Acute increase in blood pressure during inhalation of coarse particulate matter air pollution from an urban location

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Abstract

Particulate matter (PM) air pollution is a leading global risk factor for cardiovascular mortality. Although exposure to fine PM \(<2.5 \,m\text{m}\) raises arterial blood pressure (BP), few studies have evaluated the impact of coarse PM which differs in size \((2.5–10 \,m\text{m})\), sources, and chemistry. Twenty-nine healthy adults \((30.4 \pm 8.2 \text{ years})\) underwent a randomized double-blind crossover study involving 2-hour exposures to concentrated ambient coarse PM \((164.2 \pm 80.4 \,\mu g/m^3)\) at an urban location (Dearborn, Michigan) versus filtered air. Cardiovascular outcomes were measured during, immediately, and 2 hours after exposures. Both systolic (1.9 mm Hg; 95% confidence interval: 0.96, 2.8; \(P < .001\)) and diastolic (1.9 mm Hg; 95% confidence interval: 1.1, 2.7; \(P < .001\)) BP levels were higher throughout coarse PM compared with filtered air exposures by mixed-model analyses. Heart rate variability, endothelial function, and arterial compliance were not significantly affected. Brief exposure to coarse PM in an urban environment raises arterial BP. These findings add mechanistic support to the contention that coarse PM may be capable of promoting cardiovascular events. J Am Soc Hypertens 2016;10(2):133–139.

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Introduction

Fine particulate matter (PM) \(<2.5 \,\mu m\) air pollution is a leading cause of global morbidity and mortality.\textsuperscript{1,2} A multitude of studies across scientific disciplines provide consistent and coherent evidence that fine PM is causally related to cardiovascular diseases.\textsuperscript{2} Particles of this minute size are principally derived from urban-industrial combustion processes (eg, coal-fired power plants, vehicle exhaust).\textsuperscript{2} Although fine PM has been linked to a wide array of adverse biological responses, mounting evidence supports that both short- and long-term exposures are capable of raising arterial blood pressure (BP).\textsuperscript{3–7} The underlying mechanisms are likely related to sympathetic nervous system (SNS) activation and/or vascular endothelial dysfunction.\textsuperscript{2,3}

On the other hand, the cardiovascular health effects of coarse PM (2.5–10 \,\mu m) are less conclusive, despite the fact that it is an important contributor to worldwide air pollution.\textsuperscript{8–12} In addition to its larger size range, its sources and components differ from fine PM. Coarse PM is a mixture of particles typically generated from mechanical processes (eg, crushing, grinding, or resuspension of ground material) with sources ranging from agriculture, roadway dust, fugitive emissions, to construction. The
constituents substantially vary according to nearby activities and landscapes (eg, deserts, soil, vegetation) and include metals, crustal elements (eg, silicon, calcium, magnesium, iron, potassium), and bioaerosols (eg, pollen, endotoxin).8,9

We recently demonstrated that 2-hour exposure to coarse PM in a rural setting promotes an acute elevation in BP, most likely due to autonomic nervous system imbalance (ie, parasympathetic withdraw and/or SNS activation) as supported by changes in heart rate variability (HRV).7 Several metals and crustal element particle constituents were associated with the prohypertensive response.13 Because of the fact that the sources and components of coarse PM are known to substantively differ between locations (which might influence the ensuing health responses),8,9 the aims of this study were to investigate if brief exposure to coarse PM derived from an urban setting (where the ever-growing majority of the global population lives in present-day societies)14 is also capable of raising arterial BP and secondarily to explore the biological mechanisms potentially responsible.

Methods

The study was approved by the Institutional Review Board of the University of Michigan, and all participants signed a written informed consent document during a screening visit. Participants were healthy nonsmoking adults (living in nonsmoking households within 100 miles of the exposure site location) aged 18–50 years without a history of cardiovascular disease or risk factors (screening visit BP <140/90 mm Hg and fasting glucose <126 mg/dL). Screening BP was measured in triplicate in the seated position after 5 minutes or rest on the left arm using a GE ProCare Auscultatory 300 monitor. No subject was taking any medication (eg, statin, BP-lowering pill, antioxidant) that might alter study outcomes. We excluded subjects with any diagnosed pulmonary condition (eg, asthma, chronic obstructive pulmonary disease). We did not screen patients by or characterize their occupation or ambient or personal-level exposures to air pollution; however, patients were excluded if they self-reported on screening visit if they were routinely exposed to occupational air pollutants.

