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Early life stress, prenatal secondhand smoke exposure, and the development of internalizing symptoms across childhood

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Abstract

Background Prior findings relating secondhand tobacco smoke (SHS) exposure and internalizing problems, characterized by heightened anxiety and depression symptoms, have been equivocal; effects of SHS on neurodevelopment may depend on the presence of other neurotoxicants. Early life stress (ELS) is a known risk factor for internalizing symptoms and is also often concurrent with SHS exposure. To date the interactive effects of ELS and SHS on children's internalizing symptoms are unknown. We hypothesize that children with higher exposure to both prenatal SHS and ELS will have the most internalizing symptoms during the preschool period and the slowest reductions in symptoms over time.

Methods The present study leveraged a prospective, longitudinal birth cohort of 564 Black and Latinx mothers and their children, recruited between 1998 and 2006. Cotinine extracted from cord and maternal blood at birth served as a biomarker of prenatal SHS exposure. Parent-reported Child Behavior Checklist (CBCL) scores were examined at four timepoints between preschool and eleven years-old. ELS exposure was measured as a composite of six domains of maternal stress reported at child age five. Latent growth models examined associations between SHS, ELS, and their interaction term with trajectories of children's internalizing symptoms. In follow-up analyses, weighted quintile sum regression examined contributions of components of the ELS mixture to children's internalizing symptoms at each time point.

Results ELS interacted with SHS exposure such that higher levels of ELS and SHS exposure were associated with more internalizing symptoms during the preschool period ($\beta = 0.14$, $p = 0.03$). The interaction between ELS and SHS was also associated with a less negative rate of change in internalizing symptoms over time (β=-0.02, $p = 0.01$). Weighted quintile sum regression revealed significant contributions of maternal demoralization and other components of the stress mixture to children's internalizing problems at each age point (e.g., age 11 WQS $\beta = 0.26$, $p < 0.01$).

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Conclusions Our results suggest that prior inconsistencies in studies of SHS on behavior may derive from unmeasured factors that also influence behavior and co-occur with exposure, specifically maternal stress during children's early life. Findings point to modifiable targets for personalized prevention.

Keywords Secondhand Tobacco smoke, Early life stress, Internalizing problems, Child Development

Background

Although the last 50 years has seen tremendous progress towards reducing smoking among American adults [1], 13% remain active smokers [2]. Further, 11 states have no public smoking laws [3], leaving roughly 58 million non-smoking Americans exposed to secondhand, or environmental, tobacco smoke (SHS; [4]). As a result of structural racism and environmental injustice, relative to White women, Black women are disproportionately exposed to SHS [5] leading to disproportionate exposure during pregnancy. Specifically, in the workplace and public settings, Black Americans are disproportionately exposed to SHS compared to their white counterparts [6]; in private settings, such as homes and vehicles, Black individuals are also exposed to SHS at higher rates than white individuals [7, 8]. Such prenatal SHS exposure has wide reaching impacts on children's later behavior and health [1, 9].

Equivocal evidence links prenatal SHS with internalizing symptoms. Some studies report strong associations between prenatal SHS and child internalizing problems, characterized by heightened anxiety and depression symptoms [10–12]; however, other studies do not [13–16]. Recent advances in environmental epidemiology highlight the importance of examining the combined effects of multiple chemical or social exposures that act as neurotoxicants, or co-exposures [17], given that people are rarely exposed to one neurotoxicant at a time [18]. Early life stress (ELS), consisting of parental stressors and adversities shared by both parents and children, have been shown to act as neurotoxicants [19–21]. Parental adversity and psychological distress are among the most robust and well-replicated risk factors for child psychopathology and mental health symptoms [22–24]. The mechanisms driving associations between maternal stress and child mental health symptoms are diverse and intersecting. For example, maternal stress can influence parenting style [25–27], early attachment and bonding [28, 29], and family processes, such as stress, cooperative caregiving, and home environment [30–32]. Intergenerational transmission of mental health symptoms may also be biological, with emerging evidence suggesting genetic, epigenetic, and physiological (e.g., oxytocin, immune, etc.) mechanisms underlying offspring vulnerability to psychiatric disorders [33–35]. Together, these findings highlight the importance of understanding the influence of maternal stress and shared adversities on children's internalizing symptoms. In order to clarify prior conflicting findings in studies examining associations between ETS exposure and children's internalizing symptoms, we examine if maternal stress during children's early life compounds or is compounded by *prenatal* SHS exposure.

Given that maternal stress during children's early life is a known risk factor for internalizing symptoms [35], we propose that it may serve as a critical effect modifier in associations between SHS and internalizing symptoms. Moreover, SHS and stress commonly co-occur [36], which can be understood theoretically through the stress process perspective [37] and empirically through the high rates of co-occurrence of parental stressors, nicotine dependence, and child maltreatment [36, 38, 39]. Shared and cascading effects of SHS and parental adversity (e.g., parental perceived stress, psychological distress, economic hardship, intimate partner violence, maternal demoralization, neighborhood quality, and lack of social support) on children's wellbeing may also operate through shared neurobiological targets or synergistic effects on brain function [40, 41]. For example, animal models document that prenatal nicotine exposure combined with stress associated with maternal separation from pups during early infancy causes increased time spent immobile during a forced swim test, reflecting depressive-like behavior and anhedonia [42]. These exposures were also associated with an increased number of neurons in the amygdala and a decreased number of neurons in the ventral tegmental area, pointing to a possible neural mechanism by which co-exposure results in greater internalizing behaviors [42]. Although the effects of combined exposure to SHS and stress on mental health in humans have not yet been examined, their interaction has been linked with increased cognitive problems [43]. In addition to static effects on behavior, exposures may influence trajectories of development. Prior findings indicate relative stability or decreases in internalizing symptoms amongst community samples of youth before age 12 and then sharp increases into adolescence, particularly among girls [44–47]. Notably, these trajectories are shaped by stress, with maternal stress and psychopathology strongly associated with elevations in internalizing symptoms [44, 46–48]. Critically, studies reporting effects of prenatal SHS on internalizing symptoms have not examined longitudinal change in these symptoms over time [10–12]. How the combined effects of SHS and maternal stress during children's early life may influence

the trajectory of internalizing symptoms remains an important and understudied area.

The current study sought to address these gaps in knowledge by examining how combined exposure to prenatal SHS and maternal stress during children's early life increases internalizing symptoms and influences development in a prospective birth cohort of non-smoking Black and Latinx mothers and their children (N=482). Given prior findings from animal models and human epidemiologic studies, we hypothesized that prenatal exposure to SHS combined with maternal stress during children's early life would result in elevated internalizing symptoms in youth that would remain present over time.

Methods

Participants

Detailed demographic and recruitment information regarding the *Columbia Center for Children's Environmental Health (CCCEH)* Mothers and Newborns prospective birth cohort have been previously published [49]. To briefly summarize, Black and Latinx women residing in Washington Heights, Harlem, or the South Bronx in New York City (NYC) were recruited between 1998 and 2006 through local prenatal care clinics. Recruited women were non-users of tobacco products or illicit drugs, between the ages of 18 and 35 years, and free of diabetes, hypertension, or known HIV, and had initiated prenatal care by the 20th week of pregnancy. The full cohort included data from 727 mother-child dyads. Of the 727 dyads enrolled in the Mothers and Newborns cohort, 564 had available data for all predictors of interest (i.e., SHS, ELS, sex, maternal years of education, and birthweight) and so were included in the current analyses (Fig. 1). This study was approved by the Institutional Review Board of Columbia University, and mothers provided informed consent for themselves and their children at every study visit. Children provided assent beginning at age 7.

