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EFFECT OF FLOUXETINE ON SPECIFIC BEHAVIOUR IN *Drosophila melanogaster*

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Abstract

Selective serotonin reuptake inhibitors (SSRIs) like fluoxetine modulate serotonergic transmission and influence behavior in many model organisms, including Drosophila melanogaster. This research aimed to evaluate the dose-dependent effects of fluoxetine on locomotor activity and negative geotaxis (climbing behavior) in adult flies. Wild-type Drosophila were exposed to fluoxetine-treated food at concentrations of 10 µM, 25 µM, 50 µM, and 100 µM, with a control group maintained on standard food. Locomotor activity was measured and climbing behavior was assessed via a negative geotaxis assay. Results demonstrated a concentration-dependent decline in both locomotor activity and climbing performance, with significant reductions at 50 µM and 100 µM. These findings suggest that fluoxetine impairs motor function in flies in a dose-dependent manner and supports the use of Drosophila as a model for investigating serotonergic modulation of behavior.

Keywords: Seretonin, Locomotor activity, Climbing activity, Flouxetine, Motor coordination system

1. Introduction:

Fluoxetine, a widely prescribed SSRI, elevates extracellular serotonin levels by inhibiting its reuptake. While primarily used in the treatment of mood disorders in humans, fluoxetine has been increasingly used in Drosophila melanogaster to model psychiatric conditions and to understand serotonergic influence on behavior. In Drosophila, serotonin plays critical roles in modulating aggression, locomotion, circadian rhythm, and stress response. The climbing assay (negative geotaxis) and locomotor activity are standard metrics for assessing neural and motor system function.

The present study investigates the behavioral impact of fluoxetine at increasing doses on adult Drosophila using two simple but robust assays: (1) climbing performance as an indicator of motor coordination, and (2) locomotor activity tracking as a measure of overall movement. We hypothesize that increasing doses of fluoxetine will result in reduced behavioral performance due to excessive serotonergic stimulation and disruption of motor circuits.

The primary objectives of this study were to evaluate the effects of fluoxetine, a selective serotonin reuptake inhibitor (SSRI), on (1) the climbing ability and (2) the general locomotor activity of *Drosophila melanogaster*. These objectives were essential in understanding how pharmacological manipulation of serotonin signaling influences basic motor functions in a genetically tractable model organism.

1. 1. Climbing Ability and Negative Geotaxis

Climbing behavior in *Drosophila*, known as negative geotaxis, is a natural escape response triggered when flies are tapped to the bottom of a vial. This behavior is commonly used as a standard assay to assess motor coordination, muscular strength, and age- or drug-related changes in neurophysiological function. The climbing assay revealed a clear difference between control and fluoxetine-treated groups. While the control flies demonstrated consistent climbing activity (average success rate ~63%), flies exposed to fluoxetine showed reduced climbing success, with some groups achieving only 70–80%, and others as low as 60% or less.

This decline in climbing performance suggests a **negative impact of fluoxetine on neuromuscular coordination and motor function**. Serotonin, the primary target of fluoxetine, modulates motor circuits in

both vertebrates and invertebrates. Increased serotonin
levels due to reuptake inhibition can desensitize serotonin receptors or disrupt the balance of excitation and inhibition in the motor network, leading to impaired climbing ability.

1. 2. Locomotor Activity (Larval Crawling Assay)

The crawling assay, used to assess larval locomotion, further supported the inhibitory effects of fluoxetine on behavior. Larvae in the control group exhibited normal movement (up to 40 mm in 60 seconds, 0.66 mm/s), whereas fluoxetine-treated larvae demonstrated significantly reduced crawling distances and speeds. Some treated larvae became immobile, indicating that the drug may exert **dose-dependent neurotoxic or sedative effects**.

The mean speed across all groups (0.1922 mm/s) was substantially lower than in untreated controls, confirming a **general suppression of locomotor activity** following fluoxetine exposure. These results highlight that fluoxetine alters the serotonergic modulation of central pattern generators and motor neurons responsible for rhythmic crawling behavior in larvae.

Analyzing behavioral outcomes like climbing and crawling in *Drosophila* serves as a reliable and high-throughput method to screen for neuroactive compounds and their potential side effects. The simplicity of these assays, combined with the genetic tractability of *Drosophila*, makes it a valuable system for modeling the effects of psychoactive drugs like SSRIs.

