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REVIEW

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The impact of air pollution on neurodegenerative diseases: a narrative review of current evidence

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Abstract

This narrative review explores the relationship between air pollution and neurodegenerative diseases (NDs). Historically, air pollution has been linked primarily to respiratory and cardiovascular issues, but recent evidence suggests that it may also impact neurological health. With the global increase in neurodegenerative diseases, understanding environmental risk factors has become crucial. The review synthesizes findings from recent studies, highlighting the potential role of air pollutants—particularly fine particulate matter (PM2.5), ozone, nitrogen dioxide (NO2), and heavy metals—in the onset and progression of NDs. Key mechanisms under investigation include brain inflammation and microglial activation, which are believed to contribute to neurodegenerative processes. Animal and human studies have shown correlations between air pollution exposure and increased risk of cognitive decline and neurodegenerative disorders. Research indicates that air pollution may exacerbate neuroinflammation and cause white matter abnormalities, which disrupt neural communication and cognitive function. Additionally, emerging evidence suggests that environmental factors like residential greenness and climate action could mitigate some of these adverse effects. Despite advancements, significant knowledge gaps remain, particularly regarding the long-term impact of chronic exposure and the specific molecular pathways involved. This review shows the need for further research to clarify these mechanisms and develop targeted interventions. Addressing air pollution's impact on neurodegenerative diseases requires comprehensive public health strategies, including stricter environmental regulations and increased awareness, alongside continued research into preventive and therapeutic measures.

Keywords Air pollution, Neurodegenerative diseases, Environmental health, Health policy

Introduction

Air pollution, traditionally a concern primarily for respiratory and cardiovascular health, is now under scrutiny for its potential impacts on the nervous system [1, 2]. With global aging and the increasing prevalence of neurodegenerative diseases, environmental factors are gaining attention as potential contributors to the onset and progression of these debilitating conditions [3]. Neurodegenerative diseases, which involve the gradual deterioration of the nervous system, pose a significant global health challenge [4]. Conditions such as Alzheimer's disease (AD) and Parkinson's disease (PD), anxiety,

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and depression impose heavy burdens on individuals, caregivers, and healthcare systems worldwide [4]. While these diseases have complex origins that are not fully understood, growing evidence suggests that exposure to air pollutants like fine particulate matter (PM2.5), ozone, nitrogen dioxide (NO2), and heavy metals may play a role in their development [5].

The existing literature indicates that air pollution can impact neurodegenerative diseases through mechanisms such as brain inflammation and white matter abnormalities [6, 7]. However, significant knowledge gaps persist, particularly regarding the mechanisms linking air pollution to the onset and progression of neurodegenerative diseases. One critical mechanism of interest is brain inflammation, which is known to play a pivotal role in the neurotoxic effects of air pollution [8]. Chronic brain inflammation is believed to contribute to the development or exacerbation of neurodegenerative diseases such as AD and PD [9]. While this concept has been explored in several studies, a comprehensive review that synthesizes and evaluates the existing evidence is necessary to fully comprehend how air pollution-induced brain inflammation contributes to these diseases [10, 11].

Furthermore, research has identified white matter abnormalities in the brains of individuals exposed to air pollution [12, 13]. These abnormalities disrupt communication between different brain regions and have been associated with cognitive and motor impairments. Additionally, the activation of microglia, the brain's immune cells, in response to air pollution has been proposed as a potential mechanism that could exacerbate neuroinflammation and contribute to the neurodegenerative processes [14]. Additionally, abnormalities in white matter and the activation of microglia have been observed in individuals exposed to air pollution, suggesting these factors might contribute to cognitive and motor impairments. This narrative review aims to critically examine and synthesize current evidence on the relationship between air pollution and neurodegenerative diseases.

Pathophysiological mechanisms of air pollution in neurological diseases

An often-overlooked risk factor for neurodegenerative illness is air pollution, which is a common pro-inflammatory stimulation to the central nervous system [15]. It is estimated that 88 million individuals are exposed to PM2.5 and 29 million to PM10 in the USA alone [16]. It is concerning to note that although exposure is thought to be considerable, UFPM levels in the USA are not tracked or regulated [17]. Millions more are also exposed to PM during work and during natural disasters like fires, war, and the aftermath of terrorist events like the World Trade Center attack. Parkinson's disease (PD) and Alzheimer's disease (AD), two conditions that may be impacted by air pollution, are also common [18]. AD is the most common neurodegenerative disease, affecting about 4 million Americans and an estimated 27 million individuals globally. One to two percent of people over 50 suffer from Parkinson's disease (PD), a debilitating movement disorder and the second most common neurodegenerative disease. The fact that recent studies have connected air pollution to neuroinflammation and neuropathology linked to AD and PD is quite concerning in light of these figures [19].

Animal populations (feral dogs) that were naturally exposed to contaminated metropolitan surroundings were the subject of the first research examining the potential link between air pollution and neurodegenerative diseases [2]. Increased oxidative damage, early diffuse amyloid plaque development, and a marked rise in DNA damage (apurinic/apyrimidinic sites) in the olfactory bulbs, frontal, cortex, and hippocampus were all observed in feral dogs residing in high-pollution areas. The nasal pathway is implicated as a major portal of entry since dogs exposed to high levels of urban pollution also exhibit tissue damage and deposited metals (nickel and vanadium) at target brain regions in a gradient form (olfactory mucosa > olfactory bulb > frontal cortex) [20]. Early pathology in the olfactory bulb, nuclei, and pathways is shared by AD and PD, which is quite comparable. One of the first symptoms of both disorders is olfactory impairments [20]. This study established the first link between pollution exposure and the accelerated pathophysiology of neurodegenerative diseases.

