

The effects of heart medication on the heart rates of *Drosophila melanogaster*

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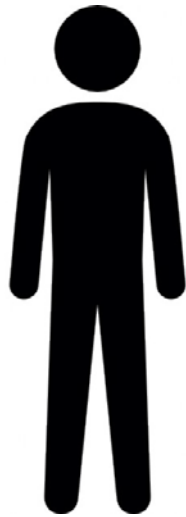
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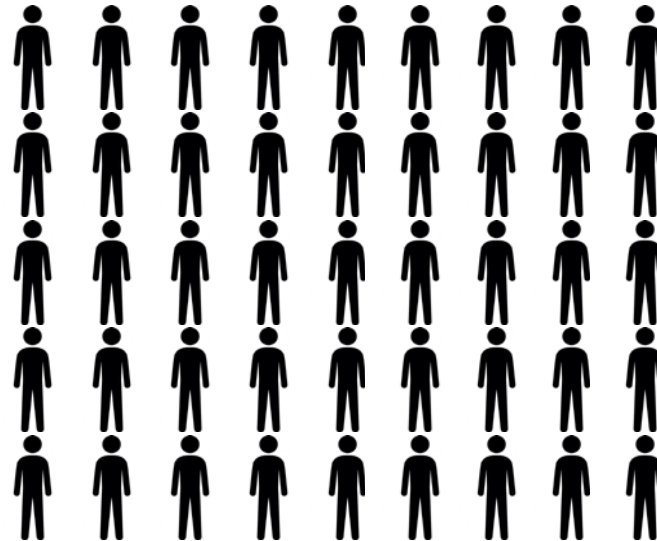
What is the leading cause of death in the United States?

Cardiovascular Disease

Every 40 seconds one
American dies.



Within this 30 minute
presentation 45 Americans
will die.



American Heart Association (2015)

Models of Cardiovascular Disease



Current Models:

- Mammals and zebra fish
- Similar in anatomy/physiology

Is a new model necessary?

- Current models expensive and tedious to work with
- Current need -- a model organism that is:
 - More efficient to work with in lab
 - Still an accurate model of human cardiac disease

Drosophila melanogaster (*D. mel*)



Is *D. mel* a more efficient organism to work with in the lab?

- Short life span
- Genome sequenced
- Easy to culture
- Low cost

Drosophila melanogaster (*D. mel*)



Is *D. mel* a potential model of human cardiovascular disease?

