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ORIGINAL ARTICLE

Impact of Air Pollutant on Heart Rate Variability in Healthy Young Adults

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Abstract

Background: Air pollution and sex independently affect cardiac autonomic control, which can be assessed by heart rate variability (HRV). The research hypothesis is that individuals exposed to low concentrations of pollution have higher cardiac autonomic modulation compared to those exposed to high concentrations and that women have better cardiac autonomic control than men.

Objective: To analyze the impact of exposure to air pollutants, specifically smoke, and sex on HRV in healthy young people exposed to different concentrations of pollution over an average period of 22 years.

Methods: From April to September 2011, 36 participants of both sexes (20-30 years old) were selected, grouped by levels of air pollution exposure according to indices provided by the Environmental Company of São Paulo State. The R-R intervals (R-Ri) of the electrocardiogram were captured using a heart rate monitor during supine rest. HRV was analyzed by spectral analysis and conditional entropy. The Queen´s College step test was used to characterize functional capacity. A between-group comparison was performed using the two-way ANOVA statistical test (post hoc Tukey) and $p<0.05$.

Results: Significant differences were found in mean R-Ri ($p<0.01$) and cardiac parasympathetic modulation between sexes in the same city ($p=0.02$) and between groups exposed to different air pollution concentrations ($p<0.01$).

Conclusion: Our results suggest that long-term exposure to air pollutants, specifically smoke, has an unfavorable impact on HRV, with reduced cardiac vagal autonomic modulation in healthy young adults, especially females.

Keywords: Air pollution; sex; autonomic nervous system; heart rate.

Introduction

Air pollution is defined as the presence of substances in the atmosphere resulting from human activity or natural processes. When these materials surpass pre-established concentrations, they can be harmful to health, as well as to normal community activities, such as activities of daily living and social participation.[1,2]

Impacts of air pollution on cardiovascular morbidity and mortality have been described,[3] and can be explained by: 1) an increase in fibrinogen and circulating inflammatory factors that lead to an increase in blood viscosity and coagulation disorders; and 2) changes in autonomic nervous system (ANS) modulation to the heart,[4–9] which can be evaluated through heart rate variability (HRV).

Studies have shown that some factors like sex and functional capacity can influence ANS modulation.[10-12] Women have a higher resting HRV than men of the same age group, indicating a parasympathetic predominance in females and a sympathetic predominance in males.[10,12-14]

Assessment of HRV is a non-invasive, simple and inexpensive method, widely used in the quantification of cardiac sympathetic and parasympathetic modulation using linear and non-linear measures.[11,15-19] An individual who exhibits efficient cardiac autonomic control

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mechanisms has a high resting HRV, characterized by a parasympathetic predominance.[8,19,20] However, some cardiac conditions (e.g., conduction disturbances and atrial fibrillation) can also induce a high HRV.[19]

Thus, the research hypothesis is that individuals exposed to low concentrations of air pollution have better cardiac autonomic modulation compared to those exposed to high concentrations, and that women have better cardiac autonomic control than men. Thus, this study aimed to analyze the long-term impact of exposure to pollutants, specifically to smoke, and the influence of sex on cardiac autonomic modulation in healthy young people exposed to two different levels of air pollution.

Methods

Study design

This was an observational, cross-sectional, prospective study.

Sample

Thirty-six participants (20 men and 16 women) between 20 and 30 years old were selected by convenience, and divided into two groups according to the place of residence: a) group 1 – 10 men and 8 women living in a city with a high concentration of air pollution (São Paulo, São Paulo State) and; b) group 2 – 10 men and 8 women living in a city with a low concentration of air pollution (São Carlos, São Paulo State).

