# Relating Major Depressive Disorder (MDD) to Circadian Signaling in Drosophila melanogaster

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In 2019, over 3.2 million adolescents aged 12-17 experienced symptoms of Major Depressive Disorder (MDD), and 73% of adolescents who experienced MDD did not get enough sleep per night. Depression, which is characterized by lower-than-normal levels of serotonin, can be modeled in Drosophila via chronic vibrational stress (VS). The purpose of this experiment was to elucidate the relationship between circadian oscillator modification and the severity of symptoms of MDD in the model Drosophila melanogaster. The Drosophila Activity Monitor and custom Python code were used to measure sleep. A custom-built circular arena was used to quantify walking behavior. VS caused arrhythmic sleep architecture in w1118 controls. During both the daytime and nighttime, fumin (insomnia-like) mutants had higher numbers of sleep bouts than the w1118 flies, indicating that the fumin mutants experienced less sleep consolidation because their arousal is characterized by enhanced alertness, since they have a higher amount of extracellular dopamine and a decreased arousal threshold. VS exposure increased the number of sleep bouts because it caused more fragmented sleep via the inhibition of 5-HT release to the 5-HT-1A receptors in the a-lobes of the MBs. Flies with elevated tryptophan hydroxylase (Trh) (generated by crossing UAS-Trh;Elav-Gal4) alleviated arrythmicity induced by VS. Trh-elevated flies walked further in 10 minutes than controls, and were minimally affected by VS. Trh is rate-limiting in serotonin synthesis, so elevating it was posited to increase brain serotonin, relieving the effects of VS. Thus, VS-induced sleep irregularity was enhanced with insomnia-like predisposition and alleviated with increased brain serotonin.

**Awards Won:**