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Review

Impact of Early-Life Exposure to Environmental Neurotoxicants on Brain Development and Risk of Neurodevelopmental Disorders in Children

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Abstract: Environmental neurotoxicants pose significant risks to the developing brain, particularly during foetal and early postnatal periods when the blood-brain barrier is immature and highly permeable. Exposure during these critical windows of development can result in long-lasting structural and functional alterations to the nervous system, potentially leading to adverse neurodevelopmental and cognitive outcomes later in life. To synthesise current evidence on major environmental neurotoxicants, their mechanisms of action, neurodevelopmental effects, vulnerability factors, and implications for prevention and policy. A narrative review of published epidemiological, experimental, neuroimaging, and meta-analytic studies examining exposure to heavy metals, pesticides, industrial solvents, air pollutants, and endocrine-disrupting chemicals, with emphasis on developmental neurotoxicity and associated health outcomes. Environmental neurotoxicants disrupt neurodevelopment through oxidative stress, inflammation, excitotoxicity, apoptosis, epigenetic modifications, and neurotransmitter dysregulation. Prenatal and early-life exposures are associated with increased risks of autism spectrum disorder, attention-deficit/hyperactivity disorder, intellectual disabilities, behavioural disorders, reduced intelligence quotient (IQ), and structural brain abnormalities. Susceptibility is influenced by genetic factors, socioeconomic conditions, nutritional status, and combined exposures to multiple toxicants. Environmental neurotoxicants remain a major threat to child neurodevelopment, while current regulatory frameworks are insufficient to adequately protect vulnerable populations. Strengthened preventive measures, child-specific regulations, coordinated international testing, and equitable public health interventions are urgently needed to reduce exposure and safeguard brain health.

Keywords: Neurotoxicants; Neurodevelopment; Early-Life Exposure; Neurodevelopmental Disorders; Children; Environmental Health

1. Introduction

Foetal and neonatal brain development is characterised by rapid in utero growth, basic structural formation, rapid proliferation, and excessive synaptogenesis. The system is highly dynamic and extremely vulnerable; thus, any

exposure may have severe effects on foetal development. Rapid neurogenesis occurs before mid-gestation, followed by neuronal migration for cortical layer formation and synaptogenesis for neural circuit development [1]. Postnatal phases include synaptic pruning and significant myelination, increasing white-matter volume for faster, more efficient information transfer [1]. In the immature stage, the blood-brain barrier still lacks fully developed junctions and transporters, which increases the passage of toxins through this system [2–4]. Heavy metals such as lead (Pb) and mercury (Hg), emitted by industry and present in contaminated water, can enter the brain and trigger oxidative stress, inflammation, and cell death, which may result in reduced intelligence and attention-deficit/hyperactivity disorder (ADHD) [5,6]. Pesticides such as organophosphates and pyrethroids, used in agriculture, impair cholinergic and other neurotransmitter functions and may be responsible for autism and developmental delay [7–9]. Infants whose mothers were exposed to solvents during pregnancy may suffer cognitive delays, attention deficit, hyperactivity disorder, speech delay, and impairment in their motor skills [10,11]. Inhaling air pollutants like fine particulate matter less than 2.5 μm (PM2.5) and polycyclic aromatic hydrocarbons (PAHs), due to traffic emissions and combustion processes, causes inflammation, excitotoxicity, and contributes to the structural development of the brain and mental health issues [12–14]. Endocrine disruptors like phthalates and Bisphenol A (BPA), which are common in plastics and consumer products, affect hormone signals and epigenetic patterns and are known to lead to behavioural disorders [15–17].

Some epidemiological studies, which include meta-analysis studies and cohort studies, show that there are dose-dependent relations between exposure of infants to neurotoxic compounds during their mother's pregnancy and an increased probability of autism spectrum disorder (ASD), ADHD, learning disabilities, and lower IQ scores. Neurotoxic effects on the infants can depend on many variables, which include genetics, socioeconomic status (low SES), nutrition deficiencies, and co-exposure, among others. For instance, infants who suffer from low SES and/or suffer from iron deficiency could be more vulnerable to toxicity at lower exposures [18,19].

There is ample evidence regarding preventive practices that reveal fragmentation and a lack of focus on addressing the issues of interaction among multiple exposures and the impact of low exposure levels [20,21]. Therefore, it is imperative to adopt a precautionary strategy that includes implementation of chemical bans and biomonitoring [20,21].

Community-level interventions such as education, nutritional supplements, and medical screening can be effective mitigations [22,23]. Moreover, economic considerations have shown positive results from previous strategies such as the ban of leaded gasoline [24,25]. This narrative review examines this issue, including relevant tables on neurotoxicants, their permissible limits, mechanisms, and risk factors to take evidence-based action for safeguarding children's neurodevelopment.

2. Methodology

This narrative review was designed to critically examine the existing literature on the effects of early-life exposure to environmental neurotoxicants on brain development and on the risk of neurodevelopmental disorders (NDDs) in children. A qualitative synthesis approach was used to gather, evaluate, and interpret relevant studies across multiple disciplines, including environmental health, toxicology, paediatrics, and neuroscience.

A comprehensive search of the published literature was conducted using databases including PubMed, ScienceDirect, Google Scholar, and Scopus. The search covered articles published between January 2000 and August 2025. The following search terms and combinations were used: "environmental neurotoxicants", "early-life exposure", "neurodevelopmental disorders", "brain development", "lead", "mercury", "pesticides", " polychlorinated biphenyls (PCBs)", and "children's health". The combination included: "environmental neurotoxicants" OR "neurotoxicity" OR "heavy metals" OR "pesticides" OR "air pollution") AND ("neurodevelopment" OR "brain development" OR "child development") AND ("children" OR "infants" OR "prenatal exposure". Articles identified through the literature search were screened by title, abstract, and full text for relevance and eligibility. Only studies that satisfied the predefined inclusion criteria and provided evidence linking early-life exposure to environmental neurotoxicants with neurodevelopmental outcomes in children were included in the review.

Included studies comprised original research articles and epidemiological studies focusing on children from the prenatal stage up to 12 years of age. Eligible studies specifically addressed exposure to environmental neurotoxicants via food, water, air, or household products and reported measurable neurological or developmental

outcomes, such as IQ, behavioural changes, autism spectrum disorder (ASD), or attention-deficit/hyperactivity disorder (ADHD). Studies were excluded if they focused solely on adults, relied exclusively on animal models without human data, were theoretical or editorial in nature, or did not explicitly link environmental exposure to neurodevelopmental outcomes.