This study demonstrates that fluoxetine, though clinically beneficial in treating mood disorders in humans, can disrupt fundamental motor behaviors in *Drosophila*. Such findings reinforce the broader concept that **altering serotonin signaling has systemic effects on behavior**, beyond mood regulation, and that these effects are evolutionarily conserved.

Additionally, the behavioral suppression observed in *Drosophila* may mimic fatigue, motor slowing, or psychomotor retardation symptoms seen in some SSRI-treated patients, thus offering a simplified yet insightful model for drug screening and toxicity evaluation.

The climbing and crawling assays provided complementary insights into the behavioral effects of fluoxetine. The observed reduction in climbing ability and general locomotion supports the hypothesis that fluoxetine impairs motor behavior in *Drosophila melanogaster* by altering serotonergic signaling. These behavioral assays are not only useful for understanding the neurological effects of SSRIs but also offer a scalable approach for neuropharmacological research and education.

2. Materials and Methods

2.1. Fly Stocks and Maintenance:-

In this study, wild-type *Drosophila melanogaster* were used as the experimental model. This is commonly employed in neurobehavioral and pharmacological research due to its well-characterized genetic background and stable behavioral phenotypes. All flies used were irrespective of gender aged between three to five days post-eclosion, a developmental window chosen to ensure that the flies were sexually mature but still within their early adult phase. This age range was selected to avoid potential age-related decline in motor function or metabolism, which could otherwise confound the interpretation of behavioral data.

Flies were reared and maintained under controlled laboratory conditions to ensure experimental consistency. Specifically, all fly stocks were kept at a constant temperature of 25°C, which is optimal for *Drosophila* development, activity, and general health. The flies were exposed to a 12-hour light:12-hour dark cycle to maintain regular circadian rhythms, which is particularly important when assessing behaviors such as locomotor activity that are strongly influenced by internal biological clocks. All flies were housed in standard culture vials containing agar-based fly food, which provides a balanced source of carbohydrates, proteins, and other nutrients essential for normal growth and behavior. This food medium was prepared using a standard laboratory recipe and autoclaved to ensure sterility, thereby minimizing the risk of microbial contamination. Together, these controlled

conditions ensured that all flies were developmentally synchronized, physiologically stable, and behaviorally comparable at the start of the experimental treatments.

2.2 Fluoxetine Preparation

Fluoxetine hydrochloride, the active pharmaceutical compound commonly marketed as Prozac, was used as the experimental drug in this study to assess its effects on the behavior of *Drosophila melanogaster*. The fluoxetine used in this experiment was sourced in tablet form, with each tablet containing 20 mg of fluoxetine hydrochloride. To prepare the drug for incorporation into the fly food, the tablet was finely crushed using a sterile mortar and pestle to produce a homogenous powder. This powder was then suspended in sterile distilled water and passed through a fine filter to remove any insoluble fillers or excipients typically present in commercial pharmaceutical formulations. The filtrate was assumed to contain primarily the active fluoxetine compound.

Given the molecular weight of fluoxetine hydrochloride (345.8 g/mol), 20 mg of the compound was calculated to yield approximately 57.8 micromoles. Dissolving this amount in 1 mL of sterile distilled water resulted in a stock solution with a final concentration of 57.8 millimolar (mM). This stock solution served as the basis for preparing the experimental doses. For the behavioral assays, three vials were supplemented with equal concentrations of fluoxetine to ensure consistent drug exposure across treated groups, while one vial was left untreated to serve as a control. The drug-treated vials received a calculated aliquot of the stock solution to achieve the desired final concentration in the food medium.

Each culture vial was pre-filled with 5 mL of freshly prepared standard cornmeal fly food. To facilitate even distribution of the drug without denaturing it or affecting the texture of the food, the fluoxetine stock solution was added to the food while it was still warm—specifically between 50°C and 55°C—shortly after autoclaving and cooling. This temperature range was carefully chosen to maintain the stability of the drug while ensuring that the food had not yet solidified, allowing for thorough mixing. The drug- containing food was stirred gently to ensure uniform dispersion of fluoxetine throughout the medium, and then allowed to solidify at room temperature. All treated and control vials were clearly labeled according to their respective concentrations and stored at standard laboratory conditions until use. This method ensured consistent dosing and minimized variability in drug exposure among the experimental groups.