These results have recently been validated and expanded in human and other animal models. Increases in CD-68, CD-163, and HLA-DR positive cells (indicating infiltrating monocytes or resident microglia activation), elevated pro-inflammatory markers (Interleukin-1β, IL1-β; cycloxygenase 2, COX2), increased Aβ42 deposition (the hallmark disease protein of Alzheimer's disease), blood–brain-barrier (BBB) damage, endothelial cell activation, and prefrontal lobe brain lesions are all observed in brain tissue from people who live in highly polluted areas [21]. Fascinatingly, the frontal cortex, substantia nigra, and vagus nerves were found to have higher levels of pro-inflammatory markers such as COX2 and IL1-β as well as the CD-14 marker for innate immune cells. Additionally, research on animals has demonstrated that air pollution results in increased MAP kinase signaling through JNK, cytokine generation, neurochemical alterations, lipid peroxidation, altered behavior, and increased expression of NFκβ [22]. These studies collectively show unequivocally that air pollution affects the central nervous system.

Both AD and PD share abnormal filamentous protein aggregates and neuroinflammation as shared characteristics. Exposure to urban air pollution has been demonstrated to cause neuroinflammation and accumulation of Aβ42 (a component of Aβ plaques) and α-synuclein (a component of Lewy Bodies) in target areas for AD and PD involvement, even though studies have not yet found a direct effect of air pollution on defined Lewy bodies (a pathological hallmark of PD) or beta-amyloid (Aβ) plaques (a pathological hallmark of AD)[23]. For instance, 10 years before their counterparts who live in clean air, dogs exposed to high levels of air pollution exhibit greater deposits of diffuse amyloid plaques. Furthermore, exposure to high concentrations of air pollution is known to start the accumulation of Aβ42 and α-synuclein early in human childhood, supporting the idea that air pollution may promote early disease processes and/or premature aging in the brain[2]. One possible explanation is that oxidative stress and nanoparticles alter the rate of protein fibrillation and aggregation, which may have an impact on soluble Aβ and α-synuclein. These alterations in protein aggregation linked to air pollution might indicate early pathology in the processes of neurodegenerative diseases [23].

A notion known as "the multiple hit hypothesis" has also been put out, according to which environmental toxins cause CNS disease by acting at several stages of human development. Research supports this theory by demonstrating that PM affects the central nervous system from an early age [24]. For instance, in children exposed to high levels of air pollution, MRI investigations have shown structural damage (hyperintense white matter lesions) localized in the prefrontal cortex, which may be linked to cognitive impairment. Interestingly, frontal lesions with vascular/endothelial disease and neuroinflammation are also seen in dogs exposed to the same air pollution [25]. As a result, young people and animals may be especially susceptible to the inflammatory effects of air pollution, which can worsen throughout the course of a person's lifetime.

Although the only CNS diseases with a known increased epidemiological risk with exposure to air pollution are ischaemic stroke, multiple sclerosis (risk is increased by secondhand smoke), and Parkinson's disease (risk is increased by manganese content in the air), it is likely that many other unstudied diseases have an even higher associated risk [26]. Given that genetic predisposition may give vulnerability to the CNS consequences of air pollution, as is the case with hereditary APOE4 allele carriers in humans and APOE knockout mice, these hazards may be dispersed across individual variances in population susceptibility[27]. However, extending both mechanistic and epidemiological studies to pursue the risks for other CNS diseases is of urgent concern to human health, given the high prevalence of AD and PD, the established CNS pathology caused by air pollution, the link between neuroinflammation and AD/PD pathogenesis, and the common high rate of human exposure to air pollution [28].

Methods

To explore the connection between air pollution and neurodegenerative diseases, we conducted a narrative review. We searched prominent academic databases like PubMed, Google Scholar, and Web of Science using a comprehensive set of keywords encompassing "Air Pollution," "Neurodegenerative diseases," and related terms like "Environmental Exposure" and "Inflammation." This search strategy ensured we captured recent studies (within the last 5 years) on the specific mechanisms under investigation (focusing on brain inflammation and microglial activation). The focus on studies from the last 5 years in our narrative review is justified by the rapid advancements in research techniques and the evolving understanding of the relationship between air pollution and neurodegenerative diseases. We ensure that the review reflects the latest evidence and trends, incorporating updated findings that address emerging mechanisms and current exposure patterns.

Inclusion criteria

Language

Only articles published in English were included to ensure comprehension and consistency.

Access

Articles had to be available in full text to allow for thorough evaluation.

Relevance

Studies must have directly addressed the connection between air pollution and neurodegenerative diseases, focusing on specific mechanisms, outcomes, or epidemiological evidence.

Exclusion criteria

Non-primary research

Reviews, conference papers, and abstracts were excluded to maintain a focus on primary research and ensure data quality.

Irrelevant content

Studies not explicitly linking air pollution with neurodegenerative outcomes or not providing original empirical data were excluded.

Two independent reviewers screened all retrieved articles against the pre-established criteria. Any discrepancies were resolved through discussion until a consensus was reached. This rigorous screening process yielded a final selection of 82 articles for in-depth analysis. We then extracted key information from these articles. This data encompassed study design, participant characteristics, methods used to assess exposure to air pollution, specific neurodegenerative disease outcomes investigated, and the most critical findings from each study.

