The Role of Dopamine in Regulating Feeding Behavior Using Optogenetics in Drosophila Melanogaster

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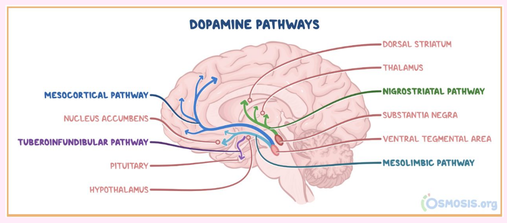
Introduction

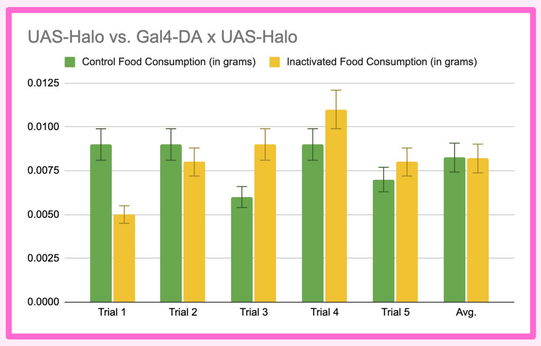
- Dopaminergic neurons (DNs) are involved in:
  - Movement
  - Pleasurable reward and motivation
  - Mood and behavior
  - Appetite
- New research suggests that DN's influence on motivation through dopaminergic reward systems can have implications for dietary decisions
  - Palatable foods can stimulate food intake even when hunger is absent
  - Reward-stimulated motivational feeding also interacts with homeostatic systems for energy balance
- Mesolimbic and mesocortical pathways of the dopamine reward system have ties to controlling food intake



  - **Mesolimbic Pathway:** Connects the VTA to the nucleus accumbens; all nerve axons communicate using dopamine
    - Structures of this pathway work to inform an individual of how rewarding a behavior might be, and are activated by palatable foods, increasing feeding without hunger (incentive salience: seeking out natural rewards; e.g. food)
  - **Mesocortical Pathway**: Connects the VTA to cortical areas
    - The cortical areas are influential in neural responses to rewards and cognitive processes related to desire (e.g. reward evaluation and decision-making related to food)
- In flies, the key dopaminergic pathways are composed of PPL1 and PPL2 neurons
  - **PPL1**: Located in the protocerebral bridge; modulates feeding behavior based on reward signals
  - **PPL2**: Located in the anterior protocerebral bridge; influences feeding via homeostatic mechanisms
- This study **investigates the influence of dopamine levels on food consumption based on the prior relationship observed between the two factors**
  - Results of this research can reflect on addressing and increasing knowledge underlying **eating disorders, obesity, and T2DM,** as food consumption levels hold major relevance for these health issues

Results

A



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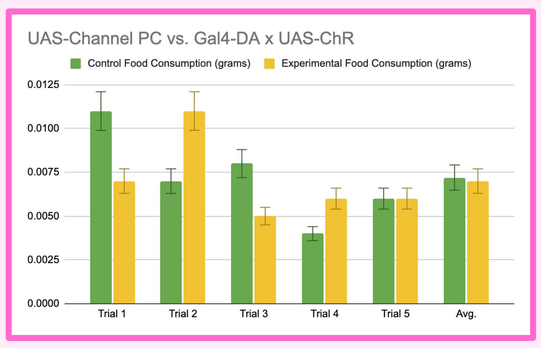

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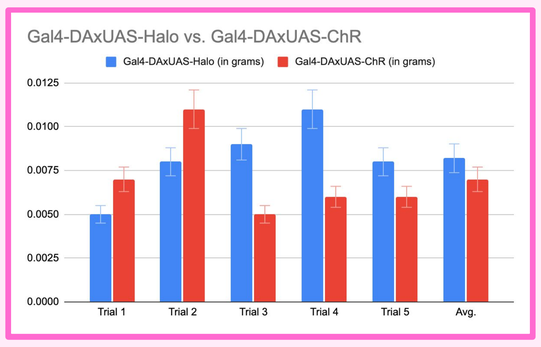

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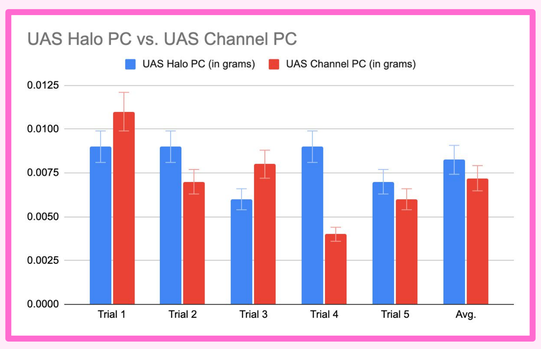

