Optogenetic Modulation of Dopamine Neurons Induces Changes in Sleep and Activity in Fruit Flies

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Introduction

- Dopaminergic neurons (DNs) are well-known to play roles in movement, motivation, and memory in both humans and animals.
- DNs are also implicated in sleep and arousal.
- In diseases where DNs are affected, sleep disorders are often present as well.
- In Parkinson's Disease, DNs degenerate, leading to symptoms of insomnia, daytime sleepiness, and restless legs syndrome in patients.
- Increased DN activity is implicated in schizophrenia. Patients also often present with insomnia and restless legs syndrome.
- In this study, we investigated the role of DNs in the sleep of fruit flies via chronic activation and inactivation.

Results

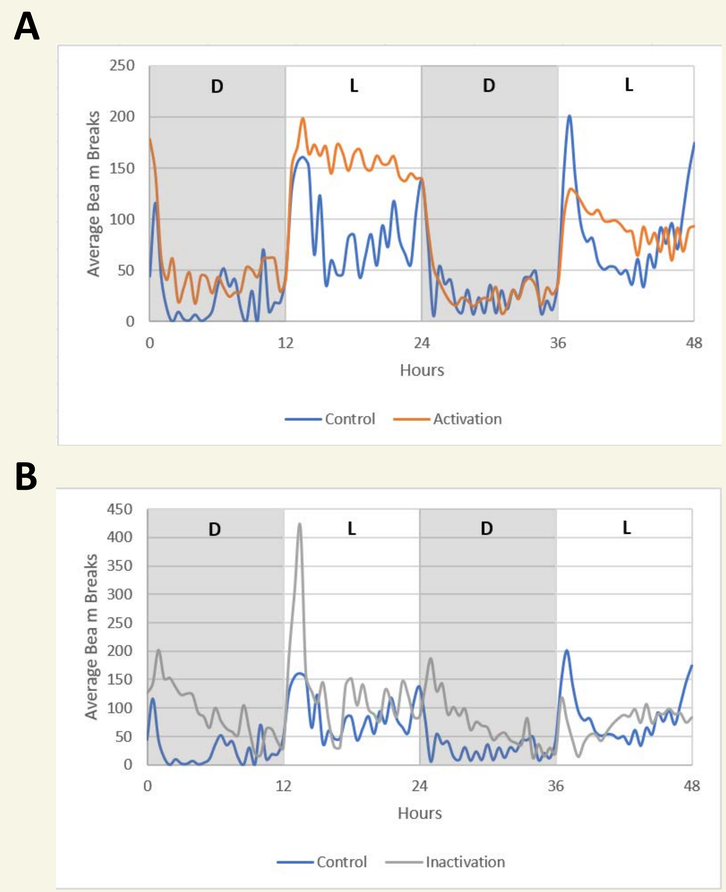

Fig. 3: Effect of DN modulation on 48-hr circadian rhythm.
A) Effect on flies with chronically activated DNs. B) Effect on flies with chronically deactivated DNs.

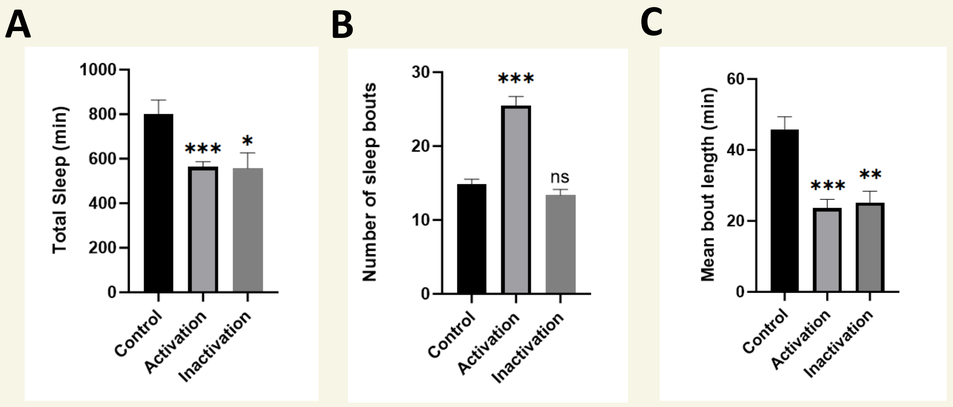

Fig. 4: Quantification of the effect of DN modulation on sleep.
Results are expressed as mean + SEM. Data was analyzed using t-test (***$p < 0.001$; **$p < 0.01$; *$p < 0.05$). A) Average total sleep for both chronic inactivation and activation of DNs. B) Average number of bouts of sleep for both chronic inactivation and activation of DNs. C) Average duration of bout for both chronic inactivation and activation of DNs.

Methods

The GAL4/UAS system is widely-used genetic tool to drive expression of a specific gene in a tissue of interest.