All volunteers were considered healthy according to the anamnesis: they did not have any disease of the respiratory, cardiovascular, or skeletal muscle systems. They lived in the same city for at least 15 years, without staying more than six months in other cities that had a concentration of air pollution different from the place of origin. It is known that short-term exposure to pollutants, depending on the concentration and type of pollutant, can acutely increase the risk of respiratory and cardiovascular mortality,[3,21] while exposure to air pollutants for a period between 15 and 30 years can cause medium and long-term impacts on human health.[22] Individuals using medications that can alter cardiac autonomic modulation, individuals who consumed alcohol, smokers, hypertensive subjects, those with diabetes mellitus, respiratory or cardiovascular diseases, sedentary lifestyle and/or a body mass index ≥ 30 kg/m^2 were excluded.

Classification of locations regarding air quality

The indices for estimating air quality and classifying the cities as “highly polluted” and “low polluted” were consulted on the website of the Environmental Company of São Paulo State (CETESB).[23] Primary standards for high pollutant concentrations were those that, when exceeded, can affect the health of the population, that is, the maximum tolerable levels. Secondary standards were defined as concentrations below which have the least impact on the population's well-being, that is, the desired levels of pollutant concentrations. In this study, we adopted 150µg/m^3 and 100µg/m^3 per day for primary and secondary standards, respectively.[24]

To obtain the annual averages of 2011, the averages of the indices from the seven air quality monitoring stations in the metropolitan region of São Paulo and from the single monitoring station in São Carlos in that same year, provided by CETESB, were calculated.[23] These data are shown in Table 1.

However, for the purposes of this research, only smoke concentrations were considered for estimation of air pollution of the two cities mentioned above (São Paulo and São Carlos), which represent only a fraction of the particulate matter that influences this type of pollution. This decision was made based on the information available on the website of CETESB,[23] which provides only smoke indices as measurements in the city of São Carlos.

Procedures

Volunteer recruitment and data collection were carried out from April to September 2011 at the Physical Education and Sport School of the University of São Paulo and the Cardiovascular Physiotherapy Laboratory of the Federal University of São Carlos.

Initially, volunteers were informed about the purposes of the study and experimental procedures and signed an informed consent form. The study was approved by the Research Ethics Committee (EEFE-USP 2011/36) and complied with the 466/12 Resolution of the National Health Council 12/12/2012.

The subjects were instructed to abstain from caffeine and alcoholic beverage intake, and from strenuous physical exercise for at least 24 hours before the HRV measurement, and to have a good night's sleep the night before the tests. The experimental procedure was carried out in the morning period (between 7 am and 12 pm), considering circadian variations.[18,25]

Table 1 – Primary and secondary smoke index standards of the cities of São Paulo and São Carlos, Brazil, in 2011

	Reference value	São Paulo, SP	São Carlos, SP
Primary standard ($\mu g/m^3$)	150	158,85	46
Secondary standard ($\mu g/m^3$)	100	109,71	38

NB: $\mu g/m^3$ = micrograms/cubic meter. Source: CETESB.[23]

On the day of the experiment, the volunteers were asked whether they had followed the instructions correctly and if they were in good health. Then, the heart rate monitor (Polar Electro, Finland, S810®) was placed on the volunteer's chest, according to the manufacturer's specifications.[18] Afterwards, the RR intervals (R-Ri) of each participant at supine rest were recorded (in ms), for 15 minutes, in a silent and climate-controlled environment, at a temperature of around 22 °C and relative humidity between 40 and 60%.

Next, the submaximal exercise test was performed with a 40.9 cm step, following the Queen´s College protocol[26] for people between 18 and 30 years old. The protocol consisted of stepping up and down on the step for three minutes, in cadence with a metronome set at 96 beats per minute (bpm). This test aimed to indirectly estimate the maximum oxygen consumption (VO_2max) reached by the volunteer, considering heart rate recovery (from the 5th to the 20th second heartbeat after the test), and the following equations proposed by the protocol:

Men → VO_2max (mL/Kg/min) = 111.33 – (0.42 x heart rate recovery)

Women → VO_2max (mL/Kg/min) = 65.81 – (0.1847 x heart rate recovery)

