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Effect of acute aerobic exercise on serum BDNF levels in patients with Chagas heart disease

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Chagas disease is an important endemic disease in Latin America and an emerging disease in non-endemic countries [1]. Chagas heart disease (CHD), the most important clinical manifestation of this infection, causes heart failure, complex arrhythmias, thromboembolism and sudden death [2]. A diffuse damage in the autonomic nervous system is a pathological feature commonly present in variable degrees in patients with CHD [3].

The neurotrophin Brain Derived Neurotrophic Factor (BDNF) plays important functions in the nervous system, such as neuronal survival and maintenance, synaptic plasticity and memory processing [4]. Moreover, BDNF has an important role in metabolic events [5], being susceptible to regulation by physical activity. Recently, it has been demonstrated that Chagas disease patients exhibit higher serum BDNF levels compared to healthy subjects [6]. Interestingly, in patients with Chagas cardiomyopathy underwent 12-week-aerobic training, the best functional capacity was associated to higher serum BDNF levels [7]. However, the acute effect of aerobic exercise on the BDNF levels in CHD remains unknown, as well as its relationship to ventricular dysfunction and exercise intensity.

Patients were recruited from an Outpatient Reference Center for Chagas Disease in the state of Minas Gerais, Brazil. The study was approved by the Institutional Review Committee and the subjects gave informed consent.

Inclusion criteria were the diagnosis of Chagas disease determined by positive serology, clinical, electrocardiographic or echocardiographic findings compatible with CHD, age between 30 and

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Table 1
Clinical data from CHD patients stratified according to left ventricular systolic function.

Variable	Non-dilated group (N = 16)	Dilated group (N = 14)	P value
BMI (kg/m^2)	26.95 ± 4.63	26.85 ± 4.55	0.802
LVEF (%)	64.57 ± 5.50	39.50 ± 9.06	<**0.001**
VO_{2peak} (mL/kg/min)	29.98 ± 6.23	21.28 ± 7.54	**0.001**
BDNF at rest (pg/mL)	15,083.10 ± 4541.22	13,203.54 ± 3527.27	0.845
BDNF after exercise (pg/mL)	12,804.17 ± 4605.47	10,870.73 ± 5387.26	0.769
Δ BDNF (pg/mL)	−2278.93 ± 4183.27	−2334.76 ± 6376.03	0.902

Data presented as mean and standard deviation (M ± SD). BMI = body mass index, LVEF = left ventricular ejection fraction; VO_{2peak} = peak oxygen uptake; Δ BDNF = changes in BDNF after exercise compared to rest; pg/mL = picograms per milliliter. The values highlighted in bold are statistically significant (P < 0.05).

60 years and sedentary lifestyle according to the International Physical Activity Questionnaire (IPAQ). Exclusion criteria were the presence of systemic or heart disease by any other causes or co-morbidities, the use of cardiac pacemaker, blood transfusion within six months and the use of antidepressant medication.

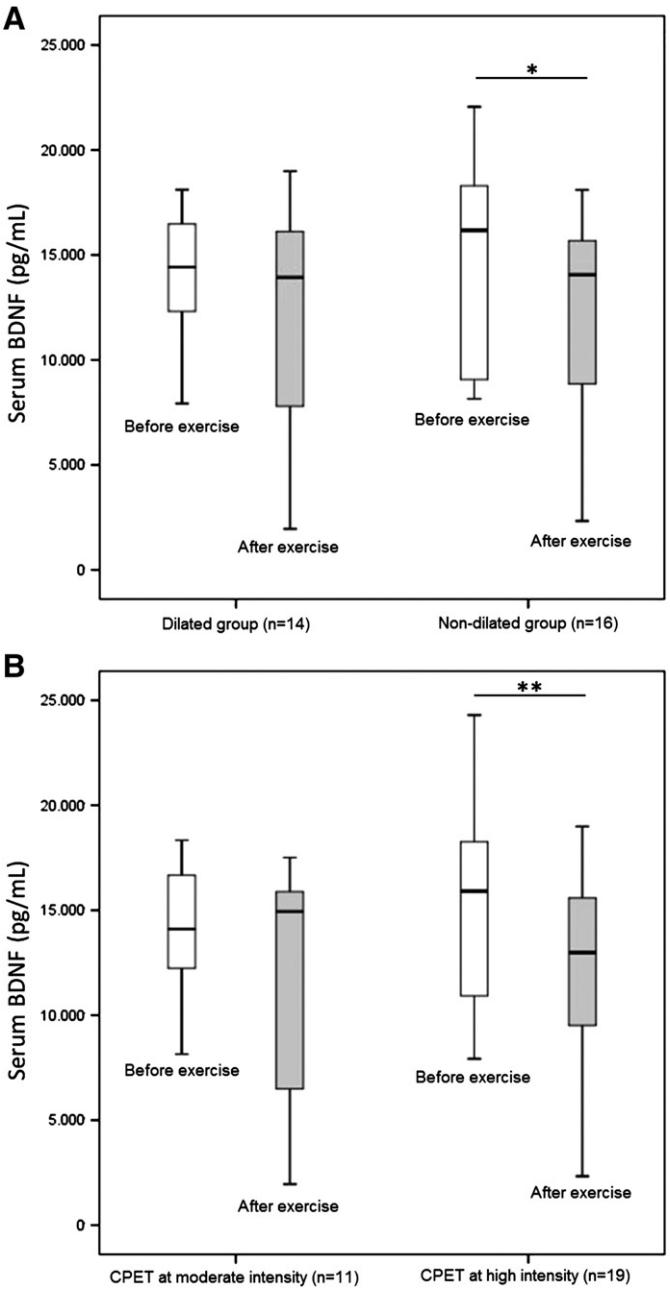

Fig. 1. Changes in serum BDNF before (white box) and after (gray box) acute exercise. A) Non-dilated and dilated group; B) chagasic patients who underwent Cardiopulmonary Exercise Test (CPET) at moderate and high intensity. *p < 0.05; **p < 0.001.

