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Background lead and mercury exposures: Psychological and behavioral problems in children

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ABSTRACT

Background: The potential harm from exposure to nonessential metals, particularly mercury (Hg) and lead (Pb), has been the focus of research for years. Initial interest focused on relatively high exposures; however, recent evidence suggests that even background exposures might have adverse consequences for child development. Identifying the extent of these consequences is now a priority.

Methods: We assessed blood Pb and Hg levels in a biracial sample of 9–11 year-old children ($N = 203$). Neurodevelopment and psychological functioning assessments included hostility, disruptive behaviors, emotion regulation, and autism spectrum disorder behaviors. Parasympathetic (vagal) responses to acute stress were indexed by heart rate variability (HRV) at rest and during stress.

Results: With increasing Pb levels, children exhibit higher levels of hostile distrust and oppositional defiant behaviors, were more dissatisfied and uncertain about their emotions, and had difficulties with communication. These significant associations were found within a range of blood Pb levels from 0.19 to 3.25 µg/dL, well below the "reference value" for children of > 5 µg/dL. Vagal reactivity interacted with Hg such that increasing Hg was associated with increasing autism spectrum behaviors for those children with sustained vagal tone during acute stress.

Conclusions: This study is the first to demonstrate an association between very low-level Pb exposure and fundamental psychological mechanisms that might explain prior associations with more complex outcomes such as delinquency. Analyses of vagal reactivity yielded entirely novel associations suggesting that Hg may increase autism spectrum behaviors in children with sustained vagal tone during acute stress. The novelty of these later findings requires additional research for confirmation and the cross-sectional nature of the data caution against assumptions of causality without further research.

1. Introduction

The adverse effects of elevated blood lead (Pb) on children's development have been studied extensively in the domain of cognitive functioning (Lanphear et al., 2005), even at concentrations below those deemed to be elevated (> 5 µg/dL) by the Centers for Disease Control and Prevention (CDC) in 2012 (Canfield et al., 2003). Effects of Pb exposure also have been examined for behaviors such as delinquency (Needleman et al., 1996); however, much of this work has focused on children with identified exposure routes (*e.g.*, proximity to a battery factory) and thereby higher Pb levels (Wasserman et al., 1998). In contrast, background metal exposures would likely occur through less

Abbreviations: ADHD, Attention Deficit and Hyperactivity Disorder; ASD, Autism Spectrum Disorder; BMI, body mass index; CDC, Centers for Disease Control and Prevention; CDI, Child Depression Inventory; CVD, cardiovascular diseases; DBD, Disruptive Behavioral Disorders; DERS, Difficulties in Emotion Regulation Scale; EECHO, Environmental Exposures and Child Health Outcomes; ECG, electrocardiogram; HF-HRV, high frequency component of HRV; LF-HRV, high frequency component of HRV; Hg, mercury; IBI, interbeat interval; MDL, method detection limits; Pb, lead; SES, socioeconomic status

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clear routes and as a result of relatively minor differences in diet (Davidson et al., 2010; Falco et al., 2006), dust exposure (Fergusson and Kim, 1991), and ambient air pollution (Boehmer et al., 2013). More needs to be learned about possible consequences of background metal exposure. Exposure at these low levels is of particular importance to public health, as background exposures would affect a much larger proportion of children.

One pair of neurodevelopmental disorders that have been evaluated, and happen to have some overlap of symptoms, are Attention Deficit and Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD). A study of 4704 children in the National Health and Nutrition Examination Survey 1999–2002 (Braun et al., 2008) revealed that higher blood Pb levels are associated with a significantly higher risk of ADHD. Notably, this association was found in children with relatively low levels of blood Pb (nearly 80% of this population had blood Pb levels < 2 μg/dL). ASD has been less consistently associated with Pb or other non-essential metal exposures. Most studies have considered metal levels in blood, hair, and urine for those with diagnosed ASD compared to controls. This research has yielded inconsistent results with respect to Pb and Hg, with most studies finding non-significant differences (Macedoni-Luksic et al., 2015; Fuentes-Albero et al., 2015) or even a reduced level of some non-essential metals (Pb) in those with ASD (Yorbik et al., 2010).

The other category of neurodevelopmental impairments that has been studied includes disruptive behaviors and found associations with delinquency (Needleman et al., 1996) and disruptive classroom behavior (Needleman, 1982). Despite these findings, very little attention has been given to the possible underlying psychological mechanisms that may contribute to the observed associations. For example, little is known about how Pb exposure may undermine children's ability to regulate their emotions and develop supportive social relationships. One of the few studies investigating Pb and emotion regulation abilities (Mendelsohn et al., 1998) did find that higher Pb was associated with poor emotion regulation in very young children; however, the children in the study had relatively high levels of Pb exposure (comparing exposed, with levels > 10 μg/dL to less exposed, with levels < 10 μg/dL).