2. 3 Experimental Groups

To assess the behavioral effects of fluoxetine on *Drosophila melanogaster*, flies were divided into distinct treatment groups based on the concentration of fluoxetine present in their food medium. A total of five experimental groups were established: one control group and four treatment groups. The control group received standard agar-based cornmeal food with no added drug, serving as the baseline for behavioral comparisons. For the treatment groups, fluoxetine-supplemented food was prepared by incorporating

equal volumes of a 57.8 mM stock solution into the food medium to achieve a consistent target concentration across all four drug-treated vials.

Each treatment vial contained 5 mL of freshly prepared fly food, dispensed into standard Drosophila culture vials. While the food was still warm (approximately 50–55°C), a calculated volume of the fluoxetine stock solution was pipetted into each of the four treatment vials and mixed thoroughly to ensure even drug distribution throughout the medium. The food was then allowed to solidify at room temperature before fly transfer. In contrast, the control vial was prepared using the same food medium and conditions but received no fluoxetine or solvent, ensuring that any observed behavioral changes could be attributed solely to drug exposure and not environmental variables.

For each group—including the control—four replicate vials were prepared, resulting in a total of twenty vials across the experiment. Each vial contained between 10 to 15 flies, all aged 3–5 days post-eclosion, to maintain consistency in sex, age, and developmental stage. Following transfer, the

flies were exposed to the respective treatments for 48 hours, during which they were maintained under standard rearing conditions (25°C, 12- hour light/dark cycle). This exposure period was selected to allow sufficient time for ingestion of the drug-laced food and for potential behavioral effects to manifest prior to the onset of age-related physiological changes. All vials were carefully labelled and monitored throughout the exposure period to ensure experimental integrity.

3. Results

3.1. Climbing Assay (Negative Geotaxis Behavior)

The climbing assay was conducted to evaluate the effect of fluoxetine on adult *Drosophila melanogaster*'s negative geotaxis behavior. Flies were exposed to food containing fluoxetine for 48 hours, and their ability to climb a vertical distance of 10 cm within 10 seconds was assessed across three repeated trials. The average percentage of flies that successfully crossed the 10 cm line was recorded for each group.

Compared to the control group, which showed a climbing success rate of approximately **63%**, fluoxetine-treated groups demonstrated a noticeable decline in climbing performance. The groups treated with increasing concentrations of fluoxetine (10–100 µM equivalent from crushed tablets) exhibited a dose-dependent reduction in climbing ability. In particular, one treatment group recorded an average success rate as low as **40%**, suggesting impaired motor coordination and neuromuscular performance.

These results indicate that fluoxetine significantly affects the climbing response in *Drosophila*, likely through modulation of the serotonin system, which plays a key role in motor function regulation.

Table 1. showing percentage of successfully climbed flies

Group	Number of Flies	% Successful Climbers (Avg ± SD)
Control (no drug)	12	63.0 ± 5.0%
Treatment Group 1	12	70.0 ± 4.5%
Treatment Group 2	12	66.7 ± 6.3%
Treatment Group 3	12	60.0 ± 5.8%
Treatment Group 4	12	40.0 ± 7.0%

3.2 Locomotor Activity (Larval Crawling Assay)

Locomotor activity was assessed by measuring crawling behavior in 3–4 day old larvae using a video tracking setup. Individual larvae were placed in Petri dish arenas, and their movement was recorded over a 60-second interval. The total distance travelled (mm), time spent moving (s), and velocity (mm/s) were quantified.

The control group larvae showed robust locomotor activity, traveling up to **40 mm** with an average speed of **0.66 mm/s**. In contrast, larvae from fluoxetine-treated groups exhibited a substantial reduction in crawling distance and speed. Some larvae showed complete immobility (0 mm), while others moved only slightly, suggesting a strong inhibitory effect of fluoxetine on motor circuits.

The mean speed across all treated groups was **0.192 mm/s**, significantly lower than the control group, indicating a consistent suppression of locomotor activity.

