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Highlights

Tainted air: The link between pollution and Alzheimer's disease

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ABSTRACT

In this issue of the *Biomedical Journal*, we learn how air pollution may contribute to cognitive decline and even increase risk for Alzheimer's disease. We also highlight original research documenting the body's response to infection with a common oral pathogen. Finally, we learn how a cellular antioxidant protein protects against mitochondrial dysfunction in Parkinson's disease.

Spotlight on reviews

Tainted air: the link between air pollution and Alzheimer's disease

Without prevention, the incidence of Alzheimer's disease (AD) is expected to triple by the year 2050 [1]. The insurmountable pressure that this would place on health care systems has intensified the search for major preventable risk factors for AD. In this issue of the *Biomedical Journal*, Kilian and Kitazawa [2] discuss how one such risk factor for AD may literally be in the air we breath, and describe the potential mechanisms linking pollution to decline in brain function and AD.

Chronic exposure to polluted air is a major health issue worldwide, with the WHO estimating that a staggering 91% of the world's population lives in places where air pollution exceeds recommended health guidelines [3]. Polluted air contains particulate matter (PM) of various sizes along with noxious compounds such as nitrogen and sulfur oxide species, carbon monoxide, metals and other inorganic compounds. PM contains sulfates, nitrates, ammonium, chlorides, carbon, and other biological material and dust, and is divided according to size: "ultrafine" (PM < 100 nm, $PM_{0.1}$), "fine" (PM < 2.5 μm, $PM2_{2.5}$), and "coarse" (PM < 10 μm, PM_{10}) [4]. Once inhaled, fine and ultrafine PM are capable of crossing into the bloodstream where they are taken up by cells leading to oxidative stress and mitochondrial damage [5]. Ultrafine PM in particular is considered the most toxic form of PM, and may even be able to penetrate the brain directly through the olfactory nerve [6].

It has long been known that exposure to polluted air affects respiratory health [7], but could the effects be more widespread to extend even to the brain? Many epidemiological studies have focused on vehicle exhaust as a source of PM, measuring how urban vs. rural or distance to roadway affects

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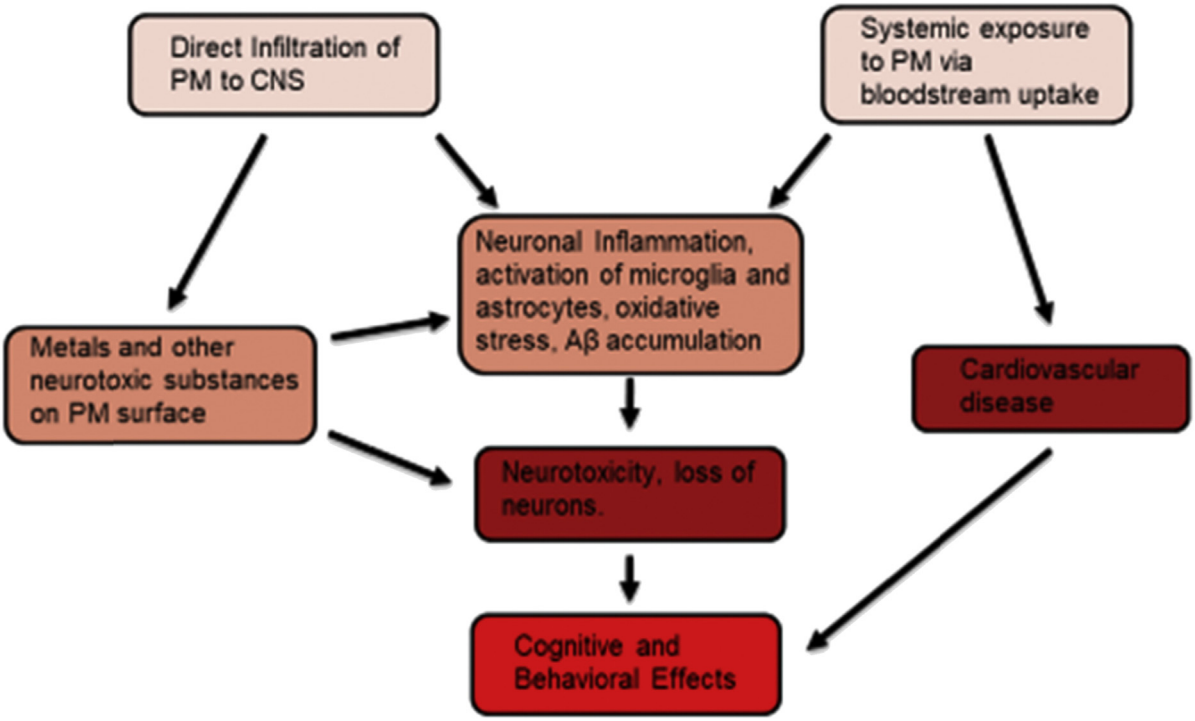

