Acute thoracoabdominal and hemodynamic responses to tapered flow resistive loading in healthy adults

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Abstract (149 words)

We investigated the acute physiological responses of tapered flow resistive loading (TFRL) at 30, 50 and 70% maximal inspiratory pressure (PI_{max}) in 12 healthy adults to determine an optimal resistive load. Increased end-inspiratory rib cage and decreased end-expiratory abdominal volumes equally contributed to the expansion of thoracoabdominal tidal volume (captured by optoelectronic plethysmography). A significant decrease in end-expiratory thoracoabdominal volume was observed from 30 to 50% PI_{max}, from 30 to 70% PI_{max}, and from 50 to 70% PImax. Cardiac output (recorded by cardio-impedance) increased from rest by 30% across the three loading trials. Borg dyspnoea increased from 2.36±0.20 at 30% PI_{max}, to 3.45±0.21 at 50% PI_{max}, and 4.91±0.25 at 70% PI_{max}. End-tidal CO_2 decreased from rest during 30, 50 and 70 %PI_{max} (26.23±0.59, 25.87±1.02 and 24.30±0.82 mmHg, respectively). Optimal intensity for TFRL is at 50% PI_{max} to maximise global respiratory muscle and cardiovascular loading whilst minimising hyperventilation and breathlessness.

Key words: Inspiratory Muscle Training, Thoracoabdominal Volumes, and Cardiac Output

1.0 – Introduction:

Inspiratory muscle training (IMT) aims to functionally overload the inspiratory muscles and has been shown to improve inspiratory muscle strength (reflected by increased maximal inspiratory pressure; PI_{max}), endurance and exercise tolerance in healthy individuals (McConnell & Romer, 2004), as well as in various respiratory (Enright et al., 2004; Gosselink et al., 2011) and cardiovascular disorders (Dall'Ago et al., 2006). IMT devices are usually small and portable allowing for training to be performed at home, with the most common training programmes consisting of 30 breaths performed twice daily (4-5 minute sessions) above 30% PI_{max}, 7 days a week for 8-12 weeks (Gosselink et al., 2011; Langer et al., 2018; McConnell, 2013).

The mechanisms of improved PI_{max} following IMT has been attributed to structural and functional adaptations to the training stimulus, including strength, speed of respiratory muscle shortening and power output (Romer & McConnell, 2003) secondary to hypertrophy of inspiratory muscles (Enright et al., 2006). In terms of improving exercise capacity, previous research has suggested significant IMT-induced physiological adaptations including the attenuation of the respiratory muscle metaboreflex (Witt et al., 2007) and improved respiratory muscle efficiency, associated with reduced oxygen requirement for the respiratory musculature (Turner et al., 2012). Lower dyspnoea levels following IMT have also been reported during exercise (Ramsook et al., 2017; Turner et al., 2011) however, research into the mechanisms behind this needs to be further explored (Ramsook et al., 2017).

The majority of studies investigating the acute effects of inspiratory muscle loading have typically used mechanical threshold loading devices, which provide a constant pressure throughout inspiration. A more recently developed tapered flow resistive loading (TFRL) device, however, provides a tapered resistance via an electronic, dynamically adjusted valve allowing pressure to be volume-dependently tapered once the initial threshold has been overcome (Langer et al., 2015). Use of this device in an IMT programme in patients with chronic obstructive pulmonary disease (COPD) has resulted in greater improvements in inspiratory muscle function (i.e. strength, endurance, power, and shortening

velocity) as well as a greater tolerance of higher training loads compared to those patients who trained with the mechanical threshold loading devices (Langer et al., 2015).

The acute effects of inspiratory muscle loading, via TFRL and mechanical threshold loading, on thoracoabdominal volumes in healthy individuals have shown significant increases in tidal volume, end-inspiratory volume and minute ventilation, along with decreases in end-expiratory volumes, albeit at moderate intensities (40% PI_{max}) (da Fonsêca et al., 2019; de Souza et al., 2016). An increase in the fractional contribution of the pulmonary rib cage compartment to tidal volume expansion during moderate inspiratory resistance (40% PI_{max}) and during a single PI_{max} manoeuvre compared to quiet breathing has previously been reported (de Souza et al., 2016). Furthermore, healthy individuals increased abdominal rib cage contribution to tidal volume expansion during moderate intensity loading only and decreased abdominal contribution during both moderate (40% PI_{max}) and maximal intensities (100% PI_{max}) (de Souza et al., 2016).

It is unclear, however, what the optimal training load is when using TFRL devices in terms of maximising respiratory muscle recruitment and mobilising central haemodynamic and local respiratory muscle oxygenation requirements. By combining these physiological measurements, we aimed to develop a greater understanding of the acute effects of separate short bouts of TFRL at low, moderate, and high intensities (corresponding to 30, 50, and 70% PI_{max}, respectively) performed at a fixed breathing frequency, and ultimately determine an optimal inspiratory muscle training load to elicit beneficial physiological responses, whilst minimising potential adverse physiological effects. It was reasoned that due to the device's inherent operational requirements (i.e. an initial threshold load that must be overcome before dynamical adjustments can arise) there would progressively be greater expiratory muscle recruitment at 50 and 70% PI_{max} compared to 30% PI_{max} to allow for the further expansion of tidal volume. This in turn was expected to maximise loading to both inspiratory and expiratory muscles making TFRL a suitable tool for both inspiratory and expiratory muscle training.

2.0 – Methods:

2.1 - Participants:

Twelve healthy individuals participated in the study. The sample was formed by 6 males and 6 females. Inclusion criteria were followed and included: healthy adults aged between 18-30 years who were free from injury and able to give full written consent. The exclusion criteria were current smokers, chronic pulmonary, cardiac, or neuromuscular disease, and users of medications that affect muscle strength or haemodynamic variables. All participants provided full informed consent prior to their participation.

2.2 – Study design:

This was a cross sectional study approved by Northumbria University Newcastle Ethics Committee (No: 16821). The study investigated the acute effects of tapered flow resistive loading at 30%, 50% and 70% PI_{max} on thoracoabdominal volumes, central haemodynamic and local respiratory muscle oxygenation responses. All trials were conducted in one visit.

2.3 – Participant preparation:

Participants were familiarised with the inspiratory muscle training device (POWERbreathe KH1; HaB International Ltd., Southam, UK) upon arrival to the laboratory. Participants performed spirometry tests using a metabolic gas exchange analyser (Cortex; METALYZER® 3B, Leipzig, Germany), and after three acceptable measurements, the highest value for forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), $FEV1_1$/FVC ratio, and peak expiratory flow (PEF) were taken (Graham et al., 2019). The participants then performed PI_{max} maneuverers using the inspiratory muscle trainer device from residual volume (Laveneziana et al., 2019). Measurements were repeated at least five times until three consecutive maneuverers had less than 10% variability. The highest value of these measurements was used as the participant's baseline PI_{max}. Optoelectronic plethysmography (OEP; BTS, Italy) markers, Physioflow (Enduro, PF-07, Manatec Biomedical,

France) and near-infrared spectroscopy (NIRS; NIRO-200NX, Hamamatsu, Hamamatsu City, Japan) electrodes were then attached to the chest wall following skin preparation. Participants were then familiarised with the modified (1-10) Borg scale (Borg, 1982).

2.4 – Inspiratory muscle loading trials:

Participants used the POWERbreathe device during 3 separate trials (30, 50 and 70% PI_{max}). Each trial lasted for 3 minutes. The first and third minute involved quiet breathing (QB) with the load being applied during the second minute and at a fixed frequency of 10 breaths per minute (2 seconds inspiration, 4 seconds expiration) as outlined by McConnell (2013). Breathing frequency was controlled to standardise inspiratory muscle loading and to allow the direct comparison of rib cage and abdominal thoracoabdominal volumes between loaded trials at different resistive loads. This frequency was controlled by an interval timer which provided auditory cues signalling when participants should initiate inspirations and expirations. The participants were instructed to inhale forcefully against the resistance during the loaded minute but were given no instructions to expire to residual volume. This allowed for differences in end-expiratory thoracoabdominal volumes and fractional contribution of the rib cage and abdominal thoracoabdominal compartments to total tidal volume expansion between inspiratory muscle loaded intensities to be observed. During expiration, there was no resistance and the load was applied in a balanced ordered sequence for both males and females (Table 1). For all variables, the QB values reported were averages of the first unloaded minutes within all trials.

Table 1. Balanced order sequence for the inspiratory loaded breathing trials for males (n=6) and females (n=6).

