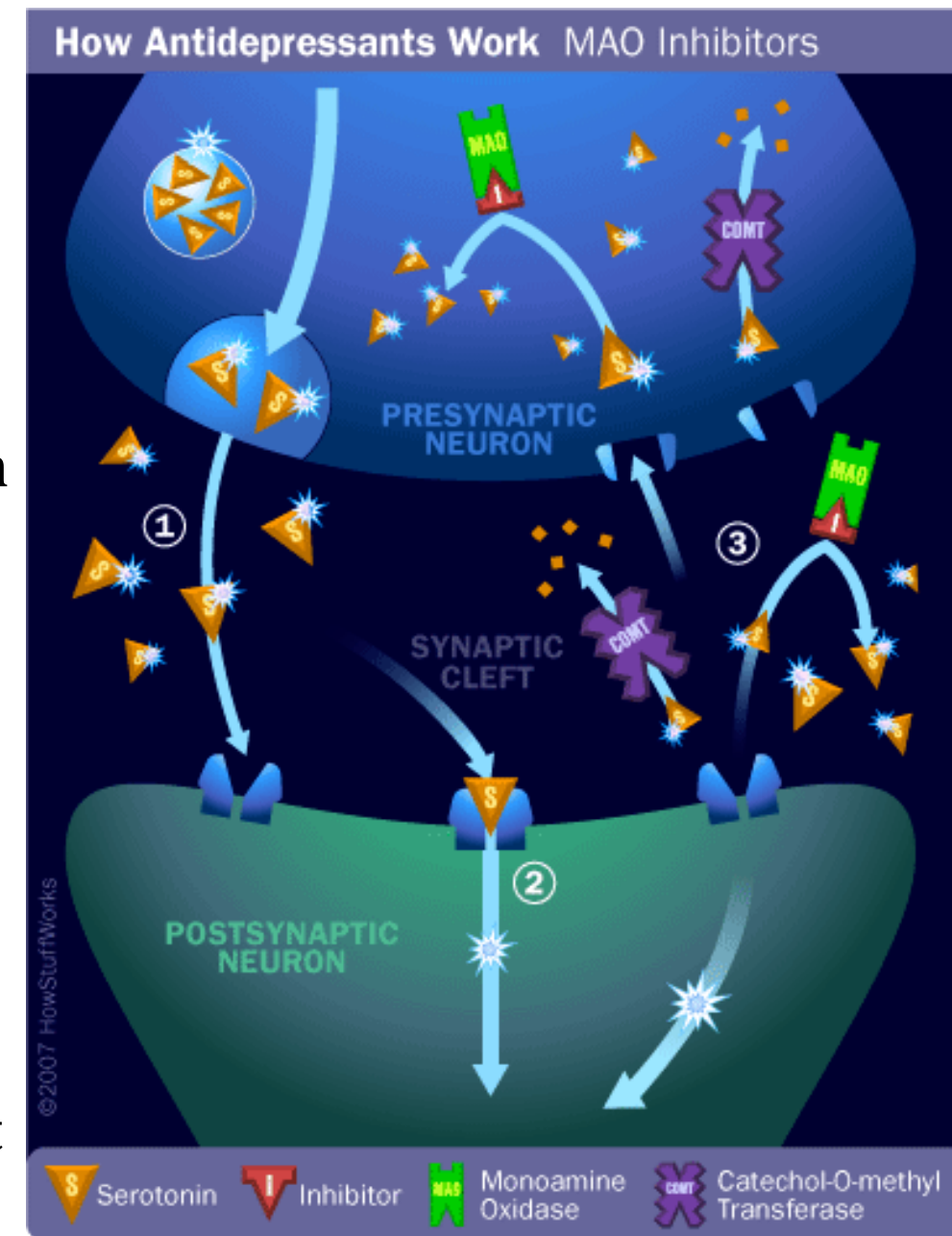


Introduction

Depression affects 264 million people worldwide and is a pressing health crisis⁽¹⁾. Despite this, research regarding the physiology of depression and mechanisms behind antidepressants is lacking⁽²⁾. This study aims to provide insight into these mechanisms by studying the biological effects of one antidepressant, selegiline, a monoamine oxidase inhibitor (MAOI), on *C. elegans*. MAOIs prevent degradation of monoamines, such as serotonin and dopamine, by inhibiting an enzyme called monoamine oxidase^(3,4). However, the mechanisms through which MAOIs achieve this inhibition is largely unknown. This study investigates how egg-laying, thrashing, and lipid composition of *C. elegans* are affected by Selegiline. These functions are modulated by homologous neurotransmitter pathways in humans and in *C. elegans*, these same pathways are implicated in depression⁽⁵⁾. This research will help to define the pathways with which MAOIs interact to treat depressive symptoms.



