previous findings from our laboratory showed that adult female mice with an history of AIE exhibit increase latency to consume a palatable reinforcer after restraint stress. These changes in negative affect were not observed in male mice.[3] We will expand these findings by evaluating if this heightened negative affect phenotype is accompanied by changes in CRF signaling in the CeA. We hypothesize that following restraint stress, adult females with AIE history will have higher activity of CeA CRF- and CRFR1-expressing neurons than male mice.

1. Gilpin et al. 2015
2. Flores-Bonilla et al. 2020
3. Kasten et al. 2020