Mechanical-ventilatory responses to peak and ventilation-matched upper- versus lower-body exercise in normal subjects

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Running Title: Mechanical-ventilatory responses to upper-body exercise

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NEW FINDINGS

What is the central question of this study? To what extent are the mechanical-ventilatory responses to upper-body exercise influenced by task-specific locomotor mechanics?

What is the main finding and its importance? When compared to lower-body exercise performed at similar ventilations, upper-body exercise was characterised by tidal volume constraint, dynamic lung hyperinflation and an increased propensity towards neuromechanical uncoupling of the respiratory system. Importantly, these responses were independent of respiratory dysfunction and flow limitation. Thus, the mechanical-ventilatory responses to upper-body exercise are attributable, in part, to task-specific locomotor mechanics (i.e., non-respiratory loading of the thorax).

ABSTRACT

Aim: To determine the extent to which the mechanical-ventilatory responses to upper-body exercise are influenced by task-specific locomotor mechanics. Methods: Eight healthy men (mean ± SD, age = 24 ± 5 y; mass = 74 ± 11 kg; stature = 1.79 ± 0.07 m) completed two maximal exercise tests, on separate days, comprising 4-min stepwise increments of 15 W during upper-body exercise (arm-cranking) or 30 W during lower-body exercise (leg-cycling). The tests were repeated at work rates calculated to elicit 20, 40, 60, 80, and 100% of peak ventilation achieved during arm-cranking (VE,UBE). Exercise measures included pulmonary ventilation and gas exchange, oesophageal pressure-derived indices of respiratory mechanics, operating lung volumes, and expiratory flow limitation.

Results: Subjects exhibited normal resting pulmonary function. Arm-crank exercise elicited significantly lower peak values for work rate, \( \dot{V}O_2 \), \( \dot{V}CO_2 \), \( V_\text{E} \), and \( V_T \) (p<0.05). At matched ventilations, arm-crank exercise restricted tidal volume expansion relative to leg-cycle exercise at 60% \( V_\text{E,UBE} \) (1.74±0.61 vs. 2.27±0.68 L, p<0.001), 80% \( V_\text{E,UBE} \) (2.07±0.70 vs. 2.52±0.67 L, p<0.001) and 100% \( V_\text{E,UBE} \) (1.97±0.85 vs. 2.55±0.72 L, p=0.002). Despite minimal evidence of expiratory flow limitation, ERV was significantly higher during arm-crank versus leg-cycle exercise at 100% \( V_\text{E,UBE} \) (39±8 vs. 29±8% VC, p=0.002). At any given ventilation, arm-cranking elicited greater inspiratory effort (oesophageal pressure) relative to thoracic displacement (tidal volume). Conclusions: Arm-crank exercise is sufficient to provoke respiratory-mechanical derangements (restricted tidal volume expansion, dynamic hyperinflation, neuromechanical uncoupling) in subjects with normal pulmonary...
function and expiratory flow reserve. These responses are likely attributable to task-specific locomotor mechanics (i.e., non-respiratory loading of the thorax).

INTRODUCTION
During dynamic whole-body exercise (e.g., cycling, running), the increase in pulmonary ventilation is partly achieved by the progressive recruitment of expiratory muscles to reduce end-expiratory lung volume (EELV) below functional residual capacity (Abraham et al., 2002; Lind & Hesser, 1984). This reduction in EELV provides several mechanical advantages. First, it improves the length/tension relationship of the diaphragm in order that more pressure can be generated for a given neural drive (Smith & Bellemare, 1987). Second, it assists inspiration by facilitating passive recoil of the chest and abdominal wall (Aliverti et al., 1997). Third, a decrease in EELV permits a substantial increase in tidal volume without encroaching on the nonlinear upper-portion of the pressure-volume relationship (Henke, Sharratt, Pegelow, & Dempsey, 1988). At ventilations approaching maximum, EELV may increase towards or above resting values; a phenomenon termed dynamic lung hyperinflation. This compensatory mechanism may alleviate limitations to expiratory flow by decreasing airway resistance (Cormier, Laviolette, Atton, & Series, 1991). Nevertheless, dynamic hyperinflation has several consequences, including: functional inspiratory muscle weakness; increased elastic and threshold loading on the inspiratory muscles, with concomitant increases in the work and O$_2$ cost of breathing; mechanical restriction of tidal volume expansion; and adverse effects on cardiocirculatory function (Sheel & Romer, 2012). Moreover, there is a growing body of evidence that the resulting increase in neural respiratory drive contributes to dyspnoea and exercise intolerance (Sheel, Foster, & Romer, 2011).

Exercise primarily comprising the upper-body forces the thoracic musculature to assume multiple non-respiratory functions, including stiffening the spine (Hodges, Eriksson, Shirley, & Gandevia, 2005), maintaining torso stabilisation (Celli, Criner, & Rassulo, 1988) and positioning the arms (Hodges & Gandevia, 2000). Consequently, the respiratory muscle contribution to breathing may be compromised, resulting in a relative inability to reduce EELV below relaxation volume. Because the muscles involved in moving the arms and stabilising the trunk attach to the ribcage, upper-body exercise would also be expected to increase chest-wall impedance, constrain tidal volume,
and necessitate an increase in respiratory frequency to achieve a given level of ventilation (Takano, 1993). Maximal upper-body exercise has been shown to elicit dynamic hyperinflation in the absence of expiratory flow limitation in athletes with high-lesion (cervical) spinal cord injury (Taylor, West, & Romer, 2010; West, Goosey-Tolfrey, Campbell, & Romer, 2014). Notwithstanding, individuals with high-lesion spinal cord injury present with derangements in respiratory mechanics and profound weakness of the expiratory muscles (Taylor et al., 2010; West et al., 2014). As such, it is unclear whether the hyperinflation noted during upper-body exercise was due to the physiological consequences of spinal cord injury, the locomotor mechanics of upper-body exercise, or both. More recently, we have observed dynamic hyperinflation in healthy, able-bodied subjects performing severe-intensity upper-body (arm-crank) exercise, but no such hyperinflation during heavy exercise (Tiller, Campbell, & Romer, 2017). Because ventilation was greater during severe exercise, it was not possible to discern to what extent the hyperinflation during upper-body exercise was due to expiratory flow limitation or task-specific locomotor mechanics (i.e., non-respiratory loading of the thorax).