Participant	Inspiratory load (cmH_2O) order		
1	30	50	70
2	30	70	50
3	50	30	70
4	50	70	30

5	70	30	50
6	70	50	30

2.5 – Operational thoracoabdominal volume measurements:

Throughout all breathing trials, optoelectronic plethysmography (OEP; BTS, Italy) was used to measure thoracoabdominal wall muscle kinematics, breathing pattern, and inspiratory and expiratory flow rates. This was achieved by attaching 89 reflective markers to the chest wall according to anatomical references outlined previously (Aliverti & Pedotti, 2002). Participants were seated and grasped handles located laterally and positioned in line with their mid sternum to ensure arms were lifted away from their chest wall. This allowed eight infrared cameras to capture the movement of the reflective markers during the trials. The three-dimensional coordinates of the markers were reconstructed by stereophotogrammetry and total and compartmental thoracoabdominal volumes were calculated by dedicated software using Gauss's theorem (Aliverti & Pedotti, 2002).

Total thoracoabdominal volume (V_{CW}) can be divided into 3 compartments: the pulmonary rib cage (RCp), the abdominal rib cage (RCa) and the abdomen (Ab) allowing for the consideration of both lung-and diaphragm-apposed sections of the rib cage (RCp and RCa respectively) (Aliverti & Pedotti, 2002). Total and compartmental end-expiratory ($V_{CW,\ EE}$) and end-inspiratory ($V_{CW,\ EI}$) thoracoabdominal volumes were measured at the beginning and end of inspiratory flow on a breath-by-breath basis and expressed as changes from those during quiet breathing (QB). Tidal volume (V_T) was calculated for total, and compartmental thoracoabdominal volume as the difference between end-inspiratory volume ($V_{CW,\ EI}$) and end-expiratory volume ($V_{CW,\ EE}$) (Aliverti & Pedotti, 2002). Inspiratory capacity (IC) manoeuvres were performed at QB, as previously described (O'Donnell & Webb, 1993), in order to calculate thoracoabdominal volume at total lung capacity (TLC). Furthermore, minute ventilation (V_E), inspiratory flow and expiratory flow rates were assessed throughout all trials by the OEP system. Finally, lung size was controlled using FVC as a surrogate when determining sex differences in thoracoabdominal volumes (V_T / FVC) as outlined previously (Vogiatzis et al., 2005).

2.6 – Central haemodynamic measurements:

Cardiac output (CO), stroke volume (SV) and heart rate (HR) were measured continuously and averaged at 6-second intervals via a non-invasive bioimpedance cardiography device (Physio-Flow, Enduro, PF-07, Manatec Biomedical, France). Six electrodes were attached to the participants. Two electrodes were placed at the left base of the neck, over the carotid artery, and two electrodes were placed on the back at the xiphoid level to transmit and receive electrical currents serving as the ECG signal (Nasis et al., 2015).

Arterial oxygen content (CaO_2) was estimated from the following equation: CaO_2 (ml O_2/100ml blood) = 1.39 x (Hb) x arterial oxygen saturation (SpO_2) (Borghi-Silva et al., 2008), where Hb is haemoglobin concentration (Borghi-Silva et al., 2008) and SpO_2 is oxygen saturation. Normal haemoglobin concentration values were assumed for males (15g/dL) and females (14g/dL) (Lewis et al., 2004) and SpO_2 was continuously monitored by a pulse oximeter (Onyx Vantage 9590, Nonin Medical Inc, USA). Systemic oxygen delivery (DO_2) was estimated from the following equation: DO_2 (L/min) = CO x CaO_2estimated (Borghi-Silva et al., 2008).

2.7 – Inspiratory muscle perfusion and oxygenation responses:

Oxyhaemoglobin (O_2HB), deoxyhaemoglobin (HHb), and tissue oxygen saturation ($StiO_2$) of the sternocleidomastoid and 7th intercostal muscle were measured continuously by near-infrared spectroscopy (NIRS; NIRO-200NX, Hamamatsu, Hamamatsu City, Japan) throughout all trials. Total haemoglobin (tHb) was calculated as the sum of O_2HB and HHb. Electrodes were attached along the sternocleidomastoid and in the left 7th intercostal space to avoid blood flow contributions from the liver on the right side of the body. Changes observed in muscle O_2Hb, HHb, and $StiO_2$ were used as an indices of inspiratory muscle oxygen delivery, oxygen extraction, and the dynamic balance between tissue oxygen delivery and utilisation, respectively, whilst tHb was used as an index of microvascular oxygenation (Grassi & Quaresima, 2016; Louvaris et al., 2020; Rodrigues et al., 2019).

2.8 – Gas exchange measurements:

Partial pressure of end-tidal carbon dioxide ($P_{ET}CO_2$) and partial pressure of end-tidal oxygen ($P_{ET}O_2$) were measured on a breath-by-breath basis by a metabolic gas exchange analyser (Cortex; METALYZER® 3B, Leipzig, Germany) throughout QB and all TFRL trials by attaching the pick-up lead of the gas exchange analyser to the mouthpiece of the POWERbreathe device.

2.9 – Dyspnoea measurements:

Following each trial, participants were required to rate their breathlessness/dyspnoea at the end of inspiratory muscle loaded breathing using the modified Borg scale (1-10) (Borg, 1982).

2.10 – Statistical analysis:

Estimation of sample size within each tapered flow resistive loading trial (i.e. 30, 50 and 70% PI_{max}) was based on the results of a previous study (McConnell & Griffiths, 2010). Using the mean difference in tidal volume expansion between 50 and 70% PI_{max} of 0.7 L and a standard deviation (SD) of 1.2 L, an alpha significance level of 0.05 (2-sided) and 80% power, a minimum total sample size of 12 subjects was required. Normality of the data was assessed using the Shapiro-Wilk test. The Friedman test was used to determine changes across trials for all variables before Wilcoxon tests were applied to determine between trial differences. The Mann-Whitney U test was used to assess differences between males and females. Data are presented as mean ± standard error of mean (SEM) unless otherwise stated. We used SEM instead of SD because the comparisons of interest were in the mean values of various physiological variables under the three different PI_{max} intensities within the same participants. The software IBM SPSS Statistics 26 was used to conduct the analysis and the level of significance for all analyses was set at $p<0.05$.

3.0 – Results:

3.1 – Participant baseline characteristics:

Demographic, spirometric, and respiratory muscle strength variables for men, women, and all participants combined are outlined in Table 2.

Table 2. Participant baseline characteristics.

Variable	All participants (n=12)	Men (n=6)	Women (n=6)
Age (years)	25 ± 3	25 ± 3	25 ± 2
Height (cm)	173.4 ± 7.5	177.6 ± 7.7	169.2 ± 4.6
Weight (kg)	73.3 ± 12.3	81.2 ± 12.1	65.3 ± 5.9
PI_{max} (cmH_2O)	102.5 ± 19.8	108.2 ± 13.9	96.8 ± 24.4
FEV_1 (L)	3.7 ± 0.6	4.2 ± 0.3	3.3 ± 0.5
FEV_1 (% predicted)	101.1 ± 9.9	102.3 ± 9.7	100.3 ± 10.9
FVC (L)	4.5 ± 0.8	5.2 ± 0.7	4.1 ± 0.4
FVC (% predicted)	106.7 ± 9.7	107.0 ± 12.9	106.5 ± 8.4
FEV_1/FVC (%)	81.0 ± 5.6	80.8 ± 5.0	81.2 ± 6.5
PEF (L/s)	8.6 ± 1.8	10.5 ± 0.7	7.4 ± 1.1
PEF (% predicted)	102.2 ± 11.6	106.5 ± 7.5	99.3 ± 13.5

Data presented as mean±SD; PI_{max}, maximal inspiratory pressure; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; PEF, peak expiratory flow.

3.2 – Thoracoabdominal volume changes during inspiratory muscle loading:

Inspiratory muscle loading induced significant increases in total end-inspiratory thoracoabdominal volume ($V_{CW,\ EI}$) across all intensities ($p<0.001$). Compared to QB (0.69±0.06 L), an increase of 2.17±0.14 L ($p=0.003$) was observed at 30% PI_{max}, 2.34±0.13 L ($p=0.002$) at 50% PI_{max}, and 2.14±0.15 L ($p=0.002$) at 70% PI_{max} (Figure 1). These changes from QB occurred as a result of significantly increased $V_{CW,\ EI}$ in all three thoracoabdominal compartments at all intensities (Figures 1 and 2). Furthermore, a significant decrease in $V_{CW,\ EI}$ of 0.19±0.08 L was observed between 50% to 70% PI_{max} ($p=0.021$), mainly due to a significant reduction in end-inspiratory abdomen volume ($V_{AB,\ EI}$) of 0.14 L±0.04 L ($p=0.010$) between these intensities (Figures 1 and 2).

