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Personal exposure to specific volatile organic compounds and acute changes in lung function and heart rate variability among urban cyclists

Scott Weichenthal [a,*], Ryan Kulka [a], Patrick Bélisle [b], Lawrence Joseph [b], Aimee Dubeau [a], Christina Martin [a], Daniel Wang [c], Robert Dales [d]

[a] Health Canada, Air Health Sciences Division, Ottawa, ON, Canada K1A 0K9
[b] McGill University, Department of Epidemiology and Biostatistics, Montreal, QC, Canada H3G 1Y5
[c] Environment Canada, Air Quality Research Division, Analysis and Air Quality Section, Ottawa, ON, Canada K1A 0H3
[d] Health Canada, Environmental Health Science Research Bureau, Ottawa, ON, Canada K1A 0K9

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ABSTRACT

Background: Few studies have examined the acute cardiorespiratory effects of specific volatile organic compound (VOC) exposures from traffic pollution.
Methods: A cross-over study was conducted among 42 healthy adults during summer 2010 in Ottawa, Canada. Participants cycled for 1-h along high and low-traffic routes and VOC exposures were determined along each route. Lung function, exhaled nitric oxide, and heart rate variability were monitored before cycling and 1–4 h after the start of cycling. Bayesian hierarchical models were used to examine the relationship between 26 VOCs and acute changes in clinical outcomes adjusted for potential confounding factors.
Results: Each inter-quartile range (IQR) increase in propane/butane exposure was associated with a 2.0 millisecond (ms) (95% CI: 0.65, 3.2) increase in SDNN (standard deviation of normal-to-normal intervals), a 24 ms^2 (95% CI: 6.6, 41) increase in HF (high frequency power), and a 65 ms^2 (95% CI: 11, 118) increase in LF (low frequency power) in the hours following cycling. IQR increases in ethane and isoprene were associated with a 5.8 ms (95% CI: −9.8, −1.7): decrease in SDNN and a 24 ms^2 (95% CI: −44, −7.9) decrease in HF, respectively. IQR increases in benzene exposure were associated with a 1.7 ppb (95% CI: 1.1, 2.3) increase in exhaled nitric oxide and each IQR increase in 3-methylhexane exposure was associated with a 102 mL (95% CI: −157, −47) decrease in forced expiratory volume in 1-s.
Conclusions: Exposure to traffic-related VOCs may contribute to acute changes in lung function, inflammation, or heart rate variability.

1. Introduction

Existing evidence suggests that traffic-related air pollution may contribute to cardiorespiratory morbidity. Indeed, time spent in traffic has been associated with acute myocardial infarction (Peters et al., 2004) and specific traffic pollutants including fine particulate matter ($PM_{2.5}$) and NO_2 have been associated with increased risks of asthma (McConnell et al., 2010), decreased survival after stroke (Maheswaran et al., 2010), increased hospitalizations for cardiovascular causes (Zanobetti et al., 2009), and increased mortality (Maynard et al., 2007; Brook et al., 2010). More recently, ultrafine particles (UFP) have emerged as potentially important traffic-related air pollutants as they are produced in large numbers by vehicle emissions and may have an important impact on physiological measures of cardiovascular health including heart rate variability (HRV) (Chan et al., 2004), ST-segment depression (Pekkanen et al., 2002), and endothelial function (Lucking et al., 2001). However, studies of the acute cardiorespiratory effects of other traffic-related air pollutants including specific volatile organic compounds (VOCs) that are produced during fuel combustion or through evaporative emissions are relatively scarce.

Tsai et al. (2010) examined the association between outdoor levels of six specific VOCs and cardiovascular mortality in Taiwan and noted increased risks for propane, iso-butane, and benzene. In addition, occupational VOC exposures have been associated with decreased HRV (Ma et al., 2010) and others have reported associations between ambient organic carbon levels and altered HRV in elderly patients with cardiovascular disease (Chuang et al., 2007; Schneider et al., 2010). Recently, we examined the impact of total VOC exposures on cardiorespiratory outcomes among healthy urban cyclists but did not identify important associations (Weichenthal et al., 2011). However, we did not examine specific

* Corresponding author at: Health Canada, Air Health Sciences Division, 269 Laurier Avenue West, AL 4903C, Ottawa, ON, Canada K1A 0K9.
Fax: +16 1 3 948 8482.
E-mail address: scott.weichenthal@hc-sc.gc.ca (S. Weichenthal).