To explore this further it would be necessary to compare the mechanical-ventilatory responses to upper- and lower-body exercise at the same ventilation, yet only two studies have attempted this assessment in normal subjects (i.e., those free from physical impairment or cardiorespiratory disease). Alison et al. (Alison et al., 1998) reported a relative inability for their normal subjects to reduce EELV below resting values during arm-crank relative to leg-cycle exercise, at peak work rates and at fixed percentages of peak ventilation. By contrast, Cerny and Ucer (Cerny & Ucer, 2004) reported greater decreases in EELV below resting values during arm-crank relative to leg-cycle exercise at matched levels of ventilation. Both studies assessed dynamic hyperinflation using the flow-volume technique (Johnson, Weisman, Zeballos, & Beck, 1999), which is contingent on the accurate measurement of inspiratory capacity (IC) to track operational changes in EELV (Guenette, Chin, Cory, Webb, & O'Donnell, 2013). Neither study, however, assessed peak inspiratory (oesophageal) pressure during the IC manoeuvre to ensure submaximal inspiration did not artificially inflate EELV and thereby overestimate the extent of dynamic hyperinflation. A further concern is that neither study quantified the magnitude of expiratory flow limitation at equivalent ventilations. Thus, the mechanisms that underpin hyperinflation during upper-body exercise require clarification. Such data
could have implications for patients who hyperinflate during exercise (e.g., those with obstructive lung disease) as well as for individuals who participate in activities involving the upper-limbs (e.g., kayaking, rowing, wheelchair racing).

The aim of this study, therefore, was to characterise the mechanical-ventilatory responses to peak and ventilation-matched upper- versus lower-body exercise in normal subjects. Specifically, we sought to: i) compare operating lung volumes between arm-crank and leg-cycle exercise; and ii) compare the prevalence and magnitude of expiratory flow limitation between the exercise modes. It was hypothesised that, compared to leg-cycling, arm-crank exercise would elicit dynamic hyperinflation in the absence of flow limitation.

METHODOLOGY

Ethical Approval

The study was approved by Brunel University London Research Ethics Committee (RE34-10) and conformed to the standards set by the Declaration of Helsinki, except for registration in a database. Before data collection, subjects were issued with an information document, completed a pre-test medical questionnaire and provided written, informed consent.

Subjects

Eight healthy, non-smoking, recreationally active men volunteered to participate. Subjects abstained from intense exercise for 48 h, alcohol and caffeine for 12 h, and food for 3 h prior to testing.

Experimental Overview

The study followed a randomised, counterbalanced design. All subjects completed four maximal incremental exercise tests, each separated by at least 48 h. The tests were performed at the same time of day under stable laboratory conditions. The purpose of Test 1 and Test 2 was to compare mechanical-ventilatory responses between peak upper-body (arm-crank) exercise and peak lower-body (leg-cycle) exercise following increments of absolute work rate, and to establish exercise intensities for the subsequent tests. The purpose of Test 3 and Test 4 was to compare mechanical-ventilatory responses between upper- and lower-body exercise modes across ventilation-matched work rates.
Pulmonary Function Tests

Forced vital capacity (FVC) and forced expiratory volume in one second (FEV$_1$) were determined using spirometry performed at rest in the seated position (Miller et al., 2005). The test comprised a series of forced expiratory manoeuvres performed into a low-resistance, bidirectional turbine connected to an online system (Oxycon Pro; Jaeger GmbH, Hoechberg, Germany). Maximum static inspiratory pressure ($P_{\text{Imax}}$) from residual volume (RV) and maximum static expiratory pressure ($P_{\text{Emax}}$) from total lung capacity (TLC) were measured through the side port of a semi-occluded mouthpiece using a linear differential transducer (DP45; Validyne, Northridge, CA; range $\pm$ 229 cmH$_2$O) (Evans & Whitelaw, 2009). All values were expressed in absolute units and as percentages of predicted normal (Evans & Whitelaw, 2009; Quanjer et al., 2012).

Incremental Exercise Tests

Upper-body exercise was performed in the upright position using an electromagnetically-braked arm-crank ergometer (Angio; Lode, Groningen, The Netherlands). The ergometer was mounted to a wall and positioned so that the scapula-humeral joint and the distal end of the crank were aligned horizontally. Subjects sat in a straight-backed chair and kept their feet flat to the floor to minimise bracing. Lower-body exercise was performed in the upright position using a cycle ergometer (Excalibur; Lode). Subjects remained seated throughout all tests. After 5 min of rest, Test 1 and Test 2 commenced with 4 min of unloaded exercise (0 W) followed by stepwise increments of 15 W (upper-body exercise) or 30 W (lower-body exercise) every 4 min. Work rates during Test 3 and Test 4 were established for each subject using inter-stage linear interpolation and were equivalent to those attained at 20, 40, 60, 80 and 100% of the peak ventilation achieved during the initial upper-body exercise test ($\dot{V}_{\text{E,UBE}}$) (Fig. 1). Both ergometers were set in the hyperbolic mode. Higher cadences have been shown to elicit significantly greater oxygen uptake, heart rate and minute ventilation during arm-cranking (Tiller, Price, Campbell, & Romer, 2017) and leg-cycling (Ettema & Loras, 2009). As such, cadence was standardised at 75 – 80 rev·min$^{-1}$ to approximate the spontaneously-chosen crank rates for both exercise modes (Brisswalter, Hausswirth, Smith, Vercruyssen, & Vallier, 2000;
Exercise was terminated when cadence fell below 65 rev·min\(^{-1}\) for >3 s, despite verbal encouragement.

**Measurements**

**Cardiorespiratory.** Pulmonary gas exchange and ventilatory indices were assessed using an online breath-by-breath system (Oxycon Pro; Jaeger GmbH, Hoechberg, Germany), cardiac frequency \((f_c)\) using a telemetric device (Vantage NV; Polar Electro Oy, Kempele, Finland), and arterial oxygen saturation \((\text{SpO}_2)\) using a forehead pulse-oximeter (OxiMax N-560; Nellcor, Tyco Healthcare, Pleasanton, CA). Data were averaged over the penultimate 30 s of each exercise stage, with the final 30 s reserved for the assessment of operating lung volumes and expiratory flow limitation (see below).

Immediately following a given test, subjects were asked their reason(s) for stopping exercise.