End-expiratory thoracoabdominal volume ($V_{CW,\ EE}$) was significantly decreased from QB when inspiratory load was applied across all intensities ($p<0.001$). A decrease from QB of 0.54±0.24 L ($p=0.026$) was observed at 30% PI_{max}, 0.67±0.23 L ($p=0.005$) at 50% PI_{max}, and 0.87±0.23 L

(p=0.002) at 70% PI_{max} (Figures 1 and 2). These changes occurred due to significantly decreased end-expiratory abdomen volume ($V_{Ab,\ EE}$) at all intensities, decreased end-expiratory abdominal rib cage volume ($V_{RCa,\ EE}$) at 50% (p=0.015) and 70% PI_{max} (p=0.005), and decreased end-expiratory pulmonary rib cage volume ($V_{RCp,\ EE}$) at 70% PI_{max} only (p=0.012) Furthermore, a significant decrease was observed in $V_{CW,\ EE}$ at 70% PI_{max} compared to 30% (p=0.016) and 50% PI_{max} (p=0.016) due to significant reductions in $V_{AB,\ EE}$ between these loaded intensities (p=0.011; p=0.012) as well as $V_{RCa,\ EE}$ (p=0.010; p=0.018). The $V_{RCa,\ EE}$ was also significantly reduced at 50% when compared to 30% PI_{max} (p=0.041; Figures 1 and 2).

An average total thoracoabdominal inspiratory capacity (IC) of 2.74±0.11 L was observed (Figure 1a), leaving participants with an inspiratory reserve volume (IRV: TLC-IC) of 2.04±0.11 L during QB which decreased to 0.60±0.11 L during 30% PI_{max}, 0.32±0.12 L during 50% PI_{max}, and 0.55±0.14 L during 70% PI_{max}.

Comparisons of thoracoabdominal compartmental distribution at end-inspiratory and end-expiratory volumes are shown in Figure 2. There were significant differences between thoracoabdominal compartments at all loaded intensities of 30, 50, and 70% PI_{max} (p=0.003, p<0.001, and p=0.001 respectively). The RCp contributed the most in terms of increasing $V_{CW,\ EI}$ during all trials and was significantly greater than RCa contribution at 30% PI_{max} (p=0.004), 50% PI_{max} (p=0.002), and 70% PI_{max} (p=0.003). RCp contribution to $V_{CW,\ EI}$ was also significantly greater than Ab at 30, 50, and 70% PI_{max} (p=0.004, p=0.003, and p=0.003 respectively). A significant difference was observed between end-inspiratory RCa and Ab volume during 70% PI_{max}, with a greater contribution from the RCa (p=0.024). No differences were observed between RCa and Ab compartments at 30% (p=0.859) and 50% PI_{max} (p=0.754).

In terms of end-expiratory thoracoabdominal volume, there were significant differences between thoracoabdominal compartments at all loaded intensities of 30, 50, and 70% PI_{max} (p=0.020, p=0.005, and p=0.005 respectively; Figure 2b). The Ab compartment had the greatest contribution in terms of lowering $V_{CW,\ EE}$ during all intensities and contributed significantly more than V_{RCa} at 30, 50, and 70% PI_{max} (p=0.016, p=0.003, and p=0.002). Furthermore, the Ab compartment contributed

significantly more at lowering $V_{CW,\ EE}$ than the RCp compartment during 50% (p=0.049) and 70% PI_{max} (0.042).

Analysis for the entire thoracoabdominal tidal volume ($V_{T,\ CW}$) and its compartments ($V_{T,RCp}$, $V_{T,RCa}$, $V_{T,Ab}$) along with minute ventilation (V_E) showed significant differences across trials (all p<0.001; Table 3). V_T in every compartment, as well as V_E, were significantly increased from QB at each loaded intensity. Furthermore, $V_{T,\ CW}$ and V_E were significantly increased at 50% and 70% when compared to values during 30% loading (p=0.033, p=0.049). Finally, $V_{T,RCa}$ was significantly increased at 70% compared to 30% PI_{max} (p=0.016).

Significant differences were observed across trials for both inspiratory flow (p<0.001) and expiratory flow rates (p<0.001). For inspiratory flow rate, these changes occurred as significant increases at all loaded intensities compared to QB values only (p=0.003; p=0.002; p=0.002), whereas for expiratory flow rate, changes occurred as significant increases at all loaded intensities compared to QB (p=0.003; p=0.002; p=0.002) along with between 50% and 30% PI_{max} (p=0.041) and 70% and 30% PI_{max} (p=0.041) (Table 3).

Table 3. Tidal volume of the total thoracoabdomen and its compartments and minute ventilation changes across trials.

	QB	30%	50%	70%
CW $_{VT}$ (L)	0.69 ± 0.06	2.71 ±0.30 [a]	3.01 ± 0.27 [a, b]	3.02 ±0.27 [a, b]
RCp $_{VT}$ (L)	0.30 ± 0.03	1.26 ±0.16 [a]	1.36 ± 0.15 [a]	1.38 ±0.16 [a]
RCa $_{VT}$ (L)	0.13 ± 0.02	0.64 ± 0.10 [a]	0.72 ± 0.09 [a]	0.76 ± 0.09 [a, b]
Ab $_{VT}$ (L)	0.27 ± 0.03	0.80 ± 0.09 [a]	0.92 ± 0.09 [a]	0.88 ± 0.08 [a]
V_E (L/min)	10.5 ± 1.06	27.4 ± 3.09 [a]	30.3 ± 2.82 [a, b]	30.6 ±2.86 [a, b,
Insp flow rate (L/s)	0.43 ± 0.04	1.48 ± 0.18 [a]	1.61 ± 0.16 [a]	1.53 ± 0.15 [a]
Exp flow rate (L/s)	0.32 ± 0.03	0.69 ± 0.09 [a]	0.76 ± 0.08 [a, b]	0.80 ± 0.08 [a, b]

Data presented as mean±SEM; CW, chest wall; RCP, pulmonary rib cage; RCA, abdominal rib cage; AB, abdomen; V_T, tidal volume; V_E, minute ventilation; Insp, inspiratory; Exp, expiratory; L, litres; L/min, litres per minute; L/s, litres per second. [a] significant difference from QB value, [b] significant difference from 30%.

The contribution of rib cage (RC) and abdominal (AB) compartments for end-inspiratory and end-expiratory volumes during inspiratory muscle loading at 30%, 50% and 70% PI_{max} is shown for each

participant in Figure 3. For end-inspiratory volumes, the contribution came mainly from the rib cage compartment (external intercostal muscles) with little contribution from the abdominal compartment (diaphragm). For end-expiratory volumes, comparable contributions between the rib cage compartment (internal intercostal muscles) and the abdomen (abdominal muscles) were observed across inspiratory muscle loaded trials.

3.3 – Central haemodynamic effects of inspiratory loading:

Regardless of intensity, inspiratory loading induced a significant increase in cardiac output (CO; $p<0.001$) and heart rate (HR; $p<0.001$), however changes failed to reach statistical significance in stroke volume (SV; $p=0.071$; Figure 4).

Changes in these variables occurred mainly as significant increases from QB values at all loaded intensities. Significant increases in CO from an average resting value of 6.11±0.28 L/min to 7.74±0.31 L/min during 30% PI_{max} ($p=0.004$), 8.38±0.66 L/min during 50% PI_{max} ($p=<0.003$), and 8.36±0.57 L/min during 70% PI_{max} ($p=0.003$) were observed. SV increased significantly from a resting value of 84.74±3.69 ml to 97.17±4.18 ml at 30% PI_{max} ($p=0.008$), 98.04±5.56 ml at 50% PI_{max} ($p=0.013$) and 98.69±5.62 ml at 70% PI_{max} ($p=0.016$). A significant increase from an average resting HR of 73±4 beats/min was observed during 30% PI_{max} (81±3 beats/min; $p=0.008$), 50% PI_{max} (86±4 beats/min; $p=0.003$) and 70% PI_{max} (85±3 beats/min; $p=0.003$). Furthermore, significant increases in HR during inspiratory loaded intensities were also observed between 30% and 50% PI_{max} ($p=0.006$) and 30% and 70% PI_{max} ($p=0.013$). No significant differences were observed between loaded intensities for CO or SV.

