Neurotoxicology and Teratology 51 (2015) 27–34

Contents lists available at ScienceDirect

Neurotoxicology and Teratology

journal homepage: www.elsevier.com/locate/neutera

Assessing new dimensions of attentional functions in children prenatally exposed to environmental contaminants using an adapted Posner paradigm☆

Audrey-Anne Ethier [a], Gina Muckle [b], Sandra W. Jacobson [c], Pierre Ayotte [d,e], Joseph L. Jacobson [c], Dave Saint-Amour [a,f,]*

[a] Centre de recherche, CHU Sainte-Justine, 3175, Chemin de la Côte Sainte-Catherine, Montréal, Québec H3T 1C5, Canada
[b] École de psychologie, Université Laval, Pavillon Félix-Antoine-Savard, 2325, rue des Bibliothèques Québec G1V 0A6, Canada
[c] Department of Psychiatry and Behavioral Neurosciences, Wayne State University, 3901 Chrysler Drive, Suite 2-C, Detroit, MI 48201, United States
[d] Axe santé des populations et pratiques optimales en santé, Centre de recherche du CHU de Québec, 2875 boul. Laurier, Québec, Québec G1V 2M2, Canada
[e] Département de médecine sociale et préventive, Faculté de Médecine, 1050, avenue de la Médecine, Pavillon Ferdinand-Vandry, Université Laval, Québec, Québec G1V 0A6, Canada
[f] Département de psychologie, Université du Québec à Montréal, 100 rue Sherbrooke Ouest, Montréal, Pavillon Adrien Pinard, Montréal, Québec H2X 3P2, Canada

ARTICLE INFO

Article history:
Received 29 September 2014
Received in revised form 18 July 2015
Accepted 22 July 2015
Available online 30 July 2015

Keywords:
Human neurotoxicity
Polychlorinated biphenyls
Methylmercury
Lead
Visuospatial attention
Vigilance
Impulsivity
Development

ABSTRACT

Chronic exposure to methylmercury (MeHg), lead (Pb) and polychlorinated biphenyls (PCBs) has been associated with a range of attention deficits in children, but it is not known whether selective spatial attention is also altered. We modified the classic Posner paradigm, which assesses visuospatial attention, to also assess vigilance and impulsivity. This paradigm is based on the well-documented findings that a target will be detected more quickly if a visual cue indicates beforehand where it will appear, and more slowly if the cue indicates a false spatial location. In our task, visual distractors were introduced, in addition to the classic Posner trials, to assess impulsivity, and a central smiley face, whose eye-movement cued the location of the targets, to measure spatial attention. This task was administered to 27 school-age Inuit children (mean age = 11.2 years) from Nunavik (Arctic Quebec, Canada), in which pre- and postnatal exposures to environmental contaminants had been documented from birth. After controlling for the impact of confounding variables, multivariable regressions revealed that prenatal exposures to PCBs and Pb were significantly associated with greater inattention and impulsivity, respectively, while current exposure to Pb was significantly associated with longer reaction times. Although a significant correlation was observed between cord blood PCB concentration and decreased visuospatial performance, no significant association was found after adjustment for confounders. No effect was found for Hg exposures. These results suggest that our adapted Posner paradigm is sensitive in detecting a range of attention deficits in children exposed to environmental contaminants; implications for future studies are discussed.

1. Introduction

Environmental contaminants are ubiquitous, and the neurotoxic effects of their exposure are of widespread concern. Children are at particular risk since the developing brain is especially vulnerable to exposure (Lidsky and Schneider, 2006). Chronic exposure to low-level concentrations of several contaminants has been associated with cognitive deficits in children from different populations. Effects on attentional abilities are of concern given the fundamental role of attention in learning. Moreover, attention deficit hyperactivity disorder (ADHD) is the most frequently diagnosed neurobehavioral disorder in children in many countries (Dodangi et al., 2014; Perou et al., 2013). Although the etiology of ADHD is a complex interaction between environmental, genetic and social factors, recent data suggest that exposure to environmental contaminants is also a relevant risk factor (Bouchard et al., 2007, 2010; Boucher et al., 2012b; Eubig et al., 2010; Roy et al., 2009; Sagiv et al., 2010; but see also Newman et al., 2014). Exposure to methylmercury (MeHg), lead (Pb) and polychlorinated biphenyls (BPCs), which have been well documented in several cohort studies including in Nunavik (Arctic Quebec, Canada) (e.g., Muckle et al., 2001b), are those most associated with ADHD manifestations in the literature.