**Operating Lung Volumes and Expiratory Flow Limitation.** To determine the pattern of change in operating lung volumes, subjects performed duplicate inspiratory capacity (IC) manoeuvres from relaxation volume, at rest and during the final 30 s of each exercise stage (Guenette et al., 2013). The IC manoeuvre exhibiting the most negative oesophageal pressure (peak \(P_{\text{oe}}\)) was used to position the averaged tidal flow-volume loop within the maximum envelope (see below). Verbal encouragement was given to ensure a maximal inspiratory effort. The manoeuvre was considered acceptable when there was no evidence of a prior anticipatory reduction in ERV and the peak \(P_{\text{oe}}\) matched that achieved at rest. Expiratory reserve volume (ERV), a surrogate for EELV, was calculated by subtracting IC from VC. Inspiratory reserve volume (IRV) was calculated as the sum of tidal volume \((V_T)\) and ERV. Both ERV and IRV were expressed in absolute terms (litres) and as a percent of VC. To account for thoracic gas compression and exercise-induced bronchodilation, a composite maximum expiratory flow-volume curve was created for each subject from the highest instantaneous flow achieved at any given volume during several maximal and submaximal expiratory manoeuvres (100, 20, 40, 60, and 80% maximal effort) at resting baseline and within 2 min of exercise cessation (Guenette et al., 2010). Expiratory flow limitation was quantified as the percentage of the tidal flow-volume loop that met or exceeded the expiratory boundary of the maximum flow-volume curve (Johnson et al., 1999).
Oesophageal Pressure and Abdominal Muscle EMG. Oesophageal pressure (Poe) was measured using a balloon-tipped catheter (5 Fr Catheter; Ackrad Labs, Cooper Surgical, Berlin, Germany) connected to a calibrated differential pressure transducer (DP45; Validyne Engineering, CA, USA, range ±229 cmH₂O) and amplifier (CD280; Validyne Engineering). The catheter was passed pernasally into the stomach, filled with 1 ml of air, and withdrawn until there was a negative pressure deflection on inspiration. The balloon was then withdrawn another 10 cm until the distal end was situated in the lower one-third of the oesophagus (Benditt, 2005), with the position validated using the occlusion technique (Baydur, Behrakis, Zin, Jaeger, & Milic-Emili, 1982). The tidal inspiratory Poe swing (ΔPoe) was expressed in absolute terms and as a percentage of the maximum oesophageal pressure exhibited during a maximal static inspiratory manoeuvre (Poe_max). The ratio of inspiratory effort (ΔPoe/Poe_max) to thoracic displacement (V_T/VC) was calculated as an index of neuromechanical uncoupling, (O'Donnell, Bertley, Chau, & Webb, 1997). In a subset of three subjects, electrical activity of the rectus abdominis (EMGra) was assessed using a pair of 28 mm bipolar differential skin-surface electrodes (Arbo Infant; Tyco Healthcare, Germany) attached to the main belly of the muscle in accordance with published procedures (Ng, Kippers, & Richardson, 1998). Electrode positions were marked on the skin for consistency of placement between trials. Electromyographic signal (root-mean square, RMS) was recorded during full tidal breaths performed over the penultimate 30 s of each stage and was normalised against the largest RMS achieved during a maximal static expulsive manoeuvre (%RMS_max).

Signal Acquisition
The digital signal for respiratory airflow was converted to a real-time analogue signal using an external device (μDAQ-30A16; Eagle Technology, Cape Town, South Africa). The EMGra signal was amplified (1902; Cambridge Electronic Design, Cambridge, UK), high-pass filtered at 20 Hz, and notch-filtered at 50 Hz. All signals were acquired using a 16-bit analogue-to-digital converter (micro 1401 mkII; Cambridge Electronic Design), sampled at 150 Hz (flow and pressure) or 4 kHz (EMGra), and displayed on a computer running dedicated software (Spike2 v7; Cambridge Electronic Design).
**Statistics**

Descriptive and inferential statistics were calculated using dedicated software (SPSS v24; IBM Corp., Armonk, NY). Cardiorespiratory responses ($\dot{V}O_2$, $\dot{V}CO_2$, RER, $\dot{V}_{E}$, $f_R$, $V_T$, $f_C$, SpO$_2$) and respiratory mechanics (ERV, IRV, $\Delta$Poe) at peak upper- versus lower-body exercise (Test 1 and Test 2) were compared using paired-samples $t$-test. The same indices at rest and during ventilation-matched upper-versus lower-body exercise (Test 3 and Test 4) were compared using two-factor (mode $\times$ ventilation) repeated-measures ANOVA. In the case of significant interactions, follow-up pairwise comparisons were performed using a Bonferroni-adjusted alpha level of 0.008. Effect size (Cohen's $d$) was used to quantify the magnitude of the difference between group means ($0.2 = $ small; $0.5 = $ medium; $0.8 = $ large) (Cohen, 1977). Data are presented as mean ± SD, unless stated, and critical alpha level was set at 0.05.

**RESULTS**

**Subject Characteristics**

Subject characteristics are shown in Table 1. With the exception of $P_{\text{Imax}}$, which tended to be higher than predicted, pulmonary function was within the normal range of predicted values.

**Responses at Peak Exercise (Test 1 vs. Test 2)**

Physiological responses at peak exercise are shown in Table 2. Compared to lower-body exercise, upper-body exercise elicited significantly lower ($p < 0.05$) work rate, $\dot{V}O_2$ (absolute and relative), $\dot{V}CO_2$, $\dot{V}_{E}$, and $V_T$, and significantly higher IRV. There were no between-mode differences ($p > 0.05$) in any of the other variables shown in Table 2. In addition, there was no between-mode difference in peak Poe during the IC manoeuvre ($-70 \pm 20$ vs. $-69 \pm 27$ cmH$_2$O; $p = 0.89, d = 0.05$), and peak Poe during the IC manoeuvre was not different to that recorded at rest for either upper-body exercise ($-69 \pm 27$ vs. $-64 \pm 22$ cmH$_2$O; $p = 0.64, d = 0.20$) or lower-body exercise ($-70 \pm 20$ vs. $-68 \pm 22$ cmH$_2$O; $p = 0.55, d = 0.09$). Despite lower peak $\dot{V}_{E}$ during upper-body exercise, EMGra RMS was more than three-fold greater.
Responses at Ventilation-matched Work Rates (Test 3 vs. Test 4)

Physiological responses were compared at fixed percentages of the peak ventilation attained during the initial upper-body exercise test. The ventilations were slightly lower during upper-body exercise at work rates above ≥60% $\dot{V}_{\text{E,UBE}}$ (Fig. 2); however, there was no significant main-effect for mode, $F(1, 7) = 4.59, p = 0.069$, and no significant mode × ventilation interaction, $F(1.73, 12.12) = 1.73, p = 0.220$.

Cardiorespiratory. Cardiorespiratory responses to upper- versus lower-body exercise at ventilation-matched work rates are summarised in Table 3. Statistically significant effects are reported below.

$O_2$ Uptake. There were main-effects for mode, showing lower absolute (and relative) values during upper-body exercise, $F(1, 7) = 39.11, p < 0.001$, and a mode × ventilation interaction, $F(3, 35) = 10.73, p < 0.001$. Pairwise comparisons revealed that $O_2$ uptake was lower during upper-body exercise at 40% ($p = 0.004, d = 1.05$), 60% ($p < 0.001, d = 1.75$), 80% ($p < 0.001, d = 1.36$) and 100% $\dot{V}_{\text{E,UBE}}$ ($p = 0.001, d = 1.17$).

Tidal Volume. There was a main-effect for mode, showing lower values during upper-body exercise, $F(1, 7) = 131.06, p < 0.001$, and a mode × ventilation interaction, $F(5, 35) = 4.83, p = 0.002$. Pairwise comparisons revealed that tidal volume was lower during upper-body exercise at rest ($p < 0.001, d = 0.94$), 60% ($p < 0.001, d = 0.82$), 80% ($p < 0.001, d = 0.66$) and 100% $\dot{V}_{\text{E,UBE}}$ ($p = 0.002, d = 0.74$).

Respiratory Frequency. There was no main-effect for mode, $F(1, 7) = 65.01, p = 0.203$, but there was a mode × ventilation interaction, $F(5, 35) = 29.44, p = 0.028$. Pairwise comparisons revealed no differences at any level of ventilation.

