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Combined effects of prenatal exposure to polycyclic aromatic hydrocarbons and material hardship on child ADHD behavior problems

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ABSTRACT

Importance: Polycyclic aromatic hydrocarbons (PAH) are carcinogenic and neurotoxic combustion by-products commonly found in urban air. Exposure to PAH is disproportionately high in low income communities of color who also experience chronic economic stress.

Objective: In a prospective cohort study in New York City (NYC) we previously found a significant association between prenatal PAH exposure and Attention Deficit Hyperactivity Disorder (ADHD) behavior problems at age 9. Here, we have evaluated the joint effects of prenatal exposure to PAH and prenatal/childhood material hardship on ADHD behavior problems.

Materials and Methods: We enrolled nonsmoking African-American and Dominican pregnant women in New York City between 1998 and 2006 and followed their children through 9 years of age. As a biomarker of prenatal PAH exposure, PAH-DNA adducts were measured in maternal blood at delivery and were dichotomized at the limit of detection (to indicate high vs. low exposure). Maternal material hardship (lack of adequate food, housing, utilities, and clothing) was self-reported prenatally and at multiple time points through child age 9. Latent variable analysis identified four distinct patterns of hardship. ADHD behavior problems were assessed using the Conners Parent Rating Scale- Revised. Analyses adjusted for relevant covariates.

Results: Among 351 children in our sample, across all hardship groups, children with high prenatal PAH exposure (high adducts) generally had more symptoms of ADHD (higher scores) compared to those with low PAH exposure. The greatest difference was seen among the children with hardship persisting from pregnancy through childhood. Although the interactions between high PAH exposure and hardship experienced at either period ("persistent" hardship or "any" hardship) were not significant, we observed significant differences in the number of ADHD symptoms between children with high prenatal PAH exposure and either persistent hardship or any hardship compared to the others. These differences were most significant for combined high PAH and persistent hardship: ADHD Index ($p < 0.008$), DSM-IV Inattentive ($p = 0.006$), DSM-IV Hyperactive Impulsive problems ($p = 0.033$), and DSM-IV Index Total ($p = 0.009$).

Conclusion: The present findings add to existing evidence that co-exposure to socioeconomic disadvantage and

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air pollution in early life significantly increases the risk of adverse neurodevelopmental outcomes. They suggest the need for multifaceted interventions to protect pregnant mothers and their children.

1. Introduction

Approximately 11% of children 4–17 years of age in the United States (U.S.) have been diagnosed with Attention-deficit/hyperactivity disorder (ADHD), making it one of the most commonly diagnosed behavioral disorders in children (Visser et al., 2014) ADHD symptoms of hyperactivity, impulsivity and inattention often persist and may lead to poor performance in the academic and occupational settings throughout the adult years (Biederman and Faraone, 2005). The etiology of ADHD is complex; genetic, environmental and social factors all contribute to the emergence and severity of the disease (Biederman and Faraone, 2005). Known or suggested risk factors include obstetrical complications, maternal smoking, alcohol use, lead exposure, polycyclic aromatic hydrocarbon (PAH) exposure, low socioeconomic status, and psychosocial adversity (Faraone et al., 2005; Grizenko et al., 2012; Sagiv et al., 2013).

As reviewed previously, exposure to PAH is prevalent in urban populations from combustion of fossil fuels and other organic material (Vishnevetsky et al., 2015). The sources of PAH include combustion of diesel, gasoline, coal, residential heating oil; tobacco smoking and chargrilling or broiling of foods (Bostrom et al., 2002; Larsen and Baker, 2003). Exposures to ambient and indoor air pollutants tend to be disproportionately high in lower income communities or communities consisting largely of racial or ethnic minorities (Hou et al., 2012; Jerrett, 2009; Mohai et al., 2009; Morello-Frosch et al., 2011; Woodruff et al., 2003), as is experience of material hardship, an indicator of economic stress. Racial disparities in self-rated health persist even after differences in socioeconomic status are controlled for (Morello-Frosch et al., 2011). Residents are also more likely to live in low quality housing and have inadequate educational and nutritional resources compared to higher income communities (Vishnevetsky et al., 2015). Socioeconomic and psychological stress experienced by the mother during pregnancy and/or stress in the early childhood years have been associated with child ADHD (Grizenko et al., 2012; Linnet et al., 2003; Russell et al., 2015). Socioeconomic stressors have been shown to exacerbate the neurodevelopmental impacts of toxic environmental exposures (Bellinger et al., 1987, 1989; Bellinger, 2000; Darmon and Drewnowski, 2008; Evans and Kantrowitz, 2002; Lansdown et al., 1986; Vishnevetsky et al., 2015).

