Role of toxic pollutants in the development of Parkinson's Disease

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Abstract:

Parkinson's disease (PD) has been of special concern among neurological disorders linked with the negative effects of environmental factors because of its higher incidence rates and early disability in healthy individuals. Exposure to numerous air pollutants and PM can increase the risk of neurophysiological alterations that lead to PD-like manifestation. PM and air pollutants play crucial roles in everything from neuromodulation to oxidative stress regulation and immunomodulation, and if any of these functions deviate, several neurodegenerative diseases, including PD, may develop. Further, air pollution can stimulate the central nervous system which could be a potential cause to trigger the neuroinflammatory process. Previous studies claimed that PM exposure could encourage the α-Synuclein pathology that increases the likelihood of PD. However, the postulated mechanism for air pollution and PM-induced PD or the subsequent activation of numerous pathological pathways has not yet been thoroughly investigated and explored. Further research is required in the future to better grasp the role of PM in the development of PD.

Keywords: *Parkinson's disease; α-Synuclein; Air Pollution; Air pollutant; Particulate Matters.*

Introduction

One of the most prevalent neurodegenerative diseases in the world, Parkinson's disease (PD) affects roughly 2% of people over the age of 60. A broad range of motor and non-motor symptoms, such as resting tremors, bradykinesia, rigidity, cognitive deficits, and sleep issues, are indicative of PD (Przedborski, 2017). It has not yet been established with certainty how PD develops. Dopaminergic neuronal loss in the substantia nigra compacta is the primary neuropathological feature of PD (Goyal et al., 2002; Lin et al., 2022). Numerous variables, including oxidative stress, autophagy, pro-inflammatory events, and alterations in neurotransmitters, have been postulated to have a synergistic pathophysiological role in PD (Acıkara et al., 2022). Further, it has been acknowledged that the pathophysiology of PD also includes the mishandling of α-synuclein in the PD-sensitive brain area (Yuan et al., 2022).

Across the lifespan, air pollution is known to pose a serious hazard to neurological health, increasing the incidence of both neurodevelopmental and neurodegenerative illnesses (Eckard et al., 2022). It has been well reported that the primary cause of air pollution is particulate matter (PM) having a diameter of fewer than 10 μm (PM 10) or less than 2.5 μm (PM 2.5) and participating in the pathology of numerous diseases via inducing oxidative stress, inflammation and DNA damage (Pignon et al., 2022; Hvidtfeldt et al., 2022). PM could affect the brain directly and its exposure may lead to the development of neurological disorders like PD (Pignon et al., 2022, Cristaldi et al., 2022). Evidence shows that environmental factor also plays a critical role in the pathogenesis of PD (Dunn et al., 2019). Epidemiological studies show that PD risk is elevated in association with exposure to fine particulate matter. Thus, PD may develop as a result of persistent exposure to gaseous air pollution and particulate matter. Hence, it is necessary to address the role of numerous air pollution and particulate matters in the development of PD-like manifestations. Several studies have been done on this subject, even though the relationship between air pollution exposure and PD is not well known. Thus the present study is designed to explore the role of various air pollutants and particulate matter in the pathology of PD.

Material and method

In order to find recent material, we used the electronic database PubMed. The following keywords are used: “Parkinson Disease” and “Parkinson’s disease” in combination with “Particulate Matter”; “Air Pollution”; “Nitrogen Dioxide”; “NO_2”; “Sulphur Dioxide”; “Sulfur Dioxide”; “SO_2”; and “Carbon Monoxide”; “CO”.

Discussion

Role of PM in the development of PD

PM is a complex mixture of dust, metals, and chemical substances suspended in the atmosphere. It also contains liquid droplets. The particle size of PM has been related to physiological effects, and smaller particles can penetrate the respiratory tract deeply and may cross the blood-brain barrier to enter the brain (Saitoh et al., 2022). The association between PM and PD has been the subject of numerous investigations, thus this review will examine these kinds of studies.

The negative effects of PM on PD may differ depending on the particle makeup. Even single exposure to PM is also associated with an increased risk of PD (Yu et al., 2021). Interestingly, it has been well-documented that exposure to PM2.5 accelerates the production of α-synuclein which promotes neurotoxicity and contributes to the development of PD (Yuan et al., 2022). Choi et al, reported that pro-inflammatory mediators were dramatically increased in the LA-4/RAW264.7 co-culture after exposure to PM10. A positive association has been illustrated between ozone exposure and mortality due to PD (Zhao et al., 2021). Another study suggested that the release of cytochrome C and cleaved caspase-3, as well as an increase in the Bax/Bcl2 ratio, were all markedly enhanced by PM in response to MPP^+. Further, MPP^+-induced PD paradigm, the protective effect of nicotine cannot reverse PM-induced synergistic neurotoxicity (Jin et al., 2021). Inhaling $PM_{2.5}$ may exacerbate the behavioral abnormalities of PD symptoms in an animal model by increasing oxidative stress, lowering autophagy and mitophagy, and promoting mitochondria-mediated neuronal death in the substantia nigra (Wang et al., 2021). These facts imply that additional, extensive prospective studies are required to establish the relationship between PD and PM.

