Prenatal Methylmercury, Postnatal Lead Exposure, and Evidence of Attention Deficit/Hyperactivity Disorder among Inuit Children in Arctic Québec

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BACKGROUND: Prenatal exposure to methylmercury (MeHg) and polychlorinated biphenyls (PCBs) has been associated with impaired performance on attention tasks in previous studies, but the extent to which these cognitive deficits translate into behavioral problems in the classroom and attention deficit/hyperactivity disorder (ADHD) remains unknown. By contrast, lead (Pb) exposure in childhood has been associated with ADHD and disruptive behaviors in several studies.

OBJECTIVES: In this study we examined the relation of developmental exposure to MeHg, PCBs, and Pb to behavioral problems at school age in Inuit children exposed through their traditional diet.

METHODS: In a prospective longitudinal study conducted in the Canadian Arctic, exposure to contaminants was measured at birth and at school age. An assessment of child behavior was conducted at school age.

RESULTS: Cord blood mercury concentrations were associated with higher TRF symptom scores for attention problems and DBD scores consistent with ADHD. Current blood Pb concentrations were associated with higher TRF symptom scores for externalizing problems and with symptoms of ADHD (hyperactive-impulsive type) based on the DBD.

CONCLUSIONS: To our knowledge, this study is the first to identify an association between prenatal MeHg and ADHD symptomatology in childhood and the first to replicate previously reported associations between low-level childhood Pb exposure and ADHD in a population exposed to Pb primarily from dietary sources.

KEY WORDS: ADHD, attention, children, exposure, externalizing behavior, lead, mercury, methylmercury, polychlorinated biphenyls. Envir Health Perspect 120:0000–0000 (2012). http://dx.doi.org/10.1289/ehp.1204976 [Online 21 September 2012]

Mercury (Hg), polychlorinated biphenyls (PCBs), and lead (Pb) are widespread environmental contaminants known for their adverse effects on neurodevelopment (Grandjean and Landrigan 2006). Organic Hg, or methylmercury (MeHg), is the most neurotoxic form of Hg and is present in fish and marine mammals (World Health Organization 1990). The adverse effects of acute MeHg exposure in utero have been documented following poisoning episodes that occurred in Japan (1953; 1960–65) and Iraq (1971–72) and include neurological symptoms and developmental delays (Amin-Zaki et al. 1974; Tsubaki and Irukayama 1977). In marine mammal- and fish-eating populations, chronic exposure to lower doses of MeHg during prenatal development has been associated with impairment in several domains of cognition including attention (Grandjean et al. 1997). However, the extent to which prenatal MeHg exposure is associated with behavioral problems at school age, in the absence of overt toxicological effects, remains unknown.

PCBs are synthetic organochlorine compounds (OCs) known for their long persistence in the environment. Like other OCs, their production and use has been banned or restricted in most industrialized countries, and population exposure to these chemicals now arises mainly from the ingestion of contaminated food (e.g., Moon et al. 2009). Several birth cohort studies have reported subtle cognitive alterations during childhood associated with prenatal PCB exposure, including response inhibition and attention deficits (Jacobson and Jacobson 2003; Stewart et al. 2005; reviewed by Boucher et al. 2009). In a recent prospective birth cohort study conducted near a PCB-contaminated harbor in New Bedford, Massachussetts, higher PCB and OC levels in umbilical cord predicted attention deficit/hyperactivity disorder (ADHD)–like behaviors reported by classroom teachers (Sagiv et al. 2010).

Pb exposure has also been associated with impaired performance on neuropsychological tasks assessing attention and inhibition (Chiodo et al. 2004; Surkan et al. 2007). Prenatal Pb exposure is related to reduced IQ scores (Schnaas et al. 2006; Wasserman et al. 1998), and the relation between postnatal Pb exposure and ADHD symptoms and diagnoses is well established (e.g., Braun et al. 2006; Froehlich et al. 2009; Ha et al. 2009; Kim et al. 2010). Exposure to Pb during childhood has also been associated with conduct disorder (CD) (Braun et al. 2008), higher rates of criminal arrests in early adulthood (Wright et al. 2008), and teachers’ ratings of anxiety and social problems (Roy et al. 2009).

The Inuit population in Nunavik (Arctic Québec, Canada) is exposed to MeHg and PCBs through consumption of marine mammals and fish (Muckle et al. 2001), and is also exposed to Pb through the use of Pb pellets for game hunting (Gauthier et al. 2003). This study was designed to examine the relation of developmental exposure to MeHg, PCBs, and Pb to behavioral problems at 11 years of age as reported by the child’s classroom teacher.