Information was manually extracted into thematic categories, including type of neurotoxicant, exposure route and timing, biological mechanisms, and reported NDDs. Emphasis was placed on identifying recurring patterns, emerging trends, and research gaps. Studies were also grouped by geographical region to assess global patterns of risk.

3. Results and Discussion

3.1. Critical Windows of Brain Development

3.1.1. Overview of Foetal and Early Postnatal Neurodevelopment

The foetal and early post-natal life are essential for the development of the brain. Rapid development, differentiation, and synaptogenesis characterise these stages. Brain cells have higher sensitivity to exogenous harmful factors. They are susceptible to such a phenomenon due to incomplete development of elimination systems and the impermeable character of the blood-brain barrier. Therefore, neurotoxic agents affect neural tissue at low concentrations [3,22].

Brain development is a long and highly coordinated process. It begins from the 3rd gestational week and lasts until adolescence. Both genetic regulation and the external environment affect the process [23]. As soon as the foetal period starts, neurogenesis starts on the 42nd day. Symmetrical cell division in the ventricular zone leads to the proliferation of neural stem cells. Later, these cells undergo asymmetric divisions, resulting in the production of neurons and maintaining the pool of progenitors. Neurogenesis reaches its peak in mid-pregnancy and finishes around the 108th day. Migration of neurons proceeds in radial orientation along glial guide cells from the ventricular zone. Thus, the six-layer structure of the neocortex forms by the inside-out principle. Moreover, migration of inhibitory interneurons from locations like the ganglionic eminences is important for balanced neuronal functioning. Formation of synapses commences during the second trimester. Thalamocortical and corticothalamic circuits start developing from week 26 of gestation. Subplate cells play an important role in establishing connections initially before withdrawal. Myelination occurs before birth but is minimal at this stage. Early fibre circuits are being prepared to facilitate efficient signal transmission [1,26].

After birth, neurogenesis occurs only within some brain regions, such as the subventricular zone, which helps develop the olfactory bulb, and the hippocampal dentate gyrus. Neurogenesis becomes rare. The migration phase lasts for a brief period as glial cells migrate to the cortex and white matter. These cells differentiate into oligodendrocytes and astrocytes that contribute to maintaining the brain. The number of synapses increases as synaptogenesis occurs at high levels. The excess synapse production is then followed by experience-driven synapse removal that reduces the synapse population by up to 50% from childhood through to adolescence. The synapse elimination process is affected by neurotrophic factors and neuronal activity. Myelination intensifies considerably. Oligodendrocyte progenitors form insulating myelin sheaths over the axons, which improves the speed of nerve impulse transmission. At the age of six, white matter volume quadruples, reaching 90% of the adult volume. White matter development continues until adolescence. Each stage makes the brain vulnerable to disruption that leads to lasting problems. In addition, the immature blood-brain barrier provides inadequate protection against toxins [27,28].

3.1.2. Blood-Brain Barrier (BBB) Immaturity and Sensitivity

Blood-brain barrier is a biological barrier that maintains balance between blood and brain tissues by regulating the passage of substances from one environment to the other. In children and infants, the BBB is not fully developed, hence it cannot perform some metabolic functions well compared to an adult. As such, there is a high possibility for neurotoxic effects due to increased ability of environmental chemicals such as heavy metals, pesticides, industry solvents, organics and air pollutants to penetrate the blood-brain barrier. The BBB starts formation within the 7th week of pregnancy but only becomes fully functional several months after birth [2,22,29].

Formation of this biological barrier begins during embryonic development when the cerebral blood vessels start forming. Formation of tight junctions and efflux transporters occurs as early as the 11–12th day of gestation

in rodents and 5–7 weeks post conception in humans. These barriers prevent paracellular diffusion and efflux of toxic materials, hence maintaining brain tissue stability. However, during the brain developmental process, the blood brain barrier (BBB) is not yet developed, hence having a wide extracellular space and pericyte coverage, resulting in increased susceptibility to neurotoxins [4,30,31].

This immature state causes an enhanced susceptibility to neurotoxic agents. In immature brains, the presence of transport mechanisms for nutrient transport also leads to the entry of toxic substances accidentally. For example, the expression of efflux mechanisms is often higher in embryos compared to adults, thus leading to susceptibility to certain substances that have no physiological role, such as manganese. These substances can accumulate via these routes. Also, the blood-cerebrospinal fluid barrier (BCSFB) at the choroid plexus becomes increasingly mature, thus increasing the susceptibility due to protein transfer and inflammation. Moreover, the higher respiratory rate, increased absorption in relation to body weight, and poor detoxification ability of children also worsen the impact of toxins [2,30].

3.2. Types and Sources of Environmental Neurotoxicants

Environmental neurotoxins like heavy metals, pesticides, solvent chemicals, airborne pollutants, and phthalates are highly dangerous for brain development at critical periods and even at low exposure levels. Neurotoxins can get inside the body either through ingestion or inhalation and through the placenta and adversely affect brain development through the induction of oxidative stress and inflammatory reactions, among other mechanisms, and hinder processes like synaptogenesis and myelination. For instance, exposure to lead causes a drop in IQ level and ADHD signs, whereas organophosphate pesticides, like chlorpyrifos, have shown increased likelihood of ASD and cognitive impairment. Neuroimaging research has revealed abnormalities in the brains of affected individuals in terms of reduced cortical thickness, among other issues. Exposure to neurotoxins results in a variety of developmental brain disorders and often worsens due to social and genetic factors. The problems caused by neurotoxins last long enough to affect adults, too and incur enormous costs to society.

3.2.1. Heavy Metals, Pesticides, Air Pollutants, Phthalates

Environmental neurotoxicants refer to environmental factors that can damage the nervous system and cause problems related to neurodevelopmental delay, cognitive impairment, and behavioural abnormalities. Environmental metals such as Pb and Hg can be mentioned among the most common environmental neurotoxicants, which may be emitted due to industrial practices and mining processes and through water contamination. Heavy metals can cross the BBB, causing neuroinflammation, oxidative stress, disturbance in neurotransmitter actions, and neuronal damage, especially during brain development [5,6]. Pesticides such as organophosphates, carbamates, pyrethroids, and neonicotinoids can be used in agriculture and enter the body via ingestion, inhalation, and absorption through contaminated food and water. Neurotoxic pesticides can disturb neurotransmitter actions and result in the development of neurodevelopmental disorders such as autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) [28,32]. Air pollution agents, such as particulate matter (PM), volatile organic compounds (VOCs), and nitrogen oxides emitted by vehicles, industries, and power plants, can cause systemic inflammation and oxidative stress in individuals after inhalation.

