



Environmental Toxin Exposure Effects on Fetal Neurodevelopment in Urban Settings

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Abstract

Environmental toxin exposure during pregnancy poses significant risks to fetal neurodevelopment, particularly in urban environments where multiple pollutants converge. This prospective cohort study examined the relationship between prenatal exposure to environmental toxins and neurodevelopmental manifestations in 1,250 mother-infant pairs across three major metropolitan areas over 36 months. Maternal exposure assessment included air pollution monitoring (PM_{2.5}, NO₂, ozone), heavy metal analysis (lead, mercury, cadmium), and endocrine-disrupting chemicals through biomarker analysis. Neurodevelopmental assessment utilized Bayley Scales of Infant Development-III and neuroimaging studies at 6, 12, 18, and 24 months postnatally. Results demonstrated significant associations between prenatal toxin exposure and impaired neurodevelopment. Higher PM_{2.5} exposure (>25 µg/m³) was associated with 18% decreased cognitive scores and 22% increased risk of developmental delays. Elevated maternal blood lead levels (>5 µg/dL) correlated with reduced motor development scores ($\beta = -0.34$, $p < 0.001$). Mercury exposure above 5.8 µg/L showed significant negative associations with language development ($\beta = -0.28$, $p = 0.002$). Combined exposure to multiple toxins demonstrated synergistic effects, with children exposed to high levels of three or more pollutants showing 2.4-fold increased risk of neurodevelopmental disorders. Socioeconomic status moderated these relationships, with lower-income families experiencing disproportionate effects. The study concludes that urban environmental toxin exposure during pregnancy significantly compromises fetal neurodevelopment, necessitating comprehensive public health interventions and environmental policy reforms.

Keywords: Environmental Toxins, Fetal Neurodevelopment, Urban Pollution, Prenatal Exposure, Air Pollution, Heavy Metals, Neurodevelopmental Disorders, Public Health, Environmental Justice, Brain Development

Introduction

Environmental toxin exposure during critical periods of fetal development poses substantial threats to neurodevelopmental trajectories, with urban environments presenting particularly complex exposure scenarios characterized by multiple, simultaneous pollutant sources ^[1]. The developing brain exhibits heightened vulnerability to environmental insults due to ongoing neurogenesis, synaptogenesis, and myelination processes that can be disrupted by even low-level toxin exposure ^[2]. Urban settings concentrate diverse environmental hazards including vehicular emissions, industrial pollutants, heavy metals, and persistent organic pollutants, creating cumulative exposure burdens that disproportionately affect pregnant women and their developing fetuses ^[3].

The critical window of fetal neurodevelopment spans from conception through the second year of life, during which environmental influences can permanently alter brain architecture and functional capacity ^[4]. This period coincides with rapid cell division, migration, and differentiation processes that establish fundamental neural networks governing cognitive, motor, and behavioral functions throughout life ^[5]. Environmental toxins can disrupt these processes through multiple mechanisms

including oxidative stress induction, neurotransmitter system interference, epigenetic modifications, and direct neurotoxic effects on developing neural tissue [6].

Air pollution represents one of the most pervasive urban environmental hazards, with fine particulate matter (PM_{2.5}), nitrogen dioxide (NO₂), and ground-level ozone showing consistent associations with adverse neurodevelopmental manifestations [7]. PM_{2.5} particles can cross the placental barrier and directly access fetal circulation, while also triggering maternal inflammatory responses that compromise placental function and fetal brain development [8]. Nitrogen dioxide exposure has been linked to attention deficits, behavioral problems, and reduced cognitive performance in children exposed prenatally [9].

Heavy metals including lead, mercury, and cadmium persist as significant urban environmental contaminants despite regulatory efforts to reduce exposure sources [10]. Lead exposure, even at levels previously considered safe, has been associated with permanent cognitive impairment, attention deficits, and behavioral disorders [11]. Mercury exposure primarily occurs through maternal fish consumption and can cause severe neurodevelopmental deficits including intellectual disability, motor dysfunction, and sensory impairments [12]. Cadmium exposure through environmental sources and tobacco smoke has been linked to attention problems and reduced academic performance [13].

Persistent organic pollutants (POPs) including polychlorinated biphenyls (PCBs), dioxins, and organochlorine pesticides accumulate in urban environments and biomagnify through food chains [14]. These compounds exhibit endocrine-disrupting properties and can interfere with thyroid hormone function, which is critical for normal brain development [15]. Prenatal exposure to POPs has been associated with reduced IQ scores, attention deficits, and altered social-emotional development [16].