Air pollution and neurodegenerative diseases

Neurodegenerative diseases present a significant global health challenge, affecting more than 50 million people worldwide, with Alzheimer's Disease (AD) alone accounting for 60 to 70% of cases according to the World Health Organization (WHO) [29]. This staggering figure is projected to rise to 152 million by 2050, underscoring the urgency of addressing these conditions [30, 31]. The prevalence of Parkinson's disease (PD) has also doubled over the past 25 years, further highlighting the growing impact of neurodegenerative diseases[32].

Huntington's disease (HD) exhibits varying prevalence rates globally, with recent studies indicating higher rates than previously estimated in Western populations[33, 34]. This discrepancy underscores the need for improved diagnostic tools, particularly genetic testing, to accurately assess the true burden of HD across different regions [35, 36].

Neurodegenerative diseases share a common characteristic of progressive brain function decline, primarily associated with age and characterized by neurodegeneration—the gradual loss of neuron structure and function [37]. This process involves synaptic dysfunction, abnormal protein accumulation, and ultimately, neuronal death, contributing to conditions such as AD, PD, HD, and ALS [38–40].

Environmental factors, including air pollution, are increasingly recognized as potential contributors to the development of neurodegenerative diseases. Air pollution, highlighted by the Lancet Commission as a leading environmental risk factor for disease and premature mortality, is notably associated with fine particulate matter (PM2.5), a significant component of air pollution responsible for millions of deaths annually worldwide [41, 42]. Research indicates a correlation between exposure to PM2.5 and neurodegenerative diseases like AD and PD [33, 43].

PM2.5 consists of organic and inorganic components originating from various sources such as residential fuel combustion, industrial emissions, vehicle exhaust, and wildfires [44]. It enters the central nervous system through multiple pathways, including olfactory neurons, the blood–brain barrier, and the microbiota-gut-brain axis, exerting neurotoxic effects through oxidative stress, inflammation, mitochondrial dysfunction, neuronal loss, and other mechanisms [19, 45]. PM2.5's ability to carry chemical compounds and pathogens further exacerbates its impact on health, affecting not only respiratory but also systemic and neurological functions [5, 46].

Results: current evidence from studies

Animal studies

A total of 24 animal studies, primarily utilizing zebrafish, mice, or rats, have demonstrated cognitive decline resembling features observed in neurodegenerative diseases [43, 47–69] (Fig. 1 and Table 1). Notably, Chuang et al. observed accelerated neurodegenerative disease development in animals with comorbid conditions such as hypertension [68]. Patten et al. and Navarro et al. identified increased microglial phagocytic activity and proinflammatory cell markers in rodent models, highlighting genetic modifiers' role in AD [53, 70]. Haghani et al.'s study involving ultrafine particulate matter (< 0.2 μm) demonstrated significant data correlation across different taxa related to Apolipoprotein E binding motifs, showing unique reactions in both mice and human tissue cultures [58].

Jew et al. and Shou et al. found that exposure to ultrafine particulate matter (UFP) at human-relevant concentrations adversely affected memory domains and blood–brain barriers in mice [48, 71]. Astaxanthin, a phytonutrient and antioxidant carotenoid, was found protective in rat glial cells, reducing PM2.5-induced inflammation by lowering levels of inducible nitric oxide synthase (iNOS) and Heme Oxygenase 1 (HO-1), thus protecting nerve cells [69].

Milani et al. compared diesel exhaust particulate (DEP) and biomass burning (BB), highlighting DEP's greater harmful effects evidenced by modulation of amyloid precursor protein (APP) and beta-secretase 1 (BACE1) protein levels, leading to oxidative stress [49]. They also noted faster inhalational deposition on the olfactory epithelium for UFP compared to translocation rates from the lungs via the blood-air barrier (BAB) [49].

Armstrong et al. investigated mixed gasoline and diesel engine emissions (MVE) exposure in young and aged mice, revealing exacerbated oxidative stress and increased levels of various neurologically relevant proteins, suggesting a link to age-related brain changes [50]. Multiple studies on nano-sized traffic-related air pollution particulate matter (nPM) observed increased oxidative stress, altered cerebral cortex, and elevated amyloid-β (Aβ) peptide production, all associated with Alzheimer's disease [51, 66].