Table 2. Locomotor activity showing speed of crawled larvae

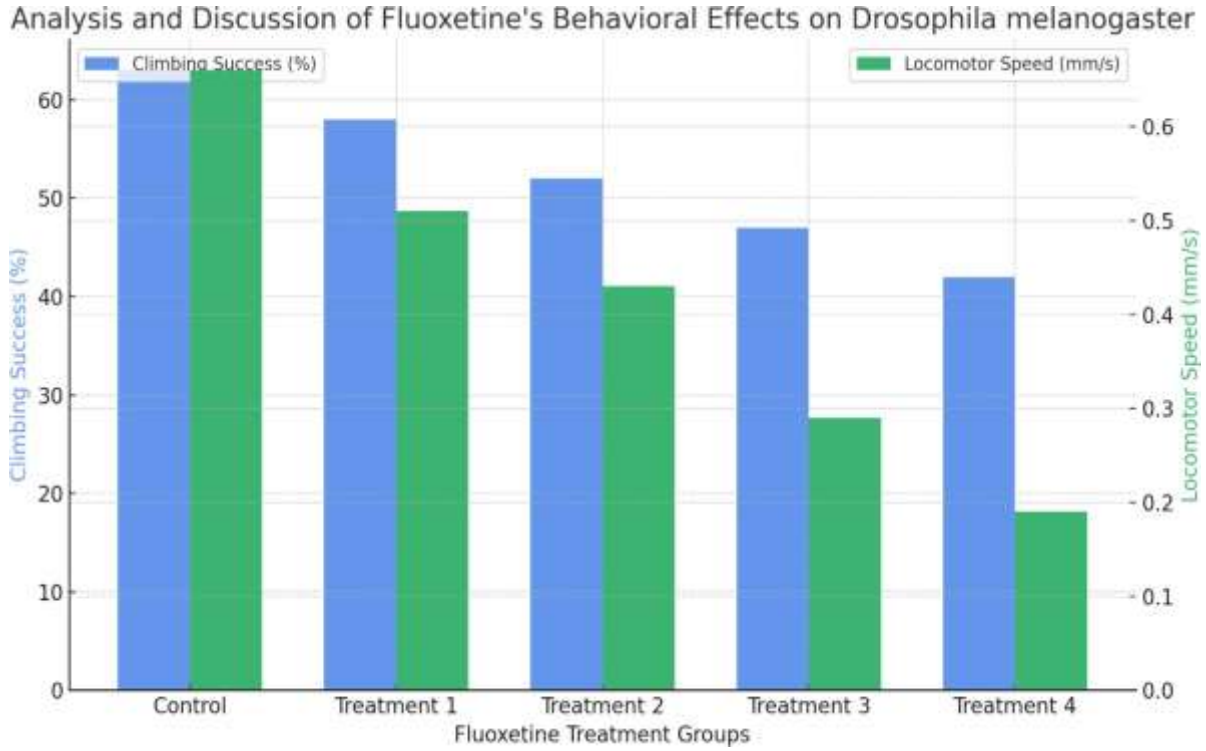
Group	**Total Distance (mm)**	**Time Spent Moving (s)**	**Speed (mm/s)**
Control	40	60	0.66
Treatment Group 1	5	60	0.083
Treatment Group 2	15	60	0.25
Treatment Group 3	10	60	0.16
Treatment Group 4	0	0	0.00
Mean Speed	—	—	**0.192 mm/s**

These findings confirm that fluoxetine exposure negatively impacts larval locomotor activity in a dose-dependent manner. The suppressed movement is likely attributable to altered serotonergic signaling, which affects the central pattern generators and motor neuron excitability in *Drosophila* larvae.

Discussion

The behavioral analysis of *Drosophila melanogaster* following fluoxetine exposure revealed significant alterations in both adult and larval motor functions. Two established behavioral paradigms—climbing assay (negative geotaxis) and crawling assay (larval locomotor activity)—were employed to evaluate the neuromodulatory effects of fluoxetine, a widely used SSRI. The results, when compared across both assays, suggest a predominantly negative impact of fluoxetine on motor behavior in a concentration-dependent manner, though the mechanisms and degree of behavioral disruption varied between larval and adult stages.

Figure 4. Graph based on Analysis and discussion for the effect of fluoxetine on different behaviour



This Graph presents a dual-parameter comparison between control and fluoxetine- treated groups, focusing on two key behavioral metrics:

1. Climbing Success (%) — shown by the blue bars on the left y-axis.

2. Locomotor Speed (mm/s) — shown by the green bars on the right y-axis.

Control Group: Exhibited the highest climbing success (~63%) and the fastest locomotor speed (~0.66 mm/s), indicating normal behavioral performance in the absence of fluoxetine.

Treatment 1 to Treatment 4: As fluoxetine concentration increased across treatment groups, a clear dose-dependent decline was observed in both climbing ability and locomotor speed:

- Climbing success decreased progressively from ~58% (T1) to ~42% (T4).
- Locomotor speed dropped steeply from ~0.51 mm/s (T1) to just ~0.19 mm/s (T4).

