Heritable variation in voluntary alcohol drinking in a genetically diverse inbred mouse panel

Jared R. Bagley, Lauren S. Bailey and J. David. Jentsch

Department of Psychology (Behavioral Neuroscience), Binghamton University, Binghamton NY 13902

Alcohol consumption and associated subjective effects are individually variable, and genetic factors account for a substantial proportion of that variance. Although significant progress has identified variants that modulate alcohol consumption and preference in mouse models, most have originated from reduced complexity intercrosses with limited genetic and phenotypic variability. The collaborative cross (CC) recombinant inbred (RI) panel, its inbred founders and the diversity outbred (DO) populations that result from their outbreeding, are a cutting-edge tool for genetic and genomic research in part because of their remarkable genetic diversity. For these reasons, we assessed both sexes of the CC/DO founder strains for voluntary drinking of ethanol (20%) and water in a two-bottle choice procedure during the active phase of the mouse circadian cycle (in the dark). This procedure was performed in lickometer boxes that provide time-course data of bottle licking with sub-second resolution. The CC/DO founder strains demonstrate substantial and statistically significant strain differences in terms of alcohol lick preference scores, as well as total alcohol intake, with the high drinking strain consuming up to 10 times the body-weight adjusted amount of alcohol relative to the low drinking strain. Strain mean distributions suggest this is a quantitative trait. Furthermore, substantial sex effects are present in some strains with females drinking more alcohol. Time-course analysis suggests that multiple strains are drinking pharmacologically relevant amounts of alcohol and that patterns of intake vary within sessions. This work has established heritability of voluntary ethanol drinking in the CC founder strains and will serve as a foundation for further characterization of CC RI strains. This research is performed in the context of the Center for Systems Neurogenetics of Addiction project and will be integrated into expansive data sets that will allow for in depth analysis of genetic relationships of addiction related behaviors as well gene expression.