Study Timeline

Longitudinal study visits began in the third trimester and occurred approximately every two years thereafter for each child in the cohort. Prenatal exposure to SHS was measured by cotinine in either maternal blood or cord blood samples taken at birth [50]. The current study leverages behavioral data collected during four visits: preschool age (age range: 22–68 months; mean age=42.85 months), age 5 (age range: 4–6 years; mean age=4.43

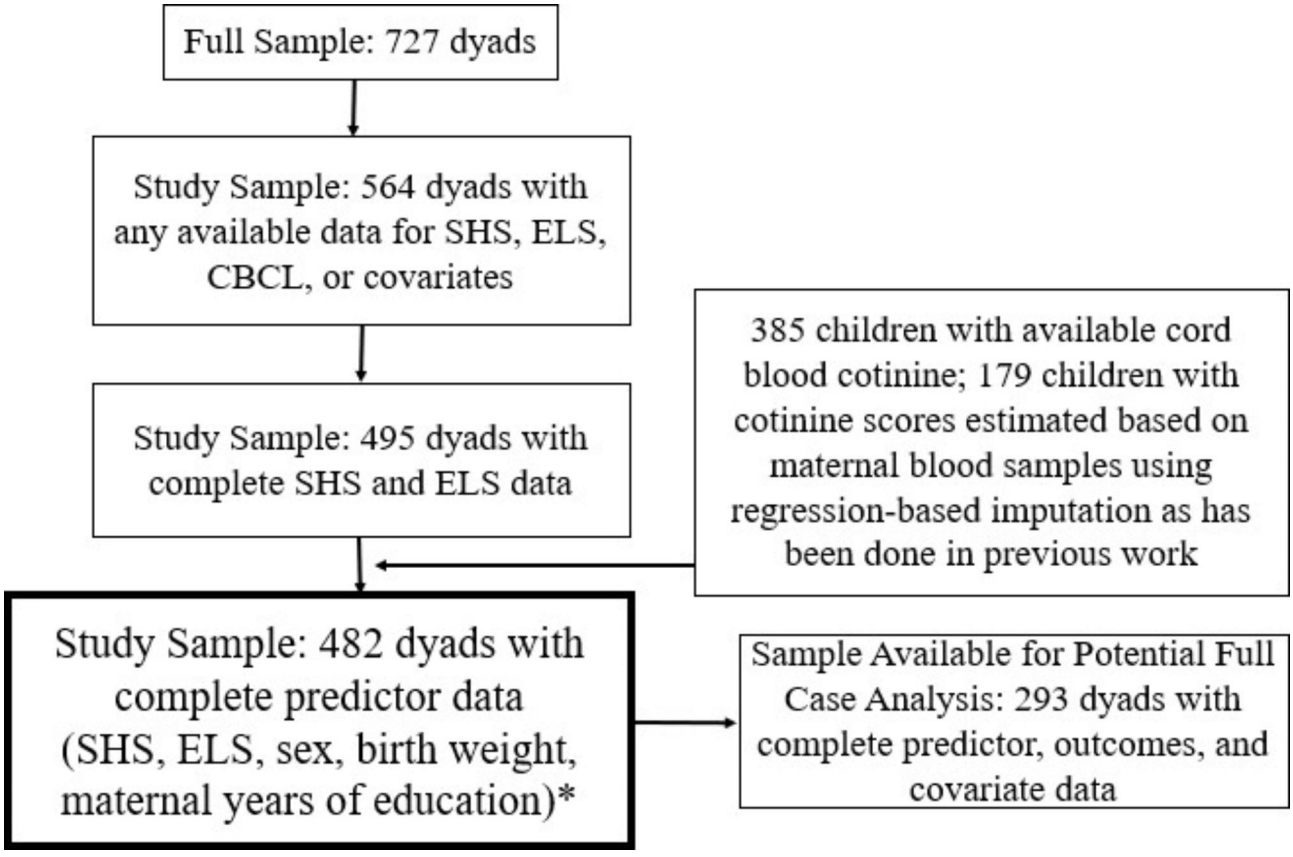

Fig. 1 Flow Chart of Participant Inclusion. *Latent growth models described in results analyzed data from 482 participants with complete predictor data. WQS analyzed all available outcome data at each timepoint as described in Table 1

Table 1 Demographic characteristics of participants at each study visit

	Preschool	Age 5	Age 7	Age 9	Age 11	Total	Full Case Analysis
N	505	513	479	445	362	564	299
Mean age (SD)	3.25 (0.99)	4.43 (0.50)	6.52 (0.51)	8.52 (0.51)	10.56 (0.58)	-	-
Sex (% male)	238 (47.13)	244 (47.56)	226 (47.18)	207 (46.52)	165 (45.58)	272 (48)	130 (43.48)
Maternal years of education at prenatal visit (SD)	11.89 (2.18)	11.9 (2.16)	11.87 (2.14)	11.89 (2.13)	11.96 (1.95)	11.89 (2.16)	11.94 (1.83)
Child birthweight in grams (SD)	3376 (469.44)	3379 (469.17)	3388 (479.98)	3371 (481.84)	3398 (481.07)	3371 (474.10)	3371 (477.99)
Early life stress composite score	0.30 (0.12)	0.30 (0.12)	0.30 (0.12)	0.30 (0.12)	0.30 (0.13)	0.30 (0.12)	0.30 (0.12)
Cotinine[a]	-2.82 (1.65)	-2.82 (1.67)	-2.86 (1.60)	-2.84 (1.57)	-2.71 (1.61)	-2.81 (1.69)	-2.70 (1.66)
Latinx (%)	315 (62)	317 (62)	296 (62)	272 (61)	227 (63)	355 (63)	183 (61)
Black (%)	190 (38)	196 (38)	183 (38)	173 (39)	135 (37)	209 (37)	116 (39)

[a]. Z-scaled natural logarithm of prenatal cotinine exposure measured in maternal blood or cord blood samples taken at birth

years), age 7 (age range: 6–8 years; mean age = 6.52 years), age 9 (age range: 8–10 years; mean age = 8.52 years), and age 11 (age range: 10–13 years; mean age = 10.56 years). Measures of children's socioemotional functioning were collected during children's preschool (3–5 years), age 7, age 9, and age 11 year visits; ELS was measured at a separate children's age 5 year study visit.

Measures

Children's Socioemotional Functioning

Children's behavior problems were measured via parent report on the Child Behavior Checklist ([51]; CBCL). We used the CBCL 1.5-5, a 100-item measure for children ages 1.5 to 5 years old which includes Emotionally Reactive, Anxious/Depressed, Somatic Complaints, Withdrawn, Sleep Problems, Attention Problems, and Aggressive Behavior subscales and the CBCL 6–18, a 113-item scale which includes Anxious/Depressed, Withdrawn/Depressed, Somatic Complaints, Social Problems, Thought problems, Attention Problems, Rule-Breaking Behavior, Aggressive Behavior subscales. The internalizing problems summary composite score for the CBCL 1.5-5 encompasses responses from the Emotionally Reactive, Anxious/Depressed, Somatic Complaints, and Withdrawn subscales. The internalizing problems summary composite score for CBCL 6–18 encompasses responses from Anxious/Depressed, Withdrawn/Depressed, and Somatic Complaints syndrome scales. Mothers were administered the CBCL age 1–5 at the child's preschool visit and the CBCL 6–18 for children's age seven, nine, and eleven visits.

