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Environmental Neurotoxins and Human Brain Health: A Critical Review of Mechanisms and Epidemiological Evidence

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ABSTRACT

Environmental neurotoxins represent a growing public health concern due to their potential to disrupt neural development, cognitive function, and brain integrity across the human lifespan. Exposure to heavy metals, pesticides, industrial chemicals, and air pollutants has been implicated in a range of neurodevelopmental and neurodegenerative disorders, including autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), Parkinson's disease (PD), and Alzheimer's disease (AD). This review synthesizes current evidence on the sources, mechanisms of action, and epidemiological links between major environmental neurotoxicants and adverse brain health outcomes. Mechanistic insights reveal that oxidative stress, mitochondrial dysfunction, neuroinflammation, and epigenetic modifications play central roles in mediating neurotoxicity. We also examine critical windows of vulnerability, particularly during prenatal and early postnatal brain development. Epidemiological studies are discussed, highlighting associations between specific toxins-such as lead, mercury, organophosphates, and fine particulate matter-and cognitive and behavioral impairments in both children and adults. Despite significant advancements, challenges remain in exposure assessment, identifying cumulative effects, and establishing causality. A multidisciplinary approach integrating toxicology, neuroscience, environmental health, and policy is essential for mitigating risk and protecting vulnerable populations. Strengthening public awareness and regulatory frameworks will be pivotal in reducing the global burden of neurotoxic exposures.

Keywords: Environmental neurotoxins, brain health, neurodegeneration, neurodevelopment, epidemiology

INTRODUCTION

Environmental exposures to neurotoxic substances have become a pressing global health issue, with implications that span from early brain development to the onset of neurodegenerative diseases later in life [1]. Unlike acute neurotoxins that cause immediate and severe neurological damage, chronic low-dose exposure to environmental pollutants often results in subtle but persistent disruptions to brain structure and function [2]. These disruptions may manifest as developmental delays in children or progressive cognitive decline in adults. The effects can be insidious and difficult to attribute directly to specific exposures, especially in settings where monitoring is inadequate. Populations in low- and middle-income countries are particularly vulnerable due to several factors, including poor environmental regulation, limited access to health information, unsafe occupational practices, and the use of hazardous materials in agriculture and industry [3]. Children, pregnant women, and the elderly are especially susceptible to neurotoxic effects, due to developmental vulnerabilities and diminished detoxification capacities [4]. This review explores the major categories of environmental neurotoxins, their known mechanisms of action on the human brain, and the epidemiological evidence linking these substances to cognitive and neurological disorders. By synthesizing current knowledge, this article aims to highlight areas of concern, research gaps, and the need for global strategies to mitigate neurotoxic exposure and protect brain health.

2. Major Classes of Environmental Neurotoxins

2.1 Heavy Metals

Heavy metals such as lead, mercury, arsenic, and cadmium are among the most studied environmental neurotoxins [5]. Lead exposure, even at low levels, has been conclusively linked to reduced IQ, attention deficit, learning disabilities, and behavioral disorders in children [6]. Prenatal exposure can cause irreversible damage to the developing brain. Mercury, particularly in the organic form methylmercury, enters the food chain through fish and seafood. It can cross the placenta and the blood-brain barrier, impairing neuronal migration and synaptogenesis [7]. Arsenic and cadmium, commonly found in contaminated water and food, have been associated with memory impairment, mood disturbances, and increased risk for Alzheimer's disease and other cognitive disorders [8].

2.2 Pesticides and Herbicides

Agricultural chemicals such as organophosphates, carbamates, and paraquat pose substantial neurotoxic risks. These compounds inhibit acetylcholinesterase, an essential enzyme for neurotransmission, leading to neural hyperactivity and subsequent cell death [9,10]. Long-term exposure, especially in agricultural workers, has been linked to increased risk of Parkinson's disease, tremors, poor motor coordination, and cognitive dysfunction [10]. Prenatal and early childhood exposure to pesticides has been correlated with developmental delays and higher rates of attention-deficit and autism spectrum disorders [11].