Estimated systemic oxygen delivery (DO_2) was significantly increased from QB across all the trials ($p=0.001$; Figure 4d). These changes occurred as increases from a QB value of 1.21±0.05 L/min to 1.53±0.07 L/min, 1.66±0.13 L/min, and 1.65±0.10 L/min at 30% ($p=0.004$), 50% ($p=0.003$), and 70% ($p=0.003$) PI_{max} respectively. No significant changes were observed between loaded intensities.

3.4 – Gas exchange analysis:

Significant changes in partial pressure of end-tidal carbon dioxide ($P_{ET}CO_2$) and partial pressure of end-tidal oxygen ($P_{ET}O_2$) were observed throughout the trials ($p<0.001$; $p=0.002$; Figure 5). These changes in $P_{ET}CO_2$ occurred as significant reductions from QB (33.44±0.91 mmHg) during 30% (26.23±0.59 mmHg; $p=0.005$), 50% (25.87±1.02 mmHg; $p=0.005$) and 70% PI_{max} (24.30±0.82 mmHg; $p=0.005$; Figure 5a). Significant differences were also found between 30% and 70% PI_{max} ($p=0.017$) and 50% and 70% PI_{max} ($p=0.037$).

Changes in $P_{ET}O_2$ occurred as significant increases from QB (109.87±2.07 mmHg) during 30% PI_{max} (124.27±1.50 mmHg; $p=0.007$), 50% PI_{max} (123.55±2.02 mmHg; $p=0.007$) and 70% PI_{max} (124.97±1.81 mmHg; $p=0.005$; Figure 5b). No significant differences in $P_{ET}O_2$ were observed between loaded intensities.

3.5 – Inspiratory local muscle oxygenation responses:

There were no significant changes from baseline in oxyhaemoglobin (O_2HB) of the intercostal ($p=0.069$) and sternocleidomastoid ($p=0.137$) muscles (Figure 6a). Increases from baseline in intercostal O_2HB from QB reached significance at 50% PI_{max} (change: 3.44±1.5 µmol/L; $p=0.037$) and 70% PI_{max} (change: 3.97±1.5 µmol/L; $p=0.028$). No significant changes were found between loaded intensities in the intercostal muscle or between all trials, including QB, in the sternocleidomastoid.

A significant change from baseline in deoxyhaemoglobin (HHb) was found across trials in the sternocleidomastoid ($p=0.009$) but not in the intercostal ($p=0.840$; Figure 6b) muscles. Wilcoxon tests identified significant decreases in sternocleidomastoid HHb compared to QB values at 30% (change: -3.05±0.74 µmol/L; $p=0.008$) and 50% PI_{max} (change: -2.64±1.06 µmol/L; $p=0.038$).

Significant changes from baseline were observed in tissue oxygen saturation ($StiO_2$) across trials in the sternocleidomastoid ($p=0.010$) but not the intercostal ($p=0.062$; Figure 6c) muscles. These changes in the sternocleidomastoid muscle $StiO_2$ occurred due to significant increases from baseline at

30% (change: 3.67±0.68 %; p=0.008) and 50% PI_{max} (change: 4.00±0.93 %; p=0.011). Although the Friedman test reported no significance in intercostal $StiO_2$, subsequent Wilcoxon tests found significant increases from baseline at 30% (change: 2.09±0.68 %; p=0.013), 50% (change: 2.51±1.12 %; p=0.022) and 70% PI_{max} (change: 2.18±0.85 %; p=0.037) but not between loaded intensities.

No significant changes from baseline were observed in total haemoglobin (tHb) across trials for intercostal (p=0.069) or sternocleidomastoid (p=0.435; Figure 6d). Wilcoxon analysis found no differences between any trial for both intercostal and sternocleidomastoid muscles.

3.6 – Dyspnoea following inspiratory loading:

The participants dyspnoea scores were significantly different between loaded trials (p<0.001). An average Borg rating of 2.36±0.20 at 30% PI_{max} significantly increased to 3.45±0.21 at 50% PI_{max} (p=0.003) and 4.91±0.25 at 70% PI_{max} (p=0.003). Furthermore, a significant increase in dyspnoea rating was observed between 50 and 70% PI_{max} (p=0.002).

3.7 – Sex differences:

No significant differences were observed between sexes in total or compartmental thoracoabdominal tidal volume (when expressed as a fraction of FVC), CO, $P_{ET}CO_2$, $P_{ET}O_2$, and dyspnoea scores (Table 4).

	30%			50%			70%		
	Male	Female	*p*	Male	Female	*p*	Male	Female	*p*
CW V_T (%FVC)	57.67±10.27	60.51±3.39	0.476	63.52±8.66	69.03±5.42	0.476	65.33±9.46	66.66±3.95	0.762
RCp V_T (%FVC)	22.42±3.92	30.79±3.30	0.111	24.08±4.31	33.96±3.94	0.114	24.29±4.93	33.69±3.90	0.171
RCa V_T (%FVC)	14.39±3.63	12.91±1.54	0.730	15.79±2.99	15.01±1.69	0.762	18.17±3.07	14.84±1.16	0.352
Ab V_T (%FVC)	20.86±3.51	16.82±1.64	0.556	23.66±2.52	20.06±2.17	0.257	22.88±2.91	18.13±1.73	0.257
ΔCO (L/min)	1.94±0.56	1.26±0.34	0.329	2.17±0.57	2.39±1.10	0.792	1.65±0.65	2.97±0.74	0.126
$\Delta P_{ET}CO_2$ (mmHg)	-6.70±1.22	-7.54±0.94	0.476	-6.74±1.26	-8.12±1.05	0.476	-9.55±1.43	-8.85±1.18	0.610
$\Delta P_{ET}O_2$ (mmHg)	13.21±4.55	15.20±1.96	0.914	12.01±5.03	14.80±2.02	0.914	15.06±4.79	15.14±1.70	0.914
Dypnoea	2.33±0.21	2.40±0.40	0.792	3.50±0.22	3.40±0.40	1.000	5.17±0.40	4.60±0.24	0.329

Table 4. Sex differences in thoracoabdominal volumes, cardiac output, gas exchange, and dyspnoea rating during inspiratory muscle loading.

Note: CW, chest wall; RCP, pulmonary rib cage; RCA, abdominal rib cage; AB, abdomen; V_T, tidal volume; CO, cardiac output; $P_{ET}CO_2$, end-tidal carbon dioxide; $P_{ET}O_2$, end-tidal oxygen; Δ, change from baseline; FVC, forced vital capacity.

4.0 – Discussion:

In healthy young adults, application of tapered flow resistive loading across different inspiratory muscle loading intensities was associated with a 5-fold increase in tidal volume, a 30% increase in cardiac output, an increase in systemic and local respiratory muscle oxygen delivery, progressively increased levels of hyperventilation, and sensations of breathlessness. Tapered flow resistive loading expectedly increased the activation of inspiratory muscles but also of the expiratory muscles, thereby making this method an important training tool for global respiratory muscle training.

4.1 - Thoracoabdominal volume regulation:

The increased tidal volume during loaded phases occurred as a result of increased end-inspiratory and decreased end-expiratory thoracoabdominal volumes. An increase in end-inspiratory volume in pulmonary and abdominal rib cage compartments reflects an increased activity of the rib cage muscles such as the external intercostal and other accessory muscles, whilst increases in abdominal end-inspiratory volumes primarily reflects greater work of the diaphragm (Aliverti et al., 1997; Chihara et al., 1996). Decreased end-expiratory volume in pulmonary and abdominal rib cage compartments reflects increased work of the internal intercostal muscles and decreased abdominal end-expiratory volume reflects increased activity of the muscles of the abdominal wall (Dellacà et al., 2001). In the present study, the increased end-inspiratory thoracoabdominal volume was due to increased end-inspiratory volume in all three compartments, whereas the decreased end-expiratory thoracoabdominal volume was mainly due to decreased end-expiratory volume of the abdomen and abdominal rib cage compartments, similar to responses observed during exercise in healthy individuals (Aliverti et al., 1997; Iandelli et al., 2002).

