Submitter Name: J. David Jentsch Submitted Email: jjentsch@binghamton.edu

Heritable differences in incentive motivation are genetically correlated with the excitability of dopamine release in the nucleus accumbens core of inbred mice

James D. Wherry[1], Anushree N. Karkhanis[1], J. David Jentsch[1]

[1]Department of Psychology, Binghamton University

Incentive motivation describes the processes by which the value or salience of rewards or associated predictive cues come to invigorate behavior, and several theoretical accounts of addictions propose that exaggerated incentive motivation plays a key role. Here, we tested the hypothesis that incentive motivation is a heritable phenotype and that genetically influenced differences in dopaminergic transmission in the ventral striatum mediate the impact of genetic variation on behavior. Male and female mice from 6 inbred strains were evaluated for operant responding for a palatable food using a progressive ratio (PR) schedule of reinforcement. Levels of responding were found to be heritable (H^2=0.2, $p<0.002$), spanning a wide range from ~200 (DBA/2J) to almost 800 lever presses (MRL/MpJ). Although lever pressing in the PR test was not genetically correlated with lever contacts in a Pavlovian autoshaping task ('sign-tracking'; r^2=0.09, p=0.64), the MRL/MpJ strain ranked highest for both measures. When mice from the same strains were evaluated for electrically stimulated dopamine release using *ex vivo* fast scan cyclic voltammetry, a genetic correlation with responding in the PR task was observed (r^2=0.7, $p<0.05$). Mice from the same strains were tested for PR responding after administration of GBR12909, a DAT inhibitor (10 mg/kg). All strains increased their responding, compared to vehicle. Although strain differences were not significant, the MRL/MpJ had the highest baseline responding and increased responding the most after GBR. These data indicate that common inbred mice differ in the excitability of mesolimbic dopamine transmission, with commensurate effects on incentive motivation.