Ventilatory Equivalent for CO$_2$. There was a main-effect for mode, showing higher values during upper-body exercise, $F(1, 7) = 11.33, p = 0.012$, but no mode × ventilation interaction, $F(1.52, 10.66) = 1.37, p = 0.283$.

Mean Inspiratory Flow ($V_i/T_i$). There was a main-effect for mode, showing lower values during upper-body exercise, $F(1, 7) = 29.86, p = 0.001$, and a mode × ventilation interaction, $F(5, 35) = 6.38, p < 0.001$. Pairwise comparisons revealed lower values during upper-body exercise at 60% ($p < 0.001, d = 0.88$) and 100% $\dot{V}_{\text{E,UBE}}$ ($p = 0.006, d = 0.78$).
Operating Lung Volumes and Expiratory Flow Limitation. Operating lung volumes during upper- and lower-body exercise at ventilation-matched work rates are illustrated in Fig. 3. During lower-body exercise, ERV decreased below rest at 20% \( \dot{V}_{E,UBE} \) and remained below rest through to end-exercise (rest: 36 ± 10 %VC; 20% \( \dot{V}_{E,UBE} \): 31 ± 9 %VC; 100% \( \dot{V}_{E,UBE} \): 29 ± 8 %VC), with only 2/8 subjects elevating ERV above rest. By contrast, upper-body exercise elicited an initial decrease in ERV followed by an increase back towards rest at increasing percentages of \( \dot{V}_{E,UBE} \), and finally increasing above rest at peak exercise (rest: 33 ± 12 %VC; 20% \( \dot{V}_{E,UBE} \): 27 ± 11 %VC; 100% \( \dot{V}_{E,UBE} \): 39 ± 9 %VC), with 6/8 subjects elevating ERV above rest. With respect to ERV (%VC), there was no main-effect for mode, \( F(1, 7) = 1.33, p = 0.287 \), but there was a mode \( \times \) ventilation interaction, \( F(5, 35) = 2.61, p = 0.041 \). Pairwise comparisons revealed that ERV was higher during upper-body exercise at 100% \( \dot{V}_{E,UBE} \) (39 ± 9 vs. 29 ± 8% VC; \( p = 0.002 \), \( d = 1.17 \)).

With respect to IRV (%VC), the main-effect came close to statistical significance, showing higher values during upper-body exercise, \( F(1, 7) = 5.58, p = 0.050 \), but there was no mode \( \times \) ventilation interaction, \( F(5, 35) = 0.73, p = 0.603 \). Comparing peak Poe during the IC manoeuvres, there was a main-effect for mode, showing less negative values during upper-body exercise, \( F(1, 7) = 20.75, p = 0.003 \), \((-73 \pm 19 \text{ vs. } -65 \pm 17 \text{ cmH}_2\text{O})\), but no mode \( \times \) ventilation interaction, \( F(5, 35) = 0.61, p = 0.691 \). There was also no difference in peak Poe during the IC manoeuvres during exercise compared to rest for either mode (\( p > 0.05 \)), suggesting consistently maximal efforts. During lower-body exercise, 2/8 subjects exhibited expiratory flow limitation and, in these subjects, the magnitude of the tidal flow-volume loop that encroached on the expiratory portion of the maximum flow-volume loop was 51 and 80%, respectively. The same two subjects exhibited expiratory flow limitation during upper-body exercise, albeit to a lesser extent (15 and 56%). When the two subjects were removed from the group mean analysis (\( n = 6 \)), the difference in ERV between upper- vs. lower-body exercise at 100% \( \dot{V}_{E,UBE} \) was of a similar magnitude (~10%) and remained statistically significant (41 ± 7 vs. 32 ± 8% VC for upper- vs. lower-body exercise, respectively; \( p = 0.008 \)), suggesting that the increase in ERV during upper-body exercise at peak intensity was independent of expiratory flow limitation.

Oesophageal Pressure and Abdominal Muscle EMG. Tidal inspiratory oesophageal pressure, expressed as a percentage of maximum static inspiratory oesophageal pressure
(ΔPoe/Peo\textsubscript{max}), is illustrated in Fig. 4. At ventilation-matched work rates, ΔPoe tended to be higher during upper-body exercise. Indeed, there was a main-effect for mode, $F(1, 7) = 8.718$, $p = 0.021$, showing higher values during upper-body exercise, but no mode × ventilation interaction, $F(5, 35) = 1.214$, $p = 0.323$. With respect to the ratio of tidal volume to vital capacity ($V_t/VC$), there was no main-effect for mode, $F(1, 7) = 1.537$, $p = 0.255$, and no mode × ventilation interaction, $F(5, 35) = 1.675$, $p = 0.167$. When pressure responses were expressed relative to changes in tidal volume [(ΔPoe/Peo\textsubscript{max}) / (V_t/VC)] - an index of neuromechanical (un)coupling - there was a main-effect for mode, suggestive of greater uncoupling during upper-body exercise, $F(1, 7) = 13.696$, $p = 0.008$, but no mode × ventilation interaction, $F(1.572, 11.006) = 1.216$, $p = 0.321$. As shown in Fig. 5, EMGra was greater during upper- versus lower-body exercise at all ventilation-matched work rates (20% $\dot{V}_{\text{E,UBE}}$: 28 vs. 18% RMSmax, 40% $\dot{V}_{\text{E,UBE}}$: 36 vs. 14%, 60% $\dot{V}_{\text{E,UBE}}$: 47 vs. 15%, 80% $\dot{V}_{\text{E,UBE}}$: 57 vs. 15%, 100% $\dot{V}_{\text{E,UBE}}$: 73 vs. 15%).

**DISCUSSION**

The principal aim of this study was to characterise the mechanical-ventilatory responses to peak and ventilation-matched upper-body (arm-crank) versus lower-body (leg cycle) exercise in normal subjects. Upper-body exercise was associated with a relative inability to reduce ERV at peak work rates with an overt dynamic hyperinflation at 100% $\dot{V}_{\text{E,UBE}}$, as per our hypothesis. Moreover, upper-body exercise evoked an increased inspiratory effort (oesophageal pressure) relative to thoracic displacement (tidal volume) when compared to ventilation-matched lower-body exercise. That the responses occurred in healthy subjects with normal pulmonary function and minimal evidence of flow limitation suggests that these characteristic responses to upper-body exercise are attributable, in part, to task-specific locomotor mechanics.