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VOCs, and as a result we may have missed potentially important relationships if some but not all VOCs were associated with acute changes in HRV and/or respiratory function. With respect to HRV, inverse associations are of particular interest as decreased HRV has been associated with increased risks of cardiovascular morbidity (Dekker et al., 1997; Liao et al., 1997; Tsuji et al., 1996). Therefore, to address limitations of our previous analysis, here we examine associations between a number of specific VOCs and acute changes in HRV, exhaled nitric oxide (NO), and lung function in the same population of urban cyclists.

2. Materials and methods

Detailed descriptions of the study design, participant characteristics, clinical measures, and exposure monitoring methods are provided elsewhere (Weichenthal et al., 2011). Briefly, during the summer of 2010, 42 healthy non-smoking adults cycled for approximately 1-h along high and low-traffic routes on two separate occasions. All cycling took place on weekdays between 1130 h and 1230 h and individual routes were separated by at least 5-days. Cycling routes were approximately 10 km in length: the high-traffic route was located on busy roadways in the downtown core of Ottawa, Canada, whereas the low-traffic route travelled along a bicycle path away from traffic along the Ottawa River. Participants were predominantly male (67%), Caucasian (95%), and ranged in age from 19–58 years. The study was approved by the Health Canada Research Ethics Board.

Each study day ran from approximately 1030 h to 1530 h. Once at the study site, participants were fit with digital Holter monitors (Seer Light Extend; GE Medical Systems Information Technologies, Inc., Milwaukee, WI, USA) and completed questionnaires to collect demographic information as well as medical history. Baseline HRV, exhaled nitric oxide (Niox Mino, Aerocrine, New Providence, NJ, USA), and lung function measurements (reported here as forced expiratory volume in 1 s (FEV_1)) (KoKo Legend spirometers, nSpire Health, Longmont, CO, US) were collected prior to cycling and follow-up measurements were collected immediately after cycling and every hour for the next 3-h (i.e., 1–4 h after the start of cycling). Time domain (SDNN, standard deviation of normal-to-normal intervals; RMSSD, root mean square of successive differences in adjacent NN intervals; pNN50, percentage of adjacent NN intervals differing by more than 50 ms) and frequency domain (LF, low-frequency power; HF, high-frequency power; LF:HF, the ratio of LF to HF) measures of HRV were based on the last 5-min of each segment of the study day. Average heart rate was also determined for each 1-h segment of the study day. Electrocardiogram data were analyzed by expert technicians at the Arrhythmia Monitoring Center in Ottawa using a GE Medical Systems Information Technology workstation (MARS version 7.2). Beat annotations were automatically assigned by the software and were verified and reviewed by technicians; only normal sinus beats were used in the analysis. HRV and exhaled NO measures were collected before spirometry procedures.

2.1. Exposure monitoring

Mean VOC exposures were determined along each route using 1-L SUMMA canisters placed in panniers located on technicians' bicycles travelling directly in front of participants. VOC analysis was conducted by GC–MS according to the United States Environmental Protection Agency method TO-15. Method detection limits ranged from 0.01–0.09 $\mu g/m^3$ for individual VOCs and in total 26 VOCs were included in the analyses as the majority of these compounds displayed at least some variation between the high and low-traffic routes. Mean personal exposure to UFPs (TSI Model 3007, TSI, St. Paul, MN, USA), $PM_{2.5}$ (TSI Dust Trak, TSI, St. Paul, MN, USA), black carbon (MicroAeth Model AE51, Magee Scientific, Berkeley, CA, USA), and CO (Langan Enhanced CO Measurer Model T15n, Langan Products, San Francisco, CA, USA) were determined using direct reading instruments mounted in panniers on participants' bicycles. Mean temperature and relative humidity during cycling were determined using HOBO Data Loggers (Onset, Cape Cod, MA, USA) in bicycle panniers and data on average outdoor NO_2 and O_3 concentrations during cycling were obtained from a fixed site monitoring station in downtown Ottawa (approximately 2 km from the main study site).