Qualifying participants were enrolled into a randomized double-blind crossover study comparing the health effects of 2-hour-long exposures to concentrated ambient coarse PM (CAP) performed at Dearborn Michigan versus filtered air (FA). The sample size target was n = 30 participants based on a priori power calculations from prior study results.7 The primary study outcomes were intrachamber systolic and diastolic BP levels in CAP versus FA exposures with an estimated power of 80% to determine approximately 1.0 mm Hg difference between exposure types using mixed model analyses with alpha error of 0.05 and n = 30. Other outcomes were measured as secondary endpoints. Of 32 patients screened, there were two screen failures (not meeting all entry criteria). Randomization was performed in blocks of 10 exposure types (five CAP and five FA exposures) using an online commercially available program (https://www.sealedenvelope.com/simple-randomiser/v1/lists). One participant dropped out after enrollment but before exposures, and thus, the final study sample size was 29 patients. The location was selected to deliver coarse CAP exposures heavily influenced by “urban sources” as we have previously characterized in detail14 to include heavy traffic and industrial activities involving iron–steel manufacturing, refining, sewage sludge incineration, and coal-fired utilities along the Detroit River.15 Seventeen participants had both CAP and FA exposures performed at Dearborn with a 1- to 3-week washout period before crossover. In prior studies,5,7 we did not observe any carry-over effect of exposures on study outcomes (ie, BP, flow-mediated dilatation [FMD]) 1 week later, and thus, this washout time is adequate to assure stability of health parameters before exposures after the crossover period. Twelve participants had CAP performed at Dearborn, although results from their individual FA “control” exposure responses were used from their prior studies done at Dexter (as per the original study design).7 Participants came to the mobile air research laboratory (AirCARE-2) each study day having fasted for 8 hours. All exposures occurred from 10 AM to noon.

Coarse CAP was generated using a two-stage virtual impactor system which concentrates ambient outdoor “real-world” PM (predominantly from 2.5 to 10 μm) without substantially altering the composition and chemical nature. FA was generated by using a high efficiency particle arrestance filter at the inlet of the concentrator to remove PM. In brief, coarse CAP mass levels were continuously monitored during exposures downstream of the concentrator using a personal DataRAM monitor (Thermo Scientific, Waltham, MA, USA), and particle size distributions were measured with a 3321 APS instrument (TSI Inc, St. Paul, MN, USA). Outdoor and within-chamber temperatures and relative humidity were also monitored. Chamber temperature was maintained at approximately 24°C during exposures. CAP filter samples were collected immediately upstream of the chambers on 47-mm Teflon filters (Pall, Ann Arbor, MI, USA) at a flow rate of 6 L/min. The samples were analyzed gravimetrically using a microbalance (MT-5; Mettler Toledo, Columbus, OH, USA) in a temperature/humidity-controlled clean laboratory. Full details regarding the AirCARE-2 facility, exposure monitoring, and ambient air pollution characteristics at the site of AirCARE-2 during have been previously published.7,13,14
Cardiovascular Outcomes

