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Short-Term Effects of Air Pollution on Heart Rate Variability in Senior Adults in Steubenville, Ohio

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Learning Objectives

- Recall what previous studies have suggested or demonstrated about relationships among altered heart rate variability (HRV), cardiovascular disorders, and exposure to air pollutants.
- Define the relationships found in this study of older persons, most of whom had cardiovascular disease, between ambient levels of traffic-related and non-traffic-related air pollutants and HRV.
- Point out whether the effects of air pollution vary according to medication usage, and whether and how they alter cardiac autonomic function.

Abstract

Objective: We examined the association between ambient air pollution levels and heart rate variability (HRV) in a panel study of 32 subjects. **Methods:** We used linear mixed models to analyze the effects of fine particles ($PM_{2.5}$), sulfate (SO_4^{2-}), elemental carbon (EC), and gases on log-transformed standard deviation of normal RR intervals (SDNN), mean square of differences between adjacent RR intervals (r-MSSD), and high- and low-frequency power (HF, LF). **Results:** An interquartile range (IQR) increase of $5.1 \mu g/m^3$ in SO_4^{2-} on the previous day was associated with a decrease of -3.3% SDNN (95% confidence = -6.0% to -0.5%), -5.6% r-MSSD (-10.7% to -0.2%), and -10.3% HF (-19.5% to -0.1%). Associations with total $PM_{2.5}$ were similar. HRV was not associated with EC, NO_2 , SO_2 , or O_3 . **Conclusion:** In addition to traffic-related particles, elevated levels of sulfate particles may also adversely affect autonomic function. (J Occup Environ Med. 2006;48:780-788)

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This work is supported by funding from the National Institute of Environmental Health Sciences (ES-09825 and ES-00002), the U.S. Environmental Protection Agency (R826780-01-0 and R827353-01-0), the Ohio Coal Development Office (CDO/D-98-2), and the U.S. Department of Energy's National Energy Technology Laboratory Award No. DE-FC26-00NT40771.

Any opinions, findings, conclusions, or recommendations expressed here are those of the authors and do not necessarily reflect the views of the U.S. Department of Energy.

Heike Luttmann-Gibson has no commercial interest related to this article.

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DOI: 10.1097/01.jom.0000229781.27181.7d

Acute exposure to increases in ambient air pollution have been associated with increased cardiovascular mortality¹⁻⁴ and morbidity,^{5,6} including increased subclinical indicators such as heart rate⁷⁻¹⁰ and blood pressure,¹¹⁻¹⁴ increased risk of cardiac arrhythmias^{15,16} and myocardial infarction,¹⁷⁻²⁰ ST-segment depression,²¹ and decreased heart rate variability (HRV).^{8,10,22-28} HRV varies with autonomic tone, and reduced HRV is believed to be either in the pathway leading to increased cardiac risk or, alternatively, a marker of poor health.

Reduced HRV as a patient characteristic has been prospectively associated with the development of clinically significant cardiovascular disease,²⁹⁻³¹ and short-term HRV changes may also have clinical significance. HRV was decreased in patients in the period immediately before ischemic sudden death³² and increased low-frequency/high-frequency (LF/HF) ratios have been reported immediately before the onset of ventricular tachycardias,³³⁻³⁵ suggesting that shorter-term increased sympathetic and reduced parasympathetic activity may trigger cardiac arrhythmias.

Although some studies investigating the relation of ambient pollution with HRV have specifically connected traffic-associated particle pollution with reduced HRV,¹⁰ less is known about the specific effects of nontraffic-related pollution on HRV. In a study of elders living near a major inner city roadway in Boston, the effect of traffic-related black carbon (BC) on reduced HRV predominated.¹⁰ In this study of elders in the small industrial town of Steuben-

ville, Ohio, we examined the association of acute nontraffic- as well as traffic-related air pollution exposures with repeatedly measured HRV using sulfate (SO_4^{2-}) as a marker of nontraffic pollution.³⁶

Subjects and Methods

Study Population and Protocol

Thirty-two nonsmoking senior adults from Steubenville, Ohio, were recruited to participate in a study on air pollution and cardiovascular health during the summer and fall of 2000. Most participants lived in one of three centrally located, subsidized apartment buildings. Before inclusion in the study, a screening appointment was held to collect information on cardiovascular and respiratory health and medications and to obtain baseline electrocardiogram (12-lead MAC6; Marquette Medical Systems Inc.) recordings. Exclusion criteria included smoking, having a pacemaker, a recent acute coronary syndrome, atrial flutter, or atrial fibrillation.