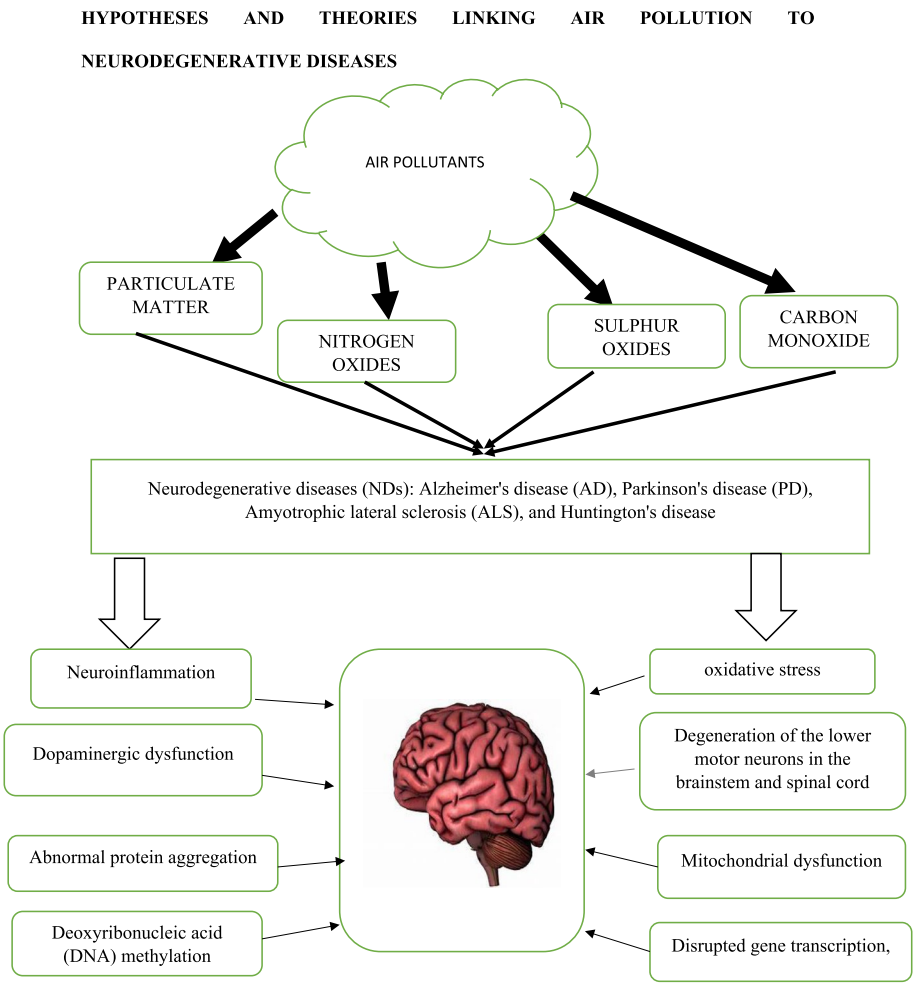

Fig. 1 Hypothesis and theories linking air pollution to neurodegenerative diseases

Studies specifically focusing on PD found that particulate matter (PM10 2.5–10 μm) deposition led to α-synuclein fibril deposition and dopaminergic neuron death in the brain parenchyma [54, 73]. Garcia et al. investigated HD and AD, revealing that nPM contributes to misfolded protein accumulation, disrupting proteostasis networks in Caenorhabditis elegans [74].

Human studies

Numerous studies have documented associations between particulate matter exposure and microglial dysfunction in AD and PD [73–79]. Table 2. Some studies have delved deeper into the pathogenesis of PD, myosclerotic conditions, and Huntington's disease (HD) [74, 80, 81]. Long-term population-based longitudinal studies and ecological studies have examined sociodemographic variables like race, age, gender, and occupational exposures [82–85].

Comparative analyses of individual air pollutants highlight sulfur dioxide (SO2) and PM2.5 as significant contributors to rapid cognitive decline [80]. Cole-Hunter et al.'s 20-year European study demonstrated higher Parkinson's mortality rates associated with PM2.5 exposure among approximately 271,000 subjects [80]. Conversely, after adjusting for age, body mass index (BMI), tobacco smoking, nitrogen dioxide (NO2), and black carbon showed null associations. Gallo et al. reported a 20% reduced risk of PD among former smokers in a cohort study, despite the presence of NO2 and black carbon, which are also found in tobacco smoke [95]. Another Canadian study linked traffic-related air pollutants to PD incidence rather than AD [91].

Li et al. explored PM2.5 exposure levels and their association with AD and allergic rhinitis in a Taiwanese population, revealing a fourfold higher risk of AD among those with allergic rhinitis [86]. Myung et al. demonstrated increased risks of acute exacerbations and emergency

Table 1 Animal studies

Authors and year	Pollutant	Participants	Neurodegenerative disease studied	Key findings
Jew et al. (2019) [71]	Ultrafine PM (UFP)	3xTgAD and non-transgenic mice	Alzheimer's disease (AD)	Short-term inhalation exposure caused memory problems in aged mice, regardless of underlying AD
Chuang et al. (2020) [68]	Fine particulate matter (PM2.5)	Hypertensive animals	Neurodegenerative diseases	Chronic low-level PM2.5 exposure may worsen neurodegeneration in subjects with hypertension
Kim et al. (2020) [69]	PM2.5	Cultured rat glial cells	Alzheimer's, Parkinson's, and other dementias	PM2.5 exposure may harm the brain by changing microglial cells. Astaxanthin may offer protection
Ha et al. (2022) [55]	Diesel exhaust particulate extract (DEPe)	Zebrafish (ZF)	Parkinson's and Alzheimer's disease	DEPe exposure damaged neurons and activated microglia. Microglia depletion did not prevent neuron loss
Shou et al. (2020) [48]	PM2.5	C57BL/6 mice	Air pollution-induced neurodegenerative disease	Chronic PM2.5 exposure led to cognitive decline in mice, possibly due to neuroinflammation and blood–brain barrier disruption
Milani et al. (2020) [49]	Biomass combustion and diesel exhaust	Mouse Brain	Alzheimer's disease markers	Both exposures caused inflammation, but diesel exhaust caused more oxidative stress. Sub-acute exposure affected APP and BACE1 protein levels
Armstrong et al. (2020) [50]	Mixed gasoline and diesel engine emissions (MVE)	Male C57BL/6 mice	Alzheimer's disease (AD)	MVE exposure increased factors in the brain linked to AD development in older mice
Cacciottolo et al. (2020) [51]	Traffic-related air pollution particulate matter (TRAP-PM)	Rodent models	Alzheimer's dementia (AD)	TRAP-PM caused oxidative stress and altered APP processing in cells, potentially contributing to AD
Navarro-Sempere et al. (2021) [70]	Hazardous gases (radon, hydrogen sulfide, carbon dioxide)	Feral mice	Neuroinflammation	Increased microglia and signs of inflammation are common features of neurodegenerative diseases
Sahu et al. (2021) [66]	PM2.5	Male C57BL/6; C3H mice (wild type and APP/PS1)	Alzheimer's disease (AD)	Chronic PM2.5 exposure worsens AD by increasing amyloid plaque buildup, gliosis, and brain inflammation
Patten et al. (2021) [53]	Particulate matter (PM)	TgF344-AD rats	Alzheimer's disease (AD)	Chronic exposure to ambient TRAP-PM promoted AD development in both healthy and AD-prone rats
Herr et al. (2021) [67]	Concentrated ambient UFP	3xTgAD and NTg mice	Alzheimer's disease (AD)	Exposure to realistic UFP levels changed tau protein phosphorylation and microglial shape, even without lung inflammation
Haghani et al. (2021) [58]	Nano-sized particulate matter (nPM)	Mice	Alzheimer's disease	Similar binding sites for factors regulating a gene cluster linked to AD risk were found in humans and mice, suggesting a potential environmental link

