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Effects of passive smoking on heart rate variability, heart rate and blood pressure: an observational study§

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Background Exposure to environmental tobacco smoke (ETS) has been shown to increase the risk for cardiovascular diseases and death, and autonomic dysfunction (specifically, reduced heart rate variability (HRV)) is a predictor of increased cardiac risk. This study tests the hypothesis that ETS exposure reduces HRV in the general population and discusses possible pathways.

Methods This cross-sectional study was conducted between 2001 and 2003 and is part of the SAPALDIA (Swiss Cohort Study on Air Pollution and Lung Diseases in Adults) study.
The analysis included 1218 randomly selected non-smokers aged 50 and above who participated in 24-h electrocardiogram recordings. Other examinations included an interview, investigating health status (especially respiratory and cardiovascular health and health relevant behaviours and exposure to ETS) and measurements of blood pressure, body height and weight.

Results Subjects exposed to ETS at home or at work for more than 2 h/day had a difference of −15% in total power (95%CI: −26 to −3%), low frequency power (−28 to −1%), low/high frequency ratio (−26 to −3%) and −18% (−29 to −4%) in ultralow frequency power of HRV compared with subjects not exposed to ETS at home or work. We also found a 2.7% (−0.01 to 5.34%) higher heart rate during the recording in exposed subjects.

Conclusions Exposure to ETS at home and work is associated with lower HRV and with higher heart rate in an ageing population. Our findings suggest that exposure to ETS increases cardiac risk through disturbances in the autonomic nervous system.

Keywords Tobacco smoke pollution, heart rate variability, autonomic nervous system, heart rate, blood pressure

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Background

Exposure to environmental tobacco smoke (ETS) and reduced heart rate variability (HRV) in middle-aged and elderly subjects,[1] survivors of myocardial infarction,[2] or patients with other cardiovascular diseases[3,4] are both known to be associated with increased cardiovascular morbidity and mortality.[5–10] HRV, a widely used measure of cardiac autonomic control,[11] reflects autonomic modulation of the rhythmic activity of the sinus node.[11] To date, little has been reported on the association between ETS exposure and HRV, heart rate, or blood pressure, the alterations of which may be steps in the pathophysiological pathway leading from ETS exposure to cardiopulmonary disease.

To our knowledge, the effect of longer-term exposures to ETS on HRV has not been analysed. Short-term effects have been described by Pope, who found a reduction in HRV in 16 never smoking subjects equipped with Holter monitors, who were moved from the non-smoking section of an airport to the smoking lounge.[12] Reports from the 1991 SAPALDIA (Swiss Cohort Study on Air Pollution and Lung Diseases in Adults) study[13] describe the effects of ETS on respiratory symptoms in never smokers[14] and on lung function in asthmatics.[15] In the follow-up study (SAPALDIA 2), we also show a higher probability of the development of asthma in subjects exposed to ETS.[16] In SAPALDIA 2, ambulatory 24-h electrocardiograms (ECG) were performed in a random sample of participants age $\geqslant$50. This analysis looks at the effect of ETS exposure on HRV and explores the role of heart rate and blood pressure in this context.

Materials and methods

Participants

The SAPALDIA cohort study was designed to measure the health effects of long-term exposure to air pollutants in the Swiss adult population. Details of its design and objectives have been reported elsewhere.[17,18] In 1991, a random sample of the Swiss population was recruited from eight areas featuring distinct geographical and environmental conditions. SAPALDIA participants were examined in 1991 and 2001–03 for risk factors of cardiovascular disease, respiratory symptoms, pulmonary function evolution and development of lung diseases.

A random sample of 2000 SAPALDIA 2 participants age $\geqslant$50 who agreed to participate were offered a 24-h ECG recording. Data on smoking status were collected during an extensive interview led by trained fieldworkers. Among the 1837 persons having performed the measurements, 1385 reported that they had not smoked cigarettes, pipes, cigarillos or cigars in the last 5 years and were included in this study. Self-reports were confirmed by end-expiratory carbon monoxide (CO) measurements using EC50 Micro-Smokerlyzers (BEDFONT, Rochester, UK); 91 participants were excluded because they had an end-expiratory CO of $\geqslant$7 ppm, indicating that they might be smokers.[19–22] One participant was excluded because of a myocardial infarction in the previous 3 months and four because of digitalis intake in the previous 30 days. None had a cardiac pacer or anaesthesia (narcosis or spinal anaesthesia) in the 8 days prior to the ambulatory ECG recording (Figure 1).