The study design was reviewed and approved by the human subjects committees of the Brigham and Women's Hospital and the Harvard School of Public Health.

Study participants were seen weekly on the same day of the week and at the same time during summer (June 4–August 18) and fall (September 25–December 15) of 2000. A short questionnaire on recent symptoms, hospital or doctor's visits, and medication use was administered followed by Holter electrocardiogram monitoring (SEER MC; GE Medical Systems) with electrodes in a modified V5 and AVF position. The Holter monitoring protocol included: 1) 5 minutes of rest in a supine position; 2) three supine blood pressure (BP) measurements (NIBP Vital Signs Monitor; Welch Allyn); 3) 5 minutes of standing with three standing BP measurements taken after 2 minutes; 4) 5 minutes of exercise (walking) outdoors (weather and health permitting); 5) 5 minutes of rest in a supine position; and 6) 2 minutes and 20 seconds of paced breathing.

TABLE 1
Participant Characteristics ($n = 32$)

Characteristic	Mean	Range
Number of visits	20.2	4–24
Age (yrs)	70.8	54–90
Body mass index (kg/m^2)	31.4	21–47
Characteristic	No.	Percent
Gender		
Male	3	9
Female	29	91
Race/ethnicity		
Black	10	31
White	22	69
Diagnoses		
Angina	6	19
Myocardial infarction	7	22
Coronary artery disease*	11	34
Congestive heart failure	6	19
Diabetes	7	22
Hypertension	23	72
Chronic obstructive pulmonary disease	9	28
Medications used†		
Beta-blocker	12	38
Calcium channel blocker	11	34
Statin	9	28
Angiotensin converting enzyme inhibitors	11	34
Digoxin	3	9
Any of the listed medications	21	66

*Angina or myocardial infarction.

†Medication use is defined as reported at least once during the study.

The Holter tapes were analyzed using a Marquette MARS Workstation (GE Medical Systems) with a 125 samples/s sampling rate following HRV guidelines.³⁷ The Holter tapes were analyzed for time-domain HRV measures, including the standard deviation of normal RR intervals (SDNN), the mean square of differences between adjacent RR intervals (r-MSSD), and the percent of RR intervals more than 50 msec different from the prior interval (PNN50), and frequency-domain HRV measures, including LF power and HF power. HRV and average heart rate was obtained for the whole protocol and for each separate interval.

Air Pollution Concentration and Meteorologic Measurements

Hourly $\text{PM}_{2.5}$ (TEOM 1400A; Rupprecht and Patashnick, East Greenbush, NY), ozone (O_3 ; API, model 400 UV), nitrogen dioxide (NO_2 ; API, model 200A Chemiluminescent), sul-

fur dioxide (SO_2 ; API, model 100UV fluorescent), and carbon monoxide (CO ; API, model 300 GFC) concentrations, temperature, relative humidity, and dew point were obtained from a centrally located ambient monitoring site at the Franciscan University of Steubenville operated by CONSOL Energy Inc. Research & Development.

We calculated apparent temperature as: $-2.653 + (0.994 \times \text{Ta}) + (0.0153 \times \text{Td}^2)$, in which Ta is the air temperature and Td is the dew point.

We also collected 24-hour integrated $\text{PM}_{2.5}$, SO_4^{2-} , EC, and gaseous pollutant (O_3 , NO_2 , SO_2) samples beginning at 9 AM each day (except Saturday) using a Harvard multipollutant monitor.³⁸ $\text{PM}_{2.5}$ was measured gravimetrically. CONSOL analyzed the SO_4^{2-} , O_3 , NO_2 , and SO_2 filters using ion chromatography and EC filters using thermal optical transmission. The concentration of nonsulfate $\text{PM}_{2.5}$ was calculated as the difference between the measured $\text{PM}_{2.5}$ and sulfate concentrations with

sulfate assumed to be in the form of ammonium sulfate ($[\text{NH}_4]_2\text{SO}_4$), that is: nonsulfate $\text{PM}_{2.5} = \text{PM}_{2.5} - (\text{SO}_4^{2-} \cdot 132/96)$.