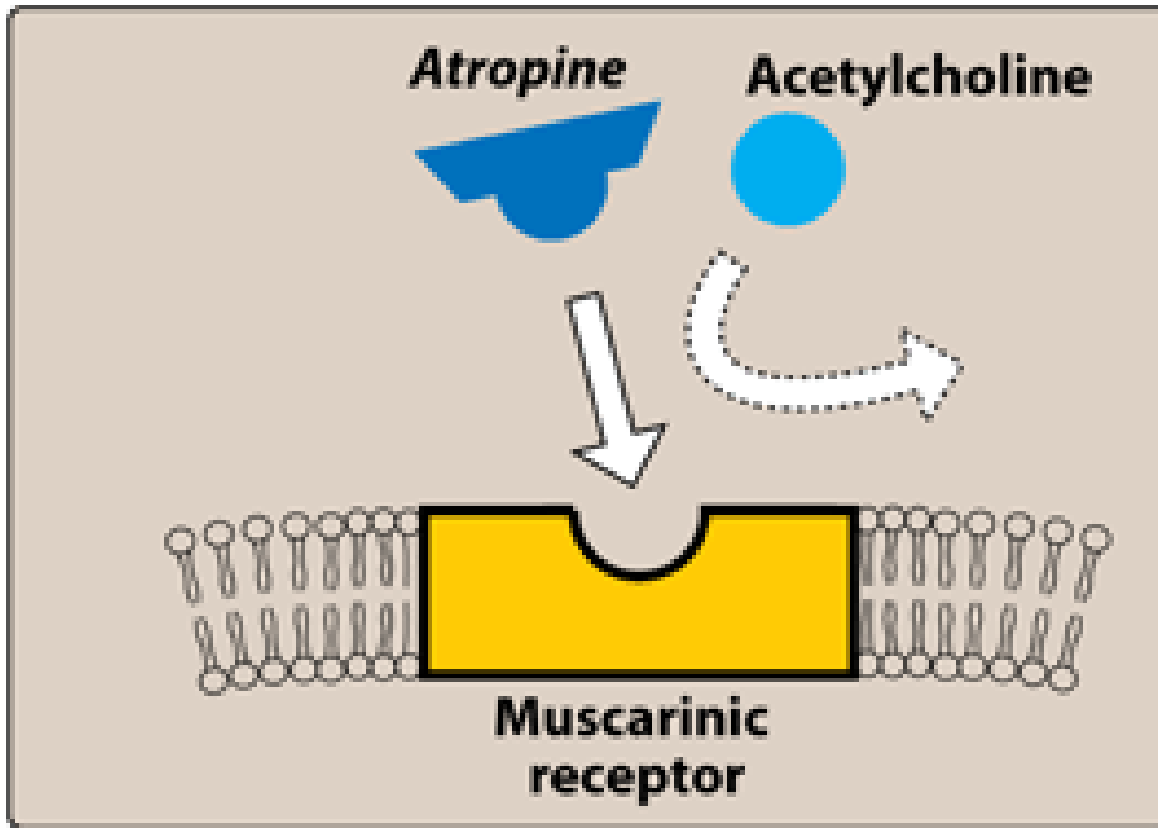
Anatomical differences:

- Only one cardiac chamber
- One layer of cardiomyocytes
- Lacks coronary arteries

Similarities:

- Protein and genetic makeup
- Physiological similarities
 - Structural defects, arrhythmias (irregular heart