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1-30 November 2020

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Effects of sertraline on *Danio rerio* embryos

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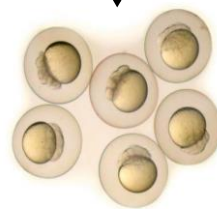


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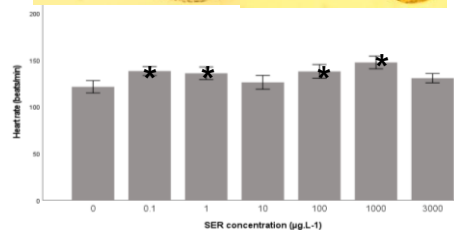
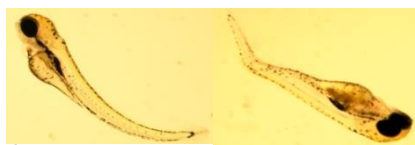
Effects of sertraline on zebrafish embryos

120h exposure to 0.1 - 3000 $\mu\text{g.L}^{-1}$

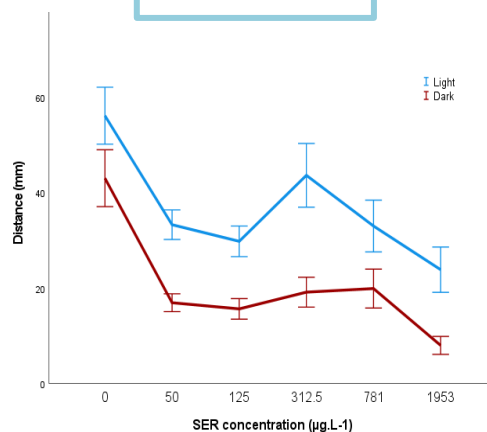
1 month exposure to 2 - 100 $\mu\text{g.L}^{-1}$



Development



Behaviour



Biochemical markers



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Abstract

The use of antidepressants has been increasing resulting in its presence in the aquatic environment. This environmental release raises concerns on potential effects to non-target organisms that have physiological systems regulated by these pharmaceuticals. Sertraline (SER) is an antidepressant belonging to the serotonin reuptake inhibitor class (SSRIs) that has a high consumption rate. However, there is little knowledge about the toxicological effects of SER in aquatic ecosystems. Thus, this study aimed to evaluate the acute (0.1 up to 3000 $\mu\text{g}\cdot\text{L}^{-1}$) and chronic (2 up to 100 $\text{ng}\cdot\text{L}^{-1}$) effects of SER on zebrafish (*Danio rerio*) focusing on different endpoints, such as development (e.g. Fish Embryo Toxicity (FET) assay and heartbeat rate), behaviour (light/dark stimulus) and biochemical markers (e.g. associated with neurotransmission (AChE), antioxidant defenses (CAT and GST) and energy metabolism (LDH)). Overall, embryos demonstrated a high sensitivity to SER (e.g. promoting an increased heartbeat rate, increased sensitivity to light/dark stimulus at low concentrations and decreased sensitivity to higher SER concentrations). These findings support further research on the long-term effects of antidepressants such as sertraline to aquatic biota and new methodologies to efficiently remove them from the environment.