Table 1 (continued)

Authors and year	Pollutant	Participants	Neurodegenerative disease studied	Key findings
Yuan et al. (2022) [54]	PM2.5	A53T transgenic mice	Parkinson's disease	PM2.5 exposure promoted α-Synuclein protein buildup, a key feature of Parkinson's disease
Xu et al. (2022) [47]	PM2.5 and NOx	Aged mice	Alzheimer's disease	This study suggests how traffic-related air pollution might impair memory and thinking
Ha et al. (2022) [55]	DEPe	Zebrafish (ZF)	Parkinson's and Alzheimer's disease	DEPe exposure damaged neurons and activated microglia. Depleting microglia did not prevent neuron loss
Parks et al. (2022) [72]	Elemental carbon (EC), nitrogen oxides (NOx), carbon monoxide (CO), fine particles (PM2			

Table 2 Evidence from human studies

Authors and year	Pollutant	No. of study participants	Neurodegenerative dx studied	Key findings
Calderón-Garcidueñas et al. (2022) [28]	Fine particulate matter (PM2.5)	179	Alzheimer's (AD) and Parkinson's (PD)	Early damage to olfactory bulb in young Mexico City residents, potentially linked to AD and PD
Shin et al. (2018) [78]	Fine particulate matter (PM2.5), nitrogen dioxide (NO2), and ozone (O3)	38,745	Parkinson's disease (PD)	Exposure to air pollution, especially PM2.5, is linked to incident PD
Li et al. (2019 [86]	Fine particulate matter (PM2.5)	National population-based cohort	Alzheimer's disease (AD)	Increased PM2.5 exposure correlated with allergic rhinitis, which could in turn increase AD risk
Myung et al. (2019) [87]	PM2.5, PM10, NO2, SO2, O3, and CO	617	Amyotrophic lateral sclerosis (ALS)	Short-term exposure to air pollution may increase the risk of acute ALS exacerbation
Toro et al. (2019) [88]	PM10, PM2.5, PMcoarse, black carbon, and nitrogen oxides	1290	Parkinson's disease (PD)	No significant positive association was observed between ambient air pollutants and PD
Calderón-Garcidueñas et al. (2019) [77]	Fine particulate matter (PM2.5) and ozone (O3)	100	Alzheimer's disease (AD)	Brainstem and olfactory areas may be initial targets in young people with high exposure, followed by cognitive deficits later
Li et al. (2019 [86]	PM2.5	National population-based cohort	Alzheimer's disease (AD)	Increased PM2.5 exposure correlated with allergic rhinitis, which could in turn increase AD risk
Shi et al. (2020) [89]	Fine particulate matter (PM2.5)	Nationwide US Medicare beneficiaries	Alzheimer's disease and Parkinson's disease (PD)	Annual mean PM2.5 exposure in the USA is significantly associated with an increased risk of hospital admission for PD and AD
Younan et al. (2020) [90]	PM2.5	Older females	Alzheimer's disease and related dementias	Long-term PM2.5 exposure linked to increased Alzheimer's disease pattern similarity scores
Yuchi et al. (2020) [91]	Fine particulate matter, black carbon, and nitrogen dioxide	678,000	Non-Alzheimer's dementia, Parkinson's disease, Alzheimer's disease, and multiple sclerosis	Road proximity is linked to these diseases, possibly mediated by air pollution
Calderón-Garcidueñas et al. (2020) [92, 93]	Fine particulate matter (PM2.5) and ozone (O3)	134	Alzheimer's disease (AD)	Air pollution control and early-life neuroprotective interventions should be prioritized
Salimi et al. (2020) [94]	PM2.5 and NO2	240,000	Parkinson's disease (PD)	Limited evidence was found for associations between long-term exposure to NO2 or PM2.5 and PD
Calderón-Garcidueñas et al. (2020) [92, 93]	Fine particulate matter (PM2.5)	575	Alzheimer's disease (AD)	Early identification of gait and balance impairment in young air pollution-exposed individuals could aid prevention efforts

