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Review article

Association between air pollution and Multiple Sclerosis: A systematic review

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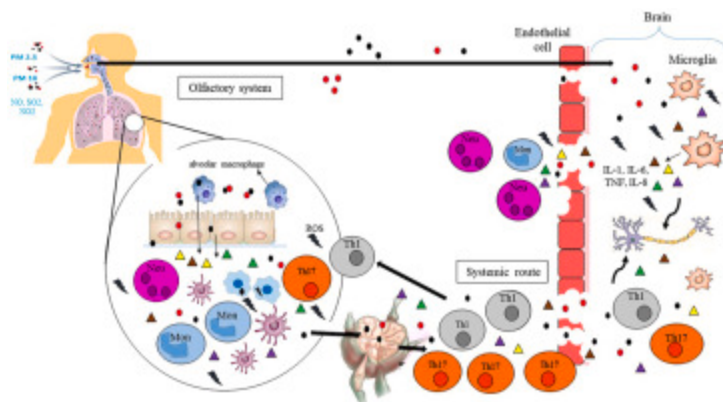
Highlights

- The role of air pollution in the development of MS is critical.
- Oxidative stress resulting from air pollutants' exposures, increases proinflammatory cytokines.
- Neuroinflammation and neurovascular damage resulting from oxidative stress could accelerate MS progression.
- Air pollution is a risk factor in the MS development and relapse episodes through the lung interaction of the immune system.

Abstract

Air pollution is a major public health threat. The present study is the first systematic review (SR) to determine the association of exposure to air pollution and Multiple Sclerosis (MS) Progression. A Literature search was carried out using relevant keywords within several international databases. A comprehensive literature search was carried out systematically and yielded 24 eligible studies concerning the relationship of exposure to air pollution including criteria air pollutants such as particulate matter, NO_x and SO_x, CO₂, traffic noise, etc. and MS disease. The results of the included studies reveal that there was a significant relationship between exposure to air pollution and MS development and progression. Although the effect of air pollution in the pathogenesis of MS is not fully known, according to the results of the included studies exposure to polluted air can stimulate several mechanisms that act as risk factors for developing MS and for having disease relapses or neurological disability. The major potential mechanism is Dysimmune inflammatory responses subsequent oxidative stress (OS), which leads to neuroinflammation and breakdown of the normal balance between immunity and self-tolerance. Air pollutants induce and sustain chemical reactions that produce reactive oxygen species (ROSs) and nitrogen reactive species (RNSs) which can initiate inflammatory cascades via the redox-sensitive mitogen-activated protein kinase (MAPK) and NF- κ B that recruit and activate neutrophils, monocytes, and dendritic cells that stimulate the adaptive immune responses such as Th1 and Th17 inflammatory responses. The uncontrolled inflammatory responses following these events cause cell death and the release of self-antigens capable of stimulating the production of auto-aggressive T-cells via enhancing antigen presentation and facilitate entry of these cells to the central nervous system. Thus, oxidative stress is the culprit in the systemic inflammation and immune imbalance development and progression, powerful risk factors in MS.

Graphical abstract



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Introduction

In the recent decades, due to industrialization, urbanization, and population growth in the cities, air pollution became an emerging major public health challenges and, therefore great attention had been paid to the prevention and control of detrimental effects of air pollution (Block and Calderón-Garcidueñas, 2009; Chen et al., 2017, Zhao et al., 2019). Air pollution is defined as the presence of a mixture of various type of substances in ambient (outdoor) or indoor air including gases (such as carbon monoxide (CO), ground-level ozone, nitrogen (NO_x) and sulfur oxides (SO_x), etc.), solid (particulate matter with different aerodynamic diameter especially coarse particles (PM_{10}), fine particles ($\text{PM}_{2.5}$), very fine particles (PM_1) and ultrafine particles (UFPs) ($\text{PM}_{0.1}$)), airborne metals (such as Zn, Cu, Fe, Mn, Pb) and organic matter (bioaerosols and polyaromatic hydrocarbons (PAHs)), traffic noise, etc. (Palacios et al., 2017; Block and Calderón-Garcidueñas, 2009; Corona-Vázquez et al., 2019; Zhao et al., 2019).

