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Good wine and old data get better with age: New insights on gene-by-environment effects of drugs of abuse in mice using GeneNetwork.org

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Gene-by-environment interactions are important for all facets of biology, especially behavior. Families of isogenic strains of mice, such as the BXD family, are excellently placed to study these interactions, as the same genome can be tested in multiple environments over time. BXD strains are recombinant inbred mouse strains derived from crossing two inbred strains —C57BL/6J and DBA/2J mice. The family segregates for around 6 million variants. Many reproducible genometypes can be leveraged, collected in GeneNetwork.org, and old data can be reanalysed with new tools to produce novel insights. We obtained drug and behavioral phenotypes from Philip et al. (2010), and reanalysed their data with new genotypes from sequencing, as well as new models (Genome-wide Efficient Mixed Model Association (GEMMA) and R/qtl2). We discovered quantitative trait loci (QTLs) on chromosomes 3, 5, 9, 11, and 14, not found in the original study. We reduced the candidate genes based on their ability to alter gene expression or predicted protein function. Candidate genes included *Slitrk6* and *Cdk14. Slitrk6,* in a chromosome 14 QTL for locomotion, was found to be part of a co-expression network involved in voluntary movement and associated with neuropsychiatric phenotypes. *Cdk14,* one of only three genes in a chromosome 5 QTL that is associated with handling induced convulsions after ethanol treatment, is regulated by the anticonvulsant drug valproic acid. By using families of isogenic strains, we can reanalyse data to discover novel candidate genes involved in response to drugs of abuse.