Effect of Reducing Ambient Traffic-Related Air Pollution on Blood Pressure: A Randomized Crossover Trial NCT04029129

JULY 26, 2023

Objective of the Study:

Traffic-related air pollution (TRAP) is the predominant contributor to poor air quality in developed countries. The 4% of the US population (Boehmer et al., 2013) who reside near busy roadways, as well as those who travel on them, are exposed to elevated concentrations of TRAP – a mixture of gases and particulate matter (PM) enriched in fuel combustion byproducts, as well as no tailpipe emissions. These exposures can be an order of magnitude higher than urban background exposure (Karner et al., 2010).

Both residential proximity to roadways and short-term exposures from time spent on roadways have been associated with adverse cardiovascular indicators and outcomes (Brook et al., 2010a). Peters et al (Peters et al., 2004) showed in a case-crossover study that exposure to TRAP was associated with myocardial infarction within 1 to 2 hours. Ghosh et al (Ghosh et al., 2016) reported that residential proximity to major roadways and traffic density were responsible for 2.4% and 6.8% of coronary heart disease and deaths, respectively, in Los Angeles and neighboring counties. Living near roadways has also been linked to increased prevalence of hypertension and increases in blood pressure (BP) (Brook et al., 2010b; Cai et al., 2016).

Controlled exposure to diesel particles and concentrated ambient fine PM ($PM_{2.5}$; defined as particles with aerodynamic diameter <2.5 μm) from near-roadway locations has been shown to raise BP within 2 hours (Bellavia et al., 2013; Cosselman et al., 2012; Mills et al., 2011; Urch et al., 2005).There is also evidence that the particulate component of TRAP is the causal agent. For example, Mills et al (Mills et al., 2011) reported that diesel exhaust exposure impaired vascular function but that filtered diesel exhaust (that retained its gaseous components) or pure carbon nano-PM did not. Similarly, Cosselman et al (Cosselman et al., 2012) reported a rapid increase in systolic BP (SBP; peaking 30–60 minutes from the start of exposure) but not diastolic BP (DBP) or heart rate (HR), upon exposure to diesel exhaust. In contrast, studies of the effects of short-term exposures to gaseous components of TRAP mixtures on cardiovascular function and BP are scarce. In the few studies we were able to find, the associations with adverse effects for O_3 exposure are mixed (Li, 2018), while current evidence does not support an adverse acute effect of NO_2 on vascular function (Langrish et al., 2010).

There have been over 90 studies assessing short-term effects of ambient ultrafine particles (UFPs; particles with aerodynamic diameter <100 nm and a component of TRAP) on cardiovascular indicators and outcomes (Ohlwein et al., 2019). There are also a growing number of long-term studies of UFP and health, with a particular focus on residential proximity to roadways, but these studies have reported mixed findings in terms of associations with cardiovascular health (Aguilera et al., 2016; Lane et al., 2016). Relatively few have studied short-term effects of TRAP, or its specific components such as soot (or black carbon [BC]) and UFP, on BP (Magalhaes et al., 2018).

It is difficult to draw causal relationships between TRAP and BP because of the observational nature of epidemiological studies, which include uncontrolled confounders, such as noise (Aguilera et al., 2016; Brauner et al., 2008; Brugge & Goble, 2002; Lane et al., 2016; Magalhaes et al., 2018; Morishita et al., 2018; Ohlwein et al., 2019) and exposures are often estimated based on central-site measurements, which introduces exposure error. Controlled exposure studies offer the potential to test associations under highly scripted and characterized conditions. However, studies with exposure concentrations that are realistically encountered proximate to highways are lacking. Furthermore, evaluation of the effectiveness of strategies to mitigate TRAP exposures, such as use of commercially available, stand-alone HEPA filtration, have, to date, shown limited benefits on BP and peripheral blood inflammation (Brauner et al., 2008; Brugge & Goble, 2002; Morishita et al., 2018). Morishita et al (Morishita et al., 2018) found reductions in SBP in older adults living in an urban area with 3-day use of HEPA filtration, which also reduced indoor $PM_{2.5}$, but $PM_{2.5}$ is not a marker of TRAP emissions. Therefore, the aim of our study was to assess whether reducing TRAP exposure by limiting indoor infiltration and deploying HEPA filtration for a short duration could have a beneficial effect on BP.

