

A comprehensive narrative review of critical windows of vulnerability in brain development and environmental exposures: timing matters

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ABSTRACT

This narrative review synthesises recent evidence on how climatic and environmental exposures shape neurodevelopment across sensitive windows. A search of Embase, PubMed, Scopus, and Web of Science (January 2020–April 2026) identified 46 studies spanning epidemiology, clinical outcomes, mechanisms and neuroimaging. Climatic stressors (temperature extremes, rainfall shocks, superstorms, El Niño–Southern Oscillation) and pollutants (PM_{2.5}/NO₂/O₃/PAHs; Pb/Hg/Cd/As/Mn; organophosphates/pyrethroids; phthalates/bisphenols/PFAS) were consistently associated with increased risk of adverse neurodevelopmental outcomes across critical developmental windows, including language, attention, executive and motor function, emotion regulation and mental health. Neuroimaging studies reported changes in white matter maturation, hippocampal and amygdala development, basal ganglia and cortical morphology and large-scale functional connectivity. Converging mechanisms - including oxidative stress, neuroinflammation, endocrine and placental dysfunction, vascular injury and immune activation - provide biological plausibility; epigenetic modifications may act as shared integrators or independent pathways influencing long-term outcomes. Vulnerability peaked from periconception through early postnatal life, with infancy–toddlerhood and adolescence as additional sensitive phases. Socio-economic disadvantage, co-exposures and contextual factors (urban heat islands; mining, agricultural and flood-prone areas) amplified risk, while cash transfers, breastfeeding and adaptive practices were protective. Environmental and climatic exposures are modifiable determinants of child brain health. Environmental factors should be considered - at least - within routine maternal and childcare through brief screening of potentially modifiable exposures. Schools and communities also play a role in awareness and adaptive responses. Coordinated, context-sensitive research using harmonised exposome-based models is needed. Protecting the developing brain from environmental and climatic threats is a scientific and ethical imperative aligned with the Sustainable Development Goals.

1. Introduction

Brain development is a prolonged and dynamic process from conception through young adulthood, during which the central nervous system (CNS) undergoes coordinated stages (neurulation, neuronal migration, synaptogenesis, myelination and pruning) that shape its structural and functional architecture.¹ Each phase represents a window of vulnerability in which environmental perturbations can leave lifelong

neurobiological and psychological effects.² The concept of critical developmental windows has therefore become central in paediatric neuroscience, highlighting that the timing of exposure is often as decisive as its magnitude.³

Over the past two decades, growing evidence has shown that climatic and environmental factors, including air pollution, temperature extremes, pesticides, heavy metals and endocrine-disrupting chemicals, interfere with neurodevelopment.^{4–6} For instance, longitudinal and

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cohort studies correlate these exposures with altered cognition, language, attention, executive function, motor coordination and mental health.^{7–11} Particulate matter (PM_{2.5}), nitrogen dioxide and polycyclic aromatic hydrocarbons are associated with white-matter and cognitive impairments,^{7,12,13} while lead, manganese and arsenic produce have additive effects on motor, language and cognitive development.⁸ Increasing evidence suggests that these adverse neurodevelopmental outcomes are underpinned by converging biological mechanisms that disrupt brain maturation and neural integrity across critical developmental windows.^{2,14} In this context, mitochondrial dysfunction, oxidative stress, neuroinflammation and endocrine disruption represent shared biological pathways of nervous tissue damage.^{7,8} Moreover, epigenetic dysregulation mediates long-term vulnerability, with prenatal toxicant exposure altering DNA methylation and histone modification in neural and placental tissues.^{15,16}

Importantly, the burden of these environmental and biological risks is not evenly distributed across populations. Children in low- and middle-income or polluted urban areas are disproportionately exposed with limited protection.^{3,8}

Beyond chemical pollutants, increasing attention has recently focused on the role of climate-related environmental stressors as additional and interacting determinants of early neurodevelopment.^{17,18} In particular, thermal extremes, rainfall variability and air-quality degradation are recognised as emerging determinants of maternal-foetal health.¹⁹ As noted by Olson and Metz,²⁰ these factors may affect foetal brain development through mechanisms including maternal stress, allostatic overload, placental dysfunction and maternal immune activation.

However, despite growing recognition of the links between environmental and climate-related exposures and neurodevelopmental vulnerability, the current body of evidence remains difficult to interpret within a consistent and integrated framework. The complexity and interdependence of these mechanisms make it challenging to draw consistent conclusions across studies. Moreover, methodological heterogeneity, non-linear climatic models and inconsistent multi-exposure analyses hinder cross-study comparability and generalisability.²¹

At the same time, the field has undergone a substantial methodological transition in recent years. Contemporary environmental neuroscience increasingly adopts exposome-oriented frameworks that move beyond traditional single exposure–single outcome paradigms and instead integrate multiple environmental exposures, developmental timing, neuroimaging markers and molecular biological measures to characterise neurodevelopmental vulnerability across the life course.²² Likewise, recent advances in environmental epidemiology have promoted multi-exposure and exposome-based approaches capable of capturing cumulative and interacting environmental influences on health outcomes.²³ This shift has been accompanied by increasing attention to critical developmental windows and the biological embedding of environmental adversity across development.

Finally, recent climate-health literature suggests increasing complexity and intensification of environmental and climate-related exposures in the context of evolving climate and environmental conditions, driven by the growing frequency, co-occurrence and non-linearity of extreme climatic events and associated environmental stressors.^{24–26} Together, these conceptual, methodological and environmental changes highlight the need for updated syntheses capable of integrating emerging evidence across biological, developmental and contextual dimensions.

Therefore, the aim of this narrative review is to provide an updated and integrative overview of how climatic and environmental exposures influence neurodevelopment across sensitive periods, considering epidemiological, mechanistic and contextual perspectives. By synthesising the most recent evidence, the review seeks to address three main questions:

- (i) which critical developmental windows - from conception to adolescence - are most vulnerable;
- (ii) which neurodevelopmental outcomes are more affected, and how timing shapes them;
- (iii) which biological mechanisms and contextual modifiers explain or mediate these associations.

These findings may help inform future research and guide the development of clinical and public-health prevention strategies, strengthening the shared responsibility of paediatric and mental health professionals in safeguarding children in the face of accelerating environmental and climatic change.

2. Methods

2.1. Search strategy

This narrative review draws on the recent epidemiological, clinical, neuroimaging and mechanistic evidence on the relationship between climatic and environmental exposures and neurodevelopment across critical developmental windows.

Searches were conducted between 1 January 2020 and 30 April 2026 in PubMed, Scopus, Embase and Web of Science. The search was restricted to studies published from 2020 onwards to provide a focused synthesis of contemporary evidence within a rapidly evolving field. This time frame was intentionally selected to capture recent developments in climate and environmental health research and to align the review with current conceptual and analytical approaches, including advances in exposure assessment, longitudinal study designs, neuroimaging methodologies, and exposome-oriented frameworks integrating multiple environmental exposures across critical developmental windows.^{22,23} The following keywords were combined and applied across databases: “neurodevelopment”, “brain development”, “prenatal”, “perinatal”, “pediatric”, “air pollution”, “particulate matter”, “heat wave”, “extreme heat”, “climate change”, “extreme climate event”, “rainfall”, “heavy metal”, “lead”, “mercury”, “arsenic”, “cadmium”, “manganese”, “organophosphate”, “pyrethroid”, “pesticide”, “phthalate”, “PFAS” and “bisphenol”. Database-specific search strategy and string are reported in the Supplementary Materials (Table S1).

2.2. Eligibility criteria and data synthesis

Eligible studies were original peer-reviewed articles published in English reporting original human data from the prenatal period onwards. Studies were included if they: (i) examined climatic-related exposures and/or environmental pollutants; (ii) assessed neurodevelopmental outcomes, brain maturation and development, cognitive functioning, behavioural and emotional outcomes, or neuroimaging correlates of neurodevelopment and (iii) specifically investigated timing of exposure or critical developmental windows.

To maintain conceptual consistency across developmental domains, the review preferentially included studies conducted in general-population or non-diagnosed cohorts examining dimensional neurodevelopmental outcomes rather than studies focused primarily on categorical neurodevelopmental or psychiatric diagnoses. This approach was adopted to better characterise how environmental exposures may influence developmental trajectories and brain maturation across the neurodevelopmental continuum, independently of disorder-specific multifactorial diagnostic frameworks.

Non-english studies, review articles, editorials, commentaries, animal studies, non-peer-reviewed publications and studies without original data were excluded.

All retrieved records were imported into Zotero. Title/abstract screening and full-text assessment were independently conducted by two reviewers. Disagreements were resolved through discussion and consensus.

Findings were synthesised qualitatively according to exposure category, developmental timing, neurodevelopmental domain and proposed biological mechanisms. Particular attention was given to sex-specific effects, contextual modifiers (e.g., socioeconomic disadvantage and co-exposures) and converging neuroimaging or mechanistic evidence.

3. Results

Following the screening process, a total of 46 original studies were included. Where available, results are described in terms of the direction and magnitude of effects, critical developmental windows, sex-specific differences and contextual or co-exposure modifiers. Fig. 1 provides an overview of the biological mechanisms linking climate and environmental determinants to neurodevelopmental outcomes, as emerged from the reviewed studies.

The evidence was synthesised into two overarching domains. Climate exposures were examined across temperature variation, rainfall and superstorms and large-scale climate oscillations, while environmental pollutants encompassed air pollutants, heavy metals, pesticides and key synthetic organic compounds - including phthalates, bisphenols and PFAS.

Main characteristics and findings of the individual studies included in this review are provided in Supplementary Tables S2 and S3.

3.1. Climate exposures

To provide an integrated overview of the evidence discussed below, Table 1 summarises the main climate-related exposures, their critical developmental windows, associated neurodevelopmental outcomes and proposed biological pathways. Detailed analytical descriptions are provided in the subsequent sections.

