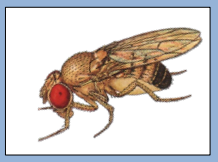
The Effect of FTD on *Drosophila* Cognitive and Motor Function

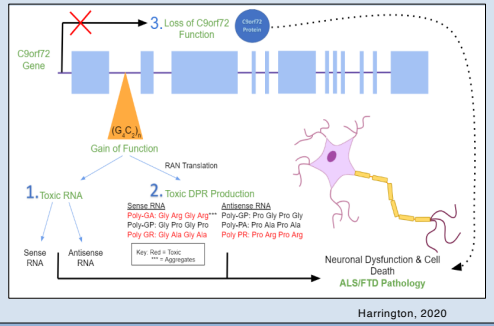
C. Barber, J. Bonavolonta, M. Depoy, O. Faro, J. Jacobs, and M. Tipping
Department of Biology, Providence College, Providence, RI 02918
Email: mtipping@providence.edu



Abstract

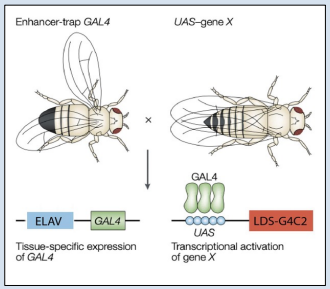
Frontotemporal dementia (FTD) is one of the most common forms of early onset dementia. This neurodegenerative disease has various symptoms such as loss of emotion/empathy, impaired judgment, mobility issues, loss of social skills, and other behavioral, motor and cognitive issues. It is well documented that many individuals with neurodegenerative diseases, including FTD, experience disruptions in sleep. The purpose of our research project is to observe the affect FTD has on sleeping pattern (circadian rhythm). We will analyze circadian rhythms in flies harboring mutations in genes known to be regulate our biological clock to verify our experimental design. We will then use this same procedure to analyze the sleeping patterns of flies modeling FTD compared to control flies. This project will provide a starting point for exploring how and why circadian rhythm is altered in FTD patients.

FTD Background



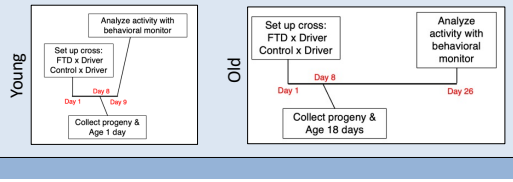
Harrington, 2020

GAL4-UAS Expression System

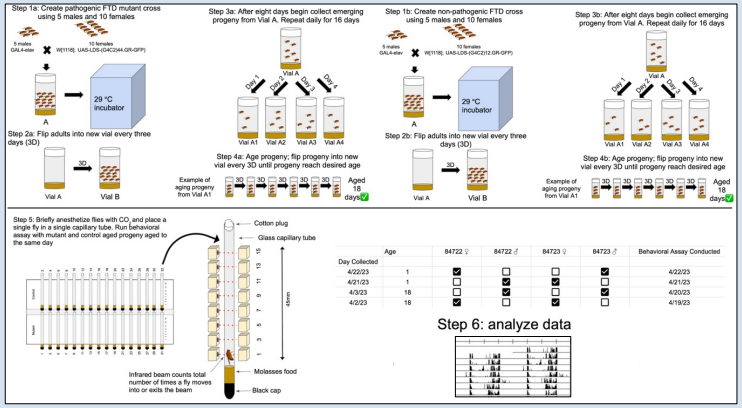


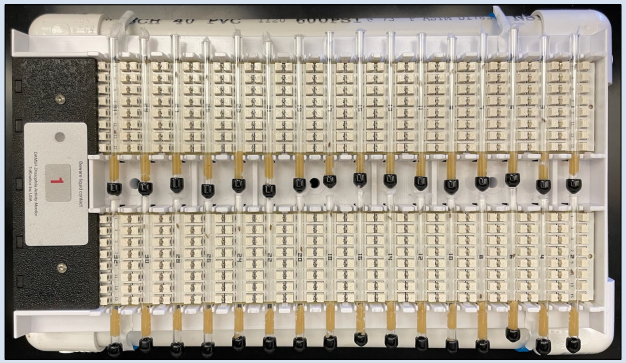
St Johnston, 2002

Activity Study Timeline

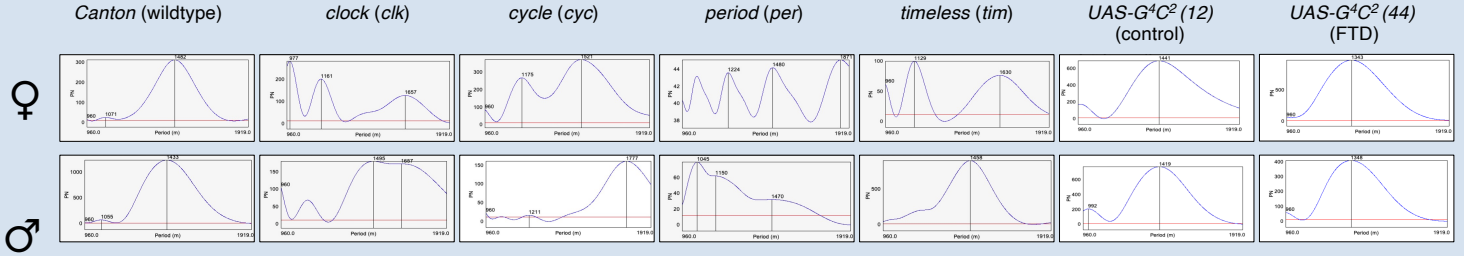


Experimental Design





Circadian rhythm analysis



Lomb-Scargle periodogram of female and male flies from wildtype, biological clock gene mutants, control and pathogenic flies for FTD. Each graph is one representative individual. For each genotype 10 flies were analyzed. All flies were kept at 25 C with a 12 hour light/12 hour dark light cycle (9am-9pm light).

Conclusions

1. We observe a normal circadian rhythm in Canton (wildtype) male and female flies.
2. Flies carrying mutations in genes that regulate the biological clock (*clk, cyc, per, tim*) demonstrate an irregular circadian rhythm, with arrhythmic patterns of sleep observed. This was observed in both males and females
3. Flies modeling FTD had shorter/shifted cycle compared to control flies, in both males and females.

Future Directions

1. Repeat these experiments with additional biological replicates.
2. Analyze free running circadian rhythm in flies modeling FTD.
3. Molecularly analyze expression of *clock*, *cycle*, *period* and *timeless* in flies modeling FTD.
4. Conduct a maze experiment to investigate the effect of reward on memory and learning.

References

1. Balendra R, Isaacs AM. C9orf72-mediated ALS and FTD: multiple pathways to disease. *Nature Reviews Neurobiology*, 14(9): 544-558. (2018)
2. Goodman, LD., et al. Toxic expanded GGGGCC repeat transcription is mediated by the PAF1 complex in C9orf72-associated FTD. *Nat. Neurosci.*, 22, 863-874 (2019).
3. St Johnston, D. The art and design of genetic screens: *Drosophila melanogaster. Nat Rev Genet* **3**, 176–188 (2002).
4. Mathieson, D. Developing and Characterizing a TDP-43 Drosophila Model of Frontotemporal Dementia. *The University of Arizona* (2017).

Acknowledgements

We would like to thank the Providence College Center for Engaged Learning for their funding of this work. Without their support we would not have been able to purchase the behavioral monitor that has allowed us to produce meaningful data on the sleeping patterns of our flies!