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Blood pressure changes in association with black carbon exposure in a panel of healthy adults are independent of retinal microcirculation

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ABSTRACT

Exposure to ambient particulate matter and elevated blood pressure are risk factors for cardiovascular morbidity and mortality. Microvascular changes might be an important pathway in explaining the association between air pollution and blood pressure. The objective of the study was to evaluate the role of the retinal microcirculation in the association between black carbon (BC) exposure and blood pressure.

We estimated subchronic BC exposure based on 1-week personal measurements (μ-Aethalometer, AethLabs) in 55 healthy nurses. Blood pressure and retinal microvasculature were measured on four different days (range: 2–4) during this week.

Subchronic BC exposure averaged (± SD) 1334 ± 631 ng/m^3 and ranged from 338 ng/m^3 to 3889 ng/m^3. An increased exposure of 631 ng/m^3 BC was associated with a 2.77 mm Hg (95% CI: 0.39 to 5.15, p = 0.027) increase in systolic blood pressure, a 2.35 mm Hg (95% CI: 0.52 to 4.19, p = 0.016) increase in diastolic blood pressure and with 5.65 μm (95% CI: 1.33 to 9.96, p = 0.014) increase in central retinal venular equivalent. Mediation analysis failed to reveal an effect of retinal microvasculature in the association between blood pressure and subchronic BC exposure.

In conclusion, we found a positive association between blood pressure and subchronic black carbon exposure in healthy adults. This finding adds evidence to the association between black carbon exposure and cardiovascular health effects, with elevated blood pressure as a plausible intermediate effector. Our results suggest that the changes in a person's blood pressure as a result of subchronic black carbon exposure operate independently of the retinal microcirculation.

1. Introduction

Short-term and long-term exposures to particulate matter air pollution contribute to cardiovascular morbidity and mortality (Brook et al., 2010; Laden et al., 2006). Altered autonomic function of the heart, changes in micro- and macrovascular reactivity, induction of systemic inflammation, endothelial dysfunction and altered peripheral resistance of the blood vessels can mediate these cardiovascular effects (Mills et al., 2009). The microcirculation determines the overall peripheral resistance and microvascular alterations may lead to blood pressure elevation and an increased risk for developing hypertension (Boudier et al., 1992; Levy et al., 2001). Adar et al. (2010) and Louwies et al. (2013) have studied the impact of air pollution on the retinal microcirculation. These authors found that retinal arteriolar narrowing is associated with long-term and short-term exposure to air pollution (Adar et al., 2010; Louwies et al., 2013). Additionally, retinal arteriolar narrowing has been associated with increased blood pressure and hypertension (Wong and Mitchell, 2007). Thus, microcirculatory changes in the retina are potentially relevant in the association between air pollution exposure and blood pressure changes.

Epidemiological research and animal studies have produced positive, negative and null associations between blood pressure and ambient air pollution (Brook, 2007). These outcomes can be explained by study-specific differences such as population characteristics, dose and duration of the exposure that are different between studies. Furthermore, the chemical composition of particulate matter is heterogeneous and varies between studies. For instance, $PM_{2.5}$ (particulate matter with a diameter smaller than 2.5 μm) exposure in high-traffic areas had a stronger effect on blood pressure compared with $PM_{2.5}$ in low-traffic

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areas (Auchincloss et al., 2008; Brook et al., 2009). Furthermore, spatial and temporal variability in pollution sources may obscure associations between PM and blood pressure. Most epidemiological studies rely on central monitor data or complex models to estimate PM concentrations at the participant's residence. Exposure is however strongly related to an individual's time–activity patterns and time spent indoor and outdoor (Dons et al., 2011).

Exposure misclassification may occur with central monitor data and may lead to incorrect estimation of cardiovascular health effects associated with air pollution exposure (Brook et al., 2011; Padro-Martinez et al., 2012).

Black carbon (BC), a by-product of fuel combustion and a constituent of particulate matter, has been associated with systemic inflammation and oxidative stress, decreased flow-mediated dilation of the brachial artery and reduced parasympathetic tone (Alexeeff et al., 2011; O'Neill et al., 2005; Park et al., 2008; Schneider et al., 2010). Mordukhovich et al. (2009) and Wilker et al. (2010) reported positive associations between short-term BC exposure, measured as the concentration averaged over the 7 days preceding each study visit, and systolic and diastolic blood pressure (Mordukhovich et al., 2009; Wilker et al., 2010). Schwartz et al. (2012) reported an association between blood pressure and modelled long-term BC concentrations. A 0.32 μg/m^3 increase in BC was significantly associated with a 2.64 mm Hg increase in systolic blood pressure and a 2.41 mm Hg increase in diastolic blood pressure (Schwartz et al., 2012). Zhao et al. (2014) measured personal BC exposure using portable measuring devices in a study that investigated the effects of BC on blood pressure in 65 persons suffering from the metabolic syndrome. A short-term BC increase of 1 μg/m^3, 10 h prior to the study visit, was associated with a 0.53 mm Hg increase in systolic blood and a 0.37 mm Hg increase in diastolic blood pressure (Zhao et al., 2014).