Methods

Participants. The participants were Inuit children from Nunavik, a region located north of the 55th parallel, about 1,500 km from Montréal. Most of the participants (n = 208) were initially recruited under the auspices of the Cord Blood Monitoring Program (1993–1998), which was designed to document prenatal exposure to a range of environmental contaminants and nutrients in newborns in Arctic Québec (Dallaire et al. 2001); the others (n = 57) were originally recruited for the Environmental Contaminants and Child Development Study (1996–2000; Muckle et al. 2001), and an additional 14 children had been involved in both studies. Mothers were contacted by phone, provided with information about the study protocol, and invited to participate with their children in the Nunavik Child Development Study.

Inclusion criteria were age between 8.5 and 14.5 years, birth weight ≥ 2.5 kg, gestation duration ≥ 35 weeks, and no major birth complications.

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We are grateful to the Nunavik population and to all people who have contributed to this study.

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The authors declare they have no actual or competing financial interests.

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defects, neurological or health problems, or pervasive development disorders. Written informed consent was provided by a parent of each participant, and oral assent was provided by each child. The research was approved by the Laval University and Wayne State University ethics committees and was conducted in accordance with ethical standards of the Helsinki Declaration (World Medical Association 2008).

Between September 2005 and February 2010, 294 children and their mothers participated in neurocognitive assessments in the three largest Nunavik villages. Participants who resided in other communities were transported by plane to one of the larger villages for testing. A maternal interview was conducted to provide information on demographic background and other factors including smoking and alcohol and drug use during pregnancy. Questionnaires for behavior assessment were filled by the child’s classroom teacher, who obtained the forms from our research nurse via the school principal. Questionnaires from eight participants were not returned by the classroom teacher, and two children were not assessed because they had not attended school since the beginning of the academic year. Of the 284 remaining children, 2 with a history of epilepsy, 1 with a history of head trauma requiring surgery, 1 with a history of meningioma, 1 with a history of head trauma requiring surgery, 1 with a history of head trauma requiring surgery, 1 with a history of meningioma, and 1 with multiple sclerosis were excluded after data collection.

Behavior assessments. The Teacher Report Form (TRF) from the Child Behavior Checklist (Achenbach and Rescorla 2001) was completed by the child’s classroom teacher. The TRF contains 112 items, each of which is rated on a 3-point scale for applicability to the child: 0 = not true; 1 = somewhat or sometimes true; 2 = very true or often true. Eight syndrome scores are computed by summing the scores of specific items: Anxious/depressed, Withdrawn/depressed, Somatic complaints, Sleep problems, Thought problems, Aggressive, Rule-breaking behavior, and Attention problems. The first three syndrome scores are summed to compute the Internalizing problems score, and the Aggressive and Rule-breaking behavior scores are summed to obtain the Externalizing problems score. To limit the number of statistical comparisons, we restricted our analyses to Internalizing, Externalizing, and Attention problem areas because no normative data are available for Inuit children, raw scores for each individual scale were used in statistical analyses.

The Disruptive Behavior Disorders Rating Scale (DBD; Pelham et al. 1992) contains 45 behavioral descriptors based on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV; American Psychiatric Association 1994). It is designed to be completed by parents and teachers to provide information required for four clinical diagnoses: ADHD–Inattentive type, ADHD–Hyperactive-impulsive type, Oppositional Defiant Disorder (ODD), and Conduct Disorder (CD). Each behavioral descriptor is rated on a 4-point scale: 1 = never/rarely; 2 = sometimes; 3 = often; 4 = very often. Symptoms are considered to be present when rated either 3 or 4. A teacher report of at least six DSM-IV symptoms of ADHD–Inattentive type, six of ADHD–Hyperactive-impulsive type, four of ODD, and three of CD is necessary for the child to be characterized as presenting these disorders, based on the DSM-IV criteria. Because most (88%) children identified as CD were also identified as ODD, children meeting criteria for either of these diagnoses were grouped together in the statistical analyses.