Phthalates, which are pervasive contaminants in plastic goods, cosmetics, and foods, are endocrine-disrupting substances that affect hormonal communication and brain growth. Prenatal and childhood exposure to these phthalates has been associated with a lower IQ, behavioural disorders, and neurodevelopmental disabilities [15,16]. Bisphenol A (BPA), one such environmental toxin, is widely present in plastics, children's toys and dishes, and canned foodstuffs [33]. Solvents like toluene and benzene, which can be found in paints, cleaners, and chemical manufacturing processes, are volatile compounds that can be ingested through inhalation or direct dermal contact. These agents can trigger neurotoxic symptoms like headache and dizziness, as well as memory impairment and peripheral neuropathy due to their solubility in cell membrane lipids and interference with neural signalling [13,34,35]. The presence of neurotoxic substances in the ambient air and water, soil, and consumer goods necessitates regulations aimed at reducing their levels in the environment, protecting people from exposure, and conducting further studies on these compounds.

3.2.2. Exposure Routes

Environmental neurotoxins, including heavy metals, pesticides, air pollution, and endocrine disrupters, gain access to our body via three primary routes: inhalation, ingestion, and skin contact. By breathing air containing fine particles, industrial gases, and wildfire smoke, the toxins affect our central nervous system via our respiratory tracts. Occasionally, some neurotoxins pass through our bodies' olfactory neurons or blood-brain barriers [13,36]. Inhalation is another common source of exposure: we ingest neurotoxins when we consume water or food contaminated by toxins or eat soils that are not clean [17,37]. It is more dangerous for small children because they tend to put everything in their mouth and consume water and food in proportions greater than their body weights [17,37]. Although skin absorption plays a smaller role in the intake of neurotoxins compared to other sources, it still occurs after we get into contact with the dust, soil, and products containing neurotoxins [17,36]. The most vulnerable periods are pregnancy and early childhood due to the transfer of the toxins from mother to foetus across the placenta or via breast milk [38].

In addition, some environments pose higher risks, such as highly polluted urban environments, agriculturally polluted areas where there is pesticide use, or home environments where products that contain neurotoxins are found [36,37]. These are some exposure methods that make us susceptible to neurodevelopmental disorders. **Table 1** below summarizes the major environmental neurotoxicants, their sources and routes of exposure.

Table 1. Major Environmental Neurotoxicants, Sources, and Routes of Exposure.

Neurotoxicant	Sources	Routes of Exposure
Lead (Pb)	Lead-based paint, water pipes, soil from emissions, batteries, and mining	Inhalation, ingestion, dermal absorption
Mercury (Hg)	Industrial emissions, fish bioaccumulation, and chloralkaline processes	Ingestion (diet), inhalation, dermal
Arsenic (As)	Groundwater, soil, air from mining, pesticides	Ingestion (water), inhalation
Cadmium (Cd)	Industrial discharges, tobacco, and contaminated crops	Inhalation, ingestion
Manganese (Mn)	Welding, mining, and air emissions	Inhalation, ingestion
Aluminium (Al)	Kitchenware, water treatment, cosmetics, antacids	Ingestion (diet), inhalation, dermal
Polychlorinated Biphenyls (PCBs)	Oils, fluids, waste, food chains (e.g., fish)	Ingestion, inhalation
Bisphenol A (BPA)	Plastics, can linings, toys, microwave ware	Ingestion, dermal absorption
Phthalates	Cosmetics, packaging, pharmaceuticals, personal care	Ingestion, dermal, inhalation
Organophosphate Pesticides (e.g., Chlorpyrifos, Diazinon)	Agriculture, insecticides	Inhalation, ingestion, dermal
Organochlorine Pesticides (e.g., DDT, Lindane)	Legacy pesticides, contaminated food, and indoor spraying	Ingestion, inhalation, dermal
Solvents (e.g., Toluene, Xylene)	Paints, inks, cleaners, and lubricants	Inhalation, dermal, ingestion
Particulate Matter (PM2.5)	Traffic, industry, wildfires, road dust	Inhalation
Polycyclic Aromatic Hydrocarbons (PAHs)	Combustion (vehicles, tobacco), industrial emissions	Inhalation, ingestion (food)
Dioxins (e.g., TCDD)	Waste incineration, chemical manufacturing	Ingestion (food chain), inhalation
Nitrates/Nitrites	Agricultural runoff, human waste	Ingestion (water, food)
Carbon Monoxide (CO)	Combustion, vehicle exhaust	Inhalation
Benzene	Industrial solvents, fuel	Inhalation, ingestion
Trichloroethylene	Degreasers, dry cleaning	Inhalation, dermal
Hexachlorophene	Disinfectants, soaps	Dermal contact

3.2.3. Regulation

There is no existing regulation or international agreement specific to neurodevelopmental toxicity in children's environment. Countries, including nations of the EU and the US, have yet to adopt mandatory developmental neurotoxicity testing before market introduction of chemicals shown to be neurotoxic, including substances such as lead, mercury, organophosphate pesticides, polychlorinated biphenyls, and flame retardants [39,40]. There is a TENDR Consensus along with experts calling out the need for a complete overhaul in the system [41]. The well-identified substances include lead, methylmercury, arsenic, polychlorinated biphenyls, organophosphate pesticides, polybrominated diphenyl ethers, and air pollutants. While there exist some regulations, such as the blood lead reference value and pesticide maximum residue level, these tend to vary across countries and often do not consider new scientific information regarding low-level exposure effects (see **Table 2**). There are many other chemicals, like pyrethroids and volatile organic compounds, that are regulated by adult toxicity studies without considering developmental effects, and the effect of mixtures is neglected [40–43].

Table 2. Global Regulatory Limits for Key Neurotoxicants in Children's Environments.

