The Association Between Personal Measurements of Environmental Exposure to Particulates and Heart Rate Variability

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Background. Epidemiologic evidence indicates that airborne particulates are associated with mortality risk, predominately from heart disease. This may occur through changes in the cardiac autonomic nervous system, witnessed by changes in heart rate variability.

Methods. This short-term longitudinal study used continuous personal particulate matter measurements to examine the effects of exposure to particulate matter less than 2.5 μm in diameter ($PM_{2.5}$) on heart rate and rate variability in 20 relatively young, healthy male workers. Continuous exposure and cardiac monitoring were performed on each subject on a nonwork day. The 5-minute standard deviation of the normal-to-normal interval was used as the main measure of heart rate variability.

Results. Mixed-effects regression models estimate an average 1.4% (95% confidence limits = −2.1, −0.6) decrease in the 5-minute standard deviation of the normal-to-normal interval for each 100 $\mu g/m^3$ increase in the 3-hour $PM_{2.5}$ moving average, and small increases in heart rate, after adjustment for potential confounding factors. Predicted effects of exposure were greatest using the 3-hour averaging interval for $PM_{2.5}$ and decreased in magnitude using shorter and longer intervals.

Conclusions. These results reveal an association between cardiac autonomic function and environmental $PM_{2.5}$ exposure. These observed associations may result from decreased vagal or increased sympathetic tone.

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Key words: particulate matter, $PM_{2.5}$, heart rate variability, cardiac autonomic function.

A number of health outcomes have been associated with particulate air pollution.[1–4] Cardiopulmonary disease has been identified as one of the main sources of morbidity and mortality associated with exposure to particulates.[4–7] One potential mechanism for those effects involves alterations in cardiac autonomic function. To date, those investigations have used elderly subjects and have not included personal exposure measurements. This study was designed to examine the magnitude of the effect of continuous personal measurements of environmental particulate matter with a mean aerodynamic diameter ≤2.5 μm ($PM_{2.5}$) on cardiac autonomic function, using standard heart rate variability (HRV) parameters.

The mechanisms responsible for the cardiac morbidity and mortality associated with particulate air pollution have not been elucidated fully. One potential mechanism is through the disruption of the autonomic nervous system.[8] The alteration in the autonomic nervous system may be induced directly through a sympathetic stress response[9] or indirectly by inflammatory cytokines produced in the lungs and released into the circulation.[10,11] These proposed mechanisms have been developed in part through the investigation of compromised animal models. Watkinson *et al.*[12] have induced arrhythmias in rat models of pulmonary hypertension after exposures to particles.

Cardiac autonomic function can be characterized using several standard heart rate variability measures in the time

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domain. Standard 5-minute HRV measurements can be collected noninvasively and afford the researcher insights into the function of the autonomic nervous system.[13] The 5-minute standard deviation (SD) of normal-to-normal intervals (SDNN) is used in this study as the main HRV indicator, representing all variation occurring within the 5-minute interval. It provides an overall measure of the parasympathetic and sympathetic components of the cardiac autonomic nervous system.

The clinical value of HRV measures has been studied in survivors of myocardial infarction. Low heart rate variability in the months after a myocardial infarction has been associated with increased mortality.[14,15] In general population cohorts, low HRV has also been associated with both increased risk of cardiac events and all-cause mortality.[16–18]

We used personal $PM_{2.5}$ measurements obtained with a continuous real-time monitor to investigate the effects of particulate matter on cardiac autonomic function in a group of relatively young boilermaker construction workers on a day when they were not working. Moving $PM_{2.5}$ averages served as the exposure metrics in this study and were generated using the continuous 5-minute $PM_{2.5}$ data. We regressed both the 5-minute SDNN and 5-minute heart rate on these exposure metrics and on the function of the cardiac autonomic nervous system.