Similar changes in operational thoracoabdominal volumes have previously been described during inspiratory muscle loading in healthy adults (da Fonsêca et al., 2019). The authors found significant increases in end-inspiratory pulmonary and abdominal rib cage volumes and observed increased electromyography activity in the sternocleidomastoid, scalene and intercostal muscles during

inspiratory muscle loading at both 20% and 40% PI_{max} in healthy adults compared to quiet breathing. These findings outline the importance of the rib cage muscles in increasing tidal volume expansion. da Fonsêca et al. (2019) also observed significant decreases in end-expiratory abdominal volumes during inspiratory muscle loading at 20% and 40% PI_{max}. The authors suggested that the decreased end-expiratory abdominal volume occurring alongside constant end-expiratory volume in rib cage compartments was a mechanism which supported diaphragmatic contraction by increasing the muscles' pre-inspiratory length and preventing excessive shortening (Aliverti et al., 1997).

In the present study, end-expiratory abdominal volume was significantly decreased at all inspiratory muscle loaded intensities, whereas end-expiratory abdominal rib cage volume was significantly decreased at 50% and 70% PI_{max}, and end-expiratory pulmonary rib cage volume was significantly decreased at 70% PI_{max} only. These findings suggest that the muscles of the abdominal wall predominantly contributed to reduce end-expiratory volume, however, as the inspiratory load was increased, expiratory muscles of the rib cage (i.e. internal intercostals) also become activated to help further decrease end-expiratory thoracoabdominal volume, thus expanding tidal volume. Furthermore, expiratory flow rate was also increased from quiet breathing with increasing inspiratory muscle loading also reflecting increased abdominal muscle recruitment (Martin et al., 1982). The present study supports previous research in that when ventilatory demand is increased, abdominal muscle recruitment during expiration is the main reason end-expiratory thoracoabdominal volume is reduced below functional residual capacity in healthy people (Aliverti et al., 1997; Iandelli et al., 2002). Thus it is likely that, if participants were unable to generate enough inspiratory pressure to overcome the initial threshold to open the valve of the training device at high inspiratory muscle loaded intensities during the fixed two seconds of inspiration for each breath, then their expiratory muscles of both the abdominal wall and the rib cage compartments contributed to increase tidal volume by reducing end-expiratory volumes. An inability to overcome the initial threshold at high intensities may explain the significant decrease in end-inspiratory thoracoabdominal volume from 50% PI_{max} to 70% PI_{max}.

Furthermore, it is well understood that reduced functional residual capacity will lengthen diaphragmatic fibres placing them at a more favourable length-tension relationship so they can

produce more pressure for a given neural output (Kikuchi et al., 1991; Martin et al., 1982). In turn, this will protect the diaphragm against contractile fatigue and improve diaphragmatic neuromechanical coupling (Laghi et al., 2014). This active contraction of abdominal muscles will store elastic energy, meaning that part of the subsequent inspiration is achieved with less activation of inspiratory muscles, thus enhancing the abdominal muscles ability to act as accessory inspiratory muscles by assisting the diaphragm and reducing inspiratory muscle work (Kikuchi et al., 1991). Kikuchi et al. (1991) also suggested that reduced functional residual capacity during inspiratory muscle loading may be due to behavioural control to minimise the sensation of dyspnoea and increase inspiratory muscle endurance.

In the present study, end-inspiratory thoracoabdominal volume was increased during inspiratory muscle loading in all compartments across all intensities. Inspiratory reserve volume was decreased from ~2.0 L during quiet breathing to 0.60 L, 0.32 L, and 0.55 L when breathing at inspiratory loads equivalent to 30%, 50%, and 70% PI_{max} respectively. This encroachment of tidal volume into the inspiratory reserve volume during inspiratory muscle loading may be one explanation to the increased dyspnoea ratings of the participants (O'Donnell et al., 2001). A “threshold” at where tidal volume expands to reach a critically low inspiratory reserve volume of ~0.5 L below total lung capacity has previously been reported (O'Donnell et al., 2007; O’Donnell et al., 2006). As mentioned above, the decrease in end-expiratory thoracoabdominal volume in our healthy participants during inspiratory muscle loading was therefore a strategy to further increase tidal volume expansion without further encroaching into their inspiratory reserve volume.

The use of tapered flow resistive loading by participants in the present study could explain the increases in end-inspiratory thoracoabdominal volume. The reduction in absolute load during inspiration once the initial threshold load is overcome consequently maintains the pressure load applied to the inspiratory muscles at the same relative intensity across the vital capacity (Langer et al., 2015). Furthermore, tapered flow resistive loading allows end-inspiratory volume to increase towards total lung capacity and greater external work be performed per breath compared to mechanical threshold loading where external work decreases during loading >60% PI_{max} due to impairment of

tidal volume expansion and premature termination of inspiration (Langer et al., 2015; McConnell & Griffiths, 2010).

Compartmental contribution to end-inspiratory and end-expiratory thoracoabdominal volumes remained fairly consistent across all loaded intensities with the predominant compartments being the pulmonary rib cage at end-inspiration and the abdomen at end-expiration. Research conducted by de Souza et al. (2016) also utilised optoelectronic plethysmography to measure thoracoabdominal volume changes during quiet breathing, moderate inspiratory resistance (40% PI_{max}) and a PI_{max} manoeuvre and found the fractional contribution of the pulmonary rib cage compartment increased significantly during 40% and at PI_{max} compared to quiet breathing. The contribution of the abdominal compartment decreased during 40% and at PI_{max} and the abdominal rib cage compartment increased during 40% and decreased at PI_{max}. However, as the authors did not report whether the reported changes in compartmental contribution were reflected within end-inspiratory or end-expiratory volumes, we are unable to draw solid comparisons. de Souza et al. (2016) also reported lower tidal volume (0.9 litres) and minute ventilation (11.6 L/min) in young healthy individuals during moderate inspiratory loading at 40% PI_{max} compared to the present study of ~3.0 litres and ~30 L/min respectively. This may be due to the application of tapered flow resistive loading in the present study compared to mechanical threshold loading in de Souza and colleagues' study, as these participants likely experienced impairment in tidal volume expansion due to the constant pressure throughout inspirations. Conversely, the tapered load applied in the present study allowed tidal volume, and consequently minute ventilation, to reach levels threefold of those observed by de Souza et al. (2016).

4.2 – Central haemodynamic and inspiratory muscle oxygenation responses:

We found a significant increase of 30-40% in cardiac output during inspiratory loaded breathing suggesting that tapered flow resistive loading placed a substantial load on the cardiovascular system. This reflects an increased energy requirement of the respiratory muscles as only these muscles were contracting. A similar increase in cardiac output has previously been reported in athletes during resting isocapnic hyperpnoea trials at ~80 L/min (Vogiatzis et al., 2009a). During hyperpnoea, this

study found that blood flow to the intercostal muscles increased linearly with work of breathing and cardiac output, with no change in intercostal muscle deoxyhaemoglobin or tissue oxygen saturation with increasing levels of respiratory muscle work. It was suggested that increasing the oxygen demand of the respiratory muscles was met by proportionally increased blood flow and oxygen delivery, emphasising the central haemodynamic response to respiratory muscle work.

An increase in cardiac output in the present study was accompanied by increased systemic oxygen delivery, increased oxyhaemoglobin, decreased deoxyhaemoglobin concentration at lower intensities, and increased tissue oxygen saturation. These findings were most pronounced in the sternocleidomastoid compared to the intercostal muscles, and combined, suggest that short bouts of tapered flow resistive loading cause an increase in inspiratory muscle perfusion and oxygen supply from arterial blood. This causes a decrease in deoxyhaemoglobin and creates a mismatch between oxygen delivery to, and extraction from, the inspiratory muscles, resulting in increased tissue oxygen saturation (Grassi et al., 2003).

Our lack of findings relating to deoxygenation of the sternocleidomastoid contrast with previous literature. In a systematic review investigating the oxyhaemoglobin, deoxyhaemoglobin and tissue oxygen saturation responses during inspiratory muscle loading, Tanaka et al. (2018) concluded that the sternocleidomastoid is the most vulnerable to deoxygenation. Studies in healthy individuals, however, have reported no changes or even increases in oxyhaemoglobin of the sternocleidomastoid and intercostal muscles during inspiratory muscle loading (Basoudan et al., 2016; Shadgan et al., 2011) compared to decreases observed in patients with chronic obstructive pulmonary disease (Reid et al., 2016). It should be noted, however, that these were incremental inspiratory muscle loading trials and do not reflect a normal bout of inspiratory muscle training. It is likely that the tendency of an increased oxygenation response to tapered flow resistive loading observed in the present study was due to the short duration of loading, and if participants were allowed to continue for longer, a deoxygenation response of the inspiratory muscle, similar to those observed previously, would likely occur.