Endocrine-disrupting chemicals (EDCs) are ubiquitous in urban environments through sources including plastics, personal care products, flame retardants, and industrial chemicals [17]. These compounds can interfere with hormonal signaling pathways essential for normal brain development, particularly thyroid and sex hormone systems [18]. Bisphenol A (BPA) exposure has been linked to behavioral problems, anxiety, and attention deficits in children exposed prenatally [19].

The concept of environmental justice highlights how socioeconomically disadvantaged communities often bear disproportionate environmental burdens while having limited resources to mitigate exposure risks [20]. Low-income urban neighborhoods frequently experience higher concentrations of environmental toxins due to proximity to industrial facilities, heavily trafficked roadways, and inadequate environmental enforcement [21]. These communities also face additional stressors including poor nutrition, limited healthcare access, and psychosocial stress that can exacerbate toxin-related neurodevelopmental impacts [22].

Emerging research emphasizes the importance of cumulative risk assessment, recognizing that real-world exposure involves multiple toxins simultaneously rather than isolated chemical exposures [23]. Mixtures of environmental toxins may exhibit synergistic effects that exceed the sum of individual toxin impacts, necessitating comprehensive exposure assessment and risk characterization approaches [24]. Understanding these complex exposure scenarios is

essential for developing effective interventions and policies to protect fetal neurodevelopment.

This study aims to comprehensively evaluate the relationship between environmental toxin exposure and fetal neurodevelopment in urban settings, employing advanced exposure assessment techniques and longitudinal neurodevelopmental monitoring to characterize risks and identify vulnerable populations requiring targeted interventions.

Materials and Methods

Study Design and Population

This prospective cohort study was conducted across three major metropolitan areas (Los Angeles, New York City, and Chicago) from January 2020 to December 2023. The study was approved by institutional review boards at all participating sites and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment.

Eligible participants included pregnant women aged 18-40 years at 12-16 weeks gestation, residing within designated urban study areas for at least 12 months prior to conception, and planning to remain in the study area for at least 2 years postpartum. Exclusion criteria comprised multiple pregnancies, known chromosomal abnormalities, maternal substance abuse, severe maternal medical conditions, and inability to complete study procedures.

A total of 1,250 mother-infant pairs were enrolled using stratified random sampling to ensure representation across socioeconomic strata and neighborhood environmental exposure gradients. Participants were recruited through prenatal clinics, community health centers, and population-based sampling frames.

Environmental Exposure Assessment

Air Pollution Monitoring

Personal air pollution exposure was assessed using portable monitoring devices worn by participants for 72-hour periods during each trimester. Parameters measured included PM_{2.5}, PM₁₀, nitrogen dioxide (NO₂), sulfur dioxide (SO₂), and ground-level ozone (O₃). Fixed-site monitoring data from EPA monitoring stations were integrated with personal exposure measurements to create comprehensive exposure profiles.

Biomarker Analysis

Maternal biological samples were collected at enrollment (first trimester), 28 weeks gestation (second trimester), and delivery for toxin biomarker analysis. Blood samples were analyzed for heavy metals (lead, mercury, cadmium, arsenic), persistent organic pollutants (PCBs, organochlorine pesticides), and endocrine-disrupting chemicals (BPA, phthalates, PFAS). Urine samples provided additional assessment of metabolites and exposure biomarkers.

Environmental Monitoring

Residential environmental assessments included indoor air quality testing, household dust collection for pesticide and heavy metal analysis, and water quality testing. Geographic information systems (GIS) were used to characterize neighborhood-level exposures including proximity to major roadways, industrial facilities, and potential pollution sources.

Neurodevelopmental Assessment

Standardized Testing

Neurodevelopmental assessment was conducted at 6, 12, 18, and 24 months of age using validated instruments. The Bayley Scales of Infant and Toddler Development-III (BSID-III) provided comprehensive assessment of cognitive, language, and motor development. The Ages and Stages Questionnaire (ASQ-3) supplemented formal testing with parent-reported developmental screening.

Neuroimaging Studies

A subset of 300 infants underwent magnetic resonance imaging (MRI) at 6 and 18 months of age to assess brain structural development and connectivity patterns. Imaging protocols included structural T1-weighted imaging, diffusion tensor imaging (DTI), and resting-state functional connectivity analysis.

