Prenatal Exposure to Air Pollution and Early-Life Stress Effects on Hippocampal Subregional Volumes and Associations With Visuospatial Reasoning

Amy E. Margolis,

New York State Psychiatric Institute and Department of Psychiatry, Vagelos College of Physicians and Surgeons

Jacob W. Cohen,

New York State Psychiatric Institute and Department of Psychiatry, Vagelos College of Physicians and Surgeons

Bruce Ramphal,

New York State Psychiatric Institute and Department of Psychiatry, Vagelos College of Physicians and Surgeons

Lauren Thomas,

New York State Psychiatric Institute and Department of Psychiatry, Vagelos College of Physicians and Surgeons

Virginia Rauh,

Department of Population and Family Health, Mailman School of Public Health

Julie Herbstman,

Columbia Center for Children's Environmental Health, Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, New York.

David Pagliaccio

New York State Psychiatric Institute and Department of Psychiatry, Vagelos College of Physicians and Surgeons

Abstract

BACKGROUND: Children from economically distressed families and neighborhoods are at risk for stress and pollution exposure and potential neurotoxic sequelae. We examine dimensions of early-life stress affecting hippocampal volumes, how prenatal exposure to air pollution might magnify these effects, and associations between hippocampal volumes and visuospatial reasoning.

METHODS: Fifty-three Hispanic/Latinx and/or Black children of ages 7 to 9 years were recruited from a longitudinal birth cohort for magnetic resonance imaging and cognitive assessment. Exposure to airborne polycyclic aromatic hydrocarbons was measured during the third trimester

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of pregnancy. Maternal report of psychosocial stress was collected at child age 5 and served as measures of early-life stress. Whole hippocampus and subfield volumes were extracted using FreeSurfer. Wechsler performance IQ measured visuospatial reasoning.

RESULTS: Maternal perceived stress associated with smaller right hippocampal volume among their children (B = −0.57, t_{34} = −3.05, 95% CI, −0.95 to −0.19). Prenatal polycyclic aromatic hydrocarbon moderated the association between maternal perceived stress and right CA1, CA3, and CA4/dentate gyrus volumes (B ≥ 0.68, t_{33} ≥ 2.17) such that higher prenatal polycyclic aromatic hydrocarbon exposure magnified negative associations between stress and volume, whereas this was buffered at lower exposure. Right CA3 and CA4/dentate gyrus volumes (B ≥ 0.35, t_{33} > 2.16) were associated with greater performance IQ.

CONCLUSIONS: Prenatal and early-life exposures to chemical and social stressors are likely compounding. Socioeconomic deprivation and disparities increase risk of these exposures that exert critical neurobiological effects. Developing deeper understandings of these complex interactions will facilitate more focused public health strategies to protect and foster the development of children at greatest risk of mental and physical effects associated with poverty.

Socioeconomic disparities place children from economically distressed families and neighborhoods at disproportionate risk for exposure to stressful life events and to air pollution. Economic disadvantage increases the likelihood of experiencing physical and social stressors, such as inadequate access to basic resources or living in neighborhoods with increased violence (1,2). In addition, air pollution is often higher in these neighborhoods, placing children at increased risk for exposure both in utero and during development (2,3). Exposures to early-life stress (ELS) (4–6) and prenatal air pollution (7–9) have been separately linked to increased risk for behavioral, psychological, and cognitive problems, which may derive from the neurobiological effects of exposure.

The hippocampus is a key region involved in stress regulation and, critically, is vulnerable to the neurotoxic effects of stress and cortisol, which can lead to deficits in hippocampal structure and volume in both animal and human research (10,11). In addition, psychological stress differentially alters subfields of the hippocampus with the CA1, CA3, and dentate gyrus generally found to be most vulnerable (12). Animal models have shown that psychological stress (e.g., restraint stress, housing in dominance hierarchies, maternal deprivation) can result in shortened dendrites, neurogenesis suppression, and the loss of spine synapses in subregions of the hippocampus (10). More specifically, chronic restraint stress results in neuronal atrophy in CA3 and CA1 (13,14). Other forms of chronic and acute stress have been shown to decrease neurogenesis in the dentate gyrus (10,13) and impair long-term potentiation and synaptic plasticity in CA1 and dentate gyrus (15). This neuronal remodeling is plausibly mediated by changes in cortisol and glutamate, both of which are involved in the stress response and have been linked to hippocampal structure and function (10). These changes likely give rise to the gross morphological differences commonly observed in human research (16). Socioeconomic disadvantage and its associated stressors, at both the household level (17–19) and neighborhood level (20), have been consistently linked to reductions in hippocampal structure, as have maternal anxiety (21,22) and the lack of maternal support (23,24). Herein, we examine potentially distinct contributions of early-life exposure to different types of maternal psychosocial and socioeconomic stress

