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ORIGINAL ARTICLE

Cardiac Autonomic Impacts of Bushfire Smoke—A Prospective Panel Study

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Background Air pollution is associated with cardiovascular disease and mortality. Most studies have focussed on urban or traffic-related pollution, and less is known about the impacts from bushfire smoke on cardiovascular autonomic function, although it is associated with increased sudden cardiac death and mortality. We sought to investigate its instantaneous and short-term impacts on heart rate variability (HRV).

Methods Twenty-four (24)-hour Holter electrocardiography (ECG) was repeated twice (during bushfire [Phase 1] and then clean air [Phase 2]) in 32 participants from two Australian towns (Warburton and Traralgon, Victoria) surrounding planned burning areas. This was compared with 10 control participants in another town (Maffra, Victoria) with two clean air assessments during the same periods. The primary HRV parameters assessed were those assessing overall HRV (Standard Deviation of Normal-to-Normal intervals [SDNN]), long-term HRV (Standard Deviation of the Average of Normal Sinus-to-Normal Sinus intervals for each 5-minutes [SDANN]), low frequency [LF]) and short-term HRV (Root Mean Square of Successive Differences between N-N intervals [RMSSD], High Frequency [HF], LF:HF ratio). Average concentrations of particulate matter <2.5 μm in diameter ($PM_{2.5}$) were measured at fixed site monitors in each location.

Results Mean $PM_{2.5}$ levels were significantly elevated during bushfire exposure in Warburton (96.5±57.7 μg/m^3 vs 4.0±1.9 μg/m^3, p<0.001) and Traralgon (12.6±4.9 μg/m^3 vs 3.4±3.1 μg/m^3, p<0.001), while it remained low in the control town, Maffra, in each phase (4.3±3.2 μg/m^3 and 3.9±3.6 μg/m^3, p=0.70). Although SDANN remained stable in controls, the exposed cohort showed significant worsening in SDANN during bushfire smoke exposure by 9.6±25.7ms (p=0.039). In univariable analysis, smoke exposure was significantly associated with higher ΔSDNN and ΔSDANN (p=0.03, p=0.01 exposed vs control). The association remained significant in ΔSDANN after adjusting for age, sex and cigarette smoking (p=0.02) and of borderline significance in ΔSDNN (p=0.06).

Conclusions Exposure to the bushfire smoke was independently associated with reduced overall and long-term HRV. Our findings suggest that imbalance in cardiac autonomic function is a key mechanism of adverse cardiovascular effects of bushfire smoke.

Keywords Air pollution • Bush fire • Heart rate variability

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Introduction

There has been a world-wide increase in severe vegetation fire events associated with climate change. The smoke from such fires has the potential to travel vast distances and affect major population centres far from the fires [1]. The cardiovascular (CV) health consequences of air pollution generally equal or exceed those due to pulmonary diseases and cancer combined [2]. Short-term associations between CV hospital admissions and particulate air pollution have been demonstrated in many multi-city studies around the world [3–5]. However, the main source of particles evaluated has been fossil fuel combustion, even though biomass combustion can be a significant contributor.

Recent epidemiological evidence suggests bushfire smoke has a multitude of deleterious effects on CV health, leading to morbidity and mortality, such as, out of hospital cardiac arrests [6–8], ischaemic heart disease [7,9], and cardiac hospital admissions [10–12], and cardiovascular emergency department (ED) attendances [13]. Although the key pathophysiological mechanism is assumed to be through autonomic function abnormalities [2,14], there is little evidence underpinning the mechanism in bushfire smoke. Bushfire smoke is composed of polycyclic aromatic hydrocarbons, gases, metals and particulate matter (PM), including $PM_{2.5}$ (particulate matter less than 2.5 μm in diameter), which can penetrate deep into the respiratory tract and bloodstream, resulting in oxidative stress and inflammation, endothelial dysfunction, and autonomic nervous system imbalance—all probable causes of adverse short-term [5,7,9,15] and long-term CV outcomes [14–17].

Heart rate variability (HRV) is a marker of cardiac autonomic function and has been used in the air pollution literature. Decreased HRV has been associated with cardiac morbidity and mortality [2,18]. In the elderly, and in those with pre-existing CV disease, air pollutant exposure resulting in reduced HRV has been explored as a precipitant of adverse cardiac events, including myocardial ischaemia, infarction, dysrhythmias and sudden cardiac death [2,14,16]. We aimed to evaluate the short-term effect of bushfire smoke on HRV.

