Impacts of Acetylcholine in Relation to Learning in Neurodevelopmental Disorders

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Introduction

- Individuals with Autism Spectrum Disorder and Attention Deficit-Hyperactivity Disorder show deficits in cognitive tasks, e.g. learning
- Because most research associates learning with dopamine and serotonin, acetylcholine (ACh) is often overlooked as a neurotransmitter in learning
- It plays a part in encoding memories, and therefore learning. Thus, lower levels predict less consolidation and impaired hippocampus function in humans[1]
- In our lab, the Drosophila melanogaster cholinergic system works as a model for neurodevelopmental disorders like ASD and ADHD due to its reduced complexity, similarity to human genetics, & behavior while allowing specific genetic modifications[2]
- In flies, the antennal lobe is in charge of learning and function for olfaction and gustation which is present in this study[3]
- The above information leads to the hypothesis that deactivated ACh neurons will block the learning and memory of a conditioned preference while activated ACh neurons will enhance it

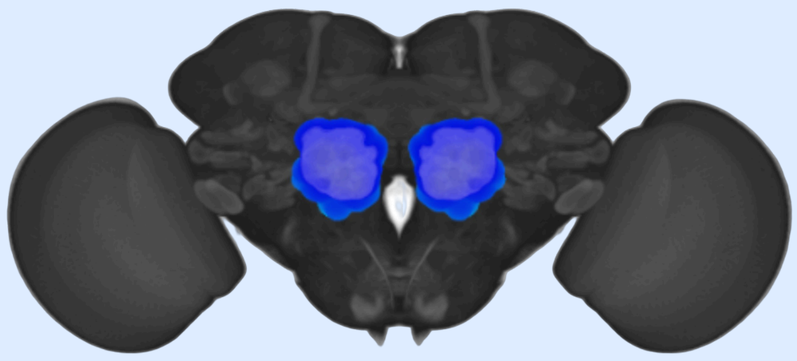


Figure 1. ACh expression in antennal lobes.[4]

Methods

- Using a *Drosophila melanogaster* model and the binary Gal4/UAS system → 6793 x 8514 for visualization, 6793 x 41752 and 6793 x 55136 for neuron manipulation via yellow and red light
- Red light Channelrhodopsin to activate ACh channels & yellow light Halorhodopsin to deactivate ACh channels for 1.5 hours prior to testing using 10% vinegar/.5g yeast as CS's
- 6 vials total: ChR/Vinegar, HaloR/Vinegar, ChR/Yeast/Neutral, ChR/Vinegar/Neutral, ChR/Yeast, HaloR/Yeast
- Drosophila Activity Monitors are used to measure fly activity after being conditioned to observe food preference, using a preference assay for 1 hour
- Finding results by investigating the amount of time the fly spent on each food in each vial

Results

- Vial 1 - control - ChR|Yeast
  - expected: Yeast, No preference
  - observed: No preference
- Vial 2 - control - ChR|Vinegar
  - expected: Vinegar
  - observed: Strong Vinegar Preference
- Vial 3 - *experimental* - ChR|Vinegar
  - expected: Vinegar
  - observed: Yeast
- Vial 4 - *experimental* - HaloR|Vinegar
  - expected: No preference, Yeast
  - observed: No preference
- Vial 5 - *experimental* - ChR|Yeast
  - expected: Yeast
  - observed: Slight Vinegar Preference
- Vial 6 - *experimental* - HaloR|Yeast
  - expected: Vinegar, No preference
  - observed: Strong Vinegar Preference for the first half, then Yeast Preference

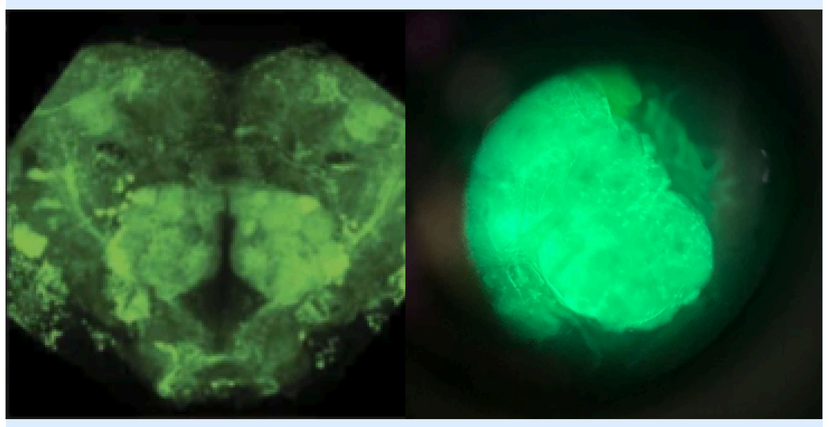
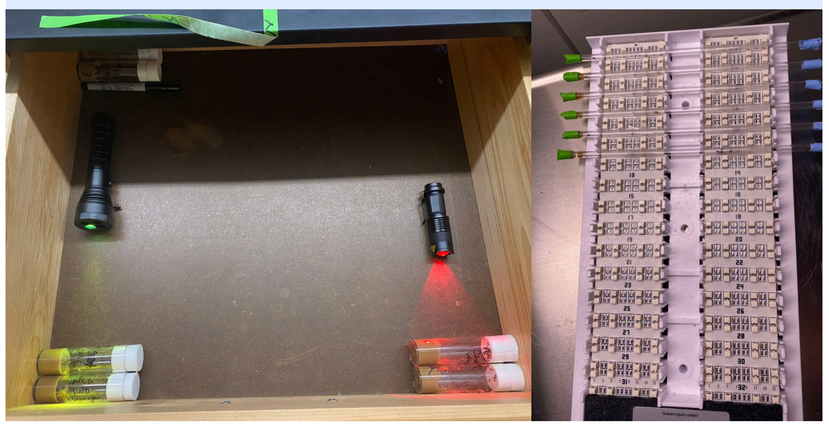


Figure 2. Cholinergic pathways in *Drosophila* brains dissected and imaged with EGFP labeling.

- add graphs later (figure desc in font size 32)

Figure 3. (R) Experimental setup for conditioning & data collection via DAMs.



Discussion

- Other studies in optogenetics show similar patterns after activation/inactivation of neural pathways, showing that the altered behaviors are consistent. However, due to time & resource constraints, this study wasn't able to research as in-depth[5]
- The control group acted successfully as sensitization tests to establish a baseline preference for the experimental groups
- The experimental groups consistently the opposite of what was hypothesized
  - Whether activated ACh neurons inhibited learning or taught conditioned aversion to the food requires further study
  - When ACh was activated, the flies avoided the food they were conditioned to and preferred the other
  - When ACh was inactivated, the flies did not learn to prefer the food they were exposed to, following their natural preference or did not show one
- Future directions:
  - Before reaching definite conclusions, the study should be replicated with more trials and bigger sample sizes
  - Measure and compare the strengths of the preferences with the baseline via a power test - most helpful for the ones that showed no preference or the opposite
- Implications:
  - More extensive research on ACh's role in learning can inform further treatments for neurodevelopmental disorders like ADHD and ASD that involve ACh
  - If results are replicated in future studies, findings can aid strategies to reverse the effects and enhance learning

References

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