Results

Egg-Laying Assay:

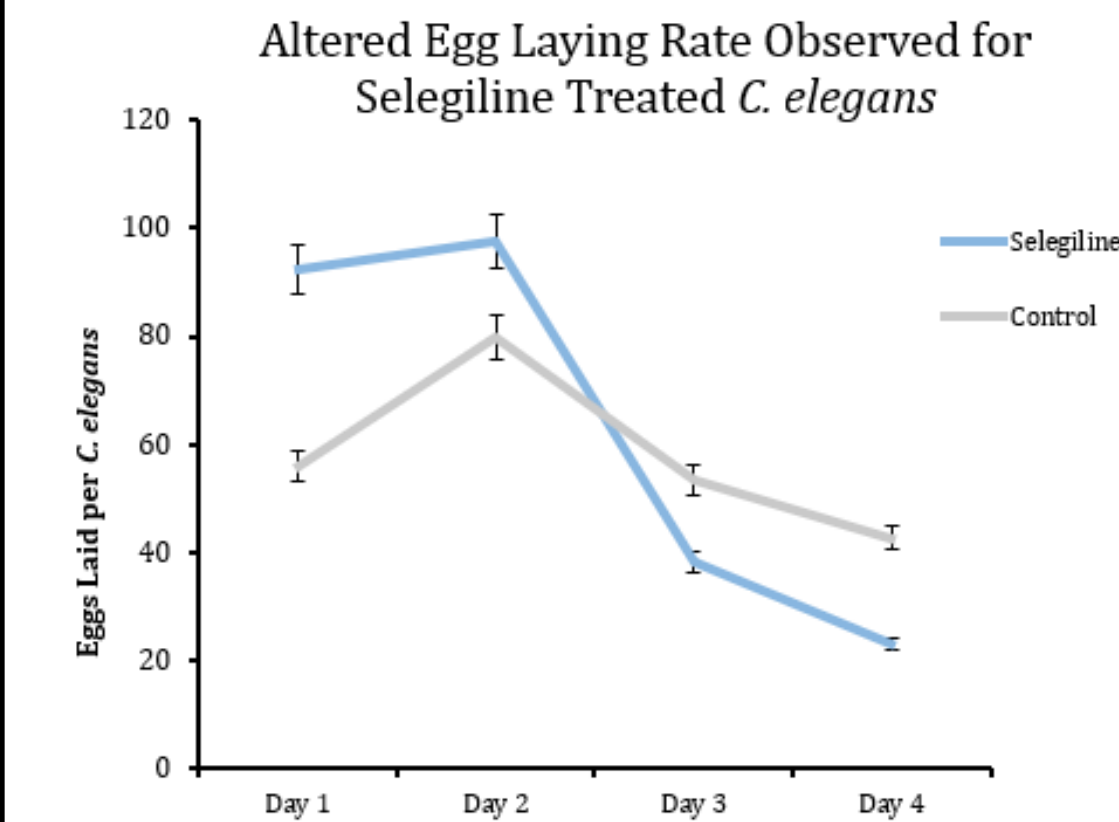


Fig. 1: Egg laying assay results indicate that selegiline redistributes egg-laying production timeline in *C. elegans* such that the number of eggs laid on days 1 and 2 increased, $f(3,36) = 3.4, p = 0.028, \eta^2 = 0.22$.