Methods

Study Subjects

The Institutional Review Board of the Harvard School of Public Health approved this study, and written informed consent was obtained. The study population consisted of 20 male (apprentice/journeyman) boilermaker construction workers. These 20 subjects, a self-selected subset from a larger occupational cohort, consented to monitoring on a day when they were not working. We used a self-administered questionnaire to collect information on medical history, including respiratory and cardiac systems, and on subjects' use of prescription and nonprescription medications.

Exposure Assessment

Exposures included ambient air pollution and multiple indoor sources of pollutants, including tobacco smoke, cooking, and cleaning. Monitoring for 16 of the 20 subjects took place between June and August 1999; an additional 3 subjects were monitored in October 1999 and 1 subject was monitored in December 1999. Each subject was monitored for one 24-hour period. Continuous $PM_{2.5}$ monitoring was conducted throughout the 24-hour monitoring period with a TSI Inc. DustTrak (Shoreview, MN), which measures airborne particles using light-scattering technology. It has a range of 0.001–100 mg/m^3 and can measure particles from 0.1 to 10 μm in size. The response of the DustTrak is linear over the size range of particles investigated in this study. This is apparently the first health-effects study to make use of the DustTrak. The monitor was placed in a padded pouch and the inlet tubing secured in the participant's breathing zone. The monitor ran throughout the 24-hour observation period. Subjects were instructed to wear the monitor while they were awake and to place the monitor on a nightstand next to their bed while they were sleeping, keeping the inlet as close as possible to their breathing zone. The monitor was programmed to record measurements every 10 seconds and to report 5-minute averages. Moving averages from 15 minutes to 9 hours were generated using these 5-minute averages.

Continuous Holter Monitoring and Tape Processing

We performed continuous heart rate monitoring using a five-lead Holter monitor, Model Dynacord 3 Channel Model 423 (Raytel Cardiac Services, Windsor, CT). Each participant's skin was shaved if necessary, cleansed, and slightly abraded to ensure proper lead contact. Electrodes were placed in a modified V1 and V5 position. Each subject was given a daily diary to record any symptoms such as chest pain and shortness of breath, as well as activities such as eating and sleeping.

Each 24-hour tape was sent to Raytel Cardiac Services (Windsor, CT) and analyzed using a Delmar Avionics (Irvine, CA) Model Strata Scan 563. Only beats with a rate ratio (*ie*, normal-to-normal) interval of 0.6–1.5 seconds and a rate ratio of 0.8–1.2 were included in the analysis. Trained personnel performed all analyses, and all normal and abnormal findings could either be accepted or rejected on the basis of standard criteria to ensure quality control. Tapes were analyzed in the time domain, and reports summarizing heart rhythm, rate analysis, and ST changes were generated. The mean heart rate and the SDNN were calculated in 5-minute segments for the entire recording.

Statistical Methods

We used mixed-effects regression models (SAS Version 8[19]) to investigate the effects of $PM_{2.5}$ on heart rate variability parameters. Previous studies have reported that heart rate variability is associated with $PM_{2.5}$ exposure in the preceding few hours.[5] Limited reports in elderly subjects found that a 4-hour average has the strongest correlation, although a recent study has reported even shorter averaging times (2 hours).[20] To address this issue, we examined averaging times ranging from 15 minutes to 9 hours, although the primary hypothesis of the present study was focused on averaging times of 2–4 hours. The $\log_{10}$-transformed response variables, 5-minute heart rate, and 5-minute SDNN were regressed on these moving averages. The response variables were $\log_{10}$ transformed to improve normality and

TABLE 1. Summary Statistics Stratified by Current Smoking Status

	Smokers	Nonsmokers
Number of Subjects	9	11
Age (years)		
Mean	42 ± 15	44 ± 11
Range	21–58	21–58
Years as boilermaker		
Mean	17 ± 16	20 ± 12
Range	0–40	1–34
Heart rate (5-minute mean, beats/minute)	79 ± 6	81 ± 11
SDNN (5-minute mean, ms)	56.6 ± 22.2	58.1 ± 17.9
SDNN (5-minute mean, ms), $\log_{10}$ (msec)	1.7 ± 0.2	1.71 ± 0.2

Data presented are mean ± standard deviation unless otherwise indicated. SDNN = standard deviation of normal-to-normal intervals.

stabilize the variance. A random effect for each study subject, as well as fixed covariates such as time of day, smoking status, age, and heart rate, were included in the models. The modifying effects of individual characteristics such as hypertension were also investigated. Analyses examining the effects of outliers on regression results were also performed.

