Effects of fluoxetine in zebrafish under ecologically relevant exposure scenarios

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• Introduction

Psychiatric drugs are among the most commonly prescribed pharmaceuticals, being used in the treatment of mental health and behavioral disorders (Csoka & Szyf, 2009). Being widely detected in the aquatic environment, they can lead to behavioral changes in aquatic organisms, especially in fish, even when exposed to environmentally relevant concentrations (Ford & Fong, 2015). Fluoxetine is usually prescribed for the treatment of human depression, obsessive-compulsive disorder, anxiety, panic, compulsive behavior, eating and personality disorders. It belongs to a group of most detected drugs in the aquatic environment called selective serotonine reuptake inhibitors (SSRIs). These act on the central nervous system, binding to presynaptic receptors, which block serotonin reuptake (5-HT) in the presynaptic membrane, leading to a build-up of this neurotransmitter in the synaptic cleft and affecting neuronal signal transmission. This increase in serotonin levels consequently leads to an increase in serotonergic neurotransmission through post-synaptic receptors (Barry, 2013; Cunha et al., 2018; Duarte et al., 2019; Dzieweczynski et al., 2012; Farias et al., 2018).

Behavior is being increasingly used, showing to be a highly sensitive endpoint for neuronal and endocrine disruption (Andrade, 2015; Klüver et al., 2015; Magno et al., 2015).

Thus, this work aimed to evaluate the effects of fluoxetine on the behaviour of adult zebrafish (Danio rerio) when subject to a chronic exposure (21 days) to concentrations of 1000, 100, 10 and 1 ng/L plus control.

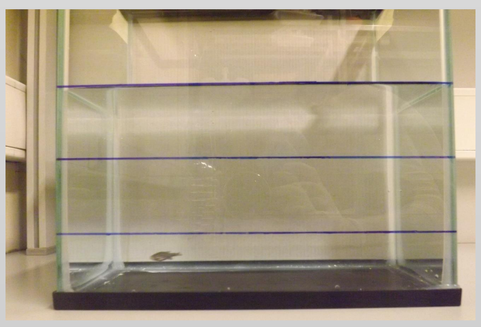
• Material and Methods

Fluoxetine exposure (21 days)

Test conditions
- Concentration: 0; 10; 100; 1000 ng/L;
- Photoperiod: 14:10 (L:D);
- Temperature: 27 ± 1º C;
- 3 replica per treatment;

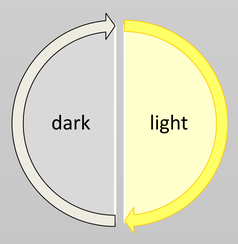
Behavior analysis (96h, 8 days, 15 and 21 days)

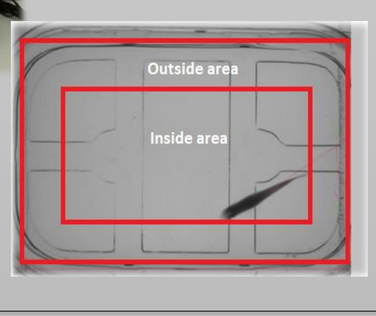
Novel Tank dive test



- 5 minutes recording of fish movement in each of the 3 areas of the aquarium (top layer, middle and bottom);
- Evaluation of time travelled in each area;
- N= 12 fish per treatment.

Light - Dark Stimulus





- 6 min recording of fish movement;
- Light-dark cycles (3 minutes of duration);
- Aquarium divided into outside area and inside area for thigmotaxis evaluation;
- Evaluation of TD travelled in each of the areas;
- N= 12 fish per treatment

• Results

1. Novel Tank dive test

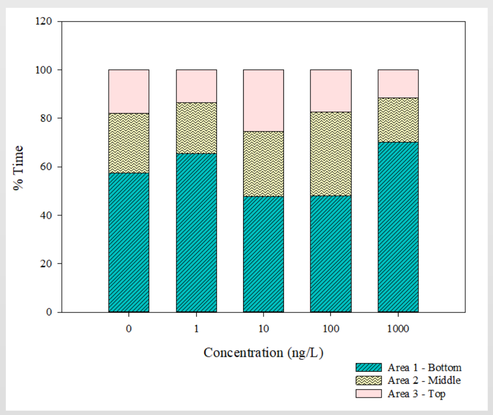


Fig 1 – Fluoxetine exposure effects on the total swimming time (% TT) of adult zebrafish.

Fish exposed to the highest concentration of fluoxetine appear to spend more time in the bottom layer of the aquarium compared to the control group. The differences, however, are not statistically significant (Area 1 (bottom): p = 0.107; Area 2 (middle): p = 0.027; Area 3 (top): p = 0.272).

2. Light – Dark stimulus

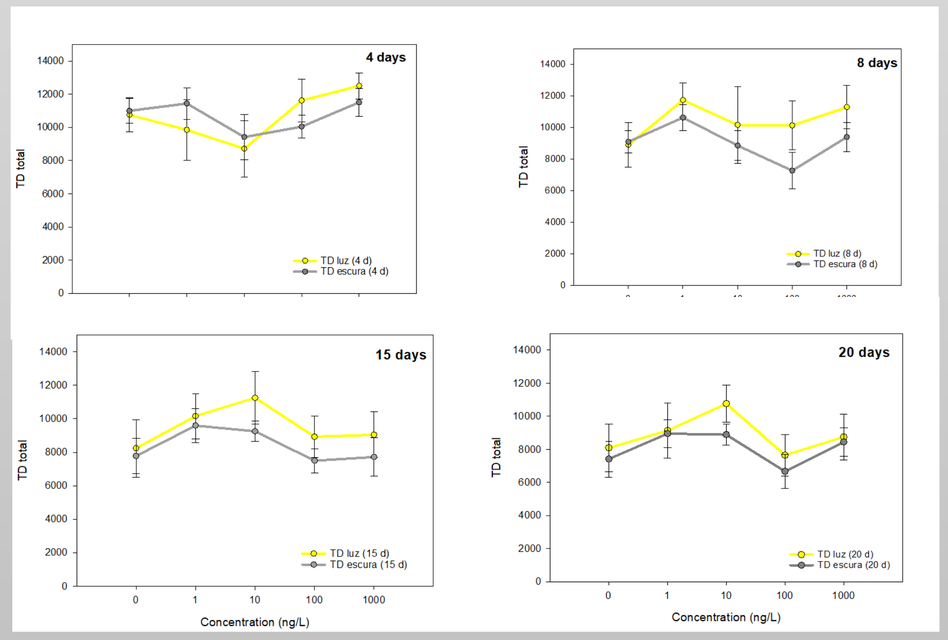


Fig 2 – Total distance (TD total) traveled by the zebrafish exposed to fluoxetine, during periods of light and dark stimulus.

Locomotion of adult fish (TD total) did not change between dark and light periods. Chronic exposure to fluoxetine did not seem to change locomotor activity (data not shown).

• Discussion and Conclusion

The present data suggest that the exposure of the adult zebrafish to the drug fluoxetine in environmentally relevant concentrations (ng / L) does not lead to any observable effect on behavior.

• **References**

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