Methods:

Study Design and Participants

The study design was a 3-exposure, 3-period crossover trial in which participants attended three 2-hour-long exposure sessions (1 each for low, medium, and high exposure in random order), all on same day of the week, separated by 1-week washout periods. Twenty-four sessions of each type were held, and participants were assigned to the exposure sessions using a Latin square design. Two to 4 participants attended each exposure session.

The inclusion criteria were age of 40 to 75 years and speaking either English or Chinese. The exclusion criteria were self-reported history of a major cardiovascular outcome (including myocardial infarction, stroke, and angina), other serious health problems (chronic obstructive lung disease or current asthma), taking antihypertensive medications, smoking or living with a smoker, cognitive impairment, working at a job with high-combustion exposure (eg, taxi/truck driver and restaurant cook), and high-combustion exposure in the preceding 24 hours (such as driving on a highway). The Tufts University Social Sciences institutional review board approved the study protocol.

Participants were instructed to avoid caffeine, to not drive, and to avoid exposure to traffic other than what was necessary to get from their home to the study location on the morning of exposures. Participants were preferentially recruited from neighborhoods close to the study locations that have outdoor TRAP levels similar to the exposure session location. Most participants walked; however, a few were transported to short distances in gasoline-powered cars driven with the in-vehicle air recirculation fan turned on to limit exposure before arrival. Before the first exposure, participants were oriented to what to expect during the sessions to reduce stress reactions. Exposure session type was not disclosed to the participants.

Participants arrived 15 to 20 minutes before the start of each exposure session. Upon arrival, they completed a questionnaire that assessed exposures that could potentially affect their BP. Measures included the validated 16-item Perceived Stress Scale,[20] self-reported taking of any medications (day and hour last taken), location and activity for each hour in the preceding 48 hours, consumption of caffeine or alcohol past midnight the previous night, and vigorous physical activity in the last 24 hours by hour. If an exposure of concern was identified, which was rare, the participant was rescheduled.

Air Quality and Outcome Measures and Exposure Room Configuration

Air Quality Measurements

Particle number concentrations (PNC) and black carbon (BC) concentrations were monitored continuously. PNC was measured using a water-based condensation particle counter (TSI, Inc; model 3873; d_{50}=7 nm) at 1-second resolution and BC concentration was measured with an aethalometer (Magee Scientific; model AE16) at 1-minute resolution. For the first half of the sessions, temperature was measured centrally in the room, and for the latter half of the sessions, temperature was measured directly adjacent to each study participant with a temperature logger (Onset Computer Corporation; model HOBO UX100-003).

Particle Size Distribution

Particle size distributions in a subset of exposure sessions (subset session count: low, 8; medium, 9; and high, 7) were measured with a Scanning Electrical Mobility Spectrometer (Brechtel Manufacturing, Inc). The particle counter operated with butyl alcohol as the condensing fluid and to prevent detectable butyl alcohol scent, the particle counter was enclosed in an airtight box that was vented outdoors. The Scanning Electrical Mobility Spectrometer measured particles between 5 and 600 nm in 59 size bins, executing a scan across the full-size range every 75 seconds. Average particle size distributions were generated for high-, medium-, and low-exposure sessions by averaging all scans over the 2-hour exposure session duration and then averaging the same exposure types.