Statistical Methods

We examined the associations between air pollution and log-transformed HRV parameters and HR over the entire 30-minute protocol with linear mixed models, including random subject effects, fixed effects of pollution, age, gender, race, obesity (defined as body mass index $>30 \text{ kg/m}^2$), season, time of day, apparent temperature, and a first-order autoregressive process for the within-subject residuals.³⁹ In the main analysis, 24-hour integrated pollution measurements (ending at 9 AM on the day of the electrocardiogram recording) were used as the exposure variable. Exposures also were assessed using moving averages (4–72 hours) of $\text{PM}_{2.5}$ and gaseous pollutant hourly concentrations before the electrocardiogram.

We assessed effect modification by medical conditions and medication intake in regression models, including interaction terms between air pollution effects and potential effect modifiers. Results are restricted to r-MSSD as an outcome and $\text{PM}_{2.5}$ and SO_4^{2-} as exposure variables. Hypertension, coronary artery disease (angina or myocardial infarction), and congestive heart failure were defined as subject-specific conditions. Medication intake was defined as a time-varying condition. Results were similar when we defined medication intake as subject-specific (subject defined as "on medication" when medication was taken on most days).

Results are reported as estimated percent differences and 95% confidence interval (CI) in HRV or heart rate associated with an interquartile range (IQR) increase in each pollutant. All analyses were done with SAS software version 9.1 (SAS Institute, Inc., Cary, NC).

TABLE 2

Average Heart Rate Variability (HRV) and Average Heart Rate During 30-Minute Protocol for 32 Subjects (638 valid measurements)

	No.	Mean (standard deviation)
SDNN (ms)	638	86.4 (32.6)
r-MSSD (ms)	638	36.3 (37.4)
PNN50 (%)	638	7.7 (13.5)
High frequency (ms^2)	634	239 (425)
Low frequency (ms^2)	635	355 (589)
Heart rate (beats/min)	638	79.7 (12.0)

TABLE 3

Average Air Pollution Concentrations During the Two Study Periods (June 1–August 25, 2000 and September 20–December 15, 2000)

	Pollutant	No.	Mean	Percentile		Interquartile Range
				25th	75th	
Daily data 9 AM to 9 AM	$\text{PM}_{2.5}$ ($\mu\text{g}/\text{m}^3$)	137	19.7	11.6	25.0	13.4
	SO_4^{2-} ($\mu\text{g}/\text{m}^3$)	133	6.9	3.3	8.5	5.1
	Nonsulfate $\text{PM}_{2.5}$ ($\mu\text{g}/\text{m}^3$)	133	10.0	6.3	11.5	5.3
	EC ($\mu\text{g}/\text{m}^3$)	127	1.1	0.7	1.3	0.6
	NO_2 (ppb)	133	10.5	6.0	13.4	7.3
Hourly data Averaged over Calendar days	SO_2 (ppb)	134	4.1	0.4	4.7	4.3
	O_3 (ppb)	134	22.2	12.1	28.5	16.4
	$\text{PM}_{2.5}$ ($\mu\text{g}/\text{m}^3$)	118	20.0	11.3	26.5	15.2
	NO_2 (ppb)	113	10.9	7.4	14.7	7.3
	SO_2 (ppb)	151	10.8	5.4	13.2	7.8
	O_3 (ppb)	144	27.3	15.7	36.3	20.6

TABLE 4

Pearson Correlation Coefficients Between Daily Air Pollution Concentrations During the Two Study Periods (June 1–August 25, 2000 and September 20–December 15, 2000)

	SO_4^{2-}	Nonsulfate $\text{PM}_{2.5}$	EC	NO_2	SO_2	O_3
$\text{PM}_{2.5}$	0.90	0.87	0.59	0.40	0.33	0.23
SO_4^{2-}		0.57	0.47	0.24	0.31	0.36
Nonsulfate $\text{PM}_{2.5}$			0.62	0.54	0.31	0.01
EC				0.54	0.38	-0.10
NO_2					0.26	-0.29
SO_2						-0.03

Results

Study Population

Of 53 subjects screened, 32 were recruited for the study. There were 645 health visits, with an average of 20 (range, 4–24) per subject (Table 1). The mean age at screening was 71 years; 91% of the participants were female, and 69% were white. Most participants (84%) had one or more cardiovascular condition, and two thirds were on one or more medications (Table 1). Twenty subjects (63%) with body mass index greater

than 30 kg/m^2 were classified as obese. Average HRV and heart rate measurements are listed in Table 2.