on hippocampal volumes, specifically, maternal perceived stress, maternal psychological distress, material hardship, neighborhood quality, and maternal intimate partner violence.

Exposure to air pollution also alters the hippocampus and exhibits differential effects on hippocampal subfields. Decreased structural integrity across the hippocampus (25), decreased neurogenesis in the dentate gyrus, and activated microglia in the dentate gyrus and CA1 subfields (26) have all been observed following perinatal air pollutant exposure in animal models. Decreased dendritic branching in CA1 and CA3 subregions (27) and reductions in hippocampal brain-derived neurotrophic factor (BDNF) expression (28) have been shown to follow prenatal particulate matter (PM) 2.5 ($PM_{2.5}$) exposure. Prior human research has also focused on exposure to polycyclic aromatic hydrocarbons (PAHs)—a group of air pollutants resulting from the incomplete combustion of organic matter and tobacco smoke, grilling, oil- and coal-burning power plants, and vehicular emissions (29). Prenatal PAH exposure—estimated by land use regression models or directly measured personal exposure—has been associated with structural alterations in the brain, specifically cortical thinning in brain regions in both hemispheres (30), volume reductions in the corpus callosum (31), and reduced left hemisphere white matter (32). In addition, consistent with findings from animal models, infants born after the closing of a coal-burning factory in China had decreased markers of exposure to PAH and increased level of mature BDNF (33). Yet, few human studies have focused on the effects of air pollution exposure on specific neuroanatomical regions implicated in cognitive development and, of particular interest here, the hippocampus. Such findings would enhance our understanding of the etiologic mechanisms by which air pollution affects neurodevelopment. Consistent with the findings from animal models, extant human research demonstrates an association between concurrent air pollution exposure in adulthood and smaller hippocampal volume, while controlling for socioeconomic status (29,34–37), which was further supported in a meta-analysis (38). Similarly, prenatal exposure to air pollution (estimated by land use regression models) was shown to associate with smaller left hippocampal volumes in school-age children (39). The effects of air pollution on hippocampal subfields remain understudied.

Overall, the hippocampus may represent a common site of the neurotoxic effects of air pollution and stress, particularly experienced prenatally and in early life, which can lead to deleterious downstream cognitive and neurodevelopmental outcomes. Conceptual work suggests that models describing threats to neurodevelopment must account for the amplified effects of multiple exposures (40). Specifically, recent findings indicate that the effects of exposure to ELS and air pollution on brain and behavior may be compounding (41–43). Herein, we investigate potential interactions between prenatal exposure to PAH and ELS on the hippocampal structure in school-age children. Understanding these aggravated effects may facilitate a comprehensive public health campaign that targets distinct patterns of risk for child development.

Finally, structural and functional neuroimaging studies have demonstrated an integral role for the hippocampus in learning, remembering, and flexibly navigating spatial information (44–48). This relationship has been observed bilaterally (49) and across different subfields (47). Larger hippocampal volume has been associated with greater navigational experience in taxi drivers (50,51), and both severe hippocampal damage (45) and CA1 atrophy in

patients with multiple sclerosis (52) are correlated with impaired spatial recall. Structural differences have been similarly identified in children with nonverbal learning disorder, which is characterized by visuospatial deficits (53). These visuospatial deficits are independently associated with differences in stress and air pollution exposure in early life (54–56), with 1 study reporting that higher PAH DNA-adducts, a biological marker of exposure, were associated with lower visuospatial intelligence among children who experienced material hardship (41). Importantly, additional animal research has begun to place hippocampal subfields as potential mediators in the relationship between adversity and visuospatial cognitive skills (57,58).

