



Maternal prenatal urinary phthalate metabolite concentrations and visual recognition memory among infants at 27 weeks



Khristina N. Ipapo^{a,b}, Pam Factor-Litvak^{a,c}, Robin M. Whyatt^{a,b}, Antonia M. Calafat^d,
Diurka Diaz^{a,b}, Frederica Perera^{a,b}, Virginia Rauh^{a,e}, Julie B. Herbstman^{a,b,*}

^a Columbia Center for Children's Environmental Health, Columbia University, New York, NY, USA

^b Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, NY, USA

^c Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA

^d National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, GA, USA

^e Department of Population and Family Health, Mailman School of Public Health, Columbia University, New York, NY, USA

ARTICLE INFO

Keywords:

Phthalates

Fagan

Infant cognition

Visual recognition memory

ABSTRACT

Background: Prior research has demonstrated inverse associations between maternal prenatal urinary phthalate metabolite concentrations and cognitive development assessed in preschool and school-aged children. While there are a limited number of studies that evaluated these associations during infancy, no study has evaluated whether these associations exist when using the Fagan Test of Infant Intelligence (FTII), which captures novelty preference as a function of visual recognition memory.

Objective: We evaluated associations between phthalate metabolite concentrations in maternal prenatal urine and cognition in infancy using the FTII at 27 weeks and determine if these associations are sex-specific.

Methods: Mono-*n*-butyl phthalate (MnBP), monobenzyl phthalate (MBzP), monoisobutyl phthalate (MiBP), mono-ethyl phthalate (MEP), mono-3-carboxypropyl phthalate (MCPP) and four di-2-ethylhexyl phthalate metabolites (DEHP) were quantified in urine samples collected from 168 minority women living in urban neighborhoods during their third trimester of pregnancy. The FTII was administered to infants at 27 weeks to measure visual recognition memory and was recorded as the novelty preference score.

Results: There were no associations between prenatal phthalate metabolite concentrations and novelty preference score in the full sample. However, there was evidence of effect modification by infant sex. Sex-stratified models demonstrated that compared to girls in the lowest tertile of MBzP concentrations, girls in tertiles 2 and 3 had, on average, 3.98 and 4.65 points lower novelty preference scores (*p*-value=0.04 and 0.03, respectively). The relationship was similar for Σ DEHP, MiBP, and MEP. Effects among boys were inconsistent and generally not significant.

Conclusion: Maternal prenatal exposure to some phthalates was negatively associated with visual recognition memory as measured by the FTII among girls at age 27 weeks.

1. Introduction

Phthalates are a class of high production volume chemicals that are widely used as plasticizers and additives for consumer products such as toys, and personal care products such as cosmetics and perfumes (Sathyanarayana, 2008). Several phthalates are endocrine disruptors that act by various mechanisms, including the inhibition of testosterone production and the modulation of thyroid hormone functions (Howdeshell et al., 2008; Sathyanarayana, 2008). In animal studies, some phthalates have been shown to interfere with estrogen synthesis by suppressing aromatase enzyme activity in the brain, suggesting that

phthalates could affect males and females differently (Andrade et al., 2006). Humans can be exposed to phthalates via oral, dermal and inhalation routes (CDC, 2011). Due to widespread use of products containing phthalates, exposure is ubiquitous (Sathyanarayana, 2008). Phthalates rapidly hydrolyze to monoester metabolites and oxidative metabolites, which are excreted primarily in urine (Heudorf et al., 2007). Urinary concentrations of phthalate metabolites are used as internal dosimeters of exposure because urinary enzymatic activity is negligible. Therefore, the metabolite concentration in urine accurately reflects an individual's exposure to phthalates as opposed to the external contamination with phthalates during sample collection and

* Correspondence to: 722 W 168th St., Room 1217, New York, NY 10032, USA.
E-mail address: jh2678@columbia.edu (J.B. Herbstman).

processing (Whyatt et al., 2012).

Animal studies have suggested that prenatal phthalate exposure is likely to increase the risk of neurodevelopment impairment (Miodovnik et al., 2014). There are a number of studies demonstrating associations between prenatal exposure to phthalates and adverse cognitive development in school-age children. Among New York City children at 3 years of age, Whyatt et al. (2012) demonstrated an inverse association between prenatal urinary concentrations of mono-*n*-butyl phthalate (MnBP) and monoisobutyl phthalate (MiBP) and psychomotor development index (PDI) of the Bayley Scales of Infant Development II (BSID) in both boys and girls. MnBP was also inversely associated with mental development index (MDI) of BSID in girls only (Whyatt et al., 2012). Among the same NYC children at age 7 years, Factor-Litvak et al. (2014) found that full-scale IQ as measured by the Wechsler Intelligence Scale for Children (WISC) was inversely associated with prenatal urinary metabolite concentrations of MnBP and MiBP. Additionally, Factor-Litvak et al. (2014) found that associations between MBzP and perceptual reasoning speed, and MiBP and verbal comprehension were stronger among boys than girls (Factor-Litvak et al., 2014). However, studies examining the effects of prenatal phthalate exposures on cognitive development among infants have been limited. Among Korean infants at 6 months, Kim et al. (2011) found that prenatal urinary concentration of mono-2-ethyl-5-hydroxyhexyl phthalate (MEHHP), mono-2-ethyl-5-oxohexyl phthalate (MEOHP) and MnBP were inversely associated with MDI and PDI of the BSID. In sex-stratified analyses, male infants demonstrated a stronger inverse association between phthalate metabolites and developmental indices, whereas female infants exhibited no significant associations (Kim et al., 2011).

