Science of the Total Environment 432 (2012) 338–343

Contents lists available at SciVerse ScienceDirect

Science of the Total Environment

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

Prenatal exposure to polychlorinated biphenyls and child neuropsychological development in 4-year-olds: An analysis per congener and specific cognitive domain

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ARTICLE INFO

Article history:
Received 28 February 2012
Received in revised form 4 June 2012
Accepted 5 June 2012
Available online xxxx

Keywords:
Child development
Polychlorinated biphenyls
Neuropsychology
Environmental exposure

ABSTRACT

Polychlorinated biphenyls (PCB) are synthetic organochlorine compounds with potential neurotoxic effects. Although negative effects on neuropsychological development have been observed in previous studies on PCB exposure, there are inconsistencies in these effects at current exposure levels of these compounds which are much lower than for previous generations. This study aimed to disentangle the effects of prenatal and postnatal PCB exposure on neuropsychological development at 4 years of age. This study is based on a population-based birth cohort design established in Menorca (Spain) as part of the INMA [Environment and Childhood] Project. We assessed general neuropsychological development using the McCarthy Scales of Children's Abilities (MCSA). A total of 422 4-year old children were assessed with the MCSA. Levels of PCBs were measured in cord blood (n = 405) and in blood samples taken at 4 years (n = 285). We found no statistically significant effects of the sum of prenatal PCBs on MCSA scores. Nevertheless, individual congener analyses yielded significant detrimental effects of prenatal PCB153 on the majority of MCSA scores, while no effects were reported for other congeners. The levels of PCBs at 4 years of age were not associated with neuropsychological development. Thus, prenatal exposure to low-level concentrations of PCBs, particularly PCB153, was associated with an overall deleterious effect on neuropsychological development at 4 years of age, including negative effects on executive function, verbal functions and visuospatial abilities, but not on motor development.

1. Introduction

Polychlorinated biphenyls (PCBs) are synthetic organochlorine compounds that have been widely used as insulators, coolants, and lubricants in electrical transformers, capacitors, and hydraulic equipment, and as plasticizers in plastic and rubber products since the 1930s.

Despite the ban on PCBs in most industrialized countries in the 1970s, their presence is still detectable due to their high biostability and lipophilicity and because they are resistant to both chemical and biological degradation (Govarts et al., 2011; Ibarluzea et al., 2011; Ribas-Fito et al., 2001).

Two recent systematic reviews (Ribas-Fito et al., 2001; Goodman et al., 2010) and one literature review (Boucher et al., 2009), present the existing evidence on the effects of PCBs on neuropsychological development. The conclusions of the literature review are that prenatal exposure to PCBs has a negative effect on neuropsychological development in children, with specific impairments in executive functions (Boucher et al., 2009). Since the poisoning episodes in which the link between PCB exposure and developmental neurotoxicity was recognized (Hsu et al., 1985; Guo et al., 2004), birth cohort studies have been established in several countries to study the effects of prenatal, perinatal and postnatal exposures to these compounds on child neuropsychological development. Differences among studies on the effects of PCBs on neuropsychological development were reported. Four of these studies demonstrated a decrease in intelligence quotient

Abbreviations: (PCB), polychlorinated biphenyls; (HCB), hexachlorobenzene; (pp'DDT), dichlorodiphenyltrichloroethane; (pp'DDE), dichlorodiphenyl dichloroethylene; INMA, [Environment and Childhood] Project; (OCs), organochlorine compounds; (Coef), coeficient; (MSCA), McCarthy Scales of Children's Abilities; (LOD), limits of detection.

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doi:10.1016/j.scitotenv.2012.06.012

score during childhood (Stewart et al., 2005; Vreugdenhil et al., 2002; Walkowiak et al., 2001; Jacobson et al., 1990) while the other two did not find any association (Gray et al., 2005; Gladen and Rogan, 1991). Nevertheless, despite the relatively large body of literature on the neurotoxic effects of early-life exposure to PCBs on neuropsychological development, controversy still exists over whether PCBs are in fact neurotoxicants at current levels of exposure (Goodman et al., 2010).

We have previously studied the effects of dichlorodiphenyltrichloroethane (DDT)/dichlorodiphenyl dichloroethylene (DDE) and hexachlorobenzene (HCB) on neuropsychological development in the Menorca cohort, due to the high concentrations of these chemicals reported in Spain (Ribas-Fitó et al., 2003, 2007), but we did not include PCBs in these analyses. The aim of this study was to assess any potential detrimental effects of prenatal and postnatal exposure to current levels of PCBs, which are lower than for previous generations, on general neuropsychological development and specific cognitive domains.

2. Material and methods

2.1. Study design and participants

This study was based on a population-based birth cohort design established in Menorca (Spain) as part of the INMA [Environment and Childhood] Project, which focuses on environmental exposures and growth, development and health in children (Guxens et al., 2011). All women presenting for antenatal care in a 12-month period beginning in mid-1997, were considered eligible and were invited to participate. 482 mothers (94% of those eligible) were finally enrolled into the cohort. At 4 years of age, 470 mother–child pairs (98% of those enrolled) remained in the follow-up. All families signed a consent form to participate in the study.