3.1.1. Temperature exposure

Eight studies across diverse populations have related temperature extremes to adverse neurodevelopmental outcomes, with timing and socioeconomic status (SES) emerging as key modifiers of risk. In a large U.S. retrospective analysis of 2352,529 singleton births across 525 counties, maternal exposure to extreme ambient heat (≥ 95 th percentile, mean $\approx 25.3^\circ\text{C}$) during organogenesis (3–12 weeks post-conception) was associated with higher odds ratio of major structural anomalies (OR = 1.05, 95% CI 1.00–1.11), particularly of the central nervous system (OR = 1.17, 95% CI 1.01–1.37). Effects were more pronounced in socially vulnerable areas and among infants with multiple anomalies, while co-exposure to high PM_{2.5} further intensified risks.²⁷ Similarly, a population-based case-control study in Georgia, USA (825 neural tube defect cases and 3300 controls), revealed a clear dose-response relationship between periconceptional heatwaves and neural tube defects: adjusted odds ratios rose from 1.09 (95% CI 1.01–1.17) for 1–2 hot days

to 1.29 (95% CI 1.04–1.58) for ≥ 6 days, identifying the neurulation phase (17–28 days post-fertilisation) as the critical window.²⁸

Beyond congenital anomalies, several studies connect thermal stress to early developmental functioning and later cognition. In Western Australia, cumulative heat exposure from conception through early childhood ($n = 59,771$) increased developmental vulnerability at age 5 (OR = 1.29, 95% CI 1.05–1.58), especially after prenatal exposure (OR = 1.34, 95% CI 1.10–1.65), mainly affecting communication, language and school-based cognitive skills. Cold exposure, instead, showed weaker and inconsistent effects.²⁹ A large Chinese cohort ($n = 67,453$) confirmed these findings: prenatal heatwaves, particularly in the first and third trimester, increased risks of fine motor, language and adaptive delays (OR = 1.19–1.38), independent of air pollution, birth outcomes and postnatal temperature.³⁰ Similarly, in a French cohort ($n = 12,163$), higher night-time temperatures at 14–19 weeks of gestation correlated with smaller expressive vocabularies (RR = 0.968, 95% CI 0.940–0.996), and while early postnatal heat (first 28 weeks) was associated with even lower scores (RR = 0.852, 95% CI 0.769–0.944). The authors suggested that sleep disruption or neuroendocrine stress may underlie these effects, pinpointing mid-gestation to early infancy as a potential critical developmental window.³¹ A subsequent causal re-analysis of the same cohort using longitudinal modified treatment policy modelling further suggested that projected temperature increases ($+2^\circ\text{C}$ to $+3^\circ\text{C}$) could further compromise early language development, with the strongest effects observed for rising night-time temperatures.³²

Evidence of heat-related neurodevelopmental vulnerability has also been observed in older children, with chronic heat exposure associated with cognitive deficits. In 11,878 participants (mean age 9.9 ± 0.6 years) of the ‘Adolescent Brain Cognitive Development Study’ (ABCD), higher cumulative days above the 95th percentile predicted lower composite ($B = -0.067$, $p < 0.001$), fluid ($B = -0.053$) and crystallised intelligence ($B = -0.061$), as well as pattern recognition ($B = -0.064$) and reading ($B = -0.050$) scores, within learning domains; the associations were stronger in low-income urban areas.³³

Neuroimaging data further explore the association between temperature exposure, critical developmental windows and the underlying neurobiological mechanisms. In 2681 participants from the Generation R study, early-life temperature exposure was associated with altered white matter microstructure at 9–12 years of age. Cold exposure ($\approx 2.6^\circ\text{C}$) from the third month of gestation to 15 months of life and heat exposure ($\approx 20.2^\circ\text{C}$) from 9 months to approximately 2.6 years were each linked to higher mean diffusivity, suggesting reduced myelination and delayed white matter maturation, with stronger effects under socioeconomic disadvantage.³⁴ A follow-up, fMRI study on the same cohort ($n = 2229$) showed that higher ambient temperatures during the week preceding imaging were associated with reduced within-network connectivity in the medial parietal default-mode, salience and hippocampal networks ($\beta \approx -0.05$, $p < 0.01$), again accentuated in

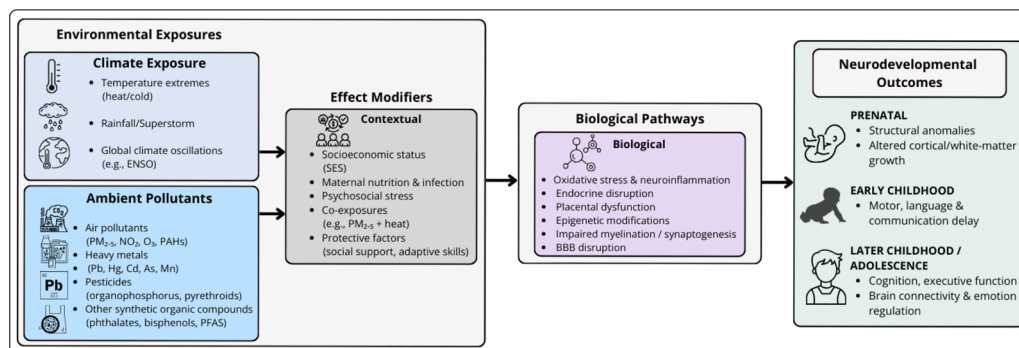


Fig. 1. Conceptual framework of climate and environmental determinants of neurodevelopment.

Note. As: Arsenic; BBB: Blood-Brain Barrier; Cd: Cadmium; ENSO: El Niño-Southern Oscillation; Hg: Mercury; Mn: Manganese; Pb: Lead; PFAS: Per- and Polyfluoroalkyl Substances.

Table 1

Summary of studies examining climate exposures and child neurodevelopmental outcomes.

Climate exposure	Critical developmental window	Neurodevelopmental outcomes / Neuroimaging	Putative mechanisms	Key modifiers
<i>Extreme heat / temperature extremes</i>	Periconception; organogenesis; gestation; early infancy; childhood	Neural tube defects; language delay; fine motor impairment; cognitive deficits Structural anomalies; altered white matter and functional connectivity	Oxidative stress; placental dysfunction; endocrine dysregulation; neuroinflammation; sleep disruption; altered myelination	SES; urbanicity; PM _{2.5} co-exposure
<i>Rainfall shocks</i>	Prenatal period; first 1000 days	Lower working memory; delayed cognitive development	Food insecurity; undernutrition; reduced household resources	Social protection; income support
<i>Superstorms / climate disasters</i>	Prenatal	Altered temperament; externalising behaviour; hippocampal Amygdala, basal ganglia and orbitofrontal alterations	Placental immune activation; epigenetic regulation; inflammatory signalling; altered hormonal transfer	Adaptive behaviour; genetic susceptibility (COMT); concurrent heat exposure
<i>Large-scale climate oscillations and shocks</i>	Second–third trimester; infancy	Lower cognition; language and memory deficits; developmental delay; lower educational and occupational outcomes	Nutritional disruption; infection burden; placental and metabolic dysfunction; epigenetic programming	Sex; regional climate; socioeconomic conditions

Note. SES: Socio-economic Status.disadvantaged neighbourhoods.³⁵

Overall, evidence suggests that temperature-related neurodevelopmental vulnerability may be shaped by both timing and context. The periconceptional and early gestational periods appear most critical for neural tube and structural anomalies, while exposure from the mid-second trimester through early infancy seems to be associated with language, fine motor and adaptive delays, likely mediated by sleep disruption and endocrine imbalance. During gestation, infancy and toddlerhood, heat and cold stress may alter myelination and functional connectivity, especially under social disadvantage, while prolonged exposure throughout childhood has been associated with poorer cognitive and academic performance. These effects may be mediated by intersecting biological mechanisms, such as increased oxidative stress, activation of neuroimmune pathways, placental and endocrine maladaptation, impaired vascular and immune regulation, and perturbation of sleep–wake cycles, all of which can be exacerbated by concurrent air-pollution exposure and socioeconomic adversity.

3.1.2. Rainfall and superstorm

Evidence from four studies across both low- and high-income settings identifies rainfall shocks and extreme storm events as emerging risk factors for neurodevelopment. In Peru, Pazos et al.³⁶ linked gridded precipitation data with the ‘Young Lives’ cohort ($n = 1728$) to examine how early-life rainfall variability influences cognitive development. Rainfall shocks - defined as monthly deviations from typical precipitation levels - affected 27% of children, occurring more frequently post-natally than *in utero*.

Each additional shock during the first 1000 days of life was associated with a 0.066 SD decrease in working memory performance at ages 5–12 yrs, with the strongest effects following gestational exposure. These deficits appeared to operate primarily through indirect pathways: rainfall variability reduced household income and food security, leading to undernutrition and consequently, poorer cognitive outcomes. Interestingly, participation in a conditional cash transfer programme mitigated part of these effects, underscoring the protective role of socioeconomic support during climate shocks.

In high-income contexts, Buthmann et al.³⁷ explored the effect of prenatal exposure to Superstorm Sandy (SS, 2012) on child temperament in 33 mother-infant dyads. Higher levels of maternal “storm stress” (combining objective and subjective measures) were associated with lower infant Extraversion temperament scores at 6–12 months. In the same study, placental RNA sequencing identified 646 differentially expressed genes enriched in immune, extracellular-matrix and sensory-perception pathways. Theoretically, these alterations are consistent with a placental response to prenatal environmental stress, as maternal exposure to SS was the strongest predictor of infant temperament. The enriched regulatory signatures, implicating polycomb-complex components, estrogen-receptor targets and

microRNA-processing pathways, suggest that environmental stress may induce transcriptional repression and structural remodelling in the placenta. Such changes may affect placental barrier integrity, inflammatory signalling, and nutrient/hormonal transfer, thereby shaping early neurodevelopment.

