Assessment of the Cardiac Autonomic Nervous System in Mercury-Exposed Individuals via Post-Exercise Heart Rate Recovery

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Mercury · Cardiac autonomic dysfunction · Heart rate recovery · Exercise stress testing

Abstract
Objective: The aim of this study was to assess exercise heart rate recovery (HRR) indices in mercury-exposed individuals when evaluating their cardiac autonomic function. Subjects and Methods: Twenty-eight mercury-exposed individuals and 28 healthy controls were enrolled. All the subjects underwent exercise testing and transthoracic echocardiography. The HRR indices were calculated by subtracting the first- (HRR1), second- (HRR2) and third-minute (HRR3) heart rates from the maximal heart rate. The two groups were evaluated in terms of exercise test parameters, especially HRR, and a correlation analysis was performed between blood, 24-hour urine and hair mercury levels and the test parameters. Results: The mercury-exposed and control groups were similar in age (37.2 ± 6.6 vs. 36.9 ± 9.0 years), had an identical gender distribution (16 females and 12 males) and similar left ventricular ejection fractions (65.5 ± 3.1 vs. 65.4 ± 3.1%). The mean HRR1 (25.6 ± 6.5 vs. 30.3 ± 8.2 beats per min (bpm); p = 0.009), HRR2 (43.5 ± 5.3 vs. 47.8 ± 5.5 bpm; p = 0.010) and HRR3 (56.8 ± 5.1 vs. 59.4 ± 6.3 bpm; p = 0.016) values were significantly lower in the mercury-exposed group than in the healthy controls. However, there were no significant correlations between blood, urine and hair mercury levels and exercise test parameters. Conclusions: Mercury-exposed individuals had lower HRR indices than normal subjects. In these individuals, mercury exposure measurements did not show correlations with the exercise test parameters, but age did show a negative correlation with these parameters. Therefore, cardiac autonomic functions might be involved in cases of mercury exposure.

Introduction
Mercury is considered to be one of the most toxic heavy metals in the world and exposure can occur by various means [1]. Many studies that have researched mercury-related health problems were carried out in study populations mostly exposed through the consumption of mercury-contaminated fish and other seafood [2, 3]. Other sources important for mercury toxicity include occupational exposure, dental amalgam, fluorescent lamps,
The cardiac autonomic nervous system (ANS) plays an important role in maintaining cardiovascular functions and is based on a sensitive balance between the parasympathetic and sympathetic systems [11]. There are several tools used for evaluating and also measuring cardiac ANS functions, including heart rate recovery (HRR), heart rate variability (HRV) and baroreflex sensitivity [12]. HRR, after graded exercise, is one of the most commonly used techniques to represent autonomic activity [13, 14]. Sympathetic activity increases during exercise and diminishes during recovery; hence, previously suppressed parasympathetic activity becomes dominant during recovery and reduces the heart rate (HR) [15]. This decline is blunted by a decreased myocardial function and reduced exercise capacity [16, 17]. An abnormal HRR independently predicts increased cardiovascular and all-cause mortality rates [18]. ANS functions have previously been assessed in mercury-exposed individuals using HRV, such as in the study by Lim et al. [12] which showed that mercury might affect the cardiac ANS through parasympathetic dysfunction even at low mercury exposure levels. However, HRR in mercury-exposed individuals has not been evaluated. Therefore, the aim of the present study was to evaluate ANS function using HRR indices in mercury-exposed individuals compared to control subjects.