Neurotoxicant	Medium	Regulatory Body	Limit	Notes
Lead	Drinking Water	WHO	10 µg/L (provisional)	Associated with neurodevelopmental effects in children, including decreased IQ.
Lead	Drinking Water	US EPA	0 µg/L (action level 15 µg/L)	MCLG is 0, the action level for treatment.
Lead	Air	WHO	0.5 µg/m^3 (annual mean, older guideline)	Not in the 2021 guidelines, but a previous recommendation.
Lead	Air	US EPA	0.15 µg/m^3 (rolling 3-month average)	NAAQS for lead.
Lead	Soil (residential/playgrounds)	US EPA	400 ppm	The threshold for concern where children play.
Lead	Soil (residential/playgrounds)	California DTSC	80 ppm	Screening threshold.
Lead	Paint	Global (common)	90 ppm	Adopted by 29 countries, including the US, the EU, and many in Africa/Asia.
Lead	Paint	Global (alternative)	600 ppm	Used in several Latin American countries.
Lead	Children's Toys/Products	US CPSC	90 ppm (surface coatings), 100 ppm (substrates)	Banned above these levels.
Mercury	Drinking Water	WHO	6 µg/L (inorganic)	Potential neurodevelopmental disorders.
Mercury	Drinking Water	US EPA	2 µg/L	MCL for inorganic mercury.
Mercury	Air	WHO	No specific guideline	Not in classical pollutants, but general air quality impacts neurohealth.
Mercury	Soil	Limited global standards	Varies by country	Often based on site-specific risk assessments.
Arsenic	Drinking Water	WHO	10 µg/L (provisional)	Peripheral neuropathy, cognitive impairment.
Arsenic	Drinking Water	US EPA	10 µg/L	MCL.
Arsenic	Soil (residential)	US EPA	0.39 ppm (cancer risk-based)	Varies; some states are higher.
Cadmium	Drinking Water	WHO	3 µg/L	Potential neurodevelopmental impacts via renal dysfunction.
Cadmium	Drinking Water	US EPA	5 µg/L	MCL.
Cadmium	Soil (residential)	US EPA	71 ppm	Based on kidney effects.
Manganese	Drinking Water	WHO	80 µg/L (provisional health-based), or 400 µg/L (aesthetic)	Neurobehavioral changes and cognitive impairment in children.
Manganese	Air	WHO	No specific, but in PM	Part of the particulate matter guidelines.
Fluoride	Drinking Water	WHO	1.5 mg/L	Potential cognitive development impacts at high levels.
PM2.5 (particulate matter, neurotoxic via inflammation)	Air	WHO	5 µg/m^3 (annual mean), 15 µg/m^3 (24-h)	Linked to neurodevelopmental delays.
NO_2 (nitrogen dioxide)	Air	WHO	10 µg/m^3 (annual), 25 µg/m^3 (24-h)	Respiratory and potential neuro effects.

3.3. Mechanisms of Neurotoxicity

Neurotoxicants, such as heavy metals, pesticides, particulates, and industry-derived chemicals, induce neurotoxic effects by means of multiple overlapping mechanisms (see **Figure 1**). Common mechanisms include blood-brain barrier (BBB) damage, oxidative stress, mitochondrial dysfunction, inflammation, and alteration in gene expression. The result of these mechanisms could be immediate neuronal injury or the development of neurodevelopmental disorders, depending on various factors, including the type of neurotoxic agent, the level of exposure, duration of exposure, and individual-related variables (age, genetics) [44–46]. The mechanism involved in the toxicity induced by environmental neurotoxicants includes the utilisation of the immature nature of the BBB and increased permeability in children, resulting in the passage of toxic substances and induction of inflammation. Additionally, the toxic substance is known to influence gene expression. Acute insults like hypoxia, ischemia or infections result in an increase in BBB permeability due to the induction of matrix metalloproteinase (MMP), inflammatory cytokines, and oxidative stress.

There are various challenges preterm infants encounter, including germinal matrix intraventricular haemorrhage, which predisposes them to hydrocephalus and seizures. Since they have not attained full maturation in the BBB, their exposure to neurotoxicants in their infancy is more dangerous compared to adults, who have reached maturity with respect to their body barriers [2, 4, 30, 47]. Oxidation and mitochondrial malfunction are some of the pathways through which the effects are realized in the body. Most of the neurotoxicants stimulate oxidative

stress by increasing levels of reactive oxygen species (ROS). Some of the neurotoxicants, for instance, particulate matter (PM), are known to cause oxidative stress directly. When such neurotoxicants are present during foetal development, there is usually systemic oxidative stress in the mother because of her inability to provide adequate antioxidants that neutralize the oxidative stress [48]. The mitochondrial malfunction interferes with adenosine triphosphate (ATP) formation and initiates cell death. For instance, the presence of heavy metals such as iron within brain cells increases oxidative stress through the Fenton reaction due to an overload of ROS in the brain cells.

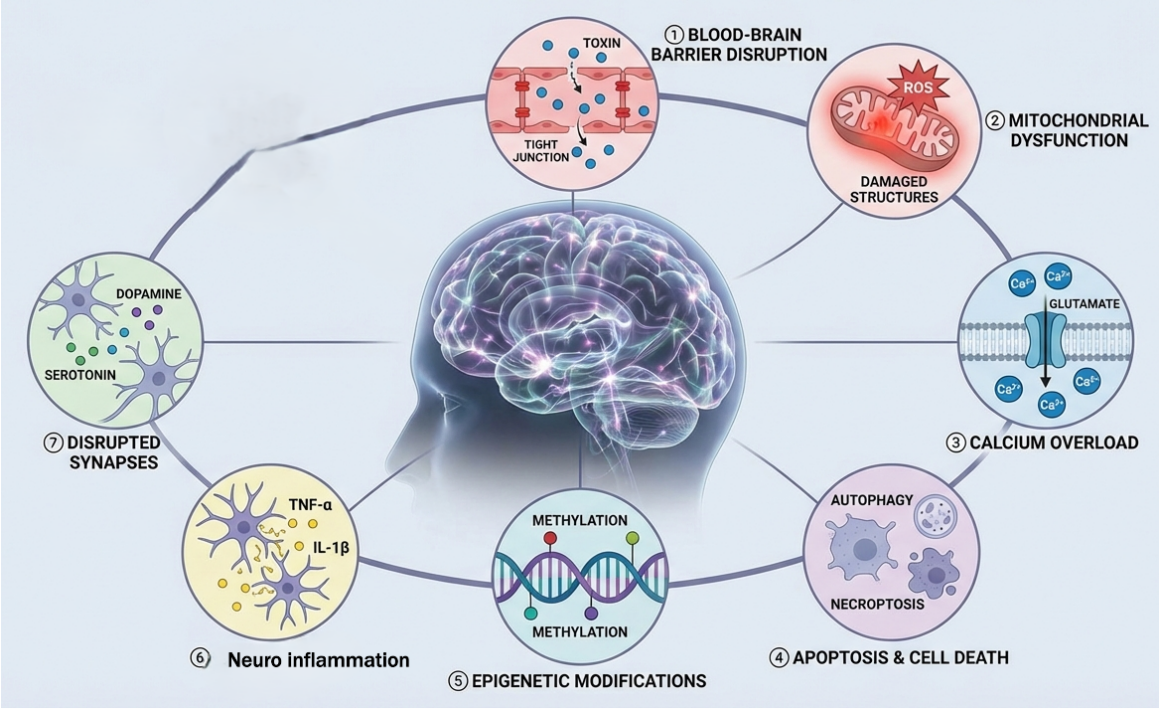

Figure 1. Mechanistic Pathways of Neurotoxicity in the Developing Brain.