ETS exposure was assessed for different environments by the question 'How many hours per day are you exposed to other people's tobacco smoke (i) at home (ii) at the workplace (iii) in bars and restaurants (iv) elsewhere?' We focused on exposure to ETS at home and work since these two sources dominate overall exposure in most subjects and because it is usually easier to recall routine exposure to ETS at home and at work than in other places. For seven subjects, information on ETS exposure was missing. On the basis of previous work,[14] ETS exposure was categorized into three exposure groups: none, $\leqslant$2 h per day but not none, and >2 h per day.

Cardiovascular risk factors

Blood pressure was measured twice on the left upper arm with the subject sitting and at rest, by an automatic device (705CP, OMRON, Tokyo, Japan) according to WHO recommendations.[23] Blood pressure values used in the regression model were the arithmetic mean of the two measurements. High blood pressure was defined as either a systolic blood pressure (SBP) $\geqslant$140 mmHg, or a diastolic blood pressure (DBP) $\geqslant$90 mmHg, or having answered yes to the question 'Do you have the following condition: Hypertension?'

Body height and weight were measured with participants not wearing any shoes or coats and body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). For two participants, information for calculating BMI was missing.

Data on education, hypertension and current medications were collected during the interview.

The highest degree of education, which is correlated to income,[24] was used as a proxy for social position.

Blood samples were taken from subjects, and several known cardiovascular risk factors were determined by the Institute for Clinical Chemistry of the University Hospital Zürich: A Hitachi Modular Autoanalyser (Rotkreuz, Switzerland); assays from Roche Diagnostics (Mannheim, Germany) were used to measure serum levels of uric acid and total cholesterol (both enzymatic tests) and high-sensitive C-reactive protein (CRP) was measured with a latex-enhanced immunoturbidimetric assay. High-density lipoprotein cholesterol (HDL) was measured with a homogenous assay (Roche diagnostics, Mannheim, Germany) using Roche Cobas Integra (Rotkreuz, Switzerland). HDL values were only used if the participants had a triglyceride level of $\leqslant$9.4 mmol/l. As additional atherogenic markers, the difference between total cholesterol and HDL (non-HDL-cholesterol) and the ratio between total cholesterol and HDL were calculated.

Ethical approval for the study was given by the central ethics committee of the Swiss Academy of Medical Sciences and the Cantonal Ethics Committees for each of the eight examination areas; subjects gave informed consent at the examination. These procedures were in accordance with the recommendations of the Helsinki Declaration.

HRV data

For 24-h ECG (Holter) recording, digital devices (Aria, Del Mar Medical Systems, Irvine, CA) with a frequency response of 0.05–40 Hz and a resolution of 128 samples/s were

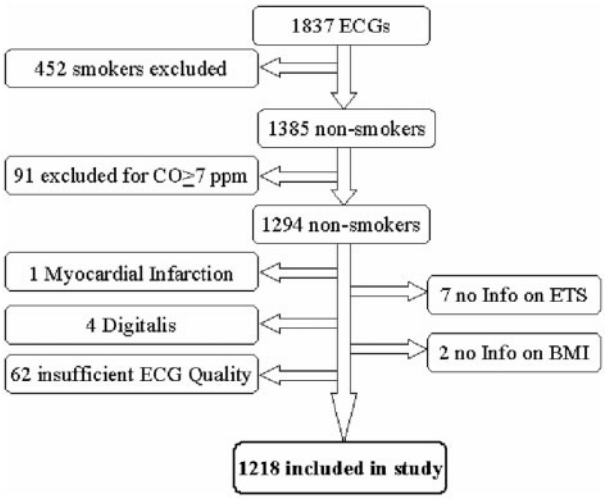

Figure 1 Flow chart of participants and exclusion criteria

used. The recorders were hooked up after the interview. Three leads (V_1, altered V_3 with the electrode on the left midclavicular line on the lowest rib and altered V_5 with the electrode on the left midclavicular line on the lowest rib) were recorded over 24 h. We excluded the first 2 h of recording to avoid bias from the effects of methacholine administered in the preceding broncho-challenge test. Recordings with insufficient quality ($n = 32$) or <18 h ($n = 30$) were not used (Figure 1). Mean duration of the remaining 1218 recordings was 22.3 ± 2.1 h. Participants were asked to follow their regular daily life and to fill in a time-activity diary during the recording time.