Biological samples. Umbilical cord blood samples (30 mL) collected at birth for the Cord Blood Monitoring Program on Environmental Contaminants and Child Development Study were previously analyzed for concentrations of Hg, PCBs, Pb, polyunsaturated fatty acids, and selenium used to indicate prenatal exposure. Child blood samples (20 mL) collected for the present study were analyzed for the same contaminants and nutrients to document current body burden. Contaminant and Se analyses were performed at the Laboratoire de Toxicologie, Institut National de Santé Publique du Québec (Québec, Canada). Omega-3 fatty acid composition of phospholipids was analyzed at the University of Guelph Lipid Analytical Laboratory (Guelph, Ontario, Canada). Detailed analytical procedures for cord and child blood samples are described in the supplemental Material, pp. 2–4 (http:// dx.doi.org/10.1289/ehp.1204976).

Confounding variables. The following potential confounding variables were considered based on prior studies of the effects of environmental contaminants and our knowledge of socioeconomic and demographic factors associated with child development in the Inuit population: a) child characteristics: age, sex, birth weight, duration of gestation, adoption status (yes/no), and breast-feeding status (yes/no); b) maternal and family characteristics: age of biological mother at birth, parity of biological mother before child’s birth, maternal education (years), marital status (single vs. married/living with partner), socioeconomic status (SES) based on the summation of predefined scores given for parental occupation status (lowest: unemployed/farm laborers/menial service workers; highest: higher executives, proprietors of large businesses, and major professionals) and education (lowest: < 7th grade; highest: graduate professional training; Hollingshead 1975), nonverbal reasoning ability (Raven Progressive Matrices; Raven et al. 1992), residential crowding (number of persons living in the house per room), and food insecurity (mother reporting at least 1 day without sufficient food or funds to purchase food in the month preceding the study; yes/no); c) seafood nutrients: docosahexaenoic acid (DHA) and Se concentrations in cord and child blood samples; and d) other prenatal exposures: maternal tobacco use (yes/no), binge drinking (at least one episode of ≥ 5 standard alcohol drinks; yes/no), and illicit drug use (yes/no) during pregnancy. When data on maternal substance use during pregnancy were available from previous assessments, the information obtained closest to delivery was used to minimize the accuracy of responses (1-month postpartum interview: n = 71; 5-year interview: n = 83). Otherwise, information provided for the present study was used. Correlations between previous and current maternal reports of substance use during pregnancy were in the moderate-to-strong range (r between 0.42–0.80), suggesting reasonably robust validity of maternal reports provided a full decade after delivery.
were added to models of the effects of other contaminant exposures on the outcome without control for confounding without considerable loss in statistical power.

In a second set of analyses, covariates were selected using a forward strategy (Greenland and Rothman 1998). Specifically, potential confounders that correlated with the end point in question at \( p < 0.20 \) were added to models and retained if they altered the standardized regression coefficient for the contaminant by \( \geq 10\% \), with order of entry determined by the strength of the correlation between the confounder and end point (starting with the variable showing the strongest correlation with the outcome; see Jacobson et al. 2008). Given recent criticisms against lipid standardization for PCB analysis (Schisterman et al. 2005), all analyses were also re-conducted using cord and current plasma PCB values unadjusted for lipid values. Associations between contaminant variables and outcomes were considered significant when \( p \leq 0.05 \) after control for confounders.

**Results**

Sample characteristics. Descriptive statistics for the study sample are summarized in Table 1. About 25% of the mothers had given birth to their child before the age of 20 years, and \( <20\% \) had completed at least 11 years of schooling. About two of every five families reported food insecurity in the month preceding the study. Five children had current blood Pb concentrations above the threshold value of 10 \(\mu\text{g/dL} \) considered by U.S. and Canadian public health agencies to indicate risk for Pb neurotoxicity.

TRF behavior problem scores and the incidence of teacher ratings consistent with DSM-IV disruptive behavior disorder diagnoses according to the DBD are presented in Table 2. About 14% of the children were identified as displaying the behaviors that characterize ADHD–Inattentive type, and a similar proportion of children were identified as ADHD–Hyperactive-impulsive type. About one child in five was described by his or her teachers as exhibiting behaviors consistent with ODD and/or CD.