**Subjects and Methods**

**Study Population**

This cross-sectional study was performed at Ankara Occupational Diseases Hospital between March 2014 and March 2015. Initially, 34 mercury-exposed individuals were screened for inclusion into the study protocol. A complete history was taken and a physical examination was performed in all the subjects. Height (in meters) and weight (in kilograms) were measured and used to calculate the body mass index as weight/height squared. The measurement of blood pressure (BP) was performed in each participant using the left arm following approximately 5 min of seated rest. Standardized mercury sphygmomanometers were used. Korotkoff phase I (appearance) and phase V (disappearance) sounds were recorded for systolic BP and diastolic BP, respectively. The exclusion criteria were individuals with diabetes mellitus, hypertension, dyslipidemia, chronic renal failure, chronic liver disease, neurological diseases, known coronary artery or structural heart disease, pulmonary hypertension, rhythm abnormalities, any drug use, particularly those that have effects on the autonomic system (such as antiarrhythmics including beta-blockers and calcium antagonists, tricyclic antidepressants, antipsychotics and diuretics) and smoking. Based on the exclusion criteria, a total of 28 mercury-exposed individuals were found to be suitable and were included in our study. Twenty-eight age- and sex-matched volunteers with no previous history of cardiac disease served as the control group. The mercury-exposed and control population included in the study were all white Turks. In the mercury-exposed group 15 individuals were dentists and the source of mercury was the production and clinical application of dental amalgam. Three individuals were chronically exposed to mercury after a fluorescent light break at home or work. Ten had occupational exposure to mercury in an industrial environment. All the participants were over the age of 18 years. Electrocardiography (ECG), treadmill exercise testing and transthoracic echocardiography were performed in all of the participants. The study was approved by the Institutional Ethics Committee, and written informed consent was obtained from all subjects.

**Treadmill Exercise Testing**

Treadmill exercise testing was conducted in all the individuals using the modified Bruce protocol. Mason-Likar modification of 12-lead ECG [19] was continuously recorded at a paper speed of 25 mm/s. After the participants had all achieved an exercise time of more than 6 min, and a maximum HR (MHR) of at least 85% of the age-predicted MHR response (peak workload), they spent at least 3 min of recovery without a cool-down period in a sitting position. Exercise capacity was measured in metabolic equivalent levels (METs) at peak exercise. The HRR indices were calculated by subtracting the first-, second- and third-minute HR from the MHR obtained during stress testing and were designated as HRR1, HRR2 and HRR3, respectively. Exercise-onset HR change was calculated by subtracting the resting HR from the HR in the first minute of exercise. The HR reserve was determined by the change in HR from rest to peak exercise during the exercise test. An impaired HRR was described as a decrease in HR from peak exercise to 1 min of recovery of <12 beats per min (bpm) [18].

**Transthoracic Echocardiography**

Standard echocardiographic imaging was performed in the left lateral decubitus position using a commercially available system (Vingmed System Five GE ultrasound, Horten, Norway). Images were obtained using a 2.5- to 3.5-MHz transducer in the parasternal and apical views. Left ventricular end-diastolic and end-systolic diameters were determined with M-mode echocardiography under two-dimensional guidance in the parasternal long-axis view, according to the recommendations of the American Society of Echocardiography [20]. The left ventricular ejection fraction was calculated from the apical four-chamber view, according to the modified Simpson’s rule [20]. In the parasternal long-axis views, the maximal left atrium anterior-posterior diameter and right ventricular mid-cavity diameter in the apical four-chamber view at the end diastole were measured. Pulmonary systolic arterial pressure was estimated using CW Doppler as the peak regurgitation velocity plus an assumed right atrial pressure in relation to the size and respiratory excursion of the inferior cava vein visualized in the subcostal view [20].

thermometers and batteries [4, 5]. The toxic effects on the central nervous system of mercury are well known [6]; however, epidemiological and experimental studies have recently reported an association between mercury and the cardiovascular system, such as coronary heart disease and myocardial infarction [7, 8], hypertension [9], generalized atherosclerosis and cerebrovascular accident [9, 10].

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Laboratory Analysis
Blood samples from the antecubital vein were taken after an overnight fast of at least 12 h. Whole blood samples were drawn in 10 mm of ethylenediaminetetraacetic acid containing trace elements tubes (BD Vacutainer, Franklin Lakes, N.J., USA). The collected blood was immediately centrifuged at 4,000 rpm for 10 min to separate the plasma from red blood cells. All biochemical parameters were analyzed in the same sample. Each individual was asked to collect 24-hour urine samples and instructed not to collect urine from the first urination after waking up on the morning of the day of collection. The samples were collected in sterile plastic pots during each urination thereafter, including the first urination upon waking the following morning, and then diluted to 1 in 10 with 5% nitric acid solution. Hair samples weighing 0.1 g were cut from the top region of the scalp with surgical scissors, as close as possible to the skin, and then placed in a labelled envelope and stored at room temperature. The blood and hair samples were digested using a microwave-induced acid digestion method. A standard solution of metallic mercury was prepared by a dilution of certified standard solutions (High Purity Standards, Charleston, S.C., USA) and two levels of quality control materials were used (Seronorm, Billingstad, Norway). Mercury levels were determined in the whole blood, 24-hour urine and hair samples using Inductively Coupled Plasma Mass Spectrometry (ICP-MS; 7700 series, Agilent, Tokyo, Japan).

