Prenatal PM$_{2.5}$ Exposure and Behavioral Development in Children from Mexico City

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Abstract

Background: Childhood exposure to air pollution has been linked with maladaptive cognitive development; however, less is known about the association between prenatal fine particulate matter (PM$_{2.5}$) exposure and childhood behavior.

Objectives: Our aim was to assess the association between prenatal PM$_{2.5}$ exposure and behavioral development in 4–6 year old children residing in Mexico City.

Methods: We used data from 539 mother-child pairs enrolled in a prospective birth cohort in Mexico City. We estimated daily PM$_{2.5}$ using a 1km^2 satellite-based exposure model and averaged over each trimester of pregnancy. We assessed childhood behavior at 4–6 years of age using the parent-completed Behavioral Assessment Scale for Children (BASC-2) composite scores and subscales. We used linear regression models to estimate change in BASC-2 T-scores with trimester specific 5-μg/m^3 increases in PM$_{2.5}$. All models were mutually adjusted for PM$_{2.5}$ exposures during the other trimesters, maternal factors including age, education, socioeconomic status, depression, and IQ, child's age at study visit, and season. We additionally assessed sex-specific effects by including an interaction term between PM$_{2.5}$ and sex.

Results: Higher first trimester PM$_{2.5}$ exposure was associated with reduced Adaptive Skills scores (β: −1.45, 95% CI: −2.60, −0.30). Lower scores on the Adaptive Skills composite score and subscales indicate poorer functioning. For PM$_{2.5}$ exposure during the first trimester, decrements were consistent across adaptive subscale scores including Adaptability (β: −1.51, 95% CI: −2.72,

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−0.30), Social Skills (β: −1.63, 95% CI: −2.90, −0.36), and Functional Communication (β: −1.21, 95% CI: −2.21, −0.21). The association between 1st trimester $PM_{2.5}$ and depression was stronger in males than females (β for males: 1.52, 95% CI: −0.41, 3.45; β for females: −0.13, 95% CI: −1.99, 1.72); p-int: 0.07).

Conclusions: Exposure to $PM_{2.5}$ during early pregnancy may be associated with impaired behavioral development in children, particularly for measures of adaptive skills. These results suggest that air pollution impacts behavioral domains as well as cognition, and that the timing of exposure may be critical.

Keywords

air pollution; behavior; childhood; neurodevelopment; particulate matter

1. Introduction

Air pollution is a growing public health concern worldwide, particularly for urban populations (WHO, 2018). Fine particulate matter ($PM_{2.5}$) is one of the most common air pollutants globally and is associated with an increased risk of several adverse health outcomes including mortality, cardiovascular disease, and asthma (Lee et al., 2018; McGuinn et al., 2017). In recent years, a growing body of literature demonstrates the adverse impact of air pollution on the central nervous system, with a particular focus on the developing brain (Calderon-Garciduenas et al., 2015; Calderon-Garciduenas et al., 2014). Given the complexity of critical neurodevelopmental processes occurring in the first months of gestation, the prenatal period is thought to be a particularly vulnerable developmental window to the effects of air pollution on the brain (Rice and Barone, 2000; Sunyer and Dadvand, 2019). Systemic inflammatory responses to prenatal air pollution exposure may increase risk of neuroinflammation, neuron damage/loss, and microglia activation (Block and Calderon-Garciduenas, 2009), potentially increasing the risk of cognitive and behavioral deficits in children.

A number of recent epidemiologic studies demonstrate associations between early life air pollution exposure and diagnoses of attention deficit hyperactivity disorder (ADHD) (Aghaei et al., 2019) and autism spectrum disorder (ASD) (Kalkbrenner et al., 2015; McGuinn et al., 2020; Volk et al., 2013). While informative, studies focusing on clinical diagnoses may suffer from outcome misclassification and issues related to changes in diagnostic criteria (Sagiv et al., 2015). Further, studies focused on diagnostic outcomes may fail to capture subclinical effects on neurobiological systems that may be altered by chemical exposures (Rauh and Margolis, 2016). In this study, we focus on dimensional variation of a suite of behavioral outcomes measures using the BASC-2. Our approach focusing on behavioral symptoms rather than categorical diagnoses may be more sensitive to subtle sub-clinical toxic effects, permitting the development of dose response profiles, thus informing future testing of more complex functional relationships between brain and behavior (Rauh and Margolis, 2016). Notably, in addition to continuous measures of internalizing and externalizing behaviors, the BASC-2 includes assessments of adaptive skills and ASD-like behaviors including communication and social skills. Ultimately, assessing modifiable risk factors for childhood behavioral development is critical as

impairments in adaptive skills and greater externalizing and internalizing symptoms in childhood has been linked to later adolescent and adult health outcomes, such as depression and substance abuse (Loth et al., 2014).

