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EDITORIAL

Running in polluted air is a two-edged sword — physical exercise in low air pollution areas is cardioprotective but detrimental for the heart in high air pollution areas

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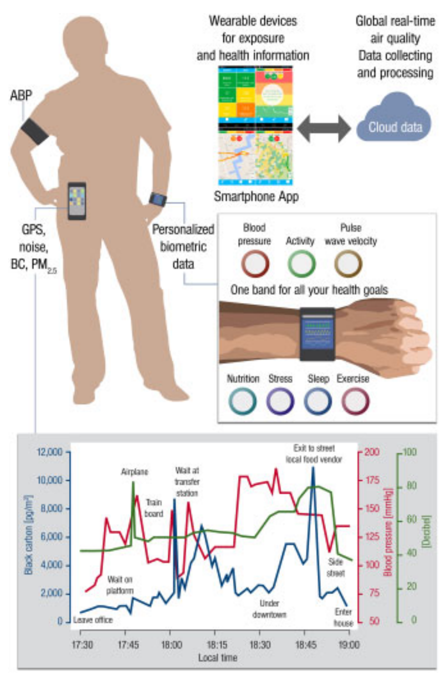

Graphical Abstract Hypothetical framework of investigations that combine technological innovation in biometric data with personalized exposure information in real-time to study interactive effects of environmental risk factors on cardiovascular endpoints. ABP, ambulant blood pressure monitoring; BC, black carbon; PM, particulate matter. With permission from Münzel *et al.*[18]

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Air pollution as a cardiovascular risk factor

In 2015, the Lancet Commission on Pollution and Health concluded that 'Pollution is the largest environmental cause of disease and premature death in the world today. Diseases caused by pollution were responsible for an estimated 9 million premature deaths in 2015—16% of all deaths worldwide'.[1] Also the World Health Organization (WHO) calculates that 12.6 million premature deaths per year are attributable to an unhealthy environment, 8.2 million of which are due to non-communicable diseases, with cardiovascular disease (CVD) (including stroke) being the largest contributor, accounting for nearly 5 million of these deaths.[2] Among all environmental pollutants, air pollution is the most important risk factor, and ambient outdoor air pollution due to particulate matter <2.5 µm ($PM_{2.5}$) exposure ranked fifth among all global risk factors in 2015, leading to 4.2 million deaths annually as estimated by the Global Burden of Diseases (GBD) study.[3] Nine out of 10 people worldwide are exposed to ambient air pollutant levels above WHO guidelines (>10 µg/m^3). Using a novel exposure response hazard function [global estimate of exposure mortality model (GEMM)], the mortality attributable to air pollution was estimated to be 9 million premature deaths at the global level[4] and 790 000 excess deaths in Europe alone.[5] These figures are also in line with the substantial impact of air pollution on cardiovascular morbidity and mortality as reported by a position paper by the American Heart Association.[6] Mounting evidence suggests that health risks attributable to $PM_{2.5}$ persist even at low levels, below WHO air quality guidelines and European standards (annual levels <10 and <25 µg/m^3, respectively).

Mitigation strategies for air pollution

Current approaches to mitigate air pollution and their impact have been previously reviewed and can be broadly classified into: (i) active personal exposure mitigation with home air cleaning and personal equipment (e.g. face masks); (ii) modification of human behaviour to reduce passive exposures; and (iii) pharmacological approaches.[7,8] The N95 respirator studied under ambient $PM_{2.5}$ exposure conditions at both high and low levels of exposure over a few hours has been shown to reduce systolic blood pressure and improve heart rate variability.[7,9] Closing car windows, air-conditioning, and cabin air filters represent approaches that could be important in those who are susceptible, but only in those spending large amounts of time in transportation microenvironments. Behavioural strategies such as air pollution avoidance by changing travel routes, staying indoors/closing windows, and limiting outdoor recreation/exercise can help limit air pollution exposure (reviewed in Munzel *et al.*[8]), but may bring other risks such as higher exposure to indoor pollutants or adverse health effects due to a sedentary lifestyle. Health impact modelling and epidemiological studies have demonstrated that the benefits of aerobic exercise nearly always exceed the risk of air pollution exposure across a range of concentrations, and for long durations of exercise for normal individuals (>75 min). Therefore, guiding healthy people to avoid outdoor activity in areas with high $PM_{2.5}$ pollution has the potential to produce greater harm than benefit, given the low absolute risk for cardiovascular or respiratory events.