**Table 1.** Descriptive characteristics of the study sample.

<table>
<thead>
<tr>
<th>Variables</th>
<th>( n )</th>
<th>Mean</th>
<th>Median</th>
<th>SD</th>
<th>Range</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child age at assessment</td>
<td>279</td>
<td>11.3</td>
<td>11.4</td>
<td>0.8</td>
<td>8.5–14.3</td>
<td>50.5</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>277</td>
<td>3.5</td>
<td>3.5</td>
<td>0.5</td>
<td>2.5–4.7</td>
<td>16.5</td>
</tr>
<tr>
<td>Duration of gestation (weeks)</td>
<td>279</td>
<td>39.1</td>
<td>39.0</td>
<td>1.5</td>
<td>35.0–44.0</td>
<td>74.6</td>
</tr>
<tr>
<td>Breast-feeding status (% yes)</td>
<td>272</td>
<td>8.5</td>
<td>9.0</td>
<td>2.5</td>
<td>0.0–15.0</td>
<td>27.3</td>
</tr>
<tr>
<td>Caregiver characteristics/family environment</td>
<td>277</td>
<td>3.9</td>
<td>3.6</td>
<td>0.3</td>
<td>0.3–0.5</td>
<td>71.8</td>
</tr>
<tr>
<td>Maternal age at delivery (years)</td>
<td>278</td>
<td>23.8</td>
<td>22.9</td>
<td>5.7</td>
<td>15.0–42.0</td>
<td>27.3</td>
</tr>
<tr>
<td>Parity before child’s birth</td>
<td>279</td>
<td>2.0</td>
<td>2.0</td>
<td>1.8</td>
<td>0.0–9.0</td>
<td>71.8</td>
</tr>
<tr>
<td>Marital status (% single)</td>
<td>279</td>
<td>8.5</td>
<td>9.0</td>
<td>2.5</td>
<td>0.0–15.0</td>
<td>27.3</td>
</tr>
<tr>
<td>Education (years of schooling)</td>
<td>278</td>
<td>15.0</td>
<td>14.0</td>
<td>1.0</td>
<td>11.0–22.0</td>
<td>27.3</td>
</tr>
<tr>
<td>Employment (% working)</td>
<td>277</td>
<td>3.6</td>
<td>3.5</td>
<td>0.8</td>
<td>0.0–7.9</td>
<td>71.8</td>
</tr>
<tr>
<td>SES score</td>
<td>279</td>
<td>28.7</td>
<td>28.0</td>
<td>1.1</td>
<td>20.0–56.0</td>
<td>27.3</td>
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<tr>
<td>Nonverbal reasoning ability</td>
<td>279</td>
<td>34.8</td>
<td>37.0</td>
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<td>Language at interview (% primarily Inuktitut)</td>
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<tr>
<td>Residential crowding (no. of persons/room)</td>
<td>277</td>
<td>1.5</td>
<td>1.3</td>
<td>0.5</td>
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<td>27.3</td>
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<tr>
<td>Food insecurity (% yes)</td>
<td>277</td>
<td>1.5</td>
<td>1.3</td>
<td>0.5</td>
<td>0.5–3.8</td>
<td>27.3</td>
</tr>
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*Assessed with the Hollingshead index, which is computed from predefined scores given for parental occupation status and education (Hollingshead 1975). Based on the Raven Progressive Matrices (Raven et al. 1992). Food insecurity was defined as mother reporting having not enough food to eat for her family at least one day in the preceding month. Binge drinking corresponds to consumption of \( >5 \) standard drinks per occasion; 1 standard drink corresponds to 0.5 oz of absolute alcohol, which is equivalent to 350 mL of beer (12 oz), 175 mL of wine (6 oz), or 44 mL of liquor (1.5 oz).

**Table 2.** Descriptive statistics for behavioral outcomes.

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<tr>
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*Endorsed until Friday 21 Sept 2012, 12:01 a.m. EST*
Risk of teacher-reported symptoms consistent with the DSM-IV diagnostic criteria for ADHD—Hyperactive-impulsive type (Egeland and Kovalik-Gran 2010). In the ERP study, we found evidence that prenatal MeHg exposure alters primary attentional mechanisms modulating early processing of sensory information (Boucher et al. 2010). It has been proposed that cortical disruption and alterations in neurotransmission, notably within the dopaminergic and GABAergic systems, are involved in the neurotoxicity of prenatal MeHg exposure (Newland et al. 2006). Because dopamine is believed to play a major role in the pathophysiology of ADHD (Del Campo et al. 2011), it is possible that this mechanism is involved in the relation of MeHg to ADHD in children.