Maternal stress during children's early life

At child age 5, mothers completed a structured interview with a trained research assistant assessing demographics and six domains of early life stress exposure. These measures assess maternal experiences of stress during the child's early life; as such, we refer to them as early life stress (ELS) because they reflect the shared experience of stress between mother and child. Items were aggregated across domains of stress exposure to create a single composite score, as has been done in previous work [52]. Items included in the composite score were extracted from several published scales examining past year material hardship [53], past month maternal perceived stress [54], intimate partner violence experienced during the child's lifetime [55], lack of current social support [56, 57], current neighborhood quality [58–60], and past year nonspecific maternal distress or demoralization (Supplementary Methods; [61]). Independently, these scales demonstrate good reliability and psychometric properties [54, 57, 62–64]. All item responses were rescaled to 0–1 for the current analysis with higher scores indicating more stress exposure. Responses were averaged within each of the six domains, and then averaged across domains to create the composite score (range = 0–1, Mean = 0.30, Supplementary Fig. 1). This age 5 ELS composite score is used in all primary analyses described below. Because some CBCL preschool measures were taken at child age 3 (before the age 5 ELS measures were acquired) we generated an abbreviated stress composite consisting of measures of material hardship, maternal stress, and maternal demoralization, as these were the only measures available at age 3. We use this age 3 abbreviated ELS score to examine the correlation between age 3 and age 5 ELS and justify our use of age 5 ELS, even though some children were seen for CBCL slightly prior to when ELS was measured at age 5 (Supplementary Results; Supplementary Fig. 2).

Secondhand Tobacco smoke exposure

Cord blood samples were used whenever available (N = 500). If a cord blood sample was not available then SHS exposure was estimated using maternal blood samples (N = 197). Reported maternal smoking during pregnancy was exclusionary for enrollment in the cohort. Children born with cotinine concentrations in their cord blood above 25 ng/ml (N = 6) were excluded from this

analysis because they were likely exposed to active smoking during gestation [50]. Cotinine values were positively skewed and so the natural logarithm of prenatal cotinine was z-scaled before use in the models described below.

Analytic Plan

We estimated a latent growth model of children's internalizing symptoms assessed from preschool to age eleven years-old using the growth function of the lavaan package in R studio version 4.1.1 [65, 66]. Of note, latent growth curve models are distinct from latent class models and use the continuous effects of all predictors on the continuous, data-derived outcomes, namely the intercept and slope scores. Intervals between slope loadings were scaled to reflect the intervals (i.e., years) between study visits. Full information maximum likelihood estimation was used to address missing CBCL data. Model fit was assessed using root mean square error of approximation (RMSEA), comparative fit index (CFI), and the standardized root mean square residual (SRMR), as these are recommended for smaller sample sizes (N<500 [67, 68]). The RMSEA should be close to zero with a significance value>0.05 [69, 70], CFI>0.90 [71, 72], SRMR<0.08 [73]).

Prenatal cotinine, early life stress, and their interaction were included in latent growth models to examine our hypothesis that the SHS*ELS interaction would be associated with increases in children's internalizing symptoms and which would remain present over time. To control for potential confounding, we included as covariates the following variables which are known to be associated with SHS and ELS exposure: birthweight [74], child sex at birth [75, 76], and maternal years of education (e.g., [77]) measured at the prenatal visit in all analyses. Cotinine, ELS, birth weight, and years of education were z-scaled. CBCL internalizing T-scores were standardized using a grand mean and standard deviation derived by pooling across all time points. The SHS*ELS interaction term was calculated by multiplying the standardized SHS and ELS scores for each participant. Sensitivity analyses including maternal self-reported alcohol use were conducted (Supplementary Results, Table S4).

To explore effects of the individual components of the ELS composite while controlling for effects of SHS, weighted quantile sum (WQS) regression estimated associations between co-exposure to the six correlated measures of postnatal ELS and children's internalizing scores at each time point, controlling for sex, birth weight, maternal years of education, and cotinine. Separate WQS regressions were conducted for each age point and so leveraged all available data from participants with CBCL outcome data at each age point. The WQS index was constructed by summing the ranked concentrations (quintiles) of each individuals' exposures multiplied by the relative strength of each predictor variable's association with their internalizing scores. Importantly, WQS can determine the overall influence of the multiple early life stressors and identify the contribution of each of the individual stressors to the overall impact on internalizing symptoms [78, 79]. A higher WQS index reflects higher exposures to stress related to the outcome, while a lower WQS index indicates either lower exposures, or that the WQS index is unrelated to the outcome. Estimating the WQS index was performed across 100 bootstrap ensembles [79], thereby minimizing vulnerability to collinearity among predictors, and resulting WQS indices were tested in a traditional linear framework, as: $g(\mu) = \beta 0 + \beta 1 WQS + z'\phi$. $G(\mu)$ reflects an identity link function, given the continuous nature of the outcomes, $\beta 0$ reflects the model intercept, $\beta 1$ indicates the association between the WQS index and the outcome, and z' indicates a vector of covariates. All WQS models were tested using negative and positive constraints in order to examine the direction of the effect (either negative or positive) of the mixture components on the outcome. Sensitivity analyses were conducted to test the resolution of quantiling using tertiles and quartiles.

Results

Participants

Table 1 presents demographic information for the study sample. Mothers included in this study did not differ from those who did not have available data on age or maternal education. Black mothers were more likely than Latinx mothers to be missing maternal and/or cord blood samples ($\chi^2=5.24$, $p=0.02$; Table S1). Across the entire sample, unscaled ELS composite scores ranged from 0.07 to 1.20 (mean=0.4, SD=0.18). Full case analysis included 293 participants with complete data across all predictors, outcomes, and covariates (Fig. 1). Children included in the full case analysis were more likely to be female ($\chi^2=5.97$, $p=0.01$; Table S2).

Combined SHS and ELS exposure are associated with higher internalizing symptoms in preschool and over time

The latent growth model indicated excellent model fit (RMSEA=0.05, RMSEA p-value=0.38, CFI=0.96, SRMR=0.03; details in Supplementary Results). Interaction effects were observed such that children with higher SHS*ELS had higher internalizing problems scores during the preschool visit ($\beta=1.17$, SE=0.53, $p=0.03$) and a slower decrease in internalizing problems over time when compared with children with lower SHS*ELS scores (β=-0.16, SE=0.06, $p=0.01$). Significant main effects show a positive association between ELS and internalizing problems during the preschool visit ($\beta=0.22$, SE=0.06, $p<0.01$) and a negative association between SHS and the slope of internalizing problems (β=-0.05, SE=0.02,

Table 2 Latent Growth Curve Model Results

Variable	Intercept			Slope		
	Coefficient	z-value	p-value	Coefficient	z-value	p-value
Sex	0.07	0.58	0.56	-0.001	-0.07	0.95
Birth Weight	0.02	0.31	0.76	0.001	0.15	0.88
Years of Education	-0.05	-1.63	0.10	0.003	0.81	0.42
SHS	0.00	0.004	0.99	-0.001	-0.16	0.87
ELS	0.22	3.60	0.00	0.01	0.79	0.43
Interaction (SHS X ELS)	0.14	2.19	0.03	-0.02	-2.49	0.01
Overall Model	0.673	1.94	0.05	-0.057	-1.35	0.18

Note: SHS = Secondhand Smoke Exposure; ELS = Early Life Stress

Table 3 Weighted Quantile Sum Results

	Coefficient	t-value	p-value
Age 5			
WQS	0.27	5.40	> 0.001
Sex	-0.002	-0.02	0.98
Birth Weight	-0.08	-1.27	0.21
Years of Education	-0.05	-2.09	0.04
SHS	-0.04	-0.55	0.58
Age 7			
WQS	0.37	6.03	> 0.001
Sex	0.23	2.04	0.04
Birth Weight	0.08	1.33	0.19
Years of Education	-0.03	-1.03	0.31
SHS	-0.05	-0.79	0.43
Age 9			
WQS	0.17	2.66	0.008
Sex	0.03	0.26	0.80
Birth Weight	0.10	1.44	0.15
Years of Education	-0.02	-0.79	0.43
SHS	0.09	1.24	0.22
Age 11			
WQS	0.26	3.91	0.0001
Sex	-0.06	-0.41	0.68
Birth Weight	-0.04	-0.59	0.59
Years of Education	-0.05	-1.49	0.14
SHS	-0.08	-1.14	0.26

Note: WQS = weighted quantile sum mixture; SHS = Secondhand Smoke Exposure

$p = 0.04$). No other significant findings were observed (Table 2).

