Science of the Total Environment 643 (2018) 378–391

Contents lists available at ScienceDirect

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Acute peat smoke inhalation sensitizes rats to the postprandial cardiometabolic effects of a high fat oral load

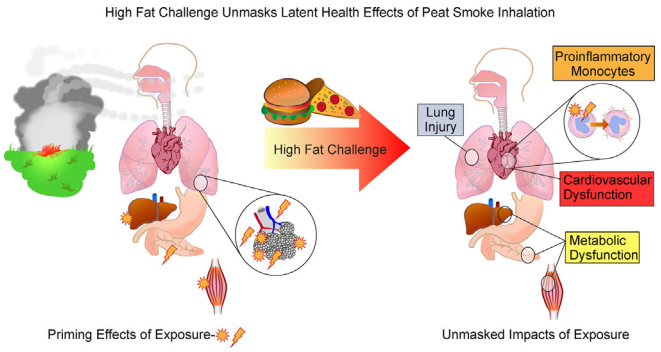
Brandi L. Martin [a,1], Leslie C. Thompson [b], Yongho Kim [b], Wanda Williams [b], Samantha J. Snow [b], Mette C. Schladweiler [b], Pamela Phillips [c], Charly King [b], Judy Richards [b], Najwa Haykal-Coates [b], Mark Higuchi [b], M. Ian Gilmour [b], Urmila P. Kodavanti [b], Mehdi S. Hazari [b], Aimen K. Farraj [b,*]

[a] Oak Ridge Institute for Science and Education, 1299 Bethel Valley Rd, Oak Ridge, TN 37830, United States
[b] Environmental Public Health Division, US EPA, 109 TW Alexander Drive, Research Triangle Park, NC, United States
[c] Toxicity Assessment Division, US EPA, 109 TW Alexander Drive, Research Triangle Park, RTP, NC, United States

HIGHLIGHTS

- Peat smoke inhalation modified cardiac functional responses to a high fat oral load.
- Peat smoke inhalation altered metabolic responses to a high fat oral load.
- Peat smoke worsened lung & systemic inflammatory responses to a high fat oral load.
- Peat smoke increased proinflammatory blood monocytes after a high fat oral load.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 28 February 2018
Received in revised form 4 June 2018
Accepted 8 June 2018
Available online xxxx

Editor: Wei Huang

Keywords:
Air pollution
Exposure
Cardiovascular

ABSTRACT

Wildland fire emissions cause adverse cardiopulmonary outcomes, yet controlled exposure studies to characterize health impacts of specific biomass sources have been complicated by the often latent effects of air pollution. The aim of this study was to determine if postprandial responses after a high fat challenge, long used clinically to predict cardiovascular risk, would unmask latent cardiometabolic responses in rats exposed to peat smoke, a key wildland fire air pollution source. Male Wistar Kyoto rats were exposed once (1 h) to filtered air (FA), or low (0.36 mg/m^3 particulate matter) or high concentrations (3.30 mg/m^3) of peat smoke, generated by burning peat from an Irish bog. Rats were then fasted overnight, and then administered an oral gavage of a HF suspension (60 kcal% from fat), mimicking a HF meal, 24 h post-exposure. In one cohort, cardiac and superior mesenteric artery function were assessed using high frequency ultrasound 2 h post gavage. In a second cohort, circulating lipids and hormones, pulmonary and systemic inflammatory markers, and circulating monocyte phenotype using flow