Study outcome methods were performed as in our prior experiment in a rural setting. The a priori determined primary outcomes for which the study was powered (targeted enrollment of n = 30) and designed were to determine exposure differences in diastolic BP during the inhalation of CAP versus FA, as well as to determine differences in brachial artery diameter (BAD) immediately after exposures based on our primary study results. Throughout the exposure period while seated within the chamber, participants had BP measured every 7 minutes using a 90217 monitor (http://www.spacelabshealthcare.com/) on the left upper arm supported at midsternal level. Continuous electrocardiogram monitoring was also performed during exposures using a Spacelabs evo Holter system. Time and frequency domain HRV metrics were analyzed at 5-minute long epochs using the Spacelabs Pathfinder software system. On completion of exposures, the following protocols were performed by a vascular technician blinded to exposure types performed by a vascular technician blinded to exposure types in a temperature-controlled human examination room of AirCARE-2. Immediately after exposures, participants rested supine for 5 minutes and then had left arm BP measured in triplicated using an Omron BP760 device (http://www.omron-healthcare.com/). Resting basal longitudinal BAD images were measured at a standardized site on the right upper arm using a portable Terason ultrasound system and a 10-mHz linear array transducer (http://www.terason.com/). All images were captured by an electrocardiogram triggered on the R-wave. Digital images were analyzed using a software package using an edge-detection system (Brachial Analyzer, Medical Imaging Applications; http://www.mia-llc.com/). Central aortic hemodynamics was measured by right radial artery tonometry using pulse waveform analyses, and large vessel compliance was measured by right carotid-to-femoral pulse wave velocity using the SphygmoCor system (AtCor Medical; http://www.atcormedical.com). Participants rested for 2 hours, and then, the identical series of postexposure tests were performed. Afterward, conduit artery endothelial function was determined by brachial artery FMD. Repeat resting BAD images were obtained at the same right arm site followed by continuous arterial imaging for 2 minutes after reactive hyperemia was induced by the release of upper arm cuff inflation for 5 minutes. Peak FMD during the 2-minute period of reactive hyperemia was used as the primary outcome. Microvascular endothelial-dependent vasodilatation (reactive hyperemia index [RHI]) was measured concomitant with brachial FMD on the ipsilateral hand by finger peripheral arterial tonometry by the EndoPAT2000 system (http://www.itamar-medical.com/). The time points of outcome measurements (during, immediately, 2 hours after exposures, and no later time points) were selected based on the sum findings of our prior exposures with fine and coarse CAP.

Statistical Methods

Summary statistics were computed for continuous measures as mean ± standard deviation, as well as median (interquartile range), and for categorical variables as frequency and proportion (%). All outcomes were visually evaluated and analyzed for normality of distribution using the Shapiro–Wilks normality test. Following the nature of data collection (crossover study design), the matched pairs of measurements obtained after exposures (post-CAP vs. post-FA) were compared using paired t-tests (for normally distributed data) and matched Wilcoxon tests for not normally distributed data (FMD, RHI). The longitudinal health measurements repetitively obtained during exposures were analyzed in mixed-effect models to evaluate for any exposure effect (Wald tests in mixed models). Random effects were included to account for within-subject correlation. The main parameter of interest this model (b2) effectively captures the average difference in parameter change (systolic or diastolic BP; or heart rate) in the CAP group versus FA at any time point. Outcomeit (eg, BP) = b0 + bi + b1 × timei + b2 × CAPi; where i represents the ith individual, t represents the ith repeated measurement, b0 represents the random intercept for participant i, CAP represents exposure (1 if CAP, 0 if FA), and time represents the duration of exposure at the time of measurement t. The changes in HRV parameters that occurred for each subject during individual exposures were calculated by subtracting the measurements obtained during the last 5 minutes at the end of the exposures from to those during the first 5 minutes at the start of exposures. These HRV changes were compared between exposure types (CAP vs. FA) by mixed models. All analyses were performed using the statistical software package R (version 2.14.1).

Results

Study participants (n = 29; nine women) were young (30.2 ± 8.2 years) with a mean body mass index of 27.5 ± 6.0 kg/m² and fasting glucose of 86.9 ± 6.9 mg/dL. Total cholesterol (164 ± 31 mg/dL), triglycerides (106 ± 81 mg/dL), high-density lipoprotein cholesterol (55 ± 16 mg/dL), and low-density lipoprotein cholesterol (89 ± 26 mg/dL) values were within normal ranges. Coarse PM concentrations were higher during CAP compared with FA exposures (Table 1). Mean systolic and diastolic BP levels during all exposures were 114.5 mm Hg (95% confidence interval [CI]: 111.3, 117.8) and 75.7 (95% CI: 72.6, 78.8), respectively. As demonstrated in Figures 1 and 2, both systolic (1.9 mm Hg; 95% CI: 0.96, 2.8; P < .001) and diastolic (1.9 mm Hg; 95% CI: 1.1, 2.7; P < .001) BP levels were higher throughout coarse PM compared with FA exposures. Heart rate did not differ between exposures (−0.04 beats/min; 95% CI: −0.76, 0.69;
P = .92). Confining the analyses to the 17 participants who had both exposure types (CAP and FA) performed within a 1- to 3-week period at the Dearborn site did not change the results. Systolic (2.1 mm Hg; 95% CI: 0.91, 3.3; P < .001) and diastolic (1.7 mm Hg; 95% CI: 0.7, 2.6; P < .001) BP levels remained higher throughout coarse PM compared with FA. The BP changes during exposures for the individual patients are presented in the online supplement (Online Supplement; Figure S1).

