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RESEARCH ARTICLE

Potentiation of the apoptotic signaling pathway in both the striatum and hippocampus and neurobehavioral impairment in rats exposed chronically to a low–dose of cadmium

Zeyneb Chouit[1] · Dounia Djellal[2] · Souhila Haddad[3] · Mourad Hanfer[2] · Messaoud Hachemi[2] · Zhoura Lakroun[1] · Smail Chafaa[2] · Hamadi Fetoui[4] · Mohamed Kebieche[1,2] · Rachid Soulimani[5]

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Abstract

Cadmium (Cd) is a highly toxic heavy metal. It accumulates in biological tissues, especially in fish which constitutes a first rank food for humans, particularly in the coastal areas. This study investigates the effect of long-term exposure to low Cd concentration (17 μg/kg/day) in rat striatum and hippocampus. In this study, the neurobehavioral ability changes were assessed by applying cognitive standard testing at the end of the rats' exposure period. In addition, the examination of mitochondrial swelling was performed at the same time of evaluation of its redox status in the brain regions studied through stress parameters (GSH, MDA, GST, and CAT). This study examined also whether this long-term exposure can modify the apoptotic signaling pathway via assessment of apoptotic markers (caspase-8 and 9, Bax, Bcl-2, and Cyt-c) in cell lysates. The results of this study showed changes in neurobehavioral abilities of animals and a stronger mitochondrial swelling associated with a significant decrease in antioxidant systems (GSH, GST, and CAT) and conversely an increase in the lipoperoxidation end product (MDA) in both the striatal and hippocampal mitochondria. In addition, the results revealed a significant increase in pro-apoptotic intracellular components such as caspase-9, Cyt-c, and Bax, and showed also an evident decrease in Bcl-2 levels. In conclusion, our results reported that chronic exposure to Cd produces behavioral and cognitive perturbations, enhances oxidative stress associated with mitochondrial edema and Cyt-c leakage, and, ultimately, potentiates apoptosis signaling pathway in both brain regions in rats.

Keywords Cd · Striatum · Hippocampus · Neurobehaviour · Oxidative stress · Apoptosis

Introduction

Over the past two decades, the industrial revolution and technological development have led to high discharges of toxic products, which considerably complicate environmental problems and their impacts on public health (Andra et al. 2017; Andjelkovic et al. 2019). Among these pollutants, Cd is a non-biodegradable industrial and environmental pollutant widely distributed which could be concentrated in the food chain (Pi et al. 2017). However, Cd, in minute quantities, has delirious effects in the body causing acute and chronic toxicities in humans (Wang et al. 2015). Recently, the studies of Abdeen and his collaborators (2017, 2019), on the effect of Cd in rat liver and kidney, showed significant increases in MDA and reduction in GSH and CAT contents in parallel to mitochondrial damage, accumulation of unfolded proteins, DNA oxidation, and upregulation of Bax and Bcl-2 expression. The U.S. Agency for the Toxic Substances and Disease Registry

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✉ Mohamed Kebieche
kebiechem2016@gmail.com

[1] Laboratory of cellular and molecular biology, University of Mohamed Seddik Ben Yahia, Jijel, Algeria

[2] Faculty of natural and life sciences, LBMBPC, University of Batna 2, Route de Constantine, 05078, Fesdis, Batna, Algeria

[3] Faculty of natural and life sciences, University of Abderrahmane Mira, Bejaia, Algeria

[4] Toxicology-Microbiology and Environmental Health Unit (UR11ES70), University of Sfax, Sfax, Tunisia

[5] Unité UR AFPA, EA3998, INRA USC 0340, MRCA, Neurotoxicologie Alimentaire et Bioactivité, Université de Lorraine, BP 4102, 57040 Metz, France

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