Neuroimaging studies conducted at school age further support storm-related alterations in brain structures, such as basal ganglia, amygdalae and specific cortical regions. In particular, DeIngénis et al.³⁸ examined 34 children (11 exposed *in utero* to SS; mean age 8.7 yrs) and observed bilateral increases in putamen (+6.2 - +6.3%) and pallidum volumes (+1.7 - +1.9%) together with a trend toward larger caudate nuclei. Moreover, concurrent prenatal exposure to extreme heat was found to further accentuated storm effects, particularly through reduction of the left nucleus accumbens volume. In a related sample ($n = 30$; 9 exposed), Shereen et al.³⁹ reported larger bilateral amygdalae and smaller medial orbitofrontal cortex (mOFC) volumes in exposed children. Crucially, storm-exposed children showed greater externalising behaviour at age 5 ($p = 0.027$); adaptive behaviours at age five - social skills, daily living and communication abilities - moderated these neural differences: higher adaptive scores predicted larger amygdala and smaller mOFC volumes, mirroring the direction of storm-related effects.

Extending these findings beyond direct exposure effects, evidence from Project Ice Storm suggests that the neurodevelopmental consequences of prenatal climate-related stress may vary according to genetic susceptibility. In a Canadian longitudinal cohort of 53 adolescents exposed *in utero* to the 1998 Québec ice storm, the association between prenatal maternal stress following the event and hippocampal volume differed according to COMT rs4680 genotype and sex, with stronger adverse effects among Val/Val carriers (boys: $\Delta R^2 = 0.122$, $p = 0.049$; girls: $\Delta R^2 = 0.244$ – 0.330 , $p \leq 0.007$).⁴⁰

Together, these findings suggest that rainfall anomalies and superstorms may disrupt neurodevelopment through both indirect socioeconomic pathways - such as reduced nutrition and household resources - and direct biological mechanisms, including placental immune dysregulation, epigenetic alterations and subcortical-limbic structural changes. Prenatal period appears to emerge as the most critical window with downstream implications for temperament, executive function and emotional regulation. Emerging evidence further suggests that individual biological susceptibility, including sex-specific gene-environment interactions, may contribute to differential neurodevelopmental responses following prenatal climate-related stress. Importantly, social protection measures and early adaptive skills may reduce these effects, offering potential targets for intervention in the face of increasing climatic extremes.

3.1.3. Climate large-scale oscillations

Beyond local temperature or rainfall variations, large-scale climatic oscillations such as the El Niño-Southern Oscillation (ENSO) have

emerged as key determinants of early brain development. Defined by periodic sea surface temperature (SST) variances across the equatorial Pacific, ENSO influences global weather, food security and infectious disease patterns, pathways that can affect foetal and early postnatal neurodevelopment.

Specifically, three large population-based studies revealed potential long-term neurocognitive effects of prenatal ENSO exposure. In 17,105 participants from the China Family Panel Studies, Tang and Di.⁴¹ found an inverted U-shaped relationship between the exposure to prenatal SST variances and adult cognition: deviations of $\pm 1^\circ\text{C}$ from neutral conditions predicted 2–4% lower mathematics scores and smaller reductions in word recognition. The second and third trimesters and 7–12 months postnatally were found as the most critical windows. Moreover, higher prenatal anomalies also predicted lower occupational prestige, particularly among women and individuals from low-income regions. Regional temperature and rainfall explained only 8–19% of the effects, confirming that global climate variability was the main driver. Interestingly, author predicted that each $\pm 1^\circ\text{C}$ deviation possibly corresponds to income losses of 0.33–1.09 billion USD per cohort. The authors suggested that ENSO-driven changes in food production, maternal nutrition and placental or immune function could modify epigenetic programming and, in turn, affect cognitive development across the lifespan.

Consistent patterns were observed in Latin America and Africa. Aguilar and Vicarelli.⁴² found that ENSO-driven rainfall during pregnancy increased maternal undernutrition (OR = 1.48, 95% CI 1.20–1.82) and infectious morbidity (RR = 1.36, 95% CI 1.11–1.65), both linked to delayed cognitive development (language, working and long-term memory and visual-spatial thinking) in children aged 2–5 yrs, particularly during El Niño years marked by heat and drought. In 187,767 East African children, Olurotimi.⁴³ reported that higher temperatures were associated with poorer cognitive performance, especially in local language scores at $>34^\circ\text{C}$ ($\beta = -0.220$), while early-life rainfall shocks were linked to lower mathematics, English and local language performance following both prenatal ($\beta = -0.020$ to -0.088) and

first-year exposure ($\beta = -0.040$ to -0.100), likely driven by malaria outbreaks, maternal anaemia and nutritional instability from reduced agricultural productivity.

Overall, ENSO and related oscillations may influence neurodevelopment through intertwined biological and social pathways - from nutritional deprivation and infectious exposure to placental and metabolic dysfunction - culminating in epigenetic changes that may mediate long-term cognitive and developmental outcomes. Converging evidence from China, Latin America and sub-Saharan Africa underscores their global relevance and biological plausibility, while exposing marked socioeconomic inequalities in vulnerability and resilience to climate-related neurodevelopmental risk.

3.2. Environmental pollutants

To provide an integrated overview of the evidence discussed below, Table 2 summarises the main classes of environmental pollutants, their associated developmental windows, neurodevelopmental outcomes, and proposed biological mechanisms. Detailed analytical descriptions are provided in the subsequent sections.

3.2.1. Air pollutants

A growing body of longitudinal and neuroimaging research ($n = 11$) has linked exposure to major air pollutants - fine particulate matter (PM_{2.5}), nitrogen dioxide (NO₂), ozone (O₃) and polycyclic aromatic hydrocarbons (PAHs) - to measurable alterations in brain structure, connectivity and cognition from the prenatal period through adolescence.

These effects may begin early, as shown in the GUSTO cohort ($n = 325$), where Buthmann et al.⁴⁴ reported that higher PM_{2.5} exposure during late gestation (weeks 36–40) predicted slower bilateral hippocampal growth (left: $\beta = -0.0024$; right: $\beta = -0.0021$, $p < 0.05$), whilst earlier exposure (weeks 1–13) was modestly associated with faster growth. Interestingly, accelerated right-hippocampal development was linked to more attentional and externalising problems, suggesting that

Table 2
Summary of studies examining environmental pollutant exposures and child neurodevelopmental outcomes.

Environmental exposure	Critical developmental window	Neurodevelopmental outcomes / Neuroimaging	Putative mechanisms	Key modifiers
Air pollutants (PM _{2.5} , NO ₂ , O ₃ , PAHs)	Prenatal period; infancy; childhood; adolescence	Attention problems; executive dysfunction; language and learning difficulties; psychotic-like experiences; lower cognition Altered hippocampal growth; delayed white-matter maturation; cortical thinning; altered functional connectivity; limbic changes	Oxidative stress; neuroinflammation; placental and vascular dysfunction; endothelial impairment; delayed myelination; epigenetic regulation	SES; psychosocial stress; neighbourhood and school environment; sex; cumulative exposure trajectories
Heavy metals (Pb, Hg, Cd, As, Mn)	Prenatal period; late childhood	Language and motor impairment; lower cognition; hot executive dysfunction; depressive symptoms Altered neurotransmission; impaired myelination; hippocampal and cerebellar vulnerability	Oxidative stress; mitochondrial dysfunction; calcium dysregulation; endocrine disruption; altered intracellular signalling	Exposure mixtures; developmental timing; metal-specific interactions
Pesticides (organophosphates, pyrethroids)	Prenatal period; early postnatal life (~2 years); school age	Motor and language deficits; executive dysfunction; reduced cognitive flexibility and inhibitory control Cortical/subcortical alterations; white-matter abnormalities; altered cerebral perfusion; DMN reorganisation	Oxidative stress; neuroinflammation; mitochondrial dysfunction; impaired oligodendrocyte maturation	Developmental timing; cumulative exposure; agricultural/high-exposure settings
Synthetic organic compounds (phthalates, bisphenols, PFAS, POPs)	First trimester; infancy; early childhood; adolescence	Communication, motor and visuospatial deficits; executive dysfunction; memory and learning impairment Grey/white matter alterations; cortical thinning; altered executive and attentional networks	Endocrine disruption; placental transfer; altered synaptogenesis; neurotransmission and myelination	Sex; developmental timing; exposure mixtures; breastfeeding; endocrine susceptibility

Note. As: arsenic; Cd: cadmium; DMN: default mode network; Hg: mercury; Mn: manganese; NO₂: nitrogen dioxide; O₃: ozone; PAHs: polycyclic aromatic hydrocarbons; Pb: lead; PFAS: per- and polyfluoroalkyl substances; PM_{2.5}: particulate matter $\leq 2.5\ \mu\text{m}$ in aerodynamic diameter; POPs: persistent organic pollutants; SES: socioeconomic status.

PM_{2.5} may disrupt hippocampal maturation through oxidative stress, neuroinflammation and placental vascular dysfunction.

Extending this evidence to the earliest measurable postnatal time-point, Blanco-Hinojo et al.⁴⁵ examined resting-state fMRI in 61 neonates at a mean postnatal age of 29 days from the Barcelona population-based cohort. Higher first-trimester PM_{2.5} exposure was associated with stronger local functional connectivity in bilateral sensorimotor regions, particularly in the premotor and right superior parietal cortex, suggesting delayed segregation of primary sensorimotor areas. Third-trimester exposure was additionally associated with visual and frontal opercular regions.

These mechanisms appear also to interact with the child's psychosocial environment. Pagliaccio et al.⁴⁶ studying 727 African American and Dominican mother-child pairs in New York City, observed that the behavioural consequences of prenatal PAH exposure depended on levels of early-life stress. Children exposed to both higher PAHs and greater family adversity at age 5 yrs showed more attention problems ($\beta = 0.22$, $p(\text{FDR}) = 0.003$) and thought problems ($\beta = 0.21$, $p(\text{FDR}) = 0.004$) by age 11. The authors proposed a "double-hit" mechanism, whereby prenatal toxicant exposure primes neural systems to heightened sensitivity to later psychosocial stress via converging oxidative, inflammatory and HPA-axis pathways.

