EXPOSURE TO PERSISTENT ORGANIC POLLUTANTS AND NEURODEVELOPMENT IN INUIT CHILDREN

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Introduction

The effects of prenatal exposure to persistent organic pollutants (POPs) on growth and neurodevelopment have been studied in prospective longitudinal studies conducted in the United States and Europe. In Michigan higher cord serum polychlorinated biphenyls (PCB) concentrations were associated with lower weight at birth, smaller head circumference and shorter gestation.[1] Similar effects were observed in the Netherlands study[2] but prenatal PCB exposure was not associated with growth in the North Carolina cohort[3]. Prenatal exposure to PCBs and methylmercury has also been linked prospectively to developmental and cognitive deficits in infancy and childhood (see reviews by Schantz et al.[4] and Davidson et al.[5]). In fish-eating populations, a high intake of n-3 polyunsaturated fatty acids (n-3 PUFAs) which has been shown to be beneficial for growth and brain development (see review by Ruxton et al.[6]) might counteract the adverse developmental effects induced by prenatal exposure to POPs.

Between 1995 and 2002, we conducted a prospective study of Inuit infants in three communities located in Nunavik, a remote coastal region of northern Quebec. The Inuit population relies on species from the marine food web for subsistence and is therefore exposed to high doses of POPs such as PCBs and methylmercury. Here we report the associations between concentrations of PCBs and mercury in biological samples collected from Inuit mothers and their infants, physical growth at birth and developmental outcomes assessed at 6.5 and 11 months of age. We also examined associations between n-3 PUFAs and developmental endpoints.

Materials and Methods

The women were recruited at their first or second prenatal medical examination. Prenatal exposure was assessed using two blood samples: one obtained from the umbilical cord and the other drawn from the mother at delivery or within a few weeks thereafter. Two maternal hair samples were collected, one at the prenatal interview and the other at the 1-month postnatal interview. A milk sample was collected from breastfeeding mothers at the 1-month postnatal interview.

Concentrations of the following OCs were measured in cord plasma, maternal plasma and breast milk samples by high resolution gas chromatography with electron capture detection: the 14 most prevalent PCB congeners (IUPAC nos. 28, 52, 99, 101, 105, 118, 128, 138, 153, 156, 170, 180, 183, and 187) and 11 chlorinated pesticides or their metabolites [aldrin, α-chlordane, γ-chlordane, *p,p´*-dichlorodiphenyltrichloroethane (DDT), *p,p´*-dichlorodiphenyldichloroethene (DDE), hexachlorobenzene (HCB), β-hexachlorocyclohexane (HCH), mirex, *cis*-nonachlor, *trans*-nonachlor, oxychlordane]. Mercury concentrations were determined by cold vapor atomic absorption in cord and maternal whole blood, as well as in the hair sample collected postnatally, which was cut into three segments of 3 cm in length, with each segment corresponding to a trimester of pregnancy. Lead concentrations were measured in cord blood; Se concentrations in cord and maternal blood;and n-3 polyunsaturated fatty acids (n-3 PUFA) in cord plasma.

The infants were assessed in the community hospital or nursing station at birth, 6.5 and 11 months of age. The tests performed included those that were used in previous PCB studies, such as the Bayley Scales of Infant Development and the Fagan Test of Infant Intelligence, as well as several new tests, such as the A-not-B test, the Haith's Visual Expectancy Paradigm, and Teller Visual Acuity Cards. Physical growth was also assessed at birth, 6.5 and 11 months of age. Maternal interviews were conducted at mid-pregnancy and at 1, 6.5 and 11-months postpartum by trained research assistants. These interviews were conducted to assess potential confounding variables pertaining to demographic background, fetal exposure to other drugs, such as nicotine, marijuana and alcohol, and quality of stimulation provided to the infant. Medical charts were reviewed to document pregnancy and perinatal medical complications.

Results and Discussion

The most prevalent PCB congeners were 153, 138 and 180. These three congeners represent about 66% of the total concentration of the 14 PCB congeners. The intercorrelations among PCB congeners that were detected in at least 70% of cord plasma samples were very high (median $r = 0.90$). The predominant chlorinated pesticides were *p,p'*-DDE, hexachlorobenzene, oxychlordane, and *trans*-nonachlor. The intercorrelations among the chlorinated pesticides detected in at least 70% of samples were strong (median $r = 0.76$). Moreover, the chlorinated pesticides measured were strongly associated with PCB congener 153, except for *p,p'*-DDT, for which the association was moderate. Based on these data, it seems reasonable to use the concentration of PCB congener 153, the most prevalent congener, as a marker of exposure to the organochlorine mixture present in the Arctic marine food chain.