Specific components of ELS are associated with children's internalizing problems

WQS regression indicated that the weighted ELS index was positively associated with children's internalizing scores at all age points. At age 5, every quintile-increase in the exposure index, a 0.27 (95% confidence interval: 0.16, 0.40) increase in children's internalizing problems scores was detected ($p < 0.001$; Table 3). Maternal demoralization, intimate partner violence, and perceived stress particularly contributed to children's internalizing scores at age 5 (weight > 45%, 19%, 19% respectively; Table 4). The contribution maternal perceived social support, neighborhood quality, and material hardship to this association was negligible (weights ≤ 14%). Negative constraints yielded no significant results.

At age 7, every quintile-increase in the exposure index, a 0.44 (95% confidence interval: 0.32, 0.57) increase in children's internalizing problems scores was detected ($p < 0.001$; Table 3). Intimate partner violence, maternal demoralization, and perceived stress particularly contributed to children's internalizing scores at age 7 (weight > 45%, 18%, 18% respectively; Table 4). The contribution maternal perceived social support, neighborhood quality, and material hardship to this association was negligible (weights ≤ 10%). Negative constraints yielded no significant results.

At age 9, every quintile-increase in the exposure index, a 0.23 (95% confidence interval: 0.10, 0.37) increase in children's internalizing problems scores was detected ($p < 0.001$; Table 3). Maternal demoralization, intimate partner violence, and perceived stress particularly contributed to children's internalizing scores at age 9 (weight > 32%, 31%, 27% respectively; Table 4). The contribution maternal perceived social support, neighborhood quality, and material hardship to this association was negligible (weights ≤ 6%). Negative constraints yielded no significant results.

For every quintile-increase in the ELS exposure index, children's age 11 internalizing problems scores increased by 0.26 scaled T-score points (95% confidence interval: 0.12, 0.40; $p < 0.001$; Table 3), controlling for effects of SHS. Maternal demoralization and material hardship contributed significantly to children's internalizing scores at age 11 (weight > 44%, 32% respectively; Table 4). The contributions of maternal social support, neighborhood quality, intimate partner violence, and maternal perceived stress were not significant (weights ≤ 16%). Models examining tertiles, quartiles, and outcomes at other ages yielded similar results (Table 4). Negative constraints yielded no significant results.

Table 4 Weights of ELS Mixture Components at Each Age Point

Component	Tertile Weight	Quartile Weight	Quantile Weight
Age 5			
Maternal Demoralization	0.44*	0.40*	0.45*
Intimate Partner Violence	0.16	0.22*	0.19*
Maternal Perceived Stress	0.13	0.21*	0.19*
Maternal Perceived Social Support	0.27*	0.13	0.14
Neighborhood Quality	0.002	0.009	0.02
Material Hardship	0.01	0.01	0.02
Age 7			
Maternal Demoralization	0.29*	0.14	0.18*
Intimate Partner Violence	0.44*	0.51*	0.45*
Maternal Perceived Stress	0.09	0.15	0.18*
Maternal Perceived Social Support	0.07	0.06	0.004
Neighborhood Quality	0.03	0.05	0.10
Material Hardship	0.09	0.09	0.09
Age 9			
Maternal Demoralization	0.31*	0.34*	0.18*
Intimate Partner Violence	0.34*	0.32*	0.45*
Maternal Perceived Stress	0.12	0.15	0.18*
Maternal Perceived Social Support	0.15	0.16	0.004
Neighborhood Quality	0.002	0.01	0.10
Material Hardship	0.08	0.09	0.09
Age 11			
Maternal Demoralization	0.28*	0.31*	0.44*
Intimate Partner Violence	0.19*	0.18*	0.16
Maternal Perceived Stress	0.03	0.04	0.06
Maternal Perceived Social Support	0.22*	0.25*	0.008
Neighborhood Quality	0.03	0.01	0.02
Material Hardship	0.25*	0.21*	0.32*

*indicates significant contribution to the mixture model as defined by weight greater than the cutoff $\tau = 0.167$, or the inverse of the number of elements in the mixture (7)

Discussion

The current study examined the interacting effects of maternal stress during children's early life and SHS on children's internalizing symptoms and their development over time. Exposure to SHS interacted with maternal stress during children's early life to result in higher internalizing symptoms during the preschool period. In addition, they interacted to result in slower decreases in symptoms across childhood. Children with the highest levels of both SHS and ELS failed to show the expected normative decreases in internalizing symptoms when ELS and SHS are not present. By examining this interaction, we clarify prior equivocal findings of associations between SHS and internalizing symptoms. Critically, maternal demoralization and material hardship, but not the four other domains of ELS, were significantly associated with children's internalizing symptoms across childhood. Such findings are consistent with translational work showing that material hardship causes behaviors in rodents analogous to internalizing problems in humans [80]. Our findings underscore the importance of longitudinal studies to understand effects of exposure on children's mental health outcomes. Moreover, our study points to the importance of modeling effects of multiple sources of neurotoxic exposures, including those in both the chemical and social environment. Identifying and intervening on modifiable factors such as prenatal SHS, maternal demoralization, and material hardship may reduce the prevalence of internalizing problems in youth.

SHS exposure primes vulnerability to ELS for preschool internalizing symptoms

Exposure to SHS and ELS resulted in higher internalizing problems scores at in preschool, supporting our hypothesis that the interaction between SHS and ELS would be associated with more internalizing symptoms. We were not able to look at causal or directional effects of SHS and ELS measured concurrently. However, we observed a positive association between ELS and internalizing problems in preschool, suggesting prenatal SHS exposure might compound effects of stress. Such conjecture is supported by animal models showing that prenatal nicotine exposure alters central nervous system nicotinic acetylcholine receptors (nAChR; [81]) which are involved

in the development and regulation of dopaminergic systems [80–83]. These dopaminergic systems play a critical role in processing threat [83–86] and are disrupted by ELS [86–89]. Thus, the interactive effects of SHS and ELS may operate through effects on the dopaminergic system. Future studies should examine these pathways to identify potential pharmacologic treatment targets in youth with pollution and stress-related internalizing disorders.

Combined SHS and ELS exposure is Associated with slower decline in internalizing symptoms across childhood

Combined exposure to SHS and ELS was associated with a slower decrease in internalizing symptoms over time, consistent with our hypothesis that the interaction between SHS and ELS would disrupt normative patterns of reduced internalizing symptoms across childhood [45, 90]. Our findings align with prior studies showing that maternal stress is associated with children's increased internalizing symptoms over development [44, 46, 47]. If the combined targeting of dopamine circuits by SHS and ELS reorganizes neural development, these effects may become magnified over time. The reorganization of dopamine-dependent circuitry in infancy and early childhood may result in a behavioral phenotype that is primed for increased sensitivity to threat and greater expression of internalizing symptoms. In typical development, children overcome these challenges and there is a subsequent reduction in internalizing symptoms over time [45, 91, 92]. However, ELS exacerbates the internalizing phenotype, resulting in altered fear processing [92], hyperresponsivity to threat [93], and changes in dopamine functioning [92, 94, 95], which ultimately leads to greater vulnerability and risk for persistent internalizing symptoms [96]. Future work should examine these neural pathways as a possible mechanism for the interactive effects of ELS and SHS. Genetic risk for internalizing symptomatology may also increase vulnerability to the interactive effects for SHS and ELS. Given that our study was performed in an epidemiological birth cohort unweighted for clinical symptoms, we are unable to examine this question. Future studies examining similar exposures in a sample weighted for anxiety or mood problems would allow for the examination of gene by environment interactions.