Several recent studies demonstrate the adverse impact of *postnatal and childhood* air pollution exposure on behavioral development in children (Forns et al., 2016; Harris et al., 2016; Newman et al., 2013). We build on this growing body of literature by focusing on the prenatal period, a vulnerable window of brain development (Sunyer and Dadvand, 2019) that is currently understudied with respect to air pollution exposure and behavioral outcomes (Perera et al., 2012). Our longitudinal study examines a broad range of clinical and adaptive behavioral outcomes in children. Finally, of the previous studies on this specific research topic, the majority have been based in the United States or Europe. The effects of early life air pollution exposure on behavioral development in children residing in low- and middle-income countries, often in the presence of high levels of environmental and social stressors, remain largely unknown.

In this study, we examine the impact of prenatal air pollution exposure and behavioral development in a cohort of children living in Mexico City, a megacity with comparatively high air pollution levels (Calderon-Garciduenas and Torres-Jardon, 2012). Specifically, we aim to assess the association between trimester-specific prenatal $PM_{2.5}$ exposure and behavioral development in 4–6 year old children. Additionally, given previous sex-specific $PM_{2.5}$ findings (Chiu et al., 2014), we additionally aim to assess sex-specific associations between $PM_{2.5}$ and behavioral development in children.

2. Methods

2.1. Study sample

This study takes place among mothers and their children enrolled in the Programming Research in Obesity, Growth, Environment and Social Stressors (PROGRESS) study, a prospective birth cohort study in Mexico City. Briefly, pregnant women were recruited between 2007 and 2011 at 12–24 weeks' gestation through the Mexican Social Security System (IMSS). Women were eligible to participate in the study if they were 18 years or older, planned to live in Mexico City after their child's birth, were less than 20 weeks gestation, had completed primary education, had no medical history of heart or kidney disease, and did not consume alcohol daily (Braun et al., 2014). In total, 948 women enrolled in the 2nd trimester and delivered a live child who was then followed longitudinally. For this analysis, we used data from 539 mother-child pairs with complete exposure, outcome, and covariate information.

Protocols were approved by the institutional review boards at the Icahn School of Medicine at Mount Sinai, Harvard School of Public Health, and Mexican National Institute of Public Health. All women provided informed consent.

2.2. Air pollution exposure assessment

Early life exposure to $PM_{2.5}$ was estimated using a hybrid satellite-based exposure model developed by our team (Just et al., 2015). Briefly, we used satellite-derived Aerosol Optical

Depth (AOD) measurements from the MODIS satellite, meteorological data, and land use regression variables (such as roadway density, temperature, relative humidity, planetary boundary layer height, and daily precipitation) to predict observations from ground monitoring sites. The hybrid land use regression approach used mixed effect models with temporal and spatial predictors and day-specific random effects to calibrate the satellite AOD and account for temporal variation in the $PM_{2.5}$-AOD relationship as well as temporal and spatial predictors. Spatiotemporal smoothing was used for gap-filling with predictions output at a daily temporal and 1*1 km spatial resolution across the entire study area. Model performance was evaluated using monitor-level leave one out cross-validation with an R^2 of 0.74. Further details on this model, including methods and performance, can be found elsewhere (Just et al., 2015).

The nearest 1km exposure grid was linked to each participant based on GPS coordinates collected at her residential address by study personnel during mid-pregnancy. Gestational age was used to link the air pollution exposures on time. Gestational age was based on last menstrual period, as reported by the mother, and by a standardized physical examination to determine gestational age at birth. Average levels of $PM_{2.5}$ were calculated for each trimester of pregnancy (1st trimester: 1–13 weeks, 2nd trimester: 14–27 weeks, 3rd trimester: 28 weeks-delivery) by averaging the daily $PM_{2.5}$ levels across these time periods.

