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# Arterial blood pressure responses to short-term exposure to fine and ultrafine particles from indoor sources – A randomized sham-controlled exposure study of healthy volunteers



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#### ABSTRACT

*Objectives*: Particulate air pollution is linked to adverse cardiovascular effects. The aim of the study was to investigate the effect of short-term exposure to indoor particles on blood pressure (BP).

Methods: We analyzed the association of particle emissions from indoor sources (candle burning, toasting bread, frying sausages) with BP changes in 54 healthy volunteers in a randomized cross-over controlled exposure study. Particle mass concentration (PMC), size-specific particle number concentration (PNC) and lung-deposited particle surface area concentration (PSC) were measured during the 2 h exposure. Systolic and diastolic blood pressure were measured before, during, directly, 2, 4 and 24 h after exposure. We performed multiple mixed linear regression analyses of different particle metrics and BP.

Results: BP significantly increased with increasing PMC, PSC and PNC resulting from toasting bread. For example, an increase per  $10~\mu g/m^3$  PM $_{10}$  and PM $_{2.5}$ , systolic BP increased at all time points with largest changes 1 h after exposure initiation of 1.5 mmHg (95%-CI: 1.1; 1.9) and of 2.2 mmHg (95%-CI: 1.3; 3.1), respectively. Conclusions: Our study suggests an association of short-term exposure to fine and ultrafine particles emitted from toasting bread with increases in BP. Particles emitted from frying sausages and candle burning did not consistently affect BP.

#### 1. Introduction

Exposure to ambient particulate matter (PM) is a leading cause of global morbidity and mortality Lim et al. (2012). Among the many health effects linked to PM exposure, a large number of epidemiological studies have confirmed the association between air pollution and adverse cardiovascular effects Brook et al. (2010). Cesaroni et al. (2014); It is possible that this association between ambient air pollution and cardiovascular mortality is mediated through high blood pressure, a major cardiac risk factor worldwide Brook et al. (2009). Increases in blood pressure have serious health ramifications, as an increase in

1 mmHg in systolic blood pressure is estimated to increase the risk of cardiovascular mortality by 2–4% Stamler et al. (1993). van den Hoogen et al. (2000); Even more, short-term increases in BP have been linked to PM-related triggering of cardiovascular events Brook et al. (2010). Giorgini et al. (2016);

The proposed mechanisms behind pulmonary exposure and cardiovascular effects are through direct translocation of specific constituents of the PM "mixture" into circulation and via pulmonary derived mediators causing oxidative stress and systemic inflammation, (Mills et al., 2009) leading to vasoconstriction, endothelial dysfunction, atherosclerosis, thrombosis, coagulation and elevated blood pressure

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Brook and Rajagopalan (2010). Particulate matter may also cause an imbalance in ANS (autonomic nervous system) favoring sympathetic over parasympathetic tone due to the stimulation of pulmonary receptors, baroreceptors, and carotid body chemoreceptors, leading to increased heart rate, stroke volume, arrhythmia, vasoconstriction and increases in blood pressure Brook et al. (2009).

Controlled human exposure studies and observational data have shown short-term PM exposure with concentrated ambient particles and diesel engine exhaust particles to have rapid adverse effects promoting vasoconstriction and a rapid increase in BP Brook et al. (2009). Brook and Rajagopalan (2009); Urch et al. (2005); Brook (2002); Cosselman et al. (2012); Bellavia et al. (2013):

In addition to this, evidence is emerging that indoor air pollution, especially the use of solid fuels for cooking and heating, are important risk factors for coronary heart diseases Fatmi and Coggon (2016). Recent studies focused on the effects of using solid fuels indoors on blood pressure and found a positive association with higher blood pressure or prevalence of hypertension. In contrast to this, two cross-sectional surveys have failed to demonstrate significant associations with blood pressure Fatmi and Coggon (2016).

To date, the majority of studies have focused on the investigating the adverse health effects associated with exposure to ambient outdoor particles. Much less evidence is available on the effects of short-term exposures to inhalable particles from indoor sources. However, initial studies indicate that specific indoor activities and combustion processes, like candle burning or open fireplace use, emit high amounts of fine and ultrafine particles (UFP), leading to human exposure levels that possibly cause pulmonary as well as systemic inflammation Ghio et al. (2012). Sørensen et al. (2005); Ward and Noonan (2008); Afshari et al. (2005); Afshari et al. (2005) have shown that candle burning, cooking food, cleaning activities and use of electric engines or furnaces emit high amounts of fine and ultrafine particles leading to considerable human exposure Afshari et al. (2005). Since populations of industrialized countries spend up to 16 h per day indoors on average, regular and prolonged exposure to particles from various indoor sources may lead to significant adverse health effects Brasche and Bischof (2005). Dorre (1997); In our previous publication on respiratory effects of fine and ultrafine particles from indoor sources, we found suggestive evidence that short-term exposure to common indoor sources is associated with decreases in lung function Soppa et al. (2014).