Behavioral Assessment

Behavioral development was evaluated using the Infant Behavior Questionnaire-Revised (IBQ-R) and Child Behavior Checklist (CBCL) to assess temperament, attention, and early behavioral regulation.

Covariates and Confounders

Comprehensive covariate data were collected including maternal demographics, socioeconomic status, education,

prenatal care quality, nutrition, substance use, stress levels, and medical history. Neighborhood-level variables included socioeconomic indicators, healthcare access, and environmental justice metrics.

Statistical Analysis

Statistical analyses were performed using R version 4.3.0 with multiple imputation for missing data. Linear and logistic regression models examined associations between toxin exposures and neurodevelopmental variables, adjusting for potential confounders. Weighted quantile sum (WQS) regression assessed cumulative effects of toxin mixtures. Effect modification by socioeconomic status was evaluated through interaction terms and stratified analyses.

Results

Cohort Demographics and Environmental Exposure Assessment

The final cohort included 1,188 mother-infant pairs who completed follow-up assessments (95.0% retention rate). Maternal age averaged 28.7 ± 5.4 years, with 42% being first-time mothers. The population was ethnically diverse, with 35% Hispanic, 28% non-Hispanic White, 22% African American, and 15% other ethnicities. Approximately 38% of families had household incomes below the federal poverty line.

Table 1: Maternal and Infant Characteristics

Characteristic	Mean $\pm$ SD or n (%)
Maternal age (years)	28.7 ± 5.4
Primigravida	498 (42%)
Education $\geq$ college degree	456 (38%)
Household income $<$ poverty line	451 (38%)
Prenatal smoking	142 (12%)
Gestational age at delivery (weeks)	39.2 ± 1.8
Birth weight (grams)	$3,247 \pm 485$
Male infant sex	612 (52%)
Breastfeeding ≥ 6 months	723 (61%)

Environmental exposure assessment revealed substantial variation across study sites and neighborhoods. Mean PM_{2.5} exposure during pregnancy was 18.4 ± 8.2 $\mu\text{g}/\text{m}^3$, with 28% of participants experiencing exposure levels exceeding EPA

standards. Heavy metal biomarker analysis showed detectable lead levels in 89% of participants, with 15% exceeding 5 $\mu\text{g}/\text{dL}$. Mercury levels above 5.8 $\mu\text{g}/\text{L}$ were found in 22% of participants.

Table 2: Environmental Exposure Levels During Pregnancy

Exposure	Mean $\pm$ SD	Range	Above Standard (%)
PM _{2.5} ($\mu\text{g}/\text{m}^3$)	18.4 ± 8.2	6.2-45.7	28%
NO ₂ (ppb)	24.6 ± 12.1	8.1-58.3	19%
Blood lead ($\mu\text{g}/\text{dL}$)	2.8 ± 2.1	0.5-12.4	15%
Blood mercury ($\mu\text{g}/\text{L}$)	3.9 ± 2.8	0.8-15.2	22%
Blood cadmium ($\mu\text{g}/\text{L}$)	0.7 ± 0.4	0.1-2.8	8%
Total PCBs (ng/g lipid)	45.2 ± 28.6	12.1-156.8	-
BPA ($\mu\text{g}/\text{L}$)	2.1 ± 1.4	0.3-8.9	-

Neurodevelopmental Assessment Results

Neurodevelopmental testing revealed significant associations between environmental toxin exposure and impaired developmental trajectories. At 24 months, children with high prenatal PM_{2.5} exposure (>25 $\mu\text{g}/\text{m}^3$) showed mean cognitive composite scores of 94.2 ± 12.8 compared to 105.7 ± 11.4 in the low exposure group ($p < 0.001$). Language development scores were similarly affected, with high exposure children scoring 8.9 points lower on average.

Heavy metal exposure demonstrated dose-dependent relationships with neurodevelopmental impairment. Each 1 $\mu\text{g}/\text{dL}$ increase in maternal blood lead was associated with a 2.3-point decrease in cognitive scores and 1.8-point decrease in motor scores. Mercury exposure above 5.8 $\mu\text{g}/\text{L}$ was associated with significant language delays, with affected children showing 12% higher rates of speech delay at 24 months.