2.3. Assessment of childhood behavior

Children's behavior was assessed using the second edition of the Behavioral Assessment System for Children (BASC-2) Parent Rating Scale, validated in English and Spanish. The BASC assesses children's adaptive and problem behaviors in the home and community settings (Reynolds and Kamphaus, 2004). The Spanish version of the BASC-2 was administered to mothers (or primary caregivers) at the 4–6 year study visit. Our primary analysis focused on relationship between $PM_{2.5}$ and adaptive behavior using the Adaptive Skills composite score (which include subscales of Adaptability, Social Skills, Daily Living, and Functional Communication). In addition, we used the BASC-2 Developmental Social Disorders (DSD) content scale to assess associations with ASD-like behaviors, including difficulties with social skills and communication (Reynolds and Kamphaus, 2004). Previous studies have shown that the BASC-2 DSD scale has high sensitivity and specificity for identifying children with high-functioning ASD, when using a threshold of 60 (1 SD from the population mean) (Volker et al., 2010). We also examined associations between $PM_{2.5}$ and the three BASC-2 composite clinical indices; Externalizing Problems, Internalizing Problems, and the Behavioral Symptoms Index (an overall level of behavioral problems). The Externalizing Problems composite score includes subscales of Aggression and Hyperactivity; Internalizing Problems include subscales of Anxiety, Depression, and Somatization; Behavioral Symptoms Index includes subscales of Attention, Atypicality, and Withdrawal (see Supplemental Table S1 for included BASC-2 measures). Higher scores on BASC-2 Attention and Hyperactivity subscales at this age have shown to be predictive of a later diagnosis of ADHD (Harvey et al., 2009).

Raw scores from all composite measures and subscales were converted to age- standardized T-scores (mean=50, SD=10). Spanish-speaking parents and children were included in the

normative sample; however, separate Spanish norms are not available for the BASC-2. Higher scores on the BASC-2 DSD scale and three clinical scales (Externalizing, Internalizing and Behavioral Skills Index) indicate more problematic behaviors; lower scores on the Adaptive Skills composite score and subscales indicate poorer functioning.

2.4. Covariates

Covariate information was obtained from standardized questionnaires administered to mothers at baseline and follow-up study visits. Questionnaires collected sociodemographic information such maternal age at enrollment, years of education, and socioeconomic status (SES). Thirteen variables derived from questionnaire results were used to classify study participants into six levels based on the SES index created by the Asociación Mexicana de Agencias de Investigación de Mercados y Opinión Pública (Carrasco, 2002). We further collapsed these six levels into low, medium, and high SES based on the distribution in our study population (Stroustrup et al., 2016). The Spanish version of the Edinburgh Postnatal Depression Scale (EPDS) was administered to women to screen for the presence of depressive symptoms during pregnancy (Alvarado-Esquivel et al., 2014; Murray and Cox, 2007). EPDS scores were dichotomized at a score of 13, based on previous studies in Spanish speaking populations (Alvarado-Esquivel et al., 2014; Murray and Cox, 2007). Finally, a subset of mothers completed the Home Observation for Measurement of the Environment (HOME) at the 24-month study visit (Bradley and Caldwell, 1979). The HOME evaluation measures the quality and support of the child's home environment and was measured in the participant's home during a separate visit.

A directed acyclic graph (DAG) was used to identify the minimally sufficient adjustment set; we additionally used the DAG to avoid adjustment for potential mediating variables on the causal pathway. Our DAG-identified adjustment set includes the following variables: maternal age in years, maternal education (less than high school, high school, or greater than high school), maternal SES (low, medium, high), maternal EPDS score (<13, 13), maternal IQ (using the Wechsler Adult Intelligence Scale, Spanish version), child's age at BASC-2 assessment, and season of conception. Season of conception was categorized as cold-dry (November-February), warm-dry (March-April), and rainy (May-October).

2.5. Statistical analyses

We examined the distribution and summary statistics for all variables using univariate and bivariate models. The distributions of trimester-specific and entire pregnancy $PM_{2.5}$ concentrations and BASC-2 scores (including the DSD scale, and adaptive skills, externalizing, internalizing, and BSI composite scores and subscales) measured at age 4–6 were examined.