Methods

This study was an analysis of prospectively collected panel data from participants in three locations: Warburton, Traralgon, and Maffra in Victoria, Australia. Warburton and Traralgon were affected by smoke from bushfires (mostly planned burns), whilst Maffra was the control town. Assessments were made in two phases, in February–March 2014 and then April–May 2014. These dates were selected by careful liaison with the planned burning team in Victoria. They targeted autumn (in the southern hemisphere) for the efficient fuel reduction burning at that time, and avoided summers and winters because of the risk of complications such as uncontrollable fires. We aligned our schedule to theirs. Phase 1 of assessment saw Warburton and Traralgon affected by bushfire smoke (i.e, during fuel reduction burning), while Phase 2 was in clean air conditions. Maffra experienced clean air conditions throughout both phases (Figure 1). Participants were coded as exposed for the Phase where exposure to bushfire smoke occurred; the other phase was coded as unexposed. This study was approved by the Monash University Human Research Ethics Committee (CF12/3097-2012001570).

This study is a part of a large project titled "Health effects of smoke from prescribed burning", which included (1) Lung inflammation test: exhaled nitric oxide (eNO); (2) Blood pressure and endothelial function (using finger plethysmography); (3) Heart rate variability and markers of cardiac ischaemia using 24-hour electrocardiography; and (4) Blood markers of inflammation and coagulation. Based on two previous similar panel studies—one study in California had 19 participants [19]; another in Brazil had 48 participants [20]— we aimed to recruit 50 participants. Our recruitment was commenced in late 2013 with one-on-one engagement, media advertising, online promotion, and site visits. A marketing company was utilised to recruit potential participants through a process of cold-calling people in the three study sites.

Exposure Measurement

$PM_{2.5}$ was measured using fixed site monitors (E-sampler-9800, Met One Instruments Inc., Grants Pass, OR, USA) in each study location. The monitors were calibrated for local conditions and provided continuous air particulate measurements based on light-scattering, collected on a 47 mm Teflon filter.

Outcomes

The outcome of interest for this study was the change in HRV parameters. Outcomes were assessed with the aid of DR200/HE Holter monitors (NorthEast Monitoring, Maynard, MA, USA). Holter monitors with five electrocardiograph (ECG) leads, were worn by participants for 18–24-hour sessions depending on individual availability. Data from each session was subsequently transferred to be analysed by the software "Holter LX Analysis" (NorthEast Monitoring). The primary HRV parameters assessed were those assessing overall HRV (the Standard Deviation of Normal-to-Normal intervals [SDNN]), long-term HRV (the Standard Deviation of Average values of Normal-to-Normal intervals for each 5-minute [SDANN]; low frequency power [LF], which is influenced by both sympathetic and parasympathetic activities), and short-term HRV (the Root Mean Square of Successive Differences between N-N intervals [RMSSD]; high frequency power [HF], which is influenced by parasympathetic activity; and the ratio of HF:LF [HF:LF], representing the balance of parasympathetic and sympathetic activities). Differences in HRV parameters were calculated as Phase 2–Phase 1 results.

Covariates and Confounders

Information regarding possible confounders was collected via questionnaire. Participant age, sex, and cigarette smoking

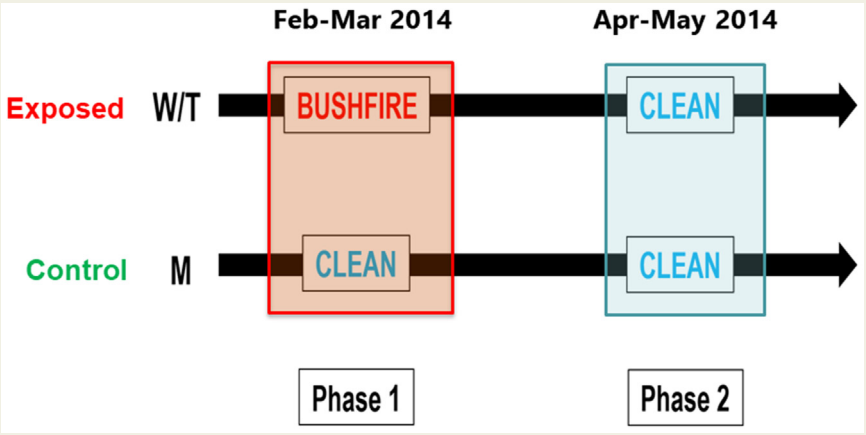

Figure 1 Study design. Representation of the timing of HRV assessments during the two phases of the study. Phase 1 spanned between February and March of 2014, while Phase 2 was between April and May 2014.
Abbreviations: W/T, Warburton/Traralgon; M, Maffra.

history (never smoked, ex-smoker, current smoker) were chosen *a priori* as potential confounders based on previous large cohort-studies having demonstrated these as significant determinants [21–23]. Participants' medical history of diabetes, hypertension and hyperlipidaemia was also documented.