Statistical Analysis
Statistical analyses were performed using SPSS 20 for Windows (SPSS Inc., Chicago, Ill., USA). Numerical variables with a normal distribution are presented as the mean ± standard deviation (SD) and those with a skewed distribution are presented as the median and interquartile range (IQR). Categorical variables are presented as the number and percentage. For numerical variables, an independent sample’s t test and Mann-Whitney U test were used for intergroup comparisons. The χ² test and Fischer’s exact χ² test were used for the comparison of categorical variables. The relationship between numerical variables was evaluated using Pearson’s or Spearman’s correlation tests. Multiple linear regression analysis was used to determine predictors of risk factors thought to be related to first-, second- and third-minute HRR parameters in the mercury-exposed group. Two-tailed p values <0.05 were considered to first-, second- and third-minute HRR parameters in the mercury-exposed group. Two-tailed p values <0.05 were considered to be statistically significant.

Results
General Characteristics of the Study Population
The baseline characteristics and echocardiographic parameters of our study population are shown in Table 1. There was no statistically significant difference between the mercury-exposed and control groups in terms of baseline demographic and clinical characteristics. All mercury-exposed and control group participants had normal values for left ventricular end-diastolic diameter (43.6 ± 3.3 vs. 44.2 ± 2.6 mm; p = 0.64), left ventricular end-systolic diameter (27.7 ± 3.7 vs. 28.1 ± 2.9 mm; p = 0.43), left ventricular ejection fraction (65.5 ± 3.1 vs. 65.4 ± 3.1%; p = 0.96) and systolic arterial pressure (24.0 ± 5.0 vs. 23.3 ± 6.4 mm Hg; p = 0.65). The right ventricular and left atrium diameters were also found to be similar in the two groups. The laboratory and serological data of the two groups are shown in Table 2.

In the mercury-exposed group the median mercury exposure time was 12 months (range 2–30, IQR 12). The median blood mercury levels in the mercury-exposed and control groups were 14.8 μg/l (IQR 4.1) vs. 0.9 μg/l (IQR 0.5; p < 0.001), respectively. The median 24-hour urine mercury levels were 51.4 μg/l (IQR 137.2) vs. 1.3 μg/l (IQR 0.6; p < 0.001), respectively, and the median hair mercury levels were 2.1 μg/g (IQR 3.0) vs. 0.2 μg/g (IQR 0.1; p < 0.001), respectively. In the mercury-exposed group, females had a longer mercury exposure time (median 12 months, IQR 7) compared to males (median 6 months, IQR 11) with a statistical significance of p = 0.04. On the other hand, in the mercury-exposed group there were no significant differences between females and males in blood mercury levels (median 13.9 μg/l, IQR 3.1 vs. median 15.5 μg/l, IQR 3.8; p = 0.08), 24-hour urine mercury levels (median 70.3 μg/l, IQR 138.2 vs. median 27.1 μg/l, IQR 109.5; p = 0.24) and hair mercury levels (median 2.4 μg/g, IQR 3.0 vs. median 1.4 μg/g, IQR 3.0; p = 0.28).

Table 1. Demographic characteristics, BP and ECG parameters of the groups

| Variable | Mercury-exposure group (n = 28) | Control group (n = 28) | p value |
|----------|-------------------------------|------------------------|---------|
| Age, years | 37.2 ± 6.6 | 36.9 ± 9.0 | 0.49 |
| Female/male | 16/12 | 16/12 | 0.99 |
| Body mass index | 24.3 ± 4.4 | 26.3 ± 4.0 | 0.07 |
| SBP, mm Hg | 117.3 ± 12.1 | 116.4 ± 13.0 | 0.89 |
| DBP, mm Hg | 72.4 ± 8.9 | 69.1 ± 7.8 | 0.14 |
| End-diastolic diameter, mm | 43.6 ± 3.3 | 44.2 ± 2.6 | 0.64 |
| End-systolic diameter, mm | 27.7 ± 3.7 | 28.1 ± 2.9 | 0.43 |
| LVEF, % | 65.5 ± 3.1 | 65.4 ± 3.1 | 0.96 |
| sPAP, mm Hg | 24.0 ± 5.0 | 23.9 ± 5.2 | 0.82 |
| Right ventricle diameter, cm | 2.56 ± 0.2 | 2.57 ± 0.2 | 0.94 |
| Left atrium diameter, mm | 31.4 ± 3.7 | 31.5 ± 3.5 | 0.95 |

