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IMPACT OF AIR POLLUTION ON BRAIN HEALTH: RELATIONSHIP WITH NEURODEGENERATIVE DISEASES AND NEUROLOGICAL CONDITIONS

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Abstract: Objective: To analyze the relationship between exposure to air pollution and the development of neurodegenerative diseases and other neurological conditions, based on recent scientific evidence. Methodology: Bibliographic review based on the analysis of articles indexed in electronic databases. The search terms included "air pollution", "neurodegenerative diseases", "neuroinflammation" and their combinations. Twenty-five studies were selected for detailed analysis. Discussion: Evidence indicates that prolonged exposure to particulate matter (PM2.5, PM10), nitrogen dioxide (NO_2) and ultrafine particles can trigger neuroinflammatory processes, oxidative stress and mitochondrial dysfunction, increasing the risk of diseases such as Alzheimer's, Parkinson's and multiple sclerosis. Studies suggest that nanoparticles can cross the blood-brain barrier, favoring the deposition of neurotoxic proteins and contributing to neurodegeneration. In addition, the impact of air pollution also extends to other neurological conditions, including stroke, neurodevelopmental disorders and depression. Genetic and socioeconomic factors influence vulnerability to the effects of pollution, making higher risk populations more susceptible to neurological impairment. Final considerations: Air pollution is a significant risk factor for neurological diseases, requiring preventive measures and effective public policies to reduce exposure to pollutants. Future research should further identify biomarkers of susceptibility and explore interventions that minimize the neurotoxic effects of pollution on the nervous system.

Keywords: Air pollution, neurodegenerative diseases, neuroinflammation, oxidative stress, environmental exposure.

INTRODUCTION

Air pollution is a global environmental problem that has a significant impact on human health and is responsible for millions of premature deaths every year. Although the association between exposure to air pollutants and cardiovascular and respiratory diseases is widely documented, recent studies have shown a worrying correlation between pollution and the development of neurological and neurodegenerative diseases (Peters *et al.*, 2024). Prolonged exposure to fine particulate matter (PM2.5), nitrogen dioxide (NO_2) and ultrafine particles (UFP) has been associated with structural, metabolic and functional changes in the central nervous system (CNS), increasing the risk of diseases such as Alzheimer's, Parkinson's, multiple sclerosis and cognitive decline (Kim *et al.*, 2024; Mussalo *et al.*, 2024).

Epidemiological studies show that individuals chronically exposed to high levels of air pollutants have a higher incidence of cognitive deficits, accelerated aging and neuroinflammation (Wang *et al.*, 2024). Studies indicate that nanoparticles present in polluted air can cross the blood-brain barrier (BBB) and deposit in vulnerable regions of the brain, such as the hippocampus and cerebral cortex. This process can trigger neuroinflammation, mitochondrial dysfunction and the accumulation of neurotoxic proteins such as beta-amyloid and alpha-synuclein (Dang *et al.,* 2024). These findings suggest that air pollution may play a crucial role in the pathogenesis of neurodegenerative diseases, potentiating already established genetic and environmental factors (Ji *et al.*, 2024).

In addition to neurodegenerative diseases, air pollution has also been associated with other neurological conditions, including stroke, autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD) and depression (Chatterjee *et al.*, 2024). Studies suggest that prenatal and childhood exposure to pollutants can affect neurocognitive development by compromising synaptic plasticity and neuronal functioning (Ji *et al.*, 2024).

The impacts of air pollution are not uniform and vary according to environmental, genetic and socioeconomic factors. Individuals living in densely polluted urban areas, especially those in vulnerable socioeconomic groups, are more exposed to high levels of pollutants and consequently at greater risk of neurological damage (Peters *et al.*, 2024).

Although the correlation between air pollution and neurodegenerative diseases is becoming increasingly evident, there are still challenges in demonstrating direct causality, due to the complexity of the mechanisms involved and the need for more robust longitudinal studies. However, the growing body of scientific evidence suggests that preventive strategies and public policies aimed at reducing exposure to pollutants may represent an effective approach to reducing the incidence of neurological diseases and promoting global public health (Wang *et al.*, 2024).

Against this backdrop, this review aims to critically analyze the relationship between air pollution and the development of neurodegenerative diseases and other neurological conditions, highlighting pathophysiological mechanisms, epidemiological evidence, gaps in the literature and potential mitigation strategies.