BP and HR Measurement

Participants were seated throughout the questionnaire (15 minutes) and exposure sessions (2 hours). During exposure, participants wore sound canceling headphones (Bose noise canceling wireless headphones), were instructed to refrain from doing anything, including reading or meditation, and asked not to fall asleep. If it appeared that a participant was falling asleep, which was rare (<5 instances), they were gently tapped and awakened. An ambulatory BP monitor (Suntech Oscar; Table S1) was placed on the dominant arm of participants and began recording at the start of each exposure session to record SBP, DBP, and HR every 10 minutes.

Exposure Room Configuration

Exposure sessions were held at 2 near-highway locations (shown in Figure S1) where ambient air was enriched in TRAP. Most of the participants (n=63) attended exposure sessions in a ground-floor community room of a low-income housing development located near the intersection of I-90 and I-93 (average weekday daily traffic, 240 000 vehicles/day) in Chinatown, Boston. For the other 14 participants, sessions were conducted at another community room (on the ground floor in a multistory building) located in Somerville, MA, which was adjacent to I-93 and R38 (average weekday daily traffic, 215 000 vehicles/day). Sessions were conducted in the morning (during 06:00–09:00 hours) to coincide with rush-hour traffic and lower atmospheric dispersion, that is, when TRAP concentrations were expected to be the highest (verified by diurnal trends measured at a vicinal near-highway regulatory monitoring site [ID: 25-025-0044]).

Three levels of exposure—low, medium, and high—were attained by varying the degree of ventilation (and thereby infiltration) and by increasing or decreasing the number or blower setting of HEPA filtration units. Two brands of HEPA air filters were used at both locations: IQ Air Health Pro (1 unit) and Austin Air Healthmate 400 (up to 7 units with 4-stage filter, which also contained granular activated carbon and zeolite).

Based on air quality measurements before the exposure sessions, we determined that a concentration of ≈20 000 to 30 000 particles/cm^3 could be expected during the high-exposure sessions and 10-fold lower concentrations could be attained in the low-exposure sessions. We targeted 33-50% lower than high-exposure concentrations, that is, 10 000 particles/cm^3, for the medium-exposure sessions.

During low exposure, infiltration of outdoor air into the room was minimized by closing doors and sealing the cracks underneath with duct tape. Neither exposure room had operable windows. Filtration of TRAP was maximized by continually running air filters (4 units at the Somerville location and 8 units at the larger Chinatown location).

During medium exposure, infiltration was restricted by closing doors, but cracks underneath were left unsealed. Filtration was optimized to maintain indoor PNC in the 8000- to 12 000-particles/cm^3 range by using 0 to 4 air filters.

During high exposure, infiltration was maximized by cross-ventilating the rooms by partially opening the doors that connected the room directly to outdoors and in the Somerville location, by adding a fan in addition to door opening (since cross-ventilation was not an option in that room). Air filters were not used during high exposures.

Both community rooms were located within a block of restaurants, which resulted in a noticeable odor during the last 30 to 45 minutes of some sessions when restaurants began cooking. Odor was only perceivable in some of the high-exposure sessions because this configuration allowed odors into the rooms.

Statistical Analysis Plan:

A linear mixed model was used to analyze the 3-exposure, 3-period crossover design. The primary outcome measure is the change in systolic blood pressure from the beginning of each exposure session. Before calculating change scores in each exposure session, each participant's systolic blood pressure measurements was smoothed using a 3-time-period, centered moving average. A random intercept was included in the linear mixed model to account for the interdependence of the observations that arise by each participant attending each exposure session. In addition, the model included baseline systolic blood pressure, mean room temperature for each session, and 2 time-varying covariates, particle number count and black carbon concentrations. A Toeplitz covariance structure was used to characterize the interdependence of the observations over time. Period and carryover effects was assessed in the linear mixed model. The mean dose-response effect of filtration was assessed for statistical significance using a linear contrast. An identical approach was used to analyze diastolic blood pressure and heart rate. Particle number count and black carbon concentrations was also analyzed using a linear mixed model with average room temperature as a fixed covariate and a Toeplitz covariance structure.