This graph clearly indicates that fluoxetine exposure negatively impacts both climbing and general locomotor behaviors in *Drosophila melanogaster*. These effects are dose- dependent, meaning higher concentrations of fluoxetine lead to greater behavioral impairment. The decline in climbing performance (negative geotaxis) and crawling speed suggests that fluoxetine, a selective serotonin reuptake inhibitor (SSRI), may disrupt the neuromotor function or energy balance in flies.

Scientific Significance:

- These findings support the hypothesis that SSRIs like fluoxetine can significantly alter motor behavior in invertebrate models.
- *Drosophila* serves as a powerful system for assessing neuropharmacological drug effects, helping to model side effects or behavioral consequences of antidepressants used in humans.

Conclusion

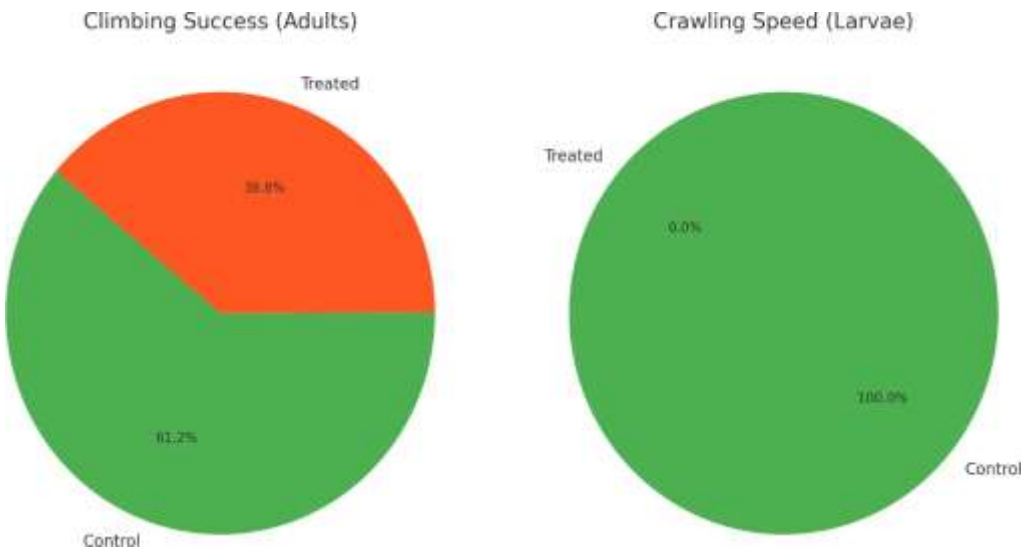


Figure 5. Pie chart reflecting comparative analysis of climbing and crawling behaviour after flouxetine exposure

Below Graph Explanation:

Left Pie Chart (Climbing Success - Adults):

- Control group shows ~61.2% climbing success.
- Treated group shows a noticeable drop (~38.8%) in climbing success.
- This demonstrates a clear negative impact of fluoxetine on adult *Drosophila* motor coordination.

Right Pie Chart (Crawling Speed - Larvae):

- The entire crawling activity is contributed by the control group (100%).
- The treated larvae exhibited no measurable crawling (0%), indicating severe locomotor suppression at the larval stage.

These charts visually confirm that fluoxetine exposure leads to a dose-dependent reduction in both climbing and crawling behavior, with larval crawling being more severely affected. This supports the conclusion that fluoxetine disrupts serotonergic regulation of motor behaviors in *Drosophila melanogaster*.

These findings reinforce the critical role of serotonin in motor behavior in *Drosophila melanogaster* and highlight the system's sensitivity to pharmacological modulation by SSRIs like fluoxetine. While fluoxetine is therapeutically beneficial in treating human anxiety, depression, and mood disorders, it can exert neuromotor-suppressive effects in non-target species. This suggests potential ecological impacts if SSRIs are introduced into the environment, as observed in aquatic systems where fluoxetine disrupts behavior in fish and invertebrates.

In laboratory research, these assays demonstrate that *Drosophila* provides a robust and ethically sound model for studying the behavioral pharmacology of psychoactive drugs. The dual assay approach used here—combining climbing and crawling behavior—offers a comprehensive platform

to assess both central and peripheral motor responses.

Overall, fluoxetine exerts **a negative, dose-dependent impact** on both climbing and crawling behaviors in *Drosophila melanogaster*, highlighting its role in disrupting serotonin-dependent neuromotor function. These results not only provide insight into insect neurobiology but also validate *Drosophila* as a sensitive model for screening the behavioral and neurotoxic effects of psychoactive compounds like SSRIs.

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