METHODOLOGY

A literature review developed according to the criteria of the PVO strategy, which stands for: population or research problem, variables and outcome. This strategy was used to develop the research question "What is the relationship between exposure to air pollution and the development of neurodegenerative diseases and other neurological conditions,

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according to current scientific evidence?". The searches were carried out using the PubMed - MEDLINE (Medical Literature Analysis and Retrieval System Online) databases. The search terms were used in combination with the Boolean terms "**AND", "OR",** using the following search strategy: (("Neurodegenerative Diseases") OR ("Neurological Disorders")) AND (("Air Pollution") OR ("Particulate Matter") OR ("Traffic-Related Air Pollution")). From this search, **312** articles were found, which were then submitted to the selection criteria. The inclusion criteria were: articles in **English; free full text**; published between 2024 and 2025 and which addressed the themes proposed for this research, review-type studies, meta-analysis, observational studies, experimental studies. The exclusion criteria were: duplicate articles, articles available in abstract form, articles that did not directly address the proposal studied and articles that did not meet the other inclusion criteria. After applying the search strategy to the database, a total of **42** articles were found. After applying the inclusion and exclusion criteria, **22** articles were selected from the PubMed database to make up this study's collection.

DISCUSSION

Air pollution is an emerging risk factor for neurodegenerative diseases and other neurological conditions, as demonstrated in the studies analyzed. Evidence indicates that different types of pollutants - such as particulate matter (PM2.5 and PM10), nitrogen dioxide (NO_2) and ultrafine particles (PM0.1) - are associated with neuroinflammatory processes, oxidative stress and epigenetic deregulation, fundamental mechanisms in the development of pathologies such as Alzheimer's disease (AD), Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS). In addition, recent studies suggest that specific pollutants, such as coke oven emissions (COE), can directly compromise synaptic plasticity and neuronal function, amplifying the deleterious effects of pollution on the central nervous system (Wu *et al.,* 2024).

Chronic exposure to pollutants can trigger cognitive dysfunction through epigenetic changes and neuroinflammation. The study by Oliver *et al.* (2024) found that prolonged maternal exposure to PM2.5 affects the cognition of offspring differently, showing a gender-dependent impact. Males were found to have significant memory deficits, while females were relatively protected. This protection was attributed to the greater expression of the histone demethylases Kdm6a and Kdm5c, which modulate the transcription of genes related to neuroprotection and mitochondrial function. These findings reinforce the hypothesis that epigenetic modifications play an essential role in susceptibility to the effects of pollution, modulating the neuronal response to environmental stress (Oliver *et al.*, 2024).

In addition, evidence indicates that chronic exposure to heavy metals, pesticides and other environmental contaminants can trigger epigenetic modifications that favor neurodegenerative processes. The study by Stoccoro and Coppedè (2024) demonstrated that these compounds are capable of altering DNA methylation patterns, impacting the regulation of genes involved in neuronal homeostasis and the response to oxidative stress. Hypermethylation of inflammation suppressor genes and hypomethylation of pro-inflammatory promoters can intensify microglial activation, exacerbating neuronal damage induced by environmental pollutants. These findings reinforce that epigenetic modifications not only increase individual vulnerability to air pollution, but can also perpetuate neurodegenerative predispositions over generations (Stoccoro & Coppedè, 2024).

The changes induced by atmospheric pollution are not restricted to the molecular and epigenetic level, but directly affect cellular function. The study by Sapienza *et al.* (2024) showed that exposure to PM0.1 leads to dysfunction of the endoplasmic reticulum and deregulation of calcium homeostasis in motor neurons. This mechanism is similar to that observed in the pathogenesis of ALS, and is characterized by alterations in the activity of the SERCA2 and SERCA3 pumps and in calcium influx via SOCE (Store-Operated Calcium Entry). These changes compromise neuronal integrity and contribute to progressive neurodegeneration. Additionally, the study by Wu *et al.* (2024) demonstrated that exposure to COE induces significant deficits in memory and learning, accompanied by reduced expression of miR-145a-5p and increased expression and phosphorylation of SIK1, a kinase involved in the regulation of synaptic plasticity. This alteration inhibits the cAMP/PKA/CREB signaling pathway, which is essential for memory consolidation, resulting in a decrease in synaptic proteins such as PSD95 and synaptophysin (SYP), which reinforces the direct impact of pollution on the central nervous system (Wu *et al.*, 2024).

