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Association between prenatal exposure to polybrominated diphenyl ethers and young children's neurodevelopment in China

Guodong Ding[a,b,1], Jing Yu[c,1], Chang Cui[d,1], Limei Chen[e], Yu Gao[e], Caifeng Wang[e], Yijun Zhou[e], Ying Tian[a,e,*]

[a] MOE and Shanghai Key Laboratory of Children's Environmental Health, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China
[b] Department of Pediatrics, Shanghai East Hospital, Tongji University School of Medicine, Shanghai, China
[c] Department of Endocrinology and Metabolism, Shanghai Jiao Tong University Affiliated Sixth People's Hospital, Shanghai, China
[d] Research Base of Key Laboratory of Surveillance and Early-warning on Infectious Disease in China CDC, Shanghai Pudong New Area Center for Disease Control and Prevention, Shanghai, China
[e] Department of Environmental Health, School of Public Health, Shanghai Jiao Tong University School of Medicine, Shanghai, China

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ABSTRACT

The use of polybrominated diphenyl ethers (PBDEs) has been dramatically increasing over the last two decades in China. Animal studies suggest that prenatal exposure to PBDEs may result in neurodevelopmental deficits. Two hundred thirty-two participating mothers were recruited from a prospective birth cohort in rural northern China between September 2010 and February 2012. We analyzed 232 cord blood specimens for selected PBDE congeners and examined their association with children's developmental quotients (DQs) at 12 ($n=192$) and 24 ($n=149$) months of age based on the Gesell Developmental Schedules (motor, adaptive, language, and social domains). There were no substantial differences by demographic characteristics among the three time points: baseline, 12 and 24 months of age. Median cord blood levels of PBDE congeners 47, 99, 100, and 153 were 3.71, 6.70, 2.63, and 2.19 ng/g lipid, respectively. At 12 months of age, neither the individual nor total (the sum of BDEs 47, 99, 100, and 153) congener levels were associated with any of the four domain DQs. However, at 24 months of age, a 10-fold increase in BDE-99 levels was associated with a 2.16-point decrease [95% confidence interval (CI): −4.52, −0.20] in language domain DQs and a 10-fold increase in BDE-47 levels was associated with a 1.89-point decrease (95% CI: −3.75, −0.03) in social domain DQs. Prenatal exposure to PBDEs was associated with lower DQs in young children. The results contribute to the growing evidence that PBDEs could act as developmental neurotoxicants,and the findings have implications for children's environmental health in China.

1. Introduction

Flame retardants are chemicals that are added to plastics, electronics, textiles, and construction material to protect against fire. Brominated flame retardants (BFRs) are the largest group on the market due to their low cost and high efficiency and account for 39% of worldwide flame retardant production (Mazdai et al., 2003). Within this group, the polybrominated diphenyl ethers (PBDEs) have been used in large quantities as flame retardant additives, and the worldwide market demand for PBDEs increased from 40,000 tons in 1992 to 67,000 tons in 2001 (Hale et al., 2011; Voorspoels et al., 2003). Because PBDEs are semivolatile and not chemically bound to substrates, they are more likely to migrate from such substrates during their lifetime. Furthermore, PBDEs are considered to be a group of persistent organic pollutants (POPs) due to similar properties with polychlorinated biphenyls in terms of lipophilicity, bioaccumulation, and persistence in the environment (Hooper and McDonald, 2000; Chen et al., 2011). Human exposure to PBDEs comes primarily from ingestion of dietary products such as fish and cow's milk. Exposure to PBDEs can also occur through dust and inhalation. Airborne contamination has been implicated, particularly in the electronics and computer industries (Mazdai et al., 2003). Over the last several decades, PBDE levels in human blood, breast milk, and adipose tissue have been dramatically increasing globally (Thomsen et al., 2002; Akutsu et al., 2003; Sjödin et al., 2004; Moon et al., 2012; Ni et al., 2013; Chen et al., 2014b), suggesting that the elevated body burden of PBDE in humans could be an important public health issue.

* Corresponding author at: MOE and Shanghai Key Laboratory of Children's Environmental Health, Xinhua Hospital, Shanghai Jiao Tong University School of Medicine, 1665 Kongjiang Road, 200092 Shanghai, China. Fax: 86 21 64663944.
E-mail address: tianmiejp@sjtu.edu.cn (Y. Tian).
[1] Guodong Ding, Jing Yu, and Chang Cui contributed equally to this work

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The most pressing current concern for potential adverse health effects of PBDEs relates to their developmental neurotoxicity (Birnbaum and Staskal, 2004; Costa and Giordano, 2007). Numerous animal studies have demonstrated that prenatal or early-life exposure to PBDEs can cause long-lasting behavioral alterations, including changes in spontaneous motor activity characterized by hyperactivity, decreased habituation, and disruption of learning and memory (Eriksson et al., 2001; Viberg et al., 2003; Kuriyama et al., 2005; Rice et al., 2007; Koenig et al., 2012). Although the association between prenatal exposure to PBDEs and adverse neurodevelopmental effects has been observed in animal models, it has not been adequately explored in human populations. Several human epidemiological studies have investigated the effects of prenatal PBDE exposures on child neurodevelopment, but these studies were mostly conducted in North America and Europe. For example, Herbstman et al. (2010) reported that prenatal BDE-47 levels were adversely associated with the 12-month (Bayley Scales of Infant Development-II) Psychomotor Development Index (PDI) ($n=118$), 24-month Mental Development Index (MDI) ($n=117$), and 48-month full-scale and verbal IQ (the Wechsler Preschool and Primary Scale of Intelligence, Revised Edition) (n=104) in children from New York. In contrast, Chen et al. (2014) reported that prenatal BDE-47 levels were not associated with PDI or MDI at ages 1–3 years ($n=285$ at 1 year, 239 at 2 years, 220 at 3 years) but negatively associated with Full-Scale IQ (the Wechsler Preschool and Primary Scale of Intelligence-III) and hyperactivity score (the Behavioral Assessment System for Children-2) at age 5 years ($n=179$) in children from Cincinnati. In a study of 62 Dutch children at age 5–6 years, Roze et al. (2009) reported that prenatal PBDE (including BDEs 47, 99, 100, 153, and 154) levels were negatively associated with fine motor coordination and sustained attention, although such levels improved coordination and visual perception and led to fewer internalizing and externalizing behaviors.