MeHg, a contaminant found in fish and marine food, has been associated with attention problems in children from several coastal populations. In studies of school-age children, prenatal and current exposures to MeHg were associated with poorer short-term memory,

☆ This manuscript is dedicated to the memory of our friend and colleague, Dr. Éric Dewailly. As a physician-scientist, Éric was dedicated to assessing the impact of environmental contaminants on the life-style and health of Indigenous peoples worldwide.

* Corresponding author at: Université du Québec à Montréal, 100 rue Sherbrooke Ouest, Montréal, Pavillon Adrien Pinard, Montréal, Québec H2X 3P2, Canada.
E-mail address: saint-amour.dave@uqam.ca (D. Saint-Amour).

http://dx.doi.org/10.1016/j.ntt.2015.07.005
0892-0362/

a brain function that is closely dependent on attention (Grandjean et al., 1997, 1999b). Using a Continuous Performance Task (CPT), which is specifically designed to assess impulsivity and sustained attention, prenatal exposure to MeHg was associated with increased reaction time in children (Grandjean et al., 1997), an effect that continued to be evident at 14 years old (Debes et al., 2006; Julvez et al., 2010). An association between prenatal exposure to MeHg and the behavioral symptomatology of ADHD in school-age children was also found in different studies (Boucher et al., 2012b; Sagiv et al., 2012b).

The association of exposure to Pb, a contaminant found ubiquitously in the environment, with attention deficits in children is well established, even at low exposure levels. Postnatal exposure to Pb was related with a poorer performance on a visual attention task (Surkan et al., 2007). Current Pb level was also associated with several indicators of impulsivity and inattention in children such as behavioral indicators (Plusquellec et al., 2007, 2010), parental and teacher reports (Fergusson et al., 1993), performance on the Go/No-Go task (Boucher et al., 2012a) or on the CPT (Kim et al., 2010; Walkowiak et al., 1998). Such associations have been identified early in development (Plusquellec et al., 2007), and there is evidence that impulsivity and attention deficits might persist in adolescence (Fergusson et al., 1993). Current Pb exposure was also related to ADHD and conduct disorders in several cohorts of children and adolescents (Braun et al., 2006, 2008; Kim et al., 2013).

Although their production has been banned worldwide for several decades (Xu et al., 2013), PCBs are still highly persistent organochlorine compounds in the environment and bioaccumulate in fish and sea mammals. Chronic prenatal exposure to PCBs at low-levels was associated with a reduction of alertness in a sample of newborn infants (Sagiv et al., 2008). In studies conducted at school-age, prenatal PCB exposure was related to executive dysfunctions (Forns et al., 2012b), greater reaction time variability (Sagiv et al., 2012a), inattention (Jacobson and Jacobson, 2003; Sagiv et al., 2012a), impulsivity (Jacobson and Jacobson, 2003; Stewart et al., 2003, 2005) and more ADHD-like behaviors (Sagiv et al., 2010). Postnatal exposure to this contaminant was also associated with various measures of inattention across multiple tests (Boucher et al., 2012a; Forns et al., 2012a; Verner et al., 2015).

