

Impulsivity and Alcohol Drinking in an Animal Model of Alcoholism

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Abstract

Alcoholism is a widespread problem, and although we are beginning to characterize genes that mediate its heritable nature, we still do not understand how a family history of alcoholism places individuals at risk for this disorder. One trait that is consistently elevated, both in alcoholics and those who suffer from a variety of addictive disorders, is impulsivity. Impulsivity can be defined as a self-defeating tendency to choose immediate, but small rewards over large rewards given at following a delay. Normally, instituting a delay to a reward decreases its subjective value, a phenomenon called delay discounting. In alcoholics, the slope of this decline in value as a function of time is steeper than in non-drinkers, but it has been difficult to demonstrate in humans whether this results from a lifetime of drinking, or causes problem drinking in the first place. In the present studies we utilized an animal model of alcoholism, the selectively bred High Alcohol Preferring (HAP) mouse, comparing them to Low Alcohol Preferring (LAP) mice as well as non-selected, outbred mice using the translational measure of impulsivity, delay discounting. By using alcohol naïve mice, we were able to assess whether genes promoting alcohol drinking increase impulsivity without the potential confound of a history of alcohol exposure. In follow-up studies, we assessed whether pharmacotherapies for alcoholism decrease impulsivity as well as alcohol consumption in HAP mice. Alcohol naïve HAP, LAP, and HS/Ibg mice were subjected to a saccharin-motivated delay discounting procedure in which the value of an immediate reward was titrated until it was subjectively equivalent to a delayed reward. As expected, time to the delayed reward decreased its value, and did so more steeply in HAP mice than in LAP and unselected HS/Ibg mice, supporting the hypothesis that impulsivity plays a causal role in initiating high drinking behavior. In related studies, we assessed whether two pharmacotherapies for alcoholism, memantine (an NMDA antagonist) and naltrexone (an opioid antagonist), altered delay discounting behavior and (in separate mice) alcohol drinking. Although these two drugs decreased free-choice drinking in HAP mice, consistent with their beneficial effects on alcoholism, they did not alter impulsivity. Amphetamine, a general dopamine agonist with known anti-impulsive actions, decreased impulsivity in HAP mice, but did not alter alcohol consumption in a behaviorally selective manner. These findings support a role for impulsivity in the development of alcoholism, but leave unanswered the question of which neural systems would serve as the best pharmacological targets for the development of medications aimed at treating those with, or at a high risk for, alcoholism.