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ENDOCANNABINOID-MEDIATED PLASTICITY AT INHIBITORY SYNAPSES ONTO DOPAMINE NEURONS AS A POSSIBLE MARKER OF INNATE PREFERENCE TO ALCOHOL
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The predominance of rewarding effects of alcohol over its aversive properties likely contributes to the transition from its occasional use to dependence. The balance between drug-induced reward and aversion is regulated by many factors, including the activity of dopamine (DA) neurons in the ventral tegmental area (VTA) and GABA projections from the rostromedial tegmental nucleus (RMTg). Since cannabinoids suppress RMTg inputs to VTA DA cells and CB1 receptors affect alcohol intake in rodents, we hypothesized that the endocannabinoid system by modulating this pathway might contribute to a shift towards alcohol preference. Sardinian alcohol-prefering (sP) or -non preferring (sNP) rats are one of the few pairs of lines of rats selectively bred for their innate opposite alcohol preference. In this study, we found ex vivo that VTA DA cells from alcohol-naïve sP rats displayed a decreased probability of GABA release and a larger endocannabinoid-mediated depolarization-induced suppression of inhibition (DSI). This difference was due to the rate of 2-arachidonoylglycerol (2-AG) degradation. In vivo, we found a reduced RMTg-induced inhibition of putative DA neurons in sP rats that negatively correlated with an increased firing. Finally, alcohol failed to enhance RMTg spontaneous activity and to prolong RMTg-induced silencing of putative DA neurons in sP rats. Our results indicate functional modulations of RMTg projections to DA neurons that might impact the reward/aversion balance of alcohol attributes, which may contribute to the innate preference observed in sP rats and to their elevated alcohol intake.