We did not observe downward sloping trajectories of internalizing problems during pre-adolescence as has been observed in prior work [44–47]. Notably, prior studies of internalizing symptom trajectories in community youth have examined majority white, middle class samples [44–47]. Our sample consists entirely of Black and Latinx dyads, with the majority of our sample falling at or below the poverty line. Given the common co-occurrence of multiple stressors facing this population [18], including elevated parental psychological distress, racism, and economic hardship, it is likely that these factors contributed to relative stability in the slope of youth's internalizing symptoms. As described below, our data support this hypothesis, such that distinct components of adversity contributed to children's internalizing symptoms at every age.

Distinct components of ELS contribute to internalizing symptoms beyond Effects of prenatal SHS

Examining components of the ELS composite revealed that maternal demoralization and material hardship significantly contributed to internalizing problems at age eleven whereas the other four domains of stress did not. Maternal demoralization reflects mothers' subjective feelings of incompetence and associated feelings of psychological distress [97] that have been linked to risk for maternal depression [98, 99], which in turn has been linked to poor child emotional outcomes [99–103]. Material hardship – the inability to meet basic needs – has been directly linked with children's risk for internalizing problems [104, 105]. In humans, material hardship increases risk for postpartum depression [105–108]. In rodent models, postpartum material hardship induces depression like behaviors in the dam, which in turn leads to disrupted maternal care-giving behaviors and altered dopamine functioning in offspring [80]. The combined targeting of dopaminergic systems by material hardship and maternal demoralization may serve as an etiologic mechanism for internalizing symptoms in offspring. Future translational research should examine the biological mechanism by which maternal demoralization and material hardship influence internalizing symptoms. Interventions addressing material hardship in young families, such as food stamps, unconditional cash transfer, and earned income tax credits, can improve health outcomes for both mothers and children [108–112]. Additionally, though understudied, interventions addressing maternal psychological distress show promising positive effects on parenting [112–116], which in turn has been linked to more positive health outcomes in youth [113, 117].

Limitations

Our study is not without limitations. First, our cohort is not weighted for clinical outcomes, limiting our ability to examine trajectories of internalizing symptoms in both clinical and nonclinical populations. Future studies should examine these trajectories in a cohort weighted for clinical symptoms in order to assess these effects. Next, maternal demoralization is a proxy for maternal psychological distress, including maternal anxiety and depression; however, our study does not contain a clinical measure of maternal anxiety or depression symptoms. Future studies should include a measure of

maternal psychopathology. Additionally, our stress composite score was measured during children's age 5 study visit; whereas, our first measure of children's internalizing symptoms occurred during their preschool (age 3–5) visit. Future studies should measure ELS prior to children's first visit to understand the temporally predictive effects of these associations. Finally, data missingness may limit generalizability. Primary reasons for data missingness include inability to participate in a particular study visit, participants' moving out of state, or loss of contact.

Conclusions

Our study shows for the first time that combined exposure to prenatal SHS and maternal stress during children's early life increases children's internalizing symptoms in early childhood and that these effects persist across middle childhood. Clinically, our findings indicate that maternal demoralization and material hardship are important targets for personalized prevention and intervention to reduce the development of children's internalizing problems. The study has a number of strengths including the relatively large prospective longitudinal birth cohort design that includes individuals who have historically been excluded from developmental research, as well as using a biomarker of exposure. Importantly, our study helps to clarify previous equivocal findings linking internalizing symptoms and SHS exposure by examining the interactive effects of SHS and ELS. It is possible that these interactive effects offer one potential mechanism through which prenatal SHS exposure may prime vulnerability to ELS and increase risk for psychopathology. Further these findings point to a pathway through mental health inequities may arise in Black youth, whose mothers are differentially exposed to SHS. Better understanding of the underlying mechanism of action of these profiles is necessary and may help address the current public health crisis in adolescent mental health [118, 119].

Abbreviations

SHS	Secondhand tobacco smoke (measured prenatally)
ELS	Maternal Stress During Children's Early Life
CBCL	Child Behavior Checklist
CCCEH	Columbia Center for Children's Environmental Health
WQS	Weighted quantile sum

Supplementary Information

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Supplementary Material 1

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Authors' contributions

MD generated the study idea, compiled, analyzed, and interpreted participant data, and was primarily responsible for writing the manuscript. JWC participated in data compilation and analysis. JDD and JAS provided statistical expertise and editorial feedback. BR was the primary data manager. JBH provided access to the data and assisted in data interpretation. DP provided statistical code and support with data interpretation. AEM provided primary editorial feedback and support through study design and completion. All authors read, provided feedback, and ultimately approved the final manuscript.

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Data Availability

This study leveraged data from the CCCEH Mothers and Newborns prospective, longitudinal birth cohort. Data is available upon written request.

Declarations

Competing interests

The authors declare no competing interests.

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Columbia University (AAAA6110, AAAT9287). Mothers provided informed consent for themselves and their children at every study visit. Children provided assent beginning at age 7.

Consent for publication

NA.

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References

1. CDCTobaccoFree. 2014 SGR: The health consequences of smoking—50 years of progress [Internet]. Centers for Disease Control and Prevention. 2022 [cited 2022 Jun 17]. Available from: https://www.cdc.gov/tobacco/sgr/50th-anniversary/index.htm?CDC_AA_refVal=https://www.cdc.gov/tobacco/data_statistics/sgr/50th-anniversary/index.htm.
2. CDC. Current cigarette smoking among adults in the United States [Internet]. Centers for Disease Control and Prevention. 2022 [cited 2023 Jan 3]. Available from: https://www.cdc.gov/tobacco/data_statistics/fact_sheets/adult_data/cig_smoking/index.htm.
3. STATE system smokefree indoor air fact sheet [Internet]. 2022 [cited 2023 Jan 3]. Available from: https://www.cdc.gov/statesystem/factsheets/sfia/SmokeFreeIndoorAir.html.

