The Effects of Antidepressant Drugs on *C. elegans*

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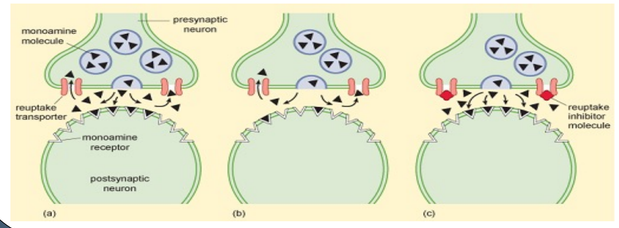
Introduction

- Hypothesized that depression causes depleted monoamine levels in synapse
- Decreased levels of monoamines (transmitters such as epinephrine, norepinephrine, dopamine, and serotonin) = shown to have a direct correlation with depressive symptoms (1).
- Monoamine oxidase inhibitors (MAOI) = class of antidepressants that look to target monoamine receptors and affect their degradation (2).

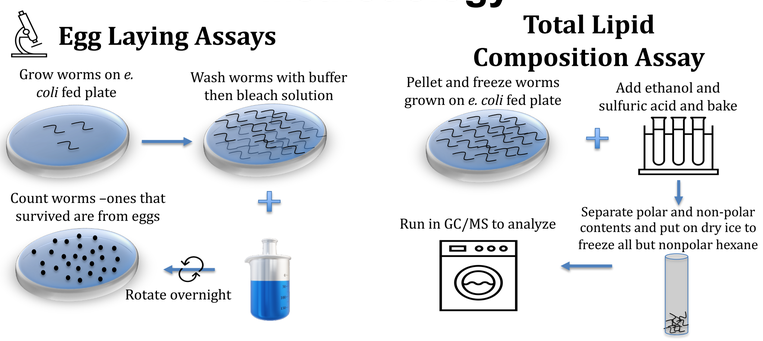


Receptors in a normal brain (a) vs. depressed brain (b). (c) shows how monoamine oxidase inhibitors likely work (3).

Model Organism - *C. elegans*

- Have common neurotransmitters and homologs to neuron receptors and proteins found in humans.
- Short lifespan, quick replication time, easily genetically manipulated
- For all experiments they were fed *E. coli*, which contains proteins, carbohydrates, and lipids that get broken down into fatty acids, as well as amino acid precursors and sugars.
- Have lipid stores which serve as structural component and as bioactive signaling molecules (5).

Methodology



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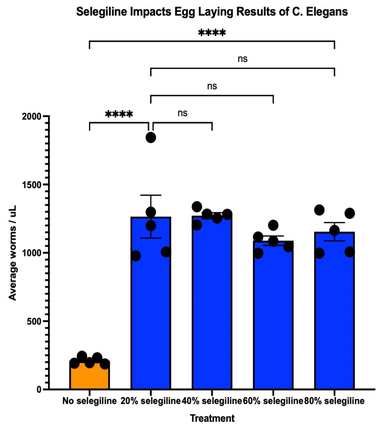
Varying Selegiline Concentration

Determining optimal concentration of drug used to maximize effects but minimize negative side effects.

Egg Laying

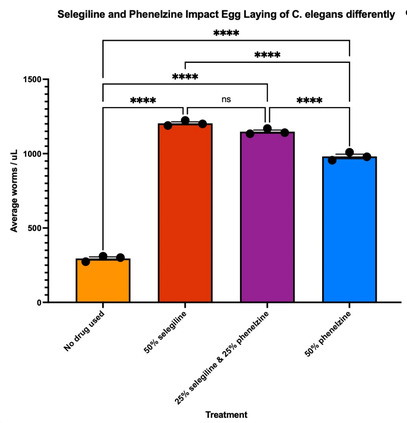


- Drug presence increased egg laying behavior, indicating increased motor neuron activity
- No significant difference in worm's egg-laying behavior based on amount of drug used
- Possible that the selegiline is more selective in inhibiting the MAO-B at lower concentrations, so as concentration of the drug increases, the binding selectivity does not change accordingly.

Combined Drug Therapy

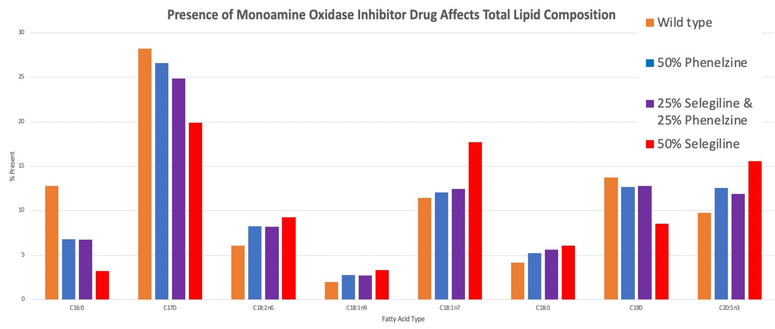
- Common treatment option used for depressed patients who do not get better with a single drug.
- These studies used varied concentrations of selegiline and phenelzine, two monoamine oxidase inhibitor drugs administered to depressed patients in the United States.
- Selegiline and phenelzine impact different biological pathways.

Egg Laying



- Makes a difference as to what percentages of the various MAO-Is are used.
- Higher rate of egg-laying when selegiline is used as compared to when it is combined with phenelzine, or when phenelzine was the only drug used.

Lipid Composition



- Saturated = C16:0, C17D, C18:0, C19D
- Unsaturated = C18:2n6, C18:1n9, C18:1n7, C20:5n3
- Drug caused worms to produce more polyunsaturated FA and remove saturated FA
- All delta FAs (bacteria based so indicative of feeding) saw a decrease, most drastic with 50% selegiline

Conclusions

<u>Increased levels of polyunsaturated FAs indicates</u>:

- Drug is causing change that causes decreased neurological defects - enzymes such as elongase I and elongase II are being upregulated (speeding up elongation process)
- Shift in which signaling molecules are being expressed (polyunsaturated FAs are precursors)
- Difference between which drug was used and the FA composition likely because the two drugs impact a different pathways
- The neurological pathway impacted likely varies from one depressed patient to another, as different drugs are effective for different people

Future Research

- Looking at negative side effects and complications worms face when concentration is varied, or combined drug therapy is used (such as thrashing activity)
- Use serotonin deficient worms to better understand the roles of the various monoamines
- Determine if there is a correlation between motor neuron activity (egg laying) and FA composition

References

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