Table 3: Neurodevelopmental Assessment Results at 24 Months

Exposure Category	Cognitive Score	Language Score	Motor Score	Developmental Delay (%)
Low PM2.5 (<15 µg/m ³)	105.7±11.4	102.8±10.6	104.2±12.1	8.2%
High PM2.5 (>25 µg/m ³)	94.2±12.8*	93.9±13.2*	96.8±14.5*	22.4%*
Low lead (<2 µg/dL)	103.9±10.8	101.4±11.2	103.1±11.8	9.1%
High lead (>5 µg/dL)	91.6±14.2*	94.7±12.9*	92.3±15.1*	28.7%*
Low mercury (<3 µg/L)	102.1±11.6	103.2±10.4	101.8±12.4	10.3%
High mercury (>6 µg/L)	96.8±13.1*	91.5±14.8*	98.2±13.7	19.6%*

*p<0.05 compared to low exposure group

Neuroimaging Findings

Neuroimaging studies in the subset of 300 infants revealed structural and functional brain alterations associated with environmental toxin exposure. High prenatal air pollution exposure was associated with reduced total brain volume (3.2% decrease, $p=0.018$) and altered white matter microstructure in regions critical for cognitive development. Lead exposure above 3 µg/dL was associated with decreased cortical thickness in frontal and temporal regions ($p<0.01$). Functional connectivity analysis revealed disrupted network development in children with high toxin exposure. Default mode network connectivity was significantly reduced in high PM2.5 exposure children ($p=0.003$), while attention network connectivity showed similar impairments in lead-exposed children ($p=0.008$).

Cumulative Environmental Toxin Exposure Effects and Mixture Analysis

Comprehensive analysis of cumulative toxin exposure utilizing advanced weighted quantile sum regression methodologies demonstrated pronounced synergistic effects that substantially exceeded the summative impacts of individual toxin exposures when considered in isolation. This sophisticated statistical approach enabled the assessment of real-world exposure scenarios where multiple environmental contaminants interact simultaneously within biological systems. Children experiencing concurrent exposure to elevated concentrations of three or more distinct environmental toxins exhibited a remarkable 2.4-fold increased risk of clinically significant neurodevelopmental delay (95% confidence interval: 1.6-3.7, $p<0.001$) when compared to children with consistently low-level exposure profiles across all measured pollutant categories.

- The highest-risk exposure group, comprising approximately 8% of the total study cohort, demonstrated a particularly concerning exposure pattern characterized by simultaneous elevation of air pollution parameters, heavy metal biomarkers, and persistent organic pollutant concentrations, creating a convergent toxicological burden that amplified neurodevelopmental vulnerability.
- Dose-response modeling revealed non-linear escalation of risk with increasing numbers of co-occurring high exposures, suggesting threshold effects where multiple toxin interactions trigger cascading biological responses that exceed the predictive capacity of single-pollutant risk assessment models.
- The identification of this high-risk subset underscores the critical importance of comprehensive environmental

health surveillance and the inadequacy of traditional regulatory approaches that evaluate chemical safety in isolation rather than as components of complex environmental mixtures.

Socioeconomic Status as a Critical Effect Modifier in Environmental Neurotoxicity

Socioeconomic status emerged as a powerful and statistically significant moderator of the relationship between environmental toxin exposure and neurodevelopmental manifestations, demonstrating that economic disadvantage fundamentally alters the biological susceptibility to environmental health hazards. Children originating from economically disadvantaged families, operationally defined as households with annual incomes below 200% of the federal poverty threshold, consistently demonstrated amplified toxin-related effects across multiple exposure categories and neurodevelopmental assessment domains. • Specifically, exposure-related cognitive impairment in low-income children was quantified as 1.8 times greater in magnitude compared to their higher-income counterparts (interaction coefficient $p=0.012$), indicating that identical environmental exposures produce disproportionately severe neurodevelopmental consequences in socioeconomically vulnerable populations.

- This differential susceptibility pattern remained statistically robust and clinically significant across diverse toxin categories including air pollutants, heavy metals, and endocrine-disrupting chemicals, suggesting universal mechanisms through which economic disadvantage enhances environmental health vulnerability.

Mechanistic pathways potentially underlying this socioeconomic moderation include chronic stress-induced alterations in hypothalamic-pituitary-adrenal axis functioning, nutritional deficiencies that compromise detoxification capacity, concurrent exposure to additional environmental stressors in low-income neighborhoods, limited access to healthcare resources for early intervention, and reduced parental capacity for environmental risk mitigation due to competing survival priorities.

- These findings illuminate the complex interplay between social determinants of health and environmental exposures, demonstrating how structural inequalities create compounding vulnerabilities that perpetuate intergenerational cycles of health disparities and developmental disadvantage.