Herein, we use structural magnetic resonance imaging (MRI) data acquired from Black and/or Latinx children from economically disadvantaged families enrolled in a prospective longitudinal birth cohort to examine several hypotheses. Though these longitudinal data are powerful, our sample size was limited, and thus we opted for analyses to minimize multiple testing. First, we hypothesized that individual differences in ELS, measured by maternal report at child age 5, would associate with reduced children's hippocampal volumes at ages 7 to 9. We aimed to parse which of the 5 measured domains of ELS would have the most potent influence. Next, given prior work showing interactions between prenatal exposure to air pollution and ELS on children's neurodevelopmental outcomes (42), we hypothesized that greater prenatal PAH exposure would potentiate stress-related reductions in hippocampal volumes. Last, given the effects of air pollution and stress on cognitive development and the role of the hippocampus in visuospatial processing (44–49), we explored the extent to which hippocampal volume associated with performance IQ (PIQ) scores, as a measure of visuospatial abilities.

METHODS AND MATERIALS

Participants

As described previously (59), we recruited $N = 53$ children of ages 7 years and older from the Sibling-Hermanos birth cohort at Columbia University for a neuroimaging visit (see Supplemental Methods). Mothers were nonsmokers. Five children opted out of the study, 5 were unable to complete the MRI scan, and 3 were excluded during quality control checks. In total, $n = 40$ children had available hippocampal subfield volumes and ELS data, $n = 37$ of those participants had prenatal air pollution exposure data, and $n = 35$ had visuospatial ability data ($n = 64$ children had available PAH, ELS, and IQ data). The Institutional Review Boards at Columbia University and New York State Psychiatric Institute approved the study; children and guardians provided written informed assent and consent.

Early-Life Stress

Each participant's mother completed validated scales measuring 5 aspects of ELS at child age 5: maternal perceived stress over the past month (60), maternal psychological distress (61), material hardship (62), neighborhood quality (63–65), and intimate partner violence (66). All items were rescaled 0–1 and averaged for each scale so that each scale yields a continuous score, with higher scores indicating more stress. These scales have good reported reliability and psychometric properties and have been reported on extensively in our prior

work (42). Our primary analyses used maternal reports of stress to measure 5 distinct domains of ELS.

Air Pollution

Maternal personal exposure to air pollution was measured and analyzed as previously described (67,68). Briefly, during the third trimester of pregnancy, mothers wore an air monitoring backpack for 48 continuous hours. The backpack contained a filter that collected airborne vapors, aerosols, and $PM_{2.5}$ from which 8 PAHs (benz[*a*]anthracene, benzo[*a*]pyrene, chrysene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, indeno-[1,2,3-*cd*] pyrene, disbenz[*a,h*]anthracene, and benzo[*g,h,i*]perylene) were extracted and measured at Southwest Research Institute. Exposure was computed as the sum of these 8 carcinogenic PAHs (see Supplemental Methods). The distribution of exposure was assessed, and participants were subsequently grouped by a median split of total PAH exposure (median = 1.60 ng/m^3) (Figure S1) as our predictor of interest, aligned with previous work (59,69). The median split separates higher and lower exposure groups minimizing measurement error in the estimate of exposure, i.e., how well the 48-hour assessment captures cumulative exposure. Furthermore, we did not expect the individual variance at the low end, reflecting minimal to no exposure, to systematically relate to biological/psychological outcomes. Exploratory analyses using PAH as a continuous variable are reported in Supplemental Results.

Visuospatial Reasoning

As part of the cohort study, participants completed neuropsychological assessment at age 7 to 9, including the Wechsler Abbreviated Scale of Intelligence, Second Edition (70). The Wechsler Abbreviated Scale of Intelligence assesses verbal IQ (VIQ) reflecting verbal reasoning and PIQ reflecting visuospatial reasoning, such that VIQ and PIQ can be combined into a full-scale IQ score. VIQ is composed of the Vocabulary subtest, measuring word knowledge, and the Similarities subtest, measuring analogical reasoning. PIQ is composed of the Matrix Reasoning and Block Design subtests and is considered a gold standard measure of visuospatial abilities (70). Each Index score is a continuous variable with a mean of 100 and SD of 15 points. Two participants were missing PIQ data.