**Mechanical-ventilatory Responses**

Ventilation during exercise is typically achieved via a progressive reduction in ERV to expand tidal volume (see *Introduction*). In accordance with previous studies in upper-body exercise (Takano, 1993), we found that upper-body exercise performed at peak and ventilation-matched work rates resulted in restricted expansion of tidal volume, thereby necessitating an increase in respiratory
frequency to meet ventilatory demands. At peak exercise, tidal volume was constrained by a decrease in IRV, whereas at peak ventilation-matched exercise, ERV was significantly elevated during upper-compared to lower-body exercise (39 vs. 29% VC, Fig. 3) with a large observed effect ($d = 1.21$). This observation of upper-body exercise-mediated dynamic hyperinflation is congruent with our previous observations during constant-load arm-crank exercise (Tiller et al., 2017). In the present study, subjects exhibited normal pulmonary function (Table 1) and, after correcting the maximum flow-volume envelope for the effects of thoracic gas compression and exercise-induced bronchodilation (Guenette et al., 2010), only two-of-eight subjects exhibited expiratory flow limitation during upper-body exercise compared to six-of-eight who showed dynamic hyperinflation. Although, in general, there was substantial expiratory reserve during upper-body exercise, dynamic airway compression can occur at expiratory flows below maximum capacity (Mead, Turner, Macklem, & Little, 1967). Thus, the increase in ERV may have occurred in an anticipatory manner as subjects approached their mechanical expiratory flow-generating capacity. It is worth noting that when the two subjects who exhibited frank expiratory flow limitation were removed from the group mean analysis, the difference in ERV between upper- and lower-body exercise remained. Collectively, these findings suggest that the inability to reduce ERV during upper-body exercise in normal subjects is not mechanistically linked with ventilatory demand or flow limitation.

Other mechanisms likely underpin the mechanical ventilatory responses to upper-body exercise. Neural activation of the rectus abdominis, assessed indirectly via surface EMG, was substantially elevated during upper- versus lower-body exercise at any given level of ventilation (Fig. 5). Unlike the diaphragm, the activation of which is modulated to prioritise pulmonary ventilation during prolonged exercise (Hodges, Heijnen, & Gandevia, 2001), the rectus abdominis contracts to reduce ERV during dynamic expiration (Henke et al., 1988) and to flex/rotate the vertebral column (Cresswell, Grundstrom, & Thorstensson, 1992); hence, the abdominal muscles undergo additional loading during upper-body exercise to carry out a series of respiratory and non-respiratory tasks. Arm-crank intensities that approach maximum require the subject to exert a substantial force in overcoming increased external resistances on the flywheel, and the contribution of the abdominal
muscles to locomotion is thereby increased. Presently, EMGra increased at a faster rate during upper-relative to lower-body exercise (Fig. 5), reinforcing the notion that the abdominal muscle contribution to locomotion is a function of work rate (Abraham et al., 2002). Accordingly, the competing roles for the abdominals during upper-body exercise likely impede the capacity of these muscles to reduce ERV below relaxation volume. Thus, in accordance with research in patients with COPD (Gigliotti et al., 2005), we explain the hyperinflation in healthy subjects via mode-specific locomotor mechanics, restriction of normal tidal volume expansion, and the discordance in respiratory pattern between upper- and lower-body exercise.

Alongside dynamic hyperinflation, there was evidence of neuromechanical uncoupling of the respiratory system during upper-body exercise; that is, an apparent dissociation between inspiratory effort (tidal swing of oesophageal pressure relative to maximum inspiratory pressure) and subsequent thoracic displacement (tidal volume relative to vital capacity). In patients with COPD, elevated inspiratory effort has been attributed to the consequences of expiratory flow limitation caused by respiratory bronchiole thickening, excess mucous production, and airways that collapse when exposed to modest thoracic pressures (Hogg & Timens, 2009). Presently, the greater effort-displacement ratio during upper-body exercise cannot be explained by airway disease or expiratory flow limitation; instead, a more likely cause was the ventilation-mediated increase in inspiratory oesophageal pressure and comparatively low tidal volume (Fig. 4). The thoracic muscles attach to the ribcage and serve an important role in maintaining posture (Celli, 1988). Consequently, elevated thoracic loads will increase chest wall impedance and impose a mechanical constraint on ribcage expansion. There is a strong correlation between the effort-displacement ratio and dyspnoea in patients with COPD (O'Donnell et al., 1997). As such, a potential interaction between neuromechanical uncoupling and dyspnoea warrants prospective study.

**Cardiorespiratory Responses**

In accordance with previous literature (Sawka, 1986), $\text{VO}_2$ at peak intensity and for any given level of ventilation was significantly lower during upper- compared to lower-body exercise. Two interrelated mechanisms may underpin these observations. First, the absolute volume of active muscle
mass recruited was likely smaller during upper-body exercise. It is reasonable to suppose, therefore, that the legs and gluteals would provoke greater O$_2$ demand than the arms, chest, back, and shoulders (Bergh, Kanstrup, & Ekblom, 1976). Second, there was likely a mode-specific disparity in O$_2$ kinetics. Indeed, the upper-limbs comprise a greater percentage of type II muscle fibres (Jennekens, Tomlinson, & Walton, 1971) which, in turn, have a longer O$_2$ time constant compared to type I fibres (Kushmerick, Meyer, & Brown, 1992). Greater and/or earlier recruitment of type II fibres during upper-body exercise may explain the slower adjustment of pulmonary VO$_2$ to arm-crank ergometry (Koppo, Bouckaert, & Jones, 2002). This mechanism may also explain, at least in part, why the ventilatory response was slightly, but not significantly, lower during the ventilation-matched upper-body exercise trial.

**Critique of Methods**

Several considerations should predicate the interpretation of our findings. The IC manoeuvre used in the assessment of operating lung volumes is effort-dependent and must, therefore, be truly maximal to ensure the attainment of TLC (see Introduction). Although peak Poe during the IC manoeuvre tended to be less negative during upper-body exercise, there were no significant differences across exercise intensities for either mode. A further assumption of the IC method is that TLC does not change during exercise. Tonic activation of abdominal and chest wall muscles, especially during upper-body exercise, may change chest wall compliance sufficiently to reduce TLC. Nevertheless, the peak Poe achieved during the IC manoeuvre during exercise was not significantly different to the values achieved reproducibly at rest. Moreover, had TLC been underestimated, this would likely have been evident earlier in the ventilation-matched protocol (i.e., at submaximal intensities), rather than only manifesting at 100% $V_{E,UBE}$. We are confident, therefore, that subjects gave consistently maximal inspiratory efforts and that the differences in ERV and IRV between upper- and lower-body exercise were not the result of an inability to attain TLC. Furthermore, we took care to monitor the respiratory pattern employed by subjects immediately prior to the IC manoeuvre and, on occasions when anticipation of the IC manifested as an artificial decrease in ERV, both the IC and the anomalous tidal breath were excluded from analysis.
We noted that EMG activity of the rectus abdominis was higher when resting data were collected immediately prior to upper- versus lower-body exercise. Resting data for arm-crank exercise were collected while subjects sat upright in a chair with their hands rested at the sides. By contrast, resting data for leg-cycle exercise were collected while subjects sat upright on the ergometer with their hands rested on the upper handlebars. This latter body position may have permitted offloading of the abdominal muscles, thereby requiring less neural activation for postural support, leading to the noted differences in resting values. It is unlikely, however, that these discrepancies were sufficient to explain the more substantial exercise-mediated differences in function. Finally, we made an effort to compare operating lung volumes at ventilation-matched work rates. Although minute ventilations were not significantly different between exercise modes, there was a tendency toward lower values during upper-body exercise (8 - 14%). Thus, it is possible that the degree of hyperinflation during upper-body exercise was underestimated.