In an effort to understand further the effects of short-term exposure to indoor particles, we investigated whether exposure to particles from candle burning (CB), frying sausages (FS), and toasting bread (T) leads to changes in blood pressure among healthy volunteers in a controlled chamber study. We performed an in-depth characterization of emitted particles combining established exposure metrics, e.g., size-specific particle mass concentration (PMC), with less common exposure metrics such as size-specific particle number concentration (PNC) and lung deposited surface area concentration (PSC) to investigate a possible link between specific characteristics of the emitted particles and blood pressure changes.

#### 2. Experimental section

The "Effects of fine and ultrafine Particles from Indoor Activities" (EPIA) project is a cross-over sham-controlled exposure study with healthy volunteers, which integrates a detailed exposure characterization, the investigation of biological pathways with toxicological methods, and human health effect analyses. It was approved by the Ethics Committee of the Heinrich-Heine-University of Düsseldorf, in accordance with the Declaration of Helsinki. All participants gave written informed consent.

The study protocol has been described in detail elsewhere Soppa et al. (2014). In short, 54 adult men and women were recruited for this study. Inclusion criteria comprised age between 18 and 79 years, ability

to speak and understand German, and non-smoker or ex-smoker status for at least ten years. Predefined exclusion criteria were: existing or planned pregnancy (within the next six months), planned surgery in the following six months, workplace and residential exposure to environmental tobacco smoke or air pollutants (e.g. career as a welder, roadman, chemical worker), end stage fatal disease, heart attack or stroke in the past three months, uncontrolled arterial hypertension, diabetes mellitus, chronic respiratory disease, chronic infectious disease and neurologic or mental disease (claustrophobia, psychosis).

All subjects were asked to abstain from alcohol and extreme physical exercise for 24 h and from caffeine drinks for at least 4 h before the beginning of each exposure and before the examination 24 h post exposure. On the morning of study days participants were asked to eat only a light breakfast before arriving at the study center. Before medical examinations and the start of exposure, each participant was interviewed regarding his or her current health status, their mode of transportation and travel time to the site of investigation. If a participant had a current infection or had taken anti-inflammatory drugs during the previous 7 days, the exposure was rescheduled. On average four participants were exposed on each exposure day.

To identify which indoor sources, may be important for human health, we first characterized the emissions of fine and ultrafine particles from various indoor sources (candle burning, toasting bread, baking pizza, frying sausages, operating a fireplace, vacuum cleaning, hot air radiator, butane and spirit burner, engine emissions of the vacuum cleaner, grinding of nanoparticle containing paint) by their physico-chemical characteristics. Candle burning, toasting bread and frying sausages showed, in comparison to the other indoor sources, stable increases in particle number and mass concentrations of ultrafine and submicron particles that could be reproduced in an experimental setting. Subsequently, these sources were further characterized and selected for the exposure of the participants.

Each exposure session lasted for two hours and took place in an air-conditioned custom-made laboratory room. The air conditioning system worked in a circulating mode, therefore there was no additional air exchange. Air flow rate was approximately 240 m $^3$ /h. During exposure, temperature (24 °C) and relative humidity were controlled.

Participants were exposed on separate occasions at the same time of day at least two weeks apart. Every 30 min a participant entered the exposure chamber and started his exposure session. The start time for the individual participant was the same on all days of exposure to prevent diurnal variation of BP from influencing the results. The order of the exposure sessions was randomized. Participants were not blinded against the type of exposure because the particle sources were placed inside the exposure chamber so that the subjects could see them and smell source-specific odors. A sham exposure with only room air (RA) was conducted, in which an air ventilator was placed in the chamber and the participants were told that this was one of the exposure situations. Participants did not exercise and were mostly sitting during exposure sessions so breathing patterns corresponded to usual quiet indoor activities.

In the experimental exposure scenarios, participants were exposed to candle burning (CB), toasting bread (T) and frying sausages (FS). Every participant was exposed to the sham exposure RA, but not all subjects participated in all exposure sessions with CB, T and FS, due to sick leave, premature study discontinuation or other personal reasons. Indoor sources were operated by staff present continuously inside the chamber. Exposure scenarios were performed on two different exposure levels for each emission source. During CB, 20 white Christmas-tree candles (exposure level 1, CB1) or 40 candles (exposure level 2, CB2) were burning simultaneously. During the T exposure scenario, bread was toasted with one (exposure level 1, T1) or two (exposure level 2, T2) identical time controlled 2-slice-toasters. The duration of each toasting period lasted up to 3 min. To ensure constant emission and in order to prevent the toaster from overheating, the toasting process was done alternately in different toasters of the same type. During the FS

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