Longitudinal neuroimaging studies showed that the impact of air pollution extends well beyond infancy, influencing white-matter development till pubertal age. In 4108 participants (5422 MRI scans between ages 10 and 14), Kusters et al.⁴⁷ found that higher exposure to PM_{2.5}, PM₁₀, and nitrogen oxides - both prenatally and during early childhood - was associated with lower fractional anisotropy and higher mean diffusivity, consistent with delayed myelination. Prenatal PM_{2.5} corresponded to an estimated of more than five-month lag in white-matter maturation, and additional exposure during adolescence contributed to further microstructural alterations, indicating a prolonged developmental vulnerability.

Extending these observations, complementary findings from the ABCD Study showed pollutant-specific effects on brain morphology.

At the level of cortical grey matter, Jara et al.⁴⁸ investigated longitudinal cortical-thickness changes in 10,947 ABCD participants followed from early to mid-adolescence. Higher PM_{2.5} and NO₂ exposure were associated with accelerated cortical thinning in the bilateral transverse temporal gyrus, left insula, orbitofrontal cortex and temporal pole (all β s < -0.016 , FDR-corrected $p < 0.05$), with effects increasing with age. O₃ showed no significant associations.

Similarly, Cotter et al.⁴⁹ found that these patterns seem to align with established mechanisms of pollution-related neurotoxicity - especially systemic inflammation and endothelial dysfunction - that can compromise neurovascular integrity, including blood-brain barrier function.

In a subsequent analysis ($n = 8182$; 12,195 scans, ages 9–13), females exposed to higher PM_{2.5} and NO₂ showed greater restriction of diffusion (RNI, RND) and slower microstructural development, while males exposed to O₃ displayed reduced diffusion and flatter growth trajectories.⁵⁰ These convergent results suggest sex-dependent susceptibilities and a persistent influence of urban pollutants on both structural and functional brain organisation.

Moreover, the social environment confirmed its role in shaping these neurobiological outcomes. Kong et al.⁵¹ analysing 6778 ABCD participants, showed that higher prenatal O₃ exposure predicted reduced left-hippocampal growth ($\beta = -0.009$, $p < 0.01$) among adolescents attending unsafe, resource-poor schools - an effect mediating poorer cognitive performance ($\beta = 0.068$, $p < 0.05$) and more psychotic-like experiences (indirect $B = -0.0013$, $p = 0.01$). In more violent or insecure neighbourhoods, the same exposure correlated with larger right-amygdala volume ($\beta = -0.009$, $p = 0.03$), consistent with stress-related limbic alterations.

At a broader population level, chronic exposure trajectories reveal cumulative behavioural and educational consequences. Hobbs et al.⁵² identified four exposure profiles from conception to age 10 yrs ($n = 1265$

participants). Adolescents experiencing persistently high or early-life peaks of pollution displayed increased odds of attentional difficulties (OR = 2.1 to 3.1), conduct problems (OR = 2.0), lower educational attainment and substance-use disorders (OR = 0.4 and 2.7 to 3.5).

In a nationwide retrospective cohort study, Oh and Song.⁵³ analysed 1436,685 South Korean children followed up to 13 years and found that each 0.01-ppm increase in prenatal NO₂ was associated with an 18% higher hazard of clinically diagnosed neurodevelopmental disorders (aHR 1.18, 95% CI 1.17–1.19; $p < 0.001$), including intellectual disability, developmental delay, and behavioural/emotional disorders. SO₂ showed smaller but significant associations (aHR 1.01, 95% CI 1.01–1.02; $p = 0.008$).

Interestingly, emerging evidence also implicates wildfire-derived PM_{2.5} as a neurodevelopmental risk factor. In 86 mother-child dyads, Buthmann et al.⁵⁴ found that first-trimester wildfire smoke exposure was associated with enrichment of maternal proteomic pathways related to immune, epigenetic and neurodevelopmental processes, and predicted lower fearfulness ($B = -0.067$) and higher exuberance ($B = 0.043$) at ages 3–5, suggesting that gestational wildfire smoke may affect foetal developmental programming through immune-, chromatin/epigenetic-, and neurodevelopment-related biological pathways.

In summary, these findings outline a coherent developmental continuum: prenatal and early-life exposure to PM_{2.5}, NO₂, O₃ and PAHs seems to be associated with altered hippocampal and white-matter growth, cortical thinning, functional connectivity and limbic regulation, leading to difficulties in attention, learning, executive and socio-emotional functioning that may persist into adolescence. Oxidative stress, neuroinflammation, vascular and placental dysfunction, together with delayed myelination, endothelial impairment, and immune-mediated epigenetic mechanisms emerge as core biological pathways, while social disadvantage and psychosocial stress operate as powerful amplifiers. Air pollution thus may represent not only a neurotoxic burden but also a social one, embedding inequality into the architecture of the developing brain.

3.2.2. Heavy metals

Evidence from longitudinal cohorts ($n = 5$) consistently indicates that exposure to heavy metals during critical developmental windows is associated with poorer neurodevelopmental outcomes, with both single-metal and mixture effects varying by timing, magnitude and affected domains.

In a large Japanese cohort of over 63,000 mother-child pairs, Yamamoto et al.⁵⁵ examined prenatal manganese (Mn) exposure, discovering substantial foetal accumulation, as indicated by high Mn levels in maternal and cord blood. Interestingly, higher cord blood concentrations were consistently linked to lower communication ($\beta = -0.19$), gross-motor scores ($\beta = -0.32$) and motor delay. The authors suggested that excessive Mn disrupts redox homeostasis and mitochondrial function, leading to oxidative stress, impaired dopaminergic transmission and altered myelination during critical phases of synaptogenesis.

Further insights into mixed-metal exposure come from the Mexico City PROGRESS cohort. In 604 mother-child pairs, Florez-García et al.⁵⁶ developed a multi-media biomarker (MMB) index combining prenatal exposure to 13 essential and non-essential metals. Higher MMB-cadmium and MMB-arsenic scores were associated with lower general cognitive index (GCI) scores ($\beta = -1.52$ and -1.53), while manganese, selenium and molybdenum showed positive associations ($\beta = +2.28$, $+2.07$, $+1.76$). These results support the dual role of metals: toxic elements such as cadmium and arsenic impair cognition through oxidative stress, mitochondrial damage and endocrine disruption, whereas essential elements like manganese, selenium and molybdenum may support antioxidant activity, thyroid function and neuronal growth.

In the same cohort, Lane et al.⁵⁷ investigated the effects of childhood blood lead (Pb) on executive functioning between 6 and 9 years. Pb exposure was significantly associated with poorer 'hot' executive

function (linked to emotional regulation and reward-based decision-making; $\beta = -0.13$, $p = 0.004$), but not with 'cold' EF, reflecting purely cognitive control ($\beta = 0.06$, $p = 0.39$). The authors proposed that Pb preferentially disrupts orbitofrontal and ventromedial prefrontal regions reliant on dopaminergic and glutamatergic balance during synaptic pruning, thereby producing selective vulnerabilities in affective and motivational regulation.

Further evidence linking lead exposure to emotional vulnerability was provided by Hoover et al.⁵⁸ who analysed serial blood lead levels from ages 1 to 12 years in 218 children from the HOME cohort. Surprisingly, each doubling in mean childhood blood lead was associated with higher risk of self-reported depressive symptoms at age 12 (RR 1.90; 95% CI 1.00–3.66; $p = 0.05$) and combined child-/caregiver-reported depressive symptoms (RR 1.76; 95% CI 1.12–2.78; $p = 0.02$). Associations strengthened through age 8, with larger effects for exposures occurring in late childhood, suggesting this period as an additional critical window for Pb-related affective vulnerability. No associations emerged for anxiety symptoms or according to sex or race.

Extending this evidence to low-resource, high-exposure settings, Nyanza et al.⁵⁹ studied 310 Tanzanian mother-child pairs from artisanal gold-mining communities, assessing combined prenatal exposure to lead (Pb), mercury (Hg), cadmium (Cd) and arsenic (As). At age 3–4 years, significant mixture effects emerged, with poorer language (aPR = 0.45, 95% CI 0.31–0.64), gross motor (aPR = 0.82, 95% CI 0.70–0.97) and overall developmental performance (aPR = 0.87, 95% CI 0.75–1.01). Lead accounted for nearly 60% of total mixture weight and synergistic Pb-Hg interactions amplified neurotoxicity beyond additive effects. Combined metal exposure was thought to induce oxidative stress and calcium dysregulation, activating MAPK/ERK/JNK pathways that damage hippocampal and cerebellar circuits essential for motor and language functions. Cadmium's weaker independent effect was attributed to limited placental transfer due to metallothionein binding.

Collectively, these findings delineate a consistent pattern of potential risk. Specifically, prenatal exposure to Pb, Hg, Cd, As and excess Mn may primarily affect motor, language and overall neurodevelopment, while postnatal Pb exposure may disrupt emotional-motivational ("hot EF") regulation, executive dysfunction and depressive symptoms, with late childhood emerging as an additional critical window for affective vulnerability. Mixture analyses further reveal synergistic and antagonistic interactions overlooked by single-pollutant models. Mechanistic evidence converges on oxidative stress, disrupted neurotransmission and altered intracellular signalling as key pathways through which heavy metals - individually or in combination - interfere with brain maturation during critical developmental periods.

3.2.3. Pesticides: neurodevelopmental effects of organophosphates and pyrethroids

Evidence from human studies ($n = 5$) consistently links pesticide exposure to alterations in brain structure, connectivity and cognitive-behavioural functioning with developmental timing emerging as a critical determinant of outcome.

