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SCIENCE DIRECT
NeuroToxicology 27 (2006) 210–216
NeuroToxicology

Neuropsychological correlates of hair arsenic, manganese, and cadmium levels in school-age children residing near a hazardous waste site

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Received 7 July 2005; accepted 12 October 2005
Available online 28 November 2005

Abstract

A pilot study was conducted to explore the potential associations between hair metal levels and the neuropsychological function and behavior of school-aged children. Thirty-two children, 11–13 years old, were administered a battery of tests that assessed general intelligence, visual-motor skills, receptive language, verbal memory, nonverbal problem-solving, and behavior problems. Parents and teachers rated the children's attention, executive functions, and behavior problems. The concentrations of manganese (Mn), arsenic (As), and cadmium (Cd) were measured in hair samples provided by 31 of the children. The mean hair metal levels were: Mn, 471.5 parts per billion (ppb); As, 17.8 ppb; Cd, 57.7 ppb. Children's general intelligence scores, particularly verbal IQ scores, were significantly related, inversely, to hair Mn and As levels, as were scores on tests of memory for stories and a word list. In some cases, a significant Mn-by-As interaction was found. It appeared that it was the low scores of children for whom both Mn and As levels were above the median values in the sample that were responsible for the main effects observed for each metal. No other significant relationships were found. These results suggest the need to study further the neuropsychological correlates of developmental exposure to Mn and As, particularly as a mixture.

Keywords: Children; Neuropsychology; Behavior; Manganese; Arsenic; Cadmium; Metal mixtures

1. Introduction

Many studies indicate that children exposed, at low levels, to metals such as lead (Pb) and mercury present signs of neurotoxicity, including reduced performance on neuropsychological tests and altered behavior (Bellinger and Adams, 2001). The extent to which low-level exposures to other metals, such as arsenic (As), manganese (Mn), and cadmium (Cd), are also neurotoxic is considerably less certain.

As has generally been considered to be a peripheral neurotoxicant, producing a clinical picture of severe polyneuropathy after acute poisoning. Recent mechanistic and neurobehavioral studies in animal models (Rao and Avani, 2004; Chaudhuri et al., 1999) and in humans (Calderon et al., 2001; Tsai et al., 2003; Wasserman et al., in press) suggest that this neurotoxicity includes the central nervous system as well. Mn, a transition metal, is both a nutrient and toxicant. Occupational exposures to Mn produce a clinical syndrome of memory loss, behavioral/mood changes and, in its final stages, a Parkinsonian-like motor dysfunction. Some studies suggest that Mn is a neurodevelopmental toxicant at environmental levels of exposure (Takser et al., 2003; He et al., 1994; Crinella et al., 1998). The central nervous system has generally not been considered to be an important target organ for Cd, although neurotoxicity has been reported in both adults and children (Bellinger et al., 2003).

In this cross-sectional pilot study, we evaluated the associations between the hair levels of As, Mn, and Cd and

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0161-813X/$ – see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuro.2005.10.001

neurospsychological function and behavior in school-aged children. The study was conducted among children residing in Ottawa County, an area of northeast Oklahoma with a 100-year history of Pb and zinc (Zn) mining. Part of this region, called the Tar Creek Superfund site, was first listed on the U.S. Environmental Protection Agency's National Priorities List in 1983 and remains on the NPL (EPA site ID 0601269 (http://www.epa.gov/superfund/sites/npl/ok/htm). More than 75 million tonnes of mining waste (referred to as ''chat'') was left on the surface in piles reaching as much as 200 ft in height. Chat contains metals other than Pb and Zn, including Cd and Mn. Mine tailings also contaminate more than 800 acres of flotation ponds in the Tar Creek region. Although As is not found in chat at levels above background environmental concentrations, Oklahoma is known to have high background levels of As. Due to community concerns about As, we included this metal in our study.

2. Methods

2.1. Study sample

In order to minimize a volunteer bias that might have resulted from community-wide requests for participants, the study sample was recruited from two science classes in the Miami, OK, school system. A letter describing the study was sent home with each child, along with a postcard for parents to return indicating interest in being contacted about participating. Positive responses were received from the parents of 32 of 80 children (40%), and appointments with the examiner (DCB) were scheduled. The examiner made five visits to Miami in 2004 to conduct the evaluations. Each child was given $50 for participating. This study was approved by the Committee on Clinical Investigation of Children's Hospital Boston. Each child provided assent, and a parent or guardian provided consent. In addition, a Certificate of Confidentiality was obtained from the National Institutes of Health.

Table 1 presents the demographic characteristics of the study sample. Children ranged in age from 11 years 7 months to 13 years 8 months. Almost one-third of the parents self-identified themselves as American Indian. Fewer than half of the children were living with both biological parents, although 85% were living with at least one biological parent. Approximately 56% of the women and 40% of the men serving in a guardianship role had attended or graduated from college.

Table 1
Characteristics of study participants

Age in months (mean, S.D., range)	151.5, 6.8, 139–164
Sex	47% male
Ethnicity	31% American Indian 69% White, non-Hispanic
Family structure	44% two parent household: both biological parents 25% two parent household: one biological and one step/adoptive parent 16% one parent household: biological parent
Maternal education	22% less than high school 22% high school graduate 19% some college 37% college graduate or graduate degree
Paternal education	10% less than high school 50% high school graduate 23% some college 17% college graduate or graduate degree
Number of children <18 years in the home (mean, S.D.)	1.9, 1.3
Hair metals (ppb)	
Arsenic	17.8, 14.1, 1.4–55.4
Manganese	471.5, 455.5, 89.1–2145.3
Cadmium	57.7, 57.7, 16.4–293.1
Lead	1680, 5178, 137–29,343

2.2. Data collection

2.2.1. Neuropsychological evaluation

Each child was administered a 2-h battery of neuropsychological tests in a private room at the public library or in a small conference room at the local hospital. Because of limited knowledge about potential neuropsychological correlates of children's exposures to the metals of interest, the battery was broad-based *and included assessments of most major domains*. The battery included the following instruments: Wechsler Abbreviated Intelligence Scale (WASI) (The Psychological Corporation, 1999), Wide Range Assessment of Visual Motor Ability (WRAVMA) (Adams and Sheslow, 1995), the 3 receptive scales of the Clinical Evaluation of Language Fundamentals-Third Edition (CELF-3) (Semel et al., 1995), the Children's Category Test-Level II (CCT) (Boll, 1993), the California Verbal Learning Test-Children (CVLT-c) (Delis et al., 1994), and the story memory subtest of the Wide Range Assessment of Memory and Learning (WRAML) (Sheslow and Adams, 1990). Children also completed two self-report instruments, the Children's Depression Inventory (CDI) (Kovacs, 2001), and the Behavior Assessment System for Children (BASC) (Reynolds and Kamphaus, 1992). Both parents and the teacher completed the appropriate versions of the CADS-IV (Connors, 1997, 1999), a questionnaire that assesses attention, and the Behavior Rating Inventory of Executive Functions (BRIEF) (Gioia et al., 2000). The children's teacher also completed the BASC.

Parents also completed a brief questionnaire that elicited information about ethnicity, primary language spoken in the home, family structure, maternal and paternal education, the child's medical history (conditions, hospitalizations, medications), and the child's educational history (grade retention, receipt of remedial services).

2.2.2. Hair sampling and analysis

Before the neuropsychological evaluation, a hair sample was collected from each child. Approximately 30–40 strands were taken from the occiput. If necessary to obtain a sufficient