Keywords: *Danio rerio*; antidepressant; behaviour; biochemical endpoints



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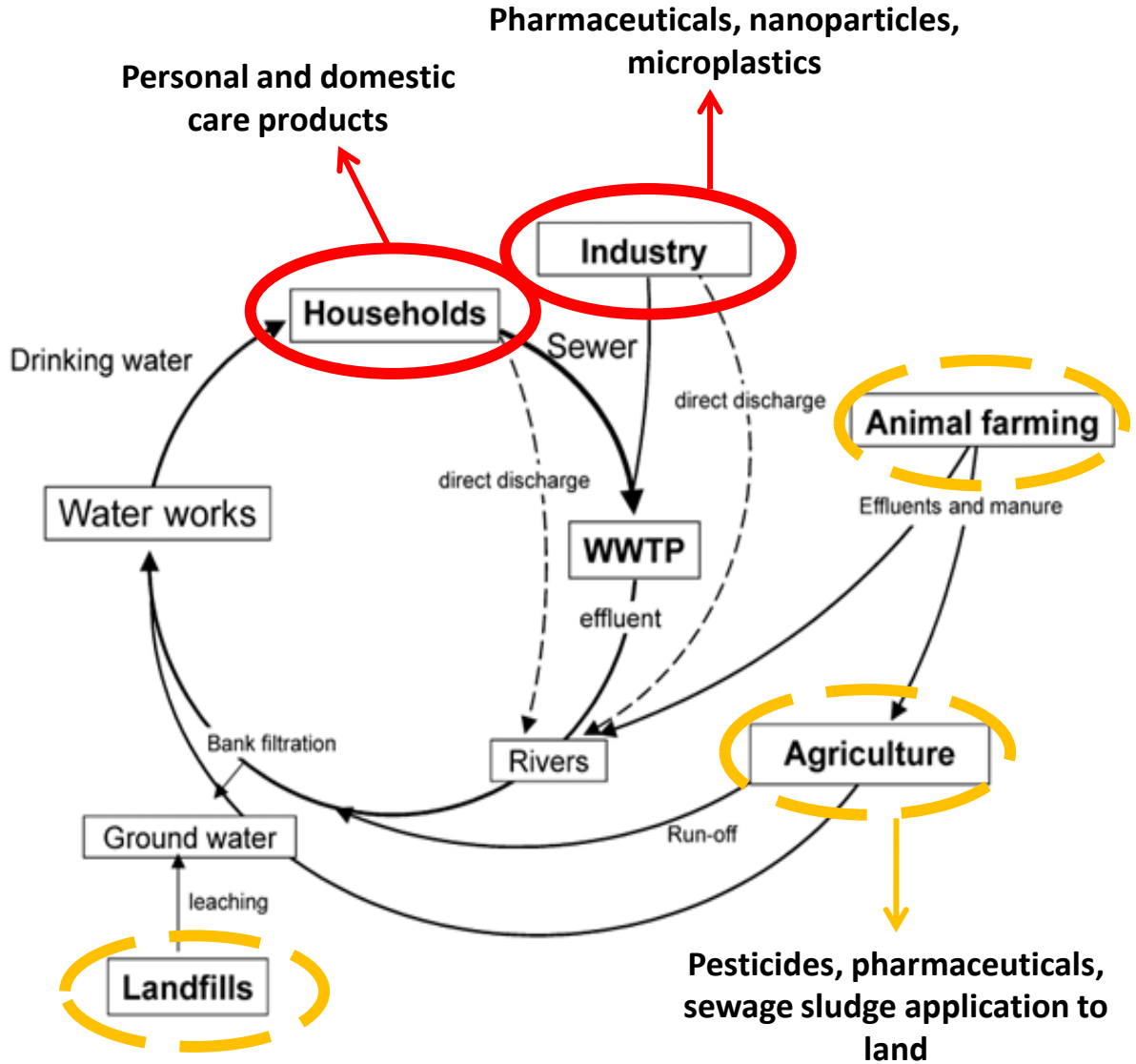
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Introduction

Emerging contaminants (EC)



Result of inadequate management of the synthesised products and residues allied with inefficient wastewater treatment plants (WWTP)



Petrović et al., (2003) Analysis and removal of emerging contaminants in wastewater and drinking water. 2003 Nov;22(10):685-96