In a longitudinal birth cohort from Northern Manhattan and the South Bronx (NYC, U.S.), Peterson et al.⁶⁰ examined 270 children aged 6–14 yrs with prenatal chlorpyrifos (CPF) exposure quantified from umbilical cord or maternal plasma. Increasing CPF levels were associated with widespread cortical and subcortical changes, including greater cortical thickness in frontal, temporal and posteroinferior regions, reduced local white-matter volumes, higher fractional anisotropy and lower diffusivity in the internal capsule, decreased regional cerebral blood flow and lower N-acetyl-aspartate concentrations - markers of reduced neuronal density. These neuroimaging abnormalities paralleled poorer fine motor speed ($\beta = -0.30$, $p < 0.001$) and motor programming ($\beta = -0.27$, $p < 0.001$). The authors attributed these findings to CPF-induced oxidative stress, neuroinflammation, mitochondrial dysfunction and impaired oligodendrocyte maturation, leading to disrupted grey-white matter differentiation and perfusion deficits

underlying motor impairment.

Functional alterations were also reported in younger cohorts. Using resting-state fMRI, Bahrami et al.⁶¹ investigated 78 Latin children aged 8–9 yrs, comparing those from rural farmworker (FW) families - at higher risk of chronic pesticide exposure - to urban non-farmworker (NFW) peers. FW children showed significant changes in the default mode network (DMN) with reduced global efficiency and clustering coefficients. Within the FW group, cumulative exposure from the prenatal period to age eight was associated with progressively greater DMN reorganisation, suggesting a dose-response effect.

At earlier developmental stages, Ramos et al.⁶² examined 299 Norwegian infants and preschoolers, finding that higher prenatal exposure to organophosphorus pesticides (dimethyl- and diethyl-phosphates) predicted poorer communication skills at 18 months ($\beta = -0.15$; 95% CI -0.27 , -0.04), which indirectly led to reduced expressive language at preschool age (indirect $\beta = -0.04$; 95% CI -0.08 , -0.004). Low-molecular-weight phthalates were likewise associated with poorer teacher-rated language ($\beta = -0.13$, 95% CI -0.24 , -0.01). In contrast, organophosphate ester metabolites showed no consistent associations.

Extending the evidence beyond the prenatal window, Li et al.⁶³ investigated postnatal pyrethroid (PYR) exposure in 263 children from rural Yunnan, measuring urinary metabolites (3-PBA, 4-F-3-PBA, DBCA) at ages 1 and 2 yrs, and assessing neurodevelopment at age 4 using the Griffiths Development Scales. Nearly all children showed detectable exposure (~98%). Higher 3-PBA levels at age two were associated with lower locomotor ($\beta = -14.61$; 95% CI -24.93 , -4.30) and language scores ($\beta = -10.89$; 95% CI -19.38 , -2.41), as well as a threefold increased risk of low language development (OR = 3.23; 95% CI 1.33–7.83), highlighting age 2 as a critical postnatal window of vulnerability.

The neurodevelopmental impact of pesticides beyond early life was further examined by Viglietti et al.⁶⁴ in 445 South African children and adolescents (mean age 10.6 years) from the Child Health Agricultural Pesticide Study (CapSA). Higher urinary levels of organophosphate and pyrethroid pesticide metabolites were consistently associated with poorer executive functioning, particularly in cognitive flexibility and spatial working memory. Associations were observed for 3,5,6-trichloro-2-pyridinol (TCPy), 2,4,5-trichlorophenoxyacetic acid (BCP), and cis-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylic acid (cis-DCCA), with effect sizes ranging from $\beta = -0.08$ to -0.18 . Higher levels of TCPy and BCP were associated with poorer cognitive flexibility, while higher TCPy, BCP, cis-DCCA and OH-P levels were associated with poorer inhibitory control. No significant associations were observed for visuospatial working memory. These findings may suggest that chronic postnatal exposure to organophosphate and pyrethroid pesticides may continue to affect selective executive domains in school-aged children, particularly in high-exposure agricultural settings.

Altogether, these studies delineate a coherent developmental pattern: prenatal exposure to organophosphorus and pyrethroid pesticides could lead to an alteration of cortical and subcortical architecture, white-matter integrity, functional-connectivity and neuronal metabolism, leading to persistent motor, language and executive-function deficits. Early postnatal exposure, particularly around age 2 yrs, seems to further compromises locomotor and language development, while chronic exposure during later childhood appears to be linked to selective executive dysfunction, especially in high-exposure agricultural settings. Mechanistic evidence consistently converges on oxidative stress, neuroinflammation and mitochondrial dysfunction - particularly affecting pre-oligodendrocytes - as key biological pathways linking pesticide exposure to altered brain maturation across critical developmental windows.

3.2.4. Other synthetic organic compounds and persistent organic pollutants

Evidence from prospective cohorts ($n = 8$) indicates that also prenatal and early postnatal exposure to other synthetic organic compounds - mainly phthalates, bisphenols and per- and polyfluoroalkyl substances

(PFAS) - may be associated with timing-, domain- and sex-specific differences in neurodevelopment.

In a cohort of 672 Saudi mother-child pairs, Al-Saleh et al.⁶⁵ found that higher first-trimester exposure to certain phthalates (mono-n-butyl, mono-isobutyl) and bisphenol A was linked to slightly lower motor development scores in the first 18 months of life ($\beta \approx -0.05$), while low-molecular-weight phthalates (e.g. mono-ethylphthalate) were modestly associated with better communication scores ($\beta \approx 0.04-0.05$). Later exposure to DEHP metabolites (a plasticiser used in food packaging and medical products) predicted small motor benefits, whereas MiBP (common in personal-care products) was linked to poorer social skills. Boys appeared more vulnerable in social and problem-solving domains, girls in motor skills. A minor mediation effect by lower maternal thyroid hormone levels was observed.

In a larger multi-cohort study, Park et al.⁶⁶ analysed 2378 parent-child dyads from 10 ECHO cohorts and assessed neurodevelopmental delay at ages 1–3 years. Higher prenatal exposure to selected phthalates, particularly DEHP metabolites (MEHP, MEHHP) and MBZP, was associated with increased odds of fine motor delay, with stronger associations among males. Higher MEP concentrations were associated with increased odds of problem-solving delay, whereas inverse associations were observed for MCINP/MCOMOP/MCNP in communication and MCPP in problem-solving domains. Mixture analyses showed no overall association with most neurodevelopmental domains, except for lower odds of delay in the personal-social domain.

Extending these behavioural findings to the brain structure, Werder et al.⁶⁷ examined 157 U.S. children (birth-7 years), combining repeated urinary measures with MRI data. Higher levels of monocarboxyisooctyl phthalate (MCP) were linked to smaller grey matter volume ($\approx -1.7 \text{ cm}^3$), while higher DEHP derivatives corresponded to larger white matter volume ($\approx +2.3 \text{ cm}^3$). Sex-specific patterns emerged: in boys, exposure to phthalates common in personal-care products (MEP, MiBP) predicted smaller grey matter, while in girls, exposure to DINCH (a newer plastic substitute) corresponded to slightly larger white matter, indicating sex-differentiated effects on brain morphology.

Longitudinal neuroimaging evidence was further provided by Engel et al.⁶⁸ who examined 17 phthalate and replacement plasticizer metabolites in 161 children from the UNC Chapel Hill Baby Connectome Project using resting-state fMRI and structural MRI between 2 weeks and 5 years of age. Multiple metabolites were associated with altered connectivity within the executive control and dorsal attention networks, with sex-specific patterns: in boys, exposure was associated with lower executive-network connectivity ($\beta = -0.16$ to -0.24), whereas in girls it was associated with higher connectivity in executive and dorsal attention networks ($\beta = +0.10$ to $+0.23$). In girls, mono-isobutyl phthalate (MiBP) was additionally associated with cortical thinning in temporal and orbitofrontal regions. These findings converge with the possibility that phthalates and replacement plasticizers may alter the maturation of attentional and executive brain networks during the first postnatal years in a sex-dependent manner, highlighting infancy and early childhood as critical developmental window.

Further evidence from both Asian and U.S. cohorts highlights prenatal vulnerability to PFAS. In a Chinese cohort of 716 mother-child pairs, Zhang et al.⁶⁹ found that higher perfluorooctanoate (PFOA) exposure slowed developmental-quotient gains between 1 and 3 years, while perfluorobutanesulfonate (PFBS) and perfluoroheptanoic acid (PFHpA) increased the likelihood of persistently low-development trajectories. Accordingly, in a U.S. cohort of 140 pairs, Oh et al.⁷⁰ reported that higher prenatal PFOA and perfluorononanoic acid (PFNA) levels predicted lower cognitive scores at 24–36 months, with longer breastfeeding mitigating these associations, suggesting a modest neuro-protective effect.

Similarly, Xing et al.⁷¹ followed 572 mother-child pairs with per- and polyfluoroalkyl substance (PFAS) assessments across five developmental stages - early, mid, and late pregnancy, cord blood at birth, and child serum at 4–6 years - alongside IQ testing at age 4–6 years. In boys,

higher PFAS exposure during childhood was associated with poorer visuospatial reasoning and processing speed, particularly for PFOA, PFNA, PFDA, PFHxS and 6:2Cl-PFESA. In contrast, girls showed generally positive associations, with higher prenatal PFOA and PFHxS concentrations during pregnancy associated with higher verbal comprehension scores. These findings suggest that PFAS-related cognitive effects could be both sex- and timing-dependent, with prenatal exposure appearing more strongly associated with verbal abilities in girls, whereas childhood exposure was more consistently linked to visuospatial and processing-speed deficits in boys.

