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Individual and joint effects of prenatal $PM_{2.5}$ and maternal stress on child temperament

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ABSTRACT

Prenatal fine particulate matter ($PM_{2.5}$) and maternal psychological functioning have been associated with child cognitive outcomes, though their independent and joint impacts on earlier behavioral outcomes remains less studied. We used data from 382 mother-child pairs from a prospective birth cohort in Mexico City. Temperament was measured at 24 months using the Carey Toddler Temperament Scale (TTS). Exploratory factor analysis (EFA) was used to update the factor structure of the TTS. During pregnancy, mothers completed the Crisis in Family Systems-Revised, Edinburgh Depression Scale, pregnancy-specific anxiety scale, and the Perceived Stress Scale. Pregnancy $PM_{2.5}$ was assessed using estimates from a satellite-based exposure model. We assessed the association between prenatal maternal stress and $PM_{2.5}$ on temperament, in both independent and joint models. Quantile g-computation was used to estimate the joint associations. Models were adjusted for maternal age, SES, education, child sex, and child age. In EFA, we identified three temperament factors related to effortful control, extraversion, and negative affect. Our main results showed that higher levels of $PM_{2.5}$ and several of the maternal psychological functioning measures were related to both effortful control and negative affect in the child, both individually and as a mixture. For instance, a one quartile increase in the prenatal mixture was associated with higher negative affect scores in the child (0.34, 95% CI: 0.16, 0.53). We observed modification of these associations by maternal SES, with associations seen only among lower SES participants for both effortful control (−0.45, 95% CI: -0.70, −0.20) and negative affect outcomes (0.60, 95% CI: 0.35, 0.85). Prenatal $PM_{2.5}$ and maternal psychological functioning measures were associated with toddler temperament outcomes, providing evidence for impacts of chemical and non-chemical stressors on early child health.

1. Introduction

Temperament broadly refers to early-emerging individual differences in emotional reactivity and regulation that appear early in development and are moderately stable over time (Thomas and Chess, 1977). Characterizing individual differences in early temperament is important as temperament predicts later psychopathology in adolescence and adulthood (Bould et al., 2014; De Pauw and Mervielde, 2010; Nigg, 2006; Olino et al., 2022). Thomas and Chess were among the first to classify different temperament styles in children based on their work in the New York Longitudinal Study (NYLS) (Thomas et al., 1963). From this initial work in the NYLS they derived nine temperament dimensions,

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that were further grouped into easy, difficult, and slow-to-warm-up temperament styles (Chess et al., 1963). Most subsequent research has not confirmed this hypothesized structure (De Pauw, 2017; Rothbart, 1982). Subsequently, Rothbart's model emerged as the most widely accepted temperament typology. This model posits the existence of three broad dimensions including Effortful Control, Surgency, and Negative Affect. Rothbart's model is supported by extensive psychometric evidence and is theoretically and empirically related to the structure of personality in adolescence and adulthood, with the three dimensions corresponding to Neuroticism, Extraversion and Conscientiousness, respectively (Caspi et al., 2005; Rothbart et al., 2000). This approach to characterizing temperament, particularly the construct of negative affect, has been widely used in several epidemiologic studies (Brunst et al., 2014; Cowell et al., 2021; Kopala-Sibley et al., 2016).

While temperament is often largely influenced by genetic factors (Saudino and Ganiban, 2020), an accumulating body of literature also points to environmental contributions, including during the prenatal period (Takegata et al., 2021). One of the most widely studied factors impacting infant and child temperament outcomes includes prenatal maternal stress (Brunst et al., 2014; Bush et al., 2017; Laplante et al., 2016) and maternal psychological functioning (Davis et al., 2007; Erickson et al., 2017; Stroustrup et al., 2016). Though less studied, there are additionally findings for environmental contributions to temperament outcomes (Cowell et al., 2021; Stroustrup et al., 2016; Rahman et al., 2022; Singer et al., 2017). Air pollution is of particular interest as an environmental contributor to child temperament given the growing body of literature linking early life fine particulate matter ($PM_{2.5}$) exposure and later life behavioral and mental health outcomes in children (McGuinn et al., 2020). One previous study assessed this research question and found impacts between higher $PM_{2.5}$ exposure during prenatal time windows and higher negative affect scores in infants (Rahman et al., 2022).