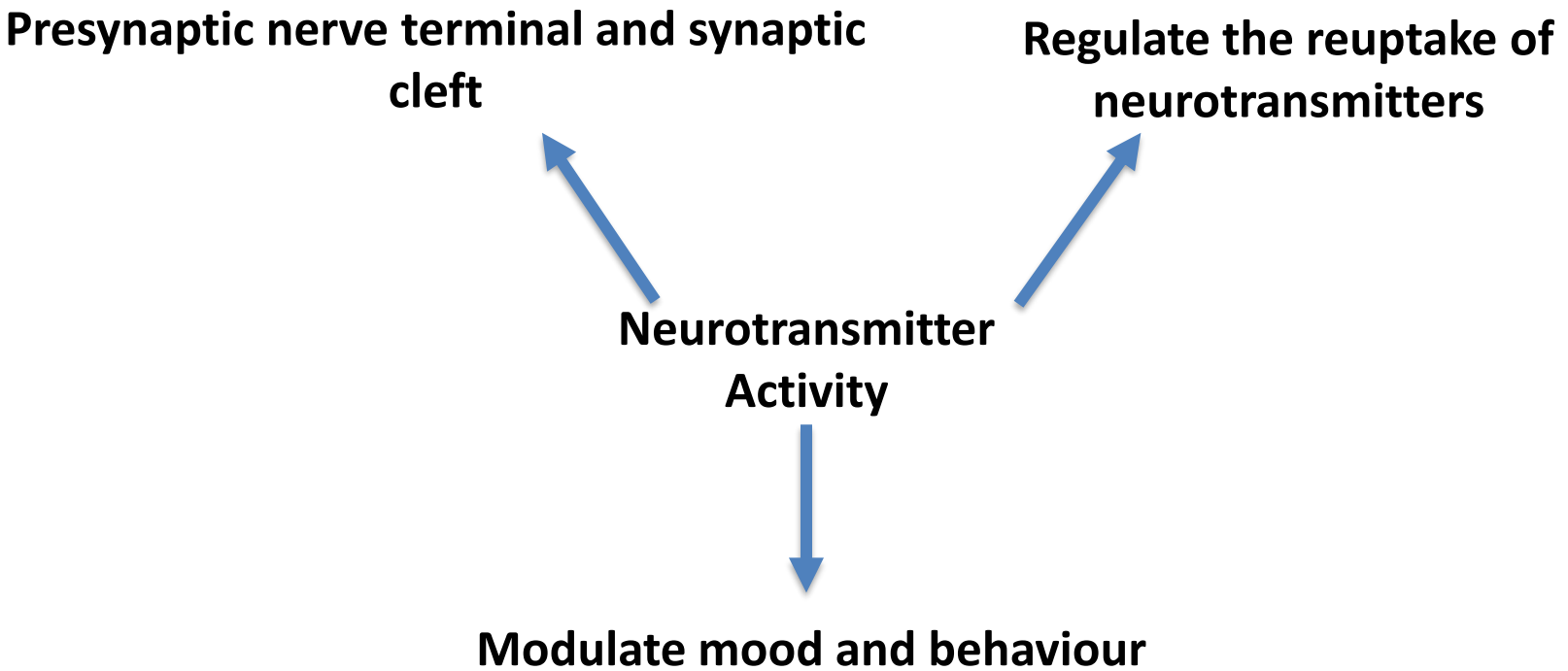


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Introduction

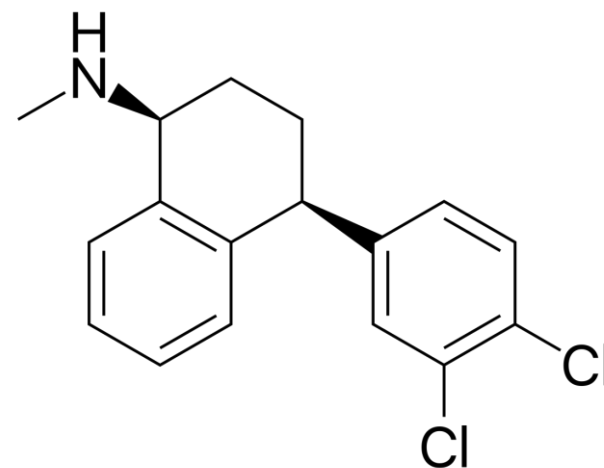
Antidepressants



Introduction

Sertraline

- IUPAC: (1S,4S)-4-(3,4-dichlorophenyl)-1,2,3,4-tetrahydro-1-naphthyl(methyl)amine
- Antidepressant included in the Selective Serotonin Reuptake Inhibitor (SSRI) class
- Applications:
 - Treatment of depression;
 - Anxiety disorders;
 - Obsessive-compulsive disorder;
 - Panic disorder
- Side Effects:
 - Agitation;
 - Minimal sedation;
 - Moderately severe gastrointestinal effects;
 - Sexual dysfunction



Material and Methods

Zebrafish (*Danio rerio*)



Embryo



Larva



Adult

- Rapid development
- Optically visible
- External development
- Genetic and embryological manipulation

- Development of major organs systems at 36h
- Optically visible

- Low cost and easy maintenance
- High fecundity rate
- Evident sexual dimorphism
- Well characterised and conserved genome

Model the health effects of environmental exposures to better understand the etiologies and mechanisms of environment-related disease in humans.



