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Effect of age-related ventilatory inefficiency on respiratory sensation during exercise

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ABSTRACT

To examine the effect of age-related respiratory function impairment on exertional dyspnea, we compared ventilatory and perceptual responses to incremental exercise under control (CTRL) and added dead space (DS) loading conditions in healthy fit older (55–79 years) and younger (20–39 years) men. Older individuals had higher ventilatory equivalents for CO_2 throughout exercise ($p < 0.05$) suggesting greater ventilatory inefficiency but operating lung volumes were similar compared to younger individuals. With added DS compared to CTRL, both groups similarly increased tidal volume (by 0.3–0.6 L) and ventilation (by 8–13 L/min) at submaximal work rates (each $p < 0.05$). At peak exercise with DS, both groups failed to further increase ventilation and had small reductions in peak work rate ($p < 0.05$). Increases in dyspnea intensity ratings with the addition of DS were similar at standardized submaximal work rates in older and younger groups. We conclude that, despite differences in ventilatory efficiency, the respiratory–mechanical and sensory responses to added chemostimulation during exercise were similar in fit older and younger individuals.

1. Introduction

The effects of aging on respiratory system function have been extensively studied (Thurlbeck and Angus, 1975; Pump, 1976; Johnson et al., 1991a,b; McClaran et al., 1999). Most studies suggest that the gradual impairment of pulmonary gas exchange and dynamic respiratory mechanics associated with aging does not compromise arterial blood gas homeostasis when metabolic requirements increase during exercise (Dempsey et al., 1985; Dempsey, 1986; Johnson and Dempsey, 1991). Thus, the decline in aerobic capacity (by 6–10% per decade) with aging is mainly thought to reflect diminished cardio-circulatory function rather than respiratory limitations, *per se* (Kasch et al., 1993). However, it remains unclear whether age-related factors such as higher physiological dead space (Johnson et al., 1991a) and inability to reduce end-expiratory lung volume (EELV) during exercise (Ofir et al., 2008) contribute to greater respiratory mechanical constraints and attendant respiratory discomfort in older individuals. This information becomes particularly important when attempting to differentiate between effects of natural aging and pathological effects that may arise, for example, from exposure to tobacco smoking in patients with early chronic obstructive pulmonary disease (COPD).

Several studies have confirmed that the respiratory system is not the proximate cause of exercise limitation in inactive younger healthy individuals (Ward and Whipp, 1980; Dempsey, 1986; Johnson and Dempsey, 1991). However, respiratory constraints may become more important in trained young athletes with markedly increased aerobic capacity (Dempsey et al., 1984) and in fit older individuals who are susceptible to arterial hypoxemia (Préfaut et al., 1994) and expiratory flow limitation (EFL) (Johnson et al., 1991b; McClaran et al., 1999) during exercise. Recent studies have reported that both the cardiovascular and respiratory systems approached or reached their physiological limits at peak oxygen uptake ($\dot{V}O_2$) in healthy older (50–80 years) individuals (Ofir et al., 2008; Chin et al., 2013). Thus, addition of dead space to the breathing circuit was not associated with increased ventilation ($\dot{V}_E$) at peak exercise and resulted in a small reduction in peak work rate (DeLorey and Babb, 1999; Chin et al., 2013).

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However, these studies enrolled both male and female participants with variable cardio-respiratory fitness and did not compare responses with younger healthy controls. It was not therefore possible to determine the relative contribution of age-related respiratory impairment to exercise limitation which is the primary focus of the current study.

This study therefore extends our previous studies (O'Donnell et al., 2000; Chin et al., 2013) by examining the differential effects of selectively stressing the respiratory system in younger and older men who were physically active and reached a similar percentage of age-specific fitness norms. The hypothesis was that combined impairment in ventilatory efficiency and dynamic respiratory mechanics related to aging, would be associated with alterations in the intensity and quality of dyspnea during exercise compared with younger fit individuals. We further postulated that these alterations of respiratory sensation would be amplified by adding dead space to the breathing circuit with corresponding ventilatory limitation and earlier exercise cessation in older but not in younger individuals. To test the hypothesis, we compared $\dot{V}_E$, breathing pattern, operating lung volumes, indices of ventilatory efficiency as well as intensity and quality of dyspnea in groups of younger and older fit healthy men before and after imposition of added dead space during incremental cycle exercise tests.

2. Methods

2.1. Subjects

Twelve non-smoker healthy active older (55–79 years) and 12 young (20–39 years) men were included. The older and young subjects were required to achieve a peak $\dot{V}O_2 \geq 35$ and ≥ 45 ml/kg/min, respectively, during the symptom-limited incremental cycle exercise tests in order to be considered physically active according to American College of Sports Medicine guidelines (Franklin et al., 2000). Exclusion criteria included: history of cardiovascular or respiratory disease; contraindication to exercise testing; and body mass index (BMI) <18.5 or $\geq$35 kg/m^2.

2.2. Study design

This randomized, controlled, cross-sectional study received ethical approval from the Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board (DMED-1243-09 and DMED-273-97). After written informed consent, subjects completed three visits scheduled 2–10 days apart at the same time of day. Visit 1 included screening for eligibility, medical history, anthropometric measurements, pulmonary function tests and symptom-limited incremental cycle exercise tests for familiarization. At visits 2 and 3, spirometry was followed by incremental exercise tests performed under either control (CTRL) or added DS conditions, in randomized order.

2.3. Study procedures

2.3.1. Pulmonary function tests

Detailed pulmonary function tests were performed using automated equipment (Vmax229d, Vs62j, and Masterscreen IOS; SensorMedics, Yorba Linda, CA) (ATS/ERS, 2002; Macintyre et al., 2005; Miller et al., 2005; Wanger et al., 2005), and measurements were expressed as percentages of predicted normal values (Briscoe and Dubois, 1958; Burrows et al., 1961; Crapo et al., 1982; Morris et al., 1988; Hamilton et al., 1995).

2.3.2. Cardiopulmonary exercise testing

Symptom-limited incremental exercise tests were performed on an electronically-braked cycle ergometer (Ergoline 800s; SensorMedics, Yorba Linda, CA) using a SensorMedics Vmax229d testing system in accordance with clinical exercise testing guidelines (ATS/ACCP, 2003). Age specific maximal effort test protocols were used: older men performed 2-min increments of 20 W while young men performed 3-min increments of 25 W. Both protocols started after a steady-state resting period, and a 1-min warm-up of unloaded pedaling.

At rest and throughout exercise, subjects breathed through a mouthpiece (with nasal passages occluded by noseclip) that was connected to a low-resistance pneumotachograph to continuously measure inspiratory and expiratory airflow, which was then integrated to obtain volume. Respired gas was sampled from a port adjacent to the mouthpiece for measurement of partial pressure of end-tidal carbon dioxide ($P_{ET}CO_2$). Oxyhemoglobin saturation was measured continuously by finger pulse oximetry and heart rate (HR) was recorded at baseline and throughout exercise using a 12-lead electrocardiogram.

Breath-by-breath measurements were evaluated as 30 s averages at rest, each work rate and at peak exercise. Due to the differences in the exercise protocols, linear interpolation was applied between individual data points in all physiological measurements to get the corresponding values at standardized $\dot{V}O_2$ and $\dot{V}_E$ levels. Subjects rated their intensity of breathing and leg discomfort at rest, each stage of exercise and at peak exercise with the modified 10-point Borg scale (Borg, 1982). At exercise cessation, subjects were asked to select qualitative descriptor choices of dyspena from a more comprehensive questionnaire (O'Donnell et al., 2000). Operating lung volumes were derived from inspiratory capacity (IC) measurements at rest, each stage of exercise and peak exercise (O'Donnell et al., 1998).

Tidal flow-volume curves at the highest equivalent work rate (HEWR) and at peak exercise were placed within their respective maximal flow-volume envelopes with the use of coinciding IC measurements. Maximal flow-volume loops were performed at rest and immediately after exercise cessation. EFL was determined by the percentage of exercise tidal volume (V_T) that overlapped the maximal expiratory flow-volume loop [V_{TFL}/V_T (%)] (Johnson et al., 1991a,b; McClaran et al., 1999) and by comparing tidal expiratory flow rates with those of the maximal envelope at isovolume [$\dot{V}/\dot{V}_{max}$ at 50% V_T (%)] (O'Donnell et al., 2000).

2.3.3. Dead space loading

An added DS of 600 mL (using 35 mm plastic tubing) was inserted between the pneumotachograph and a two-way non-rebreathing Hans Rudolph valve. The low resistance breathing circuit was similar to that used previously (O'Donnell et al., 2000; Chin et al., 2013). The pneumotachograph was calibrated with the dead space apparatus attached to the breathing circuit. The DS arrangement was not covered, but the subjects were not aware of the purpose of added DS throughout the experiment. $\dot{V}O_2$ and carbon dioxide output ($\dot{V}CO_2$) measurements were not available under DS conditions since the testing system could not accurately correct for the large dead space volume used in this study.

2.4. Statistical analysis

Characteristics of the older and young men were compared using unpaired *t*-tests. A repeated measures analysis of variance (ANOVA) with Tukey's post hoc test was performed to evaluate differences between groups and testing conditions (CTRL vs. DS) for measurements at rest, 100 W, at peak exercise and at standardized ventilation levels. Paired *t*-tests were applied to evaluate the DS-induced changes within groups at rest, standardized work rates, highest equivalent work rate and peak exercise (within each group and across conditions). Reasons for stopping exercise