Other pathways include excitotoxicity and calcium dysregulation. The imbalance between glutamate concentrations and the high activity of N-Methyl-D-aspartate (NMDA) receptors causes the inflow of calcium, which leads to excitotoxic damage of neurons. This phenomenon can be seen for substances like methylmercury, methamphetamine, and bisphenol A. Increased levels of calcium contribute to oxidative stress and induce apoptosis. For example, zinc changes the functions of glutamatergic and Gamma-aminobutyric acid (GABA) receptors, while mercury and bisphenol A affect calcium dysregulation, causing dysfunction of the endoplasmic reticulum and mitochondria. Moreover, air pollution in the form of particulate matter makes the blood-brain barrier more permeable to other neurotoxicants, ROS generation, and excitotoxicity due to neurotransmitter imbalance [12,49]. Neurotoxicants activate programmed cell death through various ways, such as apoptosis, autophagy, necroptosis, pyroptosis, and ferroptosis. Lead causes apoptosis in cells because of oxidative stress, cholinergic system malfunction, and enhanced autophagy due to the development of autophagosomes [10,50]. Electrophilic neurotoxicants like acrylamide and 2,5-hexanedione cause adduct formation and aggregation. Adducts are generated because of the formation of covalent bonds between neurotoxicants and neuronal proteins, disturbing their activity and structure. It is difficult to find key adducts among many protein changes, as neurotoxicants affect nucleophilic regions of proteins. For instance, acrylamide induces neurotoxicity by targeting the nuclear factor erythroid 2-related factor 2 (Nrf2-ARE) and nuclear factor–kappa B (NF-κB) pathways within the astrocyte and microglia cells [51,52]. The epigenetic mechanism, which includes alterations in DNA methylation and microRNA (micro-ribonucleic acid), associated with exposure to neurotoxic agents during infancy, increases the likelihood of having neurodevelopmental conditions [52]. Neurotoxicants, which include PFAS, pesticides, and methylmercury, induce both epigenetic and genotoxic effects by causing changes in DNA methylation, histone modification, and the regulation of non-coding RNA. These factors cause a change in gene expression and ultimately the outcomes of neurodevelopmental pro-

cesses. Prenatal exposure to bisphenol A leads to hypomethylation of repetitive elements in the genes related to synaptic plasticity. These disruptions affect neurogenesis, neuronal migration, synaptogenesis, myelination, and apoptosis, thus leaving the neurodevelopmental effects irreversible owing to the poor ability of repair in the developing brain [12,53].

The usual effects include neuroinflammation and glial cell impairment, which are achieved through the activation of microglia and astrocytes. Neurotoxicant exposure can easily reach the brain due to the immaturity of the BBB. Thus, neurotoxic agents induce an inflammatory reaction in the brain, causing the release of TNF-α and IL-1β cytokines [51,54]. This can affect other brain processes like neurodevelopment and synaptogenesis [48]. Other ways through which neurotoxicity occurs are by interference with neurotransmitters. Neurotoxicants can inhibit neurotransmitter receptors for dopamine, serotonin, and cholinergic neurotransmission [8,9].

3.4. Evidence Linking Exposure to Neurodevelopmental Disorders

Studies indicate that early-life exposure to environmental neurotoxins predisposes children to neurodevelopmental disabilities. Several studies have demonstrated the link between early exposure to environmental contaminants and neurological damage, as manifested in impaired cognitive function [48]. Early-life exposure to environmental contaminants is associated with low mental development index (MDI) at age three years, decreased intelligence quotient (IQ) score at age five, slow processing speed at age seven, and signs of anxiety, depression, and inattention at age six and seven [55]. Several studies have shown that environmental exposure during pregnancy and early childhood increases the risk for neurodevelopmental disabilities such as ASD, ADHD, learning disability, intellectual disability, and sensory deficits. There is an increasing focus on environmental exposures as an etiological factor of neurodevelopmental disabilities. These disabilities are characterised by impairments in social skills, communication, attention span, and cognition. In the past few decades, neurodevelopmental disabilities have increased in prevalence, hence the need to explore other etiological factors besides genetic factors. Apart from genetic factors, environmental factors, particularly those experienced during the prenatal and postnatal periods, may contribute significantly to neurodevelopmental disabilities [25,53,54].

There is substantial literature available on the relationship between ambient air pollution, especially PM2.5, nitrogen oxide 2 (NO_2), and ozone (O_3), and the effect of such exposures on child behavioural problems. Studies performed in Cincinnati and China have shown associations between PM2.5, ozone, and ASD; specifically, exposure to PM2.5 within the first three years of life was found to increase the risk of ASD [56,57]. This period encompasses critical phases of neurodevelopment, such as synaptogenesis and myelination, during which pollutants can diffuse across the blood-brain barrier and cause inflammation or oxidative stress. In addition, exposure to PM2.5 results in an increased risk of ADHD, and a comprehensive review gave highly suggestive evidence for an 82% increased risk. Cohort studies from urban settings like Pennsylvania provided support for the link between air pollutants and ASD, despite potential inconsistencies due to differences in pollutant sources. Furthermore, both nitrogen oxides and carbon monoxide demonstrated positive associations with ASD in subgroup analysis using cohort studies. Intellectual disability does not appear to be linked to air pollution, as no evidence was identified in at least one review [10].

Heavy metals are present in water, soil, food and air because of industrial activities. Heavy metals are amongst the most widely researched toxicants. Lead exposure in small quantities lowers intelligence quotient, with a study finding that for every increment in blood lead levels, there is an average drop in IQ of around 5 points. Lead exposure also causes attention deficit hyperactivity disorder (ADHD). For example, in Cincinnati Lead Study, exposure to lead results in lower grey matter volume and abnormality of white matter integrity, which are related to intellectual disabilities and behavioural impairments. Lead exposure during pregnancy is also associated with developmental defects according to Chinese research, with the concentration in blood at 3 to 5 years of age predicting future health outcomes [10,58]. Mercury is linked to ADHD behaviours in Inuit and Faroese populations, although according to a meta-analysis, there is little evidence associating mercury with autism spectrum disorder (ASD). Arsenic exposure during early life through drinking water is associated with decreased IQ and ADHD [59]. The research from Bangladesh shows dose-response effects where higher concentrations of arsenic correlate with lower performance in cognitive tests. The limitations include exposure misclassification and possible interaction of nutrition with exposure, for example, selenium reducing mercury's toxicity. This led to discussions of the safe exposure level, as some researchers argue that there is none, while others point out adaptation in the low-exposure population [59].

