

## WHEN A FIRE LEADS TO A DRINK: ENHANCEMENT OF ALCOHOL-SEEKING BY MICROINJECTIONS OF NICOTINE DIRECTLY INTO THE REWARD NEUROCIRCUITRY

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Alcohol addiction is a cyclical disorder that is characterized by periods of alcohol consumption and abstinence. The periods of abstinence are frequently brief, and the rate of relapse to alcohol consumption is typically higher than 95% within a year. Most alcoholics are not just alcoholics. The vast majority (80-95%) of alcoholics also concurrently use, or are dependent on, nicotine. During periods of alcohol abstinence, nicotine use dramatically increases. The use of nicotine can potentiate self-reported craving for alcohol and the amount of alcohol used following a relapse episode. The goal of the present project was to determine the biological basis of nicotine's ability to stimulate alcohol (EtOH)-seeking in a rodent model of alcoholism (alcohol-preferring [P] rat). Specifically, the current project examined the effect of nicotine on EtOH-seeking when administered directly into the brain reward neurocircuit (posterior Ventral Tegmental Area – pVTA). In order to determine the neurotransmitter systems regulating nicotine's ability to enhance EtOH-seeking when administered into the pVTA, two subsequent studies examined the effect of co-administration of nicotine with a acetylcholine nicotine receptor (AChN) antagonist (mecamylamine (MEC)) or with a serotonin-3 (5HT<sub>3</sub>) receptor antagonist (zacopride (Zac)). Nicotine binds with high affinity to both the AChN and 5HT<sub>3</sub> receptors. The data collected indicated that at very low concentrations nicotine microinjected into the pVTA increased EtOH-seeking in P rats. Co-administration of mecamylamine or zacopride blocked nicotine's ability to potentiate EtOH-seeking. Overall, the results show that nicotine can enhance alcohol-seeking behaviors through activation of the AChN and 5-HT<sub>3</sub> receptors in pVTA. The clinical implication of the data set would be that to reduce the amount of alcohol-craving, which could lead to relapse, nicotine use should also be terminated.