Alcohol Relapse and Interoceptive Neural Circuitry

Alcohol Use Disorder (AUD) is increasingly prevalent in society, despite widespread knowledge of the harmful effects of drug addiction. Interoception, the body's perception of its internal state, can be a powerful driver of alcohol-seeking behavior. Further, alcohol-related environmental cues (e.g. a bar, liquor bottles, etc) are reported to produce interoceptive effects reported as jitteriness, tension, and butterflies in the stomach. Thus, the presence of alcohol-related cues can drive an interoceptive state that contributes to alcohol-seeking and relapse. We hypothesize that this interoceptive information is carried to the primary interoceptive brain region, the anterior insular cortex (IC), through the nucleus reuniens (RE), a midline thalamic nucleus we have previously shown to play a role in the interoceptive effects of alcohol. In this experiment using a rat model, we silenced the RE-IC neural pathway using a chemogenetic approach to determine how this important interoceptive circuit contributes to alcohol relapse. Inhibition of the nuclear reuniens to insular cortex pathway was found to promote alcohol-seeking and diminish alcohol drinking in males only, possibly due to a lack of interoceptive feedback when the alcohol is in the rats' system, discouraging them from consuming more. Seeking and consumption were unaffected in female rats, suggesting a different interoceptive neural processing pathway that explains the sex-differences in cue-based drinking. Overall, this experiment builds a framework for understanding the neural circuitry behind interoceptive cues and alcohol relapse, and how interoceptive effects based on alcohol-associated contexts can affect both the seeking and actual consumption of alcohol.