Long-term or chronic exposure to air pollution has been associated with a broad spectrum of health conditions and chronic source of reactive oxygen species (ROSs) and neuroinflammation (Bai et al., 2018; Block and Calderón-Garcidueñas, 2009; Corona-Vázquez et al., 2019). Air pollution as a multifaceted environmental toxin is also involved in increased risk of other neurological disorders such as Alzheimer's disease, Autism Spectrum Disorders (ASD), Parkinson's diseases (PDs), and ischemic stroke (Block and Calderón-Garcidueñas, 2009; Chen et al., 2017; Roux et al., 2017; Windham et al., 2011; Zhao et al., 2019). One of the most important categories of the detrimental effects of exposure to air pollution is neurological, neurodegenerative, and autoimmune diseases (ADs) (Block and Calderón-Garcidueñas, 2009; Zhao et al., 2019). Among them, Dementia, Multiple sclerosis (MS), and Parkinson's diseases (PDs) are the most commons neurodegenerative diseases with frustrating adverse effects on individuals, families, and society, which about 55 million of the world population have these disorders (Chen et al., 2017; Roux et al., 2017; Xu et al., 2016; Zhao et al., 2019).

Multiple sclerosis (MS) is a chronic neurological disease that is marked by inflammatory central nervous system (CNS) demyelination mediated by T cells specific for a myelin antigen. MS is categorized as an autoimmune disease (ADs) that in most cases, it starts by a relapsing onset, characterized by relapses, i.e. acute inflammatory demyelination (Roux et al., 2017; Zhao et al., 2019). Compared with the healthy population, most of the MS patients show a substantially elevated risk of depression, divorce, and suicide. About fifty percent of

MS patients required mobility assistance within twenty years of diagnosis, and finally, fifty percent of all patients developed essential cognitive deficits (Lauer, 2010; Lemprière, 2020; Sawcer et al., 2014; Waubant et al., 2019).

MS is a multifactorial disease, which often starts between 20 and 40 years of age and usually women more frequently than men. Globally, around 2.5 million people were diagnosed with MS, according to the Atlas of MS database. Although the precise etiology of MS remains unknown, it is reported that both genetic and environmental factors are involved and play a crucial role in MS progression (Belbasis et al., 2015; Lauer, 2010; Sawcer et al., 2014). Similar to many other ADs, many studies have suggested that the incidence of MS shows an increasing trend. In the recent study, Jeanjean et al. concluded that the significant single-pollutant relations between exposure to PM₁₀, O₃, and NO₂ and occurrence of MS relapse. On the other hand, they also confirmed that only ozone shows significant associations with MS relapses occurrence in the multiple-pollutant model (Jeanjean et al., 2018). Additionally, Roux et al. reveals that the air pollutants such as PM₁₀ could trigger the risk of relapse in MS patients and they highlighted that probably the oxidative stress mechanism is the main mode of action of PM₁₀ (Roux et al., 2017). Therefore, the role of air pollution as an environmental factor, concerning MS development and progression must be elucidated.

Therefore, we conducted this systematic review (SR) to clarify the role of air pollutants in the occurrence and progression of MS.

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Methods

A comprehensive search was performed following “Preferred Reporting Items for SRs and Meta-Analyses”(PRISMA) and the Cochrane Reviewer's Handbook guidelines (<http://www.prisma-statement.org/Extensions/InDevelopment.aspx> ↗) (Noorimotlagh et al., 2020a, 2020b). ...

Results

A total of 261 articles were obtained in the initial search from all the above-mentioned databanks. Forty-one duplicates and 30 review papers were removed. Among them, 147 studies were excluded based on title and abstract screening. Then, the full-text of 43 records screened according to the inclusion criteria, and 20 articles excluded because a) not related to MS (12 records), and b) articles were hypothesis papers, letters to the editor, or proceeding paper (8 records). Finally, 23 papers were ...

Discussion

In recent years, the role of air pollution in the development of ADs has attracted more and more attention. Air pollution can cause and exacerbates a variety of diseases. The main sources of air pollution include industry, vehicle exhaust, forest fires, stationary fuel burners, and solid fuel combustion, which include particulate matter (PM) and a mixture of gases (carbon monoxide [CO], nitrogen dioxide [NO₂], ozone [O₃] and sulfur dioxide [SO₂]). It has been shown that exposure to air pollution ...

Conclusion

Based on the findings of the reviewed studies, it is suggested that air pollution is implicated as a risk factor in the development and relapse of MS *via* the interaction of the immune system in the different organs. The production of pro-inflammatory cytokines, T cell imbalance, systematic inflammatory, and vitamin D shortage are key factors, following exposure to air pollution cause the onset and exacerbation of MS disease. However, further evaluations are needed that help to improve our finding ...

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. ...

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