Phenotypic Behavioral Expression of Different Genetic Lines of Drosophila melanogaster as Measured by the Negative Geotaxis Assay & Their Response to Lithium Chloride: A Pharmacogenomics Study

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Annually, adverse drug reactions cause 1.5 million hospitalizations. In practice, medicine is often prescribed by trial and error to determine the best drug and dosage. Genotypes influence the level of enzymes that metabolize medications, meaning different dosages and drugs are required for effective treatment. Pharmacogenomics studies this relationship. Many studies focus research on the Cytochrome P450 (CYP450) enzyme system, as CYP450s are the major enzymes that metabolize medications. Few studies have explored the relationship between CYP450s and the metabolization of antidepressants. This led to the research on how genetic makeup in Drosophila melanogaster affects response to the same dosage of known mood stabilizer, lithium chloride. This experiment consisted of three parts. Part 1 involved a genetic screen designed to identify mutations in CYP450 genes that could result in quantifiable differences in behavioral responses that correlate with motivation, used when modeling depression in flies. In Part 2, genetic crosses were used to introduce mutations in Trh[01] into the individual CYP40 mutant backgrounds. Trh[01] is a major enzyme required for serotonin production, a compound known to influence motivation. In Part 3, experimental and control genotypes were given 50mM of LiCl and their motivation levels were tested. The four genetic backgrounds had significant differences in their response to the same dosage of LiCl ($p<.05$) indicating that genetic makeup does influence response to medication. This implies that D. melanogaster is a good system for pharmacogenomics studies and could be used to expand our knowledge about the roles of CYP450s in antidepressant treatment.

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