All recordings were scanned through a StrataScan 563 (Del Mar) and interpreted with the interactive method, with a final visual check of the full disclosure. Mean heart rate per minute was derived from Holter measurements. The length of each RR interval was manually validated during this step. Re-sampling was done at 4 Hz. Spectral analysis was performed by the fast Fourier transform method using sliding 256 PTAs windows for night periods. For 24-h periods, calculations of RR intervals were made without sliding window, to allow measurement of ultralow frequency power (ULF) and of very low frequency power (VLF). Only normal to normal (NN) intervals were used, with intervals excluded due to ectopy or artefacts being replaced by holding the previous coupling interval level throughout the time interval to the next valid coupling interval. The standard deviation of all normal to normal RR intervals (SDNN) and the following frequency domain variables were calculated: total power (≤0.40 Hz), ULF (≤0.0033 Hz), VLF (0.0033–0.04 Hz), low frequency (LF) power (0.04–0.15 Hz), high frequency (HF) power (0.15–0.40 Hz) and the ratio between LF and HF (LF/HF).

Statistical analysis

Because an initial inspection suggested that the distribution of the residuals was skewed, the HRV values were log-transformed before further analysis and the results are presented as percent differences between exposure groups.

We evaluated the effect of ETS on HRV, heart rate and blood pressure using a multivariable regression model adjusting for study site, sex, age and age squared, education, BMI, self-reported diabetes and beta-blocker intake in the previous 30 days (core model). Sensitivity analysis for additional potential confounders (hypertension, physical activity, alcohol drinking, cardioactive medication and cardiovascular risk factors in the blood) and additional analyses for the period during sleep at night to exclude shorter-term effects were carried out. To check whether former smoking would have a residual effect on cardiac autonomic function, we controlled for smoking status in a further analysis.

To assess differences of proportions and means in the three ETS exposure groups in Table 1, Chi-squared-tests and the Kruskal–Wallis test were performed.

Statistical analysis was performed using the software package Stata 9.2 (Stata corporation, College Station, TX).

Results

Among the 1218 never smokers and former smokers included in the final study group, 184 (15%) were regularly exposed to ETS at home or at work: 104 (8.5%) ≤2 h/day, and 80 (6.6%) >2 h/day.

Table 1 gives an overview of the study population's characteristics, categorized by ETS exposure. Subjects without ETS exposure were slightly older, had a lower BMI and drank less alcohol.

Table 2 shows geometric means of HRV measures, adjusted for the covariates of the core model, according to ETS exposure. In subjects exposed >2 h/day to ETS at home or at work, total power (95% CI 26 to −3%), LF (CI −28 to −1%) and LF/HF (CI −26 to −3%) were 15% lower than in unexposed subjects. ULF was 18% (CI −29 to −4%) lower. Although results for HF, VLF and SDNN showed no substantial difference between exposed and unexposed subjects, the trend was the same as for the other outcome variables. Similar results emerged when we stratified for sex (Supplementary data are available at *International Journal of Epidemiology* online). In order to test possible pathways, we analysed heart rate and blood pressure: the results are shown in Table 3 as arithmetic means adjusted for the covariates of the core model. Heart rate was 2.7% (CI 0.1 to 5.5%; $P = 0.049$) higher in subjects exposed >2 h/day to ETS than in unexposed subjects. Systolic blood SBP was similar in the two groups and DBP was 1.9% (−3.0 to 2.9%; $P = 0.174$) higher in subjects exposed to ETS > 2 h/day. Unadjusted results are presented as online supplementary material.

Figure 2 shows the relationship between ETS exposure and percent difference in LF, heart rate and DBP with control for all factors of the core model. There were trends for a lower LF with increasing ETS exposure and for higher heart rate and DBP with higher ETS exposure at home or work.