2.2. Statistical analysis

We began by creating descriptive statistics for all variables as well as Spearman's correlation matrices for VOC exposures of interest. For each pair of VOCs correlated at the level of 0.8 or higher, one of the pair was eliminated from further analysis since both essentially repeat the same information and including both in a regression model would likely split their effects. Following this procedure, we ran separate models for each VOC against each outcome adjusting for possible confounding variables including duration of cycling, relative humidity and temperature during cycling, average heart rate during cycling, and mean levels of black carbon, NO_2, O_3, $PM_{2.5}$, and UFPs during cycling. As our data consisted of baseline values together with repeated measurements at 1–4 h after the start of cycling, we created four differences for each outcome representing changes from baseline at each of the time points. We then fit Bayesian multi-level repeated measures hierarchical models for each outcome. At the first level of this hierarchical model, the change from baseline in the outcome at each time point was linearly regressed against individual-specific intercepts and slopes across time, and a beta coefficient was estimated for the effect of each VOC. At the second level of this model, individual level intercepts and slopes were assumed to collectively follow a normal distribution across subjects, with overall means and variances following prior densities that were very diffuse (non-informative), allowing for inferences to be driven by the data.

Following inspection of single-VOC models, we ran multiple-VOC models with the same hierarchical form and adjusting for the same co-variates as above. VOCs were conservatively selected for inclusion in these models. That is, a VOC was selected for multivariate modeling if single-VOC models showed a reasonable chance of an effect with a given outcome. In general, this meant that the 90% credible interval needed to exclude the null value, although we allowed some variation on this criterion. For example, if few other VOCs showed an effect for a given outcome, we lowered the threshold somewhat, typically to 85%. All statistical analyses were conducted using WinBUGS version 1.4.3 (Lunn et al. (2000)) and model estimates for each VOC reflect inter-quartile range increases in exposure.

3. Results

In total, 38 participants completed both the high and low-traffic routes whereas two participants completed only the low-traffic route and one participant completed only the high-traffic route. Baseline health outcome data were comparable to other studies of healthy adults as previously described (Weichenthal et al., 2011) and the VOC exposure database was complete for all cycling routes. In general, VOC exposure levels were higher along the high-traffic route relative to the low-traffic route for the majority of the compounds monitored; these values are listed in Table 1 along with inter-quartile range (IQR) values for both routes combined. However, for some compounds (e.g., Freons, carbon tetrachloride, chloromethane) there was little difference between routes and exposures likely reflect general background concentrations. In addition, several VOCs were strongly correlated ($r > 0.80$) and as a result 9 VOCs were dropped from statistical analysis. In general, decisions on which VOCs to drop were based on ambient concentrations and known toxicities (e.g., benzene) but in some cases there were no clear reasons to favour one compound over the others and one was selected at random. These compounds, along with those with which they were highly correlated are listed in Table 2. All other VOCs were retained for analyses. Correlations between VOCs and other air pollutants included in statistical models (NO_2, $PM_{2.5}$, O_3, UFPs) were low ($r < 0.3$). Descriptive data for other traffic-related air pollutants are available in our previous report (Weichenthal et al., 2011).

3.1. VOCs and exhaled NO

Model coefficients describing relationships between VOC exposures and changes from baseline in exhaled NO are listed in Table 3. Benzene and Freon 12 were positively associated with exhaled NO whereas inverse associations were observed for chloromethane, dichloromethane, ethane, Freon 113, and isoprene. The directions of observed associations were generally consistent between single and multiple-VOC models with the exception of Freon 12 which was inversely associated with exhaled NO in the single-VOC model and positively associated with exhaled NO in the multiple-VOC model. In all cases, however, the magnitudes of associations between specific VOCs and exhaled NO were small (i.e., < 2 ppb change per IQR increase in exposure).

3.2. VOCs and lung function (FEV_1)

Several VOCs were inversely associated with FEV_1 with the strongest association observed for 3-methlyhexane (Table 4).

Inverse relationships were also observed between $FEV_1$and chloromethane, carbon tetrachloride, Freon 113, Freon 12, 1, 4-dichlorobenzene, and isoprene in single-VOC models but the magnitudes of these relationships decreased in multiple-VOC models because correlations among these variables made it difficult to separate out their individual effects in a multivariate model. In the case of 1, 4-dichlorobenezene and isoprene, positive associations were observed with FEV_1 in multiple-VOC models.