Results

The study population consisted of 20 white men, 9 of whom were current smokers (Table 1). Their average age was 43 years (SD = 12.7 years), and they had spent an average of 19 years (SD = 14) as boilermakers. Their mean heart rate was 80 beats per minute (SD = 9 beats per minute).

The arithmetic mean $PM_{2.5}$ concentration over the 24-hour period was 150 $\mu g/m^3$ (SD = 292 $\mu g/m^3$) (Table 2). As expected, smokers had a higher mean $PM_{2.5}$ exposure than nonsmokers, with an arithmetic mean of 216 $\mu g/m^3$ (SD = 404 $\mu g/m^3$) compared with 96 $\mu g/m^3$ (SD = 158 $\mu g/m^3$) in the nonsmokers. All nonsmoking subjects lived with other nonsmokers except for one nonsmoker who lived with four current smokers. After excluding this particular subject, the mean $PM_{2.5}$ exposure measured in nonsmokers was reduced to 49 $\mu g/m^3$ (SD = 35 $\mu g/m^3$).

TABLE 2. Summary of Exposure Intensities Averaged over the 24-hour Measurement Period for All Subjects, Stratified by Current Smoking Status

	$PM_{2.5}$ Arithmetic Mean*, $\mu g/m^3$	$PM_{2.5}$ Geometric Mean*, $\mu g/m^3$	$PM_{2.5}$ Range, $\mu g/m^3$
Smokers (N = 9)	216 ± 404	61 ± 3813	19–1269
Nonsmokers (N = 11)	96 ± 158	47 ± 2582	23–566
Excluding one nonsmoker living with smokers (N = 10)	49 ± 35	37 ± 1733	23–138

Data are presented as mean ± standard deviation.

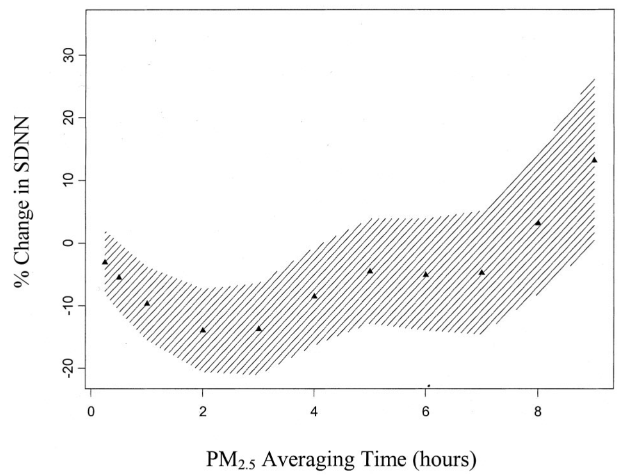

FIGURE 1. Percent change in the 5-minute standard deviation of the normal-to-normal interval (SDNN) for every 1 mg/m^3 increase in the $PM_{2.5}$ moving average (triangles). Ninety-five per cent confidence intervals are shaded. Model adjusted for time of day, age, and current smoking status.

The effects of the various moving averages of exposure on heart rate variability (presented as a percentage decrease or increase in the 5-minute SDNN) are plotted in Figure 1. There are small associations between the 5-minute SDNN and the 15-minute averaging interval. A maximum decrease in the 5-minute SDNN is observed using the 3-hour averaging interval. The association weakens using averaging intervals from 4 to 7 hours. Using 8-hour and 9-hour moving average intervals, the observed association becomes positive, indicating increases in heart rate variability with increases in $PM_{2.5}$ exposure.