Table 2 (continued)

Authors and year	Pollutant	No. of study participants	Neurodegenerative dx studied	Key findings
Calderón-Garcidueñas et al. (2020) [92, 93]	Airborne particulate matter	23	Alzheimer's disease (AD)	Suggests particulate air pollution impairs brain chromatin silencing and reduces DNA integrity, increasing AD risk in young people
Calderón-Garcidueñas et al. (2020) [92, 93]	Fe-, Al-, and Ti–rich NPs	186	Alzheimer's and Parkinson's diseases (AD, PD)	Neural damage and pathology may depend on nanoparticle characteristics and how they enter the brain
Shi et al. (2020) [89]	Fine particulate matter (PM2.5)	63,038,019	Parkinson's disease or Alzheimer's disease and related dementias	Improving air quality to reduce PM2.5 concentrations could yield substantial

hospital visits among amyotrophic lateral sclerosis (ALS) patients due to short-term air pollution exposure in a Korean case-crossover design [87]. However, Van Wijngaarden et al. found no increase in hospital admissions for PD or AD among over 63,000 residents living near PM2.5 monitoring sites in New York State [96].

Motor and physical clinical features are significant aspects of neurodegenerative diseases, with early signs often involving cognitive decline or memory loss [83, 90, 97–99]. Younan et al. stressed the importance of early detection and intervention, focusing on biomarkers such as amyloid and tau proteins [90]. Air pollutants have been implicated in accelerating motor decline and gait impairment, even in younger individuals [92].

While particulate matter (PM10) showed a weaker causal relationship with neurodegenerative diseases like multiple sclerosis, ALS, PD, and AD, a pilot study in Italy involving 132 participants found no causal link with ALS [100]. PM2.5, however, was associated with nearly double the mortality rate from multiple sclerosis among females, particularly in colder climates [85]. Weuve et al.'s study on the Nurses' Health Study Cognitive Cohort linked higher PM2.5 exposure to significantly lower cognitive memory scores in older women [101].

Semmens et al. and a panel of neurologists observed a 20% increase in cognitive decline among individuals living in urban areas with high air pollution levels over two decades [102]. This underscores the long-term impact of air pollution on cognitive health and emphasizes the need for stringent air quality regulations, as highlighted in Kulick et al.'s study [103].

Genetics plays a crucial role in the etiology of neurodegenerative diseases, with studies on DNA and epigenetic models revealing complex processes exacerbated in polluted environments [93, 104]. A study in Mexico involving humans and mice identified changes in brain molecules associated with gene regulation and DNA damage linked to markers of neurodegenerative damage such as tau and amyloid plaques, increasing the risk of early-onset AD [93]. Essers et al. analyzed brain images from children in the Generation R Study, finding that exposure to prenatal coarse particulate matter and childhood polycyclic aromatic hydrocarbons affected cerebral white matter volume, particularly in APOE ε4 carriers [82]. They also noted larger grey matter volumes associated with higher polygenic risk scores for AD, suggesting protective effects in early life but potential neurodegenerative consequences in adulthood.

Climate action and overall greenness

Research indicates that good climate action and overall greenness serve as protective factors against cortical brain loss and neurodegenerative processes [91, 105, 106]. Various air pollutants including ultrafine particulate matter (UFP), PM2.5, PM10, nitrogen oxides (NO, NO2), carbon monoxide (CO), carbon dioxide (CO2), black carbon, ozone (O3), hydrogen peroxide (H2O2), sulfur dioxide (SO2), diesel exhaust particulate extract (DEPs), biomass burning (BB), and exogenous metal-rich nanoparticles (Fe, Al, Ti) have detrimental effects on the brain, with long-term exposure above acceptable levels showing adverse effects on studied populations [58, 66, 72, 88, 104, 107–110].

A recent Chinese cohort study by Zhu et al. found that higher residential greenness was associated with lower Cox proportional hazard ratios, indicating a protective effect against neurodegenerative diseases [106]. Similarly, lower concentrations of particulate matter were linked to reduced risks of PD and AD [106]. Thus, residential greenness acts as a protective modifier in the relationship between air pollutants and neurodegenerative diseases. Several studies have explored the impact of residential greenness, defined by the availability of green spaces, parks, and vegetation in urban areas, on various health outcomes, including neurodegenerative diseases [105, 106, 111–114].

Studies have also highlighted the role of lower noise levels in green areas contributing to better cognitive health [101, 105, 111]. Environmental pollution from sources such as traffic congestion, industrial waste, solar radiation, and natural disasters like volcanic eruptions has led to long-term declines in environmental greenness, correlating with increased rates of neurological conditions [70, 112, 115]. Parks et al., in a population-based case–control study, found a significant association between increased odds of developing amyotrophic lateral sclerosis (ALS) and long-term exposure to traffic-related air pollutants (L-TRAPe) like elemental carbon (EC) [72]. Similarly, a Danish case–control study spanning from 1989 to 2013 by Nunez et al. identified a critical exposure window 6 years before ALS diagnosis, particularly involving PM2.5 [116]. Residences near roads or industries have been mapped out to show higher incidences of degenerative diseases [84, 111, 117]. Time spent in traffic leading to traffic-related air pollution (TRAP) has also shown direct associations with degenerative diseases [2, 28, 50, 53]. However, weighted daytime noise pollution levels did not show a clear causal or additive effect [91].