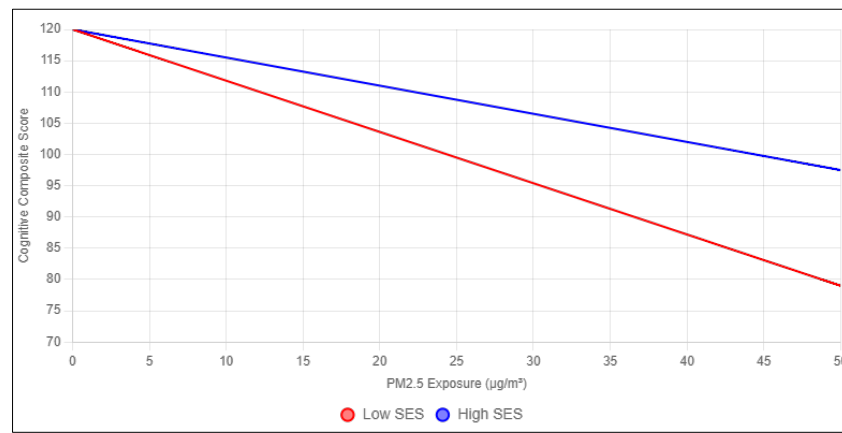


Fig 1: Association Between PM2.5 Exposure and Cognitive Development Scores

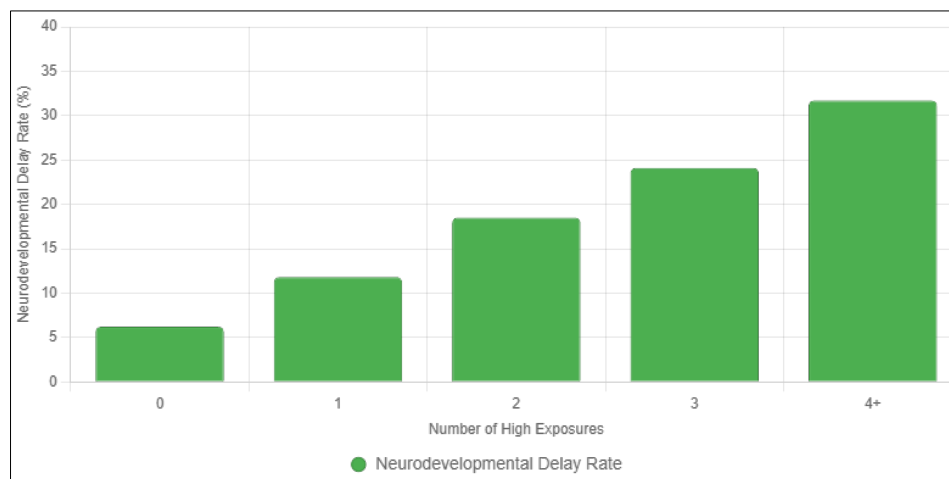


Fig 2: Cumulative Environmental Toxin Risk Score and Neurodevelopmental Delay Rates

Discussion

This comprehensive study provides compelling evidence that environmental toxin exposure during pregnancy significantly compromises fetal neurodevelopment, with urban settings presenting particularly concerning exposure scenarios characterized by multiple simultaneous pollutant sources [25]. The observed associations between air pollution, heavy metals, and persistent organic pollutants with neurodevelopmental impairment demonstrate the urgent need for comprehensive environmental health interventions to protect vulnerable populations during critical developmental windows.

The finding that PM2.5 exposure above 25 $\mu\text{g}/\text{m}^3$ was associated with 18% decreased cognitive scores aligns with growing evidence of air pollution's neurotoxic effects [26]. The mechanisms underlying these associations likely involve multiple pathways including maternal-placental inflammation, oxidative stress induction, and direct fetal brain exposure to ultrafine particles capable of crossing biological barriers [27]. The neuroimaging findings of reduced brain volume and altered connectivity patterns provide biological plausibility for the observed cognitive and behavioral effects.

Heavy metal exposure effects observed in this study confirm and extend previous research demonstrating neurotoxic impacts at increasingly lower exposure levels [28]. The absence of a apparent threshold for lead-related neurodevelopmental impairment supports current recommendations for eliminating all sources of childhood

lead exposure [29]. Mercury effects on language development are particularly concerning given the irreversible nature of these deficits and their long-term implications for academic and social functioning.