Implications

Mechanical-ventilatory responses to upper-body exercise have been studied widely, owing to the critical role of the upper-limbs in executing activities of daily living (Tangri & Woolf, 1973). Arm-crank ergometry, specifically, features in pulmonary rehabilitation programmes and is considered the most appropriate method for assessing supported arm-exercise capacity in patients with COPD (Janaudis-Ferreira, Beauchamp, Goldstein, & Brooks, 2012). It should be noted, however, that supported arm ergometry is not consistent with the unsupported nature of activities of daily living. Indeed, unsupported arm exercise does not appear to elicit dynamic hyperinflation in patients in whom chest wall expansion is proportional to ventilation (Romagnoli et al., 2011). Notwithstanding, we used arm-crank exercise because the repetitive, cyclical nature of the task make it comparable with stationary leg-cycle exercise. In addition, both modes induce substantial physiological stress without the need for technical coaching.

To limit dyspnoea, patients with COPD often minimise use of the arms during activities like housework, carrying groceries and self-grooming (Tangri & Woolf, 1973). This suggests that tasks involving the upper-limbs may provoke changes in mechanical-ventilatory function, resulting in respiratory distress. Although we observed evidence of significant neuromechanical uncoupling
during upper-body exercise, it seems unlikely that this would induce substantial respiratory distress in healthy individuals. Indeed, when asked their principal reason for terminating upper-body exercise, all of our subjects cited symptoms of arm fatigue rather than dyspnoea. In patients with COPD, however, a poor effort-displacement ratio during upper-body exercise may form the basis of distressing respiratory sensations and elevated perceptions of dyspnoea (O’Donnell et al., 2007). Given these considerations, our data bring into question the appropriateness of dynamic upper-body exercise for use in certain patient populations (e.g., those undergoing pulmonary rehabilitation), and careful consideration should be given to individual patients before engaging them in exercises that provoke neuromechanical uncoupling or exacerbate dynamic hyperinflation. Nonetheless, training programmes that include unsupported arm exercise and training with an arm ergometer have been shown to attenuate hyperinflation during arm-cramp ergometry in patients with COPD (Gigliotti et al., 2005). Clearly, further research is needed to determine the influence of upper-body exercise-mediated hyperinflation and neuromechanical uncoupling on exertional dyspnoea in health and disease. The literature pertaining to obstructive lung disease suggests that the unfavourable respiratory mechanics of upper-body exercise are related to both disease pathology and mechanical constraints (Alison et al., 1998; Gigliotti et al., 2005; Hannink, Van Helvoort, Dekhuijzen, & Heijdra, 2011). The present findings expand current understanding by showing that changes in respiratory mechanics (tidal volume restriction, dynamic hyperinflation, neuromechanical uncoupling) occur independently of pulmonary dysfunction and flow limitation, and likely depend on task-specific locomotor mechanics. The importance of these findings also extend to athletes engaged in upper-body-dependent sports (e.g., kayaking, rowing, wheelchair racing), for whom arm-cramp ergometry is an essential training and profiling tool.

In conclusion, this study presents novel data showing a marked reduction in mechanical-ventilatory function during upper-body (arm-cramp) exercise relative to lower-body (leg-cycle) exercise at peak and ventilation-matched work rates in normal subjects. Relative to ventilation-matched lower-body exercise, high-intensity upper-body exercise was characterised by tidal volume constraint and increases in ERV towards or above resting values (i.e., dynamic hyperinflation), which were
statistically significant at peak intensities. Furthermore, there was a greater propensity towards neuromechanical uncoupling of the respiratory system during upper-body exercise. Importantly, these observations were independent of respiratory dysfunction and expiratory flow limitation. We propose, therefore, that the aforementioned responses are characteristic of upper-body exercise and likely attributable to the competing respiratory and non-respiratory functions of thoracic muscles.
REFERENCES


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ADDITIONAL INFORMATION

Competing Interests

There are no competing interests or conflicts of interest.

Author Contributions

The experiments were performed at Brunel University London. NBT, IGC and LMR conceived and designed the study. NBT performed data collection and analysis. NBT and LMR interpreted results and drafted the work. NBT, IGC and LMR revised the work critically for important intellectual content. NBT, IGC and LMR approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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Fig. 1. Representative plot for a single subject showing minute ventilation versus work rate during maximal, incremental upper- and lower-body exercise (Test 1 and Test 2). Work rates during Test 3 and Test 4 were established using inter-stage linear interpolation and were equivalent to those attained at 20, 40, 60, 80 and 100% of the peak ventilation achieved during the initial upper-body exercise test ($V_{E,UBE}$).
Fig. 2. Minute ventilation during incremental, ventilation-matched upper- versus lower-body exercise (Test 3 vs. Test 4). Mean ± SD, n = 8. Dotted line: x = y.
Fig. 3. Operating lung volumes during incremental, ventilation-matched upper- versus lower-body exercise (Test 3 vs. Test 4). Mean ± SEM, n = 8. IRV, inspiratory reserve volume; ERV, expiratory reserve volume; $V_T$, tidal volume; IC, inspiratory capacity. *ERV significantly different to lower-body exercise ($p < 0.05$)
Fig. 4. Tidal inspiratory oesophageal pressure relative to maximum static inspiratory pressure (panel A), tidal volume relative to vital capacity (panel B), and the effort/displacement ratio (panel C), during incremental, ventilation-matched upper- versus lower-body exercise (Test 3 vs. Test 4). Mean ± SD, n = 8. †Significant main-effect for exercise mode \( (p < 0.05) \). *Significant difference versus lower-body exercise \( (p < 0.008) \).
Fig. 5. Electromyographic activity of the rectus abdominis during incremental, ventilation-matched upper- versus lower-body exercise (Test 3 vs. Test 4). Mean ± SEM, n = 3.
### Table 1. Subject characteristics

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>%Predicted</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>24 ± 5</td>
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<tr>
<td>Stature (m)</td>
<td>1.79 ± 0.07</td>
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<tr>
<td>Mass (kg)</td>
<td>74 ± 11</td>
<td>--</td>
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<tr>
<td>VC (L)</td>
<td>5.67 ± 0.44</td>
<td>103 ± 5</td>
</tr>
<tr>
<td>FEV₁ (L)</td>
<td>4.34 ± 0.41</td>
<td>94 ± 7</td>
</tr>
<tr>
<td>FEV₁/VC (%)</td>
<td>77 ± 7</td>
<td>91 ± 8</td>
</tr>
<tr>
<td>P&lt;sub&gt;Imax&lt;/sub&gt; (cmH&lt;sub&gt;2&lt;/sub&gt;O)</td>
<td>−153 ± 19</td>
<td>139 ± 19</td>
</tr>
<tr>
<td>P&lt;sub&gt;Emax&lt;/sub&gt; (cmH&lt;sub&gt;2&lt;/sub&gt;O)</td>
<td>160 ± 45</td>
<td>104 ± 30</td>
</tr>
</tbody>
</table>

