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Impact of metformin on feeding, behavior, and metabolism in Drosophila melanogaster.

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Introduction

- Metformin is a first-line drug used in the treatment of type II diabetes mellitus.
- It lowers blood glucose levels and increases insulin sensitivity[1].
- Despite its widespread use[2], the degree to which it affects aspects of behavior and metabolism unrelated to diabetes is not fully understood.
- Beneficial effects in numerous model organisms, including decreased triglyceride levels, lifespan extension, and slowed tumor growth[3-6], suggest that metformin could treat a range of non-diabetic conditions in humans, provided more research is done on the lesser-known effects of the drug.
- The molecular pathway by which metformin functions is conserved between humans and *Drosophila melanogaster*. We used the latter organism to conduct a preliminary assessment of metformin's impact on metabolism and physiology.

Research Questions

How does metformin affect the physiology, behavior, and metabolism of *Drosophila melanogaster*?

Specifically, how does the drug affect food consumption, body weight, sleep, and starvation resistance?

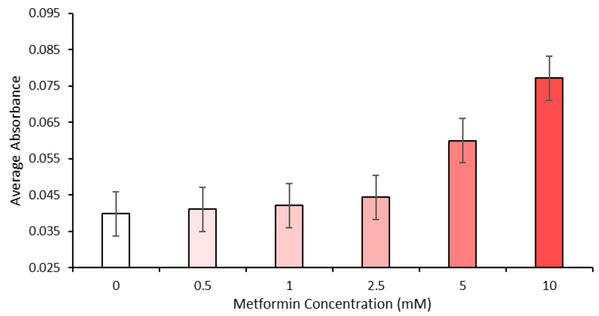
Methods

All experiments involved treatment with fly food supplemented with metformin in concentrations of 0-10.0 mM

- **Food consumption:** ConEx method[8] on supplemented food for 10 days
- **Body weight:** Empty tubes were pre-weighed, then flies were added and weighed before and after above treatment.
- **Sleep:** Drosophila Activity Monitoring (DAM) system following treatment.
- **Starvation resistance:** Metformin treatment followed by transfer to a vial with a wet tissue. Live flies were counted every 6-10 hours.

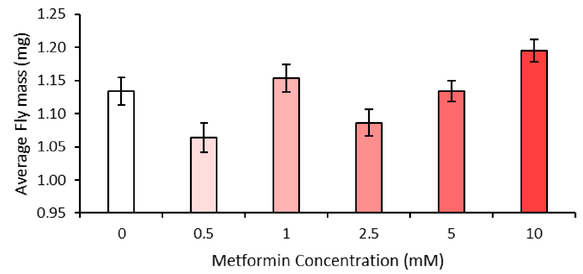
Results

Figure 1: Metformin Increases Food Consumption



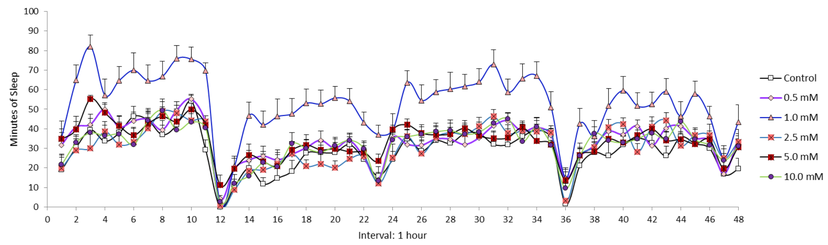
- Results from ConEx analysis of dye excreted on vial walls
- Clear trend of increased food consumption in a dosage-dependent manner
- Significant increase compared to control in 5 mM and 10 mM flies (t-test, $p<0.05$)

Figure 2: Metformin Affects Body Weight



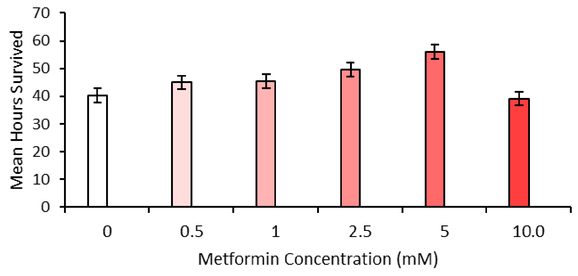
- Flies were weighed after treatment with metformin
- Statistically significant increase in body weight at 10 mM, significant decrease at 0.5 mM (t-test, $p<0.05$)

Figure 3: Metformin Does Not Significantly Affect Sleep



- Metformin did not significantly affect sleep at most concentrations
- An exception: At 1 mM, an increase in sleep was noted

Figure 4: Metformin Does Not Significantly Affect Starvation Stress



- Treatment at 4 concentrations showed a trend towards longer survival times in flies removed from a food source
- 5 mM survival compared to control was nearly significant (t-statistic of 0.064, $p<0.05$)
- At 10 mM, metformin slightly decreased mean survival time compared to the control

Discussion

- Metformin significantly increases food consumption in a dosage-dependent manner.
- The data also suggests a trend towards increased body weight with higher dosages, though the effect is not consistent enough to draw strong conclusions at this time. One reason for the decrease in weight at low concentrations could be that metformin's triglyceride-lowering effect[9] is overshadowed by increased feeding at high concentrations.
- At lower concentrations (1 mM), metformin increased sleep. This could suggest a link between metabolism and sleep.
- Treated flies were less vulnerable to starvation stress up to a drug concentration of 5 mM. The lower mean survival time at 10 mM suggests that metformin increases sensitivity to starvation stress at higher concentrations.
- Further work should include a genome-wide association study on these changes in *Drosophila Melanogaster*. This will reveal the genes that play a role in increased food consumption, which was the strongest trend observed in this preliminary study.

Acknowledgements

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