Ambient Air Pollutant Concentrations

Daily mean ambient air pollution concentrations are summarized in Table 3 for $\text{PM}_{2.5}$, SO_4^{2-} , nonsulfate $\text{PM}_{2.5}$, EC, NO_2 , SO_2 , and O_3 during the study period. Ambient concentrations of the measured criteria gases were moderate in Steubenville, whereas ambient fine particle concentrations were relatively high, with

TABLE 5
 Estimated Percent Changes (95% confidence intervals) in Heart Rate Variability (HRV) and HR Associated With an Interquartile Range (IQR) Increase in Mean Air Pollution on the Day Before* the HRV Measurement

	IQR	NO.	SDNN		r-MSSD		HF		LF		Heart Rate	
			Percent Change	95% CI	Percent Change	95% CI	Percent Change	95% CI	Percent Change	95% CI	Percent Change	95% CI
PM _{2.5}	13.4 µg/m ³	559	-4.0†	-7.0 to -0.9	-6.5‡	-12.1 to -0.6	-11.4‡	-21.5 to -0.1	-10.7‡	-20.1 to -0.3	1.1‡	0.2 to 2.1
SO ₄ ²⁻	5.1 µg/m ³	538	-3.3‡	-6.0 to -0.5	-5.6‡	-10.7 to -0.2	-10.3‡	-19.5 to -0.1	-8.4†	-17.0 to 1.2	0.8†	-0.02 to 1.7
Nonsulfate PM _{2.5}	5.3 µg/m ³	538	-2.1†	-4.3 to 0.1	-3.8†	-8.0 to 0.5	-5.9	-13.7 to 2.6	-7.2	-14.3 to 0.5	0.7†	-0.01 to 1.3
EC	0.6 µg/m ³	511	1.5	-1.1 to 4.1	-1.1	-5.8 to 3.9	3.1	-6.4 to 13.5	-4.7	-12.7 to 4.0	-0.2	-0.9 to 0.6
NO ₂	7.3 ppb	552	0.1	-2.2 to 2.4	-1.3	-5.6 to 3.2	-1.3	-9.4 to 7.7	-2.9	-10.4 to 5.2	0.0	-0.7 to 0.7
SO ₂	4.3 ppb	558	0.7	-1.0 to 2.5	0.5	-2.8 to 4.0	1.7	-4.9 to 8.7	4.9	-1.4 to 11.5	0.3	-0.2 to 0.8
O ₃	16.4 ppb	552	-1.1	-4.2 to 2.1	-2.5	-8.4 to 3.9	-3.8	-14.9 to 8.7	-3.9	-14.2 to 7.6	0.7	-0.3 to 1.6

*Previous day refers to the measurement cycle 9 AM of the previous day to 9 AM of the current day.

†P < 0.10.

‡P < 0.05.

HF indicates high frequency; LF, low frequency; CI, confidence interval.

some daily means approaching the 24-hour National Ambient Air Quality Standards (65 µg/m³ for PM_{2.5}). On 6 of the 118 days (5%), the daily mean PM_{2.5} (based on the hourly data averaged over the day) exceeded 50 µg/m³ (maximum 50.7 µg/m³). The correlation coefficients between daily particulate and gas concentrations are shown in Table 4.

Associations Between Air Pollution and Heart Rate Variability Measures

Time and frequency-domain HRV parameters, including SDNN, r-MSSD, HF, and LF were negatively associated with the mean PM_{2.5} concentration during the day before the HRV measurement (Table 5). For example, R-MSSD was -6.5% (CI = -12.1% to -0.6%, P = 0.03) lower with each IQR range increase in mean PM_{2.5} (13.4 µg/m³) on the day before the measurement. We found no suggestion of an association of HRV with mean NO₂, SO₂, or O₃ (P > 0.10). For PNN50, the results were similar in magnitude but with wider confidence intervals (data not shown). In contrast to HRV, we found that heart rate was elevated with increased PM_{2.5}. For example, heart rate was elevated by 1.1% (CI = 0.2% to 2.1%, P = 0.02) with each IQR range increase in PM_{2.5} on the day before the measurement.