MRI Acquisition and Processing

Participants completed MRI scanning on the same day as the neuropsychological assessment. Data were acquired on a 3T GE MR750 scanner (GE Healthcare) with a 32-channel head coil. Two structural T1 images were collected for each participant using a 3D-FSPGR sequence (flip angle = 11°, echo time = 2.588 ms, repetition time = 6.412 ms, 180 slices, 1-mm isotropic resolution). Structural data were processed using the standard FreeSurfer version 6.0 pipeline (recon-all) (71,72) including hippocampal subfield segmentation (73). Based on prior animal model findings on the effects of stress, we focused on the CA1, CA3, and CA4/dentate gyrus subfields.

Statistical Analyses

Distributions of continuous variables were examined (Figures S2 and S3). Cases with missing data were excluded per analysis. We report standardized regression coefficient estimates, significance tests were two-tailed, and α was set at $p < .05$. Tables S1 and S2 show simple correlations between prenatal PAH and postnatal socioeconomic and stress-related factors (child age 5): maternal perceived stress over the past month, maternal psychological distress, material hardship, neighborhood quality, intimate partner violence, and income-to-needs ratio. One participant exhibited right hippocampal total and subfield volumetric outliers ($z > 3$), which were winsorized to the next most extreme nonoutlier value. A sensitivity analysis examined whether removing this participant had any effect on the results (Supplemental Results).

Given our sample size and interest in parsing the distinct contributions of different types of maternal psychosocial and socioeconomic stress, our first analysis tested which ELS variables were associated with left or right hippocampal volume. We sought to delineate the domains of ELS at age 5 years (maternal perceived stress, maternal psychological distress, material hardship, intimate partner violence, or neighborhood instability) that were associated with children's hippocampal volumes. To do this, we entered these ELS variables into 2 multiple linear regression models ($n = 40$) predicting either left or right whole hippocampal volumes (residualized for age, sex assigned at birth, and intracranial volume to preserve degrees of freedom). We corrected for multiple comparisons using false discovery rate (FDR) across the 10 tested terms (5 domains; 2 hemispheres).

Our second analysis evaluated whether prenatal PAH exposure potentiated stress-related reductions in hippocampal volumes. We used multiple linear regression ($n = 37$) to test whether ELS, PAH, and the ELS × prenatal air pollution interaction associated with whole or subregional hippocampal volumes of that hemisphere (residualized for age, sex assigned at birth, and intracranial volume). To limit multiple testing given our sample size, we only examined domains of ELS that significantly related to whole hippocampal volumes rather than testing the interaction between prenatal PAH and all 5 ELS variables. We corrected for multiple comparisons using FDR across the number of tested interaction terms (4 volumes [whole, CA4/DG, CA3, and CA1] 3 number of domain-hemisphere associations identified in analysis 1).

Finally, in a third analysis, we explored whether visuospatial reasoning as measured by PIQ was associated with hippocampal subregions ($n = 35$). We restricted planned regression analyses to testing associations between PIQ and hippocampal subregions that were associated with the PAH × ELS interaction term in analysis 2. Control analyses evaluated the specificity of any observed associations between subfield volumes and PIQ versus VIQ. For completeness, we also present Supplemental Results from models testing associations between left hippocampal subregions and VIQ and PIQ. Furthermore, because brain structure and cognitive outcomes were measured at a single time point, we did not conduct a formal test of mediation PAH and ELS effects on PIQ by hippocampal subregions but did test the effect of the PAH × ELS interaction term on PIQ in a subset of children with available data ($n = 64$).

RESULTS

Participants

Hispanic/Latinx and/or Black children of ages 7 to 9 years participated in this study. Table 1 presents demographic, psychosocial, and cognitive data that describe the sample.

