

**Genome-wide association analysis of amphetamine sensitivity in  
*Drosophila melanogaster***

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Abuse of psychostimulants is a major public health problem with profound psychiatric, medical and psychosocial complications. Genetic factors contribute substantially to an individual's susceptibility to developing addiction; however, the search for risk alleles has yielded limited success. The initial sensitivity to psychostimulants varies significantly, and has been associated with continued use and abuse. This trait can be studied in animal models, which have emerged as powerful tools to investigate the behavioral response to drugs in a controlled and systematic manner. We are currently screening the sequenced, inbred lines of the *D. melanogaster* Genetic Reference Panel (DGRP) for amphetamine-induced behaviors, with the aim of performing genome wide association studies (GWAS) to identify new genes and gene variants associated with the sensitivity to amphetamine. The DGRP consists of 203 lines that were created by collecting mated females from a natural, outbred population followed by 20 generations of full-sibling inbreeding. The lines harbor most common variants and a representative sample of rare variants, with ~2.5 million SNPs available for analysis. We are quantifying amphetamine-induced increases in locomotor activity, changes in circadian activity, as well as amphetamine-induced mortality, at two distinct doses, using the Trikinetics *Drosophila* Activity Monitors (DAMs). Our analyses have identified substantial variation in the response to amphetamine for all 3 phenotypes. Upon completion of the screen, we will perform GWAS analyses to identify genes and gene networks associated with the psychostimulant response, with the aim of identifying novel mechanisms that modulate the neurobiology of amphetamine action and influence both the initial as well as the prolonged behavioral sensitivity to the drug.