Associations with ADHD-type behaviors were observed at cord blood Hg concentrations > 11.4 µg/L. Although such exposure levels are common among children from Nunavik, relatively few children from the general Canadian and U.S. populations are exposed to such high Hg levels (e.g., Rhaïdis et al. 1999). However, the proportion of children exposed at these levels is likely to be higher among certain subgroups. For example, in a cohort initiated after 1 November 2001 in lower Manhattan, New York City, China-born Asians showed considerably higher cord blood Hg concentrations than non-Asians (mean, 17.0 vs. 3.53 µg/L for China-born Asians and non-Asians, respectively) (Lederman et al. 2008). The exposures in such subgroups are well within the range of exposures associated with attention and ADHD in the current study.

The results reported here contrast with those of a large birth cohort study conducted in the Seychelles Islands in which prenatal exposure was not associated with impaired performance on cognitive tasks or with an increased risk of ADHD-type behaviors (Myers et al. 2003). MeHg exposure arises mainly from fish consumption in the Seychelles study population, and failure to adjust statistically for seafood nutrients has been suggested as an explanation for the absence of any evidence of MeHg-related adverse effects within this cohort, since beneficial effects of seafood nutrients may counteract adverse effects of MeHg (Strain et al. 2008). In our study population, MeHg was associated with ADHD behaviors.

**Table 3. Relation of contaminant exposures to TRF symptom scores (log transformed) ([β-coefficient (95% CI)].**

<table>
<thead>
<tr>
<th>Contaminants (log)</th>
<th>Internalizing problems</th>
<th>Externalizing problems</th>
<th>Attention problems</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Adjusted</td>
<td>Unadjusted</td>
</tr>
<tr>
<td>Cord blood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hg</td>
<td>0.09 (–0.03, 0.21)</td>
<td>0.08 (–0.04, 0.22)</td>
<td>0.08 (–0.04, 0.20)</td>
</tr>
<tr>
<td>PCB-153</td>
<td>–0.03 (–0.15, 0.09)</td>
<td>–0.02 (–0.14, 0.06)</td>
<td>–0.01 (–0.13, 0.11)</td>
</tr>
<tr>
<td>Pb</td>
<td>0.02 (–0.10, 0.14)</td>
<td>0.03 (–0.09, 0.10)</td>
<td>0.07 (–0.05, 0.19)</td>
</tr>
<tr>
<td>Current blood</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hg</td>
<td>–0.02 (–0.14, 0.10)</td>
<td>–0.01 (–0.14, 0.11)</td>
<td>0.03 (–0.09, 0.15)</td>
</tr>
<tr>
<td>PCB-153</td>
<td>–0.02 (–0.14, 0.11)</td>
<td>–0.02 (–0.15, 0.10)</td>
<td>0.01 (–0.11, 0.13)</td>
</tr>
<tr>
<td>Pb</td>
<td>0.03 (–0.03, 0.24)</td>
<td>0.06 (–0.07, 0.20)</td>
<td>0.17 (0.05, 0.29)</td>
</tr>
</tbody>
</table>

Values are standardized regression coefficients (β) and 95% confidence intervals (CI) from linear regression analyses. Adjusted models include the following control variables: child age and sex, SES, age of the biological mother at birth, maternal tobacco use during pregnancy, and birth weight. Additionally, cord Hg was included in the regression models examining the associations between prenatal Hg and ADHD–Inattentive type and ODD/CD, because their correlations with these outcomes were at p < 0.20.