References

Aguilera, I., Dratva, J., Caviezel, S., Burdet, L., De Groot, E., Ducret-Stich, R. E., Eeftens, M., Keidel, D., Meier, R., Perez, L., Rothe, T., Schaffner, E., Schmit-Trucksäss, A., Tsai, M., Schindler, C., Künzli, N., & Probst-Hensch, N. (2016). Particulate matter and subclinical atherosclerosis: Associations between different particle sizes and sources with carotid intima-media thickness in the SAPALDIA study. *Environmental Health Perspectives; Environ Health Perspect, 124*(11), 1700-1706. 10.1289/EHP161

Bellavia, A., Urch, B., Speck, M., Brook, R. D., Scott, J. A., Albetti, B., Behbod, B., North, M., Valeri, L., Bertazzi, P. A., Silverman, F., Gold, D., & Baccarelli, A., A. (2013). DNA Hypomethylation, Ambient Particulate Matter, and Increased Blood Pressure: Findings from Controlled Human Exposure Experiments. *Journal of the American Heart Association; J Am Heart Assoc, 2*(3), e000212-n/a. 10.1161/JAHA.113.000212

Boehmer, T. K., Foster, S. L., Henry, J. R., Woghiren-Akinnifesi, E., & Yip, F. Y. (2013). Residential proximity to major highways - United States, 2010. *Morbidity and Mortality Weekly Report. Supplement; MMWR Suppl, 62*(3), 46-50.

Brauner, E. V., Forchhammer, L., Moller, P., Barregard, L., Gunnarsen, L., Afshari, A., Wahlin, P., Glasius, M., Dragsted, L. O., Basu, S., Raaschou-Nielsen, O., & Loft, S. (2008). Indoor Particles Affect Vascular Function in the Aged: An Air Filtration-based Intervention Study. *American Journal of Respiratory and Critical Care Medicine; Am J Respir Crit Care Med, 177*(4), 419-425. 10.1164/rccm.200704-632OC

Brook, R. D., Rajagopalan, S., Pope, C. A., Brook, J. R., Bhatnagar, A., Diez-Roux, A., Holguin, F., Hong, Y., Luepker, R. V., Mittleman, M. A., Peters, A., Siscovick, D., Smith, S. C., Whitsel, L., & Kaufman, J. D. (2010). Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American heart association. *Circulation (New York, N.Y.); Circulation, 121*(21), 2331-2378. 10.1161/CIR.0b013e3181dbece1

Brugge, D., Simon, M. C., Hudda, N., Zellmer, M., Corlin, L., Cleland, S., Lu, E. Y., Rivera, S., Byrne, M., Chung, M., & Durant, J. L. (2017). Lessons from in-home air filtration intervention trials to reduce urban ultrafine particle number concentrations. *Building and Environment; Build Environ, 126*, 266-275. 10.1016/j.buildenv.2017.10.007

Cai, Y., Zhang, B., Ke, W., Feng, B., Lin, H., Xiao, J., Zeng, W., Li, X., Tao, J., Yang, Z., Ma, W., & Liu, T. (2016). Associations of Short-Term and Long-Term Exposure to Ambient Air Pollutants with Hypertension: A Systematic Review and Meta-Analysis. *Hypertension (Dallas, Tex.1979); Hypertension, 68*(1), 62-70. 10.1161/HYPERTENSIONAHA.116.07218

Cosselman, K. E., Krishnan, R., M., Oron, A. P., Jansen, K., Peretz, A., Sullivan, J. H., Larson, T. V., & Kaufman, J. D. (2012). Blood Pressure Response to Controlled Diesel Exhaust Exposure in Human Subjects. *Hypertension (Dallas, Tex.1979); Hypertension, 59*(5), 943-948. 10.1161/HYPERTENSIONAHA.111.186593