Cord plasma PCB 153 concentrations averaged 116.0 μg/kg lipids (geometric mean: 86.9 μg/kg lipids). Prenatal PCB exposure in Nunavik was two to three times higher than that observed in general populations in southern Québec and in Massachusetts (USA), similar to that found in the Netherlands, and about two to three times lower than in the groups of marine mammal consumers from Greenland and Faroe Islands. With regard to PCB exposure in the early neurobehavioral studies conducted in Michigan and North Carolina, prenatal PCB exposure in Nunavik was similar than observed in the Michigan study, while both were higher than prenatal exposure observed in North Carolina cohort.

Mercury concentrations found in cord blood and maternal hair samples averaged 22.7 μg/l and 4.5 μg/g, respectively (geometric means: 18.5 and 3.7 μg/l, respectively). These data confirm that prenatal exposure to methylmercury in the studied population is higher than that observed in general population samples in Canada and the United States. Prenatal methylmercury exposure in Nunavik Inuit was similar to that observed in the Faroe Islands' first and second cohorts, slightly lower than in the Seychelles Islands cohorts, and substantially lower than in the highest exposed group in the New Zealand study.

Cord blood lead concentrations averaged 0.2 μmol/l, which corresponds to 41.4 μg/l (geometric mean: 0.2 μmol/l). The average lead concentration determined in this cohort was two times higher than that found in the general population from southern Quebec and similar to that reported for the Greenlandic Inuit. Although the studied infants were exposed transplacentally to both OCs and methylmercury, exposures were only moderately confounded: cord PCB-cord Hg, $r = 0.24$; cord PCB-average hair Hg, $r = 0.34$. The associations between cord blood lead and Hg concentrations were also low, and the intercorrelations between cord blood lead and OC concentrations were even weaker. More information on the exposure variables can be found in our previous publications.[7,8]

We examined cord plasma PCB 153 concentrations in relation to duration of pregnancy, birth weight and developmental outcomes assessed at 6.5 and 11 months of age using multiple regression analyses. Pearson correlations were performed to select among the control variables those to be included in multivariate analyses. After controlling for potential confounders associated at $p \leq .10$ with the studied outcomes, higher cord plasma PCB 153 concentrations were associated with lower birth weight and marginally related to shorter duration of pregnancy. The

magnitude of the negative association between PCB and birth weight was comparable to those noted with prenatal exposure to alcohol or smoking during pregnancy. Cord plasma PCB 153 concentrations were associated with shorter length at birth in girls and were not related to head circumference.

With regard to early cognitive development, each of the major environmental contaminants examined in this study was associated with a specific aspect of early cognitive development. Whereas prenatal PCB exposure was most strongly related to visual recognition memory, cord blood lead concentrations were related to slower information processing speed, and prenatal methylmercury exposure—whether assessed in cord blood or maternal hair—to poorer performance on the A-not-B Test, which is believed to be an early precursor of executive function. n-3 PUFA levels in cord plasma phospholipids were found to be associated with elevated birth weight, longer duration of pregnancy, better visual acuity, and more optimal motor and cognitive development.

These findings are consistent with results of previous epidemiological studies conducted in populations exposed to PCBs through the consumption of PCB contaminated food. The beneficial effects of maternal n-3 PUFA intake during pregnancy were seen in a broad range of infant outcomes. In this population, the negative effects of prenatal PCB exposure on duration of pregnancy, physical growth and cognitive function are attenuated by the beneficial effects of n-3 PUFA. These data also provide support for the hypothesis that the adverse effects of prenatal exposure to PCBs, methylmercury and lead do not operate on a common neural pathway but instead impact on very different aspects of cognitive function during infancy.

A follow-up study will be performed in children at 10 years of age (± 1 year) to document the long term effects of pre- and postnatal exposure to environmental contaminants in multiple domains: growth; sensory functions (visual and auditory evoked potentials); cognitive and attentional functions (event related potentials); emotional and behavioral functions; cardiac variability.

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