The estimated VO_2max values were used considering the indices established by the American Heart Association (AHA)[27] to characterize the sample and ensure that the studied groups had similar aerobic functional classification, as this is also a factor that can affect HRV values.[10,18,25]

Data processing

R-Ri analysis

For HRV analyses, the R-Ri sequence with the highest stability, with a length of 256 points, was selected for each volunteer, excluding the initial and final stretches.[18,19]

Linear analysis of HRV

The spectral analysis of the HRV was performed by the autoregressive method[28,29] in two bands: low frequency (LF) and high frequency (HF).[13,18,25] Their values were expressed in normalized units – LFnu for cardiac sympathetic modulation and HFnu for parasympathetic modulation –[6,7] calculated as follows: LFnu = LF power/TP – VLF power × 100; HFnu = HF power/TP – VLF power × 100.[28,29] Mean R-Ri and variance were also calculated.

Nonlinear HRV analysis (conditional entropy)

The study of entropy qualifies and quantifies HRV complexity.[30] Conditional entropy based on symbolic dynamics[17] shows information about the regularity of HRV, that is, it is able to clarify whether the amount of information provided from a new sample can be determined by analyzing previous values.[15,16] This analysis provides the complexity index (CI), which was normalized by Shannon entropy, resulting in the normalized complexity index (NCI).[17] According to Porta et al.,[17] the NCI can range from 0 (null information) to 1 (maximum information). This means that the higher the NCI, the lower the regularity of the series and the greater the complexity.

Statistical analysis

The Shapiro-Wilk test was used to verify data normality. The impact of exposure to pollutants and of sex on HRV were analyzed by the two-way ANOVA statistical test, taking sex (male and female) and pollution (most polluted location – São Paulo and least polluted location – São Carlos) as factors, and analyzing the interaction between them using the post hoc Tukey's Test. Data were expressed as mean ± standard deviation. A significance level of 5% ($p<0.05$) was considered. For this purpose, the Sigma Plot 11.0 for Windows software was used.

Results

Anthropometric characteristics and age of participants are described in Table 2. There were statistical differences in body mass, height and estimated VO_2max between the sexes, where women showed lower values compared to men (as expected), regardless of the city in which they lived (Table 2). Group 1 volunteers lived in São Paulo for 21.94 ± 1.43 years and group 2 volunteers in São Carlos for 22.55 ± 4.40 years.

Table 3 shows the results of linear (time and frequency domain) and non-linear (conditional entropy) HRV analysis in supine rest of the evaluated groups. Mean R-Ri showed the impact of sex and its interaction with air pollution exposure, which was higher in men compared to women in the city of São Paulo. Likely, HFnu (cardiac parasympathetic

Table 2 – Age, anthropometric characteristics, and functional capacity of residents of São Paulo and São Carlos, included in the study

	Group 1 (São Paulo, SP)		Group 2 (São Carlos, SP)		P values		
	Men (n = 10)	Women (n = 8)	Men (n = 10)	Women (n = 8)	Impact of air pollution exposure	Impact of sex	Interaction between the impacts
Age (years)	22.2 ± 1.7	21.6 ± 1,1	22.8 ± 3.2	23.8 ± 3.2	0.109	0.822	0.363
Body mass (Kg)	74.1 ± 7.9	61.6 ± 5.8	76.4 ± 11.5	64.7 ± 16.4	0.473	0.003 *	0.918
Height (m)	1.8 ± 0.1	1.6 ± 0.1	1.8 ± 0.1	1.6 ± 0.1	0.395	< 0.001 *	0.938
BMI (Kg/m²)	23.4 ± 1.5	22.7 ± 1.9	24.7 ± 2.9	24.3 ± 6.2	0.228	0.640	0.886
Estimated VO_2max	50.5 ± 3.8	36.2 ± 3.1	50.8 ± 5.5	34.4 ± 2.7	0.559	< 0.001 *	0.443