Both unchanged values and an initial increase from resting values in tissue oxygen saturation have been observed with increasing rates of minute ventilation in the transition from rest to exercise in both healthy individuals and patients with COPD (Grassi et al., 2003; Vogiatzis et al., 2009b). An unchanged muscle oxygenation response at the transition from rest to exercise reflects a tight coupling between cardiac output and oxygen uptake (Grassi et al., 2003), whereas an increased muscle oxygenation response is attributed to the washout of deoxygenated venous blood (Grassi et al., 2003; Vogiatzis et al., 2009b). This response during increased rates of minute ventilation at the onset of exercise, and in the present studies case, the onset of inspiratory muscle loading, could reflect either a metabolic inertia, where the activation of mitochondrial respiration and muscle oxygen extraction is delayed (Grassi et al., 2003). Alternatively, this response may reflect an early increase in intracellular myoglobin deoxygenation, offset by a decrease in intravascular haemoglobin deoxygenation due to a pump-mediated increase in local perfusion (DeLorey et al., 2003).

4.3 – Gas exchange responses:

End-tidal CO_2 decreased significantly from baseline levels at all inspiratory loaded intensities in the present study. Previous literature has reported a fall in end-tidal CO_2 of 16.2 mmHg from baseline over two bouts of 30 inspiratory muscle loaded breaths at 40% PI_{max} (Ross et al., 2007). The participants in this study were instructed by Ross and colleagues (2007) to perform each loaded inspiration near residual volume and terminate toward total lung capacity with no further instructions given relating to breathing pattern. Due to the increase in tidal volume during inspiratory muscle loading, the authors noted a decreased breathing frequency from resting values and explained this as an advantageous pattern adopted to offset the effects of hypocapnia (Ross et al., 2007). In the present study, we controlled breathing frequency but did not give specific instructions relating to tidal volume. The fall of ~7-9 mmHg in end-tidal CO_2 during inspiratory loading observed in the present study compared to 16.2 mmHg in the work of Ross et al. (2007) is likely due to a much shorter duration of loading (10 breaths compared to 2x30 breaths) and a lower minute ventilation (~27-30 L/min compared to 43.1 L/min). Nevertheless, our study shows that even a short bout of inspiratory

muscle loading can result in significant reductions in end-tidal CO_2 regardless of intensity, highlighting an important caveat to recommended methods of inspiratory muscle training (30 continuous breaths) (McConnell, 2013).

4.4 – Limitations of the study:

The instructions provided regarding breathing frequency (2s inspiration, 4s expiration) is likely to have affected the level of hypocapnia experienced by the participants within this study. If breathing frequency was not controlled in the present study, the participants may have adopted a lower breathing frequency to avoid hypocapnia (Romer & McConnell, 2003) due to the increased tidal volume when using the tapered flow resistive loading device compared to studies utilising mechanical threshold loading (de Souza et al., 2016; McConnell & Griffiths, 2010).

Furthermore, although PI_{max} manoeuvres were performed from residual volume, no instructions were provided to allow participants to initiate their breaths from residual volume during the inspiratory muscle loading trials. Participants, therefore, initiated each loaded inspiration from functional residual capacity where, due to the length-tension relationship of the respiratory system and/or additional elastic recoil of the lung and chest wall, PI_{max} could be lower than when measured at residual volume (Windisch et al., 2004). This implies that the intensities applied relative to PI_{max} in this study could be higher than reported and may explain the increased dyspnoea at higher intensities.

If participants were instructed to exhale to residual volume following each loaded inspiration as observed in previous studies (Langer et al., 2015; Van Hollebeke et al., 2020), and should breathing frequency be reduced from 10 breaths/min to ~6 breaths/min, then perhaps lower levels of dyspnoea and hypocapnia would have been observed. For the purpose of this study, however, we were interested in the behaviour of end-expiratory and end-inspiratory volumes adopted by the participants between different levels of inspiratory muscle loading which would not have been observable if participants were instructed to initiate breaths from residual volume.

Surface electromyography (sEMG) of both inspiratory (i.e. external intercostals and sternocleidomastoid) and expiratory (i.e. rectus abdominus) muscles were unavailable as measurements of respiratory muscle activation. The absence of mean arterial blood pressure measurements alongside heart rate recordings also meant that we were unable to provide evidence of a metaboreflex response at any intensity of tapered flow resistive loading, which has previously been observed in healthy adults during mechanical threshold loading (McConnell & Griffiths, 2010).

4.5 – Implications for inspiratory muscle training:

While previous research has clearly outlined the benefits of tapered flow resistive loading over the more commonly used mechanical threshold loading (Langer et al., 2015), the present study highlights some of the adverse effects of this specific training method including hypocapnia caused by hyperventilation, along with significantly increased dyspnoea sensations with increasing intensity of training. Beneficial physiological responses, such as increased respiratory muscle recruitment and cardiac output were similar between 50% and 70% PI_{max}, and adverse physiological responses, such as decreased end-tidal CO_2 and increased dyspnoea scores, were significantly greater at 70% PI_{max} in the present study. These findings suggest that optimal intensity for this specific form of inspiratory muscle training at the beginning of a training programme is at 50% PI_{max} due to maximising beneficial physiological responses whilst minimising adverse responses, namely hyperventilation and breathlessness in healthy young adults. This intensity closely resembles the optimal intensity of 60% PI_{max} during mechanical threshold loading in healthy individuals in terms of maximising external work output as reported by McConnell and Griffiths (2010).

It is important to note our finding that, with increasing load, participants initiated their inspirations during inspiratory muscle loading at lower end-expiratory volumes, suggesting that in line with previous studies (Langer et al., 2015; Van Hollebeke et al., 2020), tapered flow resistive loading should be performed at residual volume. Due to our interests relating to how the participants regulated end-expiratory volumes depending on the intensity of tapered flow resistive loading, we did not instruct participants to reach residual volume within this study. However, future studies should

investigate dyspnoea and hypocapnia levels during tapered flow resistive loading from residual volume and with a decreased breathing frequency to determine whether the optimal intensity when training from these lower lung volumes is different to that observed in the present study.

4.6 – Conclusions:

The application of short bouts of tapered flow resistive loading at a fixed breathing frequency in healthy adults has shown that this method of inspiratory muscle training places a load not only the inspiratory muscles, but also on the expiratory muscles. This suggests that tapered flow resistive loading is a suitable tool for both inspiratory and expiratory (global) muscle training.

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Figure 1. Volume changes of the a) total thoracoabdomen, b) the pulmonary rib cage, c) the abdominal rib cage and d) the abdomen. *Open symbols* indicate end-inspiration, *closed symbols* indicate end-expiration and *triangles* indicate thoracoabdominal volume at total lung capacity (TLC; $V_{CW, TLC}$). *Dashed line* indicates end-expiratory volume (V_{EI}) at quiet breathing (QB). *Significant difference from QB value. **Significant difference between loaded intensities.

Figure 2. Contribution of the pulmonary rib cage (RCp), the abdominal rib cage (RCa) and the abdomen (Ab) to a) total end-inspiratory and b) total end-expiratory thoracoabdominal volumes during the inspiratory muscle loading phases at 30, 50 and 70% PI_{max}. [a] significant difference from 30%, [b] significant difference from 50%, *significant difference between other thoracoabdominal compartment.

Figure 3. Rib cage (RC) and abdomen (AB) end-inspiratory (left) and end-expiratory (right) contributions of the thoracoabdominal volume during 30% PI_{max} (a and b), 50% PI_{max} (c and d), and 70% PI_{max} (e and f). *Note:* for end-expiratory volumes, negative values towards the left side of the graphs reflect increased abdominal muscle recruitment.

Figure 4. Central haemodynamic changes in a) cardiac output (CO), b) stroke volume (SV), c) heart rate (HR), and d) estimated systemic oxygen delivery (DO_2). *Significant difference from QB value. **Significant difference between loaded intensities.

Figure 5. Partial pressure end-tidal (P_{ET}) changes in a) carbon dioxide (CO_2) and b) oxygen (O_2). *Significant difference from QB value. **Significant difference between loaded intensities.

Figure 6. Delta (Δ) changes in a) oxyhaemoglobin (O_2HB), b) deoxyhaemoglobin (HHb), c) tissue oxygen saturation ($StiO_2$), and d) total haemoglobin (tHb) in the intercostal (*circles*) and the sternocleidomastoid (*triangles*) muscles. *Significant difference from QB value.

