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**Physiological and Perceptual Responses to Incremental Exercise Testing in Healthy Men:
Effect of Exercise Test Modality**

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Running Head: Exercise responses to treadmill vs. cycle ergometry

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ABSTRACT

In a randomized cross-over study of 15 healthy men aged 20-30 years, we compared physiological and perceptual responses during treadmill and cycle exercise test protocols matched for increments in work rate – the source of increased locomotor muscle metabolic and contractile demands. The rates of O_2 consumption ($\dot{V}\text{O}_2$) and CO_2 production ($\dot{V}\text{CO}_2$) were higher at the peak of treadmill vs. cycle testing ($p \leq 0.05$). Nevertheless, work rate, minute ventilation ($\dot{V}_E$), tidal volume (V_T), breathing frequency (f_R), inspiratory capacity (IC), inspiratory reserve volume (IRV), tidal esophageal ($P_{es, \text{tidal}}$) and transdiaphragmatic pressure swings ($P_{di, \text{tidal}}$), peak expiratory gastric pressures ($P_{ga, \text{peak}}$), the root mean square of the diaphragm EMG ($\text{EMG}_{di, \text{rms}}$) expressed as a percentage of maximum $\text{EMG}_{di, \text{rms}}$ ($\text{EMG}_{di, \text{rms}}\% \text{max}$), and dyspnea ratings were similar at the peak of treadmill vs. cycle testing ($p > 0.05$). Ratings of leg discomfort were higher at the peak of cycle vs. treadmill exercise ($p \leq 0.05$), even though peak $\dot{V}\text{O}_2$ was lower during cycling. $\dot{V}\text{O}_2$, $\dot{V}\text{CO}_2$, $\dot{V}_E$, f_R , $P_{es, \text{tidal}}$, $P_{di, \text{tidal}}$ and $P_{ga, \text{peak}}$ were higher ($p \leq 0.05$), while V_T , IC, IRV, $\text{EMG}_{di, \text{rms}}\% \text{max}$, and ratings of dyspnea and leg discomfort were similar ($p > 0.05$) at all or most submaximal work rates during treadmill vs. cycle exercise. Our findings highlight important differences (and similarities) in physiological and perceptual responses at maximal and submaximal work rates during incremental treadmill and cycle exercise testing protocols. The lack of effect of exercise test modality on peak work rate advocates for the use of this readily available parameter to optimize training intensity determination, regardless of exercise training mode.

Key Words: Exercise; Bicycle; Treadmill; Mode; Symptom; Physiology

INTRODUCTION

The two most commonly used modes of exercise in research and clinical settings are the treadmill and cycle ergometer (American Thoracic and American College of Chest 2003). In the exercise training and/or rehabilitation setting, it is generally accepted that most individuals prefer to exercise on a treadmill than on a cycle ergometer. Indeed, Cumming (1977) reported that 73% of 305 normal males aged 42-70 yrs indicated preference for treadmill walking/running over cycle ergometry in part because it was felt to be less fatiguing on the legs. Over the past 45 years, many studies have sought to identify differences (and similarities) in the acute physiological response to treadmill and cycle ergometer exercise testing. The best-known difference between these modalities is in the maximal rate of O₂ consumption ($\dot{V}O_{2max}$), which is up to 20% higher when exercise testing is performed on a treadmill vs. cycle ergometer in both health and disease (Achten et al. 2003; Ciavaglia et al. 2014b; Faulkner et al. 1971; Hermansen et al. 1970; Hermansen and Saltin 1969; Jacobs and Sjodin 1985; Kalsas and Thorsen 2009; Kim et al. 1999; Matsui et al. 1978; Miles et al. 1980; Miyamura and Honda 1972; Okita et al. 1998; Pannier et al. 1980; Porszasz et al. 2003; Tanner et al. 2014). The higher $\dot{V}O_{2max}$ response to treadmill vs. cycle exercise testing has been ascribed to several factors, including: recruitment of a relatively larger muscle mass, with attainment of a higher maximal cardiac output, arteriovenous O₂ difference, lower limb blood flow and total vascular conductance during treadmill running (Hermansen et al. 1970; Hermansen and Saltin 1969; Kim et al. 1999; Matsui et al. 1978; Miyamura and Honda 1972; Niederberger et al. 1974); higher fat and lower carbohydrate oxidation rates during maximal treadmill vs. cycle ergometry (Achten et al. 2003; Cheneviere et al. 2010); and development of a less severe metabolic acidosis at maximal treadmill vs. cycle exercise (Koyal et al. 1976; Okita et al. 1998).

While the influence of exercise mode on maximal physiological responses is now well established, only a few studies have examined the influence of modality on physiological and perceptual responses at standardized submaximal exercise intensities. With few exceptions, these studies have found that carbohydrate oxidation rates, blood lactate concentrations, the respiratory exchange ratio (RER) and the ventilatory equivalent for O₂ ($\dot{V}_E/\dot{V}O_2$) are lower, while intensity ratings of breathing and leg discomfort are not different at equivalent submaximal exercise intensities during treadmill vs. cycle ergometry (Duke et al. 2014; Hermansen et al. 1970; Hermansen and Saltin 1969; Jacobs and Sjodin 1985; Koyal et al. 1976; Miles et al. 1980; Miyamura and Honda 1972; Sharma et al. 2015). In each of these studies, however, measured parameters were compared between modalities at equivalent submaximal levels of $\dot{V}O_2$, expressed either in L·min⁻¹, mL·kg⁻¹·min⁻¹ or as a percentage of $\dot{V}O_{2max}$. As such, the true impact of test modality on exercise physiological and perceptual responses is difficult to interpret from these earlier studies in as much as the protocols were not matched for increments in external work rate, which is the proximate source of increased skeletal (locomotor) muscle metabolic and contractile demands.

In 2003, Porszasz et al. (2003) first described an incremental treadmill protocol that utilizes linear increases in speed and nonlinear increases in grade that result in ramp-like increments in external work rate equivalent to those produced by an electronically-braked cycle ergometer. In this study of 22 healthy, sedentary adults, the slope of the $\dot{V}O_2$ -work rate relationship was linear and significantly higher (by 19%) during incremental treadmill vs. cycle exercise. Apart from $\dot{V}O_2$, however, Porszasz et al. (2003) did not compare cardiovascular, gas exchange, breathing pattern, operating lung volume, respiratory mechanical/muscular and/or perceptual responses at equivalent submaximal work rates between modalities.

Ciavaglia et al. (2014a; 2014b) recently compared a constellation of detailed physiological and perceptual responses to symptom-limited treadmill and cycle exercise using matched incremental work rate protocols in elderly and obese patients with chronic obstructive pulmonary disease (COPD). In these studies, $\dot{V}O_2$, the rate of CO_2 production ($\dot{V}CO_2$) and expiratory muscle activity were higher, while RER, arterial blood O_2 saturation and the $\dot{V}_E/\dot{V}O_2$ ratio were lower at any submaximal work rate during treadmill vs. cycle ergometry. Despite these differences, mean values for heart rate (HR), the ventilatory equivalent for CO_2 ($\dot{V}_E/\dot{V}CO_2$), minute ventilation ($\dot{V}_E$), tidal volume (V_T), breathing frequency (f_R), inspiratory capacity (IC), inspiratory reserve volume (IRV), neural inspiratory drive, and intensity ratings of dyspnea and leg discomfort were similar at any equivalent submaximal work rate during treadmill vs. cycle exercise. It is unlikely that these novel and important observations from elderly and obese COPD patients can be generalized to healthy, young and non-obese adults.

Accordingly, our study is the first to compare detailed assessments of cardio-metabolic function, gas exchange, breathing pattern, dynamic operating lung volumes, neural inspiratory drive, inspiratory and expiratory muscle function, dyspnea and leg discomfort in healthy, young and non-obese adults during symptom-limited treadmill and cycle exercise test protocols carefully matched for increments in work rate.