The 3-hour $PM_{2.5}$ moving average was chosen as the main exposure metric, as its effects were the largest in magnitude and most comparable with recently published investigations.[5,21] On the basis of the mixed-effects regression model, an average 1.4% decrease (95% confidence limits [CL] = −2.1, −0.6) in heart rate variability for every 100-$\mu g/m^3$ increase in the 3-hour $PM_{2.5}$ moving average was estimated (Table 3). The decreases are similar in direction and magnitude when stratified by current smoking status. However, after excluding the one nonsmoker living with smokers, the mean decrease is only 0.7% (95% CL = −3.1, 1.8).

The association between the 3-hour $PM_{2.5}$ moving average and the 5-minute heart rate is also summarized in Table 3. Small effects were observed. For the 20 subjects as a whole, there was no mean increase (0.0%; 95% CL = −0.2, 0.2) in heart rate associated with an increase of 100 $\mu g/m^3$ in the 3-hour $PM_{2.5}$ moving average after adjusting for time of day, age, and current smoking status as a

TABLE 3. Mean Heart Rate and Heart Rate Variability (SDNN) as a Function of 3-Hour Moving $PM_{2.5}$ Average

	$\log_{10}$ 5-Minute SDNN*†		$\log_{10}$ 5-Minute Heart Rate*‡	
	Mean	95% CL	Mean	95% CL
Smokers	−1.5	−2.5, −0.4	0	−0.3, 0.3
Nonsmokers	−1.2	−2.3, −0.2	−0.1	−0.4, 0.3
Excluding one nonsmoker living with smokers	−0.7	−3.1, 1.8	1.9	1.2, 2.7

SDNN = standard deviation of normal-to-normal intervals; 95% CL = 95% confidence limits.
* Coefficients expressed as % change/100 $\mu g/m^3$.
† Models adjusted for: time, age, and $\log_{10}$ heart rate.
‡ Model adjusted for: time and age.

dichotomous variable. The nonsmoking subgroup (excluding the one individual who lived with other smokers) experienced an average 1.9% increase (95% CL = 1.2, 2.7) in heart rate for every 100-$\mu g/m^3$ increase in the 3-hour moving average after adjustment for confounding variables.

The same models investigating the effects of the 3-hour moving $PM_{2.5}$ average on the $\log_{10}$ SDNN and the $\log_{10}$ heart rate were rerun with the top 5% and bottom 5% of the 3-hour moving $PM_{2.5}$ averages removed to examine the effects of outlying exposures (Table 4). The association became stronger for all subjects combined, with a mean 2.3% decrease (95% CL = −3.7, −0.9) in the heart rate variability for a 100-$\mu g/m^3$ increase in the 3-hour $PM_{2.5}$ moving average. The association in nonsmokers increases, and the greatest association is now observed in the nonsmokers' subgroup (excluding the one nonsmoker living with smokers). This subgroup showed a mean 9.5% decrease (95% CL = −14.5, −4.5) in the 5-min SDNN with every 100 $\mu g/m^3$ increase in the 3-hour $PM_{2.5}$ moving average.

When the outlying exposures were removed, the association between the $PM_{2.5}$ moving average and heart rate was also stronger. For all subjects there was a 1.2% increase (95% CL = 0.7, 1.6) associated with a 100-$\mu g/m^3$ increase in the 3-hour $PM_{2.5}$ moving average. The largest increase in heart rate, 4.7% (95% CL = 3.1, 6.2) for every 100 $\mu g/m^3$ increase in the 3-hour moving average, was observed among the nonsmoking subgroup (excluding the one nonsmoker living with smokers).

The modifying effect of hypertension on the observed association between $PM_{2.5}$ and both heart rate and SDNN was investigated. Five of the 20 men reported having been diagnosed by a physician with hypertension, although none was currently taking medication for this condition. There was little difference between the normotensive smokers and nonsmokers, with both groups experiencing decreases in the 5-minute SDNN similar to those reported in Table 3. The three hypertensive nonsmokers had a median SDNN of 38 ms, whereas the two hypertensive smokers had a median SDNN of 33 ms. For comparison, the normotensive nonsmokers had a median SDNN of 57 ms whereas the normotensive smokers had a median SDNN of 54 ms. There was little difference in median heart rate between hypertensive smokers and nonsmokers and between normotensive smokers and nonsmokers.