**Table 4. Relation of Hg and Pb exposures to DBD-based diagnoses.**

<table>
<thead>
<tr>
<th>Exposure</th>
<th>No. of cases (%)</th>
<th>OR (95% CI)</th>
<th>AOR (95% CI)</th>
<th>No. of cases (%)</th>
<th>OR (95% CI)</th>
<th>AOR (95% CI)</th>
<th>No. of cases (%)</th>
<th>OR (95% CI)</th>
<th>AOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cord Hg</td>
<td></td>
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</tr>
<tr>
<td>1st tertile (1.0–11.2; n = 90)</td>
<td>6 (6.7)</td>
<td>(referent)</td>
<td>7 (7.8)</td>
<td>(referent)</td>
<td>17 (18.9)</td>
<td>(referent)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd tertile (11.4–22.7; n = 91)</td>
<td>16 (17.6)</td>
<td>2.98 (1.11, 8.02)</td>
<td>2.77 (1.00, 7.65)</td>
<td>8 (8.8)</td>
<td>1.14 (0.40, 3.30)</td>
<td>0.95 (0.30, 3.00)</td>
<td>21 (23.1)</td>
<td>1.29 (0.68, 2.64)</td>
<td>1.19 (0.56, 2.56)</td>
</tr>
<tr>
<td>3rd tertile (22.9–99.3; n = 88)</td>
<td>17 (19.3)</td>
<td>3.35 (1.25, 8.95)</td>
<td>2.87 (1.04, 7.94)</td>
<td>8 (8.8)</td>
<td>1.14 (0.40, 3.30)</td>
<td>0.95 (0.30, 3.00)</td>
<td>21 (23.1)</td>
<td>1.29 (0.68, 2.64)</td>
<td>1.19 (0.56, 2.56)</td>
</tr>
<tr>
<td>Child Pb (µg/dL)</td>
<td></td>
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</tr>
<tr>
<td>1st tertile (0.4–1.6; n = 90)</td>
<td>10 (11.1)</td>
<td>(referent)</td>
<td>3 (3.3)</td>
<td>(referent)</td>
<td>14 (15.6)</td>
<td>(referent)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>2nd tertile (1.6–2.7; n = 94)</td>
<td>15 (16.0)</td>
<td>1.52 (0.64, 3.58)</td>
<td>1.06 (0.42, 2.66)</td>
<td>14 (14.9)</td>
<td>5.07 (1.40, 18.3)</td>
<td>4.01 (1.06, 15.23)</td>
<td>24 (25.5)</td>
<td>1.86 (0.88, 3.88)</td>
<td>1.90 (0.88, 4.11)</td>
</tr>
<tr>
<td>3rd tertile (2.7–12.8; n = 91)</td>
<td>18 (19.8)</td>
<td>7.15 (2.03, 25.2)</td>
<td>5.52 (1.38, 22.12)</td>
<td>23 (25.3)</td>
<td>1.84 (0.88, 3.85)</td>
<td>1.53 (0.67, 3.49)</td>
<td></td>
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</tr>
</tbody>
</table>

Values are unadjusted odds ratio (OR), adjusted odds ratio (AOR), and 95% confidence intervals (CI) from logistic regression analyses. Adjusted models include the following control variables: child age and sex, SES, age of the biological mother at birth, maternal tobacco use during pregnancy, and birth weight. Additionally, cord Hg was included in the regression models examining the associations between prenatal Hg and ADHD–Inattentive type and ADHD–Hyperactive-impulsive type, and child Pb was included in the models examining the associations between cord Hg and ADHD–Hyperactive-impulsive type and ODD/CD, because their correlations with these outcomes were at p < 0.20.
even without statistical adjustment for sea-
food nutrients, although MeHg and nutrient con-
centrations are moderately intercorrelated (Bo-
cher et al. 2010). An alternative explana-
tion to these diverging results points to dif-
sent sources of exposure—marine mammal
meat in the Inuit and Faroese—which is not
eaten in the Seychelles. In addition to MeHg,
marine mammals also contain an extensive
array of contaminants (Letcher et al. 2010),
some of which were measured in this study,
which may contribute to and/or accentuate
MeHg effects. Further studies are needed to
resolve this issue.

Our results relating to postnatal Pb expo-
sure replicate those of several previous stud-
ies where childhood Pb exposure was associated
with ADHD (reviewed by Eubig et al. 2010).
Studies that examined the relation of Pb expo-
sure to inattention and hyperactivity sepa-
rately have yielded inconsistent results, some
showing stronger associations with inatten-
tive symptoms (Chiado et al. 2007; Kim et al.
2010; Roy et al. 2009) and others with hyper-
activity and impulsivity (Nicolucci et al. 2010;
Nigg et al. 2010). In the present study, Pb was
associated with symptoms of the hyperactive-
impulsive type, but not the inattentive type,
of ADHD. Effects of Pb on hyperactive and
impulsive behavior are well-documented in
animal studies, as they represent core features
of Pb neurotoxicity (Brockel and Cory-Slechta
1998; Moreira et al. 2001). Child blood con-
centrations were also associated with higher
levels of impulsivity and irritability among
Nunavik children at 5 years of age (Plusquellec
et al. 2010). In an ERP analysis using a go/no-
go paradigm conducted on a subsample from
this cohort, postnatal Pb exposure was associated
with higher rates of false alarms and
with decreased brain activity (a smaller P3
component) in response to “no-go” stimu-
lants (Boucher et al. 2012), suggesting a spe-
cific deficit in response inhibition that could
be implicated in the association between Pb
and ADHD. It has been proposed that the
association of childhood Pb exposure with
hyperactivity and impulsivity is mediated by
effects of Pb on the development and func-
tion of the prefrontal cortex (Cecil et al. 2008;
Trope et al. 2010). This brain area is involved
in executive and impulsive control (Jurado
and Rossell 2007) and has been implicated in
ADHD neuropathology (Faraone and
d’Simmerman 2002).