Statistical Analyses

Data were analysed in STATA 13 (StataCorp, College Station, TX, USA). Data are expressed as mean±SD in text unless specified otherwise. Dichotomous variables were analysed using the Chi-square test or Fisher's Exact test, as appropriate. All analysed data were assessed for normality of the distribution using the Shapiro-Wilk test. Subsequently, paired *t* tests or the Wilcoxon signed-rank tests were used to analyse matched-pair data. One-way and two-way analysis of variance (ANOVA) was conducted to assess the effects of exposure and time between groups.

Missing data was accounted for using multiple imputation. Multivariable linear regression models were used to adjust for confounding in variables identified to be affected by smoke exposure after univariable analysis. The regression models adjusted the relevant indices from univariable analysis for age, sex and history of cigarette smoking. Sample size limited assessment of confounders to four variables simultaneously.

Results

Table 1 shows a summary of cohort characteristics. Among the 42 participants, 32 belonged to the exposed group (16 each in Warburton and Traralgon, respectively), while there were 10 in the control group. The mean age was 66±10 years, without any significant difference in age between the exposed and control groups. Forty-four per cent (44%) of the total participants were male, with 55%±14% males in the exposed group and 30%±3% in the control group. There

Table 1 Clinical characteristics and analysed ECG time of enrolled participants.

n	All	Exposed	Unexposed	P-value
	42	32	10	
Age (Years)*	65.9±10.5	65.3±10.8	65.0±8.7	0.93
Men	17 (40)	14 (44)	3 (30)	0.49
Hypertension†	17 (40)	11 (34)	6 (60)	0.27
Hyperlipidaemia†	16 (38)	13 (40)	3 (30)	0.72
History of smoking†	25 (60)	21 (66)	4 (40)	0.27
Asthma†	10 (24)	7 (22)	3 (30)	0.68
Diabetes†	9 (21)	6 (19)	3 (30)	0.66
Total Analysed Holter time (hh:mm)*	38:00±03:41	37:58±03:52	38:09±03:15	0.89

**Mean ± SD.*
†n (%); ***Calculated via Fisher's exact test.***

Table 2 Summary of $PM_{2.5}$ exposures in the study locations during phases of study.

Study Location (Town)	Mean $PM_{2.5}$ in Phase 1 ($\mu g/m^3$)	Mean $PM_{2.5}$ in Phase 2 ($\mu g/m^3$)	P-value#	Max $PM_{2.5}$ in Phase 1 ($\mu g/m^3$)
Warburton	96.5 ±57.7	4.0±1.9	<0.001	126
Traralgon	12.6±4.9	3.4±3.1	<0.001	181
Maffra	4.3±3.2	3.9±3.6	0.65	10.0

Phase 1: February–March 2014; Phase 2: April–May 2014.
#p-values for comparisons between Phases 1 and 2 in the same towns, 2-way ANOVA.

were no significant differences in other baseline characteristics of the exposed and unexposed groups.

A total of 78 Holter monitoring sessions were recorded, where 36 participants had paired Holter ECG data during Phases 1 and 2. Six (6) from the exposed cohort (two in Warburton and four from Traralgon) provided data during smoke exposure conditions but not for clean air ones. HRV data in these individuals for Phase 2 were imputed using multiple imputation. There were no significant baseline differences between those providing paired and unpaired data, and results were not significantly different when these participants were excluded from analysis (see Supplementary material).

$PM_{2.5}$ Exposure

The $PM_{2.5}$ exposure data during the phases of assessment are summarised in Table 2. Mean $PM_{2.5}$ concentrations were elevated to 96.5±57.7 $\mu g/m^3$ during bushfire exposure in Warburton compared to a low 4.0±1.9 $\mu g/m^3$ ($p<0.001$) in clean air assessments in Phase 2. Similarly, the $PM_{2.5}$ concentrations for Traralgon during exposure were significantly higher than in the clean air period (12.6±4.9 $\mu g/m^3$ vs 3.4±3.1 $\mu g/m^3$, $p<0.001$). In the control town of Maffra, $PM_{2.5}$ was low and stable throughout both phases (4.3±3.2 $\mu g/m^3$ vs 3.9±3.6 $\mu g/m^3$, p=0.65).