Fig. 3: Effect of DN modulation on food consumption
A: Comparison between halorhodopsin (inactivated) control and experimental groups. (p=.99867 by ANOVA test)
B: Comparison between channelrhodopsin (over-activated) control and experimental groups. (p = .99867 by ANOVA test)
C: Comparison between experimental groups. (p=.79510 by ANOVA test)
D: Comparison between parental control groups.
(p = .92662 by ANOVA test)

Discussion/ Conclusions

- The acute activation of dopamine showed **no significant difference** in the average measure of food consumption over the 2-hour duration in comparison to the control
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- Limitations to the research included:
  - Limited testing duration (2-hours)
  - Minute scale of weight preventing close investigation of differences in consumption level
- These results support the idea that levels of food consumption are not directly influenced by acute dopamine modulation
  - This contrasts with established research describing dopamine's involvement in reward-based feeding through the mesocortical and mesolimbic systems
    - The results suggest that these systems may not be directly involved in changes in short-term consumption patterns
  - Future research could look into the role of dopamine in dietary decision making (qualitative food choices over quantitative consumption)
  - These results might point to other neurological factors influencing diseases related to consumption amount (e.g. eating disorders, obesity)

Visualization

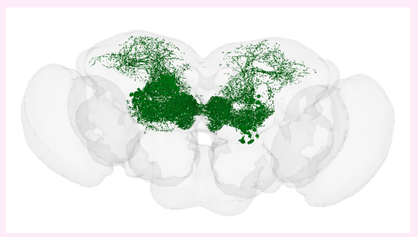

Fig. 4: Dopamine neurons highlighted in fruit fly brain.

Fig. 5: PPL2 pathway (left) and PPL1 pathway (right) in fruit fly brain.

Methods

- The **Gal4/UAS system** is a system that uses genetic crosses to achieve the ability to activate or inactivate a neurotransmitter of choice in the crossed specimen (fruit flies).
  - Gal4 8848 (dopamine) x UAS-Halorhodopsin
    - Halorhodopsin: Yellow light activated (570-590nm), Cl- ion channels
  - Gal4 8848 (dopamine) x UAS-Channelrhodopsin
    - Channelrhodopsin: Red light activated (620-750nm), Na+ ion channels
- **Optogenetics** is the tool used on the aforementioned crosses which uses different wavelengths of light to activate and inactivate the desired neurons. This replaces the biological structure of voltage-gated ion channels, making the channels sensitive to light instead.
- **Behavioral Assay:** We utilized a self-designed feeding assay that measures food consumption. Nine flies were isolated in a petri dish with an agar base layer and 0.500 grams of food present. The petri dish was left in a dark environment with either yellow or red light present. The food container was measured after 2-hours to record the difference in weight from before the trial, which translated to level of food consumption.

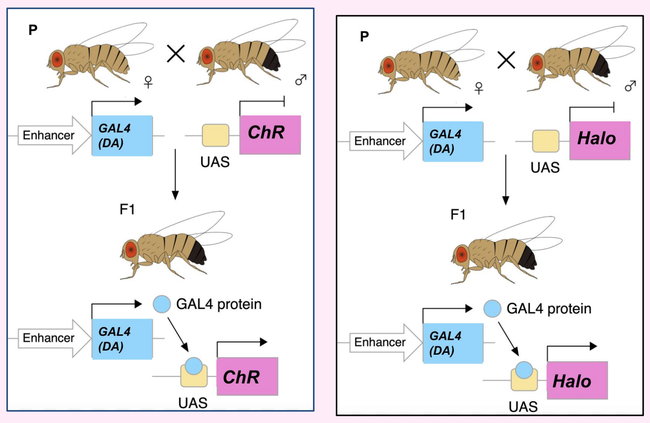

Fig 1: Gal4/UAS cross
Shows Gal4 (transcription factor) binding to UAS (coupled to target gene) and transcribing that particular gene.

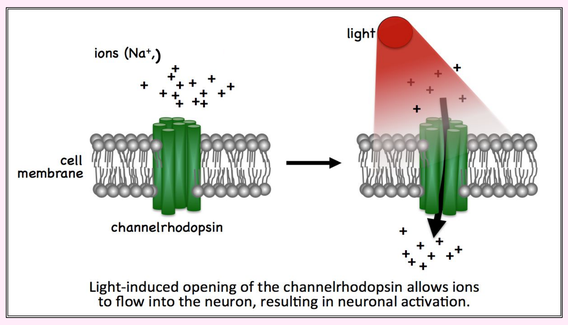

Fig 2: Optogenetics and light
Shows an optogenetic system in which Na+ ion channels have become light-gated. Red light activates the neuron firing as the sodium channels are now coupled to the channelrhodopsin.

References

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I would like to thank Dr. Gobrogge for being such a helpful and impactful mentor, Muriel Li for taking the time to help formalize my project ideas and processes, my lab mates for providing consistent support, and my family for being a constant foundation for me and making all of these experiences possible.