NEUROTOXICITY FROM CHRONIC PFOS EXPOSURE IN ADULT ZEBRAFISH INVOLVES MITOCHONDRIAL DYSFUNCTION, NEUROINFLAMMATION, AND HISTOLOGICAL BRAIN DAMAGE

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INTRODUCTION: Perfluorooctane sulfonic acid (PFOS) is a persistent environmental contaminant widely detected in aquatic ecosystems and associated with neurotoxicity. However, the mechanisms underlying its neurological effects remain unclear. OBJECTIVES: This study investigated the chronic neurotoxic effects of PFOS exposure in adult zebrafish (*Danio rerio*), focusing on behavioral alterations, mitochondrial dysfunction, neuroinflammation, and histological abnormalities in different brain regions. MATERIALS AND METHODS: Adult zebrafish (*WT*, 3-4 months old, 50:50 sex ratio) were exposed to PFOS at concentrations of 0.1, 1, and 10 μM for 14 days. Behavioral assays were conducted to evaluate locomotor activity, social preference, and aggression. High-resolution respirometry was used to assess brain mitochondrial functionality, while gene expression via qRT-PCR and histological analyses with H&E were performed after chronic exposure to examine markers of neuroinflammation, neural plasticity, and cell death. RESULTS AND CONCLUSION: Chronic exposure to PFOS at 10 μM significantly reduced aggression. Mitochondrial respirometry revealed that chronic exposure led to impairments in oxidative phosphorylation capacity, bioenergetic efficiency, and electron transport chain activity. Gene expression analysis further supported dysregulation in mitochondrial dynamics, with *mffa* and *mfn1a* downregulated. Additionally, there were alterations in the expression of inflammation-related genes, including the upregulation of *il6* and *il10*, as well as changes in apoptosis and neural activation-related genes such as *casp3a*, *cyc1*, *fosaa* and *egr1*. The histopathological evaluation showed neuronal vacuolation, architectural disorganization, Purkinje cell damage, and increased inflammation in telencephalon, optic tectum, and cerebellum reinforcing PFOS-induced neurotoxicity. Our findings indicate that mitochondrial dysfunction and inflammatory dysregulation are key events underlying PFOS-induced neurotoxicity in adult zebrafish. Given the environmental persistence and bioaccumulative nature of PFOS, further research is needed to assess long-term neurotoxic risks and develop mitigation strategies.

KEYWORDS: PFAS; environmental toxicology; histology; animal behavior; fish.