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Heritable variation and genetic correlation of addiction-related phenotypes in the CC/DO recombinant inbred mouse panel

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Research in animal and human subjects point towards impulsivity as a heritable trait that predicts relatively greater positive subjective responses to stimulant drugs. The Collaborative Cross (CC) recombinant inbred mice, their inbred founders, and the Diversity Outbred (DO) that are derived from them are a powerful genetic reference panel that has potential as a tool for revealing genetic contributions to impulsivity and addiction-related traits. Here we use eight CC/DO founder strains and nineteen CC strains to examine the heritability of impulsive action (total trials to criteria) and waiting impulsivity (premature responding) in a reversal learning test, as well as genetic correlations between these measures and other addiction-related phenotypes. *Methods.* Strains were bred at Jackson and were either studied at JAX or shipped to Binghamton University between 4-6 weeks of age. Binghamton animals underwent open field and reward sensitivity tests then were placed on food deprivation and tested on reversal learning or delay discounting. Mice at Binghamton were returned to free feed after completion and then underwent a two-bottle choice test for ethanol (20%) consumption and preference.

Results. Mouse strains demonstrate significant heritability for impulsive choice, impulsive action, ethanol consumption, and ethanol preference. A positive genetic correlation was found between impulsive action and waiting impulsivity and between waiting impulsivity and palatable food reward consumption. This research was conducted within the Center for Systems Neurogenetics of Addiction's (CSNA) inter-laboratory effort to characterize CC and DO mice for multiple, drug abuse-related traits.

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