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Arterial stiffness response to exercise in persons with and without Down syndrome

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ABSTRACT

This study compared arterial stiffness and wave reflection at rest and following maximal exercise between individuals with and without Down syndrome (DS), and the influence of body mass index (BMI), peak oxygen uptake (VO_2peak) on changes in arterial stiffness. Twelve people with DS (26.6 ± 2.6 yr) and 15 healthy controls (26.2 ± 0.6 yr) completed this study. Intima-media thickness (IMT) and stiffness of common carotid artery was examined. Hemodynamic and arterial variables were measured before and 3-min after exercise. Persons with DS had higher BMI and lower VO_2peak than controls. IMT did not differ between groups. At rest, carotid β stiffness was significantly higher in persons with DS ($P < 0.05$) but there was no difference in between groups for any of the other arterial stiffness measures. After exercise, persons with DS exhibited attenuated arterial stiffness responses in AIx-75, carotid β stiffness and Ep in contrast with controls (significant group-by-time interactions). When controlling for BMI and VO_2peak, the interactions disappeared. In both groups combined, BMI was correlated significantly with carotid Ep and β at rest. VO_2peak correlated significantly with AIx-75 and its pre-post change ($r = -0.45$, $P = 0.029$; $r = 0.47$, $P = 0.033$, respectively). The arterial stiffness responses to maximal exercise in persons with DS were blunted, potentially reflecting diminished vascular reserve. Obesity and particularly VO_2peak influenced these findings. These results suggest impaired vascular function in people with DS.

1. Introduction

Individuals with Down syndrome (DS) without congenital heart disease exhibit low levels of aerobic capacity (Fernhall, 1993; Fernhall et al., 1996; Fernhall, Tymeson, Millar, & Burkett, 1989). Chronotropic incompetence and autonomic regulatory dysfunction (Fernhall et al., 1996, 2009; Lauer, Okin, Larson, Evans, & Levy, 1996) contribute to the low aerobic fitness levels. However, arterial function and heart-artery interactions may also contribute to physical work capacity (Asanoi, Sasayama, & Kameyama, 1989; Starling, 1993). Aerobic capacity is directly related to arterial function, including endothelial function (Alomari, Solomito, Reyes, Khalil, Wood, & Welsch, 2004; Baynard, Miller, & Fernhall, 2003), arterial

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stiffness (Arena, Fei, Arrowood, & Kraft, 2007; Gando et al., 2010) and wave reflection (Binder et al., 2006). In addition, coupling of arterial and cardiac function is a major determinant of aerobic capacity (Galetta, Franzoni, Femia, Bartolomucci, Carpi, & Santoro, 2004; Hagg, Wandt, Bergstrom, Volkmann, & Gan, 2005). Thus, poor resting arterial function likely limits aerobic capacity, but it is also possible that changes in arterial function during acute exercise may play a role, although this has not been investigated. Furthermore, little is known about arterial function in individuals with DS. Information regarding arterial function may be important for individuals with DS as arterial function is not only associated with aerobic capacity, but is also an independent predictor of mortality and risk of cardiovascular disease (Chirinos et al., 2012; Vlachopoulos et al., 2013).

There are several characteristics that suggest individuals with DS may have altered arterial function. In addition to their low levels of cardiorespiratory fitness, the prevalence of overweight and obesity is significantly higher in persons with DS (Baynard, Pitetti, Guerra, Unnithan, & Fernhall, 2008), compared with the general population. Several studies have shown that obesity is associated with increased arterial stiffness (Nemes, Gavaller, Csajbok, Forster, & Csanady, 2008; Zebekakis et al., 2005), whereas higher cardiorespiratory fitness is associated with lower arterial stiffness in individuals without disabilities (Boreham, Ferreira, Twisk, Gallagher, Savage, & Murray, 2004; Gando et al., 2010; Seals, Desouza, Donato, & Tanaka, 2008). Overweight is related to higher aortic pressure wave reflection after peak exercise, as manifested by augmentation index (AIx) (Shim et al., 2011). Despite exhibiting low levels of cardiorespiratory fitness and higher prevalence of obesity, individuals with DS have lower blood pressure (BP) (Richards and Enver, 1979) and reduced BP responses to exercise (Fernhall and Otterstetter, 2003) compared to individuals without disabilities. Since BP is a major determinant of arterial stiffness and wave reflection, it is possible that arterial stiffness and wave reflection may be altered in individuals with DS both at rest and following acute exercise. However, to our knowledge, there are no data on this in persons with DS.

Physiologic responses to exercise are important as they can unmask physiological anomalies not present at rest, including arterial anomalies (Heffernan, Jae, & Fernhall, 2007c; Sacre, Holland, Jenkins, & Sharman, 2012). Exercise induced hemodynamic responses, whether measured during or immediately following exercise, are also associated with mortality and cardiovascular risk (Cole, Foody, Blackstone, & Lauer, 2000; Jae et al., 2008, 2006a, 2006b). Although the arterial response to maximal exercise has been described in people without disabilities (Aizawa and Petrella, 2008; Baynard et al., 2003; Heffernan, Collier, Kelly, Jae, & Fernhall, 2007a; Heffernan, Jae, Echols, Lepine, & Fernhall, 2007b), no data exist in persons with DS. Most of these studies examined the arterial response 10–60 min after maximal exercise. However, large artery distensibility following maximum exercise varies significantly within 3 min following exercise in healthy subjects (Naka, Tweddel, Parthimos, Henderson, Goodfellow, & Frenneaux, 2003). Therefore, the time period immediately following maximal exercise likely yields more direct insight regarding the acute effect of maximal exercise on arterial function in persons with DS.

The purpose of this study was threefold: (a) to compare baseline arterial stiffness between individuals with DS and controls without disabilities (b) to compare the arterial stiffness response to exercise between persons with DS and controls and (c) determine whether BMI and VO_2peak influence arterial stiffness at rest and in response to exercise.

2. Methods

Twenty-seven participants (12 with DS, 15 controls without disabilities) volunteered for the study. All of them were either sedentary or moderately active, but none were involved in any extensive endurance exercise training. The participants with DS were recruited from the local community and support groups. Medical history was obtained by asking both the individuals with DS and their parents/guardians to ensure that the participants did not have any underlying chronic disease that could influence their ability to complete the cycle ergometer test or affect arterial function. All participants with DS were classified as having mild intellectual disability based on their medical history. Control subjects were recruited from the local and university communities. All participants were healthy or perceived to be healthy on the basis of answers to a health questionnaire. Exclusion criteria included any form of cardiovascular disease, significant respiratory disorder, metabolic disease, atlanto-axial instability, severe or profound intellectual disability, smoking, and/or use of heart rate (HR) and BP altering or non-steroidal anti-inflammatory medications. After an explanation of the study procedures and initial screening, all participants signed informed consent. For the participants with DS, their parents/guardians also signed informed consent. This research was approved by the institutional review board of the University of Illinois at Urbana-Champaign.

2.1. Study design

All participants reported to the exercise and cardiovascular research laboratory for familiarization and testing. Participants were tested in a postprandial state (at least 3-h) and refrained from exercise 24 h before test day. Participants were also asked to refrain from caffeine ingestion on testing days. After attainment of written consent, anthropometric variables were measured. Following a 10 min supine rest period the arterial BP and HR measurements were performed in the supine position before and immediately after maximal aerobic exercise (3 min post-exercise).

2.2. Familiarization

Participants with DS attended one or two familiarization session(s) on day(s) prior to the testing day. The number and length of familiarization sessions depended on the response of the individual subject. Data collection started when a