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Orbitofrontal and accumbal dopamine function in bxd mouse strains selected for high or low impulsivity

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Impulsivity is a heritable characteristic in humans that is reportedly elevated in chronic drug users and may also be a risk factor for increased susceptibility to develop chronic use. In determining genetic underpinnings for heightened impulsivity and addiction, one hypothesis is that genetic regulation of neuronal signaling function within the orbitofrontal cortex (OFC), an area of the frontal cortex that exerts control over reward-guided behavior and plays a key role in addiction neurobiology. Here, we measured dopaminergic function within the OFC and its efferent target, the nucleus accumbens (NAc) in six recombinant BXD strains selected for a high or low impulsive phenotype through reversal learning. Adult mice underwent reversal learning or were sacrificed, and the OFC and NAc regions were collected. HPLC or rtPCR was conducted on tissue for quantification of dopamine, serotonin, and their metabolites or relative expression levels of *Drd1* and *Drd2*, respectively. HPLC analysis revealed lower dopamine and higher DOPAC levels in the NAc of high impulsive strains, while preliminary analysis of the OFC suggests lower DOPAC quantity in high impulsive strains. rtPCR identified lower expression of *Drd1* and *Drd2* in the NAc of high impulsive strains. These results thus far would indicate heritable differences in the dopaminergic system of the NAc, and potentially OFC, of high impulsive mouse strains, most notably elevated dopamine metabolism and lower *Drd1/Drd2* expression in the NAc. Data from this study facilitates understanding of dopaminergic dysfunction in the cortico-striato-thalamo-cortical pathway that may underlie impulsive behaviors and related susceptibility to substance use.