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**Initial drug sensitivity and sensitization in the Collaborative Cross/Diversity Outbred founders**

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Risk for developing a Substance Use Disorder (SUD) is driven by genetic differences, environmental exposures and gene by environment interactions. Identifying risk genes and mechanisms that contribute to SUDs requires an approach that takes into account this complex etiology. The Center for Systems Neurogenetics of Addiction (CSNA) is comprised of investigators at four institutions who study various aspects of addiction genetics using animal models. We are leveraging genetic data and genomic tools available for the Collaborative Cross (CC) and Diversity Outbred (DO) mouse populations to develop a systems level understanding of the relationship between various addiction-related phenotypes and identify risk genes. As part of the CSNA, our laboratory is examining acute locomotor sensitivity and behavioral sensitization to cocaine. As a first step toward examining the genetic architecture, we measured these behavioral traits in the eight CC/DO founder strains – 129S1/SvImJ, A/J, CAST/EiJ, C57BL/6J, NOD/ShiLtJ, NZO/HILtJ, PWK/PhJ and WSB/EiJ. Our behavioral protocol allows us to examine novelty-induced locomotor activity, acute cocaine locomotor response and initiation and maintenance of behavioral sensitization. Analysis of the founder data yielded significant strain and sex differences for many of our behavioral phenotypes with heritabilities ranging from 0.2 to 0.8. Novelty-induced locomotor activity significantly correlated with acute locomotor response to cocaine and, to a lesser extent, initial sensitization response. We will present these data along with genetic correlations with other CSNA phenotypes. We have also identified several CC strains that show divergent behavioral responses to cocaine and other psychostimulants and mapping data from these studies will be presented.