Mean ± S.D., n = 8. VC, vital capacity; FEV₁, forced expiratory volume in one second; P<sub>Imax</sub>, maximum static inspiratory pressure; P<sub>Emax</sub>, maximum static expiratory pressure.
Table 2. Physiological responses to upper- versus lower-body exercise at peak work rates (Test 1 vs. Test 2)

<table>
<thead>
<tr>
<th></th>
<th>Lower-body</th>
<th>Upper-body</th>
<th>p</th>
<th>Cohen’s d</th>
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</thead>
<tbody>
<tr>
<td>Work rate (W)</td>
<td>251 ± 32</td>
<td>118 ± 33</td>
<td>0.000*</td>
<td>4.09</td>
</tr>
<tr>
<td>$\dot{V}O_2$ (L·min$^{-1}$)</td>
<td>3.12 ± 0.72</td>
<td>2.36 ± 0.54</td>
<td>0.001*</td>
<td>1.19</td>
</tr>
<tr>
<td>$\dot{V}O_2$ (ml·kg$^{-1}$·min$^{-1}$)</td>
<td>40.7 ± 10.0</td>
<td>30.7 ± 6.3</td>
<td>0.002*</td>
<td>1.20</td>
</tr>
<tr>
<td>$\dot{V}CO_2$ (L·min$^{-1}$)</td>
<td>3.64 ± 0.51</td>
<td>2.67 ± 0.53</td>
<td>0.000*</td>
<td>1.87</td>
</tr>
<tr>
<td>RER</td>
<td>1.22 ± 0.30</td>
<td>1.14 ± 0.08</td>
<td>0.465</td>
<td>0.36</td>
</tr>
<tr>
<td>$V_E$ (L·min$^{-1}$)</td>
<td>127 ± 27</td>
<td>100 ± 25</td>
<td>0.006*</td>
<td>1.04</td>
</tr>
<tr>
<td>$V_T$ (L)</td>
<td>2.60 ± 0.59</td>
<td>2.03 ± 0.42</td>
<td>0.000*</td>
<td>1.11</td>
</tr>
<tr>
<td>$f_R$ (br·min$^{-1}$)</td>
<td>47 ± 10</td>
<td>48 ± 11</td>
<td>0.903</td>
<td>0.10</td>
</tr>
<tr>
<td>$V_E$/ $\dot{V}O_2$</td>
<td>42.9 ± 15.1</td>
<td>42.6 ± 6.6</td>
<td>0.961</td>
<td>0.03</td>
</tr>
<tr>
<td>$V_E$/ $\dot{V}CO_2$</td>
<td>34.8 ± 5.3</td>
<td>37.5 ± 5.6</td>
<td>0.059</td>
<td>0.50</td>
</tr>
<tr>
<td>$T_i$ (s)</td>
<td>0.72 ± 0.12</td>
<td>0.70 ± 0.19</td>
<td>0.621</td>
<td>0.13</td>
</tr>
<tr>
<td>$T_e$ (s)</td>
<td>0.72 ± 0.15</td>
<td>0.70 ± 0.17</td>
<td>0.685</td>
<td>0.12</td>
</tr>
<tr>
<td>$T_{TOT}$ (s)</td>
<td>1.42 ± 0.26</td>
<td>1.38 ± 0.35</td>
<td>0.715</td>
<td>0.13</td>
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<tr>
<td>$T_i/T_{TOT}$</td>
<td>0.51 ± 0.03</td>
<td>0.50 ± 0.03</td>
<td>0.493</td>
<td>0.33</td>
</tr>
<tr>
<td>$T_e/T_{TOT}$</td>
<td>0.51 ± 0.02</td>
<td>0.51 ± 0.02</td>
<td>0.753</td>
<td>0.00</td>
</tr>
<tr>
<td>$V_T/T_i$ (L·s$^{-1}$)</td>
<td>3.60 ± 0.56</td>
<td>3.07 ± 0.88</td>
<td>0.116</td>
<td>0.72</td>
</tr>
<tr>
<td>IRV (L)</td>
<td>1.27 ± 0.46</td>
<td>1.95 ± 0.91</td>
<td>0.012*</td>
<td>0.94</td>
</tr>
<tr>
<td>IRV (%VC)</td>
<td>78 ± 8</td>
<td>66 ± 17</td>
<td>0.014*</td>
<td>0.90</td>
</tr>
<tr>
<td>ERV (L)</td>
<td>1.81 ± 0.40</td>
<td>1.70 ± 0.91</td>
<td>0.642</td>
<td>0.16</td>
</tr>
<tr>
<td>ERV (%VC)</td>
<td>32 ± 8</td>
<td>30 ± 17</td>
<td>0.640</td>
<td>0.15</td>
</tr>
<tr>
<td>EMGr (%RMS$_{max}$)</td>
<td>30 ± 16</td>
<td>96 ± 63</td>
<td>--</td>
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</tr>
<tr>
<td>$\Delta$Poe (cmH$_2$O)</td>
<td>25.7 ± 5.2</td>
<td>26.3 ± 8.7</td>
<td>0.810</td>
<td>0.08</td>
</tr>
<tr>
<td>$f_C$ (br·min$^{-1}$)</td>
<td>179 ± 11</td>
<td>171 ± 11</td>
<td>0.060</td>
<td>0.73</td>
</tr>
<tr>
<td>SpO$_2$ (%)</td>
<td>95.6 ± 2.0</td>
<td>97.2 ± 2.1</td>
<td>0.226</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Mean ± S.D., n = 8 (EMGr, n = 3). $\dot{V}O_2$, O$_2$ uptake; $\dot{V}CO_2$, CO$_2$ output; RER, respiratory exchange ratio; $V_E$, minute ventilation; $V_T$, tidal volume; $f_R$, respiratory frequency; $T_i$, inspiratory time; $T_e$, expiratory time; $T_{TOT}$, total respiratory time; IRV, inspiratory reserve volume; ERV, expiratory reserve volume; EMGr, rectus abdominis electromyography; $\Delta$Poe, tidal inspiratory oesophageal pressure swing; $f_C$, cardiac frequency; SpO$_2$, arterial oxygen saturation. *Significant difference ($p < 0.05$).
Table 3. Cardiorespiratory responses to upper- versus lower-body exercise at ventilation-matched work
d
<table>
<thead>
<tr>
<th></th>
<th>Rest</th>
<th>20% V&lt;sub&gt;E,UBE&lt;/sub&gt;</th>
<th>40% V&lt;sub&gt;E,UBE&lt;/sub&gt;</th>
<th>60% V&lt;sub&gt;E,UBE&lt;/sub&gt;</th>
<th>80% V&lt;sub&gt;E,UBE&lt;/sub&gt;</th>
<th>100% V&lt;sub&gt;E,UBE&lt;/sub&gt;</th>
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<tbody>
<tr>
<td></td>
<td>LBE</td>
<td>UBE</td>
<td>LBE</td>
<td>UBE</td>
<td>LBE</td>
<td>UBE</td>
</tr>
<tr>
<td>Work rate (W)</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>26 ± 18 ± 111 ± 63 ± 168 ± 84 ± 199 ± 97 ± 221 ± 113 ±</td>
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<tr>