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Material and Methods

Assessed endpoints

Fish Embryo Toxicity assay

- Mortality
- Edema
- Malformations
- Heartbeat rate

Behaviour

- Total time
- Total distance
- % Time out
- % Distance out
- Slow, medium and rapid movements

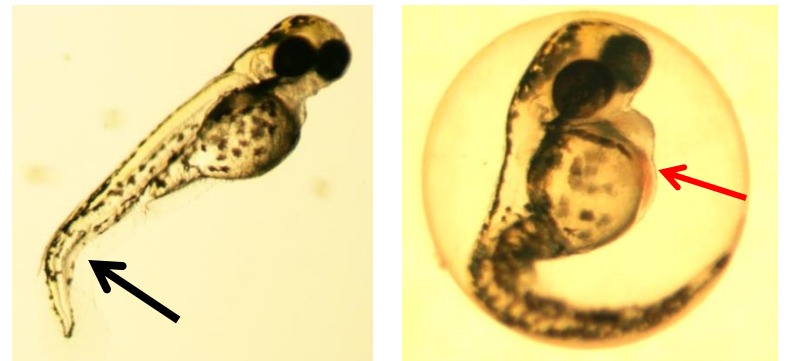
Biochemical markers

- Neurotransmission
- Antioxidant defences
- Energy metabolism

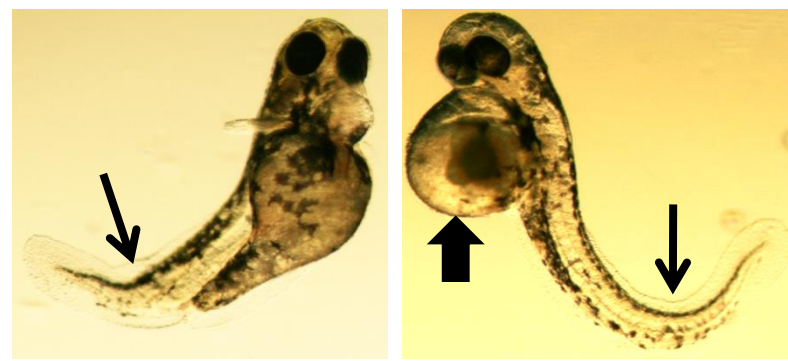


Results and discussion

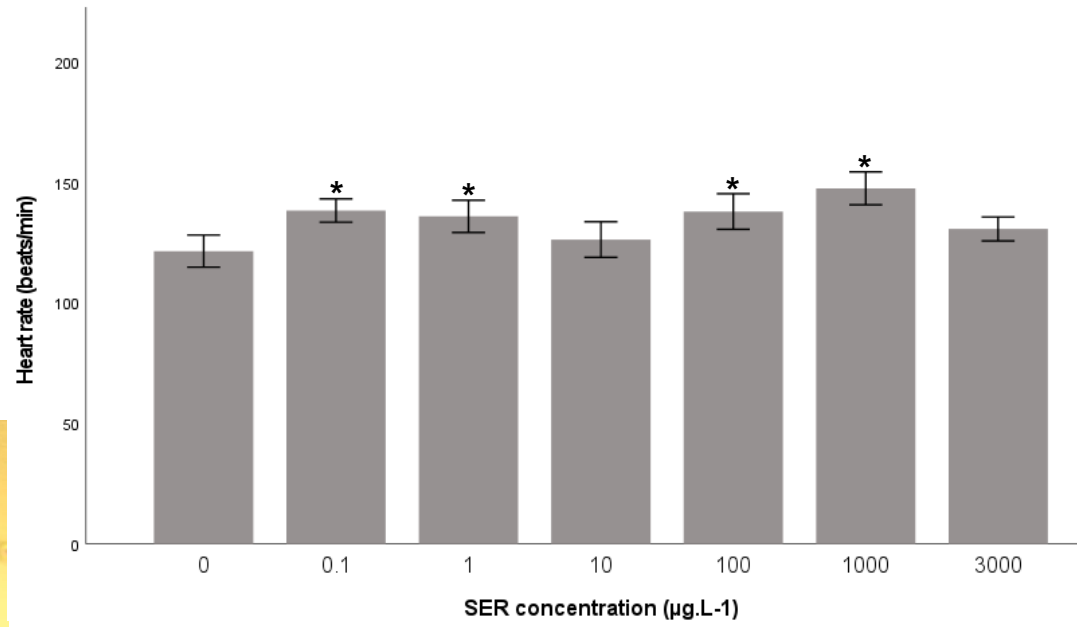
Fish Embryo Toxicity assay



24h exposure to 10 µg.L⁻¹ 48h exposure to 10 µg.L⁻¹