More recently, studies have started to assess the combined impact of multiple chemical and non-chemical stressors (Eick et al., 2023). Previous studies have often assessed the individual impacts of prenatal stressors and air pollution on health outcomes, including child temperament. Studying the combined impacts of both of these groups of stressors is important as individuals are often simultaneously exposed to both higher levels of psychosocial stressors and environmental exposures and these exposures may impact similar stress related biologic pathways (Thomson, 2019). One previous study addressed the modifying impact of prenatal maternal stress on associations between polycyclic aromatic hydrocarbon (PAH) exposure and infant temperament outcomes (Liu et al., 2022). This study found that infants exposed to both higher prenatal PAHs and maternal stress had lower orienting/-regulation outcomes (Liu et al., 2022). While studies have assessed the modifying impacts of stress on air pollution-health associations, few have examined the joint exposure of these stressors, or if this *mixture* differs by SES. This is critical as lower SES individuals are often disproportionately burdened and exposed to both higher levels of air pollution and psychosocial stress compared to higher SES individuals (Hajat et al., 2015; O'Neill et al., 2003). Assessing effect modification by SES is important particularly for temperament outcomes as several studies have found associations between family SES and child temperament (Strickhouser and Sutin, 2020), with some showing differences in impacts of prenatal maternal psychological functioning and temperament outcomes by SES (Bush et al., 2017).

We address several critical research gaps in the current analysis. Our primary objective was first to assess the individual and combined impact of multiple maternal stress and psychological functioning measures in relation to toddler temperament in our study population of mother-child pairs in a longitudinal birth cohort in Mexico City. We additionally aimed to assess the impact of prenatal $PM_{2.5}$ exposure on temperament outcomes, both individually and as a mixture with the stress measures. Finally, we assessed if there were differences in identified associations based on levels of maternal SES or child sex.

2. Materials and methods

2.1. Study population

We used data from the Programming Research in Obesity, Growth, Environment and Social Stressors (PROGRESS) longitudinal birth cohort in Mexico. Briefly, pregnant women were recruited between 2007 and 2011 at 12–24 weeks' gestation in primary care clinics of the Mexican Social Security Institute. To be included in the study, pregnant women needed to be 18 years or older and plan to live in Mexico City. Women were eligible if they 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 the current study, we used data from 382 mother-child pairs with non-missing data for all primary exposures, temperament outcomes, and covariates. Participant characteristics did not differ for those included and those in the original sample (Supplemental table 1).

Protocols were approved by the relevant institutional review boards. All women provided informed consent.

2.2. Toddler temperament

Toddler temperament was assessed around two years of age using the Carey Toddler Temperament Scale (TTS), which was developed to assess each of the nine temperament constructs originally developed by Thomas and Chess (Chess et al., 1963). The TTS is a 97-item parent-reported assessment of temperament in children aged 1–3 years (Fullard et al., 1984). Briefly, parents are presented with a statement describing a certain behavior in their child and asked to rate how often their child behaves in that way on a 6-point scale, from almost never (Thomas and Chess, 1977) to almost always (Thomas et al., 1963). Given the lack of support for the hypothesized structure of the TTS (De Pauw, 2017), we conducted an exploratory factor analysis (EFA) of the items to determine the best solution for our sample. In particular, we were interested in whether a three-factor solution resembling Rothbart's model would emerge from the EFA.

2.3. Maternal prenatal psychological functioning

We assessed the independent and combined associations of several maternal prenatal psychological functioning measures including anxiety and depressive symptoms, perceived stress, and negative life events. All of these measures have been previously validated in Spanish speaking populations (Alvarado-Esquivel et al., 2014; Rini et al., 1999; Vallejo et al., 2018; Berry et al., 2006). The Spanish version of these scales were administered to women by trained psychologists during either the second or third trimester of pregnancy.

Pregnancy-specific anxiety was assessed using an expanded set of items based on those developed by Wadhwa et al. (1993). The Pregnancy Anxiety Scale measures a woman's feelings about her health during pregnancy, the health of her baby, and her feelings about labor and delivery. The Pregnancy Anxiety Scale was previously validated and linked to health outcomes in a Latino population (Rini et al., 1999). This scale had good internal consistency in our study population (Cronbach's alpha = 0.86).

Maternal depressive symptoms during pregnancy were assessed using the validated Edinburgh Postnatal Depression Scale (EPDS) (Cronbach's alpha = 0.87). This scale measures symptoms of depression in the mother over the previous 7 days (Cox et al., 1987; Flom et al., 2018). This scale has been previously validated in Mexican adult pregnant populations (Alvarado-Esquivel et al., 2014).

Perceived stress was measured using the validated 4-item Perceived Stress Scale (PSS-4) (Cronbach's alpha = 0.72) (Vallejo et al., 2018; Cohen et al., 1983; Lee, 2012). This scale measures global perceived stress during the previous month. Responses were summed to create an overall score.