Numerical variables are expressed as the mean ± SD, unless otherwise indicated. DBP = Diastolic BP at baseline; SBP = systolic BP at baseline; sPAP = systolic pulmonary arterial BP.
Exercise Test Parameters and HRR Indices

All of the mercury-exposed and control subjects had a normal resting 12-lead ECG. All of the participants completed the exercise stress test without any complications. No rhythm abnormalities or ischemic changes were observed during the ECG stress test in either group. The duration of the treadmill exercise test (8.9 ± 2.7 vs. 9.1 ± 2.4 min; p = 0.77), peak exercise capacity (12.1 ± 2.5 vs. 12.3 ± 2.8 METs; p = 0.77), HR reserve (86.5 ± 18.2 vs. 92.3 ± 16.5 bpm; p = 0.16), baseline HR (78.3 ± 9.4 vs. 75.7 ± 10.0 bpm; p = 0.29), first-minute exercise-onset HR (14.3 ± 2.9 vs. 15.2 ± 2.6 bpm; p = 0.26) and MHR (164.5 ± 14.4 vs. 166.3 ± 11.2 bpm; p = 0.47) were similar in the mercury-exposed and control groups, respectively (table 3). The mean HRR1 (25.6 ± 6.5 vs. 30.3 ± 8.2; p = 0.01), HRR2 (43.5 ± 5.3 vs. 47.8 ± 5.5; p = 0.01) and HRR3 (56.8 ± 5.1 vs. 59.4 ± 6.3; p = 0.01) values were significantly lower in the mercury-exposed group than in the control group (fig. 1).

Correlation Analysis

The correlation analysis between the exercise test parameters and characteristics of the mercury-exposed group are shown in table 4. There were no significant correlations between any of the echocardiographic measures and laboratory values and exercise test parameters. A negative correlation was found between age and all of the exercise test parameters except HR (maximum HR, HR reserve, HRR1, HRR2 and HRR3). There was also a significant negative correlation between mercury exposure time and maximum HR and HR reserve. Nevertheless, no significant correlation was found between blood, urine or hair mercury levels and any of the exercise test parameters. The multivariate stepwise linear regression model used to determine possible independent predictors that could affect HRR1, HRR2 and HRR3 showed that baseline clinical, echocardiographic and laboratory parame-

Table 2. Laboratory and serologic data of the two groups

| Variable                        | Mercury-exposed group (n = 28) | Control group (n = 28) | p value |
|---------------------------------|--------------------------------|-----------------------|---------|
| Hemoglobin, g/dl                | 14.3±2.2                       | 14.2±1.0              | 0.82    |
| White blood cells, /μl          | 6,793±1,433                    | 7,082±1,455           | 0.45    |
| Platelet count, /μl             | 249,200±47,500                 | 247,400±46,800        | 0.88    |
| Creatinine, mg/dl               | 0.81±0.12                      | 0.79±0.19             | 0.77    |
| ESR, mm/h                       | 2 (3)                          | 3 (4)                 | 0.28    |
| ALT, U/l                        | 19.6±6.9                       | 20.4±8.2              | 0.57    |
| AST, U/l                        | 19.3±6.6                       | 23.2±7.4              | 0.06    |
| TSH, μIU/ml                     | 1.4±1.1                        | 1.2±0.8               | 0.42    |
| Triiodothyronine, pg/ml         | 2.7±0.3                        | 2.5±0.3               | 0.06    |
| Thyroxine, ng/dl                | 1.1±0.1                        | 1.1±0.1               | 0.48    |
| Blood mercury, μg/l             | 14.8±4.1                       | 0.9±0.5               | <0.001* |
| Urine mercury, μg/l             | 51.4±137.2                     | 1.3±0.6               | <0.001* |
| Hair mercury, μg/g              | 2.1±3                          | 0.2±0.1               | <0.001* |

Numerical variables are expressed as the mean ± SD or median (IQR); categorical variables are expressed as n (%). * p < 0.05. ESR = Erythrocyte sedimentation rate; ALT = alanine aminotransferase; AST = aspartate aminotransferase; TSH = thyroid-stimulating hormone.

