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Impulsivity Phenotypes are Linked with Novel Genetic Loci in Diversity Outbred Mice

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Impulsivity and impulsive behaviors are heritable traits that are predictive of risk for substance use disorders. Past studies from our laboratory using the BXD and hybrid mouse diversity panels (HMDP) have revealed that behavioral indicators of impulsivity measured in a reversal learning task are heritable and are genetically correlated with intravenous cocaine self-administration. Genome wide linkage studies in the BXD panel revealed a large quantitative trait locus on chromosome 10, but the specific genes affecting this trait remain elusive. To achieve greater precision in our mapping efforts, we have turned to the Diversity Outbred mice. A total of 332 mice (131 males, 201 females) were phenotyped using the same reversal learning test utilized in our BXD and HMDP studies. Our primary measure of impulsive responding that isolates the relative difficulty mice have with reaching performance criteria under reversal conditions revealed a genome wide significant QTL on chromosome 7 (max LOD score = 8.73, $p<0.05$). A measure of premature responding akin to that implemented in the 5-choice serial reaction time task yielded a suggestive QTL on chromosome 17 (max LOD score = 9.14, $p<0.1$). Candidate genes are being prioritized based upon expression QTL data and other relevant genetic information (e.g., presence of coding variants). These findings demonstrate the ability to map addiction-relevant traits in the DO population and to detect novel QTL not detected in other populations.