In the context of PD, the study by Huang *et al.* (2024) investigated the interaction between genetic predisposition and environmental exposure. The results indicated that individuals with a high genetic susceptibility to PD have a significantly elevated risk when exposed to high levels of NO_2 and PM10. This suggests that environmental factors can act as triggers in genetically predisposed individuals, accelerating the onset and progression of the disease. These findings corroborate the need for an integrated approach to analyzing risk factors for neurodegenerative diseases, considering both environmental and genetic aspects.

The Mendelian randomization study conducted by Liu *et al.* (2024) provides causal support for the relationship between air pollution and AD. Using genetic variants as proxies for exposure, the authors demonstrated that high levels of PM2.5 and PM10 are associated with a significantly increased risk of AD. However, no direct associations were observed between PM and PD or ALS, suggesting that the relationship with these diseases may be mediated by other biological or environmental factors that have not yet been fully elucidated.

In addition, the study by Jäntti *et al.* (2024) revealed that particles from diesel engines and compressed natural gas compromise the function of microglia, cells that are essential for the immune response of the central nervous system. This effect can intensify chronic neuroinflammatory processes, favoring the deposition of toxic proteins such as beta-amyloid and alpha-synuclein, implicated in the pathophysiology of AD and PD, respectively. These findings highlight the need for regulatory measures to minimize exposure to vehicle emissions and, consequently, reduce the burden of neurodegenerative diseases in the population.

Another point would be the direct impact of pollutants on microglial activation and neuroinflammation. Recent studies indicate that chronic exposure to urban particulate matter (uPM) can induce cellular senescence, particularly in macrophages, key cells in the innate immune response. The study by Thomas *et al.* (2024) showed that macrophages exposed to uPM exhibit a senescent phenotype characterized by increased IL-1α secretion, elevated β-galactosidase activity associated with senescence and reduced cell proliferation. This finding is relevant because it suggests that pollutant-induced immune cell senescence may compromise the immune system's ability to respond to environmental insults, favoring a chronic state of low-grade

inflammation. As microglial activation plays a central role in neurodegeneration, the contribution of macrophage senescence may amplify the inflammatory cycle, exacerbating neuronal damage in diseases such as Alzheimer's, Parkinson's and Amyotrophic Lateral Sclerosis (Thomas *et al.*, 2024).

In addition to the direct impacts of pollutants, studies show that air pollution can act synergistically with other environmental factors. The study by Kuntić *et al.* (2024) analyzed the interaction between air pollution and urban noise, showing that both contribute to increased oxidative stress and neuroinflammation. This interaction potentiates the deleterious effects on the blood-brain barrier, facilitating the entry of toxins into the central nervous system and exacerbating the risk of neurodegenerative diseases.

The study by Ramírez-Mendoza *et al.* (2024) reinforces this hypothesis by demonstrating that prolonged exposure to PM2.5 and ozone (O_3) induces a state of nitrooxidative stress, associated with the formation of neurodegenerative biomarkers. These findings suggest that chronic exposure to pollution can promote changes in cellular homeostasis that accelerate the process of neurodegeneration.

Vulnerability to air pollution is not homogeneous in the population. The study by Aretz *et al.* (2024) showed that elderly people exposed to fine particles over the long term have a higher risk of cognitive impairment, mediated by inflammatory processes and changes in the leukocyte profile. In parallel, the study by Mokhtar *et al.* (2024) identified a relationship between high levels of PM2.5 and PM10 and a reduction in the density of corneal nerve fibers, suggesting that damage to the peripheral nervous system may be an early marker of the effects of pollution on the brain.

In addition, socioeconomic disparities play a critical role in exposure to pollution. Low-income individuals, often living in areas of high population density and close to emission sources, are at greater risk of prolonged exposure, widening the inequality in the impacts of pollution on neurological health (Oliver *et al.,* 2024). Studies show that chronic maternal exposure to PM2.5 can affect cognitive development in a gender-dependent way, suggesting that biological factors modulate the response to environmental pollutants (Oliver *et al.,* 2024). As highlighted by Olloquequi *et al.* (2024), prolonged exposure to air pollutants is associated with a higher risk of cognitive impairment and an increased incidence of Alzheimer's disease, highlighting the influence of environmental factors on neurodegeneration.