The strong link of organophosphate pesticides, including chlorpyrifos, with NDDs has been shown. In a study

of an agricultural cohort like CHAMACOS, prenatal exposure relates to 60% risk increase of ASD and 35% increased risk of ADHD. There are imaging abnormalities in the form of cortical thinning and tremors in pesticide-exposed children, which indicate damage to the cholinergic system. A systematic review shows an association with cognitive impairment and attention deficit. However, some researchers find that the low exposure does not cause cognitive impairment or may even have a protective effect [60]. Sexual differences exist with endocrine disruptors like bisphenol A (BPA) and phthalates. BPA in pregnant women increases the risk of hyperactivity, anxiety in females, and aggression in males, according to research done in the United States and Europe. Phthalates, including monobutyl phthalate, have a connection with ASD as well as with psychomotor delays in meta-analyses [61]. The effect of early phthalate exposure is connected to the volumes of different brain regions in children. Exposure to polychlorinated biphenyls (PCBs), such as PCB 138, has an increased association with autism spectrum disorder. Post-mortem brain studies indicate elevated levels in individuals with autism spectrum disorder [62].

3.5. Risk Modifiers and Population Vulnerability

Lead, mercury, cadmium, certain pesticides, and air pollution, such as PM, can negatively impact the nervous system through developmental, cognitive, or behavioural problems. Some populations are more susceptible to these chemicals because of their biological and social vulnerability, as well as the presence of risk modifiers that may alter the effects of the toxins by increasing or decreasing the adverse outcome [18,63]. Risk modifiers may be genetic, socioeconomic status, nutrition, or concomitant exposures. These modifiers overlap and add up to form cumulative risks, especially among socially disadvantaged communities. Knowledge of these risk modifiers is essential in risk assessment to account for the different results obtained from exposure in different populations. **Table 3** lists both the modifiable and non-modifiable risk factors of exposure to selected neurotoxicants.

Table 3. Modifiable and Non-Modifiable Risk Factors in Exposure Outcomes.

Modifiable Risk Factors	Non-Modifiable Risk Factors
✓ Environmental exposures to specific neurotoxicants, such as lead (e.g., from paint, water pipes, soil), pesticides (e.g., organophosphates like chlorpyrifos), outdoor particulate matter (PM) pollution (e.g., from traffic, industry), endocrine-disrupting chemicals (EDCs like BPA, phthalates, PCBs), and environmental tobacco smoke.	✓ Age and developmental stage, including heightened vulnerability in fetuses, infants, children (due to immature metabolic pathways and rapid brain development), and the elderly (due to reduced plasticity and regeneration capacity).
✓ Dose, route (e.g., inhalation, ingestion, dermal), duration, and timing of exposure, which can be controlled through regulations, protective measures, or avoidance during critical periods.	✓ Genetic factors, such as polymorphisms in metabolic enzymes (e.g., PON1 for organophosphates) or DNA repair genes that influence susceptibility to toxins.
✓ Nutritional status and diet, including deficiencies (e.g., iron, calcium, vitamins) that can exacerbate toxicity, modifiable through improved nutrition or supplementation.	✓ Socioeconomic and demographic disparities, such as higher exposure burdens in low-income, racial/ethnic minority communities due to environmental racism, housing quality, and spatial distribution.
✓ Personal habits and lifestyle factors, such as smoking, alcohol consumption, illicit drug use, or co-exposures to multiple substances, which can interact with neurotoxicants.	✓ Gender-related differences in toxicokinetic or toxicodynamic responses to neurotoxicants.
✓ Residential or occupational proximity to pollution sources (e.g., near agricultural fields, industrial facilities), modifiable through relocation, urban planning, or protective equipment.	✓ Pre-existing genetic or inherent biological vulnerabilities, including species-specific differences in metabolism (relevant for risk extrapolation from animal studies).
✓ Pre-existing conditions or disorders (e.g., diabetes, neurological issues) that can be managed or treated to reduce amplified risks, along with drug interactions.	

3.5.1. Genetics as a Risk Modifier

Genetic factors, such as polymorphisms in genes coding for enzymes and proteins involved in detoxification, metabolism, and oxidative stress response, can influence individual and population susceptibility to neurotoxicants. Such factors could either contribute to increased vulnerability to toxicants through compromised metabolic detoxification or by exacerbating the toxicity of neurotoxins. Polymorphisms in detoxifying enzymes, for example, cytochrome P450 enzymes and ALAD (delta-aminolevulinic acid dehydratase) enzyme polymorphism, can affect the effect of lead exposure on neurobehavioral outcomes. Individuals carrying ALAD-2 may have increased or decreased impairment depending on the age of the person; however, the effect is stronger in adults compared to children. The apolipoprotein E4 (Apo-E4) variant is an important risk factor for adult exposure to lead, whereas the dopamine receptor D4-7 repeat (DRD4-7) can exacerbate deficits in executive functions due to lead exposure in

males. Null variants of glutathione S-transferase mu 1 (GSTM1) makes people vulnerable to air pollution because it interferes with the activity of antioxidation mechanisms, resulting in impairment of pulmonary function, increased prevalence of asthma and inflammation. Epigenetic factors like early-life DNA methylation and histone modifications because of neurotoxins can negatively influence the expression of brain-derived neurotrophic factor (BDNF), a gene that plays an essential role in neurodegenerative processes such as Alzheimer's disease [64–66]. There is an effect of genetics on the sensitivity to toxins, with some individuals being more sensitive to certain chemicals compared to others. This can be seen in certain genetic differences found in individuals from certain ethnic backgrounds or families, which predispose one to toxicity to mercury in work environments [66].

3.5.2. Socioeconomic Status (SES) as a Risk Modifier

Low SES is associated with increased susceptibility to neurotoxicants and decreased ability to protect against their effects, acting as an indicator of several susceptibilities. These include living in polluted regions, lack of access to medical services, and high levels of stress, which increase the effect of toxicants. Lead-exposed children from poor families suffer neurodevelopmental problems at lower blood concentrations compared to affluent individuals, recovering less successfully during development. SES also influences the adverse effects of air pollution by increasing connections to premature births, low birth weight, and mortality from PM10. The effect of psychosocial stress in low-SES families on the influence of lead on cognition and behaviour has been proven. It is noted in animal experiments where maternal stress worsens cognitive impairments in offspring [18,67]. The effect of low SES is also manifested through the mechanism of weathering and allostatic load, contributing to increased vulnerability [18,67]. Individuals from disadvantaged communities may be affected more heavily in combination with other modifiers like SES, genetics, nutrition, and others. For example, reading performance issues in relation to lead exposure in low-SES families appear at lower exposure rates.