Domains of ELS and Hippocampal Volume

Greater maternal perceived stress at child age 5 associated with smaller right hippocampal volume at child age 7 to 9 (B = −0.57, t_{34} = −3.05, 95% CI, −0.95 to −0.19, p_{FDR} = .04). Maternal psychological distress, material hardship, neighborhood quality, and intimate partner violence were not significantly associated with hippocampal volume after FDR correction was applied (p_{FDRs} > .14) (see Table S3). Variance inflation factors were sufficiently low to determine that collinearity was not a concern, and simple linear regressions confirmed our findings (variance inflation factor 1.75) (Table S4). We tested hemispheric specificity in a mixed-effect model and found a main effect of maternal perceived stress on smaller hippocampal volumes across hemispheres (B = −0.30, t_{76} = −1.98, p = .05) and no significant maternal perceived stress × hemisphere interaction (p = .71) (Table S5).

Joint Effects of Air Pollution and ELS on Hippocampal Volume

The maternal perceived stress × prenatal PAH interaction was associated with right CA1 (B = 0.68, t_{33} = 2.24, 95% CI, 0.06 to 1.29, p_{FDR} = .049), CA3 (B = 0.82, t_{33} = 2.86, 95% CI, 0.23 to 1.40, p_{FDR} = .029), and CA4/dentate gyrus volumes (B = 0.68, t_{33} = 2.17, 95% CI, 0.04 to 1.32, p_{FDR} = .049). Right whole hippocampus volume was not associated with the perceived stress × prenatal PAH interaction term (B = 0.49, t_{33} = 1.57, 95% CI, −0.15 to 1.13, p_{FDR} = .126), although there was still a significant main effect for maternal perceived stress (B = −0.66, t_{33} = −2.64, 95% CI, −1.17 to −0.15). Specifically, among individuals with higher prenatal PAH exposure, greater stress was associated significantly with smaller hippocampal subfield volumes; among individuals with lower prenatal PAH exposure, stress and hippocampal subfield volumes were not significantly associated (Figure 1 and Table 2). Results from all 4 models, including nonsignificant findings, are reported in Table S6.

Hippocampal Volume and Visuospatial Reasoning

PIQ was significantly associated with right hippocampal subfield volumes CA3 (B = 0.38, t_{33} = 2.39, 95% CI, 0.06 to 0.71, p = .02) and CA4/dentate gyrus (B = 0.35, t_{33} = 2.16, 95% CI, 0.02 to 0.68, p = .04) (Figure 2) but not with CA1 (B = 0.16, t_{33} = 0.95, 95% CI, −0.19 to 0.51, p = .35) (Table S7 and Figure S4). Right hippocampal subfield volumes did not predict VIQ in simple linear regressions (Table S7), nor did left hippocampal subfield volumes predict PIQ or VIQ (Table S8). For completeness, a model containing PAH, ELS, and their interaction term (PAH × ELS) did not significantly predict PIQ or VIQ (Table S9).

DISCUSSION

Our study reports on the effects of different aspects of ELS on children's hippocampal volumes, as well as the moderating effects of prenatal exposure to PAH in a community

sample of Black or Latinx children from economically disadvantaged backgrounds. Of the 5 aspects of ELS that we have previously investigated (42), maternal perceived stress was negatively associated with right hippocampal volume. Over and above the effects of perceived stress, maternal psychological distress, material hardship, neighborhood quality, and intimate partner violence were not significantly associated with hippocampal volumes. Critically, maternal perceived stress was associated with reduced right hippocampal subfield volumes (CA1, CA3, and CA4/dentate gyrus) when children had higher levels of prenatal exposure to air pollution. Finally, in exploratory analyses, hippocampal CA3 and CA4/dentate gyrus volumes were positively associated with visuospatial abilities. Overall, our results point to the need to measure and consider multiple exposures when studying threats to neurodevelopment, particularly in the context of socioeconomic deprivation.

