Autonomic Neuroscience: Basic and Clinical 197 (2016) 9–13

Contents lists available at ScienceDirect

Autonomic Neuroscience: Basic and Clinical

journal homepage: www.elsevier.com/locate/autneu

Effect of continuous and interval aerobic exercise training on baroreflex sensitivity in heart failure

Gustavo Santos Masson [a], Juliana Pereira Borges [a,b,*], Pedro Paulo Soares da Silva [c], Antônio Cláudio Lucas da Nóbrega [c], Eduardo Tibiriçá [a], Marcos Adriano Lessa [a]

[a] Laboratory of Cardiovascular Investigation, Oswaldo Cruz Institute, FIOCRUZ, Rio de Janeiro, RJ, Brazil
[b] Laboratory of Physical Activity and Health Promotion, State University of Rio de Janeiro, Brazil
[c] Department of Physiology and Pharmacology, Fluminense Federal University, Niterói, RJ, Brazil

ARTICLE INFO

Article history:
Received 9 November 2015
Received in revised form 4 February 2016
Accepted 8 March 2016

Keywords:
Cardiac function
Exercise
Arterial baroreflex

ABSTRACT

Introduction: The ability of continuous aerobic exercise training (AET) to increase baroreflex control and cardiac function in heart failure (HF) has been well described, but the comparison between continuous and interval AET on these functions is inconclusive.
Objectives: To compare the effects of continuous and interval AET on cardiac function and baroreflex sensitivity (BrS) in an experimental model of HF.
Methods: Rats were divided into the following groups: continuous training (HF-CT), intense interval training (HF-IIT), moderate interval training (HF-MIT), sedentary group (HF-SED), and sham sedentary (SHAM-SED). Animals underwent surgery to induce HF by ligation of the interventricular coronary artery. Six weeks after surgery, AET was started (8 weeks, 3 sessions/week). Echocardiography studies to assess cardiac function were performed before and after AET. At the end of the training protocols, the BrS index was assessed by stepwise intravenous infusions of sodium nitroprusside and phenylephrine.
Results: All methods of exercise prevented the HF-induced increase in left ventricular diameter in diastole observed in the HF-SED rats (0.88 ± 0.09 *vs.* 1.03 ± 0.09 cm; $P < 0.05$), but only the HF-CT (28.5 ± 6.3 *vs.* 39.2 ± 12.7%; $P < 0.05$) and HF-MIT (31.0 ± 8.5 *vs.* 42.0 ± 10.3%; $P < 0.05$) groups exhibited an increase in ejection fraction. Nevertheless, the HF-CT group was the only group that showed a tachycardia reflex higher than that of the HF-SED group (0.87 ± 0.34 *vs.* 0.20 ± 0.05 bpm/mm Hg; $P < 0.05$) and similar to that of the SHAM-SED group (1.04 ± 0.11 bpm/mm Hg).
Conclusions: These results suggest that continuous and moderate interval training induced similar improvements in cardiac function but that only continuous training induced higher BrS in HF rats.

1. Introduction

Heart failure (HF) is a complex clinical syndrome characterized by progressive cardiac dysfunction secondary to left ventricular remodeling (Laterza et al., 2007). As a compensatory mechanism to maintain cardiac function, sympathetic outflow is increased, commonly leading to sympathetic hyperactivity (Persson et al., 2002), and arterial baroreflex sensitivity (BrS) is reduced (Laterza et al., 2007). This autonomic dysfunction is associated with a negative prognosis in patients with HF and coronary artery disease (La Rovere et al., 1998). However, previous studies have demonstrated that aerobic exercise training (AET) is widely used as a powerful adjuvant therapy for HF (Piepoli et al., 2004; Tenenbaum et al., 2006). Continuous AET is well known to reduce sympathetic nerve activity, prevent left ventricular remodeling, and increase BrS in clinical (Laterza et al., 2007; Martinez et al., 2011; Haykowsky et al., 2007a; Hambrecht et al., 2000) and experimental (Gao et al., 2007; Mousa et al., 2008; Liu et al., 2002) studies involving ischemic dilated cardiomyopathy.

