PM2.5-Induced Tachycardia and Hypertension in Rats are Linked to Elemental Carbon and Specific Temperature-Resolved Carbon Fractions

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ABSTRACT

Ambient fine particulate matter (PM2.5) is associated with cardiovascular morbidity and mortality. The components responsible for adverse health effects are unknown.
OBJECTIVE: We tested the hypothesis that cardiovascular responses to PM2.5 will be enhanced in hypertensive rats and associated with specific particulate components found in an urban industrial setting.
METHODS: Spontaneously hypertensive rats were exposed by inhalation to filtered air (n=8) or concentrated PM2.5 (n=8) in Dearborn, Michigan, for four consecutive summer days. Exposures were repeated in four separate groups of rats (n=32). Blood pressure (BP), heart rate (HR) and HR variability (HRV) metrics (SDNN, RMSSD) were assessed by radiotelemetry and compared to 1h- and 8h-averaged fluctuations in PM2.5 composition, with a focus on elemental carbon (EC), organic carbon (OC) and their temperature-resolved subfractions, EC1-EC5, PC (pyrrolized carbon), and OC1-OC4.
RESULTS: Exposure-related increases in mean, systolic and diastolic BP were detected as well as increased HR and decreased HRV compared to air-exposed rats. Using 1h averages, PM2.5 EC (1 µg/m3 increase) was associated with increased HR of 11-32 bpm (4-11% increase), 22-27% decrease in HRV, 3-14 mmHg increases (1.5-8%) in systolic BP, and 4-9% increases in diastolic BP. By comparison effects of OC were negligible. Using 8h averages, EC subfractions were also associated with increased heart rate (EC1; 13bpm, EC2,EC3,PC; <5bpm) and SDNN (EC1>>EC2>EC3,EC4,PC), but with decreased RMSSD (EC2,EC5> EC3,EC4). Significant but comparatively smaller responses were associated with OC and OC1. Effects of either EC or OC subfractions on blood pressures were negligible.
CONCLUSIONS: Acute changes in cardiovascular responses associated with PM2.5 carbon species appear to be driven primarily by EC and EC1 fractions.US EPA RD83479701 & Electric Power Research Institute.

BACKGROUND

- Air pollution exposure is associated with increases in the incidence of morbidity and mortality in susceptible populations with cardiopulmonary and metabolic diseases
- Fine particulate matter (mean aerodynamic diameter ≤ 2.5 µm; PM2.5) may exacerbate pre-existing airway and cardiovascular diseases, such as asthma and hypertension.
- Residents in an industrial urban community in Dearborn, Michigan are exposed to high summer concentrations of PM2.5 originating from multiple emission sources, including a steel manufacturing plant, and diesel traffic.
- Repeated controlled exposures to combustion-derived PM causes acute cardiovascular changes in laboratory rodents.
- Spontaneously hypertensive rats are sensitive to various air pollutants (ozone, PM, diesel) and respond with changes in pulmonary, vascular and cardiac systems.

PURPOSE

•To determine the effects of source-specific PM2.5 components on acute, exposure-related cardiovascular responses as indicated by changes in blood pressure, heart rate, and heart rate variability in a susceptible rat strain

STUDY DESIGN

- Male Spontaneously Hypertensive Rats, 12-13 weeks old
- Concentrated $PM_{2.5}$ inhalation exposure
- Daily 8h-exposures (7:30AM-3:30PM) for four consecutive days (M, T, W, T)
- Repeated in 4 separate field studies:
  - STUDY 1: August 10-13, 2009
  - STUDY 2: August 17-20, 2009
  - STUDY 3: July 12-15, 2010
  - STUDY 4: July 19-22, 2010

Study Site: Industrial Urban Community in Dearborn, MI

CARDIOTELEMETRY

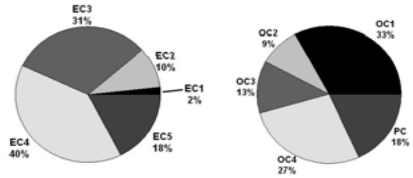
Surgical Implants: Rats were implanted with radiotransmitter units (C50-PXT; DSI). Semicontinuous data of blood pressure, ECG waveforms and heart rate were integrated over 1-h increments to correspond with air pollution data of the same 1-h increment

Inhalation Exposure to CAP: Concentrated air particulates (CAP) were generated with a Harvard - type *fine particle* concentrator, housed within a mobile air research laboratory, *AirCARE 2*, parked at Salinas Elementary School in urban Dearborn.