Prior studies have examined associations between household (17–19) and neighborhood (20) socioeconomic status and hippocampal volumes; here, we extend this work with a preliminary study of the contributions of different aspects of socioeconomic status–related stress and stressors on the hippocampus. In our study, maternal perceived stress was associated with smaller right hippocampal volume. Effects were not significant for maternal psychological distress, material hardship, neighborhood quality, or intimate partner violence (though some were trend-level significant). Note that maternal stress effects on the left hemisphere were significant but did not pass FDR correction; we also did not see significant differences in the strength of this effect in the left versus right hemisphere. Our findings are consistent with prior work showing inverse associations between maternal anxiety or psychosocial stress and hippocampal volume in animal models (10,12–15) and in newborns and children (21,22). Our measure may reflect the effect of maternal stress on children's neurodevelopment or may act as a proxy for stress in the home environment, each of which could have separate biological mechanisms; we are limited in our ability to discern this as the cohort study did not include direct report of children's experience of stress. Our findings are further limited by the measurement of maternal stress at child age 5, as we have recently shown that the effects of poverty on hippocampal volumes in these children were most salient prior to age 4.5 (74). Timing-specific effects on the hippocampus have additionally been found for general adverse experiences and maternal support (24,75,76). Future research should interrogate the timing for critical periods of vulnerability, neuroanatomical change, and the manifestation of symptoms.

Consistent with prior studies showing that prenatal PAH exposure moderates effects of ELS on neurodevelopmental outcomes (41,42), we detected a significant interaction between prenatal PAH exposure and maternal perceived stress on the right CA1, CA3, and CA4/dentate gyrus volumes. Our analyses focused on these hippocampal subregions because of the converging evidence in animal models linking both air pollution and ELS to these regions. A full multivariate model would better address the aims of the project but would be underpowered with $n = 40$ participants. Neurobiological findings converging on hippocampal subregions provide a coherent framework to understand the mutual effects of ELS to maternal perceived stress and air pollution, which may give rise to the cognitive and behavioral deficits observed in hippocampus-dependent tasks. Animal models and human epidemiological findings point to a potential biological mechanism underlying the associations observed herein. We hypothesize that effects of prenatal exposure to air

pollution on hippocampal BDNF may cause increased vulnerability to stress via reductions in hippocampal BDNF, which buffers against the deleterious effects of stress (77–79). This proposed mechanism requires further study and may offer future directions for both pharmacological and public health intervention/prevention strategies. In addition, we did not detect a significant interaction between prenatal PAH exposure and maternal perceived stress on the whole hippocampal volume, suggesting that those subfields not included in our analyses are not implicated in the PAH $\times$ stress interaction.

Finally, we observed associations between hippocampal subfield volumes and visuospatial abilities, as measured by PIQ. The contemporaneous measurement of hippocampal volume and PIQ limits our ability to establish a directional mechanism by which the compounding effects of social and physical stressors impact visuospatial abilities. Still, animal models have shown effects of stress and air pollution on visuospatial learning and memory and on hippocampal structure (57,58). Future studies should examine whether alterations to specific hippocampal subfields mediate the effects of these exposures on visuospatial processing.

Effects of prenatal exposure to air pollution can be transmitted across generations. In animal models, maternal exposure to $PM_{2.5}$ during pregnancy induced deficits in spatial learning and memory for a subsequent second generation not exposed to $PM_{2.5}$ in utero. Such findings suggest that early-life exposure to $PM_{2.5}$ may shape the intergenerational risk for neurobehavioral alterations (28). Multiple potential mechanisms may account for this intergenerational effect, e.g., maternal stress may influence the child's development via parenting or other home environment factors and/or via direct effects of maternal stress on the placenta during critical periods of brain development.

Although we account for certain factors that could have confounded our findings, there may be additional unmeasured factors that associate with living near pollution sources, such as noise or vibrations near roadways (80–82), that could contribute to the observed effects of prenatal PAH on brain structure. Prior animal and human work also suggests the potential for sex-specific effects (55), but our study was limited in sample size, and thus we could not test sex-specific effects. Future studies should investigate sex-specific effects of prenatal exposure to air pollution on visuospatial processes and their intergenerational transmission. Current findings may also inform potential etiologic pathways to nonverbal learning disability [alternatively called developmental visuospatial disorder (83)] or other neurodevelopmental disorders that are sometimes characterized by visuospatial deficits, such as autism spectrum disorder (84). Future studies should investigate this potential underlying mechanism and should attempt to measure and control for additional factors such as roadway noise and vibrations to isolate the specificity of observed effects. Given that we conducted our study in a birth cohort of Black and Latinx children from economically disadvantaged backgrounds, our results may not generalize to children from more diverse socioeconomic (parent education, occupation, income), ethnic, or racial backgrounds.