We estimated associations between trimester-specific $PM_{2.5}$ averages and changes in childhood behavioral development using both linear and logistic regression approaches. For linear models, we included the continuous BASC-2 measure. The estimates from these analyses can be interpreted as the difference in each BASC-2 measure per 5-$\mu g/m^3$ increase in $PM_{2.5}$. Logistic regression was used to assess associations between increases in $PM_{2.5}$ and the odds of clinically-relevant BASC-2 scores on the composites and subscales outcomes,

using the cutpoints provided in the BASC-2 manual. Children were categorized as being in the at risk/clinically significant group for the Externalizing Problems, Internalizing Problems, Behavioral Symptoms Index, and DSD scale if the t-scores were   60; a cut-off of   40 was used to identify children in the at risk/clinically significant group in terms of the Adaptive Skills composite score and subscale scores (Reynolds and Kamphaus, 2004). These cut-offs represent 1 SD from the population mean of 50.

Analyses were run separately for each BASC-2 composite and subscale outcome measure. Trimester-specific associations were reported separately for single models and mutually adjusted for exposures during the other trimesters (Wilson et al., 2017); for example, estimates for first trimester $PM_{2.5}$ exposure were mutually adjusted for $PM_{2.5}$ concentrations during the second and third trimesters.

Previous studies have found differences in effects of $PM_{2.5}$ exposure on males and females (Chiu et al., 2014; Lee et al., 2018). Therefore, we assessed if child sex modified $PM_{2.5}$-BASC-2 associations. In order to adjust for the quality of the caregiving environment, in sensitivity analyses we also adjusted for HOME scores for the subset of participants for whom scores were available. Finally, we assessed the confounding effects of prenatal lead exposure by adjusting for maternal lead exposure in the subset of participants who had prenatal blood lead concentrations available (Renzetti et al., 2017).

3. Results

3.1. Study population

Sociodemographic, exposure, and outcome measures for our study population are shown in Tables 1 and 2. Children were on average 4.8 years at the 4–6-year follow-up visit; there was an even distribution of females and males in our study sample. Mothers were 28 years old (± 5.6) at enrollment and primarily of low education and of low socioeconomic status. About 30% of mothers were categorized as having EPDS scores above 13. Average trimester-specific $PM_{2.5}$ levels ranged from 22.1 – 22.9 μg/m^3; the entire pregnancy average $PM_{2.5}$ level was 22.7 μg/m^3 (Table S2). Women in our study population were exposed to considerably higher levels than the Mexican Air Quality Standard of 12 μg/m^3.

3.2. Distribution of BASC-2 scores

The distributions (mean ± SD) of BASC-2 T-scores are shown in Table 2, overall and by sex. Compared to females, males tended to have higher mean scores on the Externalizing Problems, Behavioral Symptoms Index (including Attention Problems), and DSD scales, and lower mean scores on the Adaptive Skills measures. While the distributions of scores in our study sample were fairly similar to the age-standardized population (i.e., means and SDs around 50 and 10, respectively), our study sample tended to have higher mean values for Externalizing Problems, Internalizing Problems (particularly for the Anxiety subscale), and the Behavioral Symptoms Index, and lower scores for Adaptive Skills (most notably for Functional Communication) compared to the age-standardized population.

3.3. Association between prenatal PM$_{2.5}$ and childhood behavior

Figure 1 shows the difference in continuous BASC-2 Adaptive Skills composite and Developmental Social Disorders scores per 5-μg/m^3 increase in PM$_{2.5}$. Higher concentrations of PM$_{2.5}$ during the first trimester were associated with lower Adaptive Skills composites scores (β: −1.45, 95% CI: −2.60, −0.30). We did not observe significant associations between either 2nd and 3rd trimester PM$_{2.5}$ and Adaptive Skills (Figure 1, Table S3). First trimester PM$_{2.5}$ was similarly associated with lower scores of the three Adaptive subscales; Adaptability (β: −1.51, 95% CI: −2.72, −0.30), Social Skills (β: −1.63, 95% CI: −2.90, −0.36), and Functional Communication (β: −1.21, 95% CI: −2.21, −0.21) (Table S3). About 20% of children scored in the at-risk/ clinical range for Adaptive Skills (i.e., < 40); percentages for subscales ranged from 16–23% (Table S4). PM$_{2.5}$ concentration during the first trimester was associated with an increased odds of being in the at-risk/ clinical range for Adaptive Skills (OR: 1.41, 95% CI: 1.00, 1.98) and Functional Communication (OR: 1.35, 95% CI: 0.98, 1.85) subscales (Table S5).

