Neuropeptide Y in the Medial Prefrontal Cortex Modulates Ethanol Consumption in Mice

Binge-like drinking behavior has been estimated to cause about 80,000 deaths in the United States annually and is a significant risk factor for developing ethanol dependence. This behavior is partially regulated by control of the amygdala by the medial prefrontal cortex (mPFC). A neurotransmitter called neuropeptide Y (NPY) binds to interneurons in the mPFC projecting to the amygdala, thus we hypothesized that NPY regulates binge-like drinking behavior. In the mPFC, NPY has a post-synaptic receptor NPY1R, and a presynaptic receptor NPY2R. To test NPY’s affect in modulating ethanol intake, NPY1R was pharmacologically agonized and NPY2R was pharmacologically antagonized. The agonism of NPY’s post-synaptic receptor and the antagonism of NPY’s presynaptic receptor both resulted in reduced ethanol intake compared to vehicle treated animals. To further study NPY’s role, neurons in the mPFC expressing NPY1R were chemogenetically inhibited through the use of a Designer Receptor Exclusively Activated by a Designer Drug (DREADD). This specific inhibition of NPY1R in the mPFC resulted in decreased consumption of ethanol. To examine the effects of binge-like drinking on NPY activity in the mPFC, we performed immunohistochemistry and found a decrease in NPY immunoreactivity after three weeks of binge-like drinking. These results establish a role for NPY modulation of binge-like drinking behavior in mice. This study could help understand how people develop alcohol dependence and suggest therapeutic strategies.