

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 α -lobes of the MBs. Flies with elevated tryptophan hydroxylase (Trh) (generated by crossing UAS-Trh;Elav-Gal4) alleviated arrhythmicity 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.