Consistent with results from the Adaptive Skills composite score and subscales, first trimester PM$_{2.5}$ exposure was associated with deficits in social skills and communication, as measured by the Developmental Social Disorders content scale (β: 1.34, 95% CI: 0.14, 2.54) (Figure 1, Table S3).

For the clinical composite scores (Externalizing, Internalizing, and BSI), we observed similar trends. Although greater first trimester air pollution exposure was associated with more behavioral problems, confidence intervals for these results included the null (Figure 2). We did observe associations between first trimester PM$_{2.5}$ exposure and increases in a few of the behavioral subscales, including Attention Problems (β: 1.44, 95% CI: 0.17, 2.71) and Withdrawal subscales (β: 1.40, 95% CI: 0.12, 2.67) (Table S3). We did not observe associations between composite scores or DSD outcomes and PM$_{2.5}$ averaged over the entire pregnancy period (Table S6).

Our main finding of associations between first trimester PM$_{2.5}$ and Adaptability was not sex-specific (β for females: −2.45, 95% CI: −4.13, −0.77; β for males: −0.80, 95% CI: −2.47, 0.86; p-int=0.25). While we did not observe an association between PM$_{2.5}$ and the Internalizing Problems subscale of depression, child sex did modify the association between first trimester PM$_{2.5}$ and depression. In PM$_{2.5}$-sex interaction models, we observed an association between PM$_{2.5}$ and higher depression scores for males (β: 1.52, 95% CI: −0.41, 3.45) but not females (β: −0.13, 95% CI: −1.99, 1.72) (*p*-int: 0.07) (Table S7).

Among the subset of participants with available maternal blood lead concentrations (n=465), adjusting for maternal blood lead did not change any estimates significantly (Table S8). Finally, adjusting for HOME scores (n=376) did not significantly alter our results (Table S9), nor did adjusting for maternal blood lead and HOME scores in the same model.

4. Discussion

In this study, higher first trimester PM$_{2.5}$ exposure was associated with poorer BASC-2 Adaptive Skills composite score and subscales, suggesting this life stage is a critical

exposure window during which air pollution can affect the developing brain. This association was not observed with second and third trimester $PM_{2.5}$, nor with $PM_{2.5}$ averaged across the entire pregnancy. First trimester $PM_{2.5}$ was also associated with the increased DSD content scale and higher reporting of Attention and Withdrawal symptoms. Overall, our findings did not differ significantly by sex; however, first trimester $PM_{2.5}$ exposure was associated with higher depression scores for males compared to females.

Our study adds to the accumulating body of literature examining associations between early life air pollution and children's neurodevelopment by a) focusing on behavioral rather than cognitive outcomes and b) addressing air pollution exposure throughout all of pregnancy, including the first trimester. Our most robust findings were for associations between early pregnancy $PM_{2.5}$ exposure and lower adaptive functioning, including worse Communication and Social Skills scores. Early studies linking air pollution and children's neurodevelopment focused largely on cognitive outcomes (Block et al., 2012; Calderon-Garciduenas et al., 2014) with more recent studies shifting to focus on behavioral outcomes (Guxens et al., 2014; Lubczynska et al., 2017; Stingone et al., 2017; Sunyer et al., 2015). Deficits in social skills and communication, as measured using the DSD, are hallmarks of ASD (Bradstreet et al., 2017; Robertson et al., 1999). Several previous studies have found an increased risk of ASD among children with greater prenatal and/or early postnatal air pollution exposures (Flores-Pajot et al., 2016; McGuinn et al., 2020). In a population-based study of typically developing children, early prenatal $PM_{2.5}$ was associated with worse communication scores (Ha et al., 2019). Among children with ASD compared to typically developing children, first postnatal year nitrogen dioxide (a proxy for air pollution) exposure was associated with reduced adaptive skills (Kerin et al., 2018).

To date, only a limited number of studies focus on associations between *prenatal* air pollution exposure and child neurodevelopment. In a New York City based cohort, polycyclic aromatic hydrocarbons (PAH) measured in third trimester personal air monitors were associated with increased anxiety, depression and attention in young children (Perera et al., 2012). Third trimester black carbon exposure was not associated with behavioral outcomes (Harris et al., 2016). Neither study included estimates of first or second trimester air pollution exposure. To our knowledge, ours is one of the first epidemiologic studies to assess associations with childhood behavior using each trimester-specific $PM_{2.5}$ average including the first trimester.