3.3. VOCs and heart rate variability

Model coefficients describing the relationships between VOC exposures and changes in baseline HRV are listed in Tables 5 and 6. Ethane and propane were each associated with changes in SDNN with an inverse relationship observed for ethane and a positive association for propane. Isoprene and isobutane were both inversely associated with pNN50 in single-VOC models but the magnitude of these associations decreased in multiple-VOC models. A small inverse association was also observed between trichloroethane and pNN50 in both single and multiple-VOC models, but in general most VOCs were not strongly associated with acute changes in time domain measures of HRV. For frequency domain measures of HRV, evidence of a positive association was observed between propane and HF and LF whereas isoprene was inversely associated with HF. In general, the directions of observed associations were consistent between single and multiple-VOC models but in several cases the magnitude of associations decreased in multiple-VOC models. Specifically, ethane (positive association) and Freon 12 and 113 (inverse associations) were associated with HF in single-VOC models but the magnitudes of these associations decreased in multiple-VOC models. Likewise, dichloromethane was associated with increased LF:HF in single-VOC models but not in multiple-VOC models.

4. Discussion

To our knowledge this is the first study to evaluate the impact of specific VOC exposures on acute changes in cardiorespiratory outcomes among urban cyclists. Total VOC exposures were not

Table 2
Groups of highly correlated ($r > 0.8$) VOCs and those retained for analysis.

VOCs retained for analysis	VOCs removed from analysis
Benzene	Propene, 1-butene, ethylene, 2-methylpentane, 3-methylpentane, 2-methylbutane
Propane	Butane
Hexane	3-methylpentane, 2-methylpentane
Isobutane	Pentane, 2-methylpentane
m,*p*-xylene	*o*-xylene

Table 3
Model estimates for VOCs and changes in baseline FE_{NO} (ppb).

VOC	Change/IQR (95% CI)[a]	Change/IQR (95% CI)[b]
Benzene	0.92 (0.17, 1.7)	1.7 (1.1, 2.3)
Chloromethane	−0.80 (−1.5, −0.11)	−0.28 (−0.86, 0.31)
Dichloromethane	−1.0 (−1.7, −0.33)	−0.023 (−0.12, 0.074)
Ethane	−2.1 (−3.2, −0.95)	−1.3 (−2.0, −0.53)
Freon 113	−1.1 (−2.1, −0.13)	−1.2 (−2.1, −0.30)
Freon 12	−0.71 (−1.3, −0.17)	0.39 (0.012, 0.77)
Isoprene	−0.46 (−0.89, −0.028)	−0.067 (−0.27, 0.13)

[a] Single-VOC model.
[b] Multiple-VOC model including all VOCs listed in the table. All models are adjusted for duration of cycling, relative humidity and ambient temperature during cycling, average heart rate during cycling, and mean levels of black carbon, NO_2, O_3, $PM_{2.5}$, and UFPs during cycling.

Table 1
Descriptive VOC exposure data for high and low-traffic routes.