Thrashing Assay:

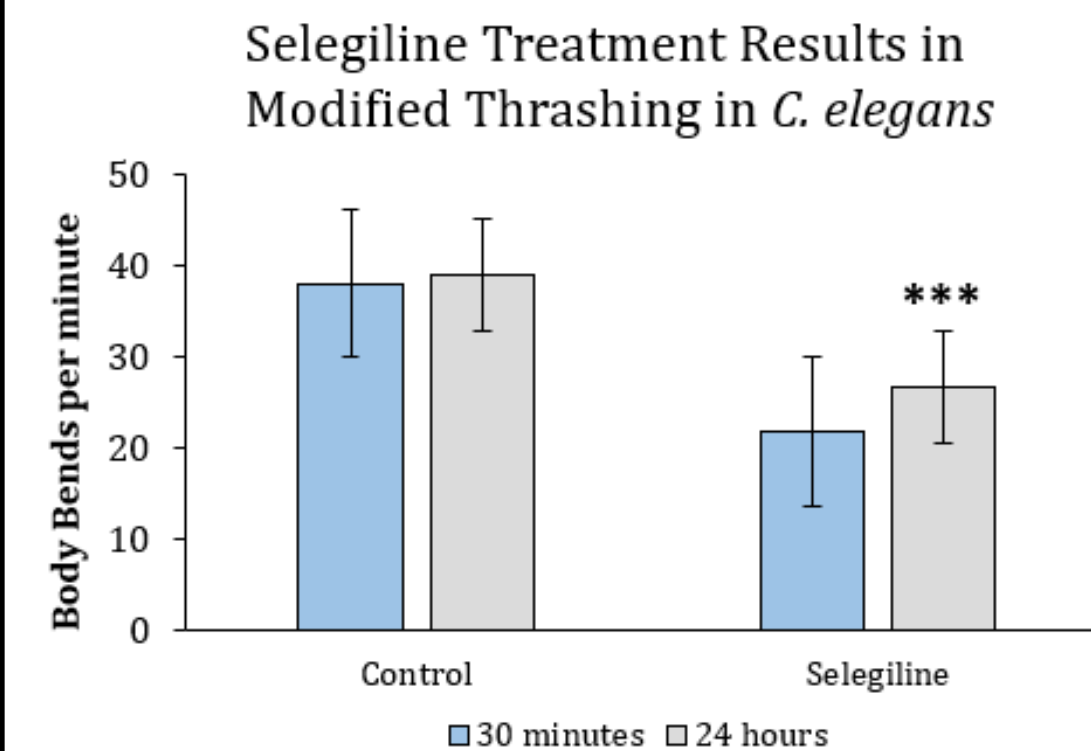


Fig. 2: Thrashing assay results indicate that selegiline significantly decreased frequency of thrashes following acute exposure and normal thrashing was not regained for at least 24 hours, $f(2,30) = 15.80, p < 0.001, \eta^2 = 0.53$.

Results Cont'd

Lipid Assay:

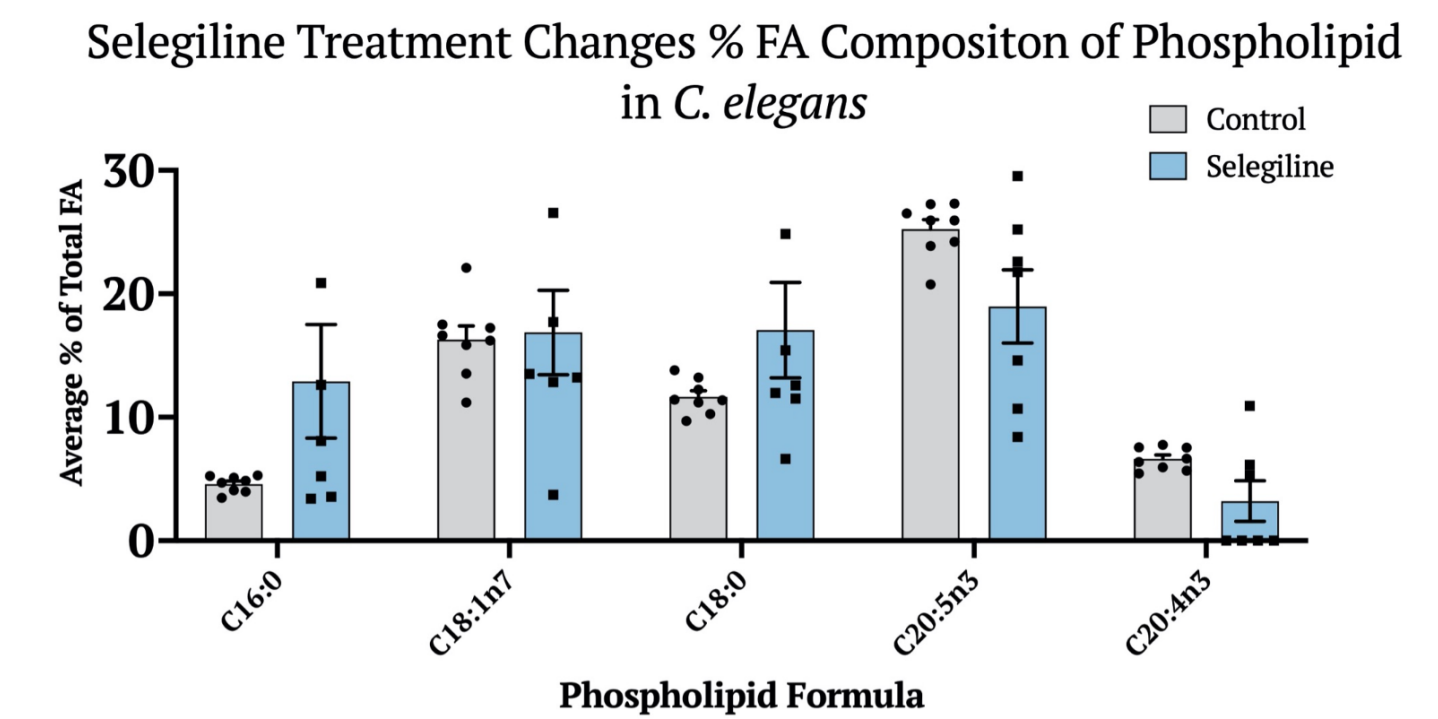


Fig. 3: Relative analysis of phospholipid GC-MS data, Independent means t-tests revealed that treatment with selegiline shows marked increases in saturated FAs while decreasing polyunsaturated FAs composition (all p 's < 0.05).

Selegiline Treatment Changes % FA Composition of Neutral Lipids in *C. elegans*

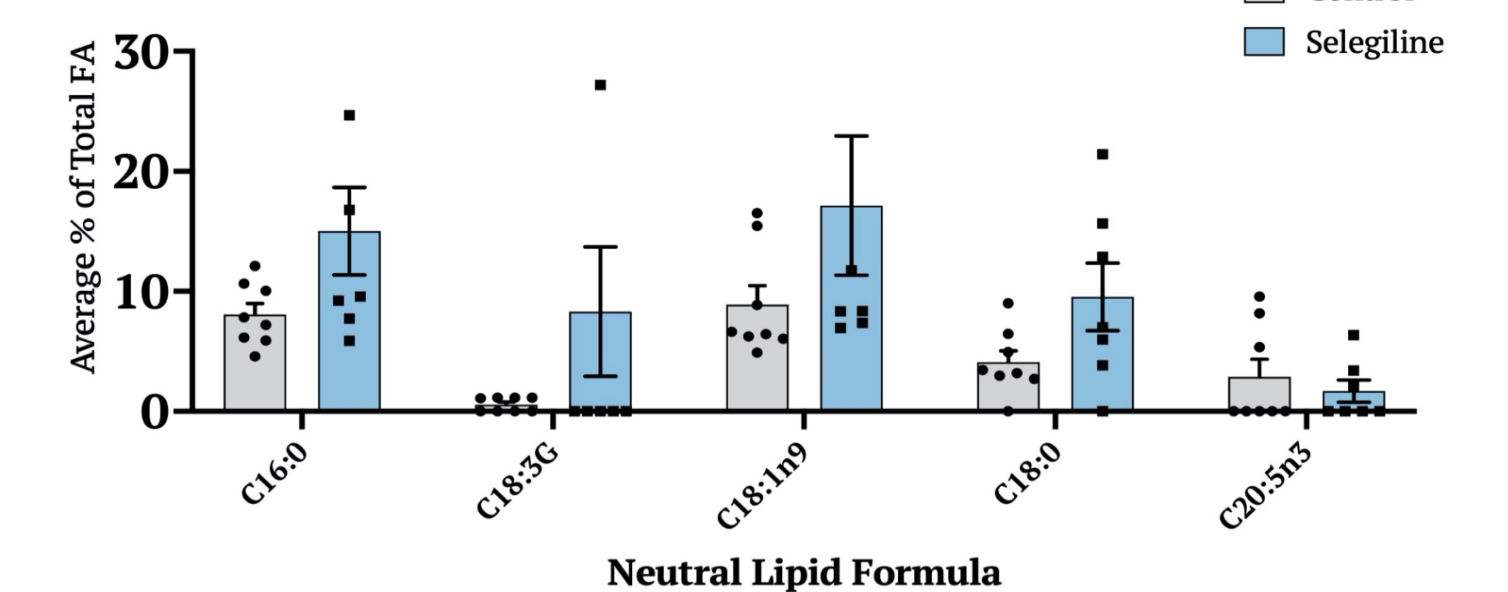
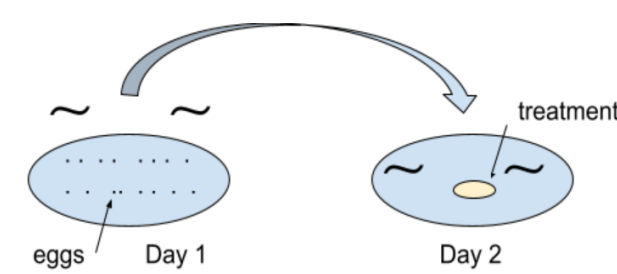