2.3 Industrial Chemicals

Industrial activities have introduced numerous persistent organic pollutants (POPs) into the environment. Compounds such as polychlorinated biphenyls (PCBs), brominated flame retardants (BFRs), and solvents, including toluene and trichloroethylene, are known to affect the central nervous system [12]. PCBs disrupt thyroid hormone balance, crucial for brain development, while solvents interfere with neuronal membrane integrity and synaptic plasticity [13]. Many of these substances are lipophilic and bioaccumulate in human tissues, making their long-term effects particularly concerning.

2.4 Air Pollutants

Airborne pollutants, including fine particulate matter (PM2.5), nitrogen oxides, sulfur dioxide, carbon monoxide, and ground-level ozone, are increasingly recognized as contributors to cognitive decline and neurodegeneration [14]. Inhaled particles can reach the brain either via the olfactory nerve or by crossing the blood-brain barrier. These pollutants initiate neuroinflammatory responses and oxidative damage in brain tissues. Long-term exposure to high levels of air pollution has been associated with decreased brain volume, accelerated brain aging, and elevated risk of dementia and stroke, particularly among urban and elderly populations [15].

3. Mechanisms of Neurotoxicity

3.1 Oxidative Stress

Oxidative stress is a common mechanism through which many environmental neurotoxins exert their harmful effects [16]. By increasing the production of reactive oxygen species (ROS), these substances damage lipids, proteins, and nucleic acids in neurons. The brain's high oxygen demand and lipid-rich environment make it highly susceptible to oxidative damage, which can disrupt synaptic communication and neuronal survival [17].

3.2 Mitochondrial Dysfunction

Mitochondria are critical for energy production and cellular metabolism in neurons [18]. Toxins like rotenone and paraquat impair mitochondrial electron transport, leading to reduced ATP generation, release of pro-apoptotic factors, and eventual cell death [19]. Mitochondrial dysfunction has been strongly linked to Parkinson's disease and other age-related neurodegenerative conditions [20].

3.3 Neuroinflammation

Exposure to neurotoxicants often activates the brain's immune cells, microglia, and astrocytes, triggering a chronic inflammatory response [21]. This sustained neuroinflammation results in the release of pro-inflammatory cytokines and chemokines, which interfere with synaptic function, neurogenesis, and neuronal repair mechanisms [22]. Inflammation is now recognized as a key contributor to the pathogenesis of diseases such as Alzheimer's, multiple sclerosis, and depression [23].

3.4 Epigenetic Modifications

Emerging evidence suggests that environmental toxins can induce long-lasting changes in gene expression through epigenetic modifications [24]. These include alterations in DNA methylation patterns, histone modifications, and changes in microRNA profiles. Such epigenetic disruptions may affect neurodevelopmental pathways and increase susceptibility to psychiatric and neurodegenerative diseases, often across multiple generations [25].

4. Epidemiological Evidence

Epidemiological studies play a vital role in elucidating the real-world impact of environmental neurotoxins on human brain health. They provide population-level insights into associations between exposures and neurological

outcomes, often highlighting vulnerable groups such as children, the elderly, and occupationally exposed individuals [26].

4.1 Neurodevelopmental Disorders

There is growing evidence that early-life exposure to environmental neurotoxins significantly affects neurodevelopment [27]. Several birth cohort studies, including the CHAMACOS (Center for the Health Assessment of Mothers and Children of Salinas) study in California, have shown that prenatal exposure to organophosphate pesticides is associated with reduced IQ scores, impaired attention, and a higher prevalence of attention-deficit hyperactivity disorder (ADHD) in children [28]. Similarly, exposure to lead during gestation and early childhood has been linked to developmental delays, lower educational attainment, and increased rates of behavioral problems [29]. Methylmercury exposure, primarily through maternal fish consumption, has been implicated in motor dysfunction and language delays [30]. The impact of such exposures during critical windows of brain development can have long-lasting consequences on cognitive capacity, academic performance, and social functioning.