VOC	High-traffic (n=39) median (μg/m^3) (range)	Low-traffic (n=40) median (μg/m^3) (range)	Mean difference (μg/m^3) (95% CI)	IQR (μg/m^3)
2-methylbutane	4.2 (0.4–31)	1.1 (0.3–8.4)	3.7 (2.1, 5.3)	3.3
Toluene	3.4 (0.4–22)	1.1 (0.3–83)	1.2 (−3.2, 5.6)	2.8
Propane	2.9 (0.8–8.0)	1.3 (0.5–4.1)	1.5 (0.9, 2.0)	2.0
Ethane	2.9 (1.6–5.7)	1.9 (1.1–4.4)	1.0 (0.6, 1.4)	1.6
Freon 12	2.6 (2.2–3.0)	2.5 (2.3–3.3)	0.05 (−0.03, 0.1)	0.2
Butane	2.6 (0.3–36)	0.8 (0.3–10)	2.3 (0.4, 4.1)	2.2
Ethylene	2.6 (0.5–6.5)	0.8 (0.3–2.8)	1.8 (1.4, 2.3)	1.8
Pentane	2.0 (0.3–15)	0.6 (0.2–4.5)	1.5 (0.7, 2.2)	1.5
Freon 11	1.5 (1.2–3.4)	1.5 (1.2–1.7)	0.07 (−0.04, 0.2)	0.1
m,*p*-xylene	1.4 (0.2–43)	0.4 (0.1–3.4)	2.1 (−0.08, 4.2)	1.1
Freon 22	1.4 (0.9–15)	1.1 (0.7–41)	0.02 (−2.2, 2.2)	0.6
Isobutane	1.3 (0.1–18)	0.4 (0.1–5.0)	1.1 (0.2, 2.0)	1
Chloromethane	1.2 (1.0–1.4)	1.2 (1.0–1.3)	0.02 (−0.02, 0.06)	0.1
2-methylpentane	1.0 (0.09–5.8)	0.3 (0.1–1.5)	0.9 (0.6, 1.2)	0.8
Benzene	0.9 (0.2–3.5)	0.3 (0.1–0.9)	0.7 (0.5, 0.9)	0.6
Propene	0.9 (0.2–3.0)	0.3 (0.2–0.9)	0.7 (0.6, 0.9)	0.6
VOC	High-traffic median (μg/m^3) (range)	Low-traffic median (μg/m^3) (range)	Mean difference (95% CI)	IQR (μg/m^3)
Hexane	0.8 (0.1–3.1)	0.3 (0.1–1.7)	0.6 (0.4, 0.7)	0.6
3-methylpentane	0.8 (0.1–3.4)	0.3 (0.1–1.2)	0.6 (0.4, 0.8)	0.6
1-butene	0.8 (0.3–3.6)	0.3 (0.2–1.2)	0.5 (0.4, 0.7)	0.5
Freon 113	0.6 (0.5–0.8)	0.7 (0.6–0.8)	−0.0005 (−0.03, 0.03)	0.1
Isoprene	0.6 (0.3–3.8)	0.9 (0.1–8.4)	−0.6 (−1.1, −0.07)	0.7
3-methylhexane	0.6 (0.1–3.5)	0.2 (0–1.4)	0.4 (0.2, 0.6)	0.4
o-xylene	0.5 (0.08–6.9)	0.2 (0.05–0.8)	0.5 (0.2, 0.9)	0.4
Dichloromethane	0.4 (0.2–1.5)	0.3 (0.2–1.3)	0.1 (0.04, 0.2)	0.3
Carbon Tetrachloride	0.4 (0.4–0.6)	0.5 (0.2–0.5)	−0.002 (−0.03, 0.02)	0.07
Trichloroethene	0.2 (0.1–0.8)	0.1 (0.03–1.4)	0.08 (−0.01, 0.2)	0.1

IQR, inter-quartile range for both routes combined; Freon 11, Trichlorofluoromethane; Freon 12, Dichlorodifluoromethane; Freon 22, Chlorodifluoromethane; Freon 113, 1,1,2-Trichlorotrifluoroethane.

associated with any of the outcomes examined in our previous analysis (Weichenthal et al., 2011), and in this study, most individual VOCs were also not strongly associated with acute changes in exhaled NO, lung function, or HRV; however, several findings are of note. First, although the magnitude of associations tended to be modest, several specific VOCs were associated with changes in either exhaled NO, FEV_1, or heart rate variability parameters. Furthermore, the direction of these associations often differed between compounds suggesting that it may not be appropriate to lump all VOCs together as "total VOCs" when evaluating the potential health effects of these compounds.

Nevertheless, caution is required in interpreting our results as many compounds were evaluated for each outcome and some associations may have occurred by chance. In addition, several compounds were highly correlated and thus we could not separate their individual effects. For example, all compounds listed as eliminated from further analysis because of high correlations with included compounds (Table 2) may have effects on the outcomes, and some effects changed between univariate and multivariate models, emphasizing the difficulties of estimating separate effects when a group of variables are highly correlated. This limitation is largely owing to the nature of the problem, and very large (likely infeasible) sample sizes would be needed to begin to untangle these effects. On the other hand, correlations between VOCs and other air pollutants (NO_2, $PM_{2.5}$, O_3, UFPs) were weaker and therefore less problematic.

Conversely, some associations were consistent with existing evidence regarding the known toxicities of the compounds examined. For example, 3-methylhexane is a known respiratory irritant and thus its inverse association with FEV_1 seems biologically plausible. Likewise, butane inhalation (abuse) is a known cause of coronary artery spasm and acute myocardial infarction in young adults and this effect depends in part on altered autonomic regulation of the heart (Menyar et al., 2005; Menyar, 2006). In this study, butane was highly correlated with propane and therefore the associations observed between propane and acute changes in heart rate variability (SDNN, LF, and HF) may be explained by butane. However, VOC exposure levels were generally low and few other studies have examined the reported associations; therefore, further evaluation is required to verify these findings. In particular, as cardiovascular morbidity is generally associated with decreased HRV the clinical implications of increased HRV require further evaluation. However, some evidence suggests that both increased and decreased HRV may be predictive of cardiovascular morbidity (de Bruyne et al., 1999).

