Regulation of endocannabinoid signalling modulates alcohol drinking and anxiety-related behaviors in alcohol-preferring rats

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This study investigates the effect of the Fatty Acid Amide hydrolase inhibitor (FAAH) inhibitor URB597 on alcohol-related behaviors in genetically selected alcohol preferring Marchigian Sardinian (msP) rats. . Previous evidences showed anxiolytic-like effect of URB597 (Busquets-Garcia et al., 2011). However, very little is known about the possibility to regulate alcohol-abuse related behavior by FAAH inhibition. MsP rats are known to drink alcohol, at least in part, to self-medicate from negative affect and anxiety. Hence, using these animals we sought interesting to investigate how FAAH inhibition and subsequent enhancement of the endocannabinoid signaling in the ventral tegmental area or in central amygdala might attenuate hyper-anxiety in msP rats, thus removing one of the triggers for the excessive drinking that characterize this rat line. To this end we administered URB597 in the central and basolateral amygdala, two brain areas known to be involved in anxiety-like responses. Results show that URB597 at 0.3 and 1.0 μg/rat significantly reduced alcohol self-administration in msP rats. Furthermore we found that at 1.0 μg/rat URB597 significantly reduced anxiety-like behavior in msP rats that previously underwent restraint stress. These results suggest that URB597 may represent a potential therapeutic agent for patients in which alcohol abuse is driven by high basal anxiety. Anandamide, besides acting as agonist at CB1 receptor, also activate PPARg receptors. Studies previously carried out in our lab have demonstrated that agonism at PPARg reduce alcohol intake. Research is underway to understand whether the modulatory effect of anandamide on alcohol abuse could involve PPARg receptors.

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