

Cameron R. Gabriel
Undergraduate
Louisiana State University, Baton Rouge, LA

Rajani Maiya, Ph.D.
Louisiana State University Health Sciences Center, New Orleans, LA

“Investigating the Role of KORs in the bed nucleus of the stria terminalis (BNSt) on Social Stress-Escalated Alcohol Consumption”

Aversive stress experiences can lead to escalated drug consumption and increase the risk of relapse to drug seeking. Individuals who consume alcohol in negative social contexts or to alleviate the effects of social stress show a higher likelihood of developing alcohol use disorder. Social stress has been most effectively modeled in animals through social defeat paradigms. Repeated social defeat stress (SDS) enhances the rewarding and reinforcing effects of several drugs of abuse, including alcohol. However, the neural mechanisms by which SDS leads to increased alcohol consumption are not well understood.

Previous studies in the lab showed that repeated social defeat stress using a resident/intruder paradigm led to escalated alcohol consumption and preference in both male and female C57BL/6J mice. The Kappa/Dynorphin system has been implicated in mediating some of the behavioral effects of SDS. Kappa opioid receptors are inhibitory G-Protein coupled receptors which upon binding to their ligand Dynorphin inhibit neuronal activity. KOR antagonists have been shown to alleviate circadian and sleep disturbances as well as anxiety-like behaviors that are precipitated by stress. Consistent with this, preliminary data show that systemic administration of the selective KOR antagonist NorBNI significantly and selectively reduced alcohol consumption in both male and female stressed mice but not in unstressed controls.

KORs are expressed in many brain regions that are implicated in mediating the many behavioral effects of stress including the basolateral amygdala (BLA), bed nucleus of the stria terminalis (BNSt), and nucleus accumbens (NAc). The overall goal of this project is to determine where in the brain KOR's are acting mediate the effects of SDS on alcohol consumption. Of these brain regions, the BNSt is the most intriguing as KORs expressed on glutamatergic terminals in the BNSt have been implicated in mediating the effects of stress on anxiety-like behavior. The BNSt is connected to numerous brain regions that regulate the behavioral effects of stress, including the amygdala, nucleus accumbens, hippocampus, and hypothalamus. Further, the BNSt contains a sub population of dynorphin-containing neurons that release dynorphin locally. We cannulated mice with canulae aimed at the BNST. We allow these mice to recover for two weeks, following which half the mice were subjected to social stress for ten days. The other half were control mice that were handled similar to the stressed mice but did not undergo social stress. Following ten sessions of social stress, the mice were housed undisturbed in their home cages for ten days after which, they were subjected to the intermittent access (IA) two-bottle choice alcohol consumption procedure. After two weeks of IA alcohol, the effects of Nor-BNI infusion into the BNST on alcohol consumption in SDS and control mice will be determined. Our results will illuminate brain regions and circuits within which KORs may be functioning to regulate stress-escalated alcohol consumption.