In a large Finnish prospective cohort, Wu et al.⁷² followed 1304 participants from childhood (ages 3–18 years) to midlife over 31 years and examined the long-term cognitive effects of childhood exposure to persistent organic pollutants (POPs), including organochlorine pesticides and polychlorinated biphenyls. Higher childhood POP mixture exposure was associated with poorer memory and learning performance in midlife ($\beta = -0.129$; 95% CI -0.244 to -0.014), corresponding to approximately 1.7 years of additional cognitive ageing. The mixture effect was found to be mainly driven by hexachlorobenzene (HCB; 23%) and dichlorodiphenyltrichloroethane (p,p'-DDT; 21%). Interestingly, associations remained significant after adjustment for adulthood exposure, and effects were stronger among participants aged 12–18 years at baseline, suggesting adolescence as a potentially critical window.

Overall, these studies identify prenatal life, infancy, early childhood and, to a lesser extent, adolescence as plausible critical windows for exposure to synthetic organic compounds and persistent organic pollutants, including phthalates, bisphenols, PFAS and organochlorine compounds. Neurodevelopmental effects appear timing-, domain- and sex-specific, involving communication, motor, visuospatial, executive and memory/learning functions, alongside alterations in grey/white matter, cortical maturation and attentional-executive brain networks. Evidence from mixture-based approaches further suggests that combined exposures may produce effects not captured by single-pollutant models and that some neurocognitive consequences may persist into midlife. Mechanistically, these compounds may interfere with endocrine regulation, placental transport, synaptogenesis, neurotransmission and myelination during critical phases of brain development.

4. Implications for global child health and prevention

The reviewed studies consistently showed that environmental and climatic exposures are not marginal concerns but central determinants of child health. The dynamic maturation of children's brains, bodies and social contexts renders them uniquely susceptible to the adverse effects of pollution, heat and other environmental stressors. Protecting neurodevelopment must therefore be a priority within both public health and climate adaptation strategies.

To this end, paediatricians and mental health professionals should integrate targeted questions about the child's and maternal proximal environmental context into history-taking, relying on parental report as the primary, and often most accessible, source of exposure-related information. This approach may support context-sensitive and risk-informed assessment strategies, particularly in populations with known environmental vulnerabilities or during critical developmental windows. Embedding brief environmental exposure screening within existing maternal and child healthcare encounters may help identify potentially modifiable exposures and inform tailored preventive and monitoring strategies, coordinating care within interdisciplinary networks.^{73,74}

Also, prenatal visits may offer key opportunities to identify and reduce exposures - heat, poor air quality, pesticides and contaminated water - through practical guidance on hydration, ventilation and cooling spaces.⁷⁵

Schools can also play a central role by fostering environmental awareness, integrating climate and health literacy into education, and adopting adaptive and protective measures during extreme weather or

pollution events.⁷⁶

At the policy level, child health agendas should align with environmental action. Cutting emissions, enforcing chemical safety and increasing urban green areas provide shared benefits for planetary and neurodevelopmental wellbeing.^{77,78} Environmental justice must guide these efforts, as children in low- and middle-income regions face overlapping risks of pollution, malnutrition and limited healthcare.⁷⁹

Finally, coordinated research and surveillance efforts are essential to monitor trends, identify emerging risks and guide evidence-based interventions. Integrating environmental metrics into paediatric cohorts, adopting exposome-based models and harmonising outcomes across contexts will clarify multi-exposure effects and regional vulnerabilities. Safeguarding the developing brain from environmental and climatic threats is both a scientific responsibility and an ethical imperative, fully aligned with the Sustainable Development Goals.¹⁷

5. Limitations and future perspectives

Interpretation of the evidence synthesised in this review requires consideration of its methodological limitations. The included studies were heterogeneous in design, ranging from large retrospective cohorts to a relatively sparse body of neuroimaging evidence and differed considerably in exposure assessment methods and neurodevelopmental measures. Given this heterogeneity and the predominantly observational nature of the available evidence, causal inference remains limited. In addition, although the range of climatic and environmental exposures covered by the search strategy was broad, it may not have been exhaustive, and other environmentally relevant agents not systematically addressed may represent additional sources of neurodevelopmental risk.

Moreover, as this was conducted as a narrative review rather than a formal systematic synthesis, study identification and selection may be more susceptible to selection bias and reduced reproducibility and the findings should therefore be considered as an interpretative synthesis of the current evidence rather than a quantitative or exhaustive assessment of the field.

Finally, the marked variability of environmental exposures across geographic regions, climatic zones and socioeconomic contexts limits the generalisability of the conclusions presented here, as exposure levels, population vulnerability and contextual modifiers differ substantially across settings.

Future research should therefore explore multi-exposure and interaction effects, adopting exposome-based and mixture models that capture cumulative and synergistic impacts. It is equally important to recognise that environmental risks are highly context-specific, varying across geographical regions, climates and socioeconomic conditions making direct comparisons between studies challenging. As the evidence base expands and methodological consistency improves, future systematic reviews and meta-analyses will also be important to quantitatively synthesise findings, estimate pooled effects and identify sources of heterogeneity across exposure types and developmental periods. Progress will depend on collaboration across disciplines - bringing together neuroscientists, environmental epidemiologists, paediatricians and mental health professionals - especially to connect biological insight with prevention. Advancing this field will require longitudinal, multi-level research that integrates biological, environmental and social data to inform early prevention and policy actions aimed at safeguarding neurodevelopment in a changing world.

6. Conclusion

This review highlights that climatic and environmental exposures are associated with increased vulnerability in cognitive, motor and emotional development, particularly when they occur during periconception, gestation and early postnatal life. Neuroimaging studies report structural and functional alterations in the developing brain,

while current evidence points to converging mechanisms including oxidative stress, neuroinflammation, vascular injury, endocrine and placental dysfunction, compounded by social and contextual adversity. These findings support the integration of climate adaptation, environmental protection, exposure reduction and early-life care into child health strategies. Future longitudinal, multi-level and exposome-oriented research is needed to translate mechanistic insight into effective prevention and public health action.

CRedit authorship contribution statement

Sergio Rinella: Writing – review & editing, Writing – original draft, Methodology, Data curation, Conceptualization. **Manuela Lo Bianco:** Writing – review & editing, Writing – original draft, Methodology, Data curation, Conceptualization. **Roberta Leonardi:** Writing – review & editing, Writing – original draft, Data curation. **Gennaro Anastasio:** Writing – review & editing, Writing – original draft, Data curation. **Piero Pavone:** Writing – review & editing, Writing – original draft, Data curation. **Martino Ruggieri:** Writing – review & editing, Validation, Supervision. **Agnese Suppiej:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Agata Polizzi:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization.

Declaration of competing interest

None of the authors has any conflict of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jpeds.2026.100353](https://doi.org/10.1016/j.jpeds.2026.100353).

References

- Wallace JL, Pollen AA. Human neuronal maturation comes of age: cellular mechanisms and species differences. *Nat Rev Neurosci.* 2024;25:7–29. <https://doi.org/10.1038/s41583-023-00760-3>.
- Dai ZP, Wang JN, Zhou HL, Zhang W, Miao J. Bridging environmental exposures and brain health with an integrative framework for understanding neurobiological impacts. *Neurosci Biobehav Rev.* 2025;179, 106444. <https://doi.org/10.1016/j.neubiorev.2025.106444>.
- Rauh VA, Margolis AE. Research Review: environmental exposures, neurodevelopment, and child mental health – new paradigms for the study of brain and behavioral effects. *Child Psychol Psychiatry.* 2016;57:775–793. <https://doi.org/10.1111/jcpp.12537>.
- Jubair H. Epigenetics and environmental exposures in early neurodevelopment: implications for pediatric neurological disorders. *Sage Open Pediatr.* 2025;12, 3050225251380331. <https://doi.org/10.1177/3050225251380331>.
- Grandjean P, Landrigan PJ. Neurobehavioural effects of developmental toxicity. *Lancet Neurol.* 2014;13:330–338. [https://doi.org/10.1016/S1474-4422\(13\)70278-3](https://doi.org/10.1016/S1474-4422(13)70278-3).
- Landrigan PJ, Fuller R, Fisher S, Suk WA, Sly P, Chiles TC, et al. Pollution and children's health. *Sci Total Environ.* 2019;650:2389–2394. <https://doi.org/10.1016/j.scitotenv.2018.09.375>.
- Calderón-Garcidueñas L, Leray E, Heydarpour P, Torres-Jardón R, Reis J. Air pollution, a rising environmental risk factor for cognition, neuroinflammation and neurodegeneration: the clinical impact on children and beyond. *Rev Neurol.* 2016;172:69–80. <https://doi.org/10.1016/j.neurol.2015.10.008>.
- Dórea JG. Environmental exposure to low-level lead (Pb) co-occurring with other neurotoxins in early life and neurodevelopment of children. *Env Res.* 2019;177, 108641. <https://doi.org/10.1016/j.envres.2019.108641>.
- Limosin F. Neurodevelopmental and environmental hypotheses of negative symptoms of schizophrenia. *BMC Psychiatry.* 2014;14:88. <https://doi.org/10.1186/1471-244X-14-88>.
- Saunders M, Magnanti BL, Correia Carreira S, Yang A, Alamo-Hernández U, Riojas-Rodríguez H, et al. Chlorpyrifos and neurodevelopmental effects: a literature review and expert elicitation on research and policy. *Env Health.* 2012;11:S5. <https://doi.org/10.1186/1476-069X-11-S1-S5>.
- Lane M, Oyster E, Luo Y, Wang H. The effects of air pollution on neurological diseases: a narrative review on causes and mechanisms. *Toxics.* 2025;13:207. <https://doi.org/10.3390/toxics13030207>.
- Guo T, Najafi ML, Zhang J. A systematic review of exposure to toxic elements and neurocognitive development in children. *Ecotoxicol Env Saf.* 2025;291, 117792. <https://doi.org/10.1016/j.ecoenv.2025.117792>.