Negative life events (NLE) within the previous six months were assessed using the validated Crisis in Family Systems-Revised survey, which inquires about 11 life event domains experienced in the last 6 months (Berry et al., 2006; Shalowitz et al., 1998). A summary score (range 0–11) was calculated by summing the number of domains that women endorsed as having at least one NLE.

2.4. Air pollution exposure assessment

Daily average $PM_{2.5}$ exposure at each participant's residence was estimated using a previously developed hybrid satellite land use regression model at a 1 × 1 km spatial resolution (Gutiérrez-Avila et al., 2022). This model ensures temporal and spatial variability throughout Mexico City (Gutiérrez-Avila et al., 2022). This model uses Extreme Gradient Boosting with inverse-distance weighted surfaces and several different meteorological and land use variables. Models were evaluated using leave-one-station-out cross-validation. Models for mean $PM_{2.5}$ exhibited good performance, with an overall cross-validated mean absolute error (MAE) of 3.68 μg/m^3. The R^2 varied year to year, ranging from 0.64 to 0.86 (Gutiérrez-Avila et al., 2022).

The nearest 1 km exposure grid was linked to each participant based on GPS coordinates collected at their residential address by study personnel. 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.

2.5. Covariates

A directed acyclic graph (DAG) was used to identify the minimally sufficient adjustment set to address potential confounding bias. This adjustment set included maternal age, maternal education, SES, child age, and child sex. Maternal age (years) and SES were assessed at enrollment. Thirteen variables (i.e. number of bedrooms, access to internet, level of education, etc.) 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 lower, medium, and higher SES based on the distribution in our study population.

2.6. Statistical analyses

We first updated the original categorization of child temperament for our study population. Therefore, exploratory factor analysis of the original 97 Carey Temperament items was conducted with an orthogonal varimax rotation. We used the eigenvalues greater than one convention and parallel analysis to help determine the number of factors to retain (Zwick and Velicer, 1986). Additionally, we placed a large emphasis on the interpretability of factors and removed factors with <3 items with loadings of at least 0.40. Factors were standardized (mean = 0; standard deviation = 1). EFA analyses were conducted using the psych package in R (Revelle, 2022).

Next, we examined descriptive characteristics of the sample, assessed the distribution of all exposure measures, and explored correlations between measures using Pearson correlation coefficients. We examined all exposures and outcomes for implausible values and removed any that fell outside the normal ranges for each specific measure. We report linear regression model coefficients (β) and 95% confidence intervals (CI) for associations between the individual prenatal exposures and the identified temperament factors. Linear regression assumptions were assessed in all models. For the individual exposure analyses, all exposures were standardized, and results are reported per interquartile range (IQR) increase in exposure.

2.7. Mixture analyses

In addition to examining impacts of individual prenatal exposures on temperament factors, we also assessed the joint impact of the mixture of prenatal exposures. For mixtures analyses, we used quantile g-computation to assess joint impacts of both maternal psychological functioning and stress measures and also prenatal $PM_{2.5}$ exposure on the identified temperament factors (Keil et al., 2020). In quantile g-computation, the model estimates the effect of simultaneously increasing all components of the mixture by one quantile. First, exposures were transformed to quantile-based scores (i.e. 0 = exposure below the first quantile, 1 = exposure between the first and second quantile, etc.). Outcomes were then regressed on the quantized exposures in a generalized linear model (Keil et al., 2020). Using this approach, each exposure in the mixture is given a positive or negative weight. Positive and negative weights sum separately to 1.0 and can be interpreted as the relative contribution of each exposure to either the positive or negative partial effects (e.g. an exposure that is negatively associated with the outcome will receive a negative weight in proportion to how large the effect of that exposure is, relative to other exposures that are negatively associated with the outcome).

We assessed the impact of the mixture of exposures both for maternal psychological functioning measures alone, and in combination with prenatal $PM_{2.5}$ exposure. Quantile g-computation coefficients and 95% CI are reported for each separate identified temperament factor. These coefficients can be interpreted as the difference in each temperament outcome for a one-quartile simultaneous increase in all exposures.

In addition to the overall mixture models, we used an extension of quantile g-computation to assess effect modification (Keil, 2021; Stevens et al., 2022). We first assessed effect modification of the maternal psychological functioning mixture by $PM_{2.5}$ levels. We additionally assessed whether the overall mixture (including $PM_{2.5}$) varies by maternal SES. For these analyses we collapsed the medium/high SES category to examine the impacts of low SES vs medium/higher SES groups. Finally, we assessed differences by child sex. From these models we were able to evaluate the product terms and report associations between the mixture and temperament factors by level of SES and sex.