We compared the associations of PM_{2.5} with those for its major components (EC, SO₄²⁻, and nonsulfate PM_{2.5}). We found that SO₄²⁻ was significantly associated with decreased SDNN, r-MSSD, HF, and LF and increased heart rate, whereas nonsulfate PM_{2.5} was moderately associated (P < 0.10) with decreased SDNN, r-MSSD, and increased heart rate. In contrast, we found no associations with HRV for the EC fraction of PM_{2.5} or for any of the gaseous pollutants (P > 0.10).

We compared the association between HRV and ambient PM_{2.5} for averaging periods at 4, 6, 12, 24, 48, and 72 hours before the electrocardiogram recordings. For all HRV mea-

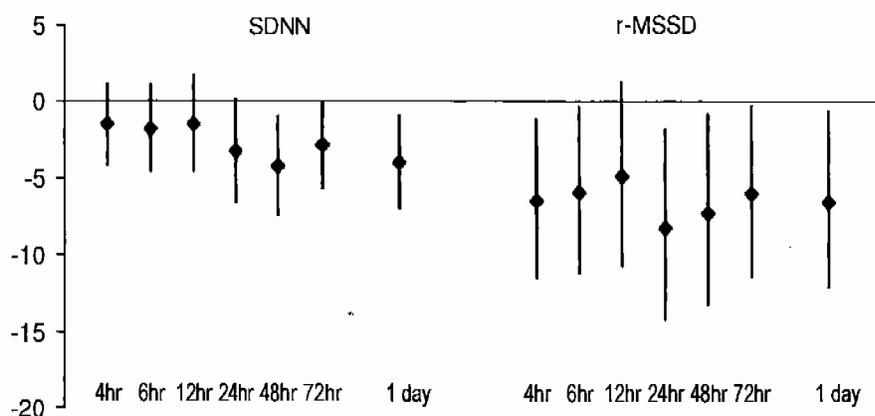


Fig. 1. Estimated percent changes (95% confidence intervals) in SDNN and r-MSSD associated with an interquartile range increase in $PM_{2.5}$ mean air pollution for different exposure metrics: moving averages for 4, 6, 12, 24, 48, and 72 hours (based on continuous data) and 1-day lag (based on filter data, 9 AM to 9 AM). Interquartile ranges are: 17.7, 17.5, 16.6, 15.2, 12.6, 11.4, and 13.4 $\mu g/m^3$, respectively.

tures, the associations between the daily mean $PM_{2.5}$ and HRV were similar to those for the 24- and 48-hour moving averages (Fig. 1).

Effect Modification

We found no consistent effect modification of the air pollution

effect by congestive heart failure, coronary artery disease, or statin intake (Table 6). However, we did find that subjects with hypertension showed very little response to increased levels of $PM_{2.5}$, whereas subjects without hypertension showed a change of -17.8% in

r-MSSD (CI = -25.8 to -8.9) associated with increased $PM_{2.5}$ (P value of interaction = 0.002). We also found stronger effects of $PM_{2.5}$ on days when subjects were not on beta-blocker medication (-10.0% r-MSSD [CI = -16.0 to -3.4] for a $PM_{2.5}$ increase of 13.4 $\mu g/m^3$) as compared with no effect (1.6% [CI = -7.6 to 11.9]) on days when subjects were on beta-blockers (interaction P value = 0.03). Similarly, we found higher $PM_{2.5}$ effects on days when subjects were not on statins (-8.4% r-MSSD [CI = -14.4 to -2.0]) as compared with days when they were (interaction P value = 0.15). Although 52% of those with hypertension and 0% of those without hypertension were on beta-blockers, the effect modification by hypertension remained significant ($P < 0.05$) in the 20 subjects not on beta-blockers. Associations between sulfates and HRV were similarly modified by hypertension and