*NB: values expressed as mean ± standard deviation; BMI: body mass index; VO_2max = maximum oxygen consumption; * significant difference according to the two-way ANOVA statistical test, with post hoc Tukey test. Source: research data.*

Table 3 – Heart rate variability assessed in the time, frequency and conditional entropy domains

	Group 1 (São Paulo, SP)		Group 2 (São Carlos, SP)		P values		
	Men (n = 10)	Women (n = 8)	Men (n = 10)	Women (n = 8)	Impact of air pollution exposure	Impact of sex	Interaction between the impacts
Mean R-Ri (ms)	1078.6 ± 138.7	816.6 ± 89.8	1005.1 ± 135.5	909.9 ± 57.4	0.798	< 0.001 *	0.0037 *
R-Ri Variance (ms²)	6373.5 ± 7263.5	2921.8 ± 2425.1	3998.4 ± 2626.7	3876.9 ± 2128.8	0.631	0.231	0.264
Spectral analysis							
LFnu (nu)	42.0 ± 20.5	46.1 ± 11.9	48.2 ± 18.3	30.2 ± 18.9	0.424	0.254	0.075
HFnu (nu)	55.8 ± 18.1	49.3 ± 12.2	47.5 ± 17.3	68.4 ± 19.1	0.351	0.217	0.022 *
Conditional Entropy							
NCI	0.8 ± 0.1	0.8 ± 0.0	0.8 ± 0.1	0.8 ± 0.1	0.589	0.291	0.472
CI	1.2 ± 0.1	1.1 ± 0.1	1.2 ± 0.1	1.2 ± 0.2	0.917	0.504	0.169

*Note: values expressed as mean ± standard deviation. R-Ri: R-R intervals; LFnu: low frequency in normalized units; HFnu: high frequency in normalized units; NCI: normalized complexity index; CI: complexity index; * significant difference according to the two-way ANOVA statistical test, with post hoc Tukey test. Source: research data.*

modulation) showed an interaction between sex and air pollution exposure, which was higher in women compared to men living in the city of São Carlos.

Moreover, HFnu was higher in women living in São Carlos, compared to those living in São Paulo. On the other hand, LFnu (cardiac sympathetic modulation) and variables related to the HRV complexity (conditional entropy) did not show an impact from pollution or sex.

The main findings of the present study were: 1) there was an impact of sex on mean R-Ri in subjects living the city with the highest concentration of air pollution (São Paulo/SP), as men had higher values than women; 2) there was an impact of sex on cardiac parasympathetic modulation in the city with the lowest concentration of air pollution (São Carlos, SP), as women had greater parasympathetic modulation compared to men; and 3) there was an impact of air pollution on cardiac parasympathetic modulation among women, as women from São Carlos, SP had greater modulation than those from São Paulo, SP.[31,32]

Discussion

The main finding of the present study was that long-term exposure to pollutants, specifically smoke, interferes with cardiac autonomic modulation, and female residents of the city with lower air pollution levels showed greater parasympathetic modulation compared to male residents.

Mean R-Ri at rest was higher in men than in women only in group 1, *i.e.*, among individuals exposed to a higher concentration of pollution, indicating an impact of sex on R-Ri regardless of air pollution levels. This may be explained by the fact that male individuals have a larger heart size[33] and, consequently, greater cardiac output and blood volume ejected by systole, presenting a lower basal heart rate compared to women.[34] A possible adaptive process related to long-term exposure to pollutants in both sexes should also be considered. Furthermore, men had a better functional capacity than women according to the AHA functional classification.[27]

Parasympathetic modulation was greater in women than in men only in group 2 (lower concentration of air pollution). The association of resting HRV with sex, with higher vagal modulation at rest among women, has been observed in several studies,[10,12,35] corroborating our finding. This may be due to a higher resting HRV and greater vagal modulation in women than men.[10,12,13] However, pollution causes a decline in parasympathetic modulation and an increment in sympathetic activity,[36,37] suggesting that a greater exposure to pollution did not equally affect the expected responses in HRV in men and women.