Recently, to overload the physiological system and stimulate greater adaptations (Stuckey et al., 2011), interval AET has been increasingly prescribed to HF patients (Wisloff et al., 2007; Nilsson et al., 2008). Interval AET consists of alternating periods of greater and lower intensity within an exercise session, whilst continuous AET is characterized by constant submaximal power output and O_2 consumption throughout the entire session. In fact, well-controlled clinical studies in HF patients have provided evidence that interval AET provides greater benefits with respect to insulin sensitivity (Tjonna et al., 2008), mitochondrial biogenesis, and body fat reduction (Daussin et al., 2008) than regular bouts of continuous AET. Nonetheless, the impact of interval AET on BrS and cardiac function in HF is not completely understood.

* Corresponding author at: Laboratory of Physical Activity and Health Promotion (LABSAU), Rua São Francisco Xavier, 524, sala 8133F, Maracanã, Rio de Janeiro, RJ, 20550-013, Brazil.
E-mail address: julipborges@gmail.com (J.P. Borges).

http://dx.doi.org/10.1016/j.autneu.2016.03.003
1566-0702/

Considering that continuous and interval exercise training have different impacts on cardiovascular regulation and autonomic activity, our objective in the present study was to evaluate the effects of continuous and interval AET, with the same duration and workload, on the BrS and cardiac function in an experimental model of ischemic dilated cardiomyopathy in rats. Our hypothesis is that continuous and interval exercise training will yield similar effects on cardiac function but different effects on BrS.

2. Materials and methods

2.1. Ethical approval

The experiments were performed according to the principles of the U.K. Animals (Scientific Procedures) Act, 1986 and the National Institutes of Health guide for the care and use of Laboratory animals (NIH Publications No. 8023, revised 1978) and were approved by the Institutional Animal Care Committee (License number: LW-34/08). The present study comply with the ARRIVE guidelines.

2.2. Animal care and experimental design

Male Wistar rats (12 weeks) provided by the animal facilities at the Oswaldo Cruz Foundation, Brazil, were kept under a 12:12-hour light-dark cycle in a temperature-controlled environment (22 °C) with free access to water and standard rat chow (Nuvital, Curitiba, PR, Brazil). HF was induced by myocardial infarction surgery. Six weeks later, the echocardiography parameters were determined, and animals with HF were randomly assigned to four groups: continuous training (HF-CT; n = 10), moderate interval training (HF-MIT; n = 9), intense interval training (HF-IIT; n = 8), and sedentary animals (HF-SED; n = 7). Another sedentary group submitted to a sham surgical procedure was used as an HF control (SHAM-SED, n = 9). The experimental design is shown in Fig. 1.

2.3. Surgery to induce myocardial infarction

To induce coronary artery occlusion, the rats were anesthetized with pentobarbital (50 mg/kg, intraperitoneally [ip]), and a left thoracotomy was performed. After accessing the mediastinum by incising the intercostal muscles between the third and fourth ribs, the heart was carefully exteriorized, and the left anterior descending (LAD) coronary artery was occluded with a 6-0 thread. After LAD coronary artery ligation, the thorax was closed, and lung collapse was prevented by the rapid withdrawal of air from the pleural cavity using a syringe. The sham-operated animals similarly underwent a left thoracotomy and cardiac exteriorization but did not undergo LAD coronary artery ligation. Therefore, sedentary-sham operated group served as a non-HF control group, ensuring that the development of heart failure was due to the coronary artery ligation itself and was not merely a consequence of the surgery. All rats received anti-inflammatory (ketoprofen; 1 mg/kg) and antibiotic (penicillin; 50,000 IU/kg) treatments, subcutaneously, during the 24-h post-surgical period.