A growing body of toxicologic literature exists supporting the biologic plausibility of an association between early life air pollution exposure and adverse impact on the developing brain (Costa et al., 2014). A number of animal studies have found increases in neuroinflammation, oxidative stress, and markers of microglial activation in response to air pollution exposure (Block and Calderon-Garciduenas, 2009). Notably, and consistent with epidemiologic literature, outcomes appear to be sex-specific, with effects often only present in male mice (Bolton et al., 2017). In humans, systemic inflammatory responses from early life air pollution exposure may reach the developing brain, increasing risk of neuroinflammation, neuron damage/loss, and microglia activation (Block and Calderon-Garciduenas, 2009). Our most consistent findings were for exposures during the first trimester, a period of rapid brain development (Rice and Barone, 2000). Prior studies have

found associations between first trimester $PM_{2.5}$ exposure and fetal growth restriction (Michikawa et al., 2017), which has been implicated in childhood behavioral disorders (Wiles et al., 2006).

While mechanistic studies linking air pollution exposure to neurodevelopmental outcomes in humans are rare, magnetic resonance imaging (MRI) offer non-invasive in vivo insight into structural and functional changes in the brain that may be associated with environmental exposures (Horton et al., 2014). Higher air pollution was associated with increased white matter brain lesions in Mexico City children compared to those children in less polluted areas (56% vs 8% respectively) (Calderon-Garciduenas et al., 2008). Another recent study observed associations between prenatal $PM_{2.5}$ and decreases in childhood corpus callosum (CC) volume (Mortamais et al., 2019). Structural changes in the CC may be one of the mechanisms linking early life air pollution exposure to childhood behavioral problems.

Our study has several limitations. We used each participant's residential location during mid-pregnancy to assign $PM_{2.5}$ exposures for the entire pregnancy period, and is possible that relocation throughout pregnancy and childhood would impact $PM_{2.5}$ exposure. However, several studies leveraging full prenatal residential address history suggest minimal exposure misclassification, and that when women do move they often stay in the same exposure category (Bell and Belanger, 2012). Personal air sampling during pregnancy, the gold standard for air pollution exposure assessment (Larkin and Hystad, 2017) was not available for these subjects. We also note that personal air sampling, while more precise, is not feasible to conduct beyond very short time periods from several days to weeks. We adjusted for HOME scores in sensitivity analyses to control for the caretaking environment, as this may impact behavioral development of the children. Adjusting for HOME scores in the subset of participants who completed the in-person home visit did not substantially impact the resulting estimates. Further, housing conditions, ventilation in the house, and other occupational exposures could potentially confound our associations. We did not have access to this data in the current analyses and we note this as a limitation. Finally, although we adjusted for several key covariates, we did not have information on other urban correlates such as environmental noise exposure. Future studies will consider additional measures of other urban correlates.

We used the BASC-2 parent reported measure to assess behavioral development in 4–6 year children. It is possible that some parents may have misreported their child's behavioral functioning; however, given the age of the children, the parent reported measure would likely be more valid at this younger age, compared to the self-reported measures (Reynolds and Kamphaus, 2004). Further, maternal mental health status may impact both the reporting of their child's behavior as well as the child's development of behavioral problems. (Leis et al., 2014). We adjusted for maternal depression in our analyses in order to control for these potential relationships. As children in the PROGRESS cohort age, we will have both self- and parent-reported BASC-2 measures, so we will be able to assess the impact of informant on the associations between air pollution and children's behavioral outcomes. Finally, given the young age of the children, instead of using strict diagnostic criteria, we assessed associations using broad behavioral symptoms.