Table 3. Exercise test parameters and HRR indices of the groups

| Variable                        | Mercury-exposed group (n = 28) | Control group (n = 28) | p value |
|---------------------------------|--------------------------------|-----------------------|---------|
| Duration of exercise test, min  | 8.9±2.7                        | 9.1±2.4               | 0.77    |
| Resting HR, bpm                 | 78.3±9.4                       | 75.7±10.0             | 0.29    |
| MHR, bpm                        | 164.5±14.4                     | 166.3±11.2            | 0.47    |
| Exercise-onset HR, bpm          | 14.3±2.9                       | 15.2±2.6              | 0.26    |
| HR reserve, bpm                 | 86.5±18.2                      | 92.3±16.5             | 0.16    |
| Maximal SBP, mm Hg              | 168.6±19.2                     | 166.3±17.1            | 0.63    |
| Maximal DBP, mm Hg              | 82.7±7.5                       | 85.1±8.0              | 0.25    |
| Peak exercise capacity, METs    | 12.1±2.5                       | 12.3±2.8              | 0.77    |
| HRR1, bpm                       | 25.6±6.5                       | 30.3±8.2              | 0.01*   |
| HRR2, bpm                       | 43.5±5.3                       | 47.8±5.5              | 0.01*   |
| HRR3, bpm                       | 56.8±5.1                       | 59.4±6.3              | 0.01*   |

Numerical variables are expressed as the mean ± SD. * p < 0.05. DBP = Diastolic BP; SBP = systolic BP.
HRR in Mercury Exposure

Table 4. Correlation analyses between exercise test parameters and some characteristics of the mercury-exposed group

| Variable                  | Baseline HR | Maximum HR | HR reserve | HRR1 | HRR2 | HRR3 |
|---------------------------|-------------|------------|------------|------|------|------|
|                           | r           | p          | r          | p    | r    | p    |
| Age                       | 0.287       | 0.139      | -0.468*    | 0.012* | -0.486* | 0.009* | -0.474* | 0.011* | -0.598* | 0.001* | -0.530* | 0.004* |
| Body mass index            | 0.037       | 0.853      | 0.005      | 0.980  | -0.002 | 0.993  | -0.188 | 0.339  | -0.318 | 0.099  | -0.121 | 0.412  |
| Systolic BP               | -0.245      | 0.209      | 0.029      | 0.885  | 0.155  | 0.431  | 0.039  | 0.846  | 0.160  | 0.415  | -0.041 | 0.836  |
| Diastolic BP              | -0.111      | 0.574      | 0.090      | 0.647  | 0.160  | 0.416  | 0.055  | 0.781  | -0.016 | 0.935  | -0.145 | 0.461  |
| Exposure (months)         | -0.018      | 0.929      | -0.670*    | 0.001* | -0.558* | 0.002* | -0.311 | 0.107  | -0.179 | 0.363  | -0.267 | 0.170  |
| Blood mercury             | -0.051      | 0.798      | 0.112      | 0.572  | 0.200  | 0.306  | -0.094 | 0.634  | 0.079  | 0.691  | 0.031  | 0.874  |
| Urine mercury             | 0.047       | 0.813      | -0.137     | 0.488  | -0.131 | 0.505  | -0.291 | 0.133  | 0.143  | 0.469  | 0.025  | 0.901  |
| Hair mercury              | -0.024      | 0.903      | -0.021     | 0.914  | -0.059 | 0.764  | 0.240  | 0.218  | -0.349 | 0.069  | -0.009 | 0.966  |

* p < 0.05. r = Correlation coefficient.

**Discussion**

The main finding of the present study was that HRR in the first, second and third minute of the recovery period after maximal exercise testing was lower in mercury-exposed individuals than in healthy controls. While there was no correlation between blood, urine or hair mercury levels and exercise test parameters, in the mercury-exposed group age showed a negative correlation with all of the exercise test parameters except baseline HR. Although many exercise test parameters, including the duration of exercise, baseline and maximum HR, HR reserve and peak exercise capacity, were similar in the two groups and there was no correlation between body mercury levels and any of the exercise test parameters, decreased HRR indices in the mercury-exposed individuals compared to the healthy controls indicate the presence and early blunting of cardiac autonomic dysfunction in this group.