Concentrated $PM_{2.5}$ Constituents
(averaged for all 4 studies)

Constituent	Mass (SEM) (mg/m³)
$PM_{2.5}$	547 ± 62.3
OC	208 ± 15.3
EC	10 ± 1.3
Sulfate	154 ± 28.8
Nitrate	24 ± 5.5
Ammonium	52 ± 11.9
Urban Dust	56 ± 8.1
Other	58 ± 14.7

$PM_{2.5}$ Temperature Resolved Carbon Fractions

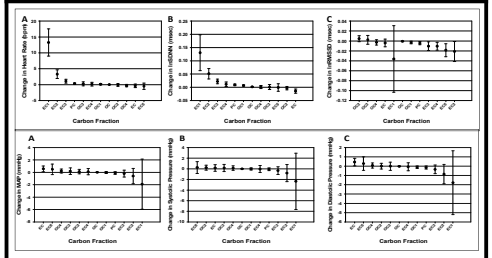


Charts depict the integrated carbon fractions from all four exposures

Results: Heart Rate & Variability

Response	Study	Component	Change per IQR	SEM	p-Value	Change per 1µg/m³ CI (lower, upper)
Heart Rate	1	$PM_{2.5}$	2.757	1.502	0.068	--
		EC	7.059	0.885	<.0001	28.1 , 36.1
		OC	-1.845	1.431	0.199	--
	2	$PM_{2.5}$	1.343	1.635	0.412	--
		EC	8.354	1.454	<.0001	19.7 , 28.1
		OC	0.879	1.107	0.428	--
	3	$PM_{2.5}$	0.719	1.344	0.593	--
		EC	3.649	0.974	0.000	8.1 , 14.1
		OC	-5.489	1.543	0.000	-2.4
	4	$PM_{2.5}$	1.086	1.375	0.431	--
		EC	5.985	1.350	<.0001	20.1 , 31.9
		OC	1.916	1.266	0.131	--
lnSDNN	1	$PM_{2.5}$	0.094	0.026	0.000	0.0615 , 0.0619
		EC	-0.031	0.018	0.086	--
		OC	0.001	0.026	0.955	--
	2	$PM_{2.5}$	0.016	0.034	0.639	--
		EC	-0.061	0.031	0.053	--
		OC	-0.009	0.023	0.693	--
	3	$PM_{2.5}$	0.024	0.029	0.415	--
		EC	0.006	0.020	0.774	--
		OC	-0.038	0.032	0.240	--
	4	$PM_{2.5}$	0.022	0.027	0.406	--
		EC	-0.051	0.024	0.039	-0.2202 , -0.2198
		OC	0.016	0.022	0.474	--
lnRMSSD	1	$PM_{2.5}$	0.001	0.017	0.942	--
		EC	-0.048	0.011	<.0001	-0.267 , -0.167
		OC	-0.011	0.016	0.494	--
	2	$PM_{2.5}$	0.019	0.016	0.236	--
		EC	-0.023	0.015	0.127	--
		OC	0.007	0.011	0.541	--
	3	$PM_{2.5}$	-0.009	0.016	0.603	--
		EC	-0.002	0.011	0.834	--
		OC	0.008	0.017	0.646	--
	4	$PM_{2.5}$	-0.008	0.018	0.659	--
		EC	-0.039	0.017	0.022	-0.244 , -0.096
		OC	0.020	0.015	0.193	--

Results: Carbon Fraction Health Effects



EC fractions associated with increased HR, BP and decreased HRV

Results: Trace Element Associations

Associations Between Major Non-Carbonaceous PM Components and Trace Elements With Diastolic Blood Pressure.

Data are expressed as change in response (effect) per IQR of pollutant, and per 1ng/m³.