3. Results

3.1. Study population

Table 1 shows descriptive characteristics of the 382 mother-child pairs included in the current analysis. Mothers in the study population were primarily low SES (56%) and had less than a high school education at study enrollment (43%). Mothers were on average 27.8 years at delivery. There was an approximately equal distribution of male and female children in the study population (52% males). Children were on average 2.0 years old at the temperament assessment study visit. We observed positive correlations between the prenatal psychological functioning measures; correlations ranged from 0.24 to 0.63 (Supplemental fig. 1).

3.2. Exploratory factor analysis

Based on our criteria, we retained three factors from the original 97 Carey Temperament items that had at least three items with factor loadings of at least 0.40 and were interpretable. No items had cross-loadings. Factor 1 was composed of 11 items (Table 2) largely related to the child's ability to regulate their behavior emotion, and cognition (Table 3, Supplemental table 2). Items on Factor 2 related to speaking with unfamilia r adults and acting acceptingly with strangers at home. Finally, Factor 3 included items involving feelings of sadness, discomfort, frustration, fear, and difficulty being soothed. Throughout this

Table 1
Characteristics of included mother-child pairs from the PROGRESS cohort (n = 382).

	N (%) or mean (SD)
Child sex	
Male	198 (52.0)
Female	184 (48.0)
Maternal age at delivery (years)	27.8 (5.7)
Maternal socioeconomic status	
Lower	214 (56.0)
Medium	131 (34.3)
Higher	37 (9.7)
Maternal education	
<High school	163 (42.7)
Some high school or HS graduate	133 (34.8)
>High school	86 (22.5)
Maternal pregnancy average $PM_{2.5}$ ($\mu g/m^3$)	22.8 (3.0)
Maternal psychological functioning	
Depressive symptoms	8.21 (5.6)
Negative life events	3.28 (2.1)
Pregnancy-specific anxiety	19.0 (5.6)
Perceived stress	5.19 (2.8)

Abbreviations: $PM_{2.5,}$ particulate matter <2.5 μm; PROGRESS, Programming Research.
in Obesity, GRowth, Environment and Social Stress; SD, standard deviation.

Table 2
Factor loadings from exploratory factor analysis with a varimax rotation.

	Factor 1 (Effortful control)	Factor 2 (Extraversion)	Factor 3 (Negative affect)
V6	0.44		
V13	0.43		
V15	0.51		
V31	0.40		
V41	0.48		
V43	0.41		
V60	0.42		
V62	0.48		
V64	0.42		
V66	0.49		
V79	0.47		
V4		0.42	
V26		0.63	
V38		0.68	
V45		0.73	
V57		0.63	
V76		0.68	
V96		0.46	
V14			0.59
V29			0.58
V37			0.46
V46			0.50
V50			0.42
V78			0.40
V84			0.41

paper we use "*effortful control*" to describe Factor 1, "*extraversion*" to describe Factor 2, and "*negative affect*" to describe Factor 3 (Rothbart, 1982; Linde et al., 2013) (Table 3).

Higher scores on the effortful control and extraversion factors are considered adaptive, whereas lower scores on the negative affect factor are considered adaptive. We observed negative correlations between the effortful control factor and each of the maternal psychological functioning measures. The negative affect factor was positively correlated with several of the maternal measures, including NLE (0.18) (Supplemental fig. 1).

3.3. Independent exposure models

We first assessed impacts of prenatal maternal exposures on childhood temperament factors in independent exposure models (Fig. 1, Supplemental table 3). For Factor 1, IQR increases in each of the maternal psychological functioning measures (modeled independently) were related to lower effortful control scores, particularly for maternal depressive symptoms (ß: 0.34, 95% CI: 0.47, −0.22) and perceived stress (ß: 0.36, −0.49, −0.23) (Fig. 1). Overall, there were no observed associations with any of the prenatal measures and extraversion scores (Factor 2).

Table 3
Description of main temperament factors identified from exploratory factor analysis of the individual Carey items.