Fig. 1 The link between PM exposure and AD. PM and other neurotoxic substances are capable of infiltrating the brain where they lead to inflammation, oxidative stress, and ultimately the neurotoxicity underlying the cognitive effects in AD. Figure kindly provided by Kilian et al. [2].

brain function and cognition. Overall, these studies reveal an alarming trend: exposure to PM at any stage of life negatively impacts cognition. In childhood, exposure to PM negatively affects performance in multiple intelligence subscales [8] and is associated with poor motor coordination and response time [9]. Similarly, elderly residents living in highly polluted areas perform poorly in cognitive tests [10] and it is estimated that every 10 $\mu g/m^3$ increase in exposure to black carbon is equivalent to 2 years cognitive decline by ageing [11]. Moreover, several studies support the notion that these cognitive effects translate into increased risk of dementia. For example, in a Canadian cohort of 2.2 million residents aged over 55 years, the incidence of dementia was significantly higher for those living within 50 m of a major roadway [12], and exposure to various pollutants including ozone [13] and nitrogen oxide [14] is associated with an increased risk of dementia. The exact risk seems to be modified by other environmental factors [15] along with genetic predisposition, since possessing copies of the APOE gene variant linked to dementia appears to exacerbate the effect of pollution [16].

These epidemiological studies are backed up by human pathological studies and animal studies revealing that PM exposure affects molecular pathways linked to AD. Individuals living in highly polluted areas accumulate higher amounts of $A\beta_{42}$ [17], a toxic form of β-amyloid, and show hyperphosphorylated tau pre-tangles in the olfactory bulb and hippocampus [18]. Likewise, in a mouse model of AD, exposure to ultrafine PM led to an increase in the expected amount of Aβ plaques and reduced neuron density in the hippocampus [16]. These findings suggest that PM exposure can affect amyloid processing in the brain. The mechanism by which this occurs is likely to involve oxidative stress and an inflammatory response gone haywire, characterized by the massive release of pro-inflammatory cytokines from glial cells, generation of reactive oxygen species and increase in cellular antioxidant proteins [19] [Fig. 1].

Still, many questions remain unanswered regarding the link between PM and AD. The reliance of epidemiological studies on proxy measures of exposure like distance to roadway means that it is difficult to determine whether any specific air pollutants increase AD risk. If this were indeed the case, it would be arguably easier to enact policy to limit the release of these compounds into the environment. There is also a need for epidemiological studies over longer time courses, since the time window for the development of AD is still unknown. Despite these unknowns, evidence is mounting that make an "airtight" case against pollution in AD, with a call to clean up our cities and urban environments of the future.

Spotlight on original articles

Tooth loss in periodontitis: the role of Fusobacterium *and inflammation*

We all know the importance of a daily a routine of brushing and flossing, or we may otherwise suffer the consequences of gingivitis, an inflammation of the gums that is caused by the build-up of bacteria. If left untreated, gingivitis can lead to periodontitis, a serious gum infection that damages soft tissue

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