2.2. Neuropsychological testing

At 4 years of age, 418 children (86% of the original cohort) were assessed using a standardized version of the McCarthy Scales of Children's Abilities (MSCA) adapted to the Spanish population (McCarthy, 2009). The general cognitive scale and the five subscales (verbal, perceptive-performance, memory, quantitative and motor) were examined. In addition, we included new measures created by Julvez et al. (2011), in such study the authors reorganized the MCSA subtests into new sub-area scores (executive functions, working memory, visual and verbal span, verbal memory, gross and fine motor skills and cognitive functions of posterior cortex) according to those tasks that are highly associated with specific neuropsychologic function. Two neuropsychologists were trained to administer and interpret the MCSA. A strict protocol was applied to avoid inter-observer variability, including inter-observer trainings and three sets of quality controls. Continuous MSCA scales and new MCSA sub-areas were standardized to a mean score of 100 with a standard deviation of 15 to homogenize all the scales. The child's age was also collected during the visit.

2.3. OCs exposure measurement

Organochlorine compounds (OCs) in umbilical cord serum (n = 405) and in blood at 4 years of age (n = 285) were measured by gas chromatography with electron capture detection and gas chromatography coupled to chemical ionization negative-ion mass spectrometry as described elsewhere (Carrizo et al., 2007). Those PCB congeners with concentrations less than the limit of detection (LOD) were substituted with the LOD divided by 2. The sum of individual PCB congener concentrations (ΣPCBs) was calculated for the most common individual congeners 118, 138, 153, and 180. Congeners 28, 52 and 101 were not considered as they were detectable in less than 21%, 25% and 40% of samples, respectively. The levels of DDE and HCB in cord blood and at 4 years of age were also analyzed. All analyses were carried out in the Department of Environmental Chemistry in Barcelona, Spain.

2.4. Other parental and child variables

Information on maternal and paternal education (primary, secondary, and university), maternal and paternal social class (non-manual, manual, and housewives) (using the United Kingdom Registrar General's 1990 classification according to parental occupation, and the 1988 International Standard Classification of Occupations code), maternal cigarette smoking during pregnancy, alcohol use during pregnancy, number of siblings at time of child's birth, and child's sex was collected after delivery. In subsequent interviews, data were collected on type and duration of any breastfeeding, marital status, maternal tobacco consumption, and child's diet at ages 4 years and 6 years. All questionnaires were administered face to face by trained interviewers. Additionally, information relating to prematurity (<37 weeks of gestational age), and low birth weight (<2500 g) taken at birth was collected from clinical records. Finally, in a subsequent visit, we assessed maternal intelligence quotient (IQ) using the 2 and 3 scales of Factor "G" of Cattell and Cattell (1977).

2.5. Statistical analysis

The MCSA scores followed a normal distribution, while serum concentrations of PCBs were skewed to the right and were normalized by logarithmic transformations. Linear regression was carried out to model the association between MCSA scores and PCB concentrations (both sum and individual congeners).

A multivariate regression model for general cognitive scale was built considering a subset of a priori selected covariates (which are related with the outcome and the exposure, the sum of PCBs) using a backwards selection procedure. Covariates retained in the model were those showing associations with MCSA general cognitive scale with p-values of <0.05 or those whose inclusion resulted in a change in the regression coefficient of the sum of PCBs ≥ 10%. The same procedure was applied for the postnatal exposure to PCBs. The same confounding variables were retained in the model for the rest of MCSA scores and PCB congeners. Potential modification of effects by duration of breastfeeding and child's fish intake (Patandin et al., 1997) were evaluated. Statistical analyses were done using Stata 10.1 (Stata Corporation, College Station, Texas).

3. Results

Our analysis was based on 355 (73%) mother–child pairs with complete information on neuropsychological development assessment and OCs levels in cord serum. The characteristics of the study population are described in full in Table 1. There were no differences in the general cognitive score of MCSA between children with organochlorine measurements (mean = 100.40; standard deviation (SD) = 15.16) and those without (mean = 97.90; SD = 13.96) (p = 0.244). Detectable concentrations of prenatal and postnatal PCB congeners 118, 138, 153, and 180 were quantified between 75 and 98% of the children (Table 2).

The association between prenatal ΣPCBs and MCSA scores at 4 years of age showed a negative trend although the associations were not statistically significant (Coefficient (Coef) general cognitive score = −2.44; p-value = 0.113) (Table 3). The analysis for each congener yielded different results. PCB153 concentrations were negatively associated with MCSA scores whereas the associations for PCB congeners 118, 138 and 180 were less precise. PCB153 showed a statistically significant negative association for general cognitive score (Coef = −3.33; p-value = 0.010), verbal, quantitative, perceptual-performance, and memory scales (Table 3). A multipollutant model,