4. Tsai J, Homa DM, Gentzke AS, Mahoney M, Sharapova SR, Sosnoff CS, et al. Exposure to secondhand smoke among nonsmokers - United States, 1988–2014. MMWR Morb Mortal Wkly Rep. 2018;67:1342–6.
5. Homa DM, Neff LJ, King BA, Caraballo RS, Bunnell RE, Babb SD, et al. Vital signs: disparities in nonsmokers' exposure to secondhand smoke–United States, 1999–2012. MMWR Morb Mortal Wkly Rep. 2015;64:103–8.
6. King BA, Homa DM, Dube SR, Babb SD. Exposure to secondhand smoke and attitudes toward smoke-free workplaces among employed U.s. adults: findings from the national adult tobacco survey. Nicotine Tob Res. 2014;16:1307–18.
7. King BA, Dube SR, Homa DM. Smoke-free rules and secondhand smoke exposure in homes and vehicles among US adults, 2009–2010. Prev Chronic Dis. 2013;10:E79.
8. Mills AL, White MM, Pierce JP, Messer K. Home smoking bans among U.S. households with children and smokers. Opportunities for intervention. Am J Prev Med. 2011;41:559–65.
9. National Institutes of Health, Department of Health & Human Services, National Cancer Institute. Health Effects of exposure to environmental Tobacco smoke. Createspace Independent Pub; 2014.
10. Cao H, Liang Y, Zhou N. Early tobacco smoke exposure, preschool cool/hot inhibitory control, and young adolescents' externalizing/internalizing problems. J Fam Psychol. 2021;35:311–23.
11. Maitre L, Julvez J, López-Vicente M, Warembourg C, Tamayo-Uria I, Philippat C, et al. Early-life environmental exposure determinants of child behavior in Europe: a longitudinal, population-based study. Environ Int. 2021;153:106523.
12. Yang HS, Lim H, Choi J, Bae S, Kim Y, Kwon H-J et al. Environmental Tobacco Smoke Exposure at Home and Attributable Problem Behaviors in Korean Children and Adolescents for 2012–2014 in a Nationally Representative Survey [Internet]. Journal of Korean Medical Science. 2018. https://doi.org/10.3346/jkms.2018.33.e229.
13. Luk TT, Wang MP, Suen YN, Koh DS-Q, Lam TH, Chan SS-C. Early childhood exposure to secondhand smoke and behavioural problems in preschoolers. Sci Rep. 2018;8:15434.
14. Park B, Park B, Kim E-J, Kim YJ, Lee H, Ha E-H, et al. Longitudinal association between environmental tobacco smoke exposure and behavioral problems in children from ages 5 to 9. Sci Total Environ. 2020;746:141327.
15. Roza SJ, Verhulst FC, Jaddoe VWV, Steegers EAP, Mackenbach JP, Hofman A, et al. Maternal smoking during pregnancy and child behaviour problems: the Generation R Study. Int J Epidemiol. 2009;38:680–9.
16. Tiesler CMT, Chen C-M, Sausenthaler S, Herbarth O, Lehmann I, Schaaf B, et al. Passive smoking and behavioural problems in children: results from the LISAplus prospective birth cohort study. Environ Res. 2011;111:1173–9.
17. Reuben A, Manczak EM, Cabrera LY, Alegria M, Bucher ML, Freeman EC, et al. The interplay of environmental exposures and mental health: setting an agenda. Environ Health Perspect. 2022;130:25001.
18. Vermeulen R, Schymanski EL, Barabási A-L, Miller GW. The exposome and health: where chemistry meets biology. Science. 2020;367:392–6.
19. Malter Cohen M, Jing D, Yang RR, Tottenham N, Lee FS, Casey BJ. Early-life stress has persistent effects on amygdala function and development in mice and humans. Proc Natl Acad Sci U S A. 2013;110:18274–8.
20. Hammen C, Hazel NA, Brennan PA, Najman J. Intergenerational transmission and continuity of stress and depression: depressed women and their offspring in 20 years of follow-up. Psychol Med. 2012;42:931–42.
21. Smith KE, Pollak SD. Early life stress and development: potential mechanisms for adverse outcomes. J Neurodev Disord. 2020;12:34.
22. Goodman SH, Rouse MH, Connell AM, Broth MR, Hall CM, Heyward D. Maternal depression and child psychopathology: a meta-analytic review. Clin Child Fam Psychol Rev. 2011;14:1–27.
23. Szekely E, Neumann A, Sallis H, Jolicoeur-Martineau A, Verhulst FC, Meaney MJ, et al. Maternal prenatal Mood, pregnancy-specific worries, and early child psychopathology: findings from the DREAM BIG Consortium. J Am Acad Child Adolesc Psychiatry. 2021;60:186–97.
24. Zhang H, Lee ZX, White T, Qiu A. Parental and social factors in relation to child psychopathology, behavior, and cognitive function. Transl Psychiatry. 2020;10:80.
25. Goodman SH, Simon HFM, Shamblaw AL, Kim CY. Parenting as a Mediator of Associations between Depression in Mothers and Children's functioning: a systematic review and Meta-analysis. Clin Child Fam Psychol Rev. 2020;23:427–60.
26. Chiesa AE, Kallechey L, Harlaar N, Rashaan Ford C, Garrido EF, Betts WR, et al. Intimate partner violence victimization and parenting: a systematic review. Child Abuse Negl. 2018;80:285–300.
27. Kaiser T, Li J, Pollmann-Schult M, Song AY. Poverty and child behavioral problems: the mediating role of parenting and parental well-being. Int J Environ Res Public Health. 2017;14:981.
28. Barnes J, Theule J. Maternal depression and infant attachment security: a meta-analysis. Infant Ment Health J. 2019;40:817–34.
29. McIntosh JE, Tan ES, Levendosky AA, Holtzworth-Munroe A. Mothers' experience of intimate partner violence and subsequent offspring attachment security ages 1–5 years: a meta-analysis. Trauma Violence Abuse. 2021;22:885–99.
30. Côté SM, Ahun MN, Herba CM, Brendgen M, Geoffroy M-C, Orri M, et al. Why is maternal Depression related to adolescent internalizing problems? A 15-Year Population-Based study. J Am Acad Child Adolesc Psychiatry. 2018;57:916–24.
31. Sheidow AJ, Henry DB, Tolan PH, Strachan MK. The role of stress exposure and family functioning in internalizing outcomes of urban families. J Child Fam Stud. 2014;23:1351–65.
32. Laskey BJ, Cartwright-Hatton S. Parental discipline behaviours and beliefs about their child: associations with child internalizing and mediation relationships. Child Care Health Dev. 2009;35:717–27.
33. Sawyer KM, Zunszain PA, Dazzan P, Pariante CM. Intergenerational transmission of depression: clinical observations and molecular mechanisms. Mol Psychiatry. 2019;24:1157–77.
34. Paananen R, Tuulio-Henriksson A, Merikukka M, Gissler M. Intergenerational transmission of psychiatric disorders: the 1987 finnish birth cohort study. Eur Child Adolesc Psychiatry. 2021;30:381–9.
35. Kessler RC, McLaughlin KA, Green JG, Gruber MJ, Sampson NA, Zaslavsky AM, et al. Childhood adversities and adult psychopathology in the WHO World Mental Health surveys. Br J Psychiatry. 2010;197:378–85.
36. Jackson DB, Testa A. The intersection between adverse childhood experiences and environmental tobacco smoke in U.s. households with children. Nicotine Tob Res. 2021;23:732–40.
37. Pearlin LI. The sociological study of stress. J Health Soc Behav. 1989;30:241–56.
38. Barr AB, Simons LG, Simons RL, Beach SRH, Philibert RA. Sharing the burden of the transition to adulthood: african american young adults' transition challenges and their mothers' health risk. Am Sociol Rev. 2018;83:143–72.
39. Pearlin LI, Aneshensel CS, LeBlanc AJ. The forms and mechanisms of stress proliferation: the case of AIDS caregivers. J Health Soc Behav. 1997;38:223–36.
40. Pagliaccio D, Luby JL, Bogdan R, Agrawal A, Gaffrey MS, Belden AC, et al. Amygdala functional connectivity, HPA axis genetic variation, and life stress in children and relations to anxiety and emotion regulation. J Abnorm Psychol. 2015;124:817–33.
41. Slotkin TA, Skavicus S, Card J, Stadler A, Levin ED, Seidler FJ. Developmental neurotoxicity of tobacco smoke directed toward cholinergic and serotonergic systems: more than just nicotine. Toxicol Sci. 2015;147:178–89.
42. Bassey RB, Gondré-Lewis MC. Combined early life stressors: prenatal nicotine and maternal deprivation interact to influence affective and drug seeking behavioral phenotypes in rats. Behav Brain Res. 2019;359:814–22.
43. Rauh VA, Whyatt RM, Garfinkel R, Andrews H, Hoepner L, Reyes A, et al. Developmental effects of exposure to environmental tobacco smoke and material hardship among inner-city children. Neurotoxicol Teratol. 2004;26:373–85.
44. Bayer JK, Sanson AV, Hemphill SA. Parent influences on early childhood internalizing difficulties. J Appl Dev Psychol. 2006;27:542–59.
45. Cohen JR, Andrews AR, Davis MM, Rudolph KD. Anxiety and depression during childhood and adolescence: testing theoretical models of continuity and discontinuity. J Abnorm Child Psychol. 2018;46:1295–308.
46. Shanahan L, Calkins SD, Keane SP, Kelleher R, Suffness R. Trajectories of internalizing symptoms across childhood: the roles of biological self-regulation and maternal psychopathology. Dev Psychopathol. 2014;26:1353–68.
47. Zhou AM, Buss KA. Trajectories of internalizing symptoms in early childhood: Associations with maternal internalizing symptoms and child physiology. Dev Psychobiol. 2021;63:1295–308.
48. Sterba SK, Prinstein MJ, Cox MJ. Trajectories of internalizing problems across childhood: heterogeneity, external validity, and gender differences. Dev Psychopathol. 2007;19:345–66.
49. Perera FP, Rauh V, Whyatt RM, Tsai W-Y, Tang D, Diaz D, et al. Effect of prenatal exposure to airborne polycyclic aromatic hydrocarbons on neurodevelopment in the first 3 years of life among inner-city children. Environ Health Perspect. 2006;114:1287–92.
50. Hopson MB, Margolis A, Rauh V, Herbstman J. Impact of the home environment on the relationship between prenatal exposure to environmental tobacco smoke and child behavior. Int J Child Health Hum Dev. 2016;9:453–64.