Both time and frequency domain metrics of HRV did not differ between exposures (Online Supplement; Table S1). Immediately post-CAP versus FA exposures, there were nonsignificant trends (P-values < .2) toward higher brachial and aortic systolic BP levels and reduced BAD values (conduit artery vasoconstriction), whereas aortic pulse pressure was significantly higher (Online Supplement; Table S2). There were no significant differences in these outcomes 2-hours after exposures, nor were there any exposure-related differences in vascular function (FMD, RHI) results (Online Supplement; Table S3).

Table 1
Coarse PM concentrations during exposures

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Median</th>
<th>25th Percentile</th>
<th>75th Percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filtered air*</td>
<td>15.5</td>
<td>6.36</td>
<td>2.7</td>
<td>27.4</td>
<td>15.4</td>
<td>11.7</td>
<td>18.7</td>
</tr>
<tr>
<td>Coarse CAP</td>
<td>164.2</td>
<td>80.4</td>
<td>70.4</td>
<td>439.8</td>
<td>147.5</td>
<td>119.8</td>
<td>183.1</td>
</tr>
</tbody>
</table>

CAP, concentrated ambient particles; FA, filtered air; PM, particulate matter; SD, standard deviation.

Coarse PM concentrations are in μg/m³ and determined by Teflon filter-based gravimetric mass measurements. The values represent the average concentration over the entire 2-hour period of exposures.

* Twelve of the 29 FA health outcome (placebo) responses (and PM data) were used from FA exposures performed for each of the individual participants during their initial rural Dexter study limb of the trial. In 15 FA exposures at urban Dearborn, the PM mass levels were below the detection limit at this site (6.8 μg/m³), and thus, these values were not included in the summary descriptive data above. The 1 value below this level in the table (2.7 μg/m³) comes from a FA exposure done at the rural Dexter site.

1 P-values < .01 for differences of median levels between exposure types compared by Wilcoxon ranked sum tests, respectively.

Figure 1. Systolic blood pressure levels during exposures. Mean systolic blood pressures with corresponding 95% confidence intervals measured every 7 minutes during coarse concentrated ambient particle (CAP) vs. filtered air (FA) exposures. BP, blood pressure.
comparison is time during exposure by site location interaction). These results mean that BP immediately increased and remained stably elevated during CAP inhalation at urban Dearborn, whereas at rural Dexter, CAP exposures caused a more gradual but steady rate of increase in BP over the 2-hour period.

Discussion

We have shown for the first time that the inhalation of coarse PM from an urban environment can promote a rapid elevation in BP. There was no evidence that autonomic balance or vascular function was substantively altered, and thus, the underlying mechanisms must remain speculative. Nevertheless, the demonstration that brief exposure to urban coarse particles significantly raises BP adds important mechanistic support to the emerging epidemiologic evidence that coarse PM may be capable of promoting acute cardiovascular events at the population level.8–12

Air Pollution and BP

The prohypertensive response observed in this present study (albeit small) closely parallels those we previously demonstrated after controlled exposures to fine PM at several different locations (roughly 1–3 mm Hg over 2 hours).5 It is also similar to those induced by coarse PM from a rural setting (Dexter, Michigan).7 Several controlled exposures to diesel exhaust (ie, minute particles ranging from 10 from 100 nm) have additionally shown that it can also increase BP.3 A recent meta-analysis of panel studies from locations across the world convincingly demonstrates that higher ambient levels of PM (of various size ranges) during the preceding few days are associated with similar BP elevations (ie, 1–3 mm Hg).4 Therefore, our findings corroborate and add to the totality of scientific evidence that short-term inhalation of PM air pollution regardless of particle size (ie, fine or coarse) and/or chemistry, composition, or sources (ie, rural or urban environments) is capable of promoting an increase in BP lasting from several hours to days.3–7