It seems likely that higher blood Pb levels adversely affect core mechanisms of psychological and social functioning, and that such outcomes can be manifested to varying degrees in clinical diagnoses. The present study considers behavioral correlates of relatively low-levels of blood Pb and blood Hg in a biracial sample of 9–11 year old children who together with their parents completed a battery of neuropsychological assessments. These assessments were designed to advance understanding beyond diagnostic dichotomies by measuring underlying functional process dimensions. Based on prior research, we hypothesized that these low-level Pb exposures would be positively associated with evidence of impairments in psychological, social, and physiological regulatory mechanisms.

The role of postnatal Hg exposure in neurodevelopment has been studied as well; but the evidence thus far does not support firm conclusions. ADHD has not shown significant associations with postnatal Hg exposure (Kim et al., 2013); however, there may be an association with ASDs (Geier et al., 2010; Hertz-Picciotto et al., 2010). One explanation for the divergent findings may be that differences in the strength or presence of associations between Hg and neurodevelopmental disorders result from a combination of Hg exposure and underlying genetic/biological susceptibility (Geier et al., 2010). One such neurobiological system that might affect the risk linked to Hg exposure is parasympathetic (vagal) regulation (Porges, 1995). Recent research has demonstrated how environmental factors might have differential impact as a function of underlying individual differences in vagal responses to acute stress (Hagan et al., 2016).

Therefore, in the present study we considered the role of parasympathetic (vagal) responses to acute stress in the associations between low-level metal exposures and neuropsychological outcomes. The focus on the parasympathetic system has been a result of efforts to integrate mechanisms of physiological control (Porges, 1995) with psychological/behavioral regulation (Suess et al., 1994; Calkins, 1997). Specifically, vagal activity when an organism is at rest is regarded as a mechanism for maintaining homeostasis (Richards, 1987). On the other hand, during changing or demanding situations (*e.g.*, stress) the vagal system is thought to function as a sort of "brake" to facilitate control (Porges et al., 1996). According to this theory, greater vagal tone ("braking") during a stress episode indicated better behavioral control, whereas decreasing vagal tone during challenging/attentional tasks reflects impaired vagal braking which undermines behavioral control and may impair social interactions (Porges et al., 1996). Environmental burdens may be particularly harmful to those with poor vagal control during challenges. A number of studies have yielded evidence that is consistent with this hypothesis (Obradovic et al., 2011; Treadwell et al., 2010). On the other hand, an excessively controlled vagal system may also be associated with neurodevelopmental disorders. For instance, relative to children who exhibited "normal" vagal withdrawal responses during stress, autistic children did not display this response but instead exhibited continued vagal tone (Toichi and Kamio, 2003). Therefore, in addition to considering the potential "main effects" of nonessential metal exposures on neurodevelopment, the present study also examined the possibility that this environmental burden may impair neurodevelopment depending on underlying differences in vagal responses to acute stress.

2. Methods

2.1. Participants

The participants were drawn from the ongoing Environmental Exposures and Child Health Outcomes (EECHO) study, a research project investigating the relationships among exposures to environmental toxicants and cardiovascular risk indices in 9–11 year old children living in low- to middle-income neighborhoods in a midsize city in upstate New York. The EECHO sample contains an approximately equal number of Black/African American and White/European American, male and female children. The study excludes any children who are not self identified as either Black or White, are not 9–11 years old, do not meet zip code residence selection criteria (designed to target low SES neighborhoods and roughly equal numbers of Black and White children), those with serious medical or developmental disabilities, and those who were on medications that might affect their cardiovascular system. We have currently recruited 210 children; however, a programming error in the online survey tool at the beginning of the study resulted in missing questionnaire data for 7 children. Therefore, the data for this paper were from 203 children (representing 170 families) recruited into EECHO thus far. With respect to joint participation, 134 children participated alone, 54 children participated with 1 sibling, and 15 children participated with 2 siblings. As we describe below, the data analysis plan reflected the nested nature of the data. The parent/caregiver informant was usually the mother (86%); in some cases the informant was a father (9%), grandmother (2%), or other custodian (*e.g.,* aunt; 3%).

3. Procedure

Participants arrived at our laboratory and blood draw center located on the Syracuse University campus and signed an assent form while a parent signed a separate consent form approved by the Institutional Review Board of Syracuse University. As part of a more extensive blood draw protocol, a certified phlebotomist drew 5-mL venous blood into a plastic lavender-top (EDTA), certified by the analyzing laboratory for measurement of blood levels of Pb and (total) Hg concentrations. Blood specimens were immediately placed on ice and within 2 h of the blood draw the samples were transferred into 5-mL cryovials (certified by the analyzing laboratory) and frozen at −80 °C pending shipment to the