51. Achenbach TM, Rescorla L. Manual for the ASEBA (Achenbach System of empirically-based Assessment) school-age forms and profiles. Burlington: Research Center for Children, Youth, and Families, Department of Psychiatry, University of Vermont; 2001.
52. Pagliaccio D, Herbstman JB, Perera F, Tang D, Goldsmith J, Peterson BS, et al. Prenatal exposure to polycyclic aromatic hydrocarbons modifies the effects of early life stress on attention and thought problems in late childhood. J Child Psychol Psychiatry. 2020;61:1253–65.
53. Mayer SE, Jencks C. Poverty and the distribution of material hardship. J Hum Resour. 1989;24:88.
54. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav. 1983;24:385–96.
55. Straus MA, Hamby SL, BONEY-McCOY SUE, Sugarman DB. The revised conflict tactics scales (CTS2). J Fam Issues. 1996;17:283–316.
56. Cohen S, Mermelstein R, Kamarck T, Hoberman HM. Measuring the functional components of social support. Social Support: theory, Research and Applications. Dordrecht: Springer Netherlands; 1985. 73–94.
57. Cohen S, Underwood LG, Gottlieb BH. Social support measurement and intervention: A guide for health and social scientists. Cohen S, Underwood LG, Gottlieb BH, editors. 2000;345. Available from: https://psycnet.apa.org/fulltext/2000-00794-000.pdf.
58. Kim SY, Nair R, Knight GP, Roosa MW, Updegraff KA. Measurement equivalence of neighborhood quality measures for european american and mexican american families. J Community Psychol. 2008;37:1–20.
59. Sampson RJ, Raudenbush SW, Earls F. Neighborhoods and violent crime: a multilevel study of collective efficacy. Science. 1997;277:918–24.
60. Sampson RJ, Raudenbush SW. Systematic social observation of public spaces: a new look at disorder in urban neighborhoods. Am J Sociol. 1999;105:603–51.
61. Dohrenwend BP, Shrout PE, Egri G, Mendelsohn FS. Nonspecific psychological distress and other dimensions of psychopathology. Measures for use in the general population. Arch Gen Psychiatry. 1980;37:1229–36.
62. Cohen S. Perceived stress in a probability sample of the United States. Social Psychol Health. 1988;251:31–67.
63. Straus MA. The conflict tactics scales and its critics: an evaluation and new data on validity and reliability. Physical violence in american families. Routledge; 2017. pp. 49–74.
64. Vega EM, O'Leary KD. Test–retest reliability of the revised conflict tactics scales (CTS2). J Fam Violence. 2007;22:703–8.
65. Rosseel Y. lavaan: An R Package for Structural Equation Modeling [Internet]. Journal of Statistical Software. 2012. p. 1–36. https://doi.org/10.18637/jss.v048.i02.
66. RStudio Team, Boston MA. RStudio: Integrated Development Environment for R [Internet]. PBC; 2022. Available from: www.rstudio.com.
67. Maas CJM, Hox JJ. Sufficient sample sizes for multilevel modeling. Methodol (Gott). 2005;1:86–92.
68. Schumacker RE, Lomax RG. A beginner's guide to structural equation modeling: Fourth Edition. Routledge; 2015.
69. Cudeck. of Assessing Model Fit. Testing structural equation models [Internet]. 1993; Available from: https://books.google.com/books?hl=en&lr=&id=FvIxxeYDLx4C&oi=fnd&pg=PA136&ots=_N_DzWXGAQ&sig=x88l8Kcc8yTFFL_xW6r-HsQZ3KA
70. Jöreskog KG, Sörbom D. LISREL 8: structural equation modeling with the SIMPLIS Command Language. Scientific Software International; 1993.
71. Browne MW, Cudeck R. Alternative Ways of assessing Model Fit. Sociol Methods Res. 1992;21:230–58.
72. Little TD. Longitudinal structural equation modeling. Guilford Press; 2013.
73. Pavlov G, Maydeu-Olivares A, Shi D. Using the standardized root mean squared residual (SRMR) to assess exact fit in structural equation models. Educ Psychol Meas. 2021;81:110–30.
74. El-Mohandes AAE, Kiely M, Gantz MG, Blake SM, El-Khorazaty MN. Prediction of birth weight by cotinine levels during pregnancy in a population of black smokers. Pediatrics. 2009;124:e671–80.
75. DiPietro JA, Voegtline KM. The gestational foundation of sex differences in development and vulnerability. Neuroscience. 2017;342:4–20.
76. Sutherland S, Brunwasser SM. Sex differences in vulnerability to prenatal stress: a review of the recent literature. Curr Psychiatry Rep. 2018;20:102.
77. Eskenazi B, Trupin LS. Passive and active maternal smoking during pregnancy, as measured by serum cotinine, and postnatal smoke exposure. II. Effects on neurodevelopment at age 5 years. Am J Epidemiol. 1995;142:19–29.
78. Brunst KJ, Sanchez Guerra M, Gennings C, Hacker M, Jara C, Bosquet Enlow M, et al. Maternal lifetime stress and prenatal psychological functioning and decreased placental mitochondrial DNA copy number in the PRISM study. Am J Epidemiol. 2017;186:1227–36.
79. Carrico C, Gennings C, Wheeler DC, Factor-Litvak P. Characterization of weighted quantile sum regression for highly correlated data in a risk analysis setting. J Agric Biol Environ Stat. 2015;20:100–20.
80. Rincón-Cortés M, Grace AA. Postpartum scarcity-adversity disrupts maternal behavior and induces a hypodopaminergic state in the rat dam and adult female offspring. Neuropsychopharmacology. 2022;47:488–96.
81. Smith AM, Dwoskin LP, Pauly JR. Early exposure to nicotine during critical periods of brain development: mechanisms and consequences. J Pediatr Biochem. 2010;1:125–41.
82. Dani JA. Overview of nicotinic receptors and their roles in the central nervous system. Biol Psychiatry. 2001;49:166–74.
83. Dani JA, Bertrand D. Nicotinic acetylcholine receptors and nicotinic cholinergic mechanisms of the central nervous system. Annu Rev Pharmacol Toxicol. 2007;47:699–729.
84. Jo YS, Heymann G, Zweifel LS. Dopamine neurons reflect the uncertainty in fear generalization. Neuron. 2018;100:916–925e3.
85. Bloomfield MA, Mccutcheon RA, Kempton M, Freeman TP, Howes O. The effects of psychosocial stress on dopaminergic function and the acute stress response. Elife [Internet]. 2019; Available from: https://elifesciences.org/articles/46797.pdf.
86. De Bundel D, Zussy C, Espallergues J, Gerfen CR, Girault J-A, Valjent E. Dopamine D2 receptors gate generalization of conditioned threat responses through mTORC1 signaling in the extended amygdala. Mol Psychiatry. 2016;21:1545–53.
87. Bonapersona V, Joëls M, Sarabdjitsingh RA. Effects of early life stress on biochemical indicators of the dopaminergic system: a 3 level meta-analysis of rodent studies. Neurosci Biobehav Rev. 2018;95:1–16.
88. Egerton A, Valmaggia LR, Howes OD, Day F, Chaddock CA, Allen P, et al. Adversity in childhood linked to elevated striatal dopamine function in adulthood. Schizophr Res. 2016;176:171–6.
89. Hanson JL, Williams AV, Bangasser DA, Peña CJ. Impact of early life stress on reward circuit function and regulation. Front Psychiatry. 2021;12:744690.
90. Olatunji BO, Cole DA. The longitudinal structure of general and specific anxiety dimensions in children: testing a latent trait-state-occasion model. Psychol Assess. 2009;21:412–24.
91. Costello EJ, Compton SN, Keeler G, Angold A. Relationships between poverty and psychopathology: a natural experiment. JAMA. 2003;290:2023–9.
92. Kraaijenvanger EJ, Pollok TM, Monninger M, Kaiser A, Brandeis D, Banaschewski T, et al. Impact of early life adversities on human brain functioning: a coordinate-based meta-analysis. Neurosci Biobehav Rev. 2020;113:62–76.
93. Agorastos A, Pervanidou P, Chrousos GP, Kolaitis G. Early life stress and trauma: developmental neuroendocrine aspects of prolonged stress system dysregulation. Horm (Athens). 2018;17:507–20.
94. Hakamata Y, Suzuki Y, Kobashikawa H, Hori H. Neurobiology of early life adversity: a systematic review of meta-analyses towards an integrative account of its neurobiological trajectories to mental disorders. Front Neuroendocrinol. 2022;65:100994.
95. Herzberg MP, Gunnar MR. Early life stress and brain function: activity and connectivity associated with processing emotion and reward. NeuroImage. 2020;209:116493.
96. Ruttle PL, Armstrong JM, Klein MH, Essex MJ. Adolescent internalizing symptoms and negative life events: the sensitizing effects of earlier life stress and cortisol. Dev Psychopathol. 2014;26:1411–22.
97. de Figueiredo JM. Distress, demoralization and psychopathology: diagnostic boundaries. Eur J Psychiatry. 2013;27:61–73.
98. Costanza A, Baertschi M, Richard-Lepouriel H, Weber K, Berardelli I, Pompili M et al. Demoralization and Its Relationship with Depression and Hopelessness in Suicidal Patients Attending an Emergency Department. Int J Environ Res Public Health [Internet]. 2020;17. https://doi.org/10.3390/ijerph17072232.
99. Liu ST, Wu X, Wang N, Zhao QQ, Xiao L, Fang CK, et al. Serial multiple mediation of demoralization and depression in the relationship between hopelessness and suicidal ideation. Psychooncology. 2020;29:1321–8.
100. Choe DE, Olson SL, Sameroff AJ. Effects of early maternal distress and parenting on the development of children's self-regulation and externalizing behavior. Dev Psychopathol. 2013;25:437–53.
101. Ciciolla L, Gerstein ED, Crnic KA. Reciprocity Among Maternal Distress, Child Behavior, and Parenting: Transactional Processes and Early Childhood Risk [Internet]. Journal of Clinical Child & Adolescent Psychology. 2014. p. 751–64. https://doi.org/10.1080/15374416.2013.812038.

