Evidence of parallels between mercury intoxication and the brain pathology in autism

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The purpose of this review is to examine the parallels between the effects mercury intoxication on the brain and the brain pathology found in autism spectrum disorder (ASD). This review finds evidence of many parallels between the two, including: (1) microtubule degeneration, specifically large, long-range axon degeneration with subsequent abortive axonal sprouting (short, thin axons); (2) dendritic overgrowth; (3) neuroinflammation; (4) microglial/astrocytic activation; (5) brain immune response activation; (6) elevated glial fibrillary acidic protein; (7) oxidative stress and lipid peroxidation; (8) decreased reduced glutathione levels and elevated oxidized glutathione; (9) mitochondrial dysfunction; (10) disruption in calcium homeostasis and signaling; (11) inhibition of glutamic acid decarboxylase (GAD) activity; (12) disruption of GABAergic and glutamatergic homeostasis; (13) inhibition of IGF-1 and methionine synthase activity; (14) impairment in methylation; (15) vascular endothelial cell dysfunction and pathological changes of the blood vessels; (16) decreased cerebral/cerebellar blood flow; (17) increased amyloid precursor protein; (18) loss of granule and Purkinje neurons in the cerebellum; (19) increased pro-inflammatory cytokine levels in the brain (TNF-α, IFN-γ, IL-1β, IL-8); and (20) aberrant nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB). This review also discusses the ability of mercury to potentiate and work synergistically with other toxins and pathogens in a way that may contribute to the brain pathology in ASD. The evidence suggests that mercury may be either causal or contributory in the brain pathology in ASD, possibly working synergistically with other toxic compounds or pathogens to produce the brain pathology observed in those diagnosed with an ASD.

Key words: autism, autism spectrum disorder (ASD), mercury (Hg), toxicity, brain pathology

INTRODUCTION

Evidence suggests that children with autism spectrum disorder (ASD) have a greater susceptibility to heavy-metal intoxication than typically developing children (Holmes et al. 2003, Kern and Jones 2006, Rose et al. 2008, Nataf et al. 2008, James et al. 2009, Geier et al. 2009a, Majewska et al. 2010, Youn et al. 2010, Kern et al. 2011a). For example, children with ASD have been found to have low plasma glutathione (GSH) and sulfate (SO4) levels (Waring and Klovrza 2000, James et al. 2004, 2006, 2009, Geier and Geier 2006, Geier et al. 2009c, Pasca et al. 2009, Adams et al. 2011), both of which are critically important for detoxification (Gutman 2002, Kern et al. 2004). Expressions such as “poor detoxifiers” and “poor excretors” have been used in reference to those with ASD (Holmes et al. 2003). In a recent analysis, DeSoto and Hitlan (2010) found that there are 58 research articles which provide empirical evidence relevant to the question of a link between autism and one or more heavy metals. Of those 58 articles, 43 supported a statistically significant link between autism and exposure to toxic metals while 15 showed no statistically significant evidence of a link between metals and autism. Thus, 74% of the studies examined showed a significant relationship between ASD and toxic metals. Moreover, several recent studies have shown that the greater the toxic metal body burden in a child, the worse the autism symptoms that the child experiences.