METHODS

Participants. Participants included healthy, non-smoking, non-obese (Body mass index (BMI) $<30\text{ kg}\cdot\text{m}^{-2}$) men aged 20–30 yrs with normal spirometry (Vestbo et al. 2013). Participants were excluded if they had a known or suspected history of cardiovascular, respiratory, musculoskeletal, endocrine, neuromuscular and/or metabolic disease; were taking doctor

prescribed medications; and/or had an allergy to lidocaine. Participants were recruited from the Montréal and surrounding area by word-of-mouth and online postings in the McGill University and Concordia University classifieds.

Study Design. Participants visited the *Clinical Exercise and Respiratory Physiology Laboratory* at McGill University on 3 separate occasions. *Visit 1* included screening for eligibility criteria, spirometry, and a symptom-limited incremental cycle exercise test followed 45-min thereafter by a symptom-limited incremental treadmill exercise test (both for familiarization purposes). *Visits 2 and 3* included spirometry and a symptom-limited incremental cycle or treadmill exercise test (randomized visit order) with added measurements of the diaphragm electromyogram and of respiratory pressures. Participants were instructed to avoid alcohol, caffeine and strenuous exercise on each test day, which were separated by ≥ 48 -hr and conducted at the same time of day (± 1 hr) for each participant. The study protocol and consent form were approved by the Institutional Review Board of the Faculty of Medicine at McGill University (A00-M74-11B) in accordance with the *Declaration of Helsinki*. All participants provided written informed consent.

Pulmonary function tests. Forced vital capacity (FVC), forced expiratory volume in 1-sec (FEV_1) and the FEV_1/FVC ratio were determined using automated testing equipment (Vmax EncoreTM; CareFusion, Yorba Linda, CA, USA). Measurements were obtained with participants seated, utilizing recommended techniques (Miller et al. 2005) and expressed as a percentage of predicted normal values (Hankinson et al. 1999).

Cardiopulmonary exercise testing. Incremental exercise tests were conducted on either an electronically braked cycle ergometer (Ergoline 800s; CareFusion, Yorba Linda, CA, USA) or a motorized treadmill (Trackmaster Model #TMX425C; Newton, KS, USA) using a Vmax EncoreTM cardiopulmonary exercise testing system; and consisted of a baseline resting period of ≥ 6 -min (while seated on the cycle ergometer and while standing on the treadmill) followed by 25-watt increases in work rate (starting at 25 watts) every 2-min to the point of symptom-limitation. The treadmill protocol was individualized for each participant based on their body mass using the formula (Jones 1997): Work rate (watts) = $m * g * v * \sin(\alpha)$, where m is the body mass of the participant in kg, g is the gravitational acceleration (9.81 m s^{-1}), v is the velocity of the treadmill in m s^{-1} , and α is the angle of inclination. The grade started at 5% and was increased by 1% every 2-min, with the increments in treadmill speed required to achieve the 25-watt 2-min^{-1} increase in work rate determined using the formula. Participants remained seated and maintained a pedaling cadence of 50-100 rev min^{-1} during cycle testing; and were not allowed to grasp the handrails during treadmill testing.

Standard respiratory and gas exchange parameters were collected breath-by-breath at rest and during exercise while participants breathed through a mouthpiece and low-resistance flow transducer with nasal passages occluded by a nose clip. Heart rate was monitored continuously using a Polar[®] heart rate monitor (Lachine, QC, Canada). Inspiratory capacity (IC) maneuvers were performed at rest, within the last 30-s of every 2-min stage during exercise, and at end exercise. Assuming that total lung capacity does not change during exercise (Stubbing et al. 1980), changes in IC and IRV (calculated as the difference between IC and the simultaneously determined V_T) reflect changes in dynamic end-expiratory and end-inspiratory lung volume, respectively.

Using Borg's 0-10 category-ratio scale (Borg 1982), participants provided ratings to the following questions at rest, within the last 30-s of every 2-min stage during exercise, and at end-exercise: How *intense* is your sensation of breathing overall? How *unpleasant* or *distressed* does your breathing make you feel? How *intense* is your sensation of leg discomfort? Breathing overall (hereafter referred to as dyspnea) was defined as "the global awareness of your breathing," which is consistent with the American Thoracic Society's most recent recommendation that "...the definition of dyspnea should be neutral with respect to any particular quality" of breathing (Parshall et al. 2012). Prior to each exercise test, participants were familiarized with the Borg scale and its endpoints were anchored such that "0" represented "no intensity (unpleasantness) at all" and "10" represented "the most severe intensity (unpleasantness) you have ever experienced or could ever imagine experiencing." At end-exercise, participants verbalized their main reason(s) for stopping exercise (dyspnea, leg discomfort, combination of dyspnea and leg discomfort, other); quantified the percentage contribution of dyspnea and leg discomfort to exercise cessation; and identified qualitative phrases that best described their breathing at end-exercise (O'Donnell et al. 2000).

Breath-by-breath measures of the root mean square of the crural diaphragm electromyogram (EMG_{di,rms}) and of esophageal (Pes), gastric (Pga) and transdiaphragmatic (P_{di}, calculated as the difference between Pga and Pes) pressure were recorded from a gastro-esophageal electrode-balloon catheter (Guangzhou Yinghui Medical Equipment Ltd., Guangzhou, China) and analyzed using published methods (Mendonca et al. 2014; Schaeffer et al. 2014). Maximum voluntary EMG_{di,rms} (EMG_{di,max}) was identified as the largest of all EMG_{di,rms} values obtained from IC maneuvers performed either at rest or during exercise. The ratio of EMG_{di,rms} to EMG_{di,max} (EMG_{di,rms}%max) was used as an index of neural

inspiratory drive. Tidal swings in P_{es} ($P_{es, tidal}$) and P_{di} ($P_{di, tidal}$) were calculated as the difference between peak tidal inspiratory and peak tidal expiratory P_{es} and P_{di} . Peak expiratory P_{ga} ($P_{ga, peak}$) was taken as an index of expiratory muscle activity (effort).

Analysis of exercise end points. Physiological parameters measured breath-by-breath were averaged in 30-s intervals at rest and during exercise. These parameters, collected over the first 30-s period of every 2-min stage during exercise, were linked with symptom ratings and IC measurements collected over the latter 30-s of the same minute to avoid contamination of averaged breath-by-breath data by subject-experimenter interaction and by irregular breaths surrounding IC maneuvers.

Four main time points were used for the evaluation of exercise parameters: (1) *pre-exercise rest*, defined as the average of the last 30-s of the baseline period after ≥ 2 -min of quiet breathing on the mouthpiece while seated on the cycle ergometer or while standing on the treadmill; (2) *ventilatory threshold* (T_{vent}), which was identified for each participant and test using the V-slope method (Beaver et al. 1986): physiological parameters and symptom ratings at the $\dot{V}O_2$ corresponding to T_{vent} were calculated by linear interpolation between adjacent measurement points for each participant and test; (3) *iso-work*, defined as the average of the last 30-sec of the highest equivalent submaximal work rate achieved by a given participant during both cycle and treadmill tests; and (4) *peak exercise*, defined as the average of the last 30-s of loaded pedaling and treadmill running. Peak work rate was identified as the highest work rate a given participant was able to sustain for ≥ 30 -s, while exercise endurance time (EET) was defined as the duration of loaded pedaling and as the duration of treadmill walking/running.