102. Dubois-Comtois K, Moss E, Cyr C, Pascuzzo K. Behavior problems in middle childhood: the predictive role of maternal distress, child attachment, and mother-child interactions. J Abnorm Child Psychol. 2013;41:1311–24.
103. Pietikäinen JT, Kiviruusu O, Kylliäinen A, Pölkki P, Saarenpää-Heikkilä O, Paunio T et al. Maternal and paternal depressive symptoms and children's emotional problems at the age of 2 and 5 years: a longitudinal study [Internet]. Journal of Child Psychology and Psychiatry. 2020. p. 195–204. https://doi.org/10.1111/jcpp.13126.
104. Lichtin RD, Merz EC, He X, Desai PM, Simon KR, Melvin SA, et al. Material hardship, prefrontal cortex-amygdala structure, and internalizing symptoms in children. Dev Psychobiol. 2021;63:364–77.
105. Zilanawala A, Pilkauskas NV. Material hardship and child socioemotional behaviors: differences by types of hardship, timing, and duration. Child Youth Serv Rev. 2012;34:814–25.
106. Chung EK, McCollum KF, Elo IT, Lee HJ, Culhane JF. Maternal depressive symptoms and infant health practices among low-income women. Pediatrics. 2004;113:e523–9.
107. Payne JL, Maguire J. Pathophysiological mechanisms implicated in postpartum depression. Front Neuroendocrinol. 2019;52:165–80.
108. Yim IS, Tanner Stapleton LR, Guardino CM, Hahn-Holbrook J, Dunkel Schetter C. Biological and psychosocial predictors of postpartum depression: systematic review and call for integration. Annu Rev Clin Psychol. 2015;11:99–137.
109. Komro KA, Markowitz S, Livingston MD, Wagenaar AC. Effects of state-level earned income tax credit laws on birth outcomes by race and ethnicity. Health Equity. 2019;3:61–7.
110. Silverman K, Holtyn AF, Jarvis BP. A potential role of anti-poverty programs in health promotion. Prev Med. 2016;92:58–61.
111. Troller-Renfree SV, Costanzo MA, Duncan GJ, Magnuson K, Gennetian LA, Yoshikawa H, et al. The impact of a poverty reduction intervention on infant brain activity. Proc Natl Acad Sci U S A. 2022;119:e2115649119.
112. Casey P, Goolsby S, Berkowitz C, Frank D, Cook J, Cutts D, et al. Maternal depression, changing public assistance, food security, and child health status. Pediatrics. 2004;113:298–304.
113. Stein A, Netsi E, Lawrence PJ, Granger C, Kempton C, Craske MG, et al. Mitigating the effect of persistent postnatal depression on child outcomes through an intervention to treat depression and improve parenting: a randomised controlled trial. Lancet Psychiatry. 2018;5:134–44.
114. Potharst ES, Kuijl M, Wind D, Bögels SM. Do improvements in maternal mental health predict improvements in parenting? Mechanisms of the mindful with your baby training. Int J Environ Res Public Health. 2022;19:7571.
115. Rokhanawati D, Salimo H, Andayani TR, Hakimi M. The effect of parenting peer education interventions for young mothers on the growth and development of children under five. Children (Basel) [Internet]. 2023;10. https://doi.org/10.3390/children10020338.
116. Galbally M, Lewis AJ. Depression and parenting: the need for improved intervention models. Curr Opin Psychol. 2017;15:61–5.
117. O'Connell LK, Davis MM, Bauer NS. Assessing parenting behaviors to improve child outcomes. Pediatrics. 2015;135:e286–8.
118. AAP-AACAP-CHA declaration of a national Emergency in Child and adolescent Mental Health [Internet]. 2021 Oct. Available from: https://www.aap.org/en/advocacy/child-and-adolescent-healthy-mental-development/aap-aacap-cha-declaration-of-a-national-emergency-in-child-and-adolescent-mental-health/.
119. Benton TD, Boyd RC, Njoroge WFM. Addressing the global crisis of child and adolescent mental health. JAMA Pediatr. American Medical Association (AMA); 2021. pp. 1108–10.

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