Factor	Description	Example items
Factor 1 Effortful control	The ability of the child to regulate behavior, emotion, and cognition.	Plays continuously for 10 min with their favorite toy; Returns to the same activity after a brief interruption.
Factor 2 Extraversion	Characterized by high activity level, high-intensity pleasure seeking, low shyness, and impulsivity.	Speaks or vocalizes immediately with unfamiliar adults; Reacts acceptingly when approached by strangers at home.
Factor 3 Negative affect	Items dealing with feelings of sadness, discomfort, frustration, fear, and difficulty to soothe	Shows a strong reaction to failure (crying, kicking); Responds intensely to frustration (cries, yells, throws tantrums)

For Factor 3, higher prenatal maternal NLE (ß: 0.22, 95% CI: 0.09, 0.35), pregnancy-specific anxiety (ß: 0.20, 95% CI: 0.04, 0.35), and perceived stress (ß: 0.16, 95% CI: 0.03, 0.29) were related to higher negative affect scores in the child (Fig. 1, Supplemental table 3). We observed differences in the association between maternal prenatal anxiety and negative affect scores by sex, with associations seen in girls (ß: 0.35, 95% CI: 0.13, 0.57) but not boys (ß: 0.01, 95% CI: 0.21, 0.23) (p-int = 0.02) (Supplemental table 3). There were no other significant differences by sex (Supplemental table 3). Finally, we observed associations between first trimester $PM_{2.5}$ exposure and higher negative affect scores in the child (ß: 0.22, 95% CI: 0.03, 0.42) (Fig. 1, Supplemental table 3).

3.4. Mixtures analyses

Based on quantile g-computation, a one quartile (i.e. the joint association) increase in the prenatal maternal psychological functioning mixture was inversely associated with effortful control scores (−0.32, 95% CI: 0.44, −0.21) (Table 4). Results were similar when assessing the joint association with the psychological functioning mixture and $PM_{2.5}$ (−0.27, 95% CI: 0.44, −0.08), though were attenuated in magnitude. For the effortful control factor, perceived stress and depressive symptoms were assigned the largest negative weights, indicating that they were negatively associated with effortful control scores (Supplemental table 4).

For the negative affect factor, a one quartile increase in the prenatal maternal psychological functioning mixture was associated with higher negative affect scores (0.22, 95% CI: 0.11, 0.34). The magnitude of the association increased when adding $PM_{2.5}$ to the mixture (0.34, 95% CI: 0.16, 0.53) (Table 4). For Factor 3, maternal perceived stress and negative life events were assigned the largest positive weights, indicating they were positively associated with negative affect scores (Supplemental table 4).

There were no observed associations with the prenatal mixture and the extraversion factor (Factor 2) (Table 4). For this factor, negative life events, anxiety, and depressive symptoms were assigned positive weights, while $PM_{2.5}$ and perceived stress were assigned negative weights (Supplemental table 4).

