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A brain proteome profile in rats exposed to methylmercury or thimerosal (ethylmercury)

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ABSTRACT

Exposure to organomercurials has been associated with harmful effects on the central nervous system (CNS). However, the mechanisms underlying organomercurial-mediated neurotoxic effects need to be elucidated. Exposure to toxic elements may promote cellular modifications such as alterations in protein synthesis in an attempt to protect tissues and organs from damage. In this context, the use of a "proteomic profile" is an important tool to identify potential early biomarkers or targets indicative of neurotoxicity. The aim of this study was to investigate potential modifications in rat cerebral cell proteome following exposure to methylmercury (MeHg) or ethylmercury (EtHg). For MeHg exposure, animals were administered by gavage daily 140 µg/kg/d of Hg (as MeHg) for 60 d and sacrificed 24 h after the last treatment. For EtHg exposure, 800 µg/kg/d of Hg (as EtHg) was given intramuscularly (im) in a single dose and rats were sacrificed after 4 h. Control groups received saline either by gavage or im. After extraction of proteins from whole brain samples and separation by two-dimensional electrophoresis (2-DE), 26 differentially expressed proteins were identified from exposed animals by matrix-assisted laser desorption ionization–time of flight (MALDI-TOF/TOF). Both MeHg and EtHg exposure induced an overexpression of calbindin, a protein that acts as a neuroprotective agent by (1) adjusting the concentration of Ca^{2+} within cells and preventing neurodegenerative diseases and (2) decreasing expression of glutamine synthetase, a crucial protein involved in regulation of glutamate concentration in synaptic cleft. In contrast, expression of superoxide dismutase (SOD), a protein involved in antioxidant defense, was elevated in brain of MeHg-exposed animals. Taken together, our data provide new valuable information on the possible molecular mechanisms associated with MeHg- and EtHg-mediated toxicity in cerebral tissue. These observed protein alterations may be considered as biomarkers candidates for biological monitoring of organomercurial poisoning.

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Mercury (Hg), as element toxic to mammals and other animals, is found in the environment in three distinct chemical forms: as elemental or metallic Hg, as inorganic Hg, or as organic Hg. In addition, toxic properties are directly related to the chemical form of Hg (Bernhoft, 2012; Carneiro et al., 2014a, 2014b; Dorea et al., 2014). The most common forms of organomercurials are methylmercury (MetHg) and ethylmercury (EtHg) (thimerosal). Eating contaminated fish and shellfish is the main source of MetHg exposure (Sweet and Zelikoff, 2001). On the other hand, EtHg has been widely used as a preservative in a number of drug products, including vaccines, to help prevent life-threatening contamination with microbes (Tan and Parkin, 2000). Almost every human and animal (domestic and farmed) that has been immunized with thimerosal-containing vaccines has been exposed to EtHg (Dorea et al., 2013).

Exposure to organic forms of Hg is associated with several neurologic disorders, including cerebellar neurodegeneration, loss of cells from the granular layer, visual impairment with loss of cells of the cortex, peripheral nerve degeneration, and sensory disturbances (Clarkson et al., 2003; Clarkson and Magos, 2006; Counter et al., 2002; Eto et al., 2002; Grandjean and Herz, 2011; Johansson et al.,

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