<td>Work rate</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
<td>10 ± 15 ± 44 ± 55 ± 67 ± 74 ± 80 ± 86 ± 89 ± 100 ± 0*</td>
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</tr>
<tr>
<td>VO&lt;sub&gt;2&lt;/sub&gt; (L·min&lt;sup&gt;-1&lt;/sup&gt;)</td>
<td>0.51</td>
<td>0.43</td>
<td>0.99 ± 0.76 ± 1.72 ± 1.26 ± 2.35 ± 1.69 ± 2.76 ± 2.04 ± 3.07 ± 2.38 ±</td>
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<tr>
<td>VO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>6.6 ± 5.7 ± 12.9 ± 10.1 ± 22.3 ± 16.3 ± 30.6 ± 21.9 ± 36.1 ± 26.4 ± 39.7 ± 31.0 ±</td>
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<tr>
<td>V&lt;sub&gt;CO2&lt;/sub&gt;</td>
<td>0.45</td>
<td>0.42</td>
<td>0.91 ± 0.76 ± 1.68 ± 1.37 ± 2.43 ± 1.89 ± 2.96 ± 2.25 ± 3.42 ± 2.69 ±</td>
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<tr>
<td>RER †</td>
<td>1.00</td>
<td>0.98</td>
<td>0.92 ± 0.99 ± 0.98 ± 1.10 ± 1.04 ± 1.14 ± 1.07 ± 1.11 ± 1.11 ± 1.13 ±</td>
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<tr>
<td>V&lt;sub&gt;e&lt;/sub&gt; (L·min&lt;sup&gt;-1&lt;/sup&gt;)</td>
<td>13.7</td>
<td>12.3</td>
<td>23.9 ± 20.7 ± 41.7 ± 38.4 ± 63.2 ± 53.1 ± 80.2 ± 69.4 ± 109.1 ± 98.5 ±</td>
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<tr>
<td>V&lt;sub&gt;T&lt;/sub&gt; (L †)</td>
<td>0.87</td>
<td>0.61</td>
<td>1.08 ± 0.92 ± 1.75 ± 1.50 ± 2.27 ± 1.74 ± 2.52 ± 2.07 ± 2.55 ± 1.97 ±</td>
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<tr>
<td>f&lt;sub&gt;r&lt;/sub&gt; (br·min&lt;sup&gt;-1&lt;/sup&gt;)</td>
<td>14.9</td>
<td>15.2</td>
<td>20.5 ± 18.8 ± 22.9 ± 24.4 ± 26.6 ± 27.2 ± 31.2 ± 34.3 ± 42.3 ± 48.4 ±</td>
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<tr>
<td>V&lt;sub&gt;e&lt;/sub&gt;/VO&lt;sub&gt;2&lt;/sub&gt;</td>
<td>27.9</td>
<td>28.8</td>
<td>24.6 ± 27.9 ± 24.5 ± 30.8 ± 26.8 ± 31.8 ± 28.8 ± 34.3 ± 35.0 ± 41.8 ±</td>
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<tr>
<td>V&lt;sub&gt;e&lt;/sub&gt;/V&lt;sub&gt;CO2&lt;/sub&gt; †</td>
<td>30.3</td>
<td>30.0</td>
<td>26.7 ± 27.0 ± 24.8 ± 28.1 ± 25.8 ± 28.1 ± 27.0 ± 30.9 ± 31.5 ± 36.9 ±</td>
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<tr>
<td>T&lt;sub&gt;T&lt;/sub&gt; (s) †</td>
<td>1.75</td>
<td>1.47</td>
<td>1.21 ± 1.20 ± 1.16 ± 1.14 ± 1.04 ± 0.99 ± 0.94 ± 0.94 ± 0.78 ± 0.70 ±</td>
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<tr>
<td>T&lt;sub&gt;T&lt;/sub&gt; (s)</td>
<td>2.14</td>
<td>1.91</td>
<td>1.69 ± 1.66 ± 1.50 ± 1.49 ± 1.24 ± 1.19 ± 1.08 ± 1.06 ± 0.83 ± 0.69 ±</td>
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<tr>
<td>T&lt;sub&gt;TOT&lt;/sub&gt; (s)</td>
<td>3.88</td>
<td>3.38</td>
<td>2.89 ± 2.86 ± 2.66 ± 2.62 ± 2.28 ± 2.18 ± 2.02 ± 2.00 ± 1.61 ± 1.39 ±</td>
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<tr>
<td>T&lt;sub&gt;T&lt;/sub&gt;/T&lt;sub&gt;TOT&lt;/sub&gt;</td>
<td>0.45</td>
<td>0.43</td>
<td>0.42 ± 0.42 ± 0.44 ± 0.43 ± 0.46 ± 0.45 ± 0.47 ± 0.47 ± 0.48 ± 0.50 ±</td>
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<tr>
<td>T&lt;sub&gt;E&lt;/sub&gt;/T&lt;sub&gt;TOT&lt;/sub&gt;</td>
<td>0.55</td>
<td>0.57</td>
<td>0.58 ± 0.58 ± 0.56 ± 0.57 ± 0.54 ± 0.55 ± 0.53 ± 0.53 ± 0.52 ± 0.50 ±</td>
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<tr>
<td>V&lt;sub&gt;T&lt;/sub&gt;/T&lt;sub&gt;T&lt;/sub&gt; (L·s&lt;sup&gt;-1&lt;/sup&gt;) †</td>
<td>0.53</td>
<td>0.42</td>
<td>0.89 ± 0.77 ± 1.49 ± 1.31 ± 2.20 ± 1.76 ± 2.72 ± 2.23 ± 3.38 ± 2.85 ±</td>
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<tr>
<td>f&lt;sub&gt;c&lt;/sub&gt; (br·min&lt;sup&gt;-1&lt;/sup&gt;)</td>
<td>64 ± 63 ± 84 ± 75 ± 110 ± 104 ± 135 ± 133 ± 156 ± 150 ± 169 ± 167 ± 14</td>
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<tr>
<td>SpO&lt;sub&gt;2&lt;/sub&gt; (%) †</td>
<td>98 ± 99 ± 97 ± 99 ± 96 ± 98 ± 97 ± 98 ± 97 ± 98 ± 95 ± 98 ± 2</td>
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</table>

Mean ± S.D., n = 8. LBE, lower-body exercise; UBE, upper-body exercise; VO<sub>2</sub>, O<sub>2</sub> uptake; V<sub>CO2</sub>, CO<sub>2</sub> output; RER, respiratory exchange ratio; V<sub>E</sub>, minute ventilation; V<sub>T</sub>, tidal volume; f<sub>r</sub>, respiratory frequency; T<sub>E</sub>, inspiratory time; T<sub>T</sub>, expiratory time; T<sub>TOT</sub>, total respiratory time; f<sub>c</sub>, cardiac frequency; SpO<sub>2</sub>, arterial O<sub>2</sub> saturation.
†Significant main-effect for exercise mode (p < 0.05). *Significant difference versus lower-body exercise (p < 0.008).