Sensitivity analyses

In order to guard against confounding by factors not considered in the core model, we conducted sensitivity analyses by including complementary categories of covariates in the model each at a time: additional control for physical exercise causing sweating and physical exercise causing slight shortness of breath did not change the difference in total power between the reference group and the highest ETS exposure group

Table 1 Overview of the study population baseline characteristics by exposure group

ETS exposure	None	⩽2 h/day	>2 h/day
n	1034 (84.9%)	104 (8.5%)	80 (6.6%)
[a]Female	556 (53.8%)	53 (51.0%)	41 (51.3%)
[a]Age (years)	61.0 (SD 6.4)	59.8 (SD 6.2)	58.4 (SD 5.0)
Blood pressure			
systolic (mmHg)	132.7 (SD 19.7)	133.7 (SD 21.0)	131.5 (SD 18.6)
diastolic (mmHg)	81.7 (SD 10.8)	82.4 (SD 10.4)	83.5 (SD 11.3)
[a]BMI (kg/m^2)	26.5 (SD 4.3)	27.8 (SD 4.8)	27.4 (SD 4.3)
[a]Self-reported diabetes	44 (4.3%)	4 (3.9%)	3 (3.8%)
[a]Education			
Primary	93 (9.0%)	15 (14.4%)	4 (5.0%)
Secondary	660 (63.8%)	69 (66.4%)	59 (73.8%)
Tertiary	281 (27.2%)	20 (19.2%)	17 (21.3%)
Light physical activity			
⩽2 d/w	496 (48.1%)	55 (52.9%)	42 (52.5%)
>2 d/w	536 (51.9%)	49 (47.1%)	38 (47.5%)
Heavy physical activity			
⩽1 h/w	763 (74.2%)	77 (74.8%)	54 (67.5%)
>1 h/w	266 (25.9%)	26 (25.2%)	26 (32.5%)
Alcohol			
<1 glass/day	776 (75.1%)	66 (63.5%)	56 (70%)
⩾1 glass/day	258 (25.0%)	38 (36.5%)	24 (30.0%)
[a]Beta-blocker medication	123 (11.9%)	17 (16.4%)	8 (10.0%)
ACE-inhibitor	64 (6.2%)	6 (5.8%)	6 (7.5%)
Antiarrhythmic drugs class I + III	4 (0.4%)	0 (0.0%)	1 (1.3%)
Calcium channel blocker	45 (4.4%)	7 (6.7%)	5 (6.3%)
Diuretics	43 (4.2%)	6 (5.8%)	2 (2.5%)
Sympathomimetics	36 (3.5%)	5 (4.8%)	0 (0.0%)
Uric acid [mol/l]	321.1 (SD 81.4)	332.6 (SD 79.0)	331.7 (SD 93.4)
Hs-CRP [mg/l]	2.6 (SD 5.9)	2.4 (SD 4.8)	2.2 (SD 3.2)
Non-HDL-cholesterol [mmol/l]	4.7 (SD 1.1)	4.8 (SD 1.2)	4.9 (SD 1.2)

[a] Covariates of the core model.

(Supplementary data are available at *International Journal of Epidemiology* online). Also, no sizeable change of the results was seen with additional control for hypertension. The difference in total power between the reference group and the highest exposure group slightly increased with additional control for consumption of red wine and alcoholic beverages or for serum levels of uric acid, high-sensitive CRP and non-HDL cholesterol or when subjects taking ACE inhibitors, antiarrhythmic medication, calcium channel blockers, diuretics or sympathomimetics were excluded. Moreover, results were not sensitive to excluding education from the model. We could also see no difference in the influence of educational level on HRV between men and women (data not shown). Additional analyses of HRV restricted to the sleep period according to diary information showed results similar to the analyses of the 24-h measures. On average, LF power at night was 15.1% (CI: −25 to −4%; $P = 0.009$) lower in subjects exposed to ETS ⩾2 h/day than in the reference group. Additional controlling for smoking status showed little evidence for a residual effect of former smoking. The strongest effect of former smoking was seen for ULF with a 5% lower ULF (CI −13 to 2%) in former smokers than in never smokers.