72h exposure to 1000 µg.L⁻¹ 72h exposure to 1 µg.L⁻¹

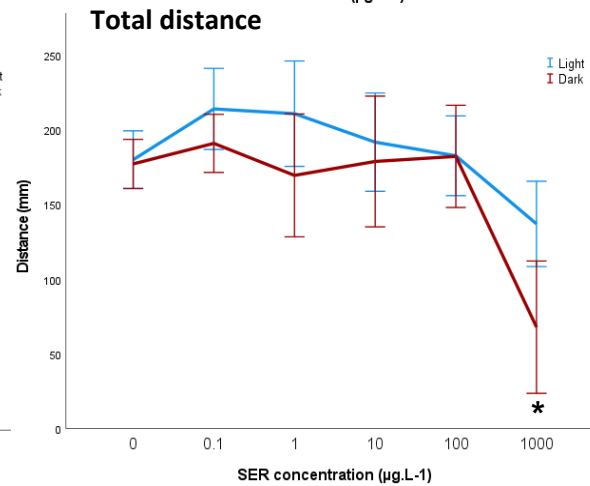
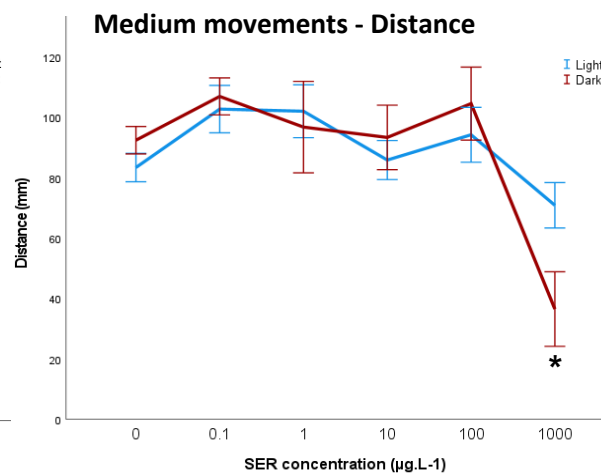
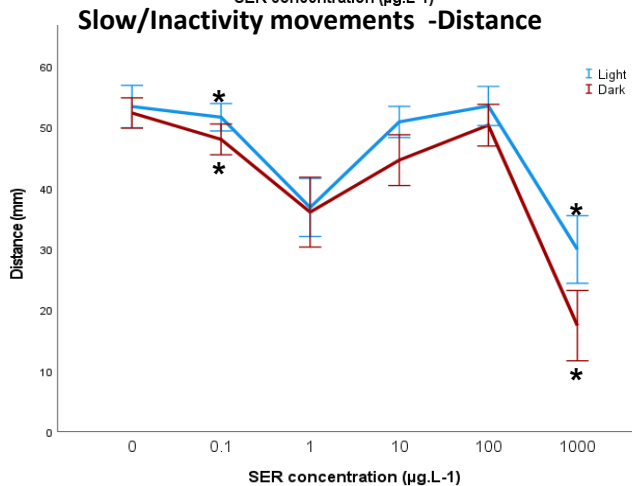
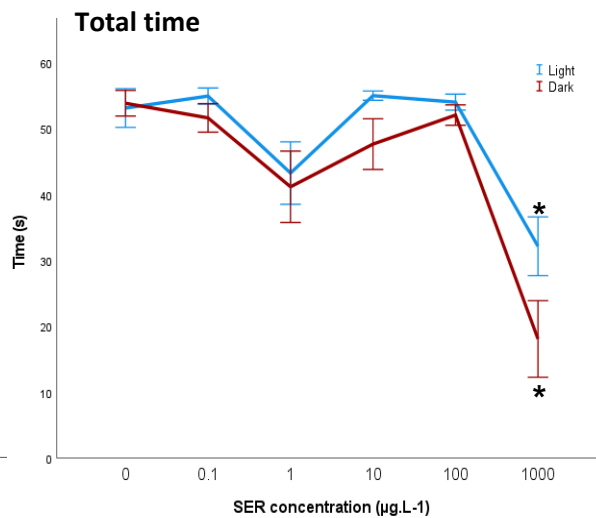
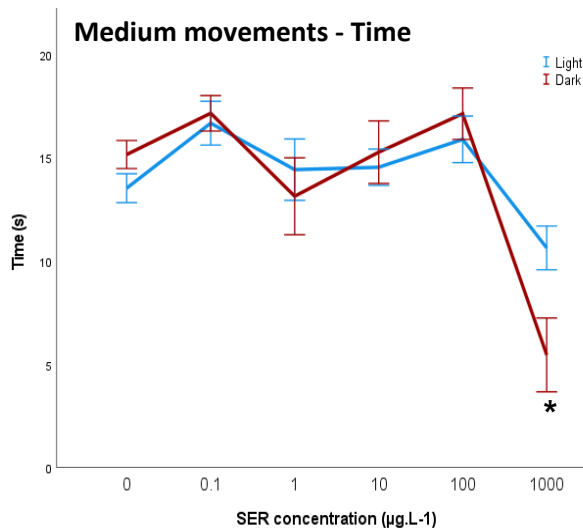
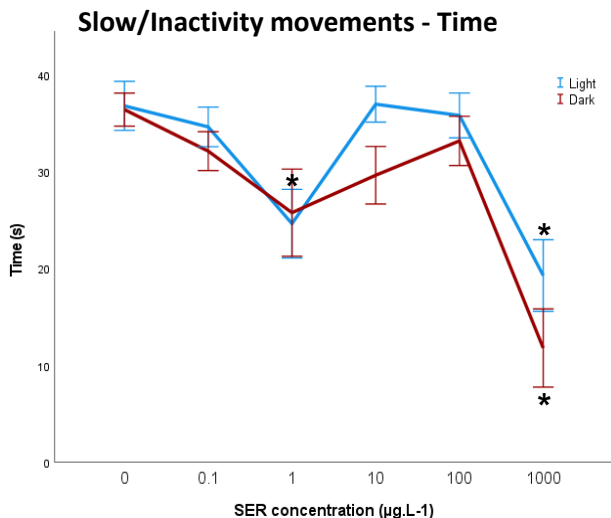