The aim of the present study was to evaluate whether effects of prenatal phthalate exposure on cognitive ability are detectable in infants at 6 months of age using the same cohort of NYC children evaluated by Whyatt et al. (2012) and Factor-Litvak et al. (2014). We used the Fagan Test of Infant Intelligence (FTII), which is an instrument that measures visual recognition memory in infants and has been shown to be predictive of IQ in children (McCall and Carriger, 1993). Based on previous reports of sex-specific differences in the effect of prenatal phthalates on cognitive endpoints in older children, we hypothesized that prenatal exposure to the precursors of MnBP, MiBP, monobenzyl phthalate (MBzP), mono-ethyl phthalate (MEP), mono-3-carboxypropyl phthalate (MCP) and di-2-ethylhexyl phthalate (DEHP) would reduce visual recognition memory as measured by the FTII and that these effects would be sex-specific.

2. Methods

2.1. Participants

This analysis includes 168 mother-infant pairs enrolled in the Columbia Center for Children's Environmental Health (CCCEH) longitudinal birth cohort of 727 pregnant women who delivered between 1998 and 2006. The original purpose of this cohort was to assess the effects of air pollutant exposures on birth outcomes and child development (Perera et al., 2002). Subjects included in this study were women who lived in the Washington Heights, Central Harlem and the South Bronx neighborhoods of New York City and self-identified as either Dominican or African-American. Women who were eligible were nonsmoking, aged 18–35, registered at the obstetrics and gynecology clinics at New York Presbyterian Medical Center and Harlem Hospital by the 20th week of pregnancy, resided in the area for at least one year, and were not diagnosed with diabetes, hypertension, or have known HIV. Mother-infant pairs were included in the present analysis if prenatal phthalate metabolite concentrations were measured in maternal spot urine samples collected during the third trimester of pregnancy and if the infant had completed the Fagan Test of Infant Intelligence (FTII) at 27 weeks. Supplemental Fig. 1 schematically

demonstrates how the 168 mother-child pairs were selected for this analysis.

2.2. Ethics statement

Institutional review boards at the Columbia University Medical Center and the Center for Disease Control and Prevention (CDC) approved the study and the consent procedures. Participating mothers provided written informed consent for themselves and on behalf of their children.

2.3. Urine sample collection and phthalate measurements

Spot urine samples were collected during the third trimester of pregnancy. Samples were first stored at -80°C at Columbia University, shipped on dry ice to the CDC and finally stored at -70°C until samples were ready for analysis. Urinary concentrations of MnBP, MBzP, MiBP, MEP, MCP and four DEHP metabolites (MEHHP, mono-2-ethyl-5-carboxypentyl phthalate (MECPP), MEOHP, and mono(2-ethylhexyl) phthalate (MEHP)) were quantified at CDC using an on-line solid-phase extraction method combined with isotope dilution high-performance liquid chromatography/tandem mass spectrometry as previously described (Kato et al., 2005). We used specific gravity, measured with a handheld refractometer (Atago PAL 10-S, Bellevue, WA), to account for urinary dilution as previously recommended (Hauser et al., 2004). Intraclass correlation coefficients (ICCs) for the phthalate metabolites in urine samples were calculated to measure reliability. In 48 women from the CCCEH cohort, urine samples were collected biweekly over 6–8 weeks in late pregnancy. There was a total of 135 samples with two to four repeats per woman. ICCs were 0.77 for MBzP, 0.65 for MnBP, and 0.60 for MiBP and ranged from 0.27 to 0.42 for DEHP metabolites after adjusting for specific gravity (Factor-Litvak et al., 2014).

2.4. Infant cognitive assessment

The Fagan Test of Infant Intelligence (FTII), which is used to measure infant visual recognition memory, can be administered at 67, 69, 79, and 92 weeks post-conception. The majority (75%) of our participants who were assessed using the FTII were tested using the 67-week version and therefore, in this analysis, we restricted to those tested using this version to eliminate variation by version. The FTII was administered to infants at 67 weeks post-conception (equivalent to 27 weeks after birth for a full-term infant) at the CCCEH by trained examiners. The average post-conception age for this cohort was 66.01 weeks. During the familiarization period, the infant is shown two identical photos. During the novelty phase, the familiar photo is shown with a new photo. The FTII measures the infant's recognition memory to the familiar photo and the infant's ability to discriminate between different visual stimuli. Infants will typically dedicate more time to the novel photo than the familiar photo because the novel photo contains more new information than the familiar photo (Fagan and Detterman, 1992). During the test, the infant completes 10 novelty trials in order to compute the novelty preference score, which is the length of fixation time devoted to the novel picture divided by the total fixation time to both the novel and familiar photo, multiplied by 100 (Fagan, 2005). The novelty preference score can be used to identify if an infant is at risk for later cognitive deficits. There are three possible outcomes of the FTII based on the novelty preference score: a novelty preference score that is greater than 54.5 indicates that an infant is at low risk for later cognitive deficits, a score that is greater than 53.1 but less than or equal to 54.5 indicates that an infant is suspected of later cognitive deficits, and a score that is less than or equal to 53.1 indicates that an infant is at risk of later cognitive deficits (Fagan, 2005).

متن کامل مقاله

دریافت فوری ←

ISIArticles

مرجع مقالات تخصصی ایران

- ✓ امکان دانلود نسخه تمام متن مقالات انگلیسی
- ✓ امکان دانلود نسخه ترجمه شده مقالات
- ✓ پذیرش سفارش ترجمه تخصصی
- ✓ امکان جستجو در آرشیو جامعی از صدها موضوع و هزاران مقاله
- ✓ امکان دانلود رایگان ۲ صفحه اول هر مقاله
- ✓ امکان پرداخت اینترنتی با کلیه کارت های عضو شتاب
- ✓ دانلود فوری مقاله پس از پرداخت آنلاین
- ✓ پشتیبانی کامل خرید با بهره مندی از سیستم هوشمند رهگیری سفارشات