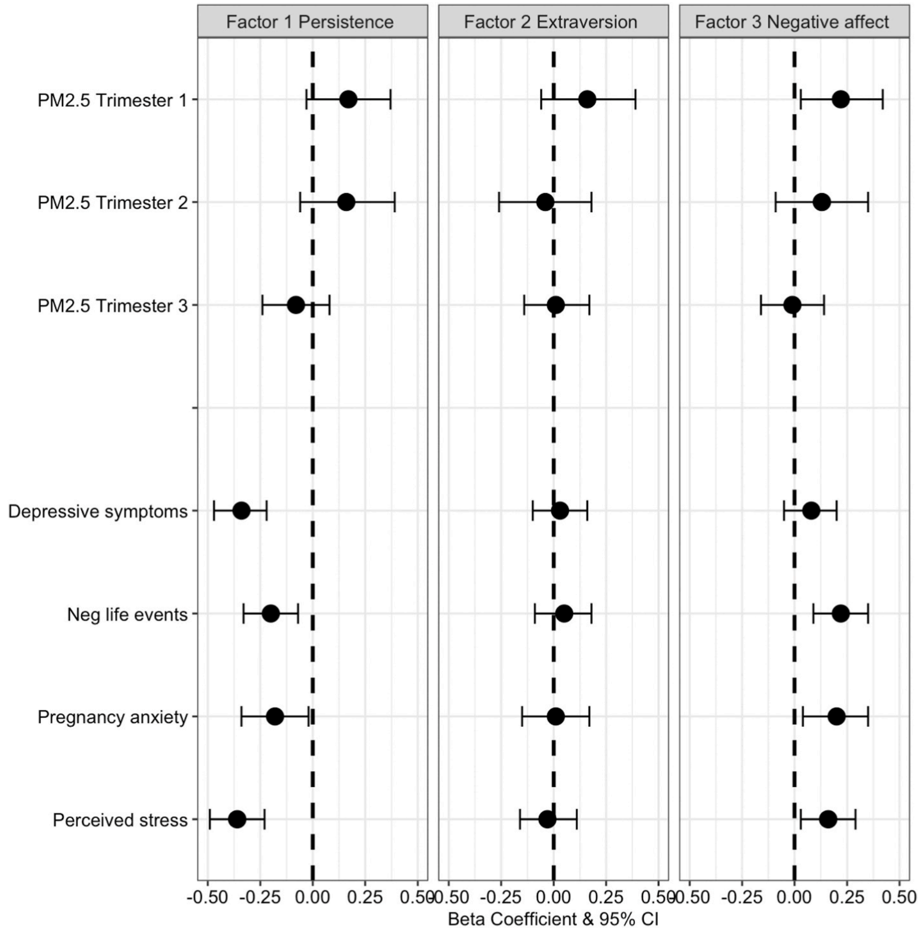

Fig. 1. Beta coefficients and 95% confidence intervals for associations between prenatal $PM_{2.5}$, maternal stressors, and temperament factor scores. Results are shown per interquartile increase (IQR) in each exposure. Models are adjusted for maternal age, SES, education, child sex, and child age.

Table 4
Quantile g-computation estimates and 95% confidence intervals for the change in temperament scores for a one quantile increase in the prenatal mixture.[a]

	Factor 1 Effortful control Beta (95% CI)	Factor 2 Extraversion Beta (95% CI)	Factor 3 Negative affect Beta (95% CI)
Prenatal maternal stress mixture[b]	−0.32 (−0.44, −0.21)	0.02 (−0.10, 0.14)	0.22 (0.11, 0.34)
Stress mixture + prenatal $PM_{2.5}$ [c]	−0.27 (−0.44, −0.08)	−0.04 (−0.23, 0.15)	0.34 (0.16, 0.53)

Abbreviations: CI, confidence interval; $PM_{2.5,}$ particulate matter <2.5 μm.
[a] Beta estimates are interpreted as the effect on temperament factor scores when increasing every exposure in the mixture by one quantile. All models are adjusted for maternal age, SES, education, child sex, and child age.
[b] Includes maternal depressive symptoms, negative life events, pregnancy-specific anxiety, and perceived stress.
[c] Additionally includes each trimester-specific $PM_{2.5}$ average. Models are additionally adjusted for season of birth.

3.5. *Modification by child sex and maternal SES*

Next, we used an extension of quantile g-computation to assess effect modification of the prenatal mixture by child sex and maternal SES. For these analyses we included trimester specific $PM_{2.5}$ averages in the prenatal maternal psychological functioning mixture. We observed differences in effortful control scores by child sex. A one quartile increase in the prenatal mixture was associated with lower effortful scores for males (−0.47, 95% CI: 0.72, −0.23), but not females (−0.06, 95% CI: 0.32, 0.20) (*p-int* 0.02) (Supplemental table 5). There were no other significant differences by sex (Supplemental table 5).

We observed significant differences by maternal SES for child effortful control and negative affect score temperament outcomes. Specifically, we observed associations between the mixture and lower effortful control scores in children in low (−0.45, 95% CI: 0.70, −0.20) but not high (−0.06 95% CI: 0.32, 0.21) SES families (*p-int*: 0.03) (Fig. 2, Supplemental table 6). Additionally, a one quartile increase in the prenatal mixture was associated with higher negative affect scores for children of low (0.60, 95% CI: 0.35, 0.85), but not high SES (0.09, 95% CI: 0.17, 0.36) families (*p-int* 0.01) (Fig. 2, Supplemental table 6).

4. Discussion

In the current study, we examined the association between maternal prenatal stress, psychological functioning, and air pollution on child temperament at age 2 in a longitudinal birth cohort in Mexico City. We found that higher levels of $PM_{2.5}$ and several of the maternal psychological functioning measures were related to both effortful control and negative affect levels in the child, both individually and as a mixture. We also observed modification of these associations by maternal SES, with associations seen only among low SES participants. Overall, we did not observe any associations with the extraversion factor.

To assess temperament, we used the Carey TTS, which consists of nine temperament dimensions (Chess et al., 1963). However, factor analyses of the TTS have often failed to confirm its hypothesized structure (De Pauw, 2017). Importantly, the original nine temperament constructs were derived from intensive observations of a very small