Role of NO_2 in the development of PD

It is well-documented the risk of developing Parkinson's disease increased after exposure to NO_2 (Jo et al., 2021). Experimental findings of Lee et al suggested that long-term exposure to traffic-related air pollution containing NO_2 contributes to the pathogenesis of PD (Lee et al., 2016). Interestingly, conflicting data is supporting a link between NO_2 and PD. Several studies reported that there is no association between exposure to NO2 and PD (Chen et al., 2017; Toro et al., 2019; Salimi et al., 2020). Further, the relative risk of PD is observed to be associated with long-term exposure, according to Kasdagli et al, however, the link does not approach the nominal level of significance (Kasdagli et al., 2019).

Role of SO_2 in the development of PD

According to a recent study, SO_2 exposure does not raise the chance of developing PD (Jo et al., 2021; Chen et al., 2017)). Further, two meta-analyses report that there is no relationship between SO_2 exposure and the risk of PD (Hu et al., 2019; Kasdagli et al., 2019). However, various designs and conflicting findings are reported by various investigations (Lee et al., 2017).

Role of CO in the development of PD

It is well known that CO has much more affinity for hemoglobin than oxygen and forms carboxyhemoglobin which decreases the oxygen-carrying capacity that leads to hypoxia. Such type of hypoxia may contribute to neuropsychological disturbances including PD (Saitoh and Mizusawa, 2022). Jo and his co-researchers reported that there is no statistically significant link between CO exposure and the occurrence of PD (Jo et al., 2021). Further, it has been documented that exposure to 0.1 ppm CO increases emergency hospital admissions in

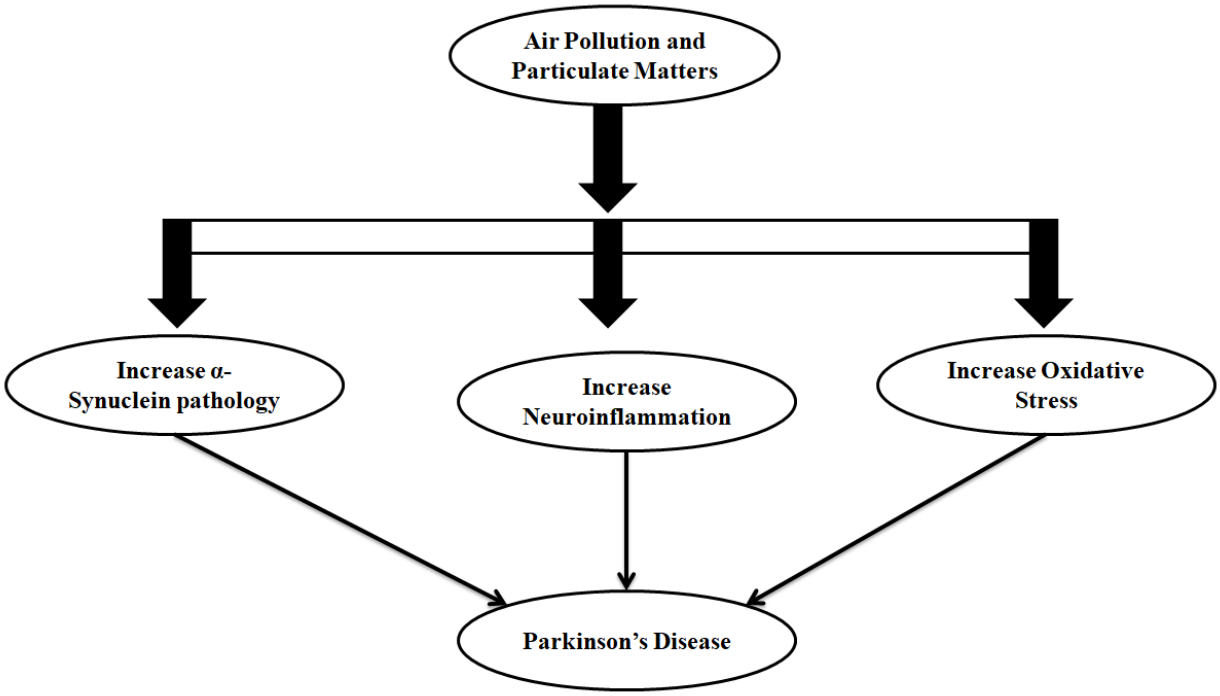
individuals with pre-existing PD (Lee et al., 2017). Lai et al., also reported that the risk of PD increased in carbon monoxide intoxication patients (Lai et al., 2015).

Conclusion

People who reside in areas with higher population densities and higher levels of pollution are at a higher risk. Particulate matter and air pollution are considered as common and important risk factors for numerous diseases including neurodegenerative diseases that have an impact on a large section of the human population. The second-most common neurodegenerative condition, PD, is thought to impact six million people worldwide. This review tries to summarise the most recent findings regarding the impact of air pollution and PM exposure on the development of PD. Both gaseous pollutants and particulate matter that get through the blood-brain barrier can affect the central nervous system, leading to oxidative stress, neuro-inflammation, and abnormal protein aggregation, which can cause PD (Figure 1). Increased expression of PD biomarkers has been linked to exposure to PM. In conclusion, it can be stated that there is a strong relationship between PM and PD, and exposure to PM might play a role in the development of PD-like manifestation. To fully comprehend the relationship between air pollution and gene expression, more research is necessary. Further, a large number of in-vivo and in-vitro research will be needed in the future to confirm the functions of PM and air pollutants in the pathophysiology of PD.

This review aims to outline current knowledge of air pollution exposure effects on neurological health.

Figure 1: Diagrammatic illustration of the role of air pollutants and particulate matter in the pathology of Parkinson's disease.



Declaration

The authors declare there is no conflict of interest and no funding agency to disclose.

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