4.2 Neurodegenerative Diseases

In adults, long-term exposure to neurotoxic substances is increasingly associated with the onset of neurodegenerative disorders. Numerous epidemiological studies have reported a higher incidence of Parkinson's disease in individuals with chronic occupational exposure to pesticides, especially paraquat and maneb [31]. Air pollution, particularly fine particulate matter ($PM_{2.5}$), has also been associated with increased risk of Alzheimer's disease and vascular dementia [32]. Data from urban populations show that sustained exposure to traffic-related air pollution correlates with smaller brain volume, hippocampal atrophy, and the accumulation of amyloid plaques, a hallmark of Alzheimer's pathology [33]. Furthermore, heavy metals such as cadmium and arsenic have been suggested as potential contributors to dementia progression through oxidative stress and inflammation [34].

4.3 Cognitive Decline

Beyond overt neurodegenerative disease, environmental neurotoxins have been associated with more subtle but widespread effects on cognitive function. Studies from the United States, Europe, and Asia have reported that cumulative exposure to lead, solvents, and industrial chemicals correlates with diminished executive function, processing speed, and working memory in adults and the elderly. For example, research from the Normative Aging Study found that cumulative lead exposure was associated with progressive cognitive decline and increased risk of depression in older men [35]. Longitudinal data also suggest that air pollution may accelerate cognitive aging and increase susceptibility to mild cognitive impairment, a known precursor to dementia [36].

5. Challenges and Gaps in Research

Despite accumulating evidence, several challenges continue to hinder the full understanding and public health translation of research on environmental neurotoxicity. One major limitation is the difficulty in quantifying lifetime exposures [37]. Most studies rely on single-point measurements or retrospective self-reports, which may not accurately capture cumulative or early-life exposures. Additionally, variability in individual susceptibility due to genetic differences, nutritional status, socioeconomic factors, and pre-existing health conditions complicates the interpretation of findings [38]. Another critical gap lies in the assessment of combined exposures. In real-life settings, individuals are rarely exposed to a single neurotoxin in isolation. Instead, they encounter complex mixtures of chemicals with potential additive or synergistic effects [39]. Yet, most toxicological and epidemiological studies continue to evaluate single-agent effects, limiting their ecological validity. Moreover, there is a lack of standardized biomarkers and validated clinical tools to detect early signs of neurotoxicity, which restricts early intervention and risk stratification [40]. Longitudinal studies with comprehensive exposure histories, consistent neurocognitive assessments, and integration of omics-based approaches (genomics, epigenomics, metabolomics) are urgently needed to uncover mechanisms and inform targeted prevention strategies.

6. Public Health and Policy Implications

Addressing the public health burden of environmental neurotoxins requires a multifaceted and collaborative approach. Regulatory interventions have already demonstrated significant benefits. The removal of lead from gasoline and paint has led to measurable improvements in population IQ scores and a decline in childhood blood lead levels [41]. Similarly, restricting the use of certain high-risk pesticides has reduced occupational poisonings and associated health impacts in some regions [42].

However, enforcement of environmental safety standards remains inconsistent, especially in low-resource settings. National and international policies must focus on stricter regulation of industrial emissions, agricultural chemicals, and air quality. Additionally, implementing surveillance systems to monitor neurotoxic exposures and associated health outcomes will be key in guiding and evaluating interventions.

Public education campaigns targeting schools, workplaces, and healthcare providers are essential in raising awareness of the risks associated with common environmental exposures. Preventive strategies should also prioritize

high-risk groups such as pregnant women, children, and workers in high-exposure occupations. Integrating environmental health into clinical practice through training, screening, and environmental history-taking can further improve early detection and risk mitigation. Ultimately, reducing the neurotoxic burden on human populations will require political will, cross-sectoral collaboration, and sustained investment in research, infrastructure, and advocacy.

CONCLUSION

Environmental neurotoxins pose a significant and underrecognized threat to human brain health. The accumulating evidence from mechanistic studies and epidemiological data underscores the urgent need for preventive strategies, improved diagnostics, and targeted interventions. Prioritizing environmental brain health should be a key component of global public health agendas, especially in protecting vulnerable populations such as children, pregnant women, and the elderly.