Fig. 4: Shows a relative analysis of neutral lipid GC-MS data. Treatment with selegiline causes marked increases in saturated FAs while decreasing most polyunsaturated FAs, with the exception of C18:1n9 (all p 's < 0.05).

Methodology

Egg-Laying Assay

- Synchronized adult WT worms on treated NGM plate
- Egg count per day

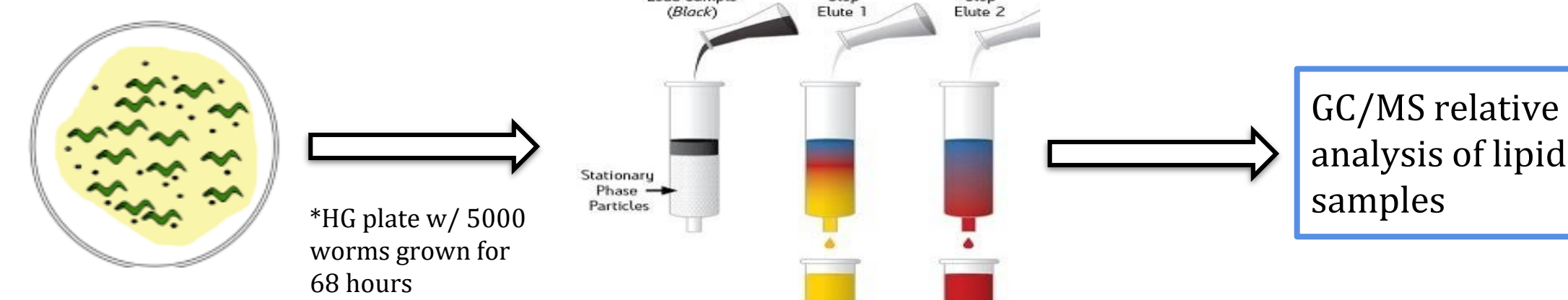


MON	TUE	WED	THU	FRI	SAT	SUN
×	×	×	×	×		

Thrashing Assay

- Thrash = bend from midline to outside
- Thrashing recorded 30 minutes & 24 hours post selegiline exposure

Lipid Assay



Acknowledgements

The success of this project was made possible thanks to the support of many individuals whom we would like to acknowledge. First and foremost, we would like to thank our advisor Dr. Jagan Srinivasan, who ceaselessly provided direction and encouragement to our group. We are especially grateful to Professor Angela Rodriguez who was an invaluable asset when it came to the presentation and integration of our studies. Our final thanks go to Professor Carissa Olsen who allowed us to work in her lab and provide interpretation skills needed to analyze our data.

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Conclusions, Limitations, and Future Directions

Conclusions:

- Increased egg laying rate and decreased thrashing indicates selegiline activates hermaphrodite specific motor neurons and VC motor neurons
- Observed pattern of up/down regulation of lipids suggests possible FAT2 and FAT7 dysregulation

Limitations:

- Stress and contamination seen in egg laying assay by day 5 causing worm death from over handling
- High variability in lipid assay selegiline trials compared to control trials

Future Research:

To better understand the molecular pathways affected by selegiline....

- Utilize FAT2 and FAT7 *C. elegans* mutants
- VC circuit knockout
- Dopamine/serotonin receptor mutants