Tsai and colleagues examined the association between ambient VOCs and daily counts of cardiovascular mortality in Taiwan between 2003 and 2006 (Tsai et al., 2010). Benzene, propane, and isobutane were each associated with increased risks of cardiovascular mortality at lag-0 day but correlations between these VOCs were high ($r > 0.85$) and thus it is not possible to attribute these effects to any single compound. Nevertheless, our finding of altered HRV in response to propane/butane is consistent with these results as impaired autonomic control of the heart is a known contributor to cardiovascular morbidity (Zareba et al., 2001). However, it is important to note that propane/butane was not associated with changes in LF:HF in the present study and thus did not appear to have an impact on the balance of sympathetic/parasympathetic modulation. Regardless, other

Table 4
Model estimates for VOCs and changes in baseline FEV_1 (mL).

VOC	Change/IQR (95% CI)[a]	Change/IQR (95% CI)[b]
Benzene	−37 (−87, 12)	35 (−39, 110)
Carbon tetrachloride	−87 (−133, −42)	−8.3 (−59, 43)
Chloromethane	−112 (−159, −65)	−51 (−105, 2.8)
1,4−dichlorobenzene	−52 (−94, −9.7)	3.9 (0.93, 6.9)
Freon 113	−92 (−155, −33)	−62 (−125, 2.3)
Freon 12	−44 (−80, −7.8)	−2.7 (−23, 18)
Isobutane	−14 (−34, 4.9)	31 (1.5, 61)
Isoprene	−28 (−57, −0.71)	9.6 (−8, 9.4)
3-methylhexane	−38 (−75, −0.77)	−102 (−157, −47)
Propane	57 (0.37, 117)	11 (−3.5, 25)
Trichloroethene	30 (−0.62, 61)	0.36 (−6.8, 7.6)

[a] Single-VOC model.
[b] Multiple-VOC model including all VOCs listed in the table. All models are adjusted for duration of cycling, relative humidity and ambient temperature during cycling, average heart rate during cycling, and mean levels of black carbon, NO_2, O_3, $PM_{2.5}$, and UFPs during cycling.

Table 5
Model estimates for VOCs and changes in baseline SDNN, RMSSD, and pNN50.

Hear rate variability	VOC	Change/IQR (95% CI)[a]	Change/IQR (95% CI)[b]
SDNN (ms)			
	Dichloromethane	5.4 (0.082, 11)	0.59 (−0.23, 1.4)
	Ethane	−7.7 (−16, 0.80)	−5.8 (−9.8, −1.7)
	Propane	8.3 (1.9, 15)	2.0 (0.65, 3.3)
	m, *p*-xylene	0.83 (−0.10, 1.8)	0.45 (−0.44, 1.3)
RMSSD (ms)			
	Isobutane	−0.59 (−1.4, 0.21)	−0.023 (−0.78, 0.75)
	Isoprene	−1.2 (−2.4, 0.012)	−0.14 (−0.63, 0.34)
pNN50 (%)			
	Freon 113	−1.8 (−3.8, 0.13)	−1.2 (−3.2, 0.86)
	Isobutane	−0.61 (−1.2, −0.0095)	0.071 (−0.62, 0.74)
	Isoprene	−1.5 (−2.4, −0.60)	−0.20 (−0.68, 0.29)
	Trichloroethene	−0.76 (−1.7, 0.19)	−0.28 (−0.53, −0.036)

[a] Single-VOC model.
[b] Multiple-VOC model including all VOCs listed in the table for a given outcome. All models are adjusted for duration of cycling, relative humidity and ambient temperature during cycling, average heart rate during cycling, and mean levels of black carbon, NO_2, O_3, $PM_{2.5}$, and UFPs during cycling.

Table 6
Model estimates for VOCs and changes in baseline HF, LF, and LF:HF.