Evidence indicates that air pollution represents a significant risk factor for neurodegenerative diseases. However, there are still gaps to be filled, especially regarding the identification of safe exposure thresholds and the characterization of specific vulnerability mechanisms. Krzyzanowski *et al.* (2024) showed, through a population-based study, that chronic exposure to air pollutants is associated with a significant increase in the incidence of Parkinson's disease, reinforcing the hypothesis that environmental particles can act as triggers for neuroinflammatory processes and mitochondrial dysfunction, which contribute to the progression of the disease (Krzyzanowski *et al.,* 2024). In addition, Ruggles and Benakis (2024) point out that pollution can contribute to cerebrovascular events, such as stroke, through the interaction of the gut-brain and lung-brain axis, which reinforces the need for studies that analyze these vulnerability mechanisms in an integrated manner (Ruggles; Benakis, 2024).

FINAL CONSIDERATIONS

Air pollution is a significant risk factor for neurological diseases, contributing to neuroinflammation, oxidative stress and mitochondrial dysfunction. In addition to its association with Alzheimer's, Parkinson's and multiple sclerosis, there is evidence of an impact on cerebrovascular diseases, neurodevelopmental disorders and mental health. However, the definition of safe exposure thresholds and individual susceptibility mechanisms are still poorly understood. The adoption of strict environmental policies and advances in biomarkers and neuroprotective strategies, such as antioxidants and epigenetic modulators, are essential to mitigate these impacts. Improved public health guidelines and collaboration between neuroscience, epidemiology and environmental health could increase knowledge about this complex interaction and provide a basis for effective preventive strategies.

REFERENCES

1. Aretz B, Doblhammer G, Heneka MT. **The role of leukocytes in cognitive impairment due to long-term exposure to fine particulate matter: A large population-based mediation analysis.** Alzheimers Dement. 2024 Dec;20(12):8715-8727.

2. Chatterjee N, González-Durruthy M, Costa MD, Ribeiro AR, Vilas-Boas V, Vilasboas-Campos D, Maciel P, Alfaro-Moreno E. **Differential impact of diesel exhaust particles on glutamatergic and dopaminergic neurons in Caenorhabditis elegans: A neurodegenerative perspective.** Environ Int. 2024 Apr;186:108597.

3. Dang M, Li Y, Zhao L, Li T, Lu Z, Lu J, Feng Y, Yang Y, Li F, Tang F, Wang X, Jian Y, Wang H, Zhang L, Fan H, Zhang G. **Causal association between particulate matter 2.5 and Alzheimer's disease: a Mendelian randomization study.** Front Public Health. 2024 May 30;12:1343915.

4. HUANG, Y. et al. **Genetic susceptibility modifies the association of long-term air pollution exposure on Parkinson's disease.** npj Parkinson's Disease, v. 10, n. 23, p. 1 - 7, 2024.

5. Jäntti H, Jonk S, Gómez Budia M, Ohtonen S, Fagerlund I, Fazaludeen MF, Aakko-Saksa P, Pebay A, Lehtonen Š, Koistinaho J, Kanninen KM, Jalava PI, Malm T, Korhonen P. **Particulate matter from car exhaust alters function of human iPSC-derived microglia.** Part Fibre Toxicol. 2024 Feb 15;21(1):6

6. Ji HW, Kang J, Kim HC, Jung J, Lee SJ, Jung JY, Lee SW. **The association between cumulative exposure to PM2.5 and DNA methylation measured using methyl-capture sequencing among COPD patients.** Respir Res. 2024 Sep 9;25(1):335.

7. KIM, B.Y. et al. **Neurodegenerative pathways and metabolic changes in the hippocampus and cortex of mice exposed to urban particulate matter: insights from an integrated interactome analysis.** Science of the Total Environment, v. 945, p. 173673, 2024.

8. Krzyzanowski B, Mullan AF, Turcano P, Camerucci E, Bower JH, Savica R. Air **Pollution and Parkinson Disease in a Population-Based Study.** JAMA Netw Open. 2024 Sep 3;7(9):e2433602.

9. Kuntić M, Hahad O, Münzel T, Daiber A. **Crosstalk between Oxidative Stress and Inflammation Caused by Noise and Air Pollution-Implications for Neurodegenerative Diseases.** Antioxidants (Basel). 2024 Feb 22;13(3):266.