We explore the association between blood pressure, short-term and subchronic BC exposure in this study. Subchronic BC exposure was calculated based on personal monitoring during one week with portable measuring devices and data from a reference station. During this 1-week period we repeatedly measured blood pressure and retinal vessel diameters. The retinal microcirculation was measured to study the potential mediating effect of the microcirculation in the relationship between BC exposure and blood pressure.

2. Methods

2.1. Study design

A total of 130 nurses working in the north of Belgium were invited and 99 (76%) agreed to participate. Fifty five nurses (56%) could be monitored in this study. The predominantly female participants were aged between 22 and 59 years and reported to be free of cardiovascular diseases and diabetes. Every participant was monitored during one average working week between April and May 2013. Clinical examinations were scheduled for every participant on Tuesday, Thursday, Saturday and Monday between 7 am and 9 pm [mean difference between repeated measurements was 1 h (range, 0.1–1.9 h)]. 75% of the participants underwent all 4 examinations, 23% completed 3 examinations, whereas 2% completed 2 examinations. Participants were not asked to fast before the visits. Blood pressure measurements and retinal images were collected during each examination. A venous blood sample was collected on the last day of the study. Gamma-glutamyl transpeptidase (γ-GT) was measured as a marker for liver function and alcohol consumption. Haemoglobin A1C was measured as a glycemic index and metabolic marker for diabetes. Participants completed a questionnaire on their smoking status, medical history and current medication use. All participants provided written informed consent. The ethics boards of Hasselt University and University Hospital Antwerp approved the study.

2.2. Blood pressure measurement

Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) were measured with an automated device (Stabilograph, Stolberg, Germany) according to the guidelines of the European Society of Hypertension (Parati et al., 2008). After the participants had rested in a sitting position for 5 min, SBP, DBP and HR were measured five times consecutively during each of the 4 study visits. The average of the last three measurements collected during the examinations was used in the analysis.

2.3. Retinal photography and grading

A Canon 45° 6.3 megapixel digital nonmydriatic retinal camera (Hospithera, Brussels, Belgium) was used. The fundus of the right eye and the left eye of each participant were photographed twice during each study visit. Participant characteristics were masked for the trained grader before review and analysis of the retinal images. IVAN retinal image analysis software was used to measure retinal vessel diameters according to previously reported protocols (Knudtson et al., 2003; Wong et al., 2004a). Retinal vessel calibres were summarized as the Central Retinal Arteriolar Equivalent (CRAE) and Central Retinal Venular Equivalent (CRVE) in each picture. The equivalents represent a summary of vessel diameters within an area equal to 0.5–1 disc diameters from the optic disc margin. Average CRAE and CRVE values were calculated for each study visit based on the four images.

2.4. Exposure assessment

2.4.1. Personal black carbon exposure

Personal exposure to black carbon (BC) was measured continuously for 7 consecutive days (from Tuesday to next week's Monday) with a portable MicroAeth Model AE51 (Aethlabs, San Francisco, California, US) on a 1-min time resolution. A short tube was attached to the inlet of the aethalometer, giving the participants the opportunity to put the device in a purse or backpack while still sampling ambient air. Air was drawn over a Teflon-coated borosilicate glass fibre filter at a flow rate of 100 ml/min, resulting in BC accumulation on the filter. The attenuation of light at 880 nm was measured and converted into a BC concentration (ng/m^3). The filter was replaced every two days to prevent filter saturation. The participants were instructed to carry the device with them at all times, but for indoor activities they were allowed to leave it in the room where the majority of the time was spent. Raw BC data were processed before they were used. Measurements with high attenuation (ATN > 75) or an error code were excluded (Dons et al., 2011). Next, data were smoothened with an algorithm that was developed by the Environmental Protection Agency (Hagler et al., 2011).

Short-term exposure windows (24 h and 48 h) were calculated by taking the average of all BC measurements 24 h or 48 h before the clinical visit.

2.4.2. Calculated personal subchronic black carbon exposure

Subchronic BC exposure was calculated based on the personal BC exposure measured during the study period. This was done using the following formula: Subchronic BC exposure = Personal BC measurement × (Refsite yearly average / Refsite week average). The personal BC measurement was calculated as the average BC exposure over the whole week for each participant. This timeframe can capture the time–activity pattern during an average working week (Dons et al., 2012). “Refsite yearly” represents the average BC concentration during the year 2013. “Refsite week average” represents the average BC concentration at the BC reference monitor during the same week as the personal BC measurements. The latter factor allows correcting for varying ambient concentrations during the study period. The monitoring station of Dessel that is operated by the Flemish Environment Agency was chosen as reference. The station is equidistant from both