Oxidative stress and the blood–brain barrier

Laboratory studies using glass models of the blood–brain barrier (BBB) suggest that exposure to oxidative stress factors like hydrogen peroxide (H2O2) can cause localized dysfunction of the BBB, potentially contributing to neurodegenerative diseases [61]. Additionally, 3D brain models have shown that exposure to PM2.5 air

pollution can damage neurons and trigger astrogliosis, a cellular response to the brain [43]. These findings provide insights into potential mechanisms by which air pollution may contribute to neurodegeneration.

Trichloroethylene: a silent killer

Trichloroethylene (TCE), a widely used industrial solvent, has emerged as a concern for its link to PD. Studies suggest exposure to TCE may increase the risk of developing PD by fivefold [118, 119]. The U.S. The Environmental Protection Agency (EPA) has classified TCE as an unreasonable risk factor due to its health effects, including carcinogenicity [89, 120, 121] Safer alternatives should be explored, and a ban on TCE use may be warranted.

Discussion

This narrative review summarizes the important themes of the relationship between air pollution and neurodegenerative diseases across both preclinical (animal) and clinical (human) data. We expanded our review to cover air pollutants such as ultra-fine particulate matter, disease emissions, particulate matter PM 2.5–10 μm, metals, black carbon, SO2, and NO2. In a review on the impact of air pollution and neurodegenerative diseases by Wang et al. in 2021, the focus was on the particulate matter with a diameter ≤ 2.5 μm (PM2.5) and it was found that (PM2.5) could significantly increase the risk of neurological disorders primarily through gaining entry to the nervous system by the Blood–Brain-Barrier or olfactory neurons [18].

Our findings also corroborate the review done by Jayaraj et al. in 2017 on the impact ambient air pollution potentially has in the development of neurodegenerative diseases [122]. The review extensively discussed the connections between air pollutants and neurodegenerative diseases and proposed a neuroinflammation hypothesis that further explains how brain cells respond to stimulation from air irritants [122, 123]. Recently in 2024, Roy and D'Angiulli shared their findings in a mini-review to highlight the current state of the subject matter [124]. They also exposed an interesting dynamic on the growing concern of air pollution in relation to mental health, precisely in depression and anxiety [124].

While the studies we have reviewed provide valuable insights into the relationship between air pollution and neurodegenerative diseases, a few limitations warrant attention. One major constraint is the methodological variability across studies, which impacts the generalizability and comparability of findings. For instance, differences in pollutant types, exposure assessment methods, and endpoints used across animal and human studies contribute to significant heterogeneity. This variability makes it challenging to draw definitive conclusions about the specific mechanisms and long-term effects of air pollution on neurodegenerative diseases. Also, our review has primarily focused on studies conducted within the past 5 years, potentially excluding older studies with relevant findings. While this approach allows us to focus on recent research, it may omit valuable historical context.

Emerging research and future directions

The current body of evidence from animal and human studies shows the multifaceted relationship between air pollution and neurodegenerative diseases, revealing both direct and indirect pathways through which environmental pollutants impact brain health. Animal studies consistently demonstrated cognitive decline and neurodegenerative-like features in response to various air pollutants, including PM and UFP. Notably, studies involving rodent models have highlighted the role of pollutants in exacerbating neuroinflammation and oxidative stress, with specific findings such as increased microglial activation and altered protein levels linked to AD and PD. The protective effects of antioxidants like astaxanthin in mitigating PM2.5-induced inflammation further emphasize the potential for therapeutic interventions.

Human studies corroborate these findings, showing associations between particulate matter exposure and neurodegenerative conditions, including AD, PD, and ALS. Longitudinal and population-based studies reveal that exposure to specific pollutants, such as PM2.5 and sulfur dioxide (SO2), correlates with accelerated cognitive decline and increased mortality rates from neurodegenerative diseases. The variability in findings, such as differing impacts of nitrogen dioxide (NO2) and black carbon, suggests that the relationship between air pollution and neurodegenerative diseases is complex and influenced by multiple factors, including sociodemographic variables and smoking status.

The protective role of residential greenness and lower noise levels in mitigating the effects of air pollution highlights the importance of environmental quality in safeguarding cognitive health. Studies suggest that increased green space can buffer against the adverse effects of air pollution, potentially offering a preventive measure against neurodegenerative diseases. Conversely, long-term exposure to high pollution levels and noise has been associated with increased disease incidence, underscoring the need for improved urban planning and environmental policies.

Oxidative stress and BBB dysfunction emerge as critical mechanisms linking air pollution to neurodegeneration. Laboratory studies demonstrate that pollutants can compromise BBB integrity and induce neuroinflammatory responses, contributing to neuronal damage. This

insight points to potential targets for therapeutic strategies aimed at protecting the BBB and mitigating oxidative stress.

Furthermore, researchers have made significant progress in unraveling the intricate relationship between air pollution and neurodegenerative diseases in recent years. Advanced neuroimaging techniques such as positron emission tomography (PET) and magnetic resonance imaging (MRI) have allowed scientists to observe and monitor brain changes in individuals exposed to air pollution. These tools offer valuable insights into the structural and functional alterations associated with neurodegenerative diseases. Additionally, researchers have focused on biomarker discovery, identifying potential biomarkers in cerebrospinal fluid, blood, and nasal samples that link air pollution exposure to neurodegenerative diseases.