TABLE 6

Effect Modification of Association of r-MSSD With $PM_{2.5}$ (13.4 $\mu g/m^3$) and SO_4^{2-} (5.1 $\mu g/m^3$) on the Previous Day by Chronic Cardiovascular Diagnoses and Medication Intake

	No. (subjects)	No. (observations)	Percent Change	$PM_{2.5}$		SO_4^{2-}	
				95% Confidence Interval	Percent Change	95% Confidence Interval	
Cardiovascular diagnoses							
Hypertension							
Yes	23	406	-2.0	-8.5 to 4.8	-3.0	-8.6 to 3.1	
No	9	153	-17.8†	-25.8 to -8.9	-14.2†	-22.6 to -5.0	
<i>P</i> Value interaction			0.002		0.03		
Coronary artery disease							
Yes	11	178	-2.9	-11.6 to 6.7	-1.5	-9.5 to 7.1	
No	21	381	-8.3†	-14.6 to -1.6	-7.7†	-13.6 to -1.5	
<i>P</i> Value interaction			0.29		0.20		
Congestive heart failure							
Yes	6	100	-13.2†	-23.8 to -1.2	-9.5	-20.2 to 2.6	
No	26	459	-5.2	-11.2 to 1.1	-4.9	-10.3 to 0.8	
<i>P</i> Value interaction			0.20		0.46		
Medication							
Beta-blocker							
Yes		164	1.6	-7.6 to 11.9	-0.3	-8.1 to 8.2	
No		395	-10.0‡	-16.0 to -3.4	-8.3†	-14.2 to -2.1	
<i>P</i> Value interaction			0.03		0.09		
Statins							
Yes		120	0.0	-10.5 to 11.8	-0.9	-9.7 to 8.7	
No		418	-8.4†	-14.4 to -2.0	-7.5†	-13.2 to -1.4	
<i>P</i> Value interaction			0.15		0.20		

* $P < 0.10$,

† $P < 0.05$,

‡ $P < 0.01$.

beta-blocker intake, with slightly higher interaction *P* values.

Discussion

We found reduced HRV in a group of elderly subjects living in Steubenville, Ohio, associated with increased total PM_{2.5} and SO₄²⁻ during the previous day. Reduced HRV was more weakly related to the nonsulfate component of PM_{2.5} and was not related to increases in pollutants generally associated with traffic sources such as EC, O₃, or NO₂. Increases in overall PM_{2.5} and SO₄²⁻ were associated not only with decreased r-MSSD and HF, suggesting reduction in vagal tone, but also with decreased LF and increased heart rate, suggesting increases in sympathetic tone.

Our sulfate effects suggest that in an environment where nontraffic sources of pollution (eg, coal combustion at power plants and steel mills) contribute significantly to ambient pollution in the community, elevated levels of particles from these sources may also adversely affect cardiac autonomic function and clinical cardiac outcomes. This conclusion is consistent with the American Cancer Society's cohort study⁴⁰ in which sulfate concentrations were a significant predictor of cardiovascular mortality, the time-series results within the Six-Cities Study (which included Steubenville) by Laden et al,⁴¹ who found sulfur was predictive of short-term mortality, and the findings by O'Neill et al,⁴² who found increased sulfate concentrations to be a significant predictor of decreased vascular reactivity in diabetics.

Within the framework of the 2000–2002 Steubenville Comprehensive Air Monitoring Program (SCAMP), Connell et al⁴³ studied fine particulate matter concentration and composition and found that SO₄²⁻ is the major constituent of PM_{2.5} in Steubenville, accounting for approximately 31% of total mass. Within the period of this study, ambient SO₄²⁻ comprised between 52% and 43% of the total PM_{2.5} mass (as [NH₄]₂SO₄).⁴⁴ The SCAMP analyses⁴³ suggest that lo-

TABLE 7
Estimated Effects of 10 µg/m³ PM_{2.5} Increase on Heart Rate Variability Measures in Selected Studies of Elderly