Zebrafish embryos heartbeat rate after 48h exposure to SER



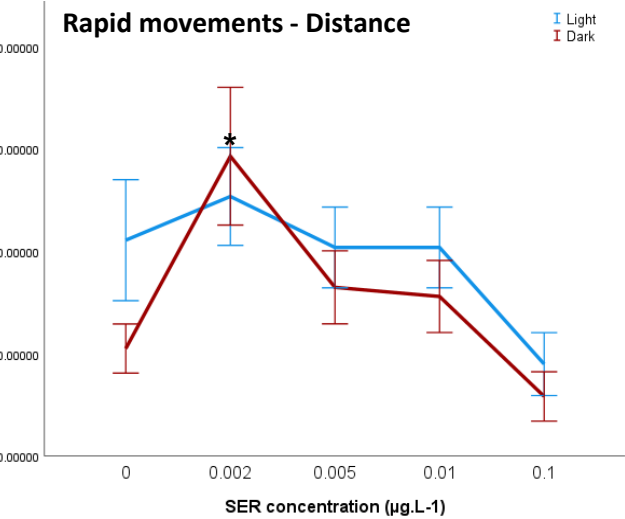
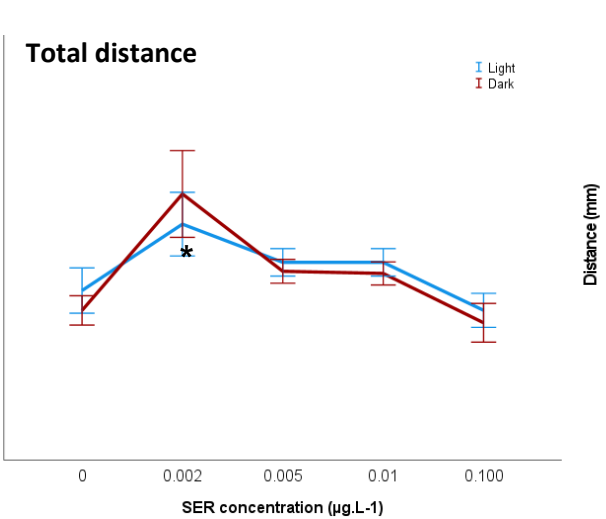
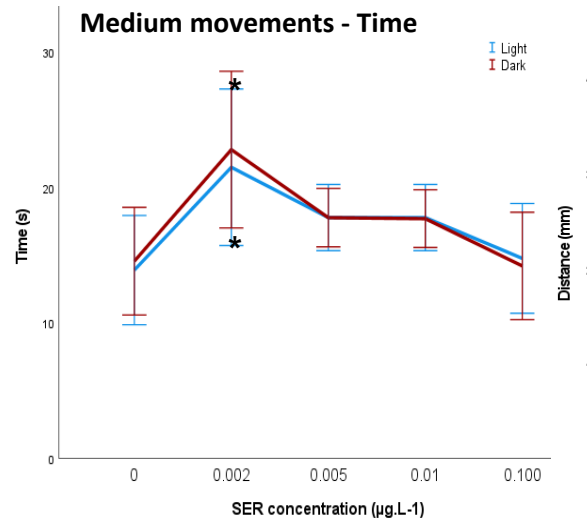
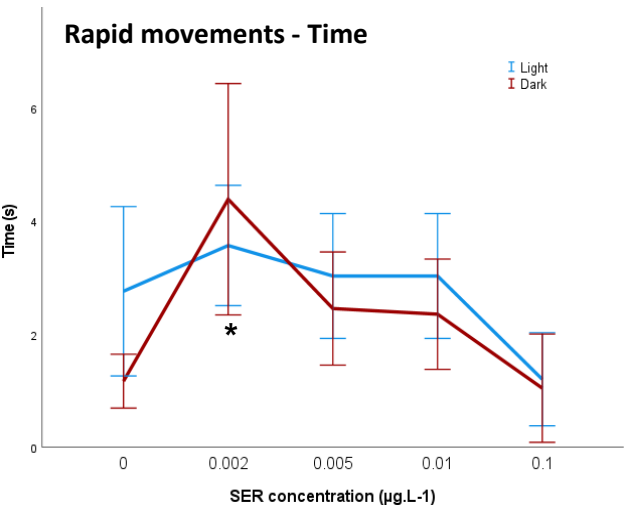
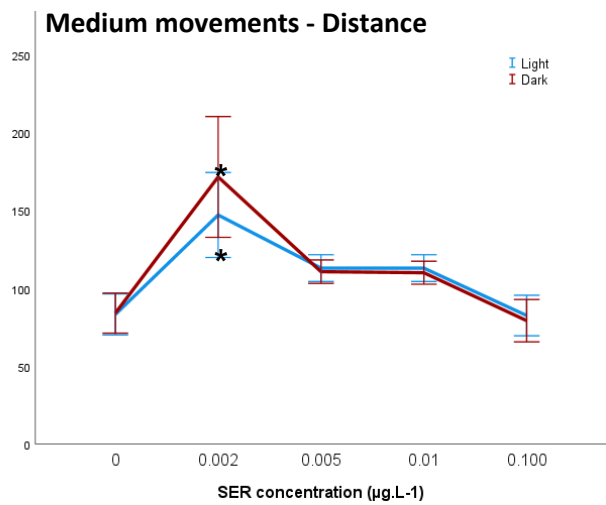
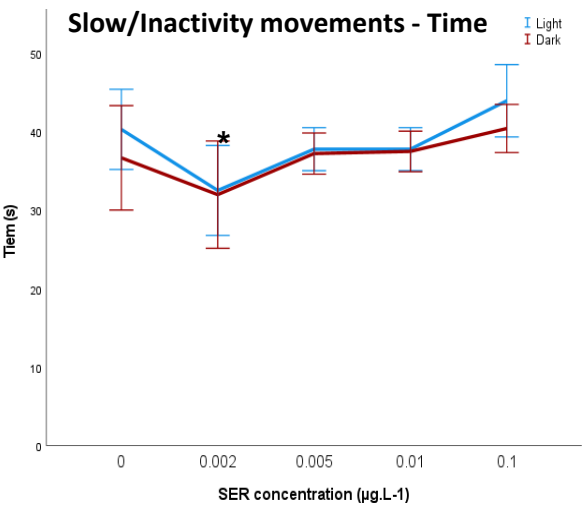
Results and discussion