2.4. Echocardiography

The echocardiographic evaluation was performed by a blinded observer before and after the end of the AET or sedentary protocol. The rats were anesthetized (30 mg/kg pentobarbital and 0.05 mg/kg fentanyl, ip), and images were obtained with a 10-MHz linear high-frequency transducer using a commercially available ultrasound system (Titan™, SonoSite, Bothell, WA, USA). Left ventricle systolic function was estimated by the ejection fraction (EF) as follows: EF (%) = $[(ED_{vol} - ES_{vol}) / EDvol] \times 100$, where ED_{vol} and ES_{vol} are the left ventricle end-diastolic and end-systolic volumes, respectively. The echocardiographic examination followed the recommendations of the American College of Echocardiography (Picard et al., 2011).

2.5. Performance test and aerobic exercise training

After adapting to a motor-driven treadmill exercise (Universidade de São Carlos, São Paulo, SP, Brazil) for more than one week (10 min per session), all animals underwent a graded treadmill exercise test until exhaustion to measure the maximum velocity achieved ($Vel_{máx}$). Briefly, the initial treadmill speed was 10 m/min, which was increased by 3 m/min every 2 min until the rats were no longer able to run. Forty-eight hours after the test, the exercise groups underwent AET 3 days per week for 8 weeks. The HF-CT group trained at 70% of Vel_{max}, which was kept unchanged throughout the entire session. The moderate interval training (HF-MIT group) was performed in such a way that rats ran during 5 min at 80% Vel_{max}, followed by 5 min intervals at 60% $Vel_{max,}$ which was repeated three times, so each HF-MIT session lasted for 30 min. In the intense interval training (HF-IIT group), rats ran during 1 min at 90% Vel_{max}, followed by 1 min at 50% $Vel_{max,}$ which was repeated 15 times, so each HF-IIT session lasted for 30 min. To maintain an identical workload and matching volume of AET between the groups, the session duration of the HF-CT group was adjusted to match the HF-MIT and HF-IIT group distances (Moreira et al., 2013). The HF-SED and

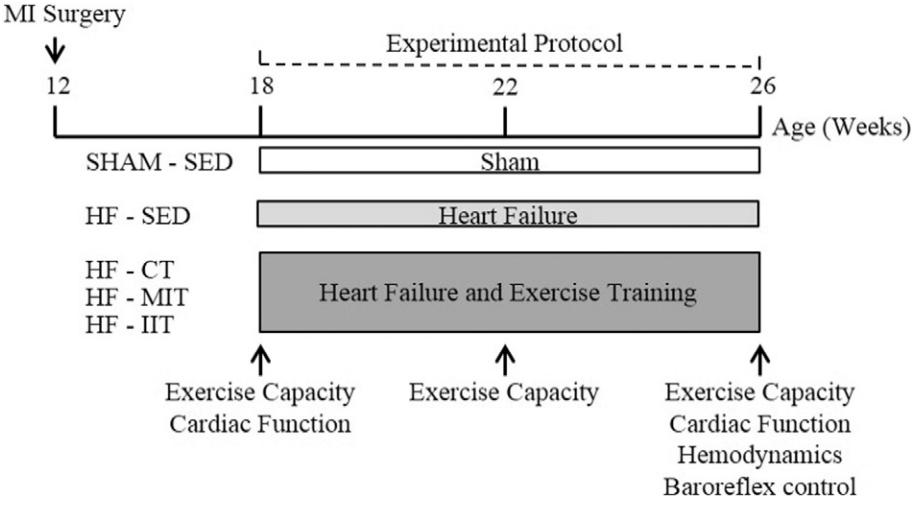

Fig. 1. Experimental design. SHAM-SED, sedentary sham; HF-SED, heart failure sedentary; HF-CT, heart failure continuous exercise training; HF-MIT, heart failure moderate interval exercise training; HF-IIT, heart failure intense interval exercise training.