As HR and BP began to decrease at the beginning of the recovery phase, increased sympathetic and decreased parasympathetic activity during exercise was replaced by increased parasympathetic and suppressed sympathetic activity within the recovery phase. This dynamic equilibrium in ANS activity in the exercise/recovery phase provides valuable information about ‘cardiac health’ in various diseases [21, 22].

In the present study, HRR was evaluated and, being easy to obtain and widely available, is assumed to be a biomarker for autonomic imbalance [23]. We found that HRR indices were blunted in mercury-exposed individuals compared to the control subjects. There have been several studies similar to ours in which the relationship between cardiac ANS function and mercury exposure was...
investigated, although HRV was the main method used for the evaluation of autonomic imbalance in these studies. In the study by Valera et al. [24] it was demonstrated that mercury exposure impaired cardiac ANS functions through the use of HRV parameters. Although in that study blood mercury levels were negatively correlated with low-frequency domains, reflecting sympathovagal balance and the standard deviation of the time interval between two consecutive R waves (RR interval) and the coefficient of variation of RR intervals, which mainly reflects parasympathetic activity, we did not find any correlation between HRR indices and body mercury levels. Furthermore, sources of mercury exposure in our study came through both occupational and environmental exposure, and metallic mercury was analyzed in blood, urine and hair samples. In another study from Japan in which cardiac ANS function and HRV were evaluated and the experimental group was exposed to methylmercury, the sources of mercury were a seafood-rich diet and mercury levels were measured from blood samples only [25]. Despite the differences in study designs and mercury sources, this interventional study also showed that long-term mercury exposure induced a sympathodominant state similar to our findings. In all these studies, the negative effects of mercury on the sympathovagal balance of the ANS are thought to be responsible for underlying mechanisms. Decreased parasympathetic activity with increased sympathetic activity causes an impairment of HRV parameters by corrupting the sympathovagal balance.

Dynamic parameters seen in exercise, such as HR and BP, depend on a healthy cardiac ANS function. Changes in sympathovagal balance in favor of sympathetic activity during recovery cause an impairment of HRR parameters, which are ANS indicators. However, through which mechanisms does mercury affect the ANS? It has been shown that mercury can cause a sympathovagal imbalance. Although their study involved children, Murata et al. [26] demonstrated that prenatal methylmercury exposure might be associated with reduced parasympathetic activity and a sympathovagal shift. Furthermore, dry umbilical cord tissue methylmercury levels collected from the study population were related negatively to parasympathetic components of cardiac autonomic indicators and positively to sympathovagal indices calculated from the electrocardiographic RR intervals. Similarly, Grandjean et al. [27] suggested that early mercury exposure might have a long-lasting effect on autonomic heart activity. These studies hypothesized that the effects of mercury on cardiac ANS could reflect the brainstem neurotoxicity of mercury. Thus, the neurotoxic effects of mercury may be one of the most important mechanisms of cardiac autonomic dysfunction [28].

In this study the significant correlation between mercury exposure time and 24-hour urine mercury confirmed the previous study of Carman et al. [29] in which a positive correlation between the duration of exposure and urinary mercury levels in mercury-exposed children was reported. The blood mercury level is useful when measured soon after a short-term and high-level exposure, but the level decreases within days of exposure. Estimation of the mercury concentration in urine is the best biomarker of long-term exposure to mercury, and is also an indicator of the bodily burden [30]. Mercury analysis of hair could be useful for assessing chronic exposure because of the abundant sulfhydryl groups in hair, but this remains controversial [30]. Ultimately, urine mercury seems to be one step ahead of blood and hair mercury for the biological monitoring of mercury exposure.

The limitations of this study include the small sample size and the very selected study population. Only HR changes were evaluated, meaning the respiratory exchange ratio, which is the most definitive and objective clinically available measure of the physiological level of effort during exercise, was not included. There was a lack of follow-up of the subjects for cardiovascular outcomes. Therefore, larger studies with the follow-up of end points are required in order to understand the clinical and therapeutic implications of cardiac involvement, as well as the pathogenesis and consequences of autonomic dysfunction in mercury exposure.

**Conclusion**

In this study, mercury exposure was associated with a blunted recovery of HR after maximal exercise. Mercury-exposed individuals might have cardiac autonomic dysfunction even without overt cardiovascular diseases.

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**Disclosure Statement**

The authors have no conflicts of interest to declare.
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