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Editorial

Editorial: Air pollution and brain health

There is increasing international recognition of air pollution as a major contributor to impaired brain health, neurological dysfunction, and a growing list of developmental and ageing disorders. Ambient air pollution is a complex mixture of particulate matter (PM), gases, organic compounds, and metals, many with known toxic effects on human cells. Anthropogenic particles derived from industrial or automotive sources such as exhaust fumes, and brake and tire wear comprise a main sources of pollutant exposure for the general population. In addition, high levels of transition metals are generated by electrical public transport systems, which contribute to the PM exposure in urban areas. As reviewed below, bushfire (wildfire) smoke is also a growing issue in many parts of the world. Often overlooked are sources of air pollution closer to home, including smoke from wood fires and biomass fuels for heating and cooking.

Air pollution is a known risk factor for stroke and vascular disease, and is also associated with exacerbated cognitive dysfunction. Imaging studies have reported metabolic and structural brain alterations in individuals exposed to air pollution. While some of the actions of air pollution on brain health may be attributed to increased inflammation and oxidative stress, there remains little understanding of the molecular basis of air pollution damage in the brain. Epidemiological studies have also identified a potentially critical association between air pollution and dementia (including Alzheimer's disease (AD), which currently affects 47 million people worldwide). Recent evidence shows that exposure to air pollutants is associated with an increased risk of AD and causes pathological changes in the brain. People who live in areas of high air pollution have a substantially increased risk of developing dementia although the specific pollutant(s) associated with increased dementia risk have not been identified. With increased urbanization, aging of the human population, and climate change, understanding the role of air pollution in brain health has taken on a new sense of urgency. This special issue brings together a broad and interesting coverage of air pollution impact on the brain and its consequences for human health and disease.

This special issue covers broad reviews of air pollution impacts on brain health and disease through to cell-specific impacts and more detailed investigation of specific pollutants. Costa et al., have provided a timely and concise analysis of the available research into developmental impacts of air pollution. The review clearly provides evidence that air pollution, especially urban vehicle exhaust, is linked to developmental disorders including autism spectrum disorder. The review delves into the mechanistic processes underlying air pollutant impact on the developing brain and highlights the critical need for continued legislative controls over air pollution. At the other end of the age spectrum, Schikowski and Altug review the association between air pollution and cognitive decline, finding strong support for a causal association, however, there remain considerable issues regarding the lack of long-term, and prospective studies. The conclusion is that further research is needed to understand the life-time impact of various forms of air pollution on cognitive abilities. These findings were reiterated by Oudin in a short but informative review on the link between Alzheimer's disease, air pollution, and associated factors such as green space, and noise pollution. The conclusion again was that biological and epidemiological support exists for air pollution impact on Alzheimer's incidence, however, further multi-exposure studies are urgently needed to determine the specific impacts of air pollutants compared to lack of green space and noise pollution, factors that are readily associated with high urban air pollution. Air pollution has, of course, been associated with other age-related neurological disorders including Parkinson's disease. Salimi et al., investigated this association, examining the literature on long-term exposure to $PM_{2.5}$ and NO_2 in NSW, Australia, and its relationship to Parkinson's disease. They found limited evidence of a causal association, a finding that support the inconsistent outcomes of epidemiological studies in this field. Whether alternative air pollution exposure scenarios are associated with Parkinson's disease remains to be determined. It is certainly clear that while studies are continuing into these long-term exposure issues, a new air pollution crisis is beginning. As reported in a review by Milton and White, climate change and other factors are driving an increase in bushfires (wildfires) in USA, Australia, South America, Asia, and many other nations and regions. This is leading to poor air quality across many areas including large cities. The impact of this on human health, and indeed brain function, has barely been investigated. This is likely to be a major area of research interest in the coming decades.

This special issue has also delved deeper into the impact of air pollution on the brain, examining research on how air pollution components affect certain brain and closely related olfactory cell types. In a review by Kanninen et al., the utility of olfactory mucosal cells for investigation of air pollution health impact was outlined. These human patient-derived cells are readily obtainable and provide a unique opportunity to study the direct impact of air pollution at the interface between environment and brain. Following from this, Gomez-Budia et al., report on the literature surrounding the action of air pollutant components on astrocytes and microglia, the key immunological cells of the brain, and likely effectors of oxidative and inflammatory responses contributing to damaging effects in the brain from air pollution. Chew et al., then delve deeper again, investigating the targeting of mitochondria, the key cellular powerhouse, by air pollutants. They report that mitochondria are a key subcellular locus for air pollution impact in the brain, with mitochondrial changes underlying many of the

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subsequent adverse events driven by air pollutants. The final two papers by Wahle et al., and Miah et al., investigate the role of specific air pollutants in brain health outcomes. In the first paper, the authors describe important effects of Zirconium-doped CeO_2 nanoparticles, which are used as fuel additives, on mouse behavior and neuroinflammation. The influence of particle redox-activity was shown by comparing the effects of inhaled CeO_2 nanoparticles that were doped with different amounts of zirconium. And the final paper by Miah et al., provides an overview of the literature, which supports potential adverse outcomes for human brain health from occupational and population-wide exposure to manganese.

These studies together provide a brief insight into the potential issues we all face from a number of sources of air pollution and a range of components some with potentially life-long toxic interactions with the brain. It is hoped that this special issue will encourage other researchers in this field to continue pursuing this key area of investigation with major implications of public health.

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