Statistical Analysis. The effect of exercise modality, measurement time and their interaction on measured parameters was examined using a two-way repeated measures analysis of variance with correction for multiple comparisons using Tukey's honest significant difference test (SigmaStat[®]; Systat[®] Software Inc., San Jose, CA, USA). Two-tailed paired *t*-tests (SigmaStat[®]) were used to examine the effect of exercise mode on 1) measured parameters at T_{vent} and 2) the percentage contribution of dyspnea and leg discomfort to exercise cessation. Reasons for stopping exercise and qualitative descriptors of dyspnea were assessed using frequency statistics. Significance was set at $p \leq 0.05$ and data are presented as mean $\pm$ SEM.

RESULTS

Participant characteristics. Participants included 15 healthy, young (22.5 ± 0.4 yrs), non-obese ($BMI = 23.8 \pm 0.5 \text{ kg m}^{-2}$) men with normal spirometry ($FEV_1 = 107 \pm 3\%$ predicted; $FEV_1/FVC = 83 \pm 2\%$) and normal-to-above normal levels of cardiorespiratory: peak $\dot{V}O_2$ on incremental cycle and treadmill exercise testing of 118 ± 5 and $135 \pm 4\%$ predicted, respectively.

Responses to cycle and treadmill exercise. Exercise mode had no effect on EET (cycle, 21.6 ± 0.8 vs. treadmill, 21.4 ± 0.9 min, $p > 0.05$) or the work rate achieved at peak exercise (cycle, 280 ± 10 vs. treadmill, 279 ± 11 watts, $p > 0.05$).

Cardiometabolic and gas exchange responses. At the symptom-limited peak of treadmill vs. cycle testing, $\dot{V}O_2$, $\dot{V}CO_2$, HR, O_2 pulse and $P_{ET}CO_2$ were higher, whereas RER, $\dot{V}_E/\dot{V}O_2$ and $P_{ET}O_2$ were lower (Table 1, Fig. 1).

As illustrated in Fig. 1, $\dot{V}O_2$, $\dot{V}CO_2$, HR and the O_2 pulse were higher, while RER was lower at most submaximal work rates during treadmill vs. cycle testing (Table 1). With the

exception of $\dot{V}_E/\dot{V}O_2$ and $P_{ET}O_2$ being higher during cycle vs. treadmill exercise at 25 and 50 watts, mean values of $\dot{V}_E/\dot{V}O_2$, $\dot{V}_E/\dot{V}CO_2$, $P_{ET}O_2$ and $P_{ET}CO_2$ were similar at all submaximal work rates between modalities (Table 1, Fig. 1).

Although participants reached their T_{vent} at the same absolute work rate during treadmill vs. cycle testing (91 ± 6 vs. 92 ± 6 watts, $p > 0.05$), mean values of $\dot{V}O_2$, $\dot{V}CO_2$, HR and the O_2 pulse were higher, while RER was lower at T_{vent} during treadmill exercise (Table 1).

Ventilatory, breathing pattern and operating lung volume responses. Despite significant differences in $\dot{V}O_2$ and $\dot{V}CO_2$ at the peak of treadmill vs. cycle exercise, $\dot{V}_E$, V_T , f_R , IC and IRV were not different between modalities at end-exercise (Table 1, Fig. 2).

As illustrated in Fig. 2, mean values of $\dot{V}_E$ were higher at all standardized submaximal work rates ≥ 75 watts (including T_{vent}) during treadmill vs. cycle exercise testing; for example, by 17.4 ± 5.6 L min^{-1} or $21 \pm 7\%$ at iso-work (Table 1, Fig. 2). The relatively greater $\dot{V}_E$ response to treadmill vs. cycle exercise was associated with the adoption of a more rapid and shallow breathing pattern (Fig. 2). Operating lung volumes were not different between modalities at any standardized submaximal work rate and at peak exercise (Fig. 2). The relationship between exercise-induced changes in IC and $\dot{V}_E$ was also similar between modalities (Fig. 2). In contrast, there was a rightward shift of the IRV- $\dot{V}_E$ relationship during treadmill vs. cycle exercise (Fig. 2), such that mean values of $\dot{V}_E$ were higher at any IRV during submaximal treadmill vs. cycle exercise; for example, by ~ 15 - 20 L min^{-1} at IRV's ranging from 0.5 to 2.0 L.

Diaphragm EMG and respiratory pressure responses. On average, EMG_{di,max} was not different when evaluated on treadmill vs. cycle exercise test days: 238.2 ± 19.8 vs. 230.0 ± 18.6 μV , respectively ($p = 0.740$). The EMG_{di,rms\%max} was higher at the peak of treadmill vs. cycle exercise (77.2 ± 3.6 vs. 67.0 ± 4.9); however, this difference did not reach statistical significance

($p=0.120$) (Table 1, Fig. 3). Neither $P_{es,tidal}$, $P_{di,tidal}$ nor $P_{ga,peak}$ were different at the peak of treadmill vs. cycle exercise (Table 1, Fig. 3).

As illustrated in Fig. 3, $P_{es,tidal}$ was higher during treadmill vs. cycle testing at standardized submaximal work rates ≥ 125 watts (Fig. 3). Similarly, $P_{di,tidal}$ was higher at iso-work, while $P_{ga,peak}$ was higher at 175 watts and at iso-work during treadmill vs. cycle testing (Fig. 3). By contrast, $EMG_{di,rms\%max}$ was not significantly different at any submaximal work rate during treadmill vs. cycle exercise (Fig. 3).

Symptom responses. A higher percentage (60% vs. 27%) of our participants identified intolerable leg discomfort as the main reason for stopping cycle vs. treadmill exercise. The relative contribution of intolerable leg discomfort to exercise cessation was also higher at the end of cycle vs. treadmill testing ($67.9 \pm 6.6\%$ vs. $43.4 \pm 7.7\%$, $p=0.023$). The majority of participants self-selected descriptor phrases alluding to a heightened sense of ‘work/effort of breathing’ and of ‘rapid breathing’ at the peak of both treadmill and cycle testing; for example, ‘Breathing in requires effort’ (cycle, 71% vs. treadmill, 64%), ‘My breathing is heavy’ (cycle, 79% vs. treadmill, 93%), ‘My breathing requires more work’ (cycle, 71% vs. treadmill, 93%) and ‘I feel that my breathing is rapid’ (cycle, 85% vs. treadmill, 93%).

Intensity ratings of leg discomfort were higher at iso-work and at peak exercise during cycle vs. treadmill testing (by 0.9 ± 0.5 and 1.2 ± 0.6 Borg 0-10 scale units, respectively) (Table 1, Fig. 4). As illustrated in Fig. 4, the relationship between increasing intensity ratings of leg discomfort and increasing $\dot{V}O_2$ was displaced to the right during treadmill vs. cycle exercise.

Borg 0-10 scale intensity and unpleasantness ratings of dyspnea were not different between modalities at any standardized submaximal work rate and at peak exercise (Table 1, Fig. 4). Compared to cycle testing, treadmill testing was associated with a rightward shift of the

dyspnea intensity- $\dot{V}_E$ relationship (Fig. 4). By contrast, the relationship between exercise-induced changes in dyspnea intensity ratings and each of EMGdi,rms%max and IRV were relatively superimposed during treadmill and cycle ergometry (Fig. 4). A similar influence of exercise mode was observed on the relationship exercise-induced changes in dyspnea unpleasantness ratings and each of $\dot{V}_E$, EMGdi,rms%max and IRV (data not shown).

DISCUSSION

The main findings of this study are that, despite significant between-test differences in $\dot{V}O_2$, $\dot{V}CO_2$, RER, HR, O_2 pulse, $\dot{V}_E$, f_R , and inspiratory and expiratory muscle pressures, detailed assessments of ventilatory efficiency and gas exchange ($\dot{V}_E/\dot{V}O_2$, $\dot{V}_E/\dot{V}CO_2$, $P_{ET}O_2$, $P_{ET}CO_2$), dynamic operating lung volumes (IC, IRV), neural inspiratory drive (EMGdi,rms%max), and exertional symptoms (dyspnea, leg discomfort) were similar at all or most submaximal work rates during incremental treadmill vs. cycle exercise testing.