All patients underwent clinical evaluation, echocardiography, the Cardiopulmonary Exercise Testing (CPET) and blood sampling for measurement of serum BDNF. Patients were classified into 2 groups: dilated cardiomyopathy characterized by the echocardiographic finding of a dilated left ventricle with impaired ventricular systolic function, and non-dilated heart disease defined as a normal left ventricular dimensions and function. The CPET, gold standard in the assessment of functional capacity, was performed on a treadmill ramp protocol and the intensity of exercise was determined as the percentage of maximum heart rate (HRmax = 220 minus the patient age) during the test. For moderate exercise the percentage was set at 60–79% and for high intensity above 80% of the HRmax. Blood samples were taken at rest and immediately after the CPET. Serum BDNF levels were determined by ELISA (Enzyme Linked Immuno Sorbent Assay), according to R&D Systems protocol (Minneapolis, MN, USA).

G Power software, version 3.1.0, was used to determine the sample size as 28 individuals, considering an alpha error of 0.05 and a statistical power of 95%. Thirty CHD patients (47.85 ± 8.71 years, 20 males) were selected for this study. Parametric paired t-test and Pearson correlation test and non-parametric Mann–Whitney and Spearman Rank correlation test were performed for data analysis, with significance levels at 0.001% and 0.05%.

In the overall study population, there was a significant decrease in serum BDNF levels after acute exercise (p = 0.006). The clinical characteristics of the CHD patients stratified according to left ventricular systolic function are presented in Table 1.

There was no significant change in serum BDNF levels after exercise in the dilated group (p = 0.136). In contrast, the non-dilated group showed a significant decrease in serum BDNF levels (p = 0.038) (Fig. 1A). Concerning the intensity of physical exercise, patients who underwent CPET at moderate intensity (n = 11; all patients in dilated group) exhibited no changes in serum BDNF levels (p = 0.477). However, the patients who underwent CPET at high intensity (n = 19, 16 in the non-dilated group and 3 in the dilated group) had a significant decrease in BDNF levels (p < 0.001) (Fig. 1B).

To the best of our knowledge, this is the first study to demonstrate the effect of acute aerobic exercise on serum BDNF levels in patients with CHD. The main findings are the decrease in serum BDNF after acute aerobic exercise and the exercise intensity-dependent BDNF response.

All patients in the non-dilated group underwent CPET at high intensity, probably because they had higher functional capacity and lower exercise intolerance than those with left ventricular dysfunction. We hypothesized that both, the dysautonomia associated to CHD and the high intensity exercise, could contribute to a stress condition leading to a decrease in the serum BDNF levels after treadmill exercise.

Aerobic exercise at high intensity increases serum glucocorticoids such as cortisol that can negatively affect hippocampal plasticity [8] and consequently reduces BDNF levels. A significant reduction in

BDNF levels after maximal exercise performed immediately after warm-up activity was also found by Rojas Vega et al. [9] in patients with a spinal cord injury. This previous study suggests that maximal effort can reduce BDNF levels by decreasing their production or release, increasing their degradation or stimulating their uptake from the blood into the brain.

A single session of moderate aerobic exercise may not be the stimulus needed to cause changes in BDNF levels in patients with CHD, since these patients have a severe autonomic dysfunction. However, the regular practice of moderate aerobic exercise might affect BDNF expression. Lima et al. [7] showed a significant increase in BDNF levels in patients with Chagas cardiomyopathy who had increased functional capacity after 12 weeks (36 sessions) of moderate exercise.

Currently, it has been suggested that high-intensity aerobic exercise is more effective to increase peak oxygen uptake in heart failure patients [10]. However, we observed that acute exercise performed at this intensity can reduce serum BDNF levels in Chagas heart disease patients, which could adversely affect neural and metabolic properties of this neurotrophic factor. In conclusion, our results suggest caution in prescribing high-intensity aerobic exercise for Chagas heart disease patients, as well as the importance of monitoring these patients during exercise. To confirm this, further longitudinal studies are necessary in encompassing a greater number of chagasic patients and exercise training at different levels of intensity.

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From abstract to peer-reviewed publication: Country matters

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Medical conferences are key in the sharing of new scientific findings. However, results reported as conference-abstracts are generally not considered final before publication in a peer-reviewed journal. It is known that approximately 1/3 of the scientific results presented as abstracts at large medical conferences are published within 2 years of presentation [1,2]. Cardiovascular research has increased substantially in the last decade, and low- and middle-income countries have now a greater share of citations than before [3]. Less is known about the relative difference between countries in

Table 1
Characteristics of abstracts.

Characteristic	Total
N	27208
Year, N (%)	
2006	9555 (35.1)
2007	8843 (32.5)
2008	8810 (32.4)
Major scientific category, %	
Basic science	22.8
Clinical science	63.1
Population science	14.1
Origin of research (first author affiliation), %	
Americas	38.2
Europe	44.8
Africa	0.2
Asia/Oceania	16.8
Median number of authors on abstract (IQR)	7 (5–9)
Abstract with >1 participating country, %	16.7

Abbreviations: AHA,American HeartAssociation; ACC, American College of Cardiology; ESC, European Society of Cardiology; GDP, gross domestic product.

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