rhythm), cardiomyopathies (disease of the heart muscle)

Atropine



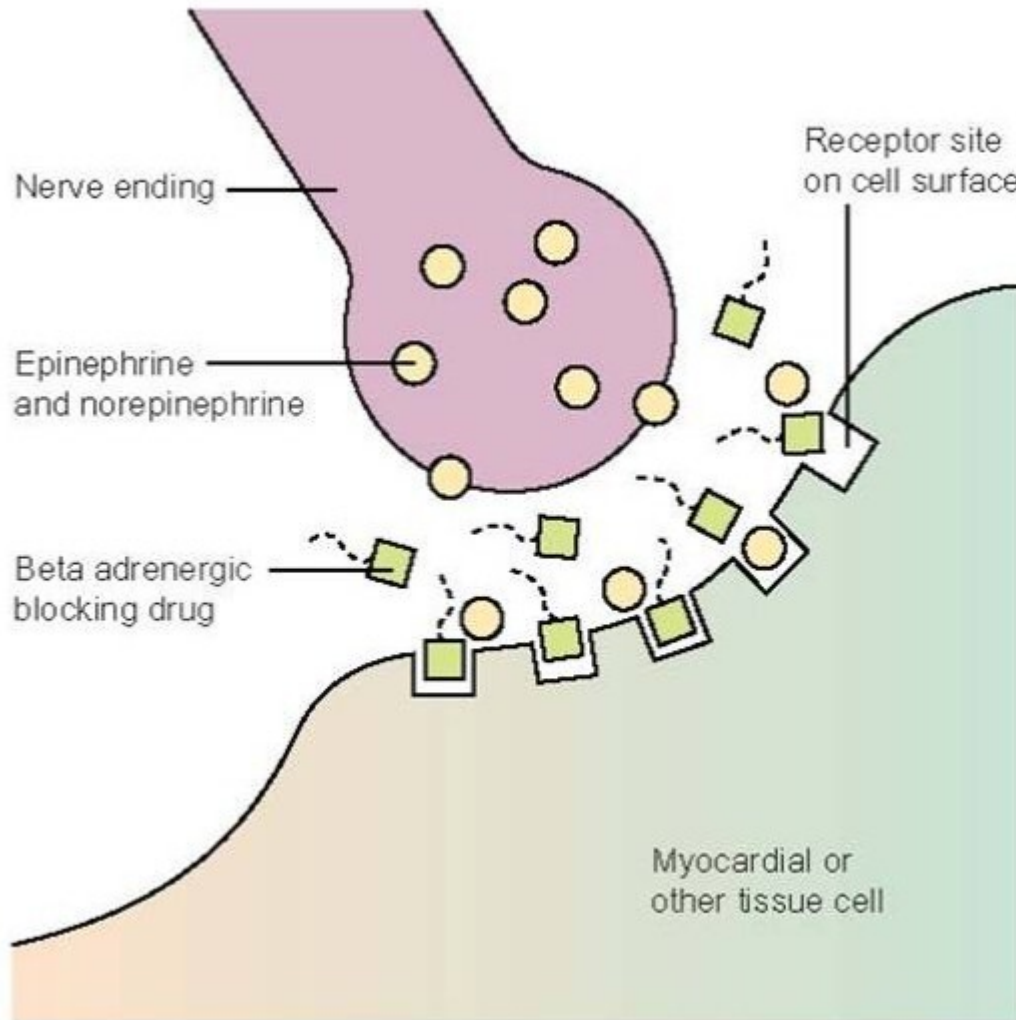
- Acetylcholine binds to muscarinic acetylcholine receptors aiding in parasympathetic influence on heart rate
- Atropine binds and blocks these receptors → Heart rate increases