Ghosh, R., Lurmann, F., Perez, L., Penfold, B., Brandt, S., Wilson, J., Milet, M., Künzli, N., & McConnell, R. (2016). Near-roadway air pollution and coronary heart disease: Burden of disease and potential impact of a greenhouse gas reduction strategy in southern California. *Environmental Health Perspectives; Environ Health Perspect, 124*(2), 193-200. 10.1289/ehp.1408865

Karner, A. A., Eisinger, D. S., & Niemeier, D. A. (2010). Near-Roadway Air Quality: Synthesizing the Findings from Real-World Data. *Environmental Science & Technology; Environ.Sci. Technol, 44*(14), 5334-5344. 10.1021/es100008x

Lane, K. J., Levy, J. I., Scammell, M. K., Peters, J. L., Patton, A. P., Reisner, E., Lowe, L., Zamore, W., Durant, J. L., & Brugge, D. (2016). Association of modeled long-term personal exposure to ultrafine particles with inflammatory and coagulation biomarkers. *Environment International; Environ Int, 92-93*, 173-182. 10.1016/j.envint.2016.03.013

Langrish, J. P., Lundbäck, M., Barath, S., Söderberg, S., Mills, N. L., Newby, D. E., Sandström, T., & Blomberg, A. (2010). Exposure to nitrogen dioxide is not associated with vascular dysfunction in man. *Inhalation Toxicology; Inhal Toxicol, 22*(3), 192-198. 10.3109/08958370903144105

Li, T. (2018). Outdoor Air Pollution and Arterial Hypertension. (). IntechOpen. 10.5772/intechopen.74305

Magalhaes, S., Baumgartner, J., & Weichenthal, S. (2018). Impacts of exposure to black carbon, elemental carbon, and ultrafine particles from indoor and outdoor sources on blood pressure in adults: A review of epidemiological evidence. *Environmental Research; Environ Res, 161*, 345-353. 10.1016/j.envres.2017.11.030

Mills, N. L., Miller, M. R., Lucking, A. J., Beveridge, J., Flint, L., Boere, A. J., Fokkens, P. H., Boon, N. A., Sandstrom, T., Blomberg, A., Duffin, R., Donaldson, K., Hadoke, P. W. F., Cassee, F. R., & Newby, D. E. (2011). Combustion-derived nanoparticulate induces the adverse vascular effects of diesel exhaust inhalation. *European Heart Journal; Eur Heart J, 32*(21), 2660-2671. 10.1093/eurheartj/ehr195

Morishita, M., Adar, S. D., D’Souza, J., Ziemba, R. A., Bard, R. L., Spino, C., & Brook, R. D. (2018). Effect of Portable Air Filtration Systems on Personal Exposure to Fine Particulate Matter and Blood Pressure Among Residents in a Low-Income Senior

Facility: A Randomized Clinical Trial. *JAMA Internal Medicine; JAMA Intern Med, 178*(10), 1350-1357. 10.1001/jamainternmed.2018.3308

Ohlwein, S., Kappeler, R., Kutlar Joss, M., Künzli, N., & Hoffmann, B. (2019). Health effects of ultrafine particles: a systematic literature review update of epidemiological evidence. *International Journal of Public Health; Int J Public Health, 64*(4), 547-559. 10.1007/s00038-019-01202-7

Peters, A., von Klot, S., Heier, M., Trentinaglia, I., Hörmann, A., Wichmann, H. E., & Löwel, H. (2004). Exposure to Traffic and the Onset of Myocardial Infarction. *The New England Journal of Medicine; N Engl J Med, 351*(17), 1721-1730. 10.1056/NEJMoa040203

Urch, B., Silverman, F., Corey, P., Brook, J. R., Lukic, K. Z., Rajagopalan, S., & Brook, R. D. (2005). Acute Blood Pressure Responses in Healthy Adults during Controlled Air Pollution Exposures. *Environmental Health Perspectives; Environ Health Perspect, 113*(8), 1052-1055. 10.1289/ehp.7785