Abbreviations: ACE, angiotensin-converting enzyme; AET, aortic ejection time; ALT, alanine amino-transferase; AP, alkaline phosphatase; BALF, bronchoalveolar lavage fluid; BSA, bovine serum albumin; CBC, complete blood count; CK, creatine kinase; CO, cardiac output; CRP, C-reactive protein; DPBS, Dulbecco's phosphate-buffered saline; ECG, electrocardiogram; EDV, end diastolic volume; EF, ejection fraction; ESV, end systolic volume; FA, filtered air; FFA, free fatty acids; FMO, fluorescence minus one; GGT, γ-glutamyl transferase; GPX, glutathione peroxidase; GSH, total reduced glutathione; GTR, glutathione reductase; HDL, high density lipoprotein; HF, high fat; IVCT, isovolumic contraction time; IVRT, isovolumic relaxation time; LDH, lactate dehydrogenase; LDL, low density lipoprotein; NAG, *n*-acetylglucosaminidase; PM, particulate matter; RH, relative humidity; SD, standard deviation; SOD, superoxide dismutase; STE, speckle tracking echocardiography; SV, stroke volume; TC, total cholesterol; US EPA, United States Environmental Protection Agency; WKY, Wistar Kyoto.

* Corresponding author at: U.S. Environmental Protection Agency, Environmental Public Health Division, 109 TW Alexander Drive, Research Triangle Park, NC 27711, Mail Code: B105-02, United States.
E-mail address: farraj.aimen@epa.gov (A.K. Farraj).

[1] Performed all of the work related to this study at the U.S. EPA location listed above.

https://doi.org/10.1016/j.scitotenv.2018.06.089
0048-9697/Published by Elsevier B.V.

Metabolic
Risk
Health

cytometry were assessed before or 2 or 6 h after gavage. HF gavage alone elicited increases in circulating lipids characteristic of postprandial responses to a HF meal. Few effects were evident after peat exposure in ungavaged rats. By contrast, exposure to low or high peat caused several changes relative to FA-exposed rats 2 and 6 h post HF gavage including increased heart isovolumic relaxation time, decreased serum glucose and insulin, increased CD11 b/c-expressing blood monocytes, increased serum total cholesterol, alpha-1 acid glycoprotein, and alpha-2 macroglobulin ($p = 0.063$), decreased serum corticosterone, and increased lung gamma-glutamyl transferase. In summary, these findings demonstrate that a HF challenge reveals effects of air pollution that may otherwise be imperceptible, particularly at low exposure levels, and suggest exposure may sensitize the body to mild inflammatory triggers.

Published by Elsevier B.V.

1. Introduction

Wildland fires represent a major source of air pollution, and are increasingly linked to adverse health impacts related to poor air quality (Haikerwal et al., 2015). Moreover, nearly 40% of total suspended black carbon (a key component of particulate matter) in the United States is linked to biomass burning (Agency, 2013), increasing the need for understanding the associated risks from exposure to various biomass combustion emissions. The cardiopulmonary effects of air pollution exposure, however, are often latent (Agency, 2009), posing a significant challenge to controlled exposure studies that rely on measures of spontaneous effects. Interestingly, air pollution exposure has been found to modify responses to stressors (e.g. exercise). For instance, Volpino et al. (2004) demonstrated that traffic policemen exposed to ambient air pollution and then subjected to exercise had exaggerated changes in cardiopulmonary function only after exercise (Volpino et al., 2004). Analogous responses to air pollution were evident in our previous findings in rodents using treadmill exercise (Carll et al., 2013) or sympathomimetic infusion (Hazari et al., 2012).

Day-to-day activities beyond exercise also stress the cardiovascular system, and when modeled experimentally, may have similar utility in demonstrating latent effects of air pollution exposure. For example, consumption of a high fat (HF) meal causes multiple transient effects including endothelial and microvascular dysfunction (Vogel et al., 1997), increases in LDL cholesterol and triglycerides (Langsted et al., 2008), oxidative stress and inflammation (de Vries et al., 2014), and altered insulin sensitivity (Robertson et al., 2002) and pulmonary function (Rosenkranz et al., 2010). Moreover, the severity of such postprandial responses varies depending upon a host of intrinsic (e.g. sex, disease, age) and extrinsic (e.g. diet, exercise) factors and as such has long been used as a tool much like exercise tests to define elevated or diminished risk. For example, postprandial responses after a HF meal revealed greater endothelial dysfunction in patients with elevated blood triglycerides (Giannattasio et al., 2005), hypotension in type 2 diabetics (Smits et al., 2014), and greater oxidative stress in men compared to women (Bloomer and Fisher-Wellman, 2010). Conversely, co-ingestion of dietary anti-oxidants improved vascular responses (Plotnick et al., 2003), while exercise diminished inflammatory responses (Fuller et al., 2017). Postprandial responses, previously unexplored in air pollution health effects studies, may prove similarly useful in indicating risk from exposure.