In all the aforementioned studies, attention capacities have been assessed with standardized questionnaires, behavioral coding or with computerized tasks that are mostly based on the CPT paradigm. Although it is widely used to assess sustained attention, the CPT does not permit examination of some important basic attentional processes, such as orientation in space. Spatial attention refers to a brain function by which a particular location in the visual field is selected for optimal processing; that is, to quickly select relevant information in the environment (Atkinson et al., 1992). This type of attention appears early in development and is particularly important for numerous tasks, including reading. Although some studies have examined some visuospatial functions (e.g., visuospatial reasoning, discrimination or memory) in relation with environmental contaminant exposure in children (Chevrier et al., 2009; Forns et al., 2012b; Grandjean et al., 1999a,b), none has specifically investigated the capacities of orienting, engaging and disengaging attention in visual space. Furthermore, many factors, such as predictability, which is known to control or influence attention deployment and performance, were often not taken into account by researchers investigating the impact of environmental contaminant exposure on brain function (with the CPT or other tests). For example, if a target is always presented at the same location, then its selection and identification can occur more quickly (and distractors become less disruptive) than if the location is not known ahead of time (Plude and Hoyer, 1986). The temporal predictability of distractor information is also important in determining the ease of maintaining the focus of attention on target information. For example, if the presentation at regular and predictable intervals of the distractors can be anticipated, then the task is likely to be less sensitive in detecting impulsivity than if the distractors are presented at random or unpredictable intervals on a trial-by-trial basis (Connor et al., 2004). Thus, assessments of spatial attention need to take into consideration the limitations of tests used in previous studies on child attention and environmental contaminants.

The current proof-of-concept study was conducted to evaluate a new protocol to measure spatial attention in children with documented exposure to environmental chemicals, while simultaneously assessing core attributes of performance such as errors of commission, omission and reaction time. To this end, we examined a small group of children from the Nunavik Child Development Study (NCDS), who displayed higher contaminant levels than those observed in the general population in North America (Jacobson et al., 2008; Muckle et al., 2001b). Prenatal exposure to Hg in Nunavik is 15 to 20 times higher than in southern Quebec's general population, and 2 to 4 times higher for PCBs and Pb (Rhainds et al., 1999). While the MeHg and PCBs are mostly found in Beluga meat and marine mammal fat, respectively (Lemire et al., 2015), the main source of Pb exposure comes from the consumption of contaminated meat from birds and animals killed with Pb bullets (Levesque et al., 2003).

2. Material and methods

2.1. Participants

School-age children from the village of Puvirnituq, who initially participated in the Cord Blood Monitoring Program in Arctic Quebec between 1993 and 1998 (Muckle et al., 1998), were invited to participate in an NCDS follow-up study between 2005 and 2010 (Boucher et al., 2010, 2012b; Ethier et al., 2012; Jacobson et al., 2015). A subsample of 30 of these children was recruited to participate in the present study in 2009–2010. Adequate data were obtained from 27 children (mean age $\pm$ SD $= 11.2 \pm 1.1$; range $= 8.6$–12.6 years; 18 boys; normal visual acuity $-$ 20/20 or better); two had technical data acquisition problems and one failed to cooperate. The research procedures were approved by the Wayne State University, Laval University, and Sainte-Justine Hospital ethics committees.

2.2. Contaminant and nutrient analyses in biological samples

Pre- and postnatal exposures to Hg, Pb and PCBs were documented at birth from the Cord Blood Monitoring Program, and at school age from a venous blood sample obtained from each child on the day of testing. Concentration of docosahexaenoic acid (DHA), an important omega-3 fatty acid, was also measured at these two time points. The analyses were performed at the *Laboratoire de Toxicologie INSPQ*, except for DHA, which was analyzed at the University of Guelph Lipid Analytical Laboratory. Detailed analytical and quality control laboratory procedures are described elsewhere (Dallaire et al., 2014; Ethier et al., 2012). The 14 most prevalent PCB congeners (IUPAC nos. 28, 52, 99, 101, 105, 118, 128, 138, 153, 156, 170, 180, 183, 187) were measured in purified plasma extracts using gas chromatography–mass spectrometry. PCB congener 153 was used as an indicator of total PCB exposure because it is highly correlated with other PCB congeners (Ayotte et al., 2003; Cartier et al., 2014; Muckle et al., 2001a; Ulbrich and Stahlmann, 2004). Furthermore, the PBC 153 congener is of particular interest because it is highly persistent with an elimination half-life of 14.4 years (Ritter et al., 2011). It is the congener found in the highest concentration in human adipose tissue (Faroon et al., 2000). Since Hg, Pb and PCB 153 concentrations followed log-normal distributions, analyses were conducted with natural log-transformed values for these variables, for both prenatal and current exposure.

2.3. Visuospatial attention-shift paradigm

An adaptation of the Posner attention-shift paradigm (Posner et al., 1980) was administered to all participants. This paradigm is based on