Discussion

In recent years, there has been increasing evidence that ETS exposure affects cardiovascular health.[5–10,25–27] Our study provides further evidence that ETS exposure is associated with cardiac autonomic dysregulation, which may be an intermediate step in the pathway to cardiac instability.[4,28] Our observations are in agreement with the findings of Pope, who described a short-term decrease in all HRV domains after acute exposure to ETS, but with relatively high standard errors in HF.[12]

LF, which is considered to represent both sympathetic and parasympathetic activities,[29] was lower in subjects with higher ETS exposure. We also observed ETS-associated increases in heart rate and, more weakly, in DBP, consistent with increases in sympathetic stimulation.

Since few people are exposed to ETS during sleep, we restricted analyses to the sleep period, when acute exposure can be excluded and found results similar to those of the 24-h measures. Therefore, we think that our findings do not reflect acute responses.

Table 2 Adjusted[a] geometric mean HRV according to ETS exposure

HRV variable	No current ETS exp.	ETS ⩽2 h/day	ETS >2 h/day
n	1034	104	80
SDNN [ms]	134.0 (131.8, 136.1)	134.0 (127.4, 140.9)	129.3 (122.1, 136.9)
Total Power [ms^2]	3866.7 (3729.6, 4008.8)	3712.1 (3308.78,4164.5)	3270.1 (2868.7, 3727.7)
HF [ms^2]	71.3 (67.5, 75.2)	61.5 (51.8, 73.1)	71.2 (58.5, 86.6)
LF [ms^2]	233.6 (224.0, 243.7)	210.3(183.8, 240.6)	197.7 (169.6, 230.5)
LF/HF	3.3 (3.2, 3.4)	3.4 (3.0, 3.8)	2.8 (2.4, 3.2)
VLF [ms^2]	626.1 (603.4, 649.7)	598.9 (532.5, 673.7)	560.0 (489.8, 640.3)
ULF [ms^2]	2741.3 (2634.1, 2852.8)	2671.6 (2352.9, 3033.6)	2256.3 (1952.4, 2607.6)

Values in parentheses are 95% CIs.

[a] Adjusted for study site, gender, age, education, BMI, diabetes and beta-blocker intake.

Table 3 Adjusted[a] geometric means of heart rate and blood pressure according to ETS exposure

Variable	No current ETS exp.	ETS ⩽2 h/day	ETS >2 h/day
Heart rate [bpm]	73.4 (72.9, 73.9)	73.4 (71.8, 75.1)	75.3 (73.5, 77.2)
SBP [mmHg]	132.7 (131.6, 133.8)	133.5 (130.1, 136.9)	132.6 (128.7, 136.5)
DBP [mmHg]	81.7 (81.1, 82.3)	82.1 (80.2, 84.0)	83.3 (81.1, 85.5)

Values in parentheses are 95% CIs.
SBP: systolic blood pressure, DBP: diastolic blood pressure.
[a] Adjusted for study site, gender, age, education, BMI, diabetes and beta-blocker intake.

ETS may affect autonomic control of the heart through activation of neural receptors of the respiratory tract. On the other hand, gaseous components, soluble fractions of the particulate component and ultrafine particle components of ETS may be absorbed in the lung and have additional systemic effects. In the experimental setting, chronic ETS exposure has been shown to increase proinflammatory cytokines and arterial resistance, to decrease concentrations of antioxidants and to increase lipid peroxidation.[30] We found no evidence of ETS-associated increases in inflammation as measured by CRP and other causal mechanisms may predominate with low-grade chronic exposure. Recent work by Bartoli and colleagues[31] suggests that particle exposures alter barometric reflexes, a pathway through which ETS exposure might also influence HRV.[31] Ultrafine particles are associated with oxidative stress,[32] as well as with reduced HRV.[33]

To better understand why exposure to ETS is associated with lower HRV, it is interesting to compare these effects with those of active smoking on HRV. In a recent publication, we showed that active smokers had lower overall and low to ULF HRV measures than never smokers, which reflect the dynamic features of sympathetic cardiovascular modulation, analogous to the results described in this work. The effect of current smoking compared with never smoking was also of magnitude similar to the effect shown in this study.[17] Thus, we could deduce that active smoking and passive smoking harm the cardiovascular system through similar toxic substances.

