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Heritable variation in voluntary alcohol drinking and blood ethanol concentrations in a genetically diverse inbred mouse panel

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Alcohol consumption and associated subjective effects are individually variable, and genetic factors account for a substantial proportion of that variance. The collaborative cross (CC) recombinant inbred (RI) mouse panel, its inbred founders and the diversity outbred (DO) populations are a cutting-edge tool for genetic and genomic research in part because of their remarkable genetic diversity. For these reasons, we assessed voluntary alcohol drinking during the active phase of the mouse circadian cycle (in the dark) in order to assess genetic effects on voluntary alcohol intake. The CC/DO founder strains demonstrate substantial and statistically significant strain differences in alcohol intake. Heritable variation in ethanol metabolism may account for at least a portion of variation in voluntary drinking. Therefore, a separate group of CC/DO founders were characterized for blood ethanol concentration (BEC) after i.p. injection (1.5 g/kg, blood collected 30 minutes post dosing). Statistically significant strain differences were detected for BEC levels, indicating potential heritable differences in ethanol metabolism. Furthermore, strain mean distributions suggest this is a quantitative trait in both sexes, however substantial sex effects are present in some strains with males tending to have higher BEC. Strain level correlations revealed no significant correlations between BECs and ethanol drinking. This work has established heritability of voluntary ethanol drinking and metabolism in the CC founder strains and will serve as a foundation for further characterization of CC RI strains.