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Chronic inorganic mercury exposure induces sex-specific changes in central TNF α expression: Importance in autism?

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Abstract

Mercury is neurotoxic and increasing evidence suggests that environmental exposure to mercury may contribute to neuropathologies including Alzheimer's disease and autism spectrum disorders. Mercury is known to disrupt immunocompetence in the periphery, however, little is known about the effects of mercury on neuroimmune signaling. Mercury-induced effects on central immune function are potentially very important given that mercury exposure and neuroinflammation both are implicated in certain neuropathologies (i.e., autism). Furthermore, mounting evidence points to the involvement of glial activation in autism. Therefore, we utilized an in vivo model to assess the effects of mercury exposure on neuroimmune signaling. In prairie voles, 10 week mercury exposure (60 ppm HgCl₂ in drinking water) resulted in a male-specific increase in TNF α protein expression in the cerebellum and hippocampus. These findings are consistent with our previously reported male-specific mercury-induced deficits in social behavior and further support a role for heavy metals exposure in neuropathologies such as autism. Subsequent studies should further evaluate the mechanism of action and biological consequences of heavy metals exposure. Additionally, these observations highlight the potential of neuroimmune markers in male voles as biomarkers of environmental mercury toxicity.

Keywords

heavy metals; environmental toxins; voles; cytokines; chemokines; autism

Introduction

Environmental exposure to heavy metals is a significant risk to human health [12]. Mercury, for example, certainly is neurotoxic and accumulation of mercury in the brain is accompanied by abnormal neuronal function in several brain regions, including in the cerebellum and the hippocampus [5, 17, 54]. Increasing evidence suggests that environmental mercury exposure may contribute to neuropathologies such as Alzheimer's disease (AD) and the autism spectrum disorders (ASD) [20-22, 28, 38-40].

Among the mechanisms implicated in mercury-induced neurotoxicity are mitochondrial dysfunction and oxidative stress [33, 45]. However, sub-lethal exposure to mercury also disrupts immunocompetence [29, 30] suggesting that changes in neuroimmune function may

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