Sophisticated in vitro and in vivo models have also played a crucial role, enabling scientists to simulate air pollution exposure more accurately. This has facilitated the study of molecular pathways and mechanisms involved in pollution-induced neurodegeneration. Large-scale epidemiological studies have further bolstered evidence of the association between air pollution and neurodegenerative diseases, shedding light on risk factors, vulnerable populations, and potential interventions.

Despite these advancements, critical knowledge gaps remain, necessitating further research. Key priorities include gaining a deeper understanding of the precise cellular and molecular mechanisms through which air pollutants trigger neurodegenerative changes. Identifying specific subpopulations more susceptible to pollution-induced neurotoxicity is another critical area, considering genetic, epigenetic, and demographic factors that contribute to differential susceptibility.

Moreover, while many studies have focused on short-term exposure effects, the long-term consequences of chronic air pollution exposure on neurodegenerative diseases are still underexplored. Longitudinal research spanning decades is essential to accurately capture these effects and understand the cumulative impact of various pollutants and their synergistic effects.

Advancements in research offer potential preventive and therapeutic implications. Early detection of neurodegenerative diseases in individuals with a history of air pollution exposure can enable timely intervention to mitigate disease progression. Stricter environmental regulations aimed at reducing air pollution levels from industrial emissions and vehicle exhausts can directly benefit public health. Additionally, personalized medicine approaches tailored to individual genetic susceptibilities to pollution-related neurodegeneration hold promise for enhancing treatment efficacy.

The intersection of air pollution and neurodegenerative diseases has significant public health implications. Neurodegenerative diseases already impose a substantial burden on healthcare systems and society due to increasing prevalence rates driven by aging populations. The additional contribution of air pollution as a risk factor exacerbates this burden, impacting healthcare planning, resource allocation, and the quality of life for affected individuals and caregivers. Moreover, the economic costs associated with neurodegenerative diseases, including medical expenses, long-term care, and lost productivity, are considerable and further compounded by air pollution-related neurodegeneration.

Addressing these challenges requires comprehensive strategies encompassing healthcare and environmental policies. Mitigating the public health impact of air pollution on neurodegenerative diseases necessitates stringent environmental policies to reduce emissions from vehicles, industrial processes, and power generation. International collaboration on air quality standards can amplify these efforts.

On the healthcare front, increasing awareness and early detection of neurodegenerative diseases in regions with high air pollution levels are critical. Public health campaigns can educate the public about the risks of air pollution exposure and promote risk reduction strategies such as wearing masks in heavily polluted areas and limiting outdoor activities during peak pollution hours.

Research into pharmaceutical interventions and personalized medicine approaches offers promise for prevention and treatment. Lifestyle modifications such as promoting physical activity, a healthy diet, and cognitive stimulation are also crucial, as these factors can influence the progression of neurodegenerative diseases.

Policy considerations should include support for affected individuals and caregivers, ensuring access to healthcare services, respite care, and financial assistance. Additionally, prioritizing research funding to address gaps in understanding the links between air pollution and neurodegenerative diseases is essential for developing effective interventions and strategies.

Conclusion

The expanding body of research into the relationship between air pollution and neurodegenerative diseases reveals a complex interaction involving environmental, genetic, and lifestyle factors. While traditionally associated with respiratory and cardiovascular issues, air pollution now emerges as a significant contributor to neurodegenerative conditions such as PD and AD. Advanced research techniques like neuroimaging, biomarker discovery, and sophisticated in vitro/in vivo models have deepened our understanding of how

air pollutants exert neurotoxic effects. However, there remain significant gaps in knowledge, particularly concerning the specific cellular and molecular pathways linking air pollution to neurodegeneration. Continued research is crucial, particularly regarding the long-term effects of chronic air pollution exposure and the combined impact of multiple pollutants.

The public health implications are profound. Neurodegenerative diseases already strain healthcare systems and society, and air pollution-related neurodegeneration exacerbates this burden. This impact extends to economic costs, diminished quality of life for patients and caregivers, and broader societal implications. Addressing these challenges requires a comprehensive approach. Implementing stricter environmental regulations to reduce air pollution levels, including controlling emissions from various sources, is essential. Healthcare strategies should emphasize early detection, public awareness campaigns, and interventions promoting lifestyle modifications such as physical activity, a healthy diet, and cognitive stimulation.

Furthermore, prioritizing research funding to investigate the links between air pollution and neurodegenerative diseases is critical. This funding should focus on filling existing knowledge gaps and developing tailored interventions. Personalized medicine approaches that consider genetic susceptibility to pollution-related neurodegeneration offer promise for both prevention and treatment strategies. By pursuing these avenues, we can mitigate the public health impact of air pollution on neurodegenerative diseases and improve outcomes for affected individuals worldwide.

Abbreviations

AD	Alzheimer's disease
ALS	Amyotrophic lateral sclerosis
APOE	Apolipoprotein E
BBB	Blood-brain barrier
CNS	Central nervous system
HD	Huntington's disease
MRI	Magnetic resonance imaging
NDs	Neurodegenerative diseases
NO2	Nitrogen dioxide
PD	Parkinson's disease
PET	Positron emission tomography
PM2.5	Particulate matter measuring 2.5 μm
PRS	Polygenic Risk Score
TCE	Trichloroethylene
WHO	World Health Organization

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NA and AA conceptualized the study. All authors were involved in the literature review. AEB, AA, and NA extracted the data from the review studies; All authors wrote the final and first drafts. All authors read and approved the final manuscript.

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