Discussion

This study used continuous personal monitors to study the effects of ambient $PM_{2.5}$ on heart rate variability among a relatively young cohort. Previous studies have used broad-area $PM_{2.5}$ monitoring and have focused specifically on elderly, compromised populations.[5,6]

Personal $PM_{2.5}$ measurements observed in this study are higher than ambient-area measurements in the suburbs of Boston, but are similar to personal $PM_{2.5}$ measurements reported by Lebret *et al.*[22] and Spengler *et al.*[23] These researchers reported average $PM_{2.5}$ levels ranging from 20 to 30 $\mu g/m^3$ in nonsmoking homes and levels ranging from 30 to 60 $\mu g/m^3$ in smoking homes. In our study, smoking subjects had the highest geometric mean $PM_{2.5}$ averaged over the 24-hour monitoring period at 61 $\mu g/m^3$, with environmental tobacco smoke presumably being the main indoor source. The nonsmoking subjects (excluding the one nonsmoker living with smokers) had a geometric mean $PM_{2.5}$ averaged over the 24-hour monitoring period of 37 $\mu g/m^3$, approximately two to three times the daily ambient average in Boston. Indoor sources of $PM_{2.5}$ other than environmental tobacco smoke, such as cooking and cleaning, may have also contributed to these levels.[24,25]

TABLE 4. Mean Heart Rate and Heart Rate Variability (SDNN) as a Function of 3-Hour Moving $PM_{2.5}$ Average After Removing Top 5% and Bottom 5% of the 3-Hour $PM_{2.5}$ Moving Average Data Points

	$\log_{10}$ 5-minute SDNN*†		$\log_{10}$ 5-minute Heart Rate*‡	
	Mean	95% CL	Mean	95% CL
Smokers	−3.1	−5.0, −1.2	0.6	0.0, 1.1
Nonsmokers	−0.5	−2.9, 1.8	2.2	1.4, 2.9
Excluding one nonsmoker living with smokers	−9.5	−14.5, −4.5	4.7	3.1, 6.2

SDNN = standard deviation of normal-to-normal intervals; 95% CL = 95% confidence limits.
* Coefficients expressed as % change/100 $\mu g/m^3$.
† Models adjusted for: time, age, and $\log_{10}$ heart rate.
‡ Model adjusted for: time and age.

The changes in HRV associated with the 3-hour moving average in this group of 20 individuals are greater than those observed in our previous analysis of the association between occupational and environmental exposure to particulates and HRV.[21] The 20 subjects in the present paper are a self-selected subset of an occupational cohort of 40 subjects. These 20 subjects do not differ from the larger occupational cohort in mean age, mean number of years worked as a boilermaker, or smoking history. The figure illustrating the effects of the various-length moving averages on the 5-minute SDNN is similar to that observed in the analysis of the entire cohort, up to 4 hours. The effects of $PM_{2.5}$ on HRV using longer moving averages (more than 4 hours) are smaller in this study, whereas the association continued to increase using longer averaging intervals in the larger cohort. Our previous study,[21] which examined the entire cohort, considering both non-work-place exposures and comparatively large work-place exposures (welding fume and residual oil fuel ash) to $PM_{2.5}$, revealed a mean decrease of 0.5% (95% CL = −0.7, −0.2) in heart rate variability for every 100 $\mu g/m^3$ increase in the 3-hour moving $PM_{2.5}$ average. When the exposures are limited to ambient and indoor sources in this study, the observed mean decrease in heart rate variability is 1.4% (95% CL = −2.1, −0.6). This is nearly a three-fold increase in the magnitude of the association when the environmental exposures are considered alone in this group of men. The differences between the two analyses may reflect the overall differences in the time course of action, the mechanism of action, and the overall toxicity of particles derived from the workplace compared with those found in ambient and indoor air pollution.