Could atropine work similarly in *D. mel*?

Ren et al. (2015)

Analysis of the protein structure of one muscarinic acetylcholine receptor in *D. mel* is similar to humans.

Propranolol hydrochloride



- Epinephrine and norepinephrine bind to beta adrenergic receptors to aid in sympathetic influence on heart rate
- Beta blockers like propranolol hydrochloride bind and block these receptors → Heart rate decreases

Could propranolol hydrochloride work similarly in *D. mel*?

Spindler et al. (2013)

D. mel have G-protein receptors similar to beta1-adrenergic receptors in humans.

Research Question

I hypothesized that atropine and propranolol hydrochloride in the growth media of third instar larvae would cause an increase and decrease respectively in the heart rates of *D. mel*.

In other words:

Give atropine to *D. mel* larvae → increase in heart rate

Give propranolol hydrochloride to *D. mel* larvae → decrease in heart rate

Methods

Day 1:

Adult flies moved to fresh vials

Days 2-5:

Adult flies mated

Larvae hatched and grew

Day 6:

Second instar larvae moved to fresh media

Atropine or propranolol hydrochloride was administered

Day 7:

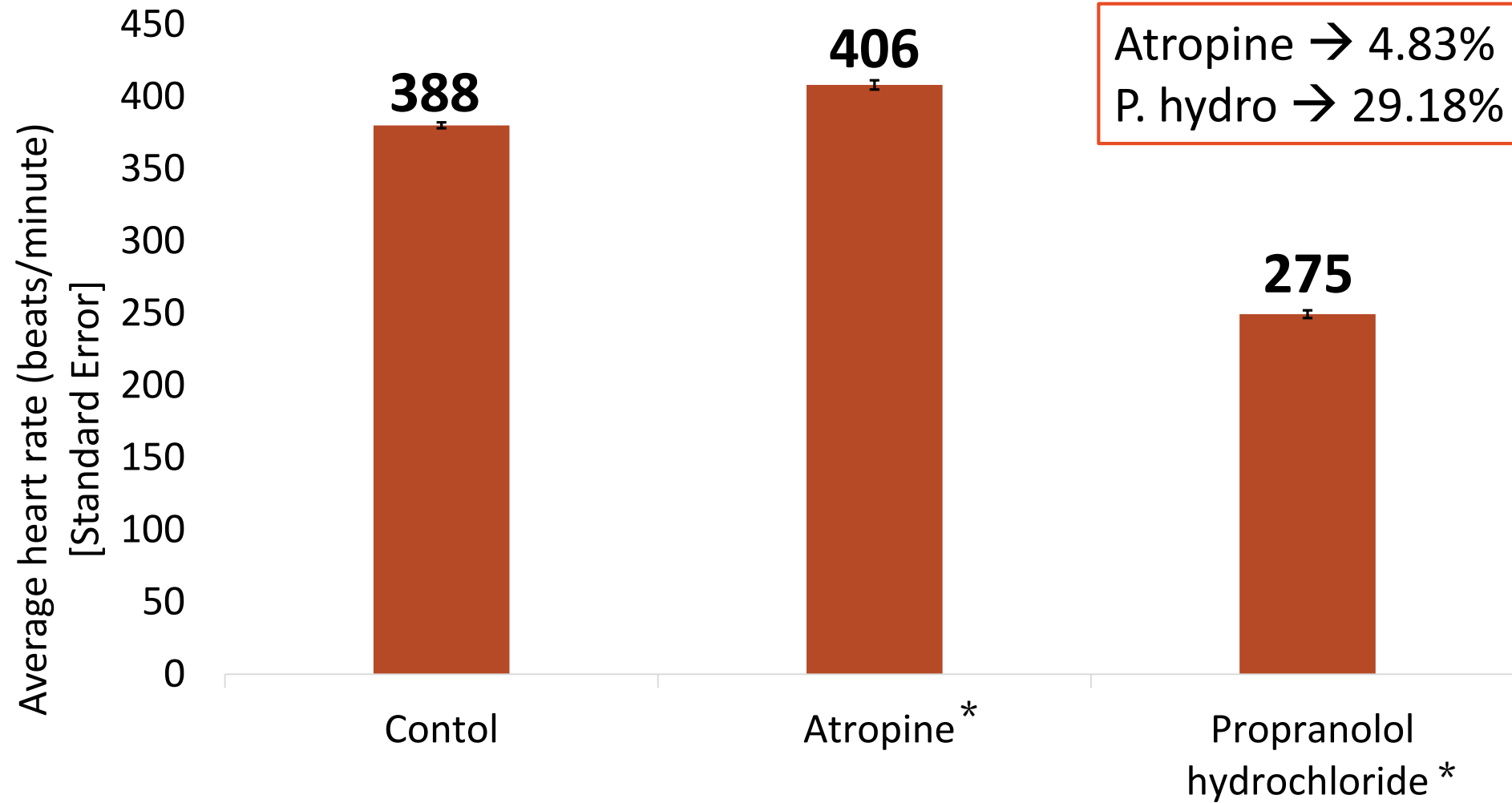
Third instar larvae heart rates recorded

Recording Heart Rate

- Heart rate recorded 3x per larva in 15 second intervals (50 total for each group)
- Tap-counter app and timed video



Results



Atropine → 4.83% increase
P. hydro → 29.18% decrease

*Significantly relevant ($p < 0.001$)

Discussion

The hypothesis was supported.

- Propranolol hydrochloride decreased heart rate
- Atropine increased heart rate

Future research:

- Eliminate bias through blinded study
- Eliminate human error with technology
- Alter concentrations to better compare to other research

Discussion

- *D. mel* could be a potential model for human cardiovascular disease research.
- Additionally, *D. mel* could be used in preliminary pharmaceutical testing for new medication.