Prenatal and ELS to chemical and social stressors are likely compounding, acting through complex biological mechanisms causing the increased risk of these exposures to exert critical biological effects. These interactions likely extend beyond exposures studied herein. For example, maternal anxiety or psychosocial stress is associated with reductions in

hippocampal volumes (21,22), but maternal support associated with increased hippocampal volumes (23), perhaps indicating a buffering effect of support. These effects have additionally been shown to interact with prenatal risk factors at the hippocampus such as preterm birth (85). By developing a deeper understanding of these complex interactions, we may develop more focused public health prevention strategies that will help protect the developmental trajectory of those children at greatest risk for mental and physical health effects associated with socioeconomic disadvantage.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGMENTS AND DISCLOSURES

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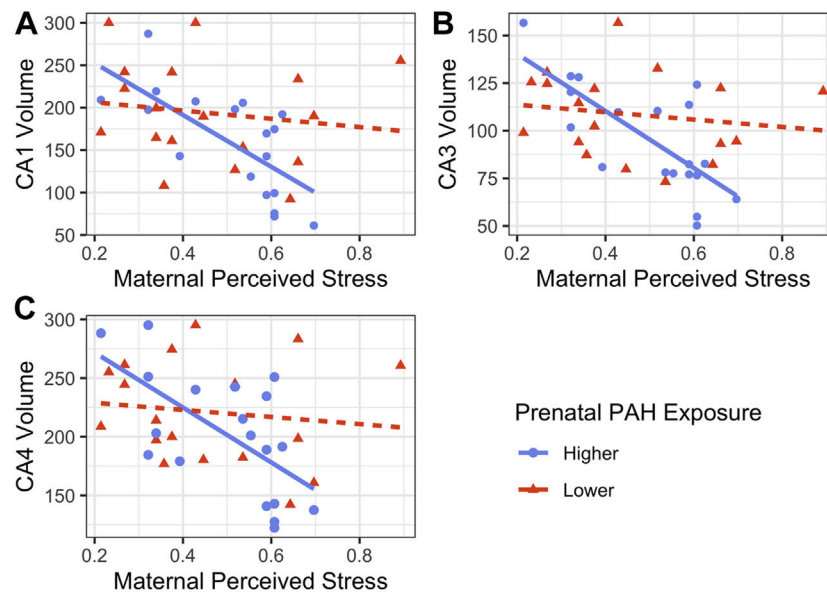
Figure 1.
Prenatal polycyclic aromatic hydrocarbon (PAH) exposure moderates the association between maternal perceived stress (0–1 scale) at age 5 and right hippocampal **(A)** CA1, **(B)** CA3, and **(C)** CA4/dentate gyrus subfield volumes (mm^3), winsorized and residualized for age, sex assigned at birth, and intracranial volume ($n = 37$: $n_{higher} = 19$, $n_{lower} = 18$).
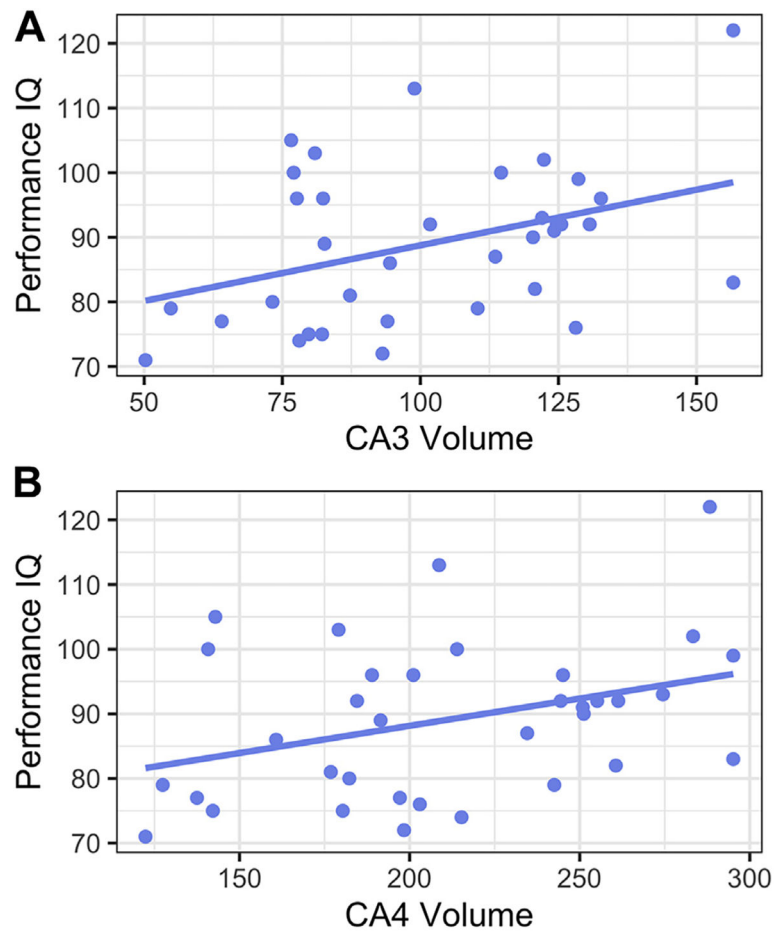
Figure 2.
Hippocampal subfield volumes CA3 (**A**) and CA4/dentate gyrus (**B**), winsorized and residualized for age, sex assigned at birth, and intracranial volume, predict visuospatial reasoning (performance IQ).

