The Influence of Imipramine on the Egg-Laying Behavior of *Caenorhabditis elegans*

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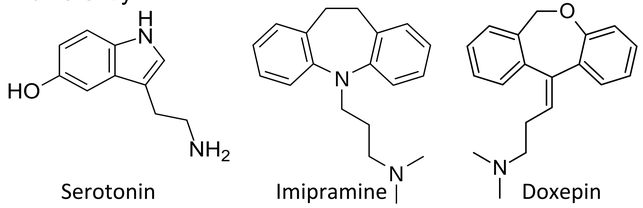
Introduction

Discovering new ways to treat mental disorders is at the forefront of scientific research due to their imposing challenges on international health. As of today, the prevalence of any mental disorder worldwide is at 13.4%. Out of this, anxiety and depressive disorders made up 6.5%, and 2.6%, respectively. Because so many people are affected by these diseases, it is imperative that treatment be given to those who need it. Current mental health treatments include psychotherapy, hospitalization and drug therapy. Current drug therapy options include imipramine and doxepin, marketed as Tofranil and Silenor, respectively. Both are classified as a tricyclic antidepressants (TCA), and are used to treat various mental disorders such as depression and general anxiety. TCA's enhance the effectiveness of the neurotransmitters, serotonin and norepinephrine, as they predominantly inhibit their reuptake. However, imipramine and doxepin also affects additional pathways such as acetylcholine, histamine and the α1-adrenergic blockade; which causes undesired side effects including lack of coordination, and blurred vision in imipramine, and dysrhythmia and severe hypotension in doxepin. Although the two TCAs are very similar in chemical structure they undergo distinct mechanisms of action which affect each pathway differently.



Materials and Methods

In order to examine the influence of imipramine, *C. elegans* were exposed to ethyl methanesulfonate (EMS) to induce mutagenesis. *C. elegans* mutants were then incubated in a 10 mg/mL imipramine solution for 70 minutes. Out of all the mutants tested, one strain of C. elegans (Strain A) was chosen due to its decreased egg-laying in imipramine solutions. Strain A worms underwent further egg-laying assays to compare the egg-laying effects of similar drugs. The worms were incubated in a 0.016 mg/mL doxepin solution, 5 mg/mL serotonin solution, 10 mg/mL imipramine solution, and a control M9 solution for 70 minutes.

Egg Laying Analysis of Mutant and N2 *C. elegans* in Imipramine and M9 Solution

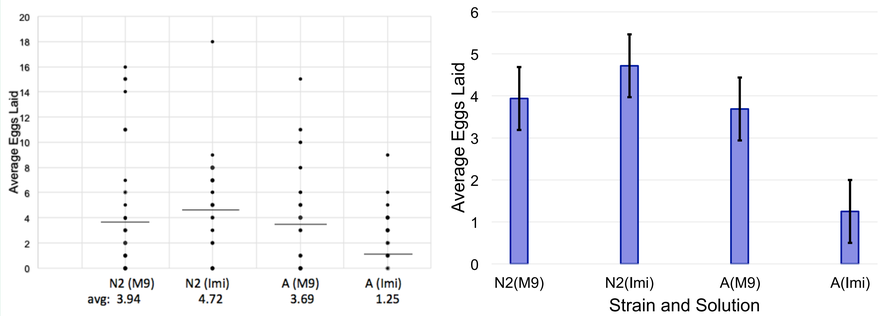


Figure 1: Wild-type worms lay more eggs in imipramine solution because imipramine stimulates the vulva muscles to induce egg laying. Mutant Strain A worms are resistant to imipramine stimulation and show decreased egg laying when compared to wild type. Strain A and N2 in Imipramine were significantly different from each other by the Mann-Whitney Test

Egg Laying Analysis of Mutant and N2 *C. elegans* in Imipramine, Doxepin, Serotonin and M9 Solution

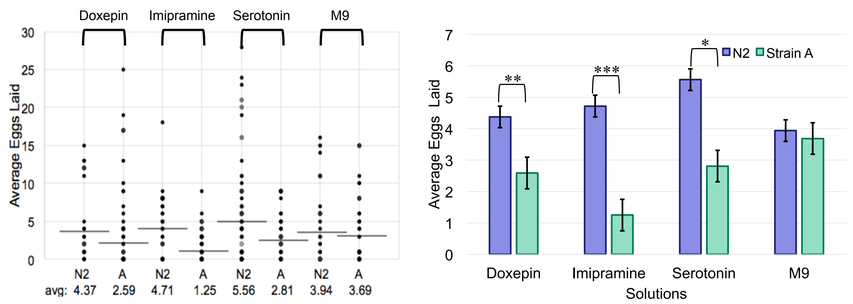
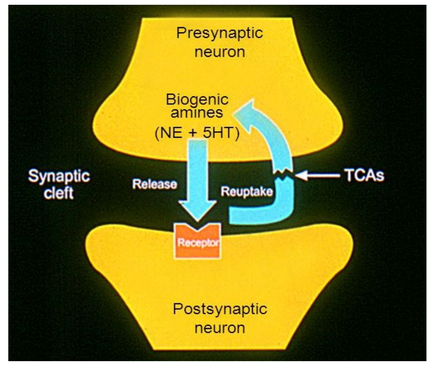


Figure 2: Wild type N2 worms demonstrate increased egg laying in both imipramine and doxepin compared to M9 control. EMS strain A worms demonstrate high resistance in imipramine and Doxepin. Serotonin has significant egg laying changes compared to M9 solution in both wild type and mutant worms. Strain A and N2 in each of the solutions, besides M9, were significantly different by the Mann-Whitney Test.

Mechanism of TCAs



Results and Conclusions

- Serotonin increases egg-laying behavior by stimulating vulvar contractions in *C. elegans*. It can be inferred that imipramine neurologically affects the vulvar muscles in a similar fashion as it increases serotonin concentration via reuptake inhibition.
- As hypothesized, the egg laying behavior of the Strain A mutants showed a resistance to the effects of imipramine and doxepin by showing decreased egg laying compared to the N2 control groups.
- Future studies would include sequencing the genome of the mutants by creating a gene map in order to identify where the mutations are taking place in genome. Also, conducting further trials with other antidepressants of different or similar classes as imipramine.

Acknowledgments

We would like to thank Zhongqiang Qiu for assisting us throughout the research processes and Dr. Myeongwoo Lee for his mentorship and providing support in the entirety of the project.

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