Component	Effect (mm Hg)	SEM	p-Value	Change per 1ng/m³ CI (lower, upper)	IQR (ng)
Uranium	15.2200	7.4500	0.0434	2.29, 149.9	0.20
Rubidium	0.1460	0.0543	0.0081	0.0045, 0.0294	8.65
Crustal	0.0760	0.0310	0.0153	5E-04, 0.0042	32.50
Manganese	0.0060	0.0029	0.0465	3E-07, 4E-05	291.50
Aluminum	0.0020	0.0010	0.0407	5E-08, 2E-06	1636.00
Potassium	0.0018	0.0007	0.0157	2E-07, 2E-06	1566.00
Magnesium	0.0014	0.0007	0.0487	5E-09, 2E-06	1590.00
Iron	0.0005	0.0002	0.0264	1E-08, 2E-07	4903.00

Results: Blood Pressures

Response	Study	Component	Change per IQR	SEM	p-Value	Change per 1µg/m³ CI (lower, upper)
MAP	1	$PM_{2.5}$	0.576	0.897	0.521	--
		EC	2.894	0.536	<.0001	10.76 , 15.64
		OC	-1.555	0.824	0.061	--
	2	$PM_{2.5}$	3.183	0.827	0.000	0.775 , 0.779
		EC	2.000	0.795	0.013	3.4 , 7.8
		OC	1.099	0.573	0.056	--
	3	$PM_{2.5}$	-0.661	0.604	0.276	--
		EC	0.369	0.411	0.370	--
		OC	-0.517	0.648	0.426	--
	4	$PM_{2.5}$	-0.377	0.555	0.498	--
		EC	0.893	0.521	0.088	--
		OC	0.876	0.473	0.065	--
Systolic	1	$PM_{2.5}$	0.454	0.992	0.647	--
		EC	3.219	0.594	<.0001	11.9 , 17.3
		OC	-1.864	0.912	0.042	-2.5 , -0.88
	2	$PM_{2.5}$	3.392	0.903	0.000	0.825 , 0.830
		EC	2.448	0.856	0.005	4.55 , 9.45
		OC	1.208	0.620	0.053	--
	3	$PM_{2.5}$	-0.268	0.673	0.690	--
		EC	0.986	0.453	0.031	1.6 , 4.4
		OC	-1.462	0.715	0.042	-1.64 , -0.55
	4	$PM_{2.5}$	0.027	0.586	0.963	--
		EC	1.156	0.548	0.036	2.61 , 7.38
		OC	0.532	0.502	0.290	--
Diastolic	1	$PM_{2.5}$	0.767	0.826	0.354	--
		EC	2.720	0.492	<.0001	10.16 , 14.64
		OC	-1.324	0.760	0.083	--
	2	$PM_{2.5}$	3.071	0.788	0.000	0.747 , 0.751
		EC	1.979	0.766	0.010	3.51 , 7.89
		OC	1.181	0.552	0.033	0.727 , 2.07
	3	$PM_{2.5}$	-0.772	0.584	0.187	--
		EC	0.258	0.398	0.517	--
		OC	-0.097	0.628	0.878	--
	4	$PM_{2.5}$	-0.404	0.569	0.479	--
		EC	1.195	0.523	0.023	2.93 , 7.47
		OC	1.320	0.473	0.006	1.16 , 2.44

SUMMARY

- Overall 4 studies: HR and BP were increased, HRV was decreased during 4-day exposures.
- Increased EC of 1 µg/m³ was associated with:
  - 4-11% increased HR (11-32bpm)
  - 22-27% decrease HRV (SDNN; 1.2-1.5ms)
  - 3-14% increase systolic pressure (3-14mmHg)
  - 4-9% increase diastolic pressure (5-12mmHg)
- EC1 and EC2 subfractions had the most associations with cardiovascular responses
- Increased OC of 1 µg/m³ was associated with minor and mixed effects; decreased systolic but increased diastolic pressures.
- Increased diastolic pressure was the only effect associated with trace elements:
  - Uranium associated with 15mmHg increase
  - Rubidium, manganese, and aluminum were associated with minor increases (< 1mmHg)

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