3.5.3. Nutrition as a Risk Modifier

Nutrition affects absorption, detoxification, and oxidative stress responses to neurotoxic substances. Lack of nutrients increases vulnerability, whereas consumption of nutritious foods provides some degree of protection. Malnutrition compromises antioxidant functions and therefore increases risk. Low consumption of iron, calcium, vitamin D, vitamin C, and folic acid is an enhancing factor that intensifies the link between lead exposure and brain impairments and increases serum lead levels. Vitamins C and E and omega-3 fatty acids protect against damage caused by exposure to air pollution, including reduction of bronchospasms in individuals with asthma or prevention of heart rate variability change in reaction to particles. If it is about fetal exposure to lead, diet-based manipulation of the gut microbiota (e.g., use of fibre or probiotics) can serve as a means of reducing neurotoxicity [68–70]. People belonging to vulnerable groups (e.g., malnourished children) are more at risk. Nutritional solutions (e.g., dietary supplements) will help address this problem [71,72].

3.5.4. Co-Exposures as a Risk Modifier

Exposure to multiple neurotoxicants simultaneously can produce combined effects that exceed the individual impacts due to mechanisms common to both substances. For example, exposure to manganese and lead leads to enhanced neurodevelopmental deficits, whereas exposure to cadmium affects kidney function and leads to albuminuria. Exposure to the combinations of lead, mercury, and cadmium alters the dopaminergic and serotonergic enzyme systems, leading to a high likelihood of being affected by neurotoxicity. Toxins such as toluene and noise affect brain tissues. Oxidative stress is exacerbated by air pollution, while PCBs and fish-derived methylmercury add to the burden. Co-exposure of carbon monoxide with reoxygenation causes oxidative stress in neurons [73–75]. Co-exposure situations occur both occupationally and environmentally; hence, cumulative assessments should consider the interactions that cannot be predicted [19,76,77].

3.6. Preventive Strategies and Policy Implications

3.6.1. Policy Frameworks (WHO, EPA, UNEP)

The threat that neurotoxicants represent to neurodevelopment is immense, causing the growing prevalence of neurological conditions in children. International and national policies developed by organisations like the World

Health Organization (WHO), the Environmental Protection Agency (EPA), and the United Nations Environment Programme (UNEP) play an integral role in prevention; yet current approaches are not adequate in their efforts to safeguard sensitive populations. Current regulatory approaches in both the United State (US) and European Union (EU) lack any mandatory pre-market assessments for developmental neurotoxicity. There are only a few chemicals that get tested for toxicity prior to their widespread utilisation. Despite the global appeals made by the WHO and UNEP for a worldwide solution to this problem, there still does not exist an international regulatory approach. Specialists have recommended setting up an international clearinghouse agency, like IARC [39,41,43].

Various agencies, including WHO, EPA, and UNEP, have created risk evaluation frameworks to manage such risks. The framework is based on initiatives such as the IPCS and includes criteria used to evaluate risks to health from environmental exposures in children. In this respect, hazards are identified through the assessment of the impact of exposure on structures, for example, neuronopathy and axonopathy, as well as functions, for instance, disruption of neurotransmitters and behaviours. The assessment of these hazards draws on data obtained from epidemiology on humans, animal studies, and in vitro experiments. In terms of dose response assessments, there are assumptions of non-linear responses in addition to the use of NOAEL, LOAEL, and BMD values while considering uncertainties. For exposure assessments, the approach entails estimating internal doses via different routes of exposure. Risk characterisation includes combining all these factors and applying margins of uncertainty by tenfold for interspecies and intraspecies variability, leading to the derivation of reference doses or MOEs, particularly among sensitive sub-populations [78–80].

Prevention techniques are aimed at decreasing exposure during important developmental stages like the embryonic stage (days 19–27 for defects in the neural tube), foetal stage (proliferation and migration), and postnatal (myelination and synaptogenesis up to adolescence). Surveillance involves the use of blood lead concentrations, metabolic markers in urine, and MRI, among other methods. Behavioural modifications involve eating organic foods that decrease exposure to pesticides, the use of eco-friendly household cleaners, and good ventilation to reduce exposure to indoor air pollution (e.g., VOCs, particulates). Breastfeeding has more advantages than disadvantages; it may be protective against prenatal neurotoxicity, but careful monitoring of maternal exposures is necessary. There are indications to establish prospective cohorts to monitor timing-based outcomes using standardised assessment techniques like the WHO Neurobehavioral Core Test Battery [20,41,62].

Policy implications underscore the need for age-specific policies that transcend adult-oriented policy approaches and take into consideration toxicokinetics based on age. The newborns, for instance, have less CYP450 enzyme activity and therefore a higher half-life of chemicals. The Environmental Protection Agency's Lautenberg Chemical Safety Act is one example of a law that mandates developmental neurotoxicity assessments using novel approaches such as zebrafish models and HTS screening. UNEP's Global Chemicals Outlook promotes the phase out of POPs and addresses a mixture of chemicals. WHO's resolutions, such as WHA67.11 on Mercury, encourage the use of conventions like Minamata to minimise neurodevelopmental outcomes. It is reported that the annual economic cost is €150 billion in Europe due to neurobehavioral deficits caused by neurotoxicant exposure. It emphasises the need for banning similar compounds like bisphenols and flame retardants and conducting tests using frameworks like REACH. There is a gap in data available from developing nations, where there is an interaction of nutrition and neurotoxins, and controversies over the threshold for endocrine disruptors [21,36,62].

3.6.2. Community-Based and Healthcare Interventions

Neurotoxicants refer to toxic compounds that affect the nervous system at specific developmental stages, such as the prenatal period and early childhood. Neurotoxicants include lead, air pollution such as particulate matter (PM), pesticides, endocrine disruptors such as BPA and phthalates, and heavy metals like mercury. These toxic chemicals may alter the structure of the brain, affect cognitive abilities, and cause behavioural conditions such as attention deficit hyperactivity disorder (ADHD), anxiety, and depression, as well as mental illnesses. The affected individuals, especially those with lower socio-economic status and certain races/ethnicities, may experience greater exposure because of environmental injustice. In terms of prevention strategies, efforts are made to minimise the risks of exposure to such chemicals, while policy interventions aim to regulate and mitigate the injustices associated with neurotoxicant exposures [62,81].