5. Conclusions

This is one of the first studies to assess the question of whether prenatal exposure to fine particulate matter impacts behavioral development in children residing in a middle-income country with considerably high levels of air pollution. We assessed this research question in a well-characterized, prospective birth cohort using state-of-the-art satellite-based air pollution exposure modeling. Adjusting for several important confounders such as maternal SES and depression, we demonstrated an inverse association between first trimester air pollution exposure and increased behavioral problems in children at 4–6 years of age.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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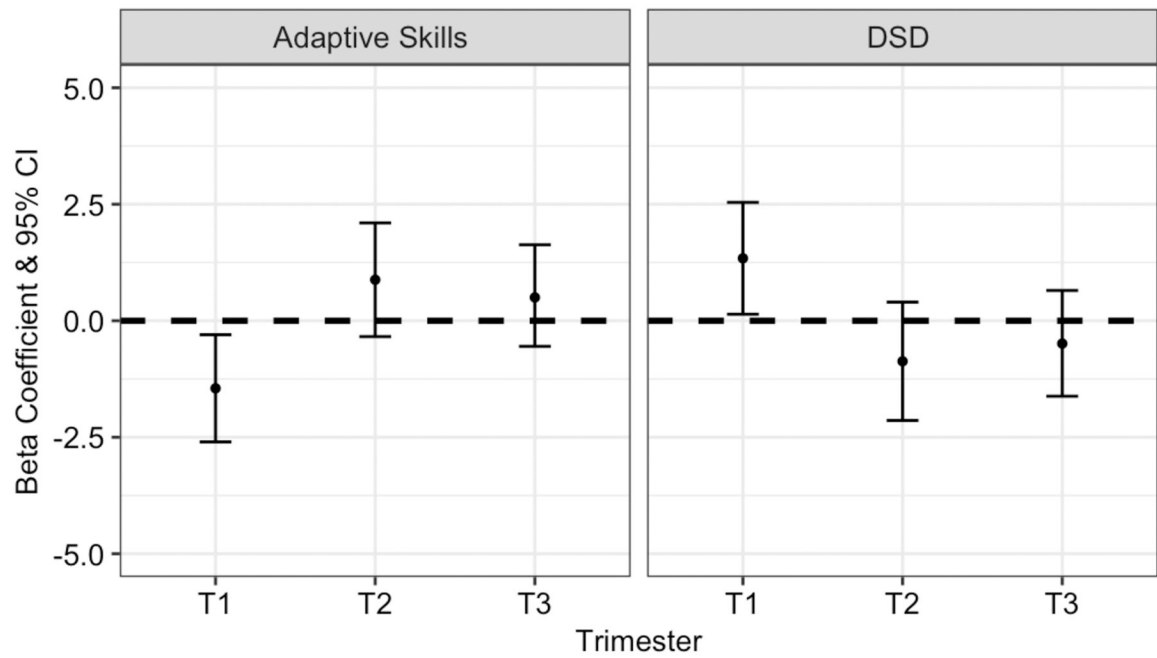
Figure 1.
Adjusted beta coefficients and 95% confidence intervals (CI) demonstrating associations between trimester-specific $PM_{2.5}$ exposure and continuous measures of BASC-2 Adaptive Skills composite and Developmental Social Disorder scores. All models are adjusted for maternal education, maternal age, maternal SES, maternal depression, maternal IQ, age of child at study visit, season of conception, and $PM_{2.5}$ exposures during the other trimesters.
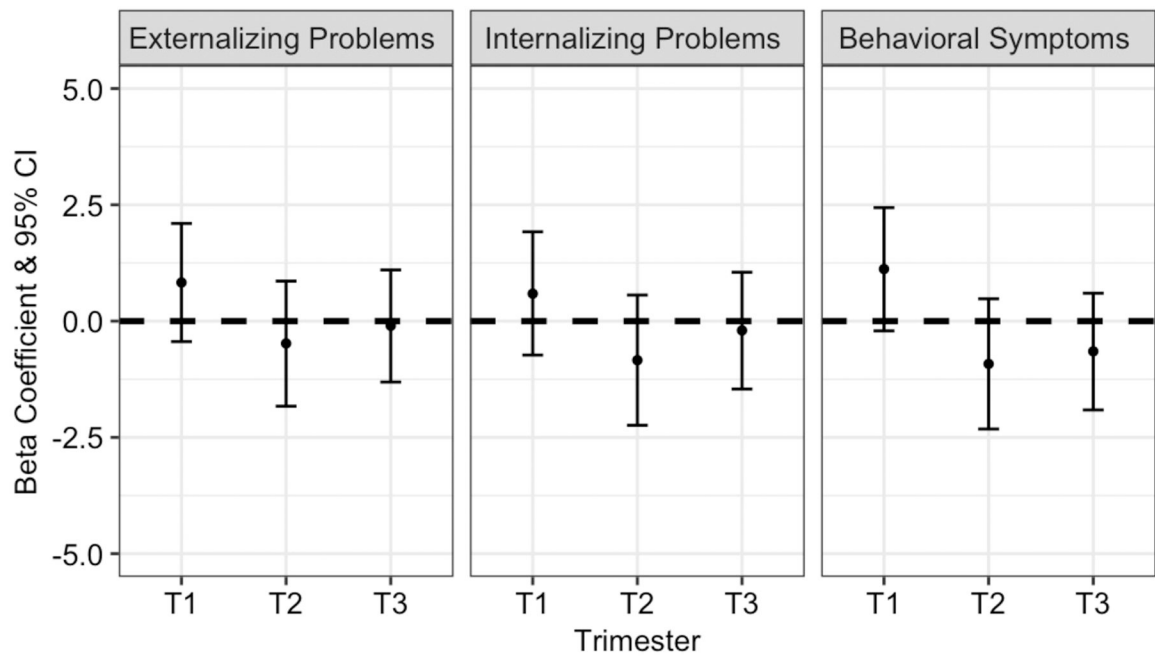
Figure 2.
Adjusted beta coefficients and 95% confidence intervals (CI) demonstrating associations between trimester-specific $PM_{2.5}$ exposure and continuous measures of BASC-2 Externalizing, Internalizing, and BSI composite T-scores. All models are adjusted for maternal education, maternal age, maternal SES, maternal depression, maternal IQ, age of child at study visit, season of conception, and $PM_{2.5}$ exposures during the other trimesters.