Difference in HRV Measures Within and Between Exposed and Unexposed Cohorts

Within the Exposed cohort, worsening in long-term and overall HRV parameters during bushfire smoke compared with clean air exposure was observed (Table 3) (SDNN difference 8.6 ±22.1 ms, p=0.058; SDANN difference 9.6±25.7 ms, p=0.039). There were no differences in shorter term HRV parameters in the exposed group, nor were there any significant differences in HRV parameters in the control group between measurement Phases. When the changes in HRV measures were compared between the cohorts, significantly larger deterioration was demonstrated in ΔSDANN (defined $SDANN_{phase2} - SDANN_{phase1}$) in the exposed cohort than in the unexposed (p=0.013). A significant difference was also observed for ΔSDNN between the groups (p=0.031). No difference in the LF:HF ratio or other short-term parameters were observed between the cohorts. Upon adjustment for age, sex, and history of cigarette smoking, the difference in ΔSDANN remained statistically significant (p=0.020), whereas mean ΔSDNN weakened to borderline statistical significance (p=0.062) (Table 4).

Table 3 Summary comparisons of differences in HRV indices.

Parameter	Exposed			Unexposed			ΔExposed vs ΔUnexposed (p-value)
	Phase 1	Phase 2	P-value	Phase 1	Phase 2	P-value	
SDNN (ms)	138.5±37.2	144.4±35.6	0.058	136.0±47.2	132.5±43.3	0.60	0.031
SDANN (ms)	117.1±35.8	124.7±34.1	0.039	118.1±37.9	113.2±32.1	0.19	0.013
RMSSD (ms)†	29.3 (18.9, 42.7)	29.9 (20.0, 42.1)	0.71	23.4 (15.8, 49.0)	26.2 (12.4, 34.3)	0.29	0.25
LF (ms^2)†	3,766 (2,319, 6,172)	3,668 (2,380, 6,207)	0.15	2,021 (1,287, 9,871)	1,920 (1,379, 6,654)	0.72	0.70
HF (ms^2)†	1,784 (707, 3,168)	1,373 (715, 2,871)	0.18	648 (414, 3,650)	598 (500, 3,322)	0.39	0.94
LF:HF ratio	2.55±0.95	2.73±1.00	0.13	2.89±0.57	2.63±0.83	0.32	0.13
Total power (ms^2)†	10,908 (5,893, 15,575)	9,886 (6,671, 14,154)	0.35	4,985 (3,661, 20,950)	57,612 (3,652, 17,917)	0.65	0.94

†Median (IQR).
Abbreviations: SDNN, Standard Deviation of Normal-to-Normal intervals; SDANN, Standard Deviation of Average of Normal-to-Normal intervals for each 5-minutes; RMSSD, Root Mean Square of Successive Differences between N-N intervals; LF, low frequency; HF, high frequency.

Table 4 Multivariable linear regression analyses of the effect of bushfire smoke exposure on HRV.

Outcome Variables	Explanatory Variables	β	95% CI	P-value
ΔSDNN	Age	0.25	-0.81, 1.32	0.63
	Sex	11.80	-10.19, 33.79	0.28
	Smoking History	-3.81	-17.63, 25.25	0.72
	Bushfire exposure	23.43	-1.22, 48.08	0.062
ΔSDANN	Age	0.097	-0.85, 1.05	0.84
	Sex	16.23	-3.33, 35.79	0.10
	Smoking History	-3.76	-22.83, 15.31	0.69
	Bushfire exposure	26.25	4.33, 48.17	0.020

Each model was adjusted for age, sex and history of cigarette smoking.
Abbreviations: SDNN, Standard Deviation of Normal-to-Normal intervals; SDANN, Standard Deviation of Average of Normal-to-Normal intervals for each 5-minutes.

Discussion

Bushfire smoke affects many individuals within Australia and worldwide [15,17,24–28], and bushfire smoke exposure is associated with cardiovascular mortality [6,7,9,29] and morbidity [10–14,30,31]. This is the first study to have assessed the effects of bushfire smoke on cardiac autonomic function. Currently, there are three principal pathways that explain the adverse effects of air pollution: disturbance of autonomic nerve activity, inflammation, and direct effects of PMs inside the bloodstream [2]. However, these pathways are mainly supported by data from urban or traffic air pollution. Similar mechanisms are assumed in the effects of bushfire smoke [32], but direct observational data is limited. This study found evidence of suppression of cardiac autonomic activity during bushfire smoke exposure, which recovered subsequently in clean air. The difference remained statistically significant after adjusting for age, sex and history of cigarette smoking in the SDANN index.