Figure 1.

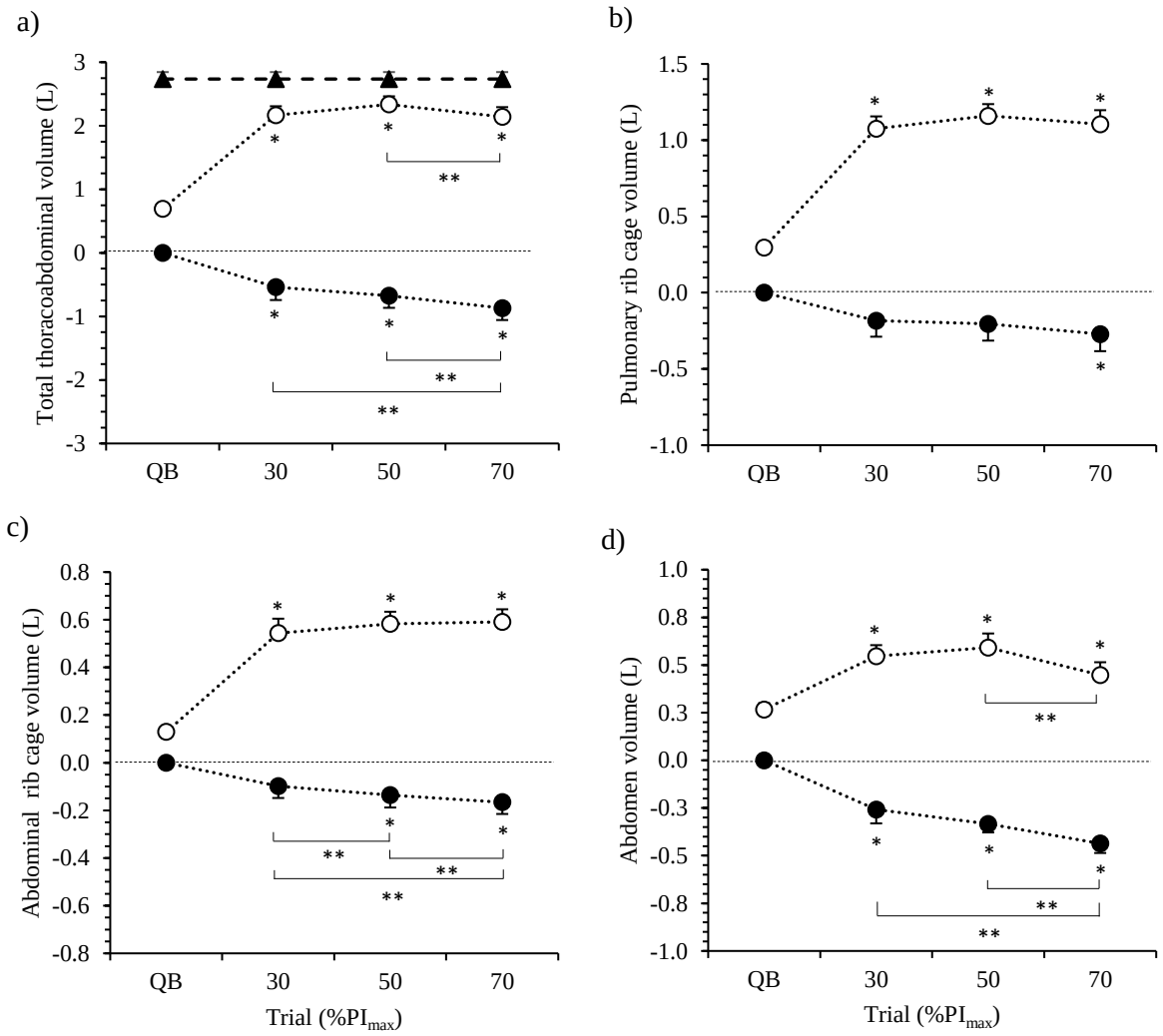


Figure 2.

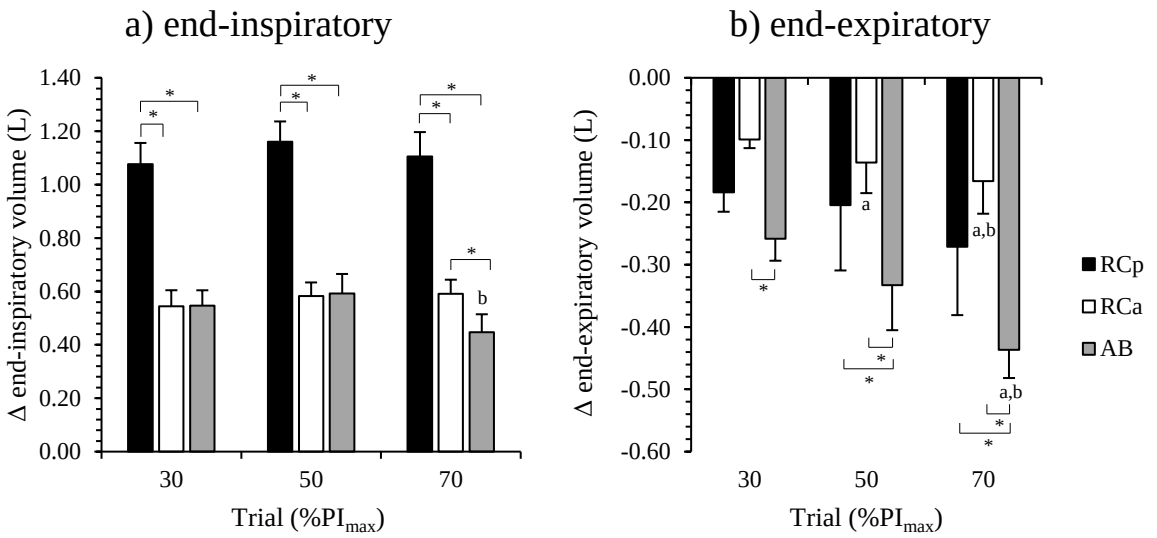

a) end-inspiratory
b) end-expiratory
Δ end-inspiratory volume (L)
Δ end-expiratory volume (L)
1.40
1.20
1.00
0.80
0.60
0.40
0.20
0.00
-0.10
-0.20
-0.30
-0.40
-0.50
-0.60
30
50
70
Trial (%PImax)
a
a,b
b
*
RCp
RCa
AB

Figure 3.