Concerning parasympathetic modulation, the within-sex analysis revealed an impact of air pollution exposure on females, as women in group 2 showed greater modulation than those in group 1. Thus, exposure to a higher concentration of pollution had an unfavorable impact on cardiac autonomic modulation in the study women. This indicates that females are more susceptible to the damage caused by pollution, as the parasympathetic modulation of men in the two cities was not significantly different. Other studies have also reported a reduction in cardiac vagal tone in individuals exposed to pollution, but they did not carry out an analysis by sex, which makes it difficult to make a comparison with the findings of the present study.[8,20]

As previously stated, we observed different HRV between sexes and, therefore, men and women may suffer different effects of the long-term exposure to air pollution on the ANS. This finding may guide future studies regarding the association among these variables.

Regarding the complexity of HRV, assessed by the conditional entropy, no statistical differences were found between the groups (São Paulo vs. São Carlos residents) or between men and women. This is in accordance with the findings of Catai et al.,[11] who assessed various age groups and, for the age range similar to our study, there were no differences between sexes, as women showed lower HRV complexity only after menopause, due to the sharp decline in the estrogen hormone, while men showed a linear decrease throughout the aging process. On the other hand, Voss et al.,[38] who also assessed different age groups, found that in the 25–34-year age range, the complexity indices varied according to sex and were higher in women than in men.

If, on the one hand, the impact of sex on the variables related to HRV is well documented in the literature, on the other hand, the relationship of these same variables with exposure to atmospheric pollution is still poorly known. Existing studies mainly cover short-term pollution,[3,4,6,7,9,36,37] making it difficult to compare their results with ours. In a meta-analysis of epidemiological studies carried out by Pieters et al.,[39] the authors found a reduction in HRV with an increase in air pollution exposure. However, when the literature search encompassed HRV, sex and long-term air pollution, we did not find any studies.

This study has some limitations. The first is that it involved only two cities in São Paulo State and, therefore, the results cannot be generalized; although there are differences in the concentrations of smoke pollution between the cities of São

Paulo and São Carlos, these may not have been enough to cause other significant changes in HRV. It is important to consider that São Carlos is a medium-sized city, with many industries and a large vehicle fleet. If the comparison had been made between São Paulo and a smaller city (and thus with lower air pollution concentrations), perhaps greater differences would have been observed; however, smaller cities usually do not have air quality control, which could lead to spurious conclusions. Also, even though the municipality of São Carlos performs the measurement of smoke indices, these represents only a fraction of the particulate-matter air pollution. Another potential limitation is the small sample size, which may have influenced the results in some of the analyses, such as of HRV complexity (conditional entropy).

Therefore, our study suggests that long-term exposure to air pollution reduces HRV in healthy young adults, especially females, with a reduction in cardiac parasympathetic modulation. Thus, our findings can be considered as a springboard for further studies with a larger sample size, focusing on the assessment of data from different cities and age groups and the relationship between HRV, long-term pollution and sex, in order to confirm and expand our findings.

Conclusion

The results suggest that long-term exposure to pollutants, specifically to smoke, has an unfavorable impact on HRV, with a reduction in cardiac vagal autonomic modulation, in healthy young adults, mainly females.

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Author contributions

Conception and design of the research: Melinski AC, Catai AM, Takito MY. Acquisition of data: Melinski AC, Moura SCG, Milan-Mattos JC. Analysis and interpretation of the data: Melinski AC, Catai AM, Moura SCG, Milan-Mattos JC, Takito MY. Statistical analysis: Catai AM, Milan-Mattos JC, Takito MY. Obtaining financing: Catai AM, Takito MY. Writing of the manuscript: Melinski AC, Catai AM, Moura SCG, Milan-Mattos JC, Takito MY. Critical revision of the manuscript for intellectual content: Melinski AC, Catai AM, Milan-Mattos JC, Takito MY.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any graduation program.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the EEFE – ESP under the protocol number 2011/36. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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