10. Liu X, Zhang X, Chang T, Zhao Z, Zhang Y, Yang X, Lu M. **Causal relationships between genetically predicted particulate air pollutants and neurodegenerative diseases: A two-sample Mendelian randomization study.** Ecotoxicol Environ Saf. 2024 Oct 1;284:116960.

11. Mokhtar SBA, Viljoen J, van der Kallen CJH, Berendschot TTJM, Dagnelie PC, Albers JD, Soeterboek J, Scarpa F, Colonna A, van der Heide FCT, van Greevenbroek MMJ, Bosm H, Kroon AA, Nuijts RMMA, Gijs M, Lakerveld J, Malik RA, Webers CAB, Stehouwer CDA, Koster A. **Greater exposure to PM2.5 and PM10 was associated with lower corneal nerve measures: the Maastricht study - a cross-sectional study.** Environ Health. 2024 Sep 4;23(1):70.

12. Mussalo L, Lampinen R, Avesani S, Závodná T, Krejčík Z, Kalapudas J, Penttilä E, Löppönen H, Koivisto AM, Malm T, Topinka J, Giugno R, Jalava P, Kanninen KM. **Traffic-related ultrafine particles impair mitochondrial functions in human olfactory mucosa cells - Implications for Alzheimer's disease.** Redox Biol. 2024 Sep;75:103272.

13. Oliver BG, Huang X, Yarak R, Bai X, Wang Q, Zakarya R, Reddy KD, Donovan C, Kim RY, Morkaya J, Wang B, Lung Chan Y, Saad S, Faiz A, Reyk DV, Verkhratsky A, Yi C, Chen H. **Chronic maternal exposure to low-dose PM2.5 impacts cognitive outcomes in a sex-dependent manner.** Environ Int. 2024 Sep;191:108971.

14. Olloquequi J, Díaz-Peña R, Verdaguer E, Ettcheto M, Auladell C, Camins A. **From Inhalation to Neurodegeneration: Air Pollution as a Modifiable Risk Factor for Alzheimer's Disease.** Int J Mol Sci. 2024 Jun 25;25(13):6928.

15. PETERS, S. et al. **Air pollution exposure and mortality from neurodegenerative diseases in the Netherlands: a population-based cohort study.** Environmental Research, v. 259, p. 119552, 2024.

16. Ramírez-Mendoza AA, Mendoza-Magaña ML, Ramírez-Herrera MA, Hernández-Nazara ZH, Domínguez-Rosales JA. Nitrooxidative Stress and **Neuroinflammation Caused by Air Pollutants Are Associated with the Biological Markers of Neurodegenerative Diseases.** Antioxidants (Basel). 2024 Mar 7;13(3):326.

17. Ruggles, A.; Benakis, C. **Exposure to Environmental Toxins: Potential Implications for Stroke Risk via the Gut– and Lung–Brain Axis.** Cells 2024, 13, 803.

18. SAPIENZA, S. et al. U**ltrafine particulate matter pollution and dysfunction of endoplasmic reticulum Ca2+ store: A pathomechanism shared with amyotrophic lateral sclerosis motor neurons?** Elsevier, v. 273, p.1 - 10, 2024.

19. Stoccoro A, Coppedè F. **Exposure to Metals, Pesticides, and Air Pollutants: Focus on Resulting DNA Methylation Changes in Neurodegenerative Diseases.** Biomolecules. 2024 Oct 27;14(11):1366.

20. Thomas SA, Yong HM, Rule AM, Gour N, Lajoie S. **Air Pollution Drives Macrophage Senescence through a Phagolysosome-15-Lipoxygenase Pathway.** Immunohorizons. 2024 Apr 1;8(4):307-316.

21. WANG, S.-n. et al. **Particulate matter 2.5 accelerates aging: Exploring cellular senescence and age-related diseases**. Ecotoxicology and Environmental Safety, v. 284, p. 116920, 2024.

22. Wu Z, Zhang H, Chen X, Zhang P, Fang J, Yang S, Chen H, Ji J, Chen L, Zheng Y, Yu D, Zhao Y. **miR-145a-5p/SIK1/cAMP-dependent alteration of synaptic structural plasticity drives cognitive impairment induced by coke oven emissions**. Ecotoxicol Environ Saf. 2024 Jun 1;277:116401.