Study	No. of Subjects	No. of Observations	Metric	SDNN			r-MSSD			HF			LF		
				Percent Change	95% Confidence Interval	95% Confidence Interval	Percent Change	95% Confidence Interval	95% Confidence Interval	Percent Change	95% Confidence Interval	95% Confidence Interval	Percent Change	95% Confidence Interval	
Boston Elders, 1997 (Gold et al, 2000) ⁶	20	163	4 hrs	-2.8	-6.4 to 0.8	-10.0	-15.4 to -4.6	-14.9	-25.9 to -2.3	-12.9	-20.6 to -4.5				
Baltimore PM Study, 1998 (Creason et al, 2001) ²⁴	56	Up to 12 per subject	1 d												
Vancouver 1998 (Ebelt et al, 2005) ⁴⁸	19	76	1 d	-8.0	-23.0 to 6.9	-13.4	-42.6 to 15.9								
Boston Elders, 1999 (Schwartz et al, 2005) ¹⁰	28	310	24 hrs	-2.6	-6.0 to 0.8	-10.1	-16.9 to -2.8								
Utah, 1990–2001 (Pope et al, 2004) ²⁵	88	250	1 d	-2.7	-3.9 to -1.4	-6.1	-9.3 to -3.0								
Mexico City, 2002 (Holguin et al, 2003) ²⁶	34	384	1 d					-19.3	-29.2 to -8.0	-8.4	-19.3 to 4.0				
Normative Aging Study, 2000–2003 (Park et al, 2005) ²⁸	497	497	24 hrs	-2.7	-9.5 to 4.5			-16.2	-28.9 to -1.2	0.8	-12.0 to 15.3				
Steubenville, 2000	32	638	1 d	-4.0	-7.0 to -0.9	-6.5	-12.1 to -0.6	-11.4	-21.5 to -0.1	-10.7	-20.1 to -0.3				

HF indicates high frequency; LF, low frequency.

cal sources in Steubenville contribute only approximately $4.6 \mu\text{g}/\text{m}^3$ (25% of the annual mean $18.4 \mu\text{g}/\text{m}^3$) to the city's $\text{PM}_{2.5}$ concentrations. The main source of $\text{PM}_{2.5}$ and sulfate in Steubenville is fossil fuel (primarily coal) combustion,³⁶ most likely produced by the steel mills and power plants located in the Ohio River Valley.

Traffic pollutant effects predominated in our two previous Boston studies conducted with a similar study design in a community of elders living next to a city roadway.^{8,10} In the first study, SO_4^{2-} and BC measurements were not available, but we found associations of ozone as well as overall $\text{PM}_{2.5}$ with reduced HRV.⁸ In the second study, reduced HRV was most strongly and consistently associated with increased BC, which is a marker for traffic exposure.¹⁰ Mean air pollution levels during the study period from June to December 2000 show that $\text{PM}_{2.5}$ and SO_4^{2-} were twice as high in Steubenville than in Boston ($\text{PM}_{2.5}$: 20 vs $10 \mu\text{g}/\text{m}^3$, SO_4^{2-} : 6.9 vs $3.0 \mu\text{g}/\text{m}^3$), whereas the traffic-related pollutant NO_2 was lower in Steubenville (10.0 vs 21.5 ppb) (Steubenville: Table 3, Boston: data not shown).

Our results for Steubenville and Boston elders, suggesting pollution-associated decreases in vagal stimulation and/or increases in sympathetic tone, are consistent with findings from many other studies that did not separate out components of $\text{PM}_{2.5}$ that might enable the investigators to distinguish traffic from nontraffic $\text{PM}_{2.5}$ effects (Table 7).

Elevation of overall particle pollution ($\text{PM}_{2.5}$ or PM_{10}) has been related to reduction in HRV or increases in heart rate in repeated-measures elders studies from Baltimore,^{23,24} Utah Valley,^{22,25} and Mexico City.²⁶ Although studies have not consistently found that elevated pollution levels increase HR at the same time as they reduce HRV, it has been proposed that the association of increased pollution with reduced HRV may be mediated, in part, through the increase in heart rate that results

