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Neuroepidemiology

Air pollution, a rising environmental risk factor for cognition, neuroinflammation and neurodegeneration: The clinical impact on children and beyond

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INFO ARTICLE

ABSTRACT

Air pollution (indoors and outdoors) is a major issue in public health as epidemiological studies have highlighted its numerous detrimental health consequences (notably, respiratory and cardiovascular pathological conditions). Over the past 15 years, air pollution has also been considered a potent environmental risk factor for neurological diseases and neuropathology. This review examines the impact of air pollution on children's brain development and the clinical, cognitive, brain structural and metabolic consequences. Long-term potential consequences for adults' brains and the effects on multiple sclerosis (MS) are also discussed. One challenge is to assess the effects of lifetime exposures to outdoor and indoor environmental pollutants, including occupational exposures: how much, for how long and what type. Diffuse neuroinflammation, damage to the neurovascular unit, and the production of autoantibodies to neural and tight-junction proteins are worrisome findings in children chronically exposed to concentrations above the current standards for ozone and fine particulate matter ($PM_{2.5}$), and may constitute significant risk factors for the development of Alzheimer's disease later in life. Finally, data supporting the role of air pollution as a risk factor for MS are reviewed, focusing on the effects of PM_{10} and nitrogen oxides.

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1. Introduction

Environmental neurology (EN) is a new field of practice and research [1] dedicated to a worldwide, comprehensive and translational study of the effects of the environment on humans. Albert Einstein defined the environment as "everything but me". Environmental medicine uses four approaches in the study of environmental factors affecting people:

- by agents (such as chemicals);
- by milieu (such as water, air);
- by population (for example, in children);
- and, of course, by pathology.

EN links neurology to public-health issues. The World Health Organization (WHO) defines air pollution as the "contamination of the indoor or outdoor environment by any chemical, physical or biological agent that modifies the natural characteristics of the atmosphere" (www.who.int/topics/air_pollution/en/).

With the industrial revolution starting in the late 18th century, air pollution increased dramatically. The combustion of fossil fuels (coal, coke, gasoline and diesel) needed to power industries, transportation and housing became responsible for the release for many hundreds of contaminants into the atmosphere. However, the mix of air pollutants changed in the 20th century: oil and diesel replaced coal, and became the major energy sources used in expanding cities (urbanization) in Western countries. By the 1960s and 1970s, two major types of pollution were recognized: the London-type smog, linked to fossil fuel combustion and emissions of particulate matter (PM); and the Los Angeles-type smog, or photochemical oxidant pollution, the main compounds of which are ozone and secondary aerosols (sulphates and nitric oxides) [2].

Nowadays, only some atmospheric air pollutants are monitored, depending on their health effects and the regulations in place in different countries; these include ozone, sulfur dioxide, carbon monoxide, nitrogen dioxide, lead and PM. However, other air contaminants referred to as "hazardous" pollutants should also be measured because they include highly neurotoxic chemicals, such as volatile organic compounds (VOCs), benzene, formaldehyde, tri- and tetrachloroethylene, toluene and polycyclic aromatic hydrocarbons (PAHs), and metals such as lead, manganese, iron, mercury, arsenic, cadmium and cobalt [3].

The neurological effects associated with sustained exposures to concentrations of outdoor air pollutants above the current international air quality standards are now an important issue for the millions of people living in megacities around the world, including the Mexico City Metropolitan Area (MCMA), Tehran and Paris. Residents of the latter are exposed to high concentrations of PM, nitrogen oxide (NOx) and PAHs, and share — with the residents of New York City, Toronto, Salt Lake City, Fairbanks in Alaska, Provo in Utah, Los Angeles–South Coast Air Basin in California, Nogales in Arizona and the MCMA — similar main sources of pollution: transport, industry and heating. Airborne PM varies in its physical and chemical composition, source and particle size, and includes PM_{10} (coarse particles $> 2.5\,\mu m$ but $< 10\,\mu m$), $PM_{2.5}$ (fine particles $> 100\,nm$ but $< 2.5\,\mu m$) and ultrafine PM (UFPM $< 100\,nm$) and their components, the key pollutants found in European cities.

The present review focuses on three topics: the detrimental impact of environmental factors on the developing brain; its long-term potential for neurodegenerative consequences; and air pollution as a risk factor for multiple sclerosis (MS). Also discussed is how to evaluate air pollutant exposures and estimates of concentrations, the relevant publications, and the uncertain and expected long-term brain effects on urban residents.

2. Assessing air pollutant exposures in people

The first issue to be faced when evaluating an individual's exposure to air pollutants is to determine how much, for how long and what type. As most people are exposed to complex mixtures of air pollutants from different sources — indoors, outdoors and occupational exposures — all of the available information has to be considered. Meteorological conditions, including precipitation, sunshine and ambient temperatures, are also included in the search for environmental factors associated with central nervous system (CNS) effects. Traffic-related air pollution is a prime exposure source for urbanites, and the highest exposures have been found near busy roads. Automated geocoding methods are being used to estimate exposures and other factors, such as road edges and centerlines, road curvature, road width and the presence of ramps, that can substantially alter exposure estimates near roadways because of the spatial gradients of traffic-related pollutant concentrations [2]. Also, land-use regression models, line-dispersion models, proximity-based assessments and personal monitors, along with interquartile range (IQR) increases in air pollutant levels, inclusion of several single-day lag evaluations and peak seasonal associations can be used to identify key air pollutants and the exposure windows conferring the greatest risk.

The primary objectives of neurological endpoints and air pollution exposures depend on analyses of neurological variables and whether the effects of interest are related to short-term or chronic air pollution exposures. Thus, a time-stratified case-crossover study design is suitable for investigating associations between acute exposures to PM and gaseous air pollutants and acute events such as stroke, whereas evaluating the risk of developing Alzheimer's disease (AD) will require years of air pollution evaluation [3–5].

Moreover, as air pollution levels are generally believed to be higher in deprived areas, this means that air pollution inequalities and means of transportation at national, regional and city levels have to be borne in mind [6]. Platt et al. [7] showed that elevated PM levels can be the consequence of "asymmetrical pollution" from two-stroke scooters that, despite constituting only a small fraction of transport modes, may yet dominate urban vehicular pollution through organic aerosol and aromatic emission factors that are up to thousands of times higher than those from other types of vehicles. Also important is the fact that air pollutant concentrations can have an impact on a neurological endpoint