The association between Pb and ADHD–
Hyperactive-impulsive type was observed at
very low blood Pb concentrations—in children
with blood Pb levels between 1.6 and 2.7 μg/
dL. These results are consistent with recent
evidence of adverse effects from postnatal Pb
exposure at levels well below the 10 μg/dL risk
level used by public health authorities (Canfield
et al. 2003; Chiado et al. 2004) and further
confirm the need to redeline downward the
tolerable level of exposure for children and to
conduct interventions to reduce their exposure.

The absence of clear evidence of adverse
effects of PCB exposure on child behavior in
this study contrasts with a recent finding
from the New Bedford (Massachusetts) cohort
study, where prenatal exposure was associated
with higher rates of teacher-reported ADHD-
like behaviors (Sagiv et al. 2010). One fac-
tor that might account for the differences in
results between these two studies relates to dif-
fences in the PCB mixtures that are found in
each study area. Unlike the residents of New
Bedford, the Nunavik Inuit live far from the
PCB contamination sources. Consequently,
they are more likely to be exposed to the more
persistent, highly chlorinated PCB congener
who have accumulated in the marine food
chain and reached the Arctic (Dewailly et al.
1993). By contrast, the children from New
Bedford were exposed to higher concentra-
tions of the lower chlorinated, mono-ortho-
and dioxin-like PCB congeners (Korrick et
al. 2000), which may be attributable to the spe-
cific PCB mixtures that were used in the
New Bedford area industries, and to dechlorination
processes that have altered PCB congeners
in the New Bedford ecosystem (Brown and

The strengths of this study include our
ability to control for confounding by other
contaminants present in seafood—specifically
for confounding in the association between
cord Hg and outcomes by child Pb, and for
confounding of the association between child
Pb and outcomes by cord Hg. Another inno-
vative aspect of this study is that we assessed
prenatal and childhood intake of nutrients
and evaluated them as potential confounders
in the neurotoxicant–behavior relationships.
Among the limitations of this study is that the
maternal report of substance use during
pregnancy was obtained in many cases about
a decade after delivery. We tried to mini-
mize this limitation by using data obtained
at 1 month or 5 years postpartum when avail-
able, although this was not possible for the
entire sample. Another limitation is that we
do not have formal diagnoses for ADHD, but
rather ADHD classifications based on
behavior ratings provided by the classroom
teachers. Although the elementary school
classroom is an optimal context for observing
the behaviors that characterize ADHD, and
teachers are in a unique position to compare
these behaviors across children, clinical diag-
noses of ADHD typically also incorporate
observations from other sources, particularly
parents. Finally, we were not able to control
for family history of ADHD. Because ADHD
was rarely recognized in the previous genera-
tion in Nunavik, this potential confounding
factor could not be reliably assessed.

Conclusions

To our knowledge, this study is the first to
report an association between prenatal MeHg
exposure and ADHD symptomatology at
school age. The associations with teach-
er-reported ADHD symptoms observed in
the current study suggest that adverse effects
of prenatal MeHg on attention previously
reported based on neuropsychological as-
sumptions may be clinically significant, and
can interfere with learning and performance in
the classroom. This study also suggests that
pre-
natal MeHg exposure may be a risk factor for
attention problems in diverse ethnic groups
from Southern Canada and the United States
who may be exposed to similar levels of MeHg
through their diet. Although the main source
of Pb exposure is our study population—lead
shot (as revealed by blood Pb isotope ratios;
Lévesque et al. 2003)—is unique in the Pb
exposure literature, this study replicates previ-
sour findings linking low-level childhood Pb
exposure to ADHD. Our results support the
need for local interventions intended to reduce
prenatal exposure to MeHg and childhood
exposure to Pb. Additionally, because MeHg
exposure in the Arctic is attributable primarily
to long-range transport of Hg from develop-
ing countries, international actions and con-
ventions aimed at limiting Hg emissions are
urgently needed.

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