Peat, a fuel source comprised of decaying vegetation found in wetlands, emits more fine particulate matter (PM) when burned than any other type of wildland fire (Rein, 2013). Moreover, short-term exposure to smoldering peat air pollution in eastern North Carolina during separate burns in 2008 and 2011 led to increased cardiopulmonary emergency room visits (Rappold et al., 2011; Tinling et al., 2016). The purpose of this study was to assess the effects of a one-time inhalation exposure to smoldering peat smoke on postprandial cardiopulmonary responses after a HF oral load in rats. To mimic a single HF meal challenge, an approach using oral gavage of a HF suspension was developed. To coincide with reported peak postprandial functional consequences, one cohort of rats was exposed to low or high concentrations of smoldering peat smoke, administered a HF gavage suspension one day later, and then examined for cardiac and superior mesenteric artery function using high frequency ultrasound 2 h post gavage. A second cohort of similarly exposed rats was assessed 24 h after exposure for time-dependent changes in systemic lipids and hormones, and pulmonary and systemic inflammatory markers immediately before, or 2 h or 6 h after HF gavage.

2. Methods

2.1. Animals

12 week-old male Wistar Kyoto (WKY) rats (Charles River Laboratories Inc., Raleigh, NC) ($n = 6–8$, depending on the experiment) were housed 2/cage in polycarbonate cages, maintained on a 12 h light/dark cycle at approximately 22 °C and 50% relative humidity in our Association for Assessment and Accreditation of Laboratory Animal Care-approved facility, and held for a minimum of one week before exposure. All animals received standard (5001) Purina pellet rat chow (Brentwood, MO) and water ad libitum unless otherwise stated. The Institutional Animal Care and Use Committee of the U.S. Environmental Protection Agency (U.S. EPA) approved all protocols.

2.2. Experimental design

2.2.1. Study layout and group size determinations

Three experiments were performed within this study to examine the impacts of air pollution exposure on postprandial responses (Fig. 1). Experiment A describes the development of a HF challenge using oral gavage administration of a HF emulsion. Experiment B describes the use of the HF oral gavage challenge to assess the priming effects of exposure on cardiovascular functional responses to a HF oral load. Experiment C describes the impacts of air pollution exposure on the time-dependent postprandial changes in metabolic, systemic and pulmonary factors after HF gavage challenge.

For Experiment A, a group size of $n = 6$ was selected since this was a pilot study and was done to match group size from a previous study with analogous species and endpoints (Farraj et al., 2016). To determine group size for Experiments B and C, sample size analysis was done based on Experiment A lipid data. Sample size analysis was performed using R Studio software with the 'pwr' package and 'pwr.anova.test' command. Original sample size analyses based on changes in triglyceride levels between the HF group and vehicle group in Experiment A were too robust to yield a meaningful sample size value (yielded $n = 2$). Instead, the analysis was based on blood LDL measurements. Sample size analysis was based on the (k) number of experimental groups ($k = 3$ groups: filtered air, low peat and high peat), a significance level = 0.05, a power = 0.8, and the effect size index (f), which is derived by multiplying the expected effect size (d) by the standard deviation (SD). We calculated d (effect range/SD), using the widest LDL SD from Experiment A, in this case the vehicle group SD. The widest effect range (i.e. range of