Acknowledgements

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References

1. Atropine. (2014). *Reactions Weekly*, 1503(1), 9.
2. Bakkers, J. (2011). Zebrafish as a model to study cardiac development and human cardiac disease. *Cardiovascular Research*, 91(2), 279–288.
3. Cammarato, A., Ahrens, C. H., Alayari, N. N., Qeli, E., Rucker, J., Reedy, M. C., ... Foster, D. B. (2011). A Mighty Small Heart: The Cardiac Proteome of Adult *Drosophila melanogaster*. *PLoS ONE*, 6(4).
4. Coppola, S., Froio, S., & Chiumello, D. (2015). β -blockers in critically ill patients: From physiology to clinical evidence. *Critical Care*, 19(1), 1-9.
5. Doke, S. K., & Dhawale, S. C. (2015). Alternatives to animal testing: A review. *Saudi Pharmaceutical Journal*, 23(3), 223–229.
6. Gibson, J. A., & Raphael, B. (2014). Understanding beta-blockers: *Nursing*, 44(6), 55–59.
7. Hasenfuss, G. (1998). Animal models of human cardiovascular disease, heart failure and hypertrophy. *Cardiovascular Research*, 39(1), 60–76.
8. Kinkade, A. (2012). Emergency Cardiovascular Pharmacotherapy: A Point-of-Care Guide. *The Canadian Journal of Hospital Pharmacy*, 65(4), 322.
9. Linford, N. J., Bilgir, C., Ro, J., & Pletcher, S. D. (2013). Measurement of Lifespan in *Drosophila melanogaster*. *Journal of Visualized Experiments*, (71), 50068.
10. Medioni, C., Sénatore, S., Salmand, P.-A., Lalevée, N., Perrin, L., & Sémériva, M. (2009). The fabulous destiny of the *Drosophila* heart. *Current Opinion in Genetics & Development*, 19(5), 518–525.

References

11. Mozaffarian, D., Benjamin, E. J., Go, A. S., Arnett, D. K., Blaha, M. J., Cushman, M., ... Turner, M. B. (2015). Executive Summary: Heart Disease and Stroke Statistics—2015 Update. *Circulation*, *131*(4), 434–441.
12. Ocorr, K., Akasaka, T., & Bodmer, R. (2007). Age-related cardiac disease model of *Drosophila*. *Mechanisms of Ageing and Development*, *128*(1), 112–116.
13. Pandey, U. B., & Nichols, C. D. (2011). Human Disease Models in *Drosophila melanogaster* and the Role of the Fly in Therapeutic Drug Discovery. *Pharmacological Reviews*, *63*(2), 411–436.
14. Patel, R., Nagueh, S. F., Tsybouleva, N., Abdellatif, M., Lutucuta, S., Kopelen, H. A., ... Marian, A. J. (2001). Simvastatin Induces Regression of Cardiac Hypertrophy and Fibrosis and Improves Cardiac Function in a Transgenic Rabbit Model of Human Hypertrophic Cardiomyopathy. *Circulation*, *104*(3), 317–324.
15. Ren, G. R., Folke, J., Hauser, F., Li, S., & Grimmelikhuijzen, C. J. P. (2015). The A- and B-type muscarinic acetylcholine receptors from *Drosophila melanogaster* couple to different second messenger pathways. *Biochemical and Biophysical Research Communications*, *462*(4), 358–364.
16. Rosenthal, N., & Brown, S. (2007). The mouse ascending: perspectives for human-disease models. *Nature Cell Biology*, *9*(9), 993–999.
17. Seyres, D., Röder, L., & Perrin, L. (2012). Genes and networks regulating cardiac development and function in flies: genetic and functional genomic approaches. *Briefings in Functional Genomics*, *11*(5), 366–374.
18. Spindler, S. R., Mote, P. L., Li, R., Dhahbi, J. M., Yamakawa, A., Flegal, J. M., ... Lublin, A. L. (2013). β 1-Adrenergic receptor blockade extends the life span of *Drosophila* and long-lived mice. *Age (Dordrecht, Netherlands)*, *35*(6), 2099–2109.

Questions?