We previously showed that prenatal PAH was significantly associated with symptoms of ADHD (Hou et al., 2012). Here we tested the hypothesis that the observed effect of prenatal PAH exposure on ADHD behavior problems is increased in the presence of material hardship experienced by the mother during pregnancy and the child's early years. Concern about prenatal exposures to PAH arises from their ready transfer across the placenta and the fetal blood brain barrier reviewed in (Brown et al., 2007; Hood et al., 2000). Moreover, the fetus is particularly susceptible to chemical insults due to the rapid, dynamic and complex brain development taking place during this period, as well as their inability to efficiently detoxify and clear chemicals and repair DNA damage (Grandjean and Landrigan, 2006; Perera et al., 2004). Prenatal exposure to PAH can be measured by PAH-DNA adducts in maternal blood or cord blood donated at delivery. Since adducts reflect not only exposure but also absorption, metabolic activation, and DNA repair, they are considered an individual biologic dosimeter of PAH. Moreover, PAH-DNA adducts in white blood cells have the advantage of providing an integrated measure of exposure over the past 3–4 months (Mooney et al., 1995). This biomarker has previously been associated with multiple adverse neurodevelopmental outcomes in children (Hou et al., 2012; Perera et al., 2008, 2011, 2012).

Material hardship assesses an individual's unmet basic needs in the areas of food, housing, and clothing (Mayer and Jencks, 1989). Because prior studies have reported adverse effects of economic disadvantage and stress experienced both during pregnancy and childhood (Bolton et al., 2013; Schoon et al., 2012), as in our prior paper on child IQ, we evaluated material hardship experienced during both of these developmental periods. We addressed the following questions: Do PAH exposure and material hardship interact to influence ADHD symptoms? Does the co-occurrence of high prenatal PAH exposure and the pattern (trajectory) of prenatal and postnatal hardship though childhood impact ADHD scores? Is there a pattern of hardship that is worse in combination with high prenatal PAH exposure?

2. Methods

2.1. The Columbia Center for Children's Environmental Health (CCCEH) cohort study

For a more detailed description of the CCCEH cohort and study design, see our prior report (Perera et al., 2006). Briefly, between 1998 and 2006 we recruited African-American and Dominican women who resided in Washington Heights, Harlem, or the South Bronx in New York City (NYC) through the local prenatal care clinics. Enrollment was restricted to women who were nonsmokers, between 18 and 35 years, non-users of other tobacco products or illicit drugs, free of diabetes, hypertension, or known HIV, and who had initiated prenatal care by the 20th week of pregnancy. The Institutional Review Board of Columbia University approved the study. The mothers provided informed consent for themselves and their younger children; beginning at age 7 children provided assent.

2.2. Personal interviews, home caretaking environment, maternal intelligence, maternal ADHD, child anxiety/depression at age 9

2.2.1. Prenatal interview

A trained bilingual interviewer administered a 45-min questionnaire during the last trimester of pregnancy to elicit demographic information, residential history, health and environmental data such as active smoking (to confirm nonsmoking status as reported on the screening questionnaire) and exposure to environmental tobacco smoke (ETS). In the cohort, the mean cotinine measured in cord blood was significantly higher in newborns whose mothers reported ETS exposure during pregnancy (t-value = −3.08, p-value = −0.002). Additionally, information was collected on dietary PAH (specifically, consumption of broiled, fried, grilled or smoked meat), income and education.

2.2.2. Postnatal interviews and assessments

Postnatal interviews were administered in-person at 6 months and annually thereafter to determine changes in residence, ETS exposure, and health and environmental conditions. At child age 3, Caldwell and Bradley's Home Observation for Measurement of the Environment (HOME) (Bradley, 1994) was used to assess the quality of the proximal caretaking environment Maternal nonverbal intelligence was measured by the Test of Non-Verbal Intelligence-Third Edition (TONI-3) administered during the infant's 6 month visit or a subsequent visit using. The TONI-3 is a 15-min, language-free measure of general intelligence, that is relatively stable and free of cultural bias (Brown et al., 1997). To address the high heritability rate of ADHD (Todd et al., 2001), mothers completed the Conners Adult ADHD Rating Scales (CAARS) (Conners et al., 1999) at the child's 7 year visit; and maternal ADHD symptoms