Autonomic Neuroscience: Basic and Clinical 188 (2015) 86–89

Contents lists available at ScienceDirect

Autonomic Neuroscience: Basic and Clinical

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

Exercise in the postural orthostatic tachycardia syndrome

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ARTICLE INFO

Article history:
Received 16 June 2014
Received in revised form 6 October 2014
Accepted 15 November 2014

Keywords:
Chronic orthostatic intolerance
Exercise intolerance
Physical activity
Cardiovascular response
Non-drug therapy

ABSTRACT

Patients with the Postural Orthostatic Tachycardia Syndrome (POTS) have orthostatic intolerance, as well as exercise intolerance. Peak oxygen uptake (VO_{2peak}) is generally lower in these patients compared with healthy sedentary individuals, suggesting a lower physical fitness level. During acute exercise, POTS patients have an excessive increase in heart rate and reduced stroke volume for each level of absolute workload; however, when expressed at relative workload (%VO_{2peak}), there is no difference in the heart rate response between patients and healthy individuals. The relationship between cardiac output and VO_2 is similar between POTS patients and healthy individuals. Short-term (i.e., 3 months) exercise training increases cardiac size and mass, blood volume, and VO_{2peak} in POTS patients. Exercise performance is improved after training. Specifically, stroke volume is greater and heart rate is lower at any given VO_2 during exercise after training versus before training. Peak heart rate is the same but peak stroke volume and cardiac output are greater after training. Heart rate recovery from peak exercise is significantly faster after training, indicating an improvement in autonomic circulatory control. These results suggest that patients with POTS have no intrinsic abnormality of heart rate regulation during exercise. The tachycardia in POTS is due to a reduced stroke volume. Cardiac remodeling and blood volume expansion associated with exercise training increase physical fitness and improve exercise performance in these patients.

1. Introduction

Over 500,000 people in the United States, primarily young women, suffer from chronic orthostatic intolerance (Robertson, 1999). Severely affected patients are unable to work, attend school, or participate in recreational activities, resulting in substantial morbidity. The Postural Orthostatic Tachycardia Syndrome (POTS, in which patients are unable to stand or remain upright for prolonged periods of time due to intolerable palpitations, dizziness, or near-syncope) is a major form of chronic orthostatic intolerance in young people, with few definitive therapies (Schondorf and Low, 1993). The underlying pathophysiology is not well understood, but recent research has suggested that physical deconditioning and reduced standing stroke volume may be important to the pathogenesis of POTS and the severity of its disability (Fu et al., 2010, 2011; Galbreath et al., 2011; Joyner and Masuki, 2008; Masuki et al., 2007b; Parsaik et al., 2012; Shibata et al., 2012).

In addition to orthostatic intolerance, patients with POTS also have exercise intolerance or low physical work performance (Low et al., 2009). Peak oxygen uptake (VO_{2peak}), an indicator of physical fitness, is generally lower in POTS patients when compared with healthy sedentary individuals (Parsaik et al., 2012; Shibata et al., 2012). Reduced VO_{2peak} is consistent with physical deconditioning, which provides a strong rationale for retraining in the treatment of POTS or chronic orthostatic intolerance. Indeed, we have found that endurance exercise training is an effective non-pharmacological therapy for POTS (Fu et al., 2010, 2011; Galbreath et al., 2011; Shibata et al., 2012). Many patients can be "cured" or at least palliated substantially after a period of exercise training or increased physical activity. Exercise performance is improved after training in POTS patients.

2. Acute exercise responses in POTS

During acute sub-maximal and maximal exercise, especially in the upright position, POTS patients have lower stroke volume and higher heart rate for each level of absolute workload compared with healthy sedentary individuals matched for sex and age (Fig. 1A and B) (Shibata et al., 2012). However, when expressed at the relative workload (percent of VO_{2peak}), the heart rate responses are not different between POTS patients and healthy individuals (Fig. 2) (Shook et al., 2007). These results suggest that POTS patients have no intrinsic abnormality of heart rate regulation during exercise.

Previous studies have found that baroreflex control of heart rate during exercise is similar between POTS patients and healthy individuals (Masuki et al., 2007a). The tachycardia in POTS patients during exercise appears to be attributed to the reduced stroke volume (Fu et al., 2010; Masuki et al., 2007b; Shibata et al., 2012), which is associated with

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http://dx.doi.org/10.1016/j.autneu.2014.11.008
1566-0702/

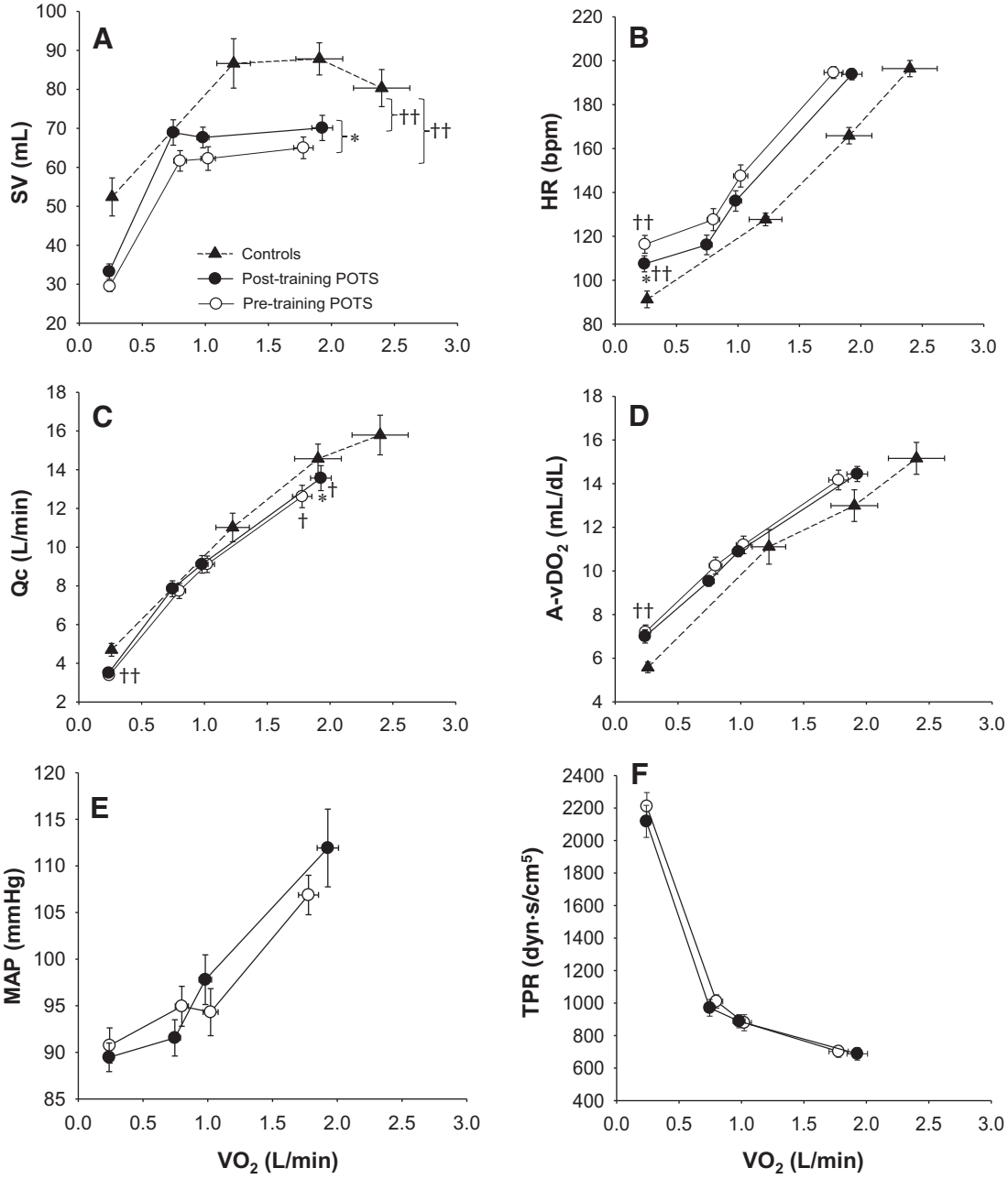

Fig. 1. Changes of stroke volume (SV, A), heart rate (HR, B), cardiac output (Qc, C), arterio–venous oxygen content difference (A-vDO_2, D), mean arterial pressure (MAP, E), and total peripheral resistance (TPR, F) in relation to changes of oxygen uptake (VO_2) during upright treadmill exercise in healthy sedentary individuals and patients with POTS before and after 3-month endurance training. Adapted with permission from Shibata et al (Shibata et al., 2012).

exercise intolerance. Recent research has shown that there are sex-specific differences in heart size and blood volume even in the healthy population (Best et al., 2014), and such sex differences are exaggerated in POTS (Fu et al., 2010). It is possible that women born with small hearts (even though within a normal range) are more susceptible to the development of POTS. Conversely, POTS patients have small hearts which are likely a secondary change due to a physiological adaptation to the reduced physical activity level (namely, decreased myocardial load and work). We previously found that physical deconditioning elicited by chronic bed rest leads to ventricular remodeling, which is not seen with equivalent degrees of acute hypovolemia (Dorfman et al., 2007; Perhonen et al., 2001). The small heart (Raj and Levine, 2013) coupled with reduced blood volume contributes to the reduced stroke volume, ultimately resulting in reflex tachycardia during exercise in POTS patients. These results support the cardiac origin of exercise intolerance in this syndrome.

We found that POTS patients and healthy individuals have a similar linear correlation between cardiac output and VO_2 during sub-maximal and maximal exercise (Fig. 1C) (Shibata et al., 2012). This observation indicates that POTS patients have a normal ability to increase cardiac output for the oxygen demand during exercise, as well as to utilize oxygen in the periphery. Many studies have shown that the slope of this relationship varies little in healthy humans with advancing age, sex, mode of exercise, overall fitness, or degree of effort (Astrand et al., 1964; Fu and Levine, 2005; Julius et al., 1967; Lewis et al., 1983; McGuire et al., 2001; Proctor et al., 1998). If oxygen utilization by working muscles is impaired, such as in patients with mitochondrial myopathy (Haller et al., 1991; Taivassalo et al., 2003) and well-compensated