Table 1.

Demographic, Psychosocial, and Cognitive Characteristics of the Sample ($n = 40$)

Characteristics	n (%) or Mean (SD) [Median]
Sex Assigned at Birth, Male	17 (42.5%)
Race/Ethnicity	
Black	18 (45%)
Hispanic/Latinx	22 (55%)
Age, Months	103.62 (9.03) [106.00]
VIQ Score	94.73 (14.44) [92.00]
PIQ Score	89.14 (11.82) [90.00]
Maternal Education, Years	12.25 (1.6) [12.00]
Total PAH, ng/m^3	1.98 (1.22) [1.60]

$n = 2$ missing PIQ. $n = 2$ missing VIQ. $n = 3$ missing total PAH.

PAH, polycyclic aromatic hydrocarbon; PIQ, performance IQ; VIQ, verbal IQ.

Table 2.

Simple Slopes Analysis for the Maternal Perceived Stress × Prenatal PAH Exposure Interaction Effect on CA1, CA3, and CA4/Dentate Gyrus Subfield Volumes

Subfields	PAH Exposure	B	SE	t	p	95% CI
CA1	Lower	−0.13	0.18	−0.70	.487	−0.50 to 0.24
	Higher	−0.81	0.24	−3.34	.002	−1.30 to −0.32
CA3	Lower	−0.12	0.17	−0.71	.484	−0.47 to 0.23
	Higher	−0.94	0.23	−4.12	<.001	−1.40 to −0.47
CA4/Dentate Gyrus	Lower	−0.10	0.19	−0.53	.598	−0.48 to 0.28
	Higher	−0.78	0.25	−3.13	.004	−1.29 to −0.27

Each simple slope was independently tested for significance using a t test ($n = 37$: $n_{higher} = 19$, $n_{lower} = 18$).

PAH, polycyclic aromatic hydrocarbon.

KEY RESOURCES TABLE

Resource Type	Specific Reagent or Resource	Source or Reference	Identifiers	Additional Information
Add additional rows as needed for each resource type	Include species and sex when applicable.	Include name of manufacturer, company, repository, individual, or research lab. Include PMID or DOI for references; use "this paper" if new.	Include catalog numbers, stock numbers, database IDs or accession numbers, and/or RRIDs. RRIDs are highly encouraged; search for RRIDs at https://scicrunch.org/resources.	Include any additional information or notes if necessary.
Antibody	none			
Bacterial or Viral Strain	none			
Biological Sample	none			
Cell Line	none			
Chemical Compound or Drug	none			
Commercial Assay Or Kit	none			
Deposited Data; Public Database	none			
Genetic Reagent	none			
Organism/Strain	none			
Peptide, Recombinant Protein	none			
Recombinant DNA	none			
Sequence-Based Reagent	none			
Software; Algorithm	R software package, FreeSurfer v6.0 pipeline (recon-all)			
Transfected Construct	none			
Other	none			