13. Gao X, Wang X, Zheng X, Zhao Y, Wang N, Chang S, et al. Chemical pollutant exposure in neurodevelopmental disorders: integrating toxicogenomic and transcriptomic evidence to elucidate shared biological mechanisms and developmental signatures. *Toxics*. 2025;13:282. <https://doi.org/10.3390/toxics13040282>.
14. Heyer DB, Meredith RM. Environmental toxicology: sensitive periods of development and neurodevelopmental disorders. *Neuro Toxicol*. 2017;58:23–41. <https://doi.org/10.1016/j.neuro.2016.10.017>.
15. Kundakovic M, Jaric I. The epigenetic link between prenatal adverse environments and neurodevelopmental disorders. *Genes*. 2017;8:104. <https://doi.org/10.3390/genes8030104>.
16. Tran NQV, Miyake K. Neurodevelopmental disorders and environmental toxicants: epigenetics as an underlying mechanism. *Int J Genom*. 2017;2017:1–23. <https://doi.org/10.1155/2017/7526592>.
17. Sisodiya SM. Climate change and neurology: time to talk and to act. *Lancet Neurol*. 2023;22:656–657. [https://doi.org/10.1016/S1474-4422\(23\)00235-1](https://doi.org/10.1016/S1474-4422(23)00235-1).
18. Sisodiya SM, Gulcebi MI, Fortunato F, Mills JD, Haynes E, Bramon E, et al. Climate change and disorders of the nervous system. *Lancet Neurol*. 2024;23:636–648. [https://doi.org/10.1016/S1474-4422\(24\)00087-5](https://doi.org/10.1016/S1474-4422(24)00087-5).
19. Conway F, Portela A, Filippi V, Chou D, Kovats S. Climate change, air pollution and maternal and newborn health: an overview of reviews of health outcomes. *J Glob Health*. 2024;14, 04128. <https://doi.org/10.7189/jogh.14.04128>.
20. Olson DM, Metz GAS. Climate change is a major stressor causing poor pregnancy outcomes and child development. *F1000Res*. 2020;9:1222. <https://doi.org/10.12688/f1000research.27157.1>.
21. Radke EG, Braun JM, Nachman RM, Cooper GS. Phthalate exposure and neurodevelopment: a systematic review and meta-analysis of human epidemiological evidence. *Env Int*. 2020;137, 105408. <https://doi.org/10.1016/j.envint.2019.105408>.
22. Liu F, Xu J, Guo L, Qin W, Liang M, Schumann G, et al. Environmental neuroscience linking exposure to brain structure and function underlying cognition and behavior. *Mol Psychiatry*. 2023;28:17–27. <https://doi.org/10.1038/s41380-022-01669-6>.
23. Santos S, Maitre L, Warembourg C, Agier L, Richiardi L, Basagaña X, et al. Applying the exposure concept in birth cohort research: a review of statistical approaches. *Eur J Epidemiol*. 2020;35:193–204. <https://doi.org/10.1007/s10654-020-00625-4>.
24. Capua GD, Rahmstorf S. Extreme weather in a changing climate. *Env Res Lett*. 2023;18, 102001. <https://doi.org/10.1088/1748-9326/acfb23>.
25. Gao H, Xu C, Wu S, Li T, Huang Y. Has the unpredictability of geological disasters been increased by global warming? *Npj Nat Hazards*. 2025;2:55. <https://doi.org/10.1038/s44304-025-00108-0>.
26. Brett L, White CJ, Domeisen DIV, Van Den Hurk B, Ward P, Zscheischler J. Review article: the growth in compound weather and climate event research in the decade since SREX. *Nat Hazards Earth Syst Sci*. 2025;25:2591–2611. <https://doi.org/10.5194/nhess-25-2591-2025>.
27. Zhang Y, Sun F, Yuan K, Du Y, Wu L, Ge Y, et al. Ambient temperature and major structural anomalies: a retrospective study of over 2 million newborns. *Sci Total Environ*. 2023;882, 163613. <https://doi.org/10.1016/j.scitotenv.2023.163613>.
28. LaPointe S, Beagle LE, Zheng X, Kancherla V, Mutic A, Chang HH, et al. Associations between exposure to extreme ambient heat and neural tube defects in Georgia, USA: a population-based case-control study. *Env Res*. 2024;261, 119756. <https://doi.org/10.1016/j.envres.2024.119756>.
29. Atalell KA, Pereira G, Duko B, Nyadanu SD, O'Donnell M, Tessema GA. Prenatal and early childhood exposure to biothermal stress and developmental vulnerability at school entry in Western Australia: a population-based cohort study. *Env Int*. 2025;202, 109642. <https://doi.org/10.1016/j.envint.2025.109642>.
30. Lin Q, Gao Y, Liu Y, Huang S, Su Y, Luo W, et al. Heat wave exposure during pregnancy and neurodevelopmental delay in young children: a birth cohort study. *Env Res*. 2025;266, 120541. <https://doi.org/10.1016/j.envres.2024.120541>.
31. Barbalat G, Guilbert A, Adelaide L, Charles MA, Hough I, Launay L, et al. Impact of early life exposure to heat and cold on linguistic development in two-year-old children: findings from the ELFE cohort study. *Env Health*. 2025;24:19. <https://doi.org/10.1186/s12940-025-01173-8>.
32. Barbalat G, Guilbert A, Charles MA, Hough I, Launay L, Kloog I, et al. Effects of projected increases in heat exposure on linguistic development in two-year-old children: a longitudinal modified treatment policy analysis. *Env Epidemiol*. 2025;9, e423. <https://doi.org/10.1097/EE9.0000000000000423>.
33. Assari S, Zare H. Extreme heat exposure is associated with lower learning, general cognitive ability, and memory among US children. *Ojn*. 2025;3:10–22. <https://doi.org/10.31586/ojn.2025.1277>.
34. Granés L, Essers E, Ballester J, Petricola S, Tiemeier H, Iniguez C, et al. Early life cold and heat exposure impacts white matter development in children. *Nat Clim Chang*. 2024;14:760–766. <https://doi.org/10.1038/s41558-024-02027-w>.
35. Granés L, Kusters MSW, Ballester J, Essers E, Petricola S, López-Vicente M, et al. Exposure to ambient temperature and functional connectivity of brain resting-State networks in preadolescents. *J Am Acad Child Adolesc Psychiatry*. 2025;64, S0890856725000462. <https://doi.org/10.1016/j.jaac.2024.11.023>.
36. Pazos N, Favara M, Sánchez A, Scott D, Behrman JR. Long-term effects of rainfall shocks on foundational cognitive skills: evidence from Peru. *SSRN J*. 2023. <https://doi.org/10.2139/ssrn.4360823>.
37. Buthmann J, Huang D, Casaccia P, O'Neill S, Nomura Y, Liu J. Prenatal exposure to a climate-related disaster results in changes of the placental transcriptome and infant temperament. *Front Genet*. 2022;13, 887619. <https://doi.org/10.3389/fgene.2022.887619>.
38. Delingenis D, Blum M, Lee RM, Shereen AD, Nomura Y. Prenatal exposure to extreme ambient heat may amplify the adverse impact of Superstorm Sandy on basal ganglia volume among school-aged children. *PLoS One*. 2025;20, e0324150. <https://doi.org/10.1371/journal.pone.0324150>.
39. Shereen AD, Delingenis D, Wu T, Rahman MS, Blum M, Newcorn JH, et al. Behavioral moderators of In-utero superstorm sandy exposure and fronto-limbic cortical development—potential role of adaptiveness in clinical intervention strategies, a pilot study. *Front Psychiatry*. 2025;16, 1481347. <https://doi.org/10.3389/fpsy.2025.1481347>.
40. Cao-Lei L, Yogendran S, Dufoix R, Elgebeil G, Laplante DP, King S. Prenatal maternal stress from a natural disaster and hippocampal volumes: gene-by-environment interactions in young adolescents from Project ice storm. *Front Behav Neurosci*. 2021;15, 706660. <https://doi.org/10.3389/fnbeh.2021.706660>.
41. Tang H, Di Q. The effect of prenatal exposure to climate anomaly on adulthood cognitive function and job reputation. *IJERPH*. 2022;19:2523. <https://doi.org/10.3390/ijerph19052523>.
42. Aguilar A, Vicarelli M. El Niño and children: medium-term effects of early-life weather shocks on cognitive and health outcomes. *World Dev*. 2022;150, 105690. <https://doi.org/10.1016/j.worlddev.2021.105690>.
43. Olurotimi O. Climate shocks and human capital:evidence from Uganda. *Envir Dev Econ*. 2025;30:421–441. <https://doi.org/10.1017/S1355770X25000105>.
44. Buthmann JL, Benmarhnia T, Huang JY, Huang P, Miller JG, Uy JP, et al. Exposure to fine particulate matter during pregnancy is associated with hippocampal development in offspring. *Biol Psychiatry Glob Open Sci*. 2025;5, 100490. <https://doi.org/10.1016/j.bpsgos.2025.100490>.
45. Blanco-Hinojo L, Pujol J, Martínez-Vilavella G, Gómez-Herrera L, Rivas I, Gómez-Roig MD, et al. Impact of prenatal exposure to airborne particulate matter on local functional connections in the cerebral cortex of neonates. *NeuroImage*. 2026;332, 121911. <https://doi.org/10.1016/j.neuroimage.2026.121911>.
46. 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. *Child Psychol Psychiatry*. 2020;61:1253–1265. <https://doi.org/10.1111/jcpp.13189>.
47. Kusters MSW, López-Vicente M, Muetzel RL, Binter AC, Petricola S, Tiemeier H, et al. Residential ambient air pollution exposure and the development of white matter microstructure throughout adolescence. *Env Res*. 2024;262, 119828. <https://doi.org/10.1016/j.envres.2024.119828>.
48. Jara CA, Jones SA, Nagel BJ. Longitudinal associations between air pollution and adolescent gray matter development: insights from the ABCD study. *Env Res*. 2026;289, 123333. <https://doi.org/10.1016/j.envres.2025.123333>.
49. Cotter DL, Campbell CE, Sukumaran K, McConnell R, Berhane K, Schwartz J, et al. Effects of ambient fine particulates, nitrogen dioxide, and ozone on maturation of functional brain networks across early adolescence. *Env Int*. 2023;177, 108001. <https://doi.org/10.1016/j.envint.2023.108001>.
50. Cotter DL, Ahmadi H, Cardenas-Iniguez C, Bottenhorn KL, Gauderman WJ, McConnell R, et al. Exposure to multiple ambient air pollutants changes white matter microstructure during early adolescence with sex-specific differences. *Commun Med*. 2024;4:155. <https://doi.org/10.1038/s43856-024-00576-x>.
51. Kong T, Yang Y, Ji F, Liu J, Liu R, Luo L. Combined effects of prenatal ozone exposure and school/neighborhood environments on youth brain, cognition, and psychotic-like experiences. *Child Psychol Psychiatry*. 2025;66:1551–1562. <https://doi.org/10.1111/jcpp.14167>.
52. Hobbs M, Deng B, Woodward L, Marek L, McLeod G, Sturman A, et al. Childhood air pollution exposure is related to cognitive, educational and mental health outcomes in childhood and adolescence: a longitudinal birth cohort study. *Env Res*. 2025;274, 121148. <https://doi.org/10.1016/j.envres.2025.121148>.
53. Oh TK, Song I. Prenatal exposure to ambient air pollution and risk of neurodevelopmental disorders in offspring: a nationwide population-based cohort study. *Child Psychol Psychiatry*. 2026, jcpp.70120. <https://doi.org/10.1111/jcpp.70120>.
54. Buthmann JL, Aghaeepour N, Burke M, Maric I, Stevenson DK, Shaw GM, et al. Prenatal wildfire smoke, first trimester proteome, and subsequent child behavioral outcomes: an exploratory study. *Env Res*. 2026;291, 123577. <https://doi.org/10.1016/j.envres.2025.123577>.
55. Yamamoto M, Eguchi A, Sakurai K, Nakayama SF, Sekiyama M, Mori C, et al. Longitudinal analyses of maternal and cord blood manganese levels and neurodevelopment in children up to 3 years of age: the Japan Environment and Children's Study (JECS). *Env Int*. 2022;161, 107126. <https://doi.org/10.1016/j.envint.2022.107126>.
56. Florez-Garcia VA, Wright RO, Keil AP, Téllez-Rojo MM, Martínez-Medina S, Estrada-Gutierrez G, et al. Essential and non-essential metals in children's intellectual functioning: a multi-media biomarker approach from a Mexico City birth cohort. *Env Res*. 2025;285, 122323. <https://doi.org/10.1016/j.envres.2025.122323>.
57. Lane JM, Liu SH, Midya V, Alcalá CS, Eggers S, Svensson K, et al. Childhood Pb-induced cognitive dysfunction: structural equation modeling of hot and cold executive functions. *J Expo Sci Env Epidemiol*. 2025;35:715–724. <https://doi.org/10.1038/s41370-025-00761-7>.
58. Hoover C, Papandonatos G, Cecil KM, Chen A, Lanphear BP, Strawn JR, et al. Blood lead concentrations and depressive and anxiety symptoms in childhood. *JAMA Netw Open*. 2026;9, e2556019. <https://doi.org/10.1001/jamanetworkopen.2025.56019>.
59. Nyanza EC, Mhara RJ, Asori M, Thomas DSK, Kisoka AP. Effects of prenatal lead, mercury, cadmium, and arsenic exposure on children's neurodevelopment in an artisanal small-scale gold mining area in Northwestern Tanzania using a multi-chemical exposure model. *PLOS Glob Publ Health*. 2025;5, e0004577. <https://doi.org/10.1371/journal.pgph.0004577>.
60. Peterson BS, Delavari S, Bansal R, Sawardekar S, Gupta C, Andrews H, et al. Brain abnormalities in children exposed prenatally to the pesticide chlorpyrifos. *JAMA Neurol*. 2025;82:1057. <https://doi.org/10.1001/jamaneurol.2025.2818>.