In China, the nationwide production of BFRs reached 10,000 tons in 2000 and the annual demand for PBDEs has been increasing at a rate of 8%, which would inevitably result in continuous increase of PBDE levels in the environmental media (Jin et al., 2009). Penta- and octa-BDEs were removed from the European (1998) and North American (2004) marketplace; however, deca-BDEs are still being produced and used globally (Huang et al., 2014). At present, there are no legal restrictions on the production and use of penta-BDEs, octa-BDEs, and deca-BDEs in mainland China. With the increasing demand for PBDEs nationwide, concerns regarding the adverse health effects of exposure to PBDEs among some susceptible populations including pregnant women and children are increasing (Chao et al., 2007; Wu et al., 2010). However, little data have been available on prenatal exposure to PBDEs and child neurodevelopment in China.

In this report, we investigated the levels of selected PBDE congeners in cord blood and evaluated the possible relationship of prenatal exposure to PBDEs with neurodevelopment as measured by the Gesell Developmental Schedules (GDS) in young children living in rural northern China. We tested the hypothesis that after adjusting for potential confounders, prenatal exposure to PBDEs would be associated with lower DQs in the motor, adaptive, language, and social domains.

2. Methods

2.1. Participants and recruitment

This study was a prospective birth cohort study which began in 2010 to determine the effects of environmental exposures on the health of pregnant women and their children living in a rural community in the southern coastal area of Laizhou Wan (Bay) of the Bohai Sea in Shandong province, northern China (LW birth cohort). The adverse consequences of the children were assessed at delivery and during the follow-up, which lasted for a period of at least 2 years. The detailed methods used in this study have been described elsewhere (Ding et al., 2013, 2014).

Pregnant women were recruited at the time they were preparing for labor and delivery in a unique county hospital located in the southern coastal area of Laizhou Wan. Eligibility criteria included a singleton pregnancy; age over 18 years old; residence in the area for at least 3 years; and no report of assisted reproduction, pregestational or gestational diabetes, chronic or pregnancy-associated hypertension, HIV infection or AIDS, and illicit drug use (Ding et al., 2013, 2014). From September 2010 to February 2012, a total of 388 women met the eligibility criteria, among whom 347 women agreed to take part in this study (response rate 89.4%). Of these women, 41 women without cord blood samples, 53 women without enough cord serum volumes, and 21 women with missing values for major confounders were excluded. Therefore, 232 mothers were included in this study. Each woman participating in the study signed an informed consent form, and the research protocol for this study was approved by the Medical Ethics Committee of Xinhua hospital, Shanghai Jiao Tong University School of Medicine. Not all mothers agreed to have their child followed after birth. Thus, among these 232 mother–infant pairs, 192 children (82.8%) completed a neurodevelopmental assessment at 12 months of age (± 1 week), and 149 (64.2%) children at 24 months of age (± 1 weeks) (Fig. 1).

2.2. Maternal interview and medical record abstraction

Standardized face-to-face interviews were conducted with the women shortly after delivery by specially trained nurses in the hospital, as described previously (Ding et al., 2013, 2014). The questionnaire included demographic information (maternal age, education level, household income, and address), maternal characteristics (cigarette smoking, alcohol use, dietary habits, and employment), potential exposures to PBDEs (working in computer or electronics manufacturing, repair, or dismantling plants) and any other chemical exposures. Other relevant information such as previous pregnancy outcomes, current pregnancy complications, date of delivery, gestational age, and sex of newborn was obtained by interview and confirmed by maternal and infant medical records.

Maternal pre-pregnancy body mass index (BMI) was calculated as the pre-pregnancy weight divided by the height squared. The women were then classified into three groups according to the 2000 WHO standards: underweight (BMI < 18.5 /m^2), normal weight (BMI 18.5 to < 23.0 /m^2), and overweight (BMI > 23.0 kg/m^2). Low birth weight was defined as < 2500 g. Preterm delivery was defined as birth at less than 37 completed gestational weeks.

2.3. Biological sample collection

Cord blood samples were collected from an umbilical vein immediately post-delivery using a syringe and two 10 mL-red topped tubes, allowed to clot, and centrifuged at 1500 rpm for 20 min; next, the serum was decanted into pre-cleaned glass vials for residue analysis. All samples were coded, frozen, and stored at -80 °C until analysis.

2.4. PBDE exposure assessment

Serum samples were stored at -80 °C until shipment on dry ice to Minzu University of China (Beijing). PBDEs extraction and gravimetric lipid determination procedures have been published