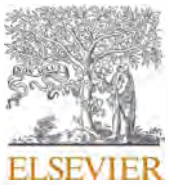
Ecotoxicology and Environmental Safety 239 (2022) 113635



Contents lists available at ScienceDirect

Ecotoxicology and Environmental Safety

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

Induction of aggression and anxiety-like responses by perfluorooctanoic acid is accompanied by modulation of cholinergic- and purinergic signaling-related parameters in adult zebrafish

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ARTICLE INFO

Edited by Dr R Pereira

Keywords:
Perfluorooctanoic acid
Aggression
Anxiety
Acetylcholinesterase
Nucleotide hydrolysis

ABSTRACT

Perfluorooctanoic acid (PFOA) is a contaminant of global concern owing to its prevalent occurrence in aquatic and terrestrial environments with potential hazardous impact on living organisms. Here, we investigated the influence of realistic environmental concentrations of PFOA (0, 0.25, 0.5, or 1.0 mg/L) on relevant behaviors of adult zebrafish (*Danio rerio*) (e.g., exploration to novelty, social preference, and aggression) and the possible role of PFOA in modulating cholinergic and purinergic signaling in the brain after exposure for 7 consecutive days. PFOA significantly increased geotaxis as well as reduced vertical exploration (a behavioral endpoint for anxiety), and increased the frequency and duration of aggressive episodes without affecting their social preference. Exposure to PFOA did not affect ADP hydrolysis, whereas ATP and AMP hydrolysis were significantly increased at the highest concentration tested. However, AChE activity was markedly decreased in all PFOA-exposed groups when compared with control. In conclusion, PFOA induces aggression and anxiety-like behavior in adult zebrafish and modulates both cholinergic and purinergic signaling biomarkers. These novel data can provide valuable insights into possible health threats related to human activities, demonstrating the utility of adult zebrafish to elucidate how PFOA affects neurobehavioral responses in aquatic organisms.

1. Introduction

Perfluorooctanoic acid (PFOA) is a representative member of the perfluoroalkyl carboxylic acids (PFCAs) which are contaminants of emerging concern. The chemical stability and thermal resistance of PFOA is related to the carbon-fluorine bonds (Giesy et al., 2001). Their ubiquity and persistence in the environment is associated with their widespread use in industrial and household applications metal plating operations, textile treatments, pharmaceuticals, cosmetics, surfactants, paper coatings, fire retardants, insecticides, refrigerants, adhesives, and lubricants (Brendel et al., 2018). Moreover, PFOA is often removed inadequately by water treatment procedures namely coagulation, filtration and oxidation (Rahman et al., 2014; Brendel et al., 2018). Unlike other recalcitrant organic pollutants, the high solubility of PFOA in water contributes to its potential ecological threat to aquatic animals. The maximum permissible level of PFOA in drinking water as established by the U.S. EPA is 70 ng/L (Cordner et al., 2019; Garnick et al., 2021). However, evidence also shows elevated levels of PFOA in aquatic environments in many countries across the globe, reaching high concentrations in China (0.970 mg/L), USA (6.57 mg/L) and Austria (1.7 mg/L) (Schultz et al., 2004; Wang et al., 2016; Arias et al., 2015).

Epidemiological studies revealed that PFOA can be detected in serum

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https://doi.org/10.1016/j.ecoenv.2022.113635
Received 6 December 2021; Received in revised form 22 April 2022; Accepted 10 May 2022