We did not observe the expected alteration in autonomic balance (ie, HRV parameters) as previously shown following rural coarse CAP exposures.7 Both conduit (FMD) and microvascular (RHI) endothelial function were also not affected. As such, the mechanisms responsible for the elevation in BP must remain speculative. However, data from several of our prior studies support that the most likely explanation is acute autonomic imbalance favoring heightened SNS activity triggered by inhaled particles interacting with a host of pulmonary receptors (eg, transient receptor potential channels).3,7 Other plausible mechanisms supported by prior human and animal experiments include vascular dysfunction (eg, reduced nitric oxide bioavailability), increased circulating levels of hemodynamically active mediators (eg, endothelins), and hypothalamic and/or perivascular oxidative stress and

Figure 2. Diastolic blood pressure levels during exposures. Mean diastolic blood pressures with corresponding 95% confidence intervals measured every 7 minutes during coarse concentrated ambient particle (CAP) vs. filtered air (FA) exposures. BP, blood pressure.
inflammation (eg, mediated by toll-like receptor activation by PM-modified biologic molecules).2,3,7

Several different metal and elemental particle components were associated with the increase in BP during coarse PM exposures we previously performed in a rural setting.13

Ongoing analyses of the composition of the coarse particles in this present study may help to elucidate the constituents and sources responsible for the BP elevation induced by coarse PM derived from an urban environment. Nevertheless, the fact that we observed highly similar responses at both rural and urban locations7 (despite widely different sources of the PM) suggests that the chemical nature of the inhaled coarse particles is of secondary importance in regard to its capacity to increase BP. We acknowledge that follow-up studies are needed to determine the underlying biological mechanisms and PM components responsible for the current findings.

Public Health Implications

Emerging epidemiologic evidence supports that short-term exposure to ambient coarse PM may be associated with an increased risk for cardiovascular events.8,9 Our findings provide one possible mechanism, an acute prohypertensive response, whereby the inhalation of coarse particles may be capable of triggering myocardial infarctions, heart failure exacerbations, and strokes among at-risk individuals.2 Although the hemodynamic changes were modest, increases in BP of 2–3 mm Hg among the hundreds of millions of people exposed to coarse PM worldwide on a daily basis can have a large public health impact.16 Moreover, prior studies demonstrate that certain susceptible subgroups of individuals respond with more robust elevations in BP (ie, exceeding 8–10 mm Hg) which may pose more substantial short-term health risks.9

From a clinical standpoint, health care providers should be aware that recent changes in outdoor air pollution levels may be a relevant risk factor responsible for alterations in BP levels among their patients. In conjunction with other exposures (eg, noise, temperature, and altitude changes), several factors within the environment are capable of mediating clinically relevant impacts on BP and potentially on hypertension control.17

Many regulations exist across the world for daily and annual levels of fine PM air pollution including the US National Ambient Air Quality Standards18 and the World Health Organization Air Quality Recommendations.18 On the other hand, no such enforcements have been promulgated specifically regarding coarse PM.2,8,9,18,19 Given the billions of individuals worldwide exposed to coarse PM from a variety of sources (rural, urban, desert sands),20–22 further studies regarding its independent health effects are urgently needed to optimally protect the global public health from air pollution.1,8,9 Although the concentrations of coarse PM in our controlled exposure protocol are higher than what is typically encountered in North American cities,22 total PM$_{10}$ mass (of which 30%–70% are coarse particles)8–10 can often exceed 100–500 µg/m$^3$ in developing nations (eg, China, India) on an hourly or even 24-hour average basis.20–22 Thus, the exposure protocol in this study has real-world relevance to hundreds of millions of people across the globe.