These results can be compared with those obtained by Gold *et al.*[5] in their study of the effects of ambient $PM_{2.5}$ on heart rate variability in 21 active Boston residents age 53–87 years. They reported an overall 0.26-ms decrease in the 6-minute SDNN for a 14.4-$\mu g/m^3$ increase in the 4-hour average $PM_{2.5}$ after controlling for heart rate. This is a 1.8-ms decrease for every-100 $\mu g/m^3$ increase in the 4-hour $PM_{2.5}$ average. To facilitate comparison with our study, we reanalyzed our data using the linear 5-minute SDNN as the outcome measure and regressed it on both the 3-hour and 4-hour moving $PM_{2.5}$ averages. Using the linear 5-minute SDNN, our data revealed a 1.9-ms decrease for every 100-$\mu g/m^3$ increase in the 4-hour $PM_{2.5}$ moving average and a 2.6-ms decrease for every 100-$\mu g/m^3$ increase in the 3-hour $PM_{2.5}$ moving average. The decreases associated with the 4-hour moving average in both studies are remarkably similar considering the overall profile of the two age groups studied.

Recognizing that the strata are small, these results suggest little modification by smoking status until outlying exposures have been removed. The magnitude of most effects on heart rate and rate variability increase with exclusion of these outlying exposures, especially among the nonsmoking subgroup (excluding one nonsmoker living with smokers). These results could imply that nonsmokers who are not consistently exposed to environmental tobacco smoke are particularly susceptible to low levels of environmental $PM_{2.5}$. Furthermore, these results could also suggest that smokers are, in some way, less susceptible to environmental $PM_{2.5}$ than nonsmokers. These results need to be confirmed in larger studies.

Again, although the strata are small, there is a suggestion that the associations outlined above are also modified by hypertension. Susceptible populations, including those with preexisting cardiopulmonary disease, have been identified in both animal and human populations,[6,9,12] and the effects of hypertension should be given further consideration in future studies.

Limitations

The observed response to non-work-place environmental particle exposures are different from that reported in our earlier study.[21] This finding may be due to several factors that were not quantified in this study. The particle composition between the two environments is not identical. Work-place particles were dominated by residual fuel oil ash and metal fume derived from welding, whereas the exposures away from work were derived from multiple sources and are likely to represent a more varied composition. Although metals and residual oil fly ash are constituents of ambient $PM_{2.5}$, they do not constitute its entirety.[26]

In addition, personal measurements of other copollutants were not gathered in this study. Confounding by other environmental copollutants such as carbon monoxide, sulfur dioxide, ozone, and nitrogen dioxide is a concern. This concern is moderated by the report of Sarnat *et al.*[27] regarding their assessment of the association between personal particulate and gaseous exposures. They report that personal $PM_{2.5}$ exposures are not well correlated with personal exposures to ozone, nitrogen dioxide, and sulfur dioxide in a group of nonsmokers. With little association between the personal $PM_{2.5}$ measurements and personal gaseous copollutants, the potential for confounding is minimized. They did not measure carbon monoxide, however, and whether a similar copollutant pattern for carbon monoxide exists in a mixed group of smokers and nonsmokers is unclear.

Also, the observed $PM_{2.5}$ exposure patterns in our first study,[21] including both work and nonwork exposures, and this study, which only includes exposures away from work, are somewhat different. The pattern of particle exposure at work included large spikes in $PM_{2.5}$ due to welding and other work activities, whereas the exposures away from work contained few spikes mainly due to smoking. An individual's physiologic response to these varied profiles may account for some of the difference shown between our two studies.

This study reveals alterations in cardiac autonomic control associated with environmental $PM_{2.5}$ exposure. Theses changes in young, otherwise healthy adult males have not been fully explored, although evidence from general population cohorts does indicate an increased risk of cardiac events and all-cause mortality associated with these changes.

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