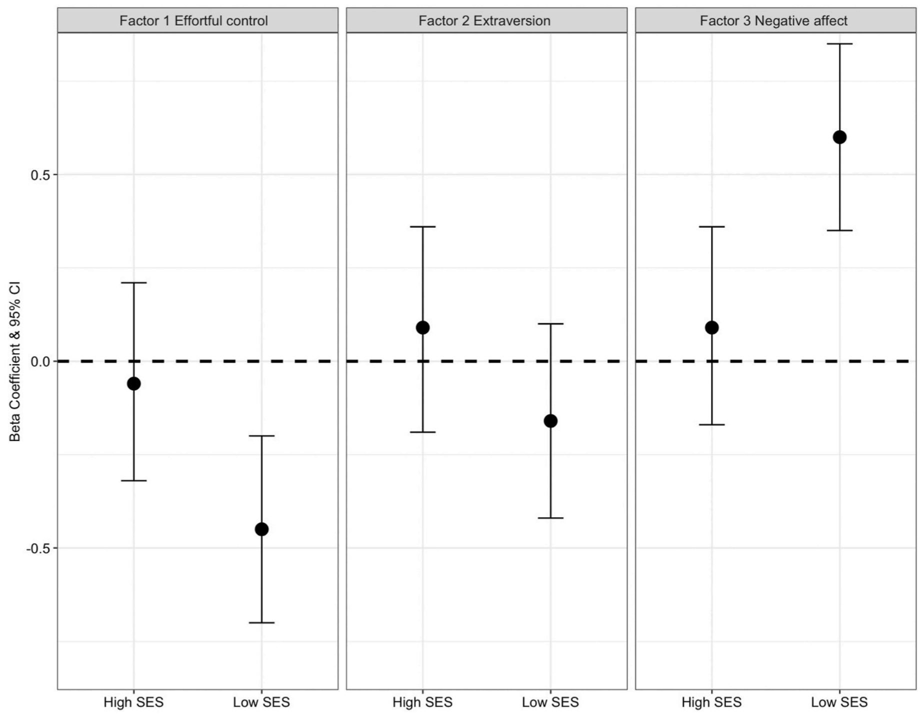

Fig. 2. Quantile g-computation estimates and 95% confidence intervals for the change in temperament scores for a one quantile increase in the prenatal mixture. Results are stratified by maternal SES. Models are adjusted for maternal age, education, child sex, and child age.

sample of primarily higher income, well-educated, white families in the New York area. Evidence suggests that the factor structure of temperament scales may be influenced by cultural factors (Bosquet Enlow et al., 2016) – thus it should not be assumed that the factor structure of the TTS is the same in the current study population as in samples from very different populations. We identified a 3-item factor structure including measures relating to effortful control, extraversion, and negative affect. Importantly, our 3-factor structure aligns closely with Rothbart's biologically based theory of temperament, which also includes three factors – effortful control, surgency, and negative affect (Rothbart et al., 2000). This approach to characterizing temperament, particularly negative affect, have been widely used in several recent epidemiologic studies (Brunst et al., 2014; Cowell et al., 2021; Kopala-Sibley et al., 2016). Characterizing individual differences in early life temperament is important as temperament has been found to be stable over time and predicts later psychopathology in adolescence and adulthood (De Pauw and Mervielde, 2010; Nigg, 2006; Olino et al., 2022).

Our finding of individual impacts of maternal psychological functioning and stress during pregnancy on child temperament is consistent with several recent studies (Takegata et al., 2021). Our most consistent findings in individual models were for maternal prenatal NLE, pregnancy anxiety, and perceived stress in relation to lower effortful control scores and higher negative affect scores in the child. Though findings have been mixed for several other prenatal measures, there have been consistent impacts of pregnancy-specific anxiety on child temperament outcomes (Erickson et al., 2017). Additionally, while some previous studies have found impacts of maternal depressive symptoms on child negative affectivity (Davis et al., 2007; Gustafsson et al., 2018), we did not observe this finding in our study population. We additionally observed an independent association between prenatal air pollution exposure and higher negative affect scores in the child. Few studies have assessed the impact of prenatal air pollution exposure on child temperament outcomes, though one recent study found an impact between higher $PM_{2.5}$ exposure during different prenatal time windows and higher negative affect scores in infants (Rahman et al., 2022).

An accumulating body of literature points to the potential combined effect of chemical and non-chemical stressors on child health outcomes (Barrett and Padula, 2019; Cowell and Wright, 2017). Several studies have investigated this research question, though the most common approach has been to assess the modifying effect of the stressor(s) by reporting stratified estimates. Few studies have investigated the combined impacts of both chemical and psychological stressors in the same mixture – or what the effect would be by simultaneously increasing every exposure in the mixture by one unit. More recently, studies have started to extend mixture modeling approaches used in environmental epidemiology to also include non-chemical stressor exposures (Eick et al., 2023). In order to comprehensively assess the combined impacts of air pollution and non-chemical stressors we used mixture modeling approaches and found an association between the mixture of exposures and both lower effortful control scores and higher negative affectivity in the child.