Behaviour – Acute exposure



Results and discussion

Behaviour – Chronic exposure



Conclusions

Comparative Biochemistry and Physiology, Part C 215 (2019) 1–8



Contents lists available at ScienceDirect

Comparative Biochemistry and Physiology, Part C

journal homepage: www.elsevier.com/locate/cbpc



Exposure to low concentration of fluoxetine affects development and acetylcholinesterase activity of zebrafish embryos

Nátalia Oliveira de Farias^{a,1}, Rhaul Oliveira^{a,b,c,e,*,1}, Diego Sousa-Moura^a, Reginaldo Carlyle Silva de Oliveira^a, Maria Augusta Carvalho Rodrigues^a, Thayres Sousa Andrade^a, Inês Domingues^d, Nichollas Serafim Camargo^{e,f}, Luís Alexandre Muehlmann^{e,f}, Cesar Koppe Grisolia^a



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Chemosphere 238 (2020) 124587



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Tissue bioconcentration and effects of fluoxetine in zebrafish (*Danio Carassius auratus*) after short-term and

^{a,1}, Hai Xu^c, Bentuo Xu^a, Lihui Jiang^a, Minghong Wu^{b,**,*}



Behavioral effects of citalopram, tramadol, and binary mixture in zebrafish (*Danio rerio*) larvae

Raougina-Laouisa Bachour^a, Oksana Golovko^b, Martin Kellner^c, Johannes Pohl^{a,*}



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and Environmental Safety 114 (2015) 67–74

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Toxicity screening of Diclofenac, Propranolol, Sertraline and Simvastatin using *Danio rerio* and *Paracentrotus lividus* embryo bioassays

Sílvia Ribeiro^{a,1}, Tiago Torres^{a,1}, Rosário Martins^{a,b}, Miguel M. Santos^{a,c,*}



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Conclusions

- Impairment of locomotor behaviour might be related to neurological alterations in neurotransmission mediated by xenobiotics. There might be a link between the decrease of locomotor activity of hatched embryos and AChE activity, or a decrease in in two serotonin receptor transcripts (SERT – serotonin transporter protein and 5-HT1A – serotonin 1A receptor transcript) therefore further studies should be performed to corroborate this hypothesis.

- The data demonstrates non monotonic responses as effects of low concentrations were not observed in higher concentrations. Data supports the need for more studies and improvements in wastewater treatment plants.



Acknowledgments

Thank you for your attention!



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Thanks are due to FCT/MCTES for the financial support to CESAM (UID/AMB/50017/2019), through national funds. MO had financial support of the program Investigador FCT, co-funded by the Human Potential Operational Programme and European Social Fund (IF/00335-2015).



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