Preventing exposure to neurotoxins involves taking a holistic approach (illustrated in **Figure 2**), guided by the precautionary principle, which considers chemicals to be guilty until proven innocent, especially concerning brain

development. This includes putting in place stricter pre-market testing and retesting of chemicals, including pesticides and industrial solvents, through proper means to dispel any assumptions of harmlessness among chemicals that have not been tested. On the other hand, it is equally crucial to address exposure pathways, including elimination of lead from paint and water, addressing air pollution, limiting the use of endocrine-disrupting chemicals in consumer goods, and encouraging alternative approaches to pest control [43]. Specific preventive strategies will target vulnerable populations through measures like monitoring exposure to neurotoxins during pregnancy and warning about the harmful impact of dangerous neurotoxins like organophosphates during pregnancy. Education campaigns can also help inform the public about potential dangers and improve product labelling. Besides offering protection, such actions will result in huge financial gains. For instance, the phasing out of leaded gasoline has saved society billions of dollars due to the lack of losses resulting from decreased intelligence quotient [36].

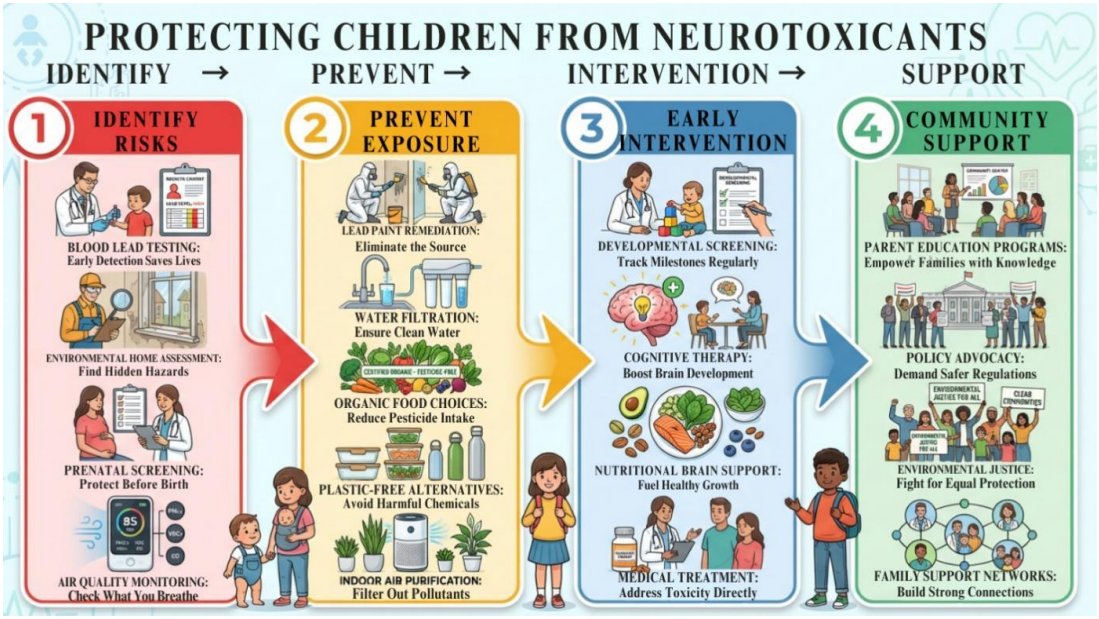

Figure 2. Integrated Model of Early-Life Exposure Prevention Strategies.

Community-based interventions are a good way to empower communities to respond to exposure issues affecting brain development. Social problems like poverty and environmental racism are common in many communities today. The interventions usually take the form of awareness and advocacy programs that involve mass campaigns educating people about mental illnesses, removing stigmas, and emphasising the effects of neurotoxicants. The community organisers push for critical pollution prevention measures to be instituted, especially in sensitive areas like schools and parks. Education and enrichment programs are important because there are programs providing early childhood enrichment and parenting programs to enhance mother-child communication. Also, education in the work environment of people exposed to neurotoxins to ensure that secondary exposure does not occur [24]. Environmental control may include pest management in schools and economic empowerment measures such as microfinance, coupled with health education to alleviate material stress and exposure risks. Finally, educating non-experts like teachers and health professionals about recognising neurodevelopmental illnesses early enough makes interventions more possible. All in all, the approaches mentioned above have been termed as effective practices in developing nations and are based on leveraging existing structures such as schools and occupational settings [20,82,83].

Healthcare facilities provide the foundation for the assessment, monitoring, and management of neurotoxicants. This is done through regular blood tests for lead content among children and prenatal tests for exposure to endocrine disruptors and air pollution, which will help detect changes in the structure of the brain. All these measures can be combined with interventions in the form of multidisciplinary approaches to deal with ADHD, holistic substance abuse treatment for expectant mothers to safeguard their offspring, and long-term birth cohorts to uncover any existing subclinical deficits. The combination of neurotoxicant awareness with routine prenatal and pae-

diatric care programs, together with mental health promotion and other community-based programs, can provide an opportunity for preventive action against neurotoxicants [25,36,43,84].

3.7. Limitations of Epidemiological Evidence

Despite providing valuable insights, epidemiological studies on environmental neurotoxicants have several inherent limitations. Residual confounding, exposure misclassification, and recall bias may affect the accuracy of exposure–outcome associations. In addition, the observational nature of most studies limits the ability to establish causality. Variations in exposure assessment methods and neurodevelopmental outcome measures, together with the complexity of evaluating combined exposures to multiple toxicants, may contribute to inconsistencies and reduce comparability across studies.

4. Conclusions

The susceptibility of the developing brain to environmental neurotoxins underscores a serious public health problem, with consequences for conditions such as ASD, ADHD, and cognitive disabilities that affect the individual's neurodevelopment. In this review, it is evident that important stages of prenatal and early postnatal life have characteristics of immature barriers and quick physiological reactions, making them more sensitive to the adverse impacts of metals, pesticides, air pollution, and endocrine-disrupting chemicals. Consistent findings from epidemiological studies reveal that even at lower levels of exposure, there are lifelong negative effects, while other determinants, such as genetics, socio-economic status, poor nutrition, and multiple exposures, affect vulnerable communities.

Addressing these risks requires immediate policy action, including establishing a unified international regulatory framework for premarket developmental neurotoxicity testing, setting consistent exposure limits, and banning high-risk chemical classes, building initiatives from the WHO, EPA, and UNEP. Improved surveillance systems, such as biomonitoring programs and long-term cohorts, are vital for tracking exposures, identifying early biomarkers, and assessing the effectiveness of interventions in real time. Alongside this, strong public awareness campaigns must equip communities, healthcare providers, and individuals with knowledge to reduce exposure through safer consumer choices, environmental advocacy, and lifestyle changes, thereby encouraging resilience and equity.

By focusing on these interconnected areas, society can protect future generations, avoid high economic and human costs, and move toward a toxin-free environment that fosters optimal brain health. The time for coordinated evidence-based action is now.

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