

Submitter Name: Lisa Tarantino

Submitted Email: lisat@med.unc.edu

Repeated exposure to cocaine produces strain specific differences in incentive sensitization in Collaborative Cross mice

Lisa M. Tarantino^{1,2,5}, Leona Gagnon^{3,5}, Ashley Charpentier^{3,5}, Savanna Julian^{3,5}, Sneha Roy^{3,5},
Elissa J. Chesler^{3,5}, and James D. Jentsch^{4,5}

¹Department of Genetics, University of North Carolina, Chapel Hill, North Carolina;

²Division of Pharmacotherapy and Experimental Therapeutics, University of North Carolina,
Chapel Hill, North Carolina;

³The Jackson Laboratory, Bar Harbor, Maine;

⁴Binghamton University, Binghamton, New York and

⁵Center for Systems Neurogenetics of Addiction, The Jackson Laboratory, Bar Harbor, Maine

Repeated exposure to psychostimulant drugs can augment locomotor responses (psychomotor sensitization), facilitate the acquisition of drug self-administration, and heighten preference for drug paired environments. These effects result, in part, from neuroadaptations within the mesolimbic dopamine system that is known to mediate each of these behaviors. These findings contributed to the incentive sensitization theory of addiction that posits that drug-induced sensitization of mesocorticolimbic circuitry in the brain alters incentive-motivational processes and imbues drugs and drug-related stimuli with enhanced salience and the ability to elicit behavior. However, direct comparisons of psychomotor and incentive sensitization are largely absent in the literature. The Center for Systems Neurogenetics of Addiction quantified psychomotor sensitization in 50 genetically heterogeneous strains from the Collaborative Cross (CC). The significant phenotypic variation present among CC strains presented a unique opportunity to study the genetic correlation between psychomotor and incentive sensitization. We established an incentive sensitization protocol and described a significant association between incentive and psychomotor sensitization in two CC strains (Bailey et al. 2023). We are currently engaged in collecting and analyzing incentive sensitization behavior in the same 50 CC strains. We have collected data on >120 mice from >25 strains. We will present our incentive sensitization procedure and preliminary data analyses that suggest that the CC strains vary significantly for incentive sensitization in a manner that does not always align with psychomotor sensitization. These findings set the stage for identifying variants that predispose individuals to extreme dopaminergic neuroadaptations and resulting effects on incentive motivation.