

Connor K. Bailey
Undergraduate
Tulane University, New Orleans, Louisiana

Mentor: Tiffany Wills, Ph. D
LSUHSC, Department of Cell Biology and Anatomy

“Stimulation of the bed nucleus of the stria terminalis produces sex-specific negative affect-like behavior and changes in activation of VTA cells in adult mice exposed to adolescent alcohol”

Adolescent alcohol use is known to produce persistent health issues through adulthood, especially within the still-developing brain (Spear, 2018). Examining the specific effects of alcohol use in adolescence on certain brain regions aids in establishing the neural basis for alcohol use disorders and other changes that may endure into adulthood.

The Bed Nucleus of the Stria Terminalis (BNST) is a sexually dimorphic basal forebrain structure that is implicated in emotional regulation, including behaviors related to alcohol withdrawal-induced anxiety-, depressive-, and pain-like behaviors (Pati et al., 2020). The BNST projects to several brain areas that modulate emotional behavior, such as the Ventral Tegmental Area (VTA). The VTA is part of the brain’s reward system and is characterized by distinct neuronal populations: dopamine (DA) neurons (~70%), gamma aminobutyric acid (GABA) neurons (~30%), glutamatergic neurons (~2-3%) (Walsh & Han, 2014).

Previous findings from behavioral testing demonstrated that females with a history of adolescent intermittent alcohol (AIE) exhibited negative affect-like behavior following adult stress. Female mice that underwent novelty induced hypophagia (NIH) testing following AIE and restraint stress experienced a significant increase in latency to consume an appetitive reinforcer. We found that chemogenetic activation of the BNST can mimic the stress effect and produce this same behavioral phenotype in female mice with a history of AIE without changes in social anxiety-like behavior. We propose that this increase in negative affect caused by activation of BNST is accompanied by suppression of the mesolimbic pathway. This could result directly from inhibition of VTA DA cells or indirectly via increasing activation of GABAergic interneurons within the VTA.

To investigate this, we employ RNAscope in situ hybridization that enables the detection of target mRNA transcripts at the single-cell level. Utilizing a set of 3 probes that hybridize to the mRNA of interest, we measure the expression of c-Fos, a general marker for cell activation, tyrosine hydroxylase (TH), an enzyme involved in dopamine synthesis, which is used to specifically label dopamine neurons, and SL32a1, a transporter protein associated with GABAergic neurotransmission, which allowed us to identify GABA neurons in the VTA of these female mice. By using this technique, we expect to observe changes in activation of specific neuronal populations in the VTA. Females with a history of AIE are expected to exhibit a reduction of double labeled c-Fos- and TH-positive cells within the VTA following chemogenetic BNST activation, indicating a direct suppression of VTA DA cells. An increase in percentage of c-Fos- and SL32a1-positive cells would suggest an indirect suppressive pathway of VTA DA cells.