Heart rate variability	VOC	Change/IQR (95% CI)[a]	Change/IQR (95% CI)[b]
HF (ms^2)			
	Carbon tetrachloride	−46 (−102, 12)	36 (−39, 109)
	Ethane	105 (13, 199)	87 (−0.0042, 178)
	Freon 11	−17 (−40, 4.9)	0.48 (−24, 25)
	Freon 12	−57 (−102, −13)	−41 (−83, 0.94)
	Freon 113	−117 (−190, −44)	−63 (−144, 19)
	Isoprene	−43 (−77, −7.5)	−24 (−41, −7.9)
	Propane	67 (−4.9, 139)	24 (6.6, 41)
LF (ms^2)			
	Carbon tetrachloride	157 (−11, 323)	134 (−61, 331)
	Chloromethane	146 (−25, 312)	92 (−89, 274)
	1,4-dichlorobenzene	139 (−33, 308)	−4.4 (−16, 6.7)
	Freon 113	232 (4.0, 457)	−14 (−261, 234)
	Isoprene	−81 (−187, 23)	−11 (−68, 44)
	Propane	264 (41, 475)	65 (11, 118)
LF:HF			
	Dichloromethane	1.2 (0.62, 1.8)	0.019 (−0.076, 0.11)
	Freon 12	0.43 (−0.052, 0.89)	0.19 (−0.048, 0.43)

[a] Single-VOC model.
[b] Multiple-VOC model including all VOCs listed in the table for a given outcome. All models are adjusted for duration of cycling, relative humidity and ambient temperature during cycling, average heart rate during cycling, and mean levels of black carbon, NO_2, O_3, $PM_{2.5}$, and UFPs during cycling.

studies have also reported significant relationships between HRV and VOC exposures. In particular, Ma et al. (2010) noted decreased SDNN and RMSSD (Ma et al., 2010) with increased exposure to total VOCs whereas Mizukoshi et al. (2010) reported an inverse association between total VOCs and HF. In addition, Ma et al. (2010) also noted that the association between total VOCS and decreased SDNN and RMSSD was independent of $PM_{2.5}$ with the strongest effects observed with 1–4 h moving averages. However, specific compounds were not examined in either of these two studies and further evaluation of the impacts of specific VOCs on HRV is warranted.

While only a small number of studies have examined the acute respiratory effects of ambient VOC exposures, some have observed positive associations between ambient VOCs and self-reported respiratory symptoms among asthmatic children (Delfino et al., 2003a; 2003b). In particular, Delfino et al. (2003a) reported increased respiratory symptoms with increasing outdoor levels of benzene, *m*,*p*-xylene, ethylbenzene, and tetrachloroethylene in Los Angeles, USA. In addition, exhaled breath concentrations (a marker of VOC exposure) of benzene were inversely associated with peak expiratory flow (Delfino et al. 2003b). Similarly, earlier studies reported significant associations between ambient benzene and hospital admissions for respiratory disease (Hagen et al., 2000), asthma exacerbation (Thompson et al., 2001) as well as childhood wheezing episodes (Buchdahl et al., 2000). In this study, we did not observe a strong association between personal exposure to benzene and lung function although benzene was associated with a small increase in exhaled NO. While this finding is not consistent with evidence discussed above, it may be explained in part by the inclusion of healthy young adults in this study as opposed to a more susceptible population such as asthmatics. Alternatively, exposures levels in Ottawa might have been below values likely to cause measureable decreases in lung function.

The major strengths and limitations of this study are discussed in detail elsewhere (Weichenthal et al., 2011). For VOCs specifically, the use of personal exposure measures for multiple compounds is an important strength as other studies of ambient VOCs have generally relied on fixed site exposure measures that can result in significant exposure measurement error for compounds with high spatial variability (Suh and Zanobetti, 2010). In addition, the availability of detailed personal exposure data for other traffic-related air pollutants is an important advantage as it was possible to adjust for these factors in the analyses; however, personal exposure data was not available for NO_2 and O_3 and fixed site measures may not have completely controlled for personal exposures to these pollutants. Co-linearity between multiple VOCs was also an issue, and in some cases it was not possible to separate the independent effects of specific compounds. In general, however, VOC exposures among cyclists in Ottawa tended to be lower than in previous studies of cyclists' exposures to VOCs (Bevan et al., 1991; van Wijnen et al., 1995) and findings should be replicated to increase confidence in the observed associations.

5. Conclusion

Twenty-six compounds were examined in this evaluation of the acute cardiorespiratory effects of VOC exposures in traffic. Evidence of possible associations were observed for a small number of compounds, and in particular, the association of propane/butane with acute changes in HRV is of interest as butane is a known cause of cardiovascular morbidity in cases of abuse. Future studies should aim to replicate this finding to verify whether or not low-level exposures may contribute to acute cardiovascular morbidity through altered autonomic modulation of the heart.

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