Limitations

All participants lived within 100 miles of the exposure facility location in southeastern Michigan and thus had been exposed to similar levels of ambient regional PM concentrations on a chronic basis before study enrollment. Although participants were excluded if they self-reported routine air pollution exposures (eg, secondhand smoke, occupational pollutants), it is possible that personal-level exposures occurred in the hours before study participation for which we cannot account that may have impacted the subsequent BP responses to controlled exposures. Future studies performing personal monitoring before controlled exposures could help to clarify this possibility. We did not measure health outcomes more than 2-hours after exposures as our prior fine CAP studies did not provide evidence that changes in BP (eg, by 24-hour ambulatory monitoring) or other health outcomes (eg, vascular function) induced by particle exposures persisted from 2–24 hours later.4 However, most health parameters (eg, brachial BP, arterial compliance, FMD) were not different either immediately or 2-hours post-CAP versus FA exposures in this present study, and it is therefore unlikely that this would have changed the following day. These observations support that the BP elevation induced by CAP exposures is triggered and resolves rapidly during and after particle inhalation, respectively. No participant reported any respiratory complaint during or after exposures (eg, cough, shortness of breath); however, we did not formally assess their breathing patterns. We therefore cannot rule out that CAP inhalation caused a subtle change in breathing patterns that may have played a role in elevating BP. The study was also not specifically powered to evaluate for changes in secondary outcomes (ie, endothelial function, HRV parameters). We acknowledge that the lack of observed impact of CAP compared with FA on these responses could in theory represent a lack of statistical power. As such, firm conclusions regarding their possible role in the mechanisms responsible for the BP elevations cannot be reached from this single study alone. However, in prior studies with a similar number of patients, we have observed changes in both HRV as well as FMD in response to both fine and coarse CAP.5,7 Further studies are thus warranted to more conclusively determine the underlying mechanisms involved in PM-induced BP elevations. Finally, HRV has many recognized limitations as a technique to assess autonomic balance. We plan to involve
more direct measures (ie, muscle sympathetic nerve activity by microneurography) in future studies to better assess the mechanistic role played by the autonomic nervous system.

Conclusions

Two-hour exposure to coarse PM air pollution within an urban location induces a small elevation in systolic and diastolic BP. Taken together with our prior studies and the published literature on air pollution, there is convincing evidence that both fine and coarse PM pollutants from a variety of sources are capable of raising BP.

References

Figure S1. Individual blood pressure responses during exposures. These figures are from the 23 “representative” participants with nearly or totally complete intrachamber BP data (i.e., no or few missing BP data points) where the totality of the intrachamber BP response can be adequately visualized. The figures are the individual patient responses for the delta BP (CAP–FA) at each time point during the 2-hour exposures (red = delta diastolic BP and blue = delta systolic BP). A visual inspection of the individual responses show that most patients had on-average higher systolic and diastolic levels during CAP vs. FA (greater number of delta values >0). As can be seen, only 2 of 23 patients (ID 17, ID 34) had all BP levels lower (delta BP < 0) throughout FA vs. CAP (“complete nonresponders”). BP, blood pressure; CAP, concentrated ambient particle; FA, filtered air.
Figure S1. (continued)
Table S1

Changes in heart rate variability (HRV) parameters during exposures

<table>
<thead>
<tr>
<th>HRV Outcome</th>
<th>^HRV_{first 5}</th>
<th>^HRV_{last 5}</th>
<th>\Delta HRV_{CAP} - \Delta HRV_{FA}</th>
<th>P^</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Study Cohort (n = 29)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Log SDNN (msec)</td>
<td>4.16 (0.45)</td>
<td>4.33 (0.57)</td>
<td>0.33 (0.84)</td>
<td>.39</td>
</tr>
<tr>
<td>Log HF peak (msec^2)</td>
<td>6.39 (1.22)</td>
<td>6.38 (1.34)</td>
<td>0.57 (1.15)</td>
<td>.11</td>
</tr>
<tr>
<td>Log LF peak (msec^2)</td>
<td>2.98 (1.62)</td>
<td>7.05 (0.97)</td>
<td>-0.21 (1.54)</td>
<td>.48</td>
</tr>
<tr>
<td>LF/HF ratio</td>
<td>2.08 (1.92)</td>
<td>3.36 (4.25)</td>
<td>0.45 (5.02)</td>
<td>.80</td>
</tr>
<tr>
<td>Results for subjects having both CAP and FA performed at Dearborn (n = 17)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Log SDNN (msec)</td>
<td>4.23 (0.43)</td>
<td>4.31 (0.57)</td>
<td>0.29 (0.90)</td>
<td>.14</td>
</tr>
<tr>
<td>Log HF peak (msec^2)</td>
<td>6.59 (1.01)</td>
<td>6.54 (1.13)</td>
<td>0.49 (1.19)</td>
<td>.15</td>
</tr>
<tr>
<td>Log LF peak (msec^2)</td>
<td>3.54 (1.16)</td>
<td>7.01 (0.96)</td>
<td>-0.24 (1.45)</td>
<td>.94</td>
</tr>
<tr>
<td>LF/HF ratio</td>
<td>1.73 (1.49)</td>
<td>2.44 (2.45)</td>
<td>-0.88 (2.60)</td>
<td>.47</td>
</tr>
</tbody>
</table>

CAP, coarse concentrated ambient particles; FA, filtered air; HF, high frequency power; LF, low frequency power; SDNN, standard deviation of the normal-to-normal R–R intervals.