61. Bahrami M, Simpson SL, Burdette JH, Lyday RG, Quandt SA, Chen H, et al. Altered default mode network associated with pesticide exposure in Latinx children from rural farmworker families. *NeuroImage*. 2022;256, 119179. <https://doi.org/10.1016/j.neuroimage.2022.119179>.
62. Ramos AM, Herring AH, Villanger GD, Thomsen C, Sakhi AK, Cequier E, et al. The association of prenatal phthalates, organophosphorous pesticides, and organophosphate esters with early child language ability in Norway. *Env Res*. 2023; 225, 115508. <https://doi.org/10.1016/j.envres.2023.115508>.
63. Li J, Song X, Luo T, Loo KK, Chen S, Gui T, et al. Effects of daily exposure to pyrethroid pesticides during infancy on children neurodevelopment at age four: a prospective study in rural Yunnan, China. *NeuroToxicology*. 2025;108:105–112. <https://doi.org/10.1016/j.neuro.2025.03.006>.
64. Viglietti PG, Jäggi L, Wey H, Petitpierre A, Lindh C, Rousseau KL, et al. Postnatal pesticide exposure and executive function in children and adolescents: findings from South Africa. *Env Res*. 2026;289, 123310. <https://doi.org/10.1016/j.envres.2025.123310>.
65. Al-Saleh I, Aljerayed Y, Gheith M, Alobaid N, Alenazi H, Elkhatib R, et al. Longitudinal analysis of maternal exposure to phthalates and bisphenol A and their impact on infant neurodevelopment and autistic behavior: the potential mediating role of thyroid hormones. *Int J Hyg Env Health*. 2025;269, 114647. <https://doi.org/10.1016/j.ijheh.2025.114647>.
66. Park S, McArthur K, Barrett E, Cordero JF, Etzel T, Ghassabian A, et al. Prenatal phthalate exposure and neurodevelopmental delay in early childhood (1 to 3 years): an environmental influences on child health outcomes (ECHO) study. *Env Int*. 2026; 208, 110100. <https://doi.org/10.1016/j.envint.2026.110100>.
67. Werder EJ, Lu K, Liu CW, Thistle JE, Rager JE, Li G, et al. Early life phthalate exposure impacts gray matter and white matter volume in infants and young children. *Env Res*. 2025;279, 121826. <https://doi.org/10.1016/j.envres.2025.121826>.
68. Engel SM, Li T, Werder EJ, Liu CW, Pacyga DC, Thistle J, et al. Early life phthalate and replacement plasticizer exposures and changes in early childhood brain functional connectivity and structural morphology. *Env Int*. 2026;208, 110119. <https://doi.org/10.1016/j.envint.2026.110119>.
69. Zhang B, Wang Z, Zhang J, Dai Y, Feng C, Lin Y, et al. Prenatal perfluoroalkyl substances exposure and neurodevelopment in toddlers: findings from SMBCS. *Chemosphere*. 2023;313, 137587. <https://doi.org/10.1016/j.chemosphere.2022.137587>.
70. Oh J, Schmidt RJ, Tancredi D, Calafat AM, Roa DL, Hertz-Picciotto I, et al. Prenatal exposure to per- and polyfluoroalkyl substances and cognitive development in infancy and toddlerhood. *Env Res*. 2021;196, 110939. <https://doi.org/10.1016/j.envres.2021.110939>.
71. Xing Y, Gan H, Xu D, Wu X, Tong J, Yan S, et al. Sensitive windows of per- and polyfluoroalkyl substances exposure and children's intelligence quotient. *Env Int*. 2026;210, 110218. <https://doi.org/10.1016/j.envint.2026.110218>.
72. Wu F, Kartiosuo N, Kaikkonen J, Magnussen CG, Rantakokko P, Kiviranta H, et al. Childhood exposure to multiple persistent organic pollutants and midlife cognitive function. *Sci Total Environ*. 2026;1020, 181552. <https://doi.org/10.1016/j.scitotenv.2026.181552>.
73. Zajac L, Landrigan PJ, the COUNCIL ON ENVIRONMENTAL HEALTH AND CLIMATE CHANGE, Zajac L, Balk SJ, Byron LG, et al. Environmental issues in global pediatric health: technical report. *Pediatrics*. 2025;155, e2024070076. <https://doi.org/10.1542/peds.2024-070076>.
74. Criswell R, Gleason K, Abuawad AK, Karagas MR, Grene K, Mora AM, et al. A call for pediatric clinicians to address environmental health concerns in rural settings. *Pediatr Clin North Am*. 2025;72:65–83. <https://doi.org/10.1016/j.pcl.2024.07.030>.
75. Atkin K, Christopoulos G, Turk R, Bernhardt JM, Simmonds K. Educating pregnant women about the dangers of extreme heat and air pollution. *J Obstet Gynecol Neonatal Nurs*. 2024;53:438–446. <https://doi.org/10.1016/j.jogn.2024.01.005>.
76. Ramadani L, Khanal S, Boeckmann M. Content focus and effectiveness of Climate change and Human health education in schools: a scoping review. *Sustainability*. 2023;15, 10373. <https://doi.org/10.3390/su151310373>.
77. Moutet L, Bernard P, Green R, Milner J, Haines A, Slama R, et al. The public health co-benefits of strategies consistent with net-zero emissions: a systematic review. *Lancet Planet Health*. 2025;9:e145–e156. [https://doi.org/10.1016/S2542-5196\(24\)00330-9](https://doi.org/10.1016/S2542-5196(24)00330-9).
78. Díaz-Martínez F, Sánchez-Sauco MF, Cabrera-Rivera LT, Sánchez CO, Hidalgo-Albadalejo MD, Claudio L, et al. Systematic review: neurodevelopmental benefits of active/passive school exposure to green and/or blue spaces in children and adolescents. *IJERPH*. 2023;20:3958. <https://doi.org/10.3390/ijerph20053958>.
79. Perera F, Nadeau K. Climate change, fossil-fuel pollution, and children's health. *N Engl J Med*. 2022;386:2303–2314. <https://doi.org/10.1056/NEJMra2117706>.