The consequence of autonomic dysfunction caused by pollutants such as ETS, air pollution and other factors can be an increased risk for ventricular arrhythmia in vulnerable patients or a contribution to the instability of a vascular plaque, eventually leading to cardiac death.[34–36]

We measured exposure to ETS using questionnaire data and used CO measures to validate smoking status. We believe that self-reporting gives a better estimate for exposure to ETS during the past year than measurement of biomarkers, which reflect the level of exposure to passive smoking in the immediate past with half-lifes of only several hours.[37] In the literature, measurement of exhaled CO in combination with self-reporting has been described to provide an acceptable degree of discrimination between smokers and non-smokers.[37]

Reporting bias might have occurred if participants with lower HRV had been more likely to report passive exposure to cigarette smoke. However, this is very unlikely since HRV is not readily apparent to the participant. Moreover, exposure to ETS is generally associated with respiratory symptoms and to a much lesser degree with cardiovascular health. In addition, we observed a 13% increase of individuals not exposed to ETS compared with 1991—which would point towards under—rather than overreporting of ETS.

A recent study has shown that social position expressed as low employment grade is associated with low HRV.[38] In our study, the effect of ETS exposure on the HRV parameters did not change

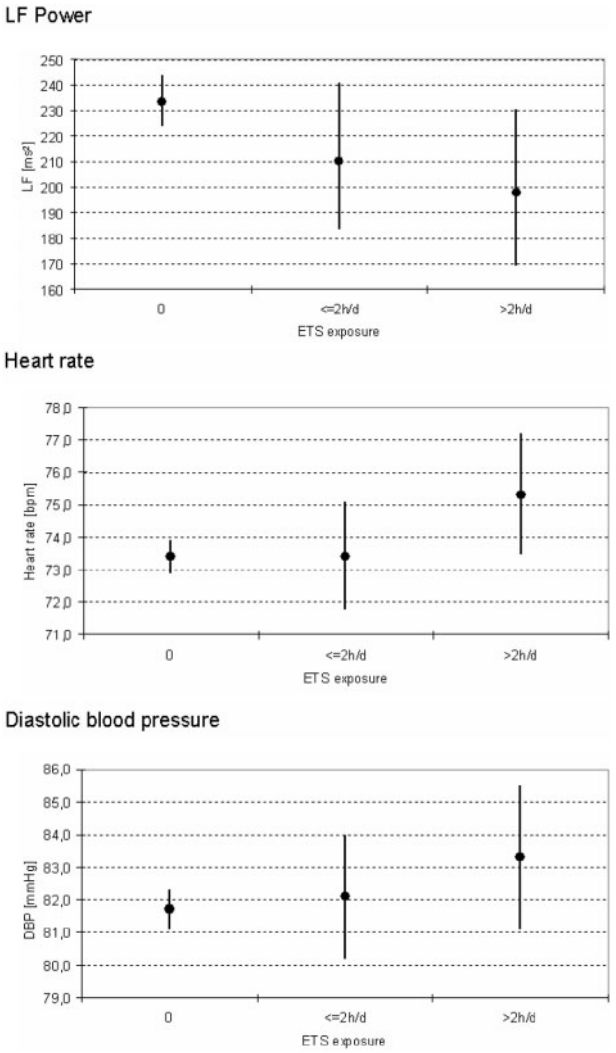

Figure 2 Hours of environmental tobacco smoke exposure at home and at work and low frequency heart rate variability, heart rate and diastolic blood pressure and respective 95% confidence intervals, adjusted for study site, sex, age, education, BMI, diabetes and beta-blocker intake

when we did not account for level of education, indicating that these results are not likely to be confounded by social position.

In conclusion, our results contribute to the evidence that exposure to second-hand smoke increases cardiac risk through cardiac autonomic dysfunction. Health benefits can be expected if people are protected from passive smoking.

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Mathematical HRV engineering: V Pichot.

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KEY MESSAGES

- ETS has been shown to be a risk factor for cardiovascular disease, but so far little is known about possible mechanisms.
- We show that subjects exposed to environmental tobacco smoke ETS for over 2 h/day at home and/or at work had a reduced heart rate variability compared with unexposed subjects.
- Exposed subjects also had a higher heart rate and a tendency for higher diastolic blood pressure, suggesting a possible pathway of increased cardiac risk through disturbances in the autonomic nervous system.

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