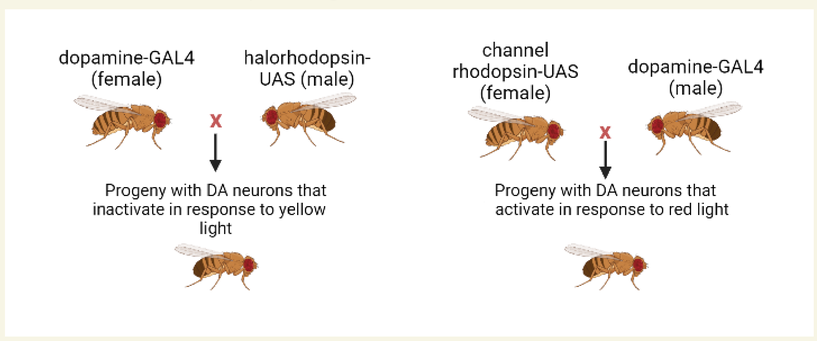

Fig. 1: Genetic crosses.

Ion channels are present in the DNs of the progeny that open in response to specific wavelengths of light. This causes the neurons to either hyperpolarize or depolarize.

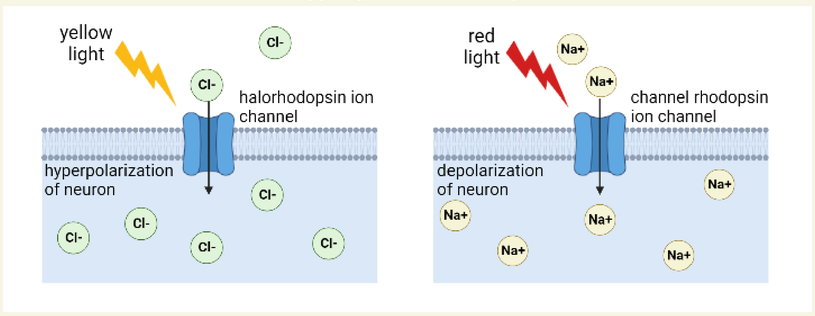

Fig. 2: Effect of light on ion channels in progeny.

Circadian Rhythm and Sleep Assay

- Progeny was placed into glass vials with food at both ends.
- Drosophila Activity Monitor System was used to monitor sleep and wake activity of the flies for 48 hours.
- Red and yellow light was shone on flies for duration of assay to chronically activate and inactivate DNs respectively.

Visualization

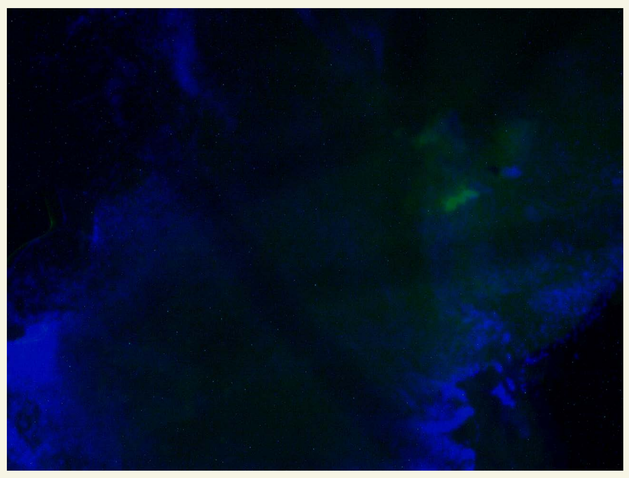

Image 1: Dopaminergic neurons highlighted in green.

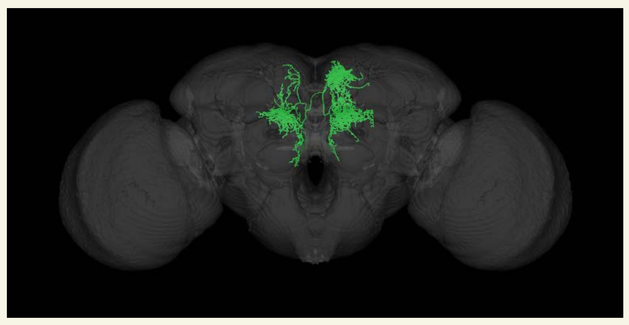

Image 2: 3D view of dopaminergic neurons in Virtual Fly Brain Database.

Discussion/ Conclusions

- Both chronic inactivation and activation of DNs causes a significant decrease of total sleep duration in fruit flies.
- Chronic activation seems to cause flies to be more active during the day, but not during the night.
- Chronic activation also causes flies to have more bouts of sleep, but less sleep per bout.
- In contrast, chronic inactivation causes flies to sleep less per bout, but have no change in bout amount.
- Due to dopamine's involvement in arousal, it was surprising to see that chronic inactivation of DNs causes flies to sleep less, both per bout and in total.
- Despite this, both activation and inactivation of DNs were able to model the sleep disorders exhibited in schizophrenia and Parkinson's respectively.
- In conclusion, this study demonstrates that DNs play a significant role in the sleep of fruit flies.

References

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