

RESEARCH ARTICLE

Developmental exposure to mercury chloride does not impair social behavior of C57BL/6 × BTBR F₁ mice

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Abstract

The effects of mercury (Hg) on social behavior and the mechanisms involved remain unknown. This study shows that Hg chloride (HgCl₂) exposure during fetal development does not impair social behavior of a mouse strain susceptible to environment-induced autistic-like behavior based on the parental phenotype. On the contrary, Hg exposure elevated the sociability of females. Since B6 mice are behaviorally normal and BTBR mice display low levels of sociability, the F₁ offspring (B6BF₁) of female B6 mice and male BTBR mice were used to investigate their social behavior and the effects of Hg. Developmental Hg-treatment increased the serum IgG levels of the post-natal day (pnd) 21 offspring, but not pnd70 offspring or the B6 dams. After Hg treatment, there were negligible levels of serum IgG anti-brain antibodies (Ab) in the pnd21 and pnd70 offspring as well as their dams. However, Hg did elevate IgG deposition in multiple assayed brain regions of the pnd21 offspring, but the higher levels were no longer present at pnd70. Cytokine levels were not changed in pnd21 or pnd70 brain by Hg exposure, suggesting neuroinflammation was not induced. Social behavior was assayed at pnd70. Surprisingly, Hg-treatment significantly enhanced sociability of female B6BF₁ offspring, but not that of the male offspring. Our data indicates that developmental exposure to HgCl₂ did not impair social behavior of B6BF₁ offspring, but it enhanced the sociability of females, which was significantly lower in adult B6BF₁ females than B6BF₁ males in the absence of any Hg exposure.

Keywords: Mercury, mouse social behavior, IgG anti-brain antibodies

Introduction

Behavioral assessment is currently the main means to diagnose autism spectrum disorders (ASD). ASD have variant degrees of social interaction and communication deficits and repetitive behaviors (American Psychiatric Association, DSM-IV-TR, 2000). The prevalence of ASD has been increasing especially in developed countries; in the US, the incidence is ~ 1 of 110 children with a ratio of 4~5 males to 1 female (Gurney et al., 2003; Mulvihill et al., 2009; Giarelli et al., 2010).

Many studies have been conducted to investigate the etiology of ASD. Genes are thought to play a substantial role in ASD pathogenesis (Kumar and Christian, 2009; Grafodatskaya et al., 2010). For instance, genes such as *MET*, *PLAUR*, and *Shank3* have been linked to abnormalities in social behavior (Eagleson et al., 2011; Peca et al., 2011). Although genetics clearly influence

ASD susceptibility, in that ASD has one of the highest concordances of genetics and disorders, a recent study of twins has suggested that environment has a greater affect on ASD prevalence than genetics (Hallmayer et al., 2011). Additionally, immune dysfunction has been suggested to contribute to ASD (Ashwood et al., 2006; Goines and Van de Water, 2010). Anti-brain antibodies (Ab) have been detected in ASD children as well as their mothers (Zimmerman et al., 2007; Braunschweig et al., 2008; Singer et al., 2008; Wills et al., 2009; Goines et al., 2011). Elevated plasma inflammatory cytokines and chemokines such as interleukin (IL)-1 β , IL-6, IL-12, IL-8, and interferon (IFN)- γ have been observed in ASD patients (Singh, 1996; Ashwood et al., 2011). Serum or plasma IgG has been reported as increased in ASD patients (Croonenberghs et al., 2002; Enstrom et al., 2009); however, decreased plasma IgG of ASD patients