Heart Rate Variability (HRV)

This study has demonstrated an impairment in two main HRV parameters in individuals who were exposed to bushfire smoke, compared with those in the control participants. The reduction in SDANN was statistically significant and independent after adjustment for possible confounders identified *a priori*. SDANN is a time-domain assessment of HRV, reflecting long-term changes in HRV and represents the balance between sympathetic and parasympathetic activities [33,34]. Our results corroborate with previous literature on the effect of PM (from non-bushfire sources) on SDANN—the majority have demonstrated an association between exposure and decrement (ie, reduction) in the parameter [19,20,35,36], including a reduction in SDANN due to $PM_{2.5}$ [35].

SDNN is an overall assessment of HRV [34] and is by far the most frequently reported HRV index in the PM literature. After adjustment for confounders, our study suggested a possible impairment (statistically borderline) in SDNN in response to bushfire smoke exposure. A strong body of literature supports the reduction of SDNN in response to a variety of sources of $PM_{2.5}$. Previous panel studies from similar aged groups participants to the present study demonstrate reductions in SDNN after $PM_{2.5}$ exposure [35,37].

Clinical Significance of SDNN and SDANN Impairment

Low HRV is an independent predictor of cardiac mortality and morbidity. Kleiger et al. were the first to report a five-time increase in all-cause mortality if SDNN is below 50 ms in participants with prior myocardial infarction [38]. Since then, many epidemiological studies have supported the observation that reduced HRV is an independent predictor of sudden cardiac death [39,40], non-fatal cardiac arrest [40], non-fatal coronary events [41] and arrhythmias [42] in participants post-acute myocardial infarction. Reduced HRV has also been implicated with poor prognosis in those with heart failure [43] or reduced left ventricular function [44]. Even in those without known cardiovascular disease (CVD), reduction in SDNN is a significant predictor of first CV events. A previous meta-analysis demonstrated that a 1% rise in SDNN results in approximately a 1% lower risk of a CV event [45].

Impact and Reduction of Air Pollution

Our results indicated that bushfire smoke causes adverse cardiovascular effects via imbalance of cardiac autonomic activity, via similar mechanisms to urban pollution. World Health Organization Guidance summarised policies and actions to reduce the emission of air pollutants in several domains, including transport system, industry, power generation, waste and wastewater, agriculture and forestry, housing, land use, and others [46]. Another emerging problem related to this is climate change: as it causes more heat waves, resulting in higher risk of bushfire not only in Australia but globally, actions to address climate change is strongly encouraged.

Limitations

Our study should be interpreted in the context of several limitations. First, this was an observational study with a small sample size although it had a similar sample size to previous reports [19,20]. Moreover, there were comparatively more participants in the exposed cohort compared to the unexposed cohort owing to only one town experiencing clean-air conditions. Despite this, we still observed a statistically significant reduction in the SDANN parameter and borderline-significant reduction in the SDNN parameter, after adjustment for confounders, in gross comparisons between those exposed and unexposed to bushfire pollution.

The magnitude of $PM_{2.5}$ exposure in Warburton was particularly high, with mean concentrations three to four times the daily acceptable maximum exposure of 25 $\mu g/m^3$ during data collection periods. However, the levels of exposure in the second exposure group in Traralgon were more erratic, with high peaks followed by periods of low concentrations. However, in attempts to minimise the possibility of type II errors, these data were included in our dichotomous exposure variable, as bushfire exposure still occurred with mean $PM_{2.5}$ levels above the Australian advisory standard.

The clinical significance of the magnitude of impairment in HRV demonstrated in this study remains to be determined with further data exploring the clinical outcomes of subclinical HRV changes. However, reduced HRV is a marker of autonomic dysfunction and a good predictor of cardiac morbidity and mortality, intimating that this may be a mechanism by which bushfire smoke causes detrimental cardiac effects.

Conclusion

In this relatively small panel study of 42 participants, exposure to the smoke from bushfires was associated with reduced long-term and possibly overall HRV. This may support the evolving hypothesis that disturbance in cardiac autonomic function serves as a mechanism for adverse cardiovascular outcomes from exposure to landscape fire smoke. Thus, further studies are warranted to investigate whether autonomic nerve system interventions, such as beta blockade, would mitigate the adverse effects from bushfire smoke.

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Appendices

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.hlc.2022.08.011

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