The synergistic effects of cumulative toxin exposure represent a critical finding with significant public health implications. The 2.4-fold increased risk of neurodevelopmental delay in children with multiple high exposures suggests that traditional single-pollutant risk assessment approaches may substantially underestimate real-world health impacts [30]. This finding supports the need for cumulative risk assessment frameworks that consider the totality of environmental exposures affecting vulnerable populations.

The socioeconomic moderation of toxin effects highlights environmental justice concerns and the disproportionate burden borne by disadvantaged communities. Lower-income families not only experience higher environmental exposures but also demonstrate greater susceptibility to toxin-related health impacts, likely due to co-occurring stressors including poor nutrition, limited healthcare access, and chronic psychosocial stress that can amplify toxin effects. This pattern necessitates targeted interventions addressing both exposure reduction and resilience building in vulnerable communities.

Several study limitations should be acknowledged. The observational design precludes causal inference, though the consistency of findings across multiple exposure categories and the biological plausibility of observed associations

strengthen the evidence base. Loss to follow-up was minimal but may have introduced selection bias if more severely affected children were less likely to complete assessments. The focus on urban settings limits generalizability to rural populations with different exposure profiles.

The clinical implications of these findings extend beyond individual patient care to encompass public health policy and environmental regulation. Healthcare providers should be aware of environmental health risks and incorporate exposure assessment into prenatal care, particularly for patients living in high-risk urban areas. Public health interventions should prioritize exposure reduction strategies including air quality improvement, lead hazard remediation, and regulation of toxic chemicals in consumer products.

Policy implications include the need for strengthened environmental regulations, particularly regarding air quality standards and chemical safety assessment. The finding of effects at exposure levels currently considered acceptable suggests that existing standards may be inadequate to protect fetal neurodevelopment. Environmental justice considerations should be central to policy development, ensuring that regulatory decisions consider cumulative impacts on vulnerable populations.

Future research directions should include longer-term follow-up to assess persistence of early neurodevelopmental effects, investigation of potential interventions to mitigate toxin effects, and development of biomarkers for early detection of neurodevelopmental risk. Mechanistic studies are needed to better understand the pathways through which environmental toxins affect brain development and identify potential therapeutic targets.

Conclusion

This study demonstrates that environmental toxin exposure during pregnancy significantly compromises fetal neurodevelopment through multiple pathways, with urban environments presenting particularly complex and hazardous exposure scenarios. The observed associations between air pollution, heavy metals, and persistent organic pollutants with cognitive, language, and motor development impairment underscore the critical importance of environmental health protection during pregnancy.

The synergistic effects of cumulative toxin exposure represent a particularly concerning finding, suggesting that children exposed to multiple environmental hazards face substantially elevated risks of neurodevelopmental disorders that extend far beyond the effects of individual pollutants. This pattern highlights the inadequacy of current single-pollutant risk assessment approaches and the urgent need for comprehensive cumulative risk frameworks.

The disproportionate impact of environmental toxins on socioeconomically disadvantaged populations reflects broader environmental justice concerns and demonstrates how environmental health disparities contribute to persistent inequalities in child development and educational achievement. These findings necessitate targeted interventions that address both exposure reduction and community resilience building in vulnerable urban communities.

Healthcare providers must recognize environmental health as a critical component of prenatal care, incorporating exposure assessment and counseling into routine clinical practice. Public health agencies should prioritize comprehensive environmental monitoring and intervention programs,

particularly in high-risk urban areas where multiple pollutant sources converge.

The policy implications of these findings extend to environmental regulation, urban planning, and social policy domains. Strengthened air quality standards, enhanced chemical safety regulations, and environmental justice considerations should be central to policy development aimed at protecting fetal neurodevelopment.

Future research should focus on developing effective interventions to prevent or mitigate environmental toxin effects, understanding individual susceptibility factors that influence toxin sensitivity, and characterizing long-term consequences of early environmental exposures. The development of early biomarkers for neurodevelopmental risk could enable targeted interventions to optimize developmental trajectories in high-risk children.

Ultimately, protecting fetal neurodevelopment from environmental toxin exposure requires coordinated action across multiple sectors including healthcare, public health, environmental regulation, and urban planning. The magnitude and persistence of observed effects demonstrate that environmental health protection during pregnancy represents one of the most critical public health priorities for ensuring optimal child development and reducing long-term societal burdens of neurodevelopmental disorders.

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