One important finding from our study was that we observed a significant interaction for the mixture and negative affect outcomes by maternal SES. This is in line with the theory that individuals are often simultaneously exposed to both higher levels of psychosocial stressors and environmental exposures, especially for lower SES populations (Morello-Frosch and Shenassa, 2006). This is particularly true for air pollution, as lower SES individuals are often disproportionately burdened and exposed to both higher levels of air pollution and psychosocial stress compared to higher SES individuals (Hajat et al., 2015; O'Neill et al., 2003). While studies have assessed the modifying impacts of stress on air pollution-health associations, few have examined the joint exposure of these stressors, or if this mixture differs by SES.

Studying the joint impact of air pollution and non-chemical stressors simultaneously is important since several of these exposures likely impact similar biologic pathways. The brain is rapidly developing during early life and several critical processes occur during these time points, including neuron formation and migration, synapse formation and pruning, generation of glial cells, and myelination (Rice and Barone, 2000). Disruptions of these critical processes during vulnerable periods could alter normal brain development (Marco et al., 2011; Paus et al., 2008). One potentially important pathway includes activation of the hypothalamic pituitary adrenal (HPA) axis and its role in the body's response to stress. Once activated, the HPA axis releases stress hormones (i.e. cortisol), which are known to have an important role in the regulation of mood (Ardayfio and Kim, 2006). Exposures, particularly during critical windows of susceptibility, may act as stressors on the body, activating the HPA axis (Henriquez et al., 2018), resulting in the release of stress hormones that impact the central nervous system. Previous studies have shown impacts between both air pollution (Thomson, 2019) and psychosocial stress (Gutteling et al., 2005) on cortisol outcomes. Future work in the PROGRESS cohort will examine this mediating impact between prenatal air pollution, stress, and behavioral and later life mental health outcomes.

Our study is not without limitations. First, our measure of child temperament was parent-reported. Though maternal characteristics may influence mothers' report of their child's temperament, studies have found this to be minimal and in particular that maternal psychopathology does not systematically bias reports of child temperament (Olino et al., 2020). While all psychological functioning and stress measures were validated in native Spanish speakers, these measures were not always validated in Mexican populations, and we acknowledge this limitation. We did not have personal air pollution measures but note that the area level measure used in the current study may help to remove confounding by personal-level factors (Weisskopf and Webster, 2017). We assessed the individual and combined impacts of the prenatal stressors on the three identified temperament outcomes. Given the different statistical models, we emphasize results that were robust across several modeling approaches rather than relying solely on statistical significance testing. We adjusted for several key covariates; however, we note the possibility for residual confounding. Finally, we collapsed SES categories in modification analyses to characterize low vs. higher SES. By doing this we may be losing variability in SES levels and acknowledge this as a limitation. These limitations should be weighed against the study's strengths. We used mother and child data from a large, prospective birth cohort in Mexico City. We used several validated assessments to measure maternal psychosocial stress and psychological functioning including the PSS and EPDS. Our study additionally made use of a state-of-the-art validated air pollution model, allowing us to examine the impacts of both chemical and non-chemical stressors during the prenatal period. This approach of assessing the impacts of both air pollution and non-chemical exposures is important as individuals are often simultaneously exposed to both types of stressors. We additionally assessed the modifying role of SES, which is critical as there are often differences in associations and inequalities by SES.

5. Conclusions

In conclusion, in the current analysis we observed both individual and combined impacts of several of the prenatal stressors on child temperament, particularly for effortful control and negative affect. These findings have important public health implications as temperament is relatively stable and is a well-established risk factor for the development of psychopathology in adolescence and adulthood, thus pointing to potential intervention opportunities earlier in life.

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CRediT authorship contribution statement

Laura A. McGuinn: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Daniel N. Klein:** Conceptualization, Methodology, Supervision, Writing – review & editing. **Iván Gutiérrez-Avila:** Data curation, Methodology, Writing – review & editing. **Alexander P. Keil:** Data curation, Methodology, Writing – review & editing. **Marcela Tamayo-Ortiz:** Data curation, Investigation, Methodology, Supervision, Writing – review & editing. **Allan Just:** Data curation, Methodology, Supervision, Writing – review & editing. **Brent Coull:** Investigation, Methodology, Supervision, Visualization, Writing – review & editing. **Mariana Torres-Calapiz:** Data curation, Resources, Writing – review & editing. **Itai Kloog:** Data curation, Investigation, Methodology, Supervision, Writing – review & editing. **Martha Maria Téllez-Rojo:** Data curation, Funding acquisition, Investigation, Project administration, Resources, Supervision, Writing – review & editing. **Rosalind J. Wright:** Writing – review & editing. **Robert O. Wright:** Data curation, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envres.2024.118432.

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