Running in areas with low air pollution is cardioprotective, whereas in highly air polluted areas exercise has detrimental effects on the heart!

The critical questions remain regarding the trade-off between the health benefits of physical activity (PA) and the potential harmful effects of increased exposure to air pollution during outdoor PA. To address this question, Kim *et al.*[10] performed a nationwide cohort study, published in this issue of the *European Heart Journal*, including 1 469 972 young adults aged 20–39 years. Air pollution exposure was estimated by the annual average cumulative level of particulate matter. PA was calculated as minutes of metabolic equivalent tasks per week (MET-min/week) based on two consecutive health examinations from 2009 to 2012. Compared with the participants exposed to low to moderate levels of $PM_{2.5}$ or PM_{10} who continuously engaged in ≥1000 MET-min/week of PA, those who decreased their PA from ≥1000 MET-min/week to 1–499 MET-min/week and to 0 MET-min/week (physically inactive) had an increased risk of CVD (*P* for trend <0.01). Among participants exposed to high levels of $PM_{2.5}$ or PM_{10}, the risk of CVD was elevated with an increase in PA above 1000 MET-min/week. The authors concluded that reducing PA may lead to subsequent elevation of CVD risk in young adults exposed to low to moderate levels of $PM_{2.5}$ or PM_{10}, whereas a large increase in PA in a high-pollution environment may adversely affect cardiovascular health.

The present study, however, has some limitations. The survey of PA was not sufficient to estimate the amount of outdoor PA because of the absence of data on whether the participants engaged in PA outdoors (e.g. running in a park) or indoors (e.g. running in a gym). Second, recall bias may occur because the data on the PA level were collected using self-reported questionnaires. Finally, the authors did not investigate the short-term effects of exposure to air pollution. Therefore, further studies are necessary to identify the association of the combined effects of short-term exposure to air pollution and changes in PA with CVD risk.

By which mechanism does air pollution cause adverse health effects and neutralize protective mechanisms induced by regular exercise?

Particulate matter (and other air pollution constituents such as reactive gases) causes recruitment of immune cells, increases oxidative stress in the vasculature and the brain, and leads to a supersensitivity of the vasculature to vasoconstricting agents, all of which contribute to vascular (endothelial) dysfunction.[11] Accordingly, particulate matter leads to subclinical, and later to full-blown, atherosclerotic and cardiometabolic disease, sharing pathomechanisms with classical cardiovascular risk factors such as hypertension or diabetes. In addition, particulate matter activates the hypothalamic–pituitary–adrenal axis and the sympathetic system, thereby triggering the release of stress hormones such as cortisol and catecholamines.[12] Of note, ultrafine particles can even cross the blood–brain barrier, thereby causing cerebral (hypothalamic) inflammation and a direct activation of the sympathetic nervous system.[13] Physical exercise may counteract these detrimental effects of air pollution by its well-known cardioprotective effects involving activation of the AMP-activated protein kinase and protective transcription factors such as NRF2 and PGC-1α that largely improve mitochondrial biogenesis/function and metabolism/energy use, as well as induction of endothelial nitric oxide synthase activity and nitric oxide signalling by shear stress, all of which mimic pre-conditioning-like protective effects with improved antioxidant and anti-inflammatory defence.[14,15]

What helps us to decide whether we can do exercise in a polluted area?

The decision to take part in outdoor exercise or not clearly depends on the assessment of external environmental exposures, especially in cities, where novel technologies may indeed bring great advancements. Sensors are becoming available nowadays to measure environmental exposures such as air pollution, noise, and temperature, and can be placed in various locations in a city to capture the variation in exposure levels within cities (for a review, see Nieuwenhuijsen[16]). Likewise, satellite data can now be used to forecast these exposure levels.[16] The use of new technologies including smartphones, other GPS devices, and small sensors can also improve personal assessment of exposure by obtaining information on the location and mobility of a person, the environmental exposure level, and PA levels.[17,18] Importantly, the combination of the assessment of personal air pollution concentrations and PA provides the opportunity to estimate the inhaled dose, which may be a better measure than area-specific exposure levels, helping to decide whether we can have our exercise without any side effects for our health (*Graphical Abstract*).

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