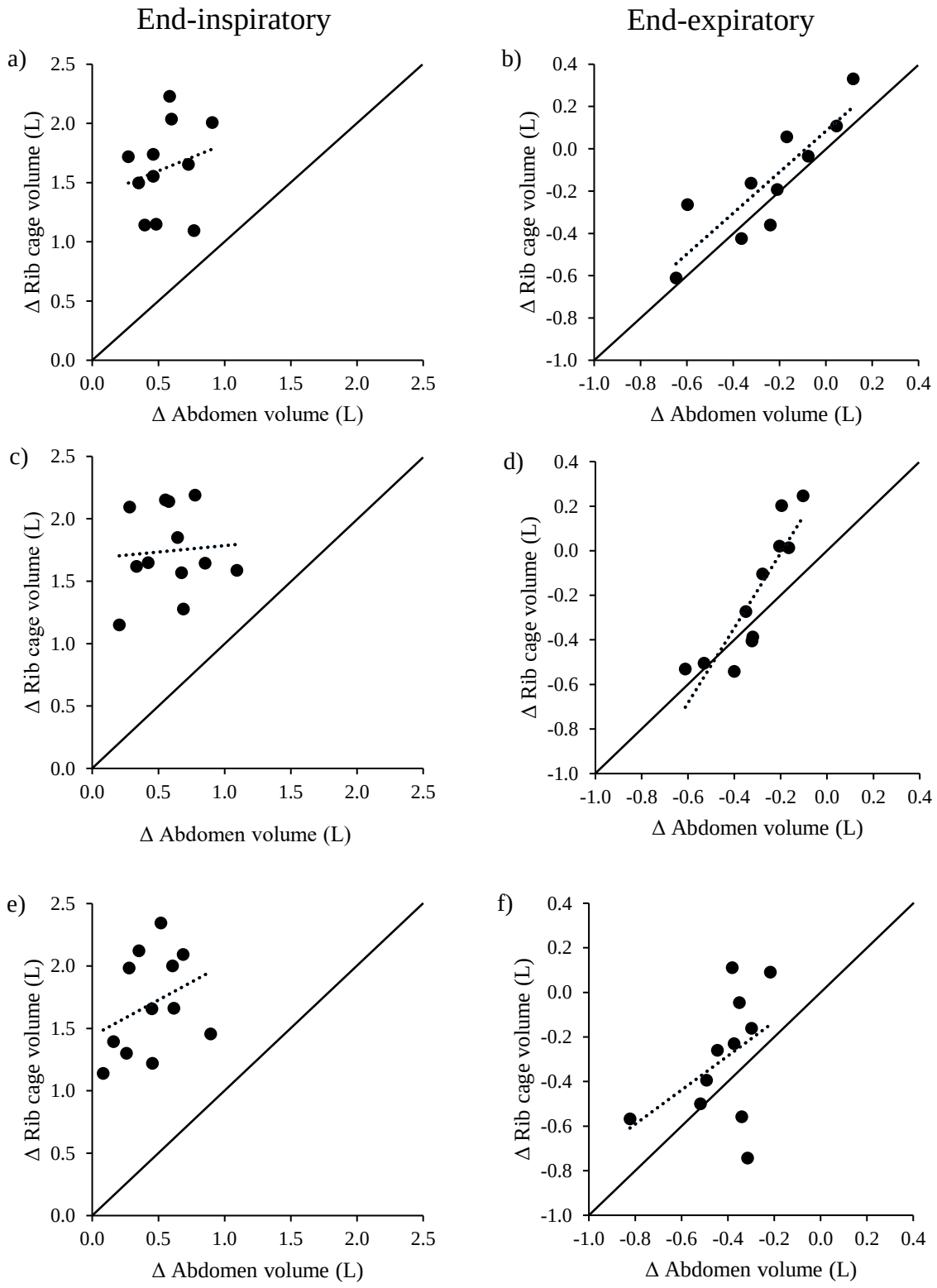

End-inspiratory
End-expiratory
a)
b)
c)
d)
e)
f)
Δ Rib cage volume (L)
Δ Abdomen volume (L)
0.0
0.5
1.0
1.5
2.0
2.5
-1.0
-0.8
-0.6
-0.4
-0.2
0.0
0.2
0.4

Figure 4.

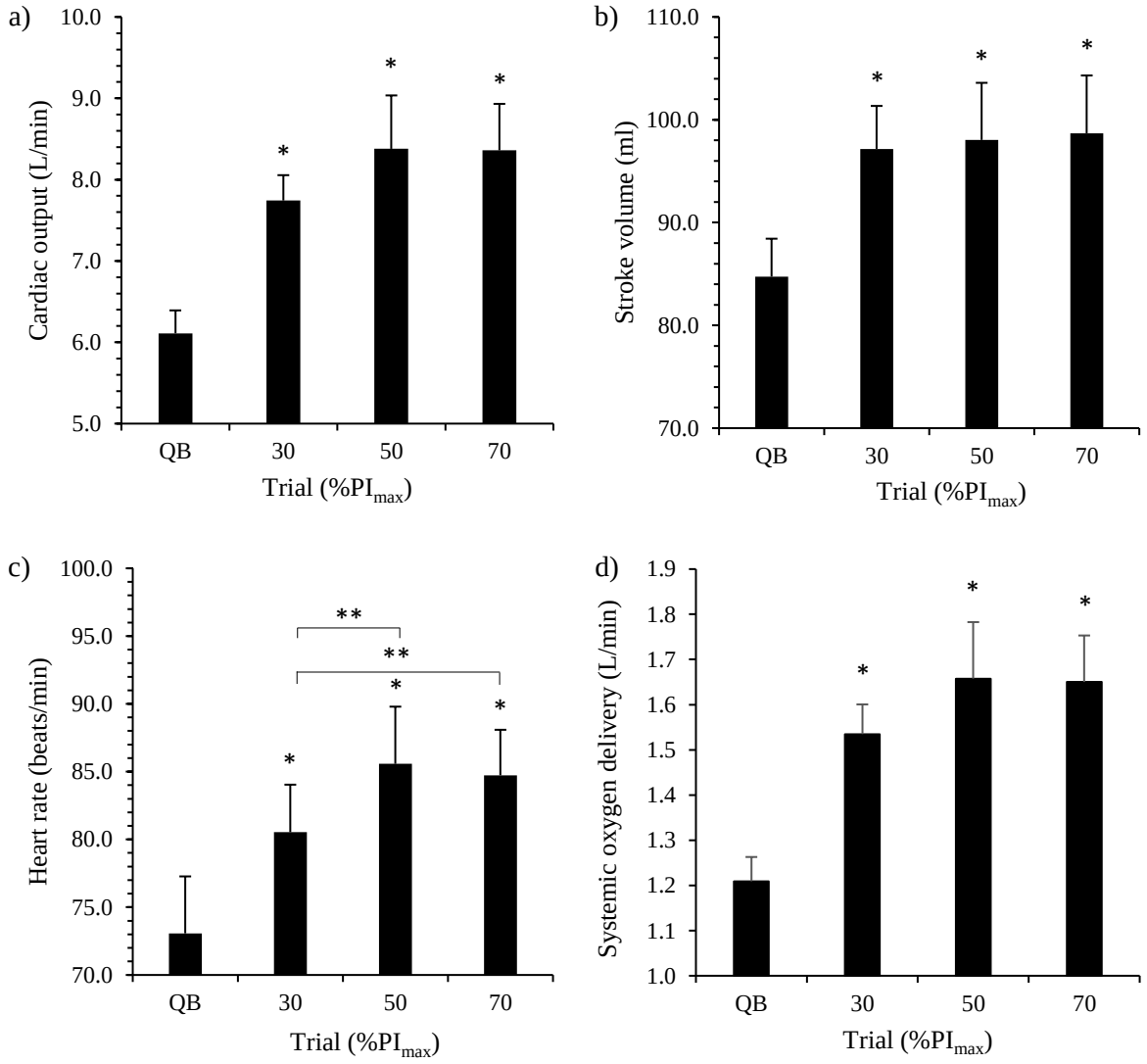

a)
Cardiac output (L/min)
10.0
9.0
8.0
7.0
6.0
5.0
QB
30
50
70
Trial (%PI$_{max}$)
b)
Stroke volume (ml)
110.0
100.0
90.0
80.0
70.0
QB
30
50
70
Trial (%PI$_{max}$)
c)
Heart rate (beats/min)
100.0
95.0
90.0
85.0
80.0
75.0
70.0
**
**
QB
30
50
70
Trial (%PI$_{max}$)
d)
Systemic oxygen delivery (L/min)
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
QB
30
50
70
Trial (%PI$_{max}$)

Figure 5.

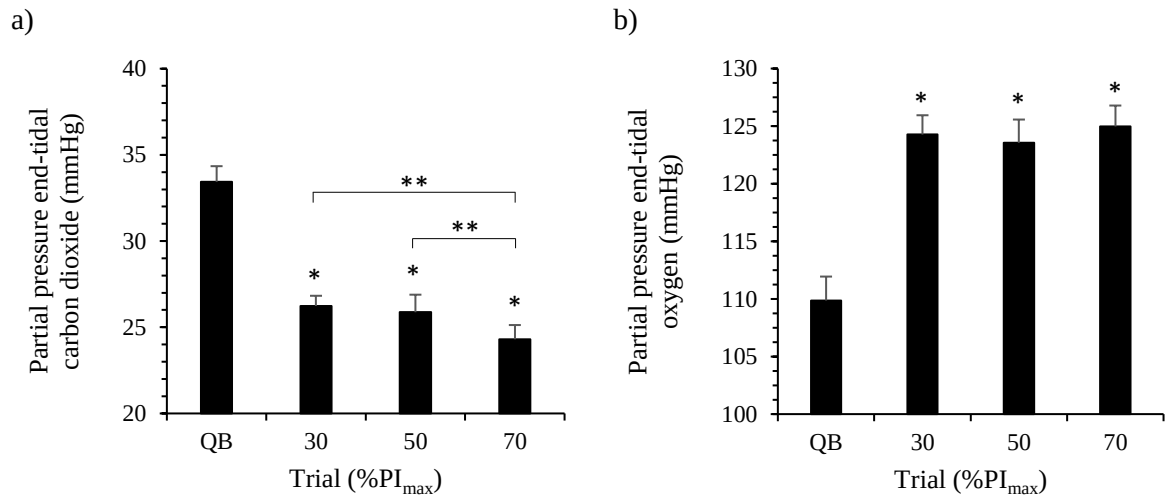