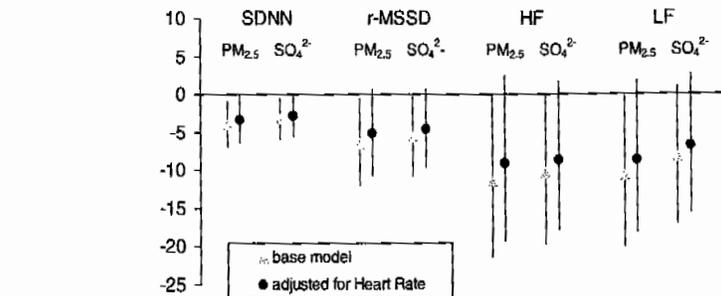


Fig. 2. Estimated percent changes (95% confidence intervals) in heart rate variability parameters associated with an interquartile range increase in $\text{PM}_{2.5}$ and SO_4^{2-} (previous day) in the base model and adjusted for heart rate.

from increased sympathetic tone. For all HRV parameters in our study, controlling for heart rate led to small changes in the magnitude of the effect estimates (Fig. 2), suggesting that a portion, but not all, of the HRV associations related to the pathways reflected by heart rate.

Similar associations of particle mass with HRV have been reported in a chamber study on elderly volunteers exposed for 2 hours to concentrated air pollution particles, in which significant decrements in HRV in both time and frequency domain were found immediately and 24 hours after exposure.⁴⁵ Although the majority of the studies point to a significant association of particle pollution with reduced HRV, effects of $\text{PM}_{2.5}$ on HRV have not been found in panel studies conducted in the northwestern United States and Canada, perhaps because of differences in particle composition or, alternatively, low power.⁴⁶⁻⁴⁸ Also, in contrast to the negative associations noted here, increases in traffic pollution were associated with increased HRV in a study of a younger healthy population of traffic police in North Carolina.⁴⁹ The investigators hypothesize that the nature of the pollution-related autonomic dysfunction may depend on the age and underlying disease states of the study participants.

Between-person comparisons of HRV show that reduced HRV may be a marker for overall ill health.²⁹ Although the significance of within-person short-term changes in HRV is somewhat less well established, a study of ischemic events showed that

they were preceded by decreased HF HRV in the hour before the event and in LF HRV in the 4 minutes before the event.⁵⁰ Similarly, a significant decrease in heart HRV has been reported to precede paroxysmal atrial fibrillation.⁵¹

We found effect modification of hypertension and beta-blocker intake in this study with stronger associations between particles and HRV among the "healthier" subjects (no hypertension, not on beta-blocker). These findings contrast with several previous studies, which showed stronger adverse effects of air pollution on HRV in subjects with preexisting cardiovascular conditions,²³ previous myocardial infarction,¹⁰ or hypertension.²⁶⁻²⁸ Two of those studies were cross-sectional analyses of large cohorts with much larger numbers of subjects.^{27,28} The small numbers of subjects in panel studies such as this one make examination of effect modification difficult, and this result may be a chance finding. Alternatively, it is possible that in sicker populations, other influences on HRV (for example, medication) predominate, making it more difficult to detect pollution effects. In support of our findings, a panel study of elderly subjects in Seattle also found associations between particles and heart rate primarily in healthy subjects.⁵²

Personal exposures to particles and gases were measured in a subset of the study population. Associations between ambient particle concentrations and corresponding personal

exposures were strong, whereas associations between ambient gases and their corresponding personal exposures were much weaker.⁴⁴ We conclude that PM_{2.5} and SO₄²⁻ ambient concentrations are very good proxies for the personal exposure of the study participants.

Recently, the scientific and regulatory communities have focused their attention on the adverse cardiac effects of ambient particles from mobile sources. This study supports the hypothesis that in an environment such as Steubenville, Ohio, where nontraffic sources of pollution contribute significantly to ambient pollution in the community, particle pollution from these sources, particularly sulfate particles, can also have adverse effects on autonomic function.

Acknowledgments

The authors thank all of the participants of the study as well as Monique Verrier, Meghan Syring, Bruce Nearing, Gail McCallum, Marisa Barr, and Marina Jacobson-Canner. The authors also thank the field team members from Franciscan University of Steubenville, in particular Kim Agnew, Michelle Bellini, Karen Gay, Sara Krilich, Debra Santarelli, Steven Shea, and Teresa Sobie. The authors are also grateful for CONSOL Energy Inc. Research and Development's laboratory analysis of air pollutant samples and for the provision of continuous ambient monitoring data.

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