Development of a Caffeine Addiction Paradigm to Examine How Dietary Restriction and Level of TOR Signaling Modulate the Effects of Drugs

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Dietary restriction (DR) studies have shown that decreasing caloric intake is beneficial in numerous organisms ranging from yeast to mammals, and genetic manipulation of the target of rapamycin (TOR) pathway can produce similar effects to those of DR. While DR and manipulation of TOR signaling can prevent disease and increase lifespan, their role in drug addiction and toxicity has not yet been investigated. This study utilized Drosophila melanogaster and caffeine to investigate whether manipulating DR and TOR signaling can protect flies against the harmful effects of caffeine. This study examined both developmental and adult responses to toxicity and also developed a model for addiction and withdrawal. I used the Capillary Feeder (CAFE) assay to measure dietary choice and drug seeking and avoiding. I used geotaxis assays as behavioral read-outs and longevity assays to measure toxicity resistance. This study found that high TOR signaling and increased caloric intake protected flies from the deleterious effects of caffeine during development while low TOR signaling and DR protected adult flies from caffeine addiction and toxicity. It was also discovered that females resisted the detrimental effects of caffeine during development as well as its toxic effects as adults significantly better than males. Efficiently combining genetic manipulation and DR can protect against the harmful effects of drugs such as caffeine.