

1 **Abstract**

2 Acute air pollutant inhalation is linked to adverse cardiac events and death, and
3 hospitalizations for heart failure. Diesel exhaust (DE) is a major air pollutant suspected to
4 exacerbate preexisting cardiac conditions, in part, through autonomic and electrophysiologic
5 disturbance of normal cardiac function. To explore this putative mechanism, we examined
6 cardiophysiologic responses to DE inhalation in a model of aged heart failure-prone rats without
7 signs or symptoms of overt heart failure. We hypothesized that acute DE exposure would alter
8 heart rhythm, cardiac electrophysiology, and ventricular performance and dimensions consistent
9 with autonomic imbalance, while increasing biochemical markers of toxicity. Spontaneously
10 Hypertensive Heart Failure rats (SHHF, 16 months) were exposed once to whole DE (4 h, target
11 $PM_{2.5}$ concentration: $500 \mu\text{g}/\text{m}^3$) or filtered air. DE increased multiple heart rate variability
12 (HRV) parameters during exposure. In the 4 h after exposure, DE increased cardiac output, left
13 ventricular volume (end diastolic and systolic), stroke volume, HRV, and atrioventricular (AV)
14 block arrhythmias while increasing electrocardiographic measures of ventricular repolarization
15 (i.e., ST- and T-amplitudes, ST area, Tpeak-Tend duration). DE did not affect heart rate relative
16 to Air. Changes in HRV positively correlated with post-exposure changes in bradyarrhythmia
17 frequency, repolarization, and echocardiographic parameters. At 24 hours post-exposure, DE-
18 exposed rats had increased serum C-reactive protein and pulmonary eosinophils. This study
19 demonstrates that cardiac effects of DE inhalation are likely to occur through changes in
20 autonomic balance associated with modulation of cardiac electrophysiology and mechanical
21 function, and may offer insights into the adverse health effects of traffic related air pollutants.

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1 **Diesel Exhaust Inhalation Increases Cardiac Output, Bradyarrhythmias, and**
2 **Parasympathetic Tone in Aged Heart Failure-Prone Rats**

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33 **Running Title:** DE alters cardiac & autonomic function

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35 **Disclaimer:** This paper has been reviewed and approved for release by the National Health and
36 Environmental Effects Research Laboratory, U.S. Environmental Protection Agency. Approval
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45 **Key Words:** echocardiography, air pollution, cardiac function, autonomic, cardiovascular,
46 electrocardiography, heart rate variability, arrhythmia, rats, heart failure

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