Heritable variation in reward sensitivity and impulsive action and choice in a genetically diverse inbred mouse panel

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Drugs of abuse, including alcohol and stimulants like cocaine, produce subjective effects that are subject to individual variability, and genetic variation accounts for at least a portion of those differences. Notably, research in both animal models and human subjects point towards reward sensitivity and impulsivity as being trait characteristics that predict relatively greater positive subjective responses to stimulant drugs. Unfortunately, past efforts have yet to yield convincing insights into underlying genetic influences on these traits due to the characteristics of the mouse panels used. The Collaborative Cross (CC) recombinant inbred mouse strains, their inbred founders, and the Diversity Outbred (DO) mice that are derived from them are a powerful genetic reference panel that has potential as a tool for revealing genetic contributions to cocaine abuse and related traits. Here we describe use of the eight CC/DO founder strains to examine the heritability of reward sensitivity and impulsivity traits, as well as genetic correlations between these measures and existing addiction-related phenotypes. *Methods.* Founder strain were all tested on open field and reward sensitivity (intake of chocolate BOOST® measured via lickometers). Mice were then divided into two counterbalanced groups and underwent reversal learning (impulsive action) or delay discounting (impulsive choice). *Results.* The founder mice demonstrate heritability for incorrect anticipatory responses within the reversal task, locomotor movement, and reward sensitivity. At this preliminary stage, significant strain differences for delay discounting are unclear. This research was conducted within the broader, inter-laboratory effort of the Center for Systems Neurogenetics of Addiction (CSNA) to characterize CC and DO mice for multiple, cocaine abuse related traits. These data will facilitate the discovery of genetic correlations between predictive traits, which will then guide discovery of genes and genetic variants that contribute to addictive behaviors.

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