\Delta HRV_{CAP} - \Delta HRV_{FA} represents the predefined secondary study outcome: difference between exposures types (CAP–FA) in the changes of each HRV parameter during exposure (mean of last 5 minutes minus the mean of the first 5 minutes).

* Results are mean (standard deviation) of CAP and FA results together.

P-values are the comparisons of the changes in HRV outcomes that occurred during the CAP vs. FA exposures by paired t-tests.

Table S2

Comparison of outcomes immediately after exposures

<table>
<thead>
<tr>
<th>Variable</th>
<th>Post-FA</th>
<th>Post-CAP</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Median</td>
</tr>
<tr>
<td>BAD</td>
<td>3.65</td>
<td>0.65</td>
<td>3.51</td>
</tr>
<tr>
<td>SBP</td>
<td>107.93</td>
<td>10.41</td>
<td>108</td>
</tr>
<tr>
<td>DBP</td>
<td>70.85</td>
<td>8.78</td>
<td>69</td>
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<tr>
<td>HR</td>
<td>60.07</td>
<td>6.99</td>
<td>63</td>
</tr>
<tr>
<td>aSBP</td>
<td>97.19</td>
<td>10.69</td>
<td>97</td>
</tr>
<tr>
<td>PP</td>
<td>25.59</td>
<td>4.91</td>
<td>25</td>
</tr>
<tr>
<td>AP</td>
<td>4.67</td>
<td>4.65</td>
<td>5</td>
</tr>
<tr>
<td>AIX@75</td>
<td>9.62</td>
<td>13.94</td>
<td>12.5</td>
</tr>
<tr>
<td>PWV</td>
<td>6.5</td>
<td>2.13</td>
<td>6.45</td>
</tr>
</tbody>
</table>

AIX@75, aortic augmentation index at a heart rate of 75 beats/min (%); AP, aortic augmentation pressure (mm Hg); aSBP, aortic systolic BP (mm Hg); BAD, brachial artery diameter (cm); CAP, concentrated ambient particle; DBP, brachial diastolic blood pressure (mm Hg); FA, filtered air; HR, heart rate (beats/min); IQR, interquartile range; max, maximum result; min, minimal result; PP, aortic pulse pressure (mm Hg); PWV, carotid-femoral pulse wave velocity (m/sec); SBP, brachial systolic blood pressure (mm Hg); SD, standard deviation.

P-values represent comparisons of the mean (or median for Wilcoxon test) of the post-CAP vs. post-FA outcome variables.
Table S3
Comparison of vascular reactivity test results 2 hours after exposures

<table>
<thead>
<tr>
<th>Variable</th>
<th>Post-FA</th>
<th>Post-CAP</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Median</td>
</tr>
<tr>
<td>RHI</td>
<td>2.09</td>
<td>0.83</td>
<td>2.08</td>
</tr>
<tr>
<td>eNMD</td>
<td>2.54</td>
<td>1.18</td>
<td>2.32</td>
</tr>
<tr>
<td>FMD-Peak</td>
<td>8.43</td>
<td>3.60</td>
<td>8.44</td>
</tr>
<tr>
<td>NMD</td>
<td>12.82</td>
<td>6.61</td>
<td>15.12</td>
</tr>
</tbody>
</table>

CAP, concentrated ambient particle; eNMD, endoPAT2000 determined nitroglycerin-mediated dilatation; FA, filtered air; FMD-peak, peak flow-mediated dilatation of the brachial artery (%); IQR, interquartile range; max, maximum result; min, minimal result; NMD, peak nitroglycerine-mediated dilatation of the brachial artery (%); RHI, reactive hyperemia index; SD, standard deviation.

P-values represent comparisons of the mean (or median for Wilcoxon test) of the post-CAP vs. post-FA outcome variables.