Table 1.

Demographics for 539 mother-child dyads participating in the PROGRESS study.

Characteristic	N (%) or mean ± SD
Sex of the child	
Male	272 (50)
Female	267 (50)
Age of child at assessment (years)	4.8 ± 0.5
Gestational age (weeks)	38 ± 1.7
Maternal age at delivery (years)	28 ± 5.6
Maternal IQ	85 ± 12
Maternal depression	
EPDS score < 13	377 (70)
EPDS score 13	162 (30)
Socioeconomic status	
Low	279 (52)
Medium	205 (38)
High	55 (10)
Maternal education	
<High school	221 (41)
High school	185 (34)
>High school	133 (25)
Season of conception	
Cold-dry (Nov - Feb)	154 (29)
Warm-dry (March - Apr)	115 (21)
Rainy (May - Oct)	268 (50)

Abbreviations: EPDS, Edinburgh Postnatal Depression Scale; IQ, intelligence quotient; PROGRESS, Programming Research in Obesity, Growth, Environment and Social Stressors Study.

Table 2.

Distribution of BASC-2 T-scores (means ± SDs), overall and by sex of the child for 539 4–6 year children enrolled in the PROGRESS study.

BASC-2 Measures	Overall	Females	Males
Adaptive Skills	48.6 ± 9.5	50.2 ± 9.0	47.1 ± 9.8
Adaptability	50.4 ± 9.8	51.0 ± 9.7	49.8 ± 9.9
Social skills	50.4 ± 10.4	51.7 ± 10.1	49.2 ± 10.5
Daily living	48.8 ± 10.2	51.0 ± 9.2	46.6 ± 10.7
Functional communication	46.2 ± 8.2	46.9 ± 8.2	45.5 ± 8.1
Developmental Social Disorders	52.2 ± 9.9	51.0 ± 9.1	53.4 ± 10.5
Externalizing Problems	51.3 ± 10.1	49.2 ± 8.6	53.3 ± 11.1
Aggression	49.1 ± 10.0	47.1 ± 8.3	51.1 ± 11.1
Hyperactivity	53.2 ± 10.2	51.3 ± 9.2	55.0 ± 10.9
Internalizing Problems	54.2 ± 10.5	53.5 ± 10.0	54.9 ± 11.0
Anxiety	57.2 ± 9.9	57.3 ± 10.0	57.0 ± 9.9
Depression	51.0 ± 11.1	49.8 ± 10.2	52.2 ± 11.9
Somatization	51.5 ± 10.3	50.8 ± 10.0	52.2 ± 10.6
Behavioral Symptoms Index	52.2 ± 10.9	50.0 ± 9.6	54.2 ± 11.7
Attention Problems	52.4 ± 10.1	50.7 ± 9.6	54.1 ± 10.4
Atypicality	53.3 ± 12.3	51.3 ± 10.4	55.3 ± 13.7
Withdrawal	49.7 ± 10.2	49.3 ± 9.6	50.1 ± 10.8

Abbreviations: BASC-2, Behavior Assessment System for Children, Second Edition; SD, standard deviation.