How does early-life exposure to anti-depressants affect zebrafish (Danio rerio)?

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Introduction

Embryonic and early juvenile development is a critical time for the proper formation of a functioning organism, during which exposure to chemicals can lead to abnormalities. This study aims to examine the physiological and behavioral effects of anti-depressant medications during embryogenesis in zebrafish (Danio rerio). The widespread use of antidepressants, even during pregnancy, raises interesting questions in two different contexts. First, the zebrafish is used to model behavioral disorders in humans; it is unknown whether exposure to antidepressants in early life alters behavior and physiology in fish in a manner similar to mammals. This study will address that knowledge gap. Second, antidepressants are increasingly being found in trace amounts in environmental water sources. The effect this could have on native wildlife populations is also unknown.

Goal:

Determine the effects of anti-depressant medications on the development and behavior of juvenile zebrafish

Methods

General Information

• Species: Zebrafish (Danio rerio)
• Antidepressants
  • Desvenlafaxine hydrochloride
  • Paroxetine hydrochloride hemihydrate (98%)

Drug Dose Preparation:

• 1M stock solutions of paroxetine and desvenlafaxine were prepared and placed into 1ML alcools
• The doses below were added to 30 ml of water, then eggs were added

<table>
<thead>
<tr>
<th>Paroxetine</th>
<th>Low 100nm</th>
<th>3µL</th>
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<tr>
<td>Medium 10µM</td>
<td>300µL</td>
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<td>High 100µM</td>
<td>3000µL</td>
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<table>
<thead>
<tr>
<th>Desvenlafaxine</th>
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<tr>
<td>Low 100nm 0.3µL</td>
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<tr>
<td>Medium 10µM 30µL</td>
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<tr>
<td>High 100µM 100µL</td>
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Mortality and Hatching Experiment

• Eggs were checked every 24 hours and the number of hatched individuals and number of deaths were recorded

Locomotor Behavior Experiment

• 9 individuals at a time were placed into 24 well plates with 1 ml of aquarium water
• 1 minute acclimation period
• 10 minutes per trial
• ANY-maze software was used to record the following variables:
  • Distance traveled (m)
  • Speed (m/s)
  • Motility time (s)
  • Total # of mobile episodes

NaCl Stress Response Experiment

• Exposures: High dose desvenlafaxine and control
• 9 individuals at a time were placed into 30ml of 100mM NaCl for 10 minutes
• After 10 minutes the animals were removed and rinsed twice in aquarium water
• They were then placed into 24 well plates for testing
• 1 minute acclimation period
• 10 minutes per trial
• ANY-maze software was used to record the same variables as the previous experiment

Desvenlafaxine Results

Paroxetine Results

Answers

Does early life exposure to anti-depressants affect:

1) Hatching - No
2) Larval Mortality - Yes
3) Locomotion - Yes
4) Stress responses - Yes

Future Directions

Does early life exposure to anti-depressants affect:

1) Cortisol levels in response to stressors
2) Locomotor behavior as adults
3) Physiology of adults (mass, lifespan, etc)
4) Stress responses of adults
5) Long-term survival

Acknowledgements

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Questions

Does early life exposure to anti-depressants affect:

1) Hatching
2) Larval Mortality
3) Locomotion
4) Stress responses

References


Exposures

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<thead>
<tr>
<th>Control</th>
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<tbody>
<tr>
<td>Desvenlafaxine: Low = 10nm</td>
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<tr>
<td>Paroxetine: Low = 100nm</td>
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Conclusion

This study investigated the effects of early-life exposure to anti-depressants on zebrafish (Danio rerio). The results showed that:

- Paroxetine treated animals spend less time being mobile than control animals; One-way ANOVA, p = 0.0278 (Fig B)
- Desvenlaxafine increased the number of mobile episodes; Two-way ANOVA, p = 0.0335 (Fig G)
- Animals that were exposed to high doses of desvenlafaxine moved more total time than control animal; One-way ANOVA, p = 0.0209 (Fig A)
- Paroxetine treated animals were mobile less total time than controls; Unpaired T- Test, one-tailed p = 0.0880 (Fig 4)

These findings suggest that early-life exposure to anti-depressants can affect the activity and behavior of zebrafish, potentially influencing their development and survival.