KAPPA OPIOID RECEPTOR-EXPRESSING CELLS IN THE BASOLATERAL AMYGDALA REGULATE SOCIAL-STRESS ESCALATED DRINKING

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Aversive stress experiences can lead to escalated drug consumption and increase the risk of relapse. Individuals who consume alcohol to alleviate the effects of social stress are more likely to develop an 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 alcohol. However, the neural mechanisms by which SDS increases alcohol consumption are not well understood. Our results show that repeated SDS enhances alcohol consumption and preference in both male and female C57BL/6J mice. The Dynorphin/Kappa opioid receptor (Dyn/KOR) system has been implicated in mediating some of the behavioral effects of SDS. 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. To further investigate Dyn/KOR mechanisms of SDS enhanced drinking, we generated a novel KOR-Cre knock in mouse line that harbors a Cre insertion in the 3'UTR of the KOR locus. Chemogenetic activation of KOR expressing neurons in the BLA (BLA^{KOR} neurons) attenuated SDS-escalated alcohol consumption. We next asked if BLA^{KOR} projections to the BNST mediate SDS-escalated alcohol consumption. KOR antagonism as well as chemogenetic inhibition of BLA^{KOR} terminals in the BNST attenuated stress-escalated alcohol consumption implicating this pathway in regulating SDS-escalated alcohol consumption. Preliminary results implicate pDyn neurons in the Dorsal Raphe Nucleus as a potential source of Dyn in the BNST that is recruited by SDS. Experiments are currently underway to determine the effects of KOR knockdown in the BLA-BNST pathway in regulating SDS-escalated alcohol consumption.

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