REFERENCES

1. Vilcins D, Cortes-Ramirez J, Currie D, Preston P. Early environmental exposures and life-long risk of chronic non-respiratory disease. Paediatric Respiratory Reviews. 2021;40:33–8. doi:10.1016/j.prrv.2021.05.004
2. Rauh VA, Margolis AE. Research Review: Environmental exposures, neurodevelopment, and child mental health – new paradigms for the study of brain and behavioral effects. Journal of Child Psychology and Psychiatry. 2016;57(7):775–93. doi:10.1111/jcpp.12537
3. Uti DE, Offor CE. Redox Signaling Disruption and Antioxidants in Toxicology: From Precision Therapy to Potential Hazards. *Cell Biochem Biophys* (2025). https://doi.org/10.1007/s12013-025-01846-8
4. Alum EU. The role of toxicology in climate change: Understanding the risks of novel environmental toxins. *Sustainable Environment, 11*(1). https://doi.org/10.1080/27658511.2025.2467485
5. Tchounwou PB, Yedjou CG, Patlolla AK, Sutton DJ. Heavy metal toxicity and the environment. EXS. 2012;133–64. doi:10.1007/978-3-7643-8340-4_6
6. Heidari S, Mostafaei S, Razazian N, Rajati M, Saeedi A, Rajati F. The effect of lead exposure on IQ test scores in children under 12 years: a systematic review and meta-analysis of case-control studies. Systematic Reviews. 2022;11(1). doi:10.1186/s13643-022-01963-y
7. Alum EU. Highlights of Heavy Metals: Molecular Toxicity Mechanisms, Exposure Dynamics, and Environmental Presence. *IAA Journal of Applied Sciences.* 2023; 10(3):8-19. https://doi.org/10.59298/IAAJAS/2023/4.2.3222
8. Egba, S Ikechukwu, Okonkwo C Onyinye, Ogbodo J Onyebuchi and Ezeh V Nzubechukwu Neuroprotective Potentials of *Alstonia boonei* extracts on Biochemical Markers of Brain Integrity in Experimental Rats, Trop J Nat Prod Res, 2021; 5(6): 1106-1109. doi.org/10.26538/tjnpr/v5i6.21
9. Egba, S.I., Ademola C F and Omoruyi L E (2021) Bucholzia coriacea seed extract attenuates mercury induced cerebral and cerebellar oxidative neurotoxicity via NO signalling and suppression of oxidative stress, adenosine deaminase and acetylcholinesterase activities in rats. Avicenna J Phytomed. 2022 Jan-Feb;12(1):42-53. doi: 10.22038/AJP.2021.18262. PMID: 35145894; PMCID: PMC8801217.
10. Silberman J, Taylor A. Carbamate toxicity. StatPearls – NCBI Bookshelf. 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482183/
11. Xu Y, Yang X, Chen D, Xu Y, Lan L, Zhao S, et al. Maternal exposure to pesticides and autism or attention-deficit/hyperactivity disorders in offspring: a meta-analysis. Chemosphere. 2022;313:137459. doi:10.1016/j.chemosphere.2022.137459
12. Egba, Simeon Ikechukwu; Okonkwo, Chibuzor Onyinye; Kalu, Uguru Grace Paul Promise, Chibuike, Sampson Nzubechi L, Egbachukwu Blessing Ifeoma, Alum Esther Ugo and Ugwu Okechukwu Paul-Chima (2024). Ameliorative potentials of methanol leaf extract of Anthocleista vogelli on mercury chloride induced neurotoxicity. INOSR Experimental Sciences 13(2):15-22. https://doi.org/10.59298/INOSRES/2024/1321522.000
13. Brown VJ. Blocking brain development: how PCBs disrupt thyroid hormone. 2005. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC1257681/
14. Meo SA, Shaikh N, Alotaibi M, AlWabel AA, Alqumaidi H. Effect of air pollutants particulate matter (PM2.5, PM10), sulfur dioxide (SO2) and ozone (O3) on cognitive health. Scientific Reports. 2024;14(1). doi:10.1038/s41598-024-70646-6
15. Kulick ER, Wellenius GA, Boehme AK, Joyce NR, Schupf N, Kaufman JD, et al. Long-term exposure to air pollution and trajectories of cognitive decline among older adults. Neurology. 2020;94(17). doi:10.1212/WNL.0000000000009314

16. Ochulor Okechukwu C., Njoku Obioma U., Uroko Robert I and Egba Simeon I. Nutritional composition of *Jatropha tanjorensis* leaves and effects of its aqueous extract on carbon tetrachloride induced oxidative stress in male Wistar albino rats. Biomedical Research 2018; 29(19): 3569-3576
17. Jové M, Mota-Martorell N, Obis È, Sol J, Martín-Garí M, Ferrer I, et al. Lipid adaptations against oxidative challenge in the healthy adult human brain. Antioxidants. 2023;12(1):177. doi:10.3390/antiox12010177
18. Casanova A, Wevers A, Navarro-Ledesma S, Pruimboom L. Mitochondria: it is all about energy. Frontiers in Physiology. 2023;14. doi:10.3389/fphys.2023.1114231
19. See WZC, Naidu R, Tang KS. Cellular and molecular events leading to paraquat-induced apoptosis: mechanistic insights into Parkinson's disease pathophysiology. Molecular Neurobiology. 2022;59(6):3353–69. doi:10.1007/s12035-022-02799-2
20. Henrich MT, Oertel WH, Surmeier DJ, Geibl FF. Mitochondrial dysfunction in Parkinson's disease – a key disease hallmark with therapeutic potential. Molecular Neurodegeneration. 2023;18(1). doi:10.1186/s13024-023-00676-7
21. Gąssowska-Dobrowolska M, Chlubek M, Kolasa A, Tomasiak P, Korbecki J, Skowrońska K, et al. Microglia and astroglia—the potential role in neuroinflammation induced by pre- and neonatal exposure to lead (Pb). International Journal of Molecular Sciences. 2023;24(12):9903. doi:10.3390/ijms24129903
22. Adamu A, Li S, Gao F, Xue G. The role of neuroinflammation in neurodegenerative diseases: current understanding and future therapeutic targets. Frontiers in Aging Neuroscience. 2024;16. doi:10.3389/fnagi.2024.1347987
23. Ogbodo John Onyebuchi, Chinazom Precious Agbo, Ugoci Olivia Njoku, Martins Obinna Ogugofor, Egba Simeon Ikechukwu, Stella Amarachi Ihim, Adaeze Chidiebere Echezona Kenneth Chibuike Brendan, Aman Babanrao Upaganlawar, and ChandrashekarDevidas Upasani (2021) Alzheimer's Disease: Pathogenesis and Therapeutic Interventions, Current Aging Science, 21:1-25.
24. Li D, Yang Y, Li Y, Zhu X, Li Z. Epigenetic regulation of gene expression in response to environmental exposures: from bench to model. Science of the Total Environment. 2021;776:145998. doi:10.1016/j.scitotenv.2021.145998
25. Bertogliat MJ, Morris-Blanco KC, Vemuganti R. Epigenetic mechanisms of neurodegenerative diseases and acute brain injury. Neurochemistry International. 2019;133:104642. doi:10.1016/j.neuint.2019.104642
26. Nabi M, Tabassum N. Role of environmental toxicants on neurodegenerative disorders. Frontiers in Toxicology. 2022;4. doi:10.3389/ftox.2022.837579
27. Uti DE, Egba SI, Ugwu OP-C, Aja PM. The Role of Phytochemicals in Age-Related Cognitive Decline: A Natural Solution for Brain Health. *Natural Product Communications.* 2025;20(6). doi:10.1177/1934578X251350761
28. Vernet C, Johnson M, Kogut K, Hyland C, Deardorff J, Bradman A, et al. Organophosphate pesticide exposure during pregnancy and childhood and onset of juvenile delinquency by age 16 years: the CHAMACOS cohort. Environmental Research. 2021;197:111055. doi:10.1016/j.envres.2021.111055
29. Santana AB, Spelta LEW, Sobalvarro JVM, Podestá MHMC, Garcia RCT, Reis TMD, et al. Gestational lead exposure and its effects on fetal/infant development—a systematic review. Reproductive Toxicology. 2023;117:108342. doi:10.1016/j.reprotox.2023.108342
30. Vejrup K, Schjølberg S, Knutsen HK, Kvalem HE, Brantsæter AL, Meltzer HM, et al. Prenatal methylmercury exposure and language delay at three years of age in the Norwegian Mother and Child Cohort Study. Environment International. 2016;92–93:63–9. doi:10.1016/j.envint.2016.03.029
31. Amaral L, Martins M, Côrte-Real M, Outeiro TF, Chaves SR, Rego A. The neurotoxicity of pesticides: implications for Parkinson's disease. Chemosphere. 2025;377:144348. doi:10.1016/j.chemosphere.2025.144348
32. Park HH, Armstrong MJ, Gorin FA, Lein PJ. Air pollution as an environmental risk factor for Alzheimer's disease and related dementias. Medical Research Archives. 2024;12(10). doi:10.18103/mra.v12i10.5825
33. S AS, Ansari MN, Elossaily GM, Vellapandian C, Prajapati B. Investigating the potential impact of air pollution on Alzheimer's disease and the utility of multidimensional imaging for early detection. ACS Omega. 2024;9(8):8615–31. doi:10.1021/acsomega.3c06328
34. Althobaiti NA. Heavy metals exposure and Alzheimer's disease: underlying mechanisms and advancing therapeutic approaches. Behavioural Brain Research. 2024;476:115212. doi:10.1016/j.bbr.2024.115212
35. Weisskopf MG, Proctor SP, Wright RO, Schwartz J, Spiro A, Sparrow D, et al. Cumulative lead exposure and cognitive performance among elderly men. Epidemiology. 2006;18(1):59–66. doi:10.1097/01.ede.0000248237.35363.29

36. Kilian J, Kitazawa M. The emerging risk of exposure to air pollution on cognitive decline and Alzheimer's disease—evidence from epidemiological and animal studies. Biomedical Journal. 2018;41(3):141–62. doi:10.1016/j.bj.2018.06.001
37. National Academies Press (US). Public health as a problem-solving activity: barriers to effective action. In: The Future of Public Health – NCBI Bookshelf. 1988. Available from: https://www.ncbi.nlm.nih.gov/books/NBK218227/
38. Hernandez LM, Blazer DG. Genetics and health. In: Genes, Behavior, and the Social Environment – NCBI Bookshelf. 2006. Available from: https://www.ncbi.nlm.nih.gov/books/NBK19932/
39. Braun G, Escher BI. Prioritization of mixtures of neurotoxic chemicals for biomonitoring using high-throughput toxicokinetics and mixture toxicity modeling. Environment International. 2022;171:107680. doi:10.1016/j.envint.2022.107680
40. Hernández AF, Lacasaña M, Garcia-Cortés H, Fernández MF, González-Alzaga B. Identification and prioritisation of biomarkers of organophosphorus compounds-induced neurotoxicity. Environment International. 2025;109446. doi:10.1016/j.envint.2025.109446
41. Kaufman AS, Zhou X, Reynolds MR, Kaufman NL, Green GP, Weiss LG. The possible societal impact of the decrease in U.S. blood lead levels on adult IQ. Environmental Research. 2014;132:413–20. doi:10.1016/j.envres.2014.04.015
42. Shekhar C, Khosya R, Thakur K, Mahajan D, Kumar R, Kumar S, et al. A systematic review of pesticide exposure, associated risks, and long-term human health impacts. Toxicology Reports. 2024;13:101840. doi:10.1016/j.toxrep.2024.101840

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