The men in our study exerted maximal (or near maximal) effort during incremental cycle and treadmill exercise testing as indicated by symptom-limited peak respiratory exchange ratio, heart rate and symptom intensity values/ratings that were, on average, ≥ 1.06 , $>95\%$ predicted (cycle, $96.3 \pm 1.2\%$; treadmill, $99.2 \pm 1.3\%$) and ~ 7 -9 Borg 0-10 scale units, respectively. Consistent with previous reports (Duke et al. 2014; Faulkner et al. 1971; Hermansen et al. 1970; Hermansen and Saltin 1969; Matsui et al. 1978; Miles et al. 1980; Miyamura and Honda 1972; Porszasz et al. 2003; Tanner et al. 2014), $\dot{V}O_2$ was higher at T_{vent} (by 23%) and at the peak of treadmill vs. cycle exercise testing (by 12%), even though work rate was not different between modalities at either measurement time. As previously discussed, these differences likely reflect 1) recruitment of a relatively larger skeletal muscle mass, with attainment of a higher maximal

cardiac output, stroke volume, arteriovenous O_2 difference, leg muscle blood flow and total vascular conductance during treadmill running (Hermansen et al. 1970; Hermansen and Saltin 1969; Matsui et al. 1978; Miyamura and Honda 1972; Niederberger et al. 1974); 2) higher fat and lower carbohydrate oxidation rates during submaximal and maximal treadmill running vs. cycling (Achten et al. 2003; Cheneviere et al. 2010); 3) higher oxidative relative to glycolytic enzyme activity in skeletal muscles predominantly used in running vs. those predominantly used in cycling (Jacobs and Sjodin 1985); and 4) less rapid rate of development of metabolic acidosis during treadmill vs. cycle ergometry (Koyal et al. 1976; Okita et al. 1998). Indeed, RER was lower, while $\dot{V}CO_2$, HR and the O_2 pulse (a surrogate measure of stroke volume (Bhambhani et al. 1994)) were higher during treadmill vs. cycle ergometry at T_{vent} , iso-work and at peak exercise.

It is clear from Fig. 1 that cardiometabolic responses were higher during incremental treadmill vs. cycle exercise at most standardized submaximal work rates. These findings, which substantiate the results of Porszasz et al. (2003) in health and Ciavaglia et al. (2014a; 2014b) in COPD, suggest that treadmill walking/running is less metabolically efficient than stationary cycling. Muscles of the upper body (e.g., arms, shoulders) and trunk (e.g., rectus abdominis) are presumably more active during treadmill vs. cycle exercise. Although activation of these muscle groups cost metabolic energy, they do not contribute to the production of external mechanical power during treadmill walking/running. It follows that, in our study, the widening disparity between work rate and each of $\dot{V}O_2$, $\dot{V}CO_2$, HR and the O_2 pulse during treadmill vs. cycle exercise may reflect, at least in part, relatively greater metabolic activity of the upper body and/or trunk muscles as work rate increased during treadmill exercise.

Exercise-induced increases in $\dot{V}_E$ are tightly coupled to $\dot{V}CO_2$ (Haouzi 2006). In our study, neither $\dot{V}_E$ nor $\dot{V}CO_2$ was significantly different between modalities at standardized work rates below T_{vent} . By contrast, $\dot{V}_E$ and $\dot{V}CO_2$ were significantly and proportionately higher during treadmill vs. cycle exercise at T_{vent} and at submaximal work rates above T_{vent} . Under these circumstances, neither $\dot{V}_E/\dot{V}CO_2$ nor $P_{ET}CO_2$ was significantly different at any submaximal work rate across modalities. Thus, ventilatory efficiency was similar during treadmill vs. cycle exercise testing when the protocols were matched for increments in work rate.

In keeping with the results of Kalsas and Thorsen (2009) and Elliott and Grace (2010), the greater $\dot{V}_E$ observed during treadmill vs. cycle exercise at T_{vent} and at submaximal work rates above T_{vent} was the result of a greater f_R with no difference in V_T . As such, f_R was higher, while V_T was lower at any $\dot{V}_E$ throughout much of treadmill vs. cycle exercise. Despite significant differences in the $\dot{V}_E$ -work rate relationship during treadmill vs. cycle ergometry, exercise mode had no effect on the relationship between IC and each of work rate and $\dot{V}_E$. Under these circumstances, adoption of a more rapid and shallow breathing pattern during treadmill vs. cycle exercise likely helped to preserve the IRV-work rate relationship between modalities.

Our study is the first to examine the effect of exercise mode on neural inspiratory drive and respiratory muscle pressure (effort) requirements in health. The higher demand for $\dot{V}_E$ during treadmill vs. cycle exercise at submaximal work rates above T_{vent} was supported by greater $P_{es,tidal}$, $P_{di,tidal}$ and $P_{ga,peak}$. Despite differences in $\dot{V}_E$ and respiratory muscle pressures between modalities, $EMG_{di,rms\%max}$ was not different at any submaximal work rate during treadmill vs. cycle exercise. By adopting a more rapid and shallow breathing pattern, our participants maintained a larger IRV (by ~200-300 mL) for any given $\dot{V}_E$ throughout the majority of treadmill vs. cycle exercise. We speculate that maintenance of a larger dynamic IRV was

associated with less elastic loading and functional weakening of the inspiratory pump muscles (e.g., diaphragm) for any given $\dot{V}_E$ during treadmill testing. We further speculate that, for these reasons, exercise mode had no effect on EMGdi,rms%max-work rate relationships.

Mean values of $\dot{V}_E$, V_T , f_R , IC, IRV, $P_{es,tidal}$, $P_{di,tidal}$ and $P_{ga,peak}$ were not different at the peak of incremental treadmill vs. cycle testing, even though $\dot{V}O_2$, $\dot{V}CO_2$ and EMGdi,rms%max were 8-15% higher in the former. These findings corroborate those of Clark et al. (1980), Johnson et al. (1992) and McClaran et al. (1999) who found that increased chemostimulation *via* hypercapnia did not elicit further increases in $\dot{V}_E$ and/or peak inspiratory and expiratory P_{es} during treadmill and cycle exercise testing near the limits of tolerance in young, endurance trained men with maximal $\dot{V}O_2$ values of 63-73 mL·kg⁻¹·min⁻¹. Collectively, these findings support the existence of critical dynamic mechanical constraints on $\dot{V}_E$ during treadmill and cycle exercise near the limits of tolerance in healthy, young, fit men with normal lung function.

A study of 20 healthy young adults by Sharma et al. (2015) recently reported that 1) intensity ratings of leg fatigue and dyspnea were not different during treadmill vs. cycle exercise at any standardized submaximal $\dot{V}O_2$ ranging from 1.0 to 2.5 L·min⁻¹; and 2) exercise mode had no effect dyspnea intensity- $\dot{V}_E$ relationships. In our study, intensity ratings of leg discomfort were similar between modalities up to 175 watts, but became greater at iso-work and at the peak of cycle vs. treadmill exercise. Moreover, the relative contribution of intolerable leg discomfort to exercise cessation was higher at the peak of cycle vs. treadmill testing. It follows that a higher percentage of our participants stopped cycle vs. treadmill exercise because of intolerable leg discomfort. We speculate that these differences reflect the sensory consequences associated with relatively greater neural activation of the lower limbs needed to produce equivalent external

work rates near the limits of tolerance during cycle vs. treadmill testing. Indeed, Bijker et al. (2002) found that the magnitude of the increase in vastus lateralis EMG and biceps femoris EMG needed to support any given increase in work rate was much greater during cycling compared to running in a group of 11 healthy young adults.

In contrast to Sharma et al. (2015), we observed a rightward shift of the leg discomfort- $\dot{V}O_2$ relationship during treadmill vs. cycle ergometry; that is, intensity ratings of leg discomfort were much lower at any standardized $\dot{V}O_2$ during treadmill vs. cycle testing (e.g., by ~3 Borg 0-10 scale units at a $\dot{V}O_2$ of 50 mL·kg⁻¹·min⁻¹). These differences may reflect the development of a more severe metabolic acidosis for any given $\dot{V}O_2$ during cycle ergometry (Koyal et al. 1976; Okita et al. 1998) and/or progressively greater activation of the upper body and trunk muscles that do not contribute to the production of external mechanical power (and, by extension, the perception of leg discomfort), but nevertheless cost metabolic energy during treadmill running.

Despite the aforementioned differences in $\dot{V}_E$ and respiratory muscle pressure responses between the two modalities, Borg 0-10 scale intensity (and unpleasantness) ratings of dyspnea were identical at submaximal work rates and at peak exercise during treadmill vs. cycle testing. Consequently, and in contrast to the results of Sharma et al. (2015), dyspnea intensity (and unpleasantness)- $\dot{V}_E$ relationships were shifted to the right throughout the majority treadmill vs. cycle exercise testing. Accumulating evidence suggests that neural inspiratory drive (and the attendant 'central corollary discharge') is the proximate source of exertional dyspnea in health (Jensen et al. 2011; Mendonca et al. 2014; Schaeffer et al. 2014) and in patients with COPD (Ciavaglia et al. 2014a; Guenette et al. 2014; Jolley et al. 2015). It follows that preservation of the EMG_{di,rms}%max-work rate relationship during treadmill vs. cycle testing in our study was likely responsible for preservation of the dyspnea intensity (and unpleasantness)-work rate

relationship, despite significant differences in $\dot{V}_E$ and contractile respiratory muscle pressure (effort) requirements. Indeed, exercise mode had no effect on dyspnea intensity (and unpleasantness)-EMG_{dI,rms}%_{max} relationships.

It is possible that the observed rightward shift of the dyspnea intensity (and unpleasantness)- $\dot{V}_E$ relationship during treadmill vs. cycle exercise may also reflect, at least in part, temporal desensitization to the sensory consequences of increased $\dot{V}_E$ and contractile respiratory muscle effort requirements during a form of exercise (walking/running) that was more familiar to and/or preferred by our participants. This hypothesis is bolstered by the results of Schneider et al. (2009) and Brummer et al. (2011) who found that familiar and/or preferred exercise modes (e.g., treadmill running) are associated with decreased neuronal activity (deactivation) in the frontal cortex of healthy recreational runners, where increased neural activation of the prefrontal cortex has been mechanistically linked to the perception of activity-related dyspnea in health and COPD (Higashimoto et al. 2011).

Methodological considerations. Our treadmill protocol employed linear increases in grade and curvilinear increases in speed, which is in contrast to previous studies that utilized linear increases in speed and curvilinear increases in grade (Ciavaglia et al. 2014a; Ciavaglia et al. 2014b; Porszasz et al. 2003). Despite these differences, all studies reported 1) a linear $\dot{V}O_2$ -work rate relationship during treadmill testing and 2) that the $\dot{V}O_2$ -work rate slope was higher during treadmill vs. cycle exercise.

Our participants were healthy, young, non-obese men with normal-to-above normal levels of cardiorespiratory fitness. As such, our results may not be generalizable to elderly men

and women; obese men and women; physically inactive/deconditioned men and women; patients with chronic cardiorespiratory and/or neuromuscular disease; or any combination thereof.

Training specificity may influence comparisons of the physiological response to treadmill vs. cycle exercise. For example, Verstappen et al. (1982) found that maximal $\dot{V}O_2$ values were 14% higher during treadmill vs. cycle ergometry in runners, but not significantly different between modalities in cyclists. Although detailed assessments of training history were not recorded in our study, all of our participants were recreationally active and none were known to be training for participation in any competitive athletic event(s) and/or involved in bicycling as a sport or common form of recreation. Nevertheless, we cannot rule out the possibility that unmeasured differences in our participants' training histories may have influenced our results.

In our study, stride frequency during treadmill testing and pedal cadence during cycle testing were not matched within- or between-subjects. Thus, maintenance of a relatively higher stride frequency vs. pedal cadence may have contributed to differences in the f_R -work rate relationship during treadmill vs. cycle exercise (Caretto et al. 1992).

Summary and implications. In summary: 1) cardiometabolic, ventilation and respiratory muscle pressure (effort) responses were consistently higher at standardized submaximal work rates during incremental treadmill vs. cycle exercise; and 2) with few exceptions, detailed assessments of ventilatory efficiency, dynamic operating lung volumes, neural inspiratory drive, dyspnea and leg discomfort were similar at equivalent submaximal work rates during treadmill vs. cycle ergometry.

Our findings suggest that physiological parameters relevant to the prescription of exercise - specifically peak $\dot{V}O_2$, peak HR and $\dot{V}O_2$ at T_{vent} - should be assessed in each exercise mode for

optimal (mode-specific) training intensity determination. Alternatively, the lack of effect of exercise mode on peak work rate in our study advocates for the use of this readily available parameter to determine optimal training intensity, regardless of exercise training mode.

In terms of evaluating an individuals' occupational readiness, our finding of a higher peak $\dot{V}O_2$ on treadmill vs. cycle exercise testing may lead to the identification of occupational tasks with higher metabolic equivalents and that may be unsafe for some adults. By contrast, our finding of a lower peak $\dot{V}O_2$ on cycle vs. treadmill exercise testing may lead to the identification of occupational tasks with metabolic equivalents deemed as "safe" but below the physical requirements of a particular position of employment.

Finally, peak $\dot{V}O_2$ is often used to evaluate pre-operative risk for major surgery, with values $<14 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ being indicative of "high-risk" (American Thoracic and American College of Chest 2003). In our study, peak $\dot{V}O_2$ was, on average, $6.5 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (or 12%) higher when testing was performed on the treadmill vs. cycle ergometer. It follows that, in a given surgical candidate, peak $\dot{V}O_2$ measured pre-operatively on a cycle ergometer may indicate "high-risk", while peak $\dot{V}O_2$ measured pre-operatively on a treadmill may indicate "low-to-moderate risk".

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REFERENCES

- Achten, J., Venables, M.C., and Jeukendrup, A.E. 2003. Fat oxidation rates are higher during running compared with cycling over a wide range of intensities. *Metabolism: clinical and experimental* **52**(6): 747-752.
- American Thoracic, S., and American College of Chest, P. 2003. ATS/ACCP Statement on cardiopulmonary exercise testing. *American journal of respiratory and critical care medicine* **167**(2): 211-277. doi: 10.1164/rccm.167.2.211.
- Beaver, W.L., Wasserman, K., and Whipp, B.J. 1986. A new method for detecting anaerobic threshold by gas exchange. *J Appl Physiol* (1985) **60**(6): 2020-2027.
- Bhambhani, Y., Norris, S., and Bell, G. 1994. Prediction of stroke volume from oxygen pulse measurements in untrained and trained men. *Canadian journal of applied physiology = Revue canadienne de physiologie appliquee* **19**(1): 49-59.
- Bijker, K.E., de Groot, G., and Hollander, A.P. 2002. Differences in leg muscle activity during running and cycling in humans. *European journal of applied physiology* **87**(6): 556-561. doi: 10.1007/s00421-002-0663-8.
- Borg, G.A. 1982. Psychophysical bases of perceived exertion. *Medicine and science in sports and exercise* **14**(5): 377-381.
- Brummer, V., Schneider, S., Abel, T., Vogt, T., and Struder, H.K. 2011. Brain cortical activity is influenced by exercise mode and intensity. *Medicine and science in sports and exercise* **43**(10): 1863-1872. doi: 10.1249/MSS.0b013e3182172a6f.
- Caretti, D.M., Szlyk, P.C., and Sils, I.V. 1992. Effects of exercise modality on patterns of ventilation and respiratory timing. *Respiration physiology* **90**(2): 201-211.

- 501 Cheneviere, X., Malatesta, D., Gojanovic, B., and Borrani, F. 2010. Differences in whole-body
 502 fat oxidation kinetics between cycling and running. *European journal of applied physiology*
 503 **109**(6): 1037-1045. doi: 10.1007/s00421-010-1443-5.
- 504 Ciavaglia, C.E., Guenette, J.A., Langer, D., Webb, K.A., Alberto Neder, J., and O'Donnell, D.E.
 505 2014a. Differences in respiratory muscle activity during cycling and walking do not
 506 influence dyspnea perception in obese patients with COPD. *J Appl Physiol* (1985) **117**(11):
 507 1292-1301. doi: 10.1152/japplphysiol.00502.2014.
- 508 Ciavaglia, C.E., Guenette, J.A., Ora, J., Webb, K.A., Neder, J.A., and O'Donnell, D.E. 2014b. Does
 509 exercise test modality influence dyspnoea perception in obese patients with COPD? The
 510 *European respiratory journal : official journal of the European Society for Clinical*
 511 *Respiratory Physiology* **43**(6): 1621-1630. doi: 10.1183/09031936.00151513.
- 512 Clark, J.M., Sinclair, R.D., and Lenox, J.B. 1980. Chemical and nonchemical components of
 513 ventilation during hypercapnic exercise in man. *Journal of applied physiology: respiratory,*
 514 *environmental and exercise physiology* **48**(6): 1065-1076.
- 515 Cumming, G.R. 1977. Comparison of treadmill and bicycle ergometer exercise in middle-
 516 aged males. *American heart journal* **93**(2): 261.
- 517 Duke, J.W., Stickford, J.L., Weavil, J.C., Chapman, R.F., Stager, J.M., and Mickleborough, T.D.
 518 2014. Operating lung volumes are affected by exercise mode but not trunk and hip angle
 519 during maximal exercise. *European journal of applied physiology* **114**(11): 2387-2397. doi:
 520 10.1007/s00421-014-2956-0.
- 521 Elliott, A.D., and Grace, F. 2010. An examination of exercise mode on ventilatory patterns
 522 during incremental exercise. *European journal of applied physiology* **110**(3): 557-562. doi:
 523 10.1007/s00421-010-1541-4.

- 524 Faulkner, J.A., Roberts, D.E., Elk, R.L., and Conway, J. 1971. Cardiovascular responses to
525 submaximum and maximum effort cycling and running. *J Appl Physiol* **30**(4): 457-461.
- 526 Guenette, J.A., Chin, R.C., Cheng, S., Dominelli, P.B., Raghavan, N., Webb, K.A., Neder, J.A., and
527 O'Donnell, D.E. 2014. Mechanisms of exercise intolerance in global initiative for chronic
528 obstructive lung disease grade 1 COPD. *The European respiratory journal : official journal*
529 *of the European Society for Clinical Respiratory Physiology* **44**(5): 1177-1187. doi:
530 10.1183/09031936.00034714.
- 531 Hankinson, J.L., Odencrantz, J.R., and Fedan, K.B. 1999. Spirometric reference values from a
532 sample of the general U.S. population. *American journal of respiratory and critical care*
533 *medicine* **159**(1): 179-187.
- 534 Haouzi, P. 2006. Theories on the nature of the coupling between ventilation and gas
535 exchange during exercise. *Respiratory physiology & neurobiology* **151**(2-3): 267-279. doi:
536 10.1016/j.resp.2005.11.013.
- 537 Hermansen, L., Ekblom, B., and Saltin, B. 1970. Cardiac output during submaximal and
538 maximal treadmill and bicycle exercise. *J Appl Physiol* **29**(1): 82-86.
- 539 Hermansen, L., and Saltin, B. 1969. Oxygen uptake during maximal treadmill and bicycle
540 exercise. *J Appl Physiol* **26**(1): 31-37.
- 541 Higashimoto, Y., Honda, N., Yamagata, T., Matsuoka, T., Maeda, K., Satoh, R., Nishiyama, O.,
542 Sano, H., Iwanaga, T., Miyara, T., Muraki, M., Tomita, K., Kume, H., Miyai, I., Tohda, Y., and
543 Fukuda, K. 2011. Activation of the prefrontal cortex is associated with exertional dyspnea
544 in chronic obstructive pulmonary disease. *Respiration; international review of thoracic*
545 *diseases* **82**(6): 492-500. doi: 10.1159/000324571.

- Jacobs, I., and Sjodin, B. 1985. Relationship of ergometer-specific V_{O2} max and muscle enzymes to blood lactate during submaximal exercise. *Br J Sports Med* **19**(2): 77-80.
- Jensen, D., O'Donnell, D.E., Li, R., and Luo, Y.M. 2011. Effects of dead space loading on neuro-muscular and neuro-ventilatory coupling of the respiratory system during exercise in healthy adults: implications for dyspnea and exercise tolerance. *Respiratory physiology & neurobiology* **179**(2-3): 219-226. doi: 10.1016/j.resp.2011.08.009.
- Johnson, B.D., Saupe, K.W., and Dempsey, J.A. 1992. Mechanical constraints on exercise hyperpnea in endurance athletes. *J Appl Physiol* (1985) **73**(3): 874-886.
- Jolley, C.J., Luo, Y.M., Steier, J., Rafferty, G.F., Polkey, M.I., and Moxham, J. 2015. Neural respiratory drive and breathlessness in COPD. *The European respiratory journal : official journal of the European Society for Clinical Respiratory Physiology* **45**(2): 355-364. doi: 10.1183/09031936.00063014.
- Jones, N. 1997. *Clinical Exercise Testing*. W.B Saunders Company, Philadelphia.
- Kalsas, K., and Thorsen, E. 2009. Breathing patterns during progressive incremental cycle and treadmill exercise are different. *Clinical physiology and functional imaging* **29**(5): 335-338. doi: 10.1111/j.1475-097X.2009.00874.x.
- Kim, S., Yamabe, H., and Yokoyama, M. 1999. Hemodynamic characteristics during treadmill and bicycle exercise in chronic heart failure: mechanism for different responses of peak oxygen uptake. *Jpn Circ J* **63**(12): 965-970.
- Koyal, S.N., Whipp, B.J., Huntsman, D., Bray, G.A., and Wasserman, K. 1976. Ventilatory responses to the metabolic acidosis of treadmill and cycle ergometry. *J Appl Physiol* **40**(6): 864-867.

- 568 Matsui, H., Kitamura, K., and Miyamura, M. 1978. Oxygen uptake and blood flow of the
569 lower limb in maximal treadmill and bicycle exercise. *European journal of applied*
570 *physiology and occupational physiology* **40**(1): 57-62.
- 571 McClaran, S.R., Wetter, T.J., Pegelow, D.F., and Dempsey, J.A. 1999. Role of expiratory flow
572 limitation in determining lung volumes and ventilation during exercise. *Journal of applied*
573 *physiology* **86**(4): 1357-1366.
- 574 Mendonca, C.T., Schaeffer, M.R., Riley, P., and Jensen, D. 2014. Physiological mechanisms of
575 dyspnea during exercise with external thoracic restriction: role of increased neural
576 respiratory drive. *J Appl Physiol* (1985) **116**(5): 570-581. doi:
577 10.1152/japplphysiol.00950.2013.
- 578 Miles, D.S., Critz, J.B., and Knowlton, R.G. 1980. Cardiovascular, metabolic, and ventilatory
579 responses of women to equivalent cycle ergometer and treadmill exercise. *Medicine and*
580 *science in sports and exercise* **12**(1): 14-19.
- 581 Miller, M.R., Hankinson, J., Brusasco, V., Burgos, F., Casaburi, R., Coates, A., Crapo, R., Enright,
582 P., van der Grinten, C.P., Gustafsson, P., Jensen, R., Johnson, D.C., MacIntyre, N., McKay, R.,
583 Navajas, D., Pedersen, O.F., Pellegrino, R., Viegi, G., and Wanger, J. 2005. Standardisation of
584 spirometry. *The European respiratory journal : official journal of the European Society for*
585 *Clinical Respiratory Physiology* **26**(2): 319-338. doi: 10.1183/09031936.05.00034805.
- 586 Miyamura, M., and Honda, Y. 1972. Oxygen intake and cardiac output during maximal
587 treadmill and bicycle exercise. *J Appl Physiol* **32**(2): 185-188.
- 588 Niederberger, M., Bruce, R.A., Kusumi, F., and Whitkanack, S. 1974. Disparities in
589 ventilatory and circulatory responses to bicycle and treadmill exercise. *Br Heart J* **36**(4):
590 377-382.

- 591 O'Donnell, D.E., Hong, H.H., and Webb, K.A. 2000. Respiratory sensation during chest wall
592 restriction and dead space loading in exercising men. *J Appl Physiol* **88**(5): 1859-1869.
- 593 Okita, K., Nishijima, H., Yonezawa, K., Ohtsubo, M., Hanada, A., Kohya, T., Murakami, T., and
594 Kitabatake, A. 1998. Skeletal muscle metabolism in maximal bicycle and treadmill exercise
595 distinguished by using in vivo metabolic freeze method and phosphorus-31 magnetic
596 resonance spectroscopy in normal men. *Am J Cardiol* **81**(1): 106-109.
- 597 Pannier, J.L., Vrijens, J., and Van Cauter, C. 1980. Cardiorespiratory response to treadmill
598 and bicycle exercise in runners. *European journal of applied physiology and occupational*
599 *physiology* **43**(3): 243-251.
- 600 Parshall, M.B., Schwartzstein, R.M., Adams, L., Banzett, R.B., Manning, H.L., Bourbeau, J.,
601 Calverley, P.M., Gift, A.G., Harver, A., Lareau, S.C., Mahler, D.A., Meek, P.M., and O'Donnell,
602 D.E. 2012. An official American Thoracic Society statement: update on the mechanisms,
603 assessment, and management of dyspnea. *American journal of respiratory and critical care*
604 *medicine* **185**(4): 435-452. doi: 10.1164/rccm.201111-2042ST.
- 605 Porszasz, J., Casaburi, R., Somfay, A., Woodhouse, L.J., and Whipp, B.J. 2003. A treadmill
606 ramp protocol using simultaneous changes in speed and grade. *Medicine and science in*
607 *sports and exercise* **35**(9): 1596-1603. doi: 10.1249/01.MSS.0000084593.56786.DA.
- 608 Schaeffer, M.R., Mendonca, C.T., Levangie, M.C., Andersen, R.E., Taivassalo, T., and Jensen, D.
609 2014. Physiological mechanisms of sex differences in exertional dyspnoea: role of neural
610 respiratory motor drive. *Experimental physiology* **99**(2): 427-441. doi:
611 10.1113/expphysiol.2013.074880.

- Schneider, S., Brummer, V., Abel, T., Askew, C.D., and Struder, H.K. 2009. Changes in brain cortical activity measured by EEG are related to individual exercise preferences. *Physiol Behav* **98**(4): 447-452. doi: 10.1016/j.physbeh.2009.07.010.
- Sharma, P., Morris, N.R., and Adams, L. 2015. The effect of different exercise modalities on dyspnea and leg fatigue in healthy subjects. *Respiratory physiology & neurobiology* **210**: 44-50. doi: 10.1016/j.resp.2015.02.001.
- Stubbing, D.G., Pengelly, L.D., Morse, J.L., and Jones, N.L. 1980. Pulmonary mechanics during exercise in normal males. *J Appl Physiol* **49**(3): 506-510.
- Tanner, D.A., Duke, J.W., and Stager, J.M. 2014. Ventilatory patterns differ between maximal running and cycling. *Respiratory physiology & neurobiology* **191**: 9-16. doi: 10.1016/j.resp.2013.10.011.
- Verstappen, F.T., Huppertz, R.M., and Snoeckx, L.H. 1982. Effect of training specificity on maximal treadmill and bicycle ergometer exercise. *International journal of sports medicine* **3**(1): 43-46. doi: 10.1055/s-2008-1026061.
- Vestbo, J., Hurd, S.S., Agusti, A.G., Jones, P.W., Vogelmeier, C., Anzueto, A., Barnes, P.J., Fabbri, L.M., Martinez, F.J., Nishimura, M., Stockley, R.A., Sin, D.D., and Rodriguez-Roisin, R. 2013. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *American journal of respiratory and critical care medicine* **187**(4): 347-365. doi: 10.1164/rccm.201204-0596PP.

Table 1. Effect of modality on physiological and perceptual responses at rest and during symptom-limited incremental exercise testing in 15 healthy, young men.

Parameter	Rest		Ventilatory Threshold		Iso-work		Peak	
	Cycle	Treadmill	Cycle	Treadmill	Cycle	Treadmill	Cycle	Treadmill
<i>Cardiometaabolic and gas exchange parameters</i>								
$\dot{V}O_2$ (L min ⁻¹)	0.40 ± 0.03	0.46 ± 0.03	1.68 ± 0.06	2.06 ± 0.08*	3.87 ± 0.15	4.53 ± 0.18*	4.24 ± 0.14	4.74 ± 0.16*
$\dot{V}O_2$ (mL.kg ⁻¹ .min ⁻¹)	5.1 ± 0.3	5.9 ± 0.3	22.0 ± 1.0	26.9 ± 1.0*	50.1 ± 1.4	58.8 ± 1.8*	55.0 ± 1.3	61.5 ± 1.5*
$\dot{V}CO_2$ (mL.kg ⁻¹ .min ⁻¹)	4.3 ± 0.3	4.5 ± 0.3	18.5 ± 1.1	21.2 ± 1.1*	52.1 ± 1.8	60.1 ± 1.9*	60.4 ± 1.9	64.9 ± 1.8*
RER	0.84 ± 0.03	0.76 ± 0.02*	0.83 ± 0.02	0.78 ± 0.01*	1.04 ± 0.01	1.02 ± 0.02	1.10 ± 0.02	1.06 ± 0.02*
Heart rate (beats.min ⁻¹)	80.9 ± 2.9	87.8 ± 4.4*	116.1 ± 2.8	122.9 ± 3.8*	178.9 ± 2.7	190.1 ± 2.1*	188.1 ± 2.3	193.8 ± 2.5*
O ₂ pulse (ml O ₂ .beat ⁻¹)	5.0 ± 0.3	5.4 ± 0.5	14.6 ± 0.6	16.9 ± 0.7*	21.7 ± 0.8	23.9 ± 1.1*	22.6 ± 0.7	24.5 ± 1.0*
$\dot{V}_E/\dot{V}O_2$	32.8 ± 1.3	29.5 ± 1.3*	21.0 ± 0.5	20.0 ± 0.4	27.4 ± 1.0	27.5 ± 0.4	33.5 ± 1.1	29.9 ± 0.6*
$\dot{V}_E/\dot{V}CO_2$	39.3 ± 1.3	38.9 ± 1.4	25.2 ± 0.5	25.6 ± 0.5	26.3 ± 0.8	27.0 ± 0.4	30.6 ± 0.9	28.4 ± 0.4
P _{ET} O ₂ (mmHg)	107.0 ± 1.8	103.8 ± 1.4*	98.6 ± 1.1	95.1 ± 1.1	107.3 ± 1.2	107.7 ± 0.6	114.0 ± 0.9	110.4 ± 0.7*
P _{ET} CO ₂ (mmHg)	34.8 ± 1.0	34.6 ± 0.8	43.1 ± 0.7	42.4 ± 0.8	40.8 ± 1.1	39.8 ± 0.7*	35.5 ± 0.9	37.9 ± 0.4*
<i>Ventilation, breathing pattern and operating lung volume parameters</i>								
$\dot{V}_E$ (L.min ⁻¹)	12.9 ± 0.9	13.4 ± 0.9	35.2 ± 1.5	41.2 ± 1.9*	107.0 ± 6.9	124.4 ± 4.8*	142.1 ± 6.2	141.0 ± 3.9
V _T (L)	0.99 ± 0.07	0.86 ± 0.06	1.82 ± 0.11	1.82 ± 0.12	3.04 ± 0.14	2.95 ± 0.10	3.08 ± 0.08	2.96 ± 0.10
f _R (breaths.min ⁻¹)	14.0 ± 0.8	17.2 ± 1.3*	20.7 ± 1.3	24.3 ± 1.4*	35.7 ± 1.9	42.7 ± 1.3*	46.4 ± 1.6	48.1 ± 1.3
IC (L)	3.63 ± 0.13	3.71 ± 0.14	3.94 ± 0.14	3.99 ± 0.13	4.01 ± 0.17	3.96 ± 0.13	3.87 ± 0.14	3.70 ± 0.15
IRV (L)	2.64 ± 0.11	2.84 ± 0.14	2.12 ± 0.16	2.17 ± 0.17	0.97 ± 0.13	1.01 ± 0.11	0.78 ± 0.13	0.74 ± 0.09
<i>Gastro-esophageal electrode-balloon catheter-derived parameters</i>								
EMGdi,rms%max	11.2 ± 2.2	10.5 ± 1.3	20.5 ± 2.6	25.0 ± 2.6	58.0 ± 4.1	63.2 ± 4.6	67.0 ± 4.9	77.2 ± 3.6
Pes,tidal (cmH ₂ O)	5.2 ± 0.5	5.2 ± 0.5	11.2 ± 0.9	12.6 ± 1.0	28.6 ± 2.0	32.8 ± 1.3*	40.0 ± 2.9	37.6 ± 1.5
Peak inspiratory Pes (cmH ₂ O)	-11.4 ± 1.0	-10.1 ± 0.9	-14.7 ± 1.2	-13.1 ± 1.4	-25.7 ± 1.8	-23.9 ± 1.3	-29.8 ± 1.8	-24.7 ± 1.3*
Peak expiratory Pes (cmH ₂ O)	-6.2 ± 0.6	-4.9 ± 0.6	-3.4 ± 0.7	-0.5 ± 1.1*	3.0 ± 1.0	8.9 ± 0.9	10.2 ± 1.8	13.0 ± 1.2
Pdi,tidal (cmH ₂ O)	10.0 ± 1.0	6.6 ± 0.7*	10.2 ± 2.0	13.0 ± 1.0	22.4 ± 1.3	27.2 ± 1.1*	26.9 ± 1.5	29.4 ± 1.6
Peak inspiratory Pdi (cmH ₂ O)	23.1 ± 1.2	20.8 ± 2.4	26.6 ± 1.8	24.8 ± 2.6	34.4 ± 1.7	35.1 ± 2.3	38.5 ± 1.9	35.2 ± 2.5
Peak expiratory Pdi (cmH ₂ O)	13.1 ± 0.8	14.2 ± 2.4	13.1 ± 1.0	11.8 ± 2.3	12.0 ± 0.9	7.9 ± 1.9	11.6 ± 0.9	5.8 ± 1.7*
Peak expiratory Pga (cmH ₂ O)	12.1 ± 0.8	11.5 ± 2.3	13.7 ± 1.0	14.8 ± 1.8	16.9 ± 1.1	22.5 ± 1.9*	23.1 ± 1.7	23.6 ± 1.9
<i>Symptom parameters</i>								
Dyspnea intensity (Borg 0-10 scale units)	0.1 ± 0.1	0.0 ± 0.0	0.7 ± 0.2	0.5 ± 0.2	5.6 ± 0.7	5.5 ± 0.5	7.8 ± 0.6	7.7 ± 0.5
Dyspnea unpleasantness (Borg 0-10 scale units)	0.1 ± 0.1	0.0 ± 0.0	0.4 ± 0.1	0.1 ± 0.1*	4.4 ± 0.8	4.5 ± 0.6	6.2 ± 0.8	6.7 ± 0.6
Leg Discomfort (Borg 0-10 scale units)	0.0 ± 0.0	0.0 ± 0.0	0.8 ± 0.2	0.4 ± 0.1*	6.3 ± 0.7	5.5 ± 0.7*	8.6 ± 0.6	7.4 ± 0.7*

Note: Values are means ± SEM. $\dot{V}O_2$ and $\dot{V}CO_2$, rate of O₂ consumption and CO₂ production, respectively; RER, respiratory exchange ratio; $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$, ventilatory equivalents for O₂ and CO₂, respectively; P_{ET}O₂ and P_{ET}CO₂, end-tidal partial pressure of O₂ and CO₂, respectively; $\dot{V}_E$, minute ventilation; V_T, tidal volume; f_R, breathing frequency; IC, inspiratory capacity; IRV, inspiratory reserve volume; EMGdi,rms%max, root mean square of the crural diaphragm electromyogram (EMGdi,rms) expressed as a percentage of maximal voluntary EMGdi,rms; Pes,tidal and Pdi,tidal, tidal esophageal and transdiaphragmatic pressure swings, respectively; Pga, gastric pressure. *p≤0.05 vs. cycle at measurement time.

Figure Legends

Figure 1. Metabolic, cardiovascular and gas exchange responses during symptom-limited treadmill and cycle exercise test protocols matched for increments in work rate. Values are means $\pm$ SEM. $\dot{V}O_2$ and $\dot{V}CO_2$, rate of O_2 consumption and CO_2 production, respectively; RER, respiratory exchange ratio; $\dot{V}_E/\dot{V}O_2$ and $\dot{V}_E/\dot{V}CO_2$, ventilatory equivalents for O_2 and CO_2 , respectively; $P_{ET}O_2$ and $P_{ET}CO_2$, end-tidal partial pressure of O_2 and CO_2 , respectively. * $p \leq 0.05$ vs. cycle at measurement time.

Figure 2. Ventilation, breathing pattern and operating lung volume responses during symptom-limited treadmill and cycle exercise test protocols matched for increments in work rate. Values are means $\pm$ SEM. f_R , breathing frequency. * $p \leq 0.05$ vs. cycle at measurement time.

Figure 3. Gastro-esophageal electrode-balloon catheter-derived responses during symptom-limited treadmill and cycle exercise test protocols matched for increments in work rate. Values are means $\pm$ SEM. EMGdi,rms%max, root mean square of the crural diaphragm electromyogram (EMGdi,rms) expressed as a percentage of maximal voluntary EMGdi,rms; $P_{es,tidal}$ and $P_{di,tidal}$, tidal esophageal and transdiaphragmatic pressure swings, respectively; P_{ga} , gastric pressure. * $p \leq 0.05$ vs. cycle at measurement time.

Figure 4. Perceptual responses during symptom-limited treadmill and cycle exercise test protocols matched for increments in work rate. Values are means $\pm$ SEM. $\dot{V}O_2$, rate of O_2 consumption; EMGdi,rms%max, root mean square of the crural diaphragm electromyogram (EMGdi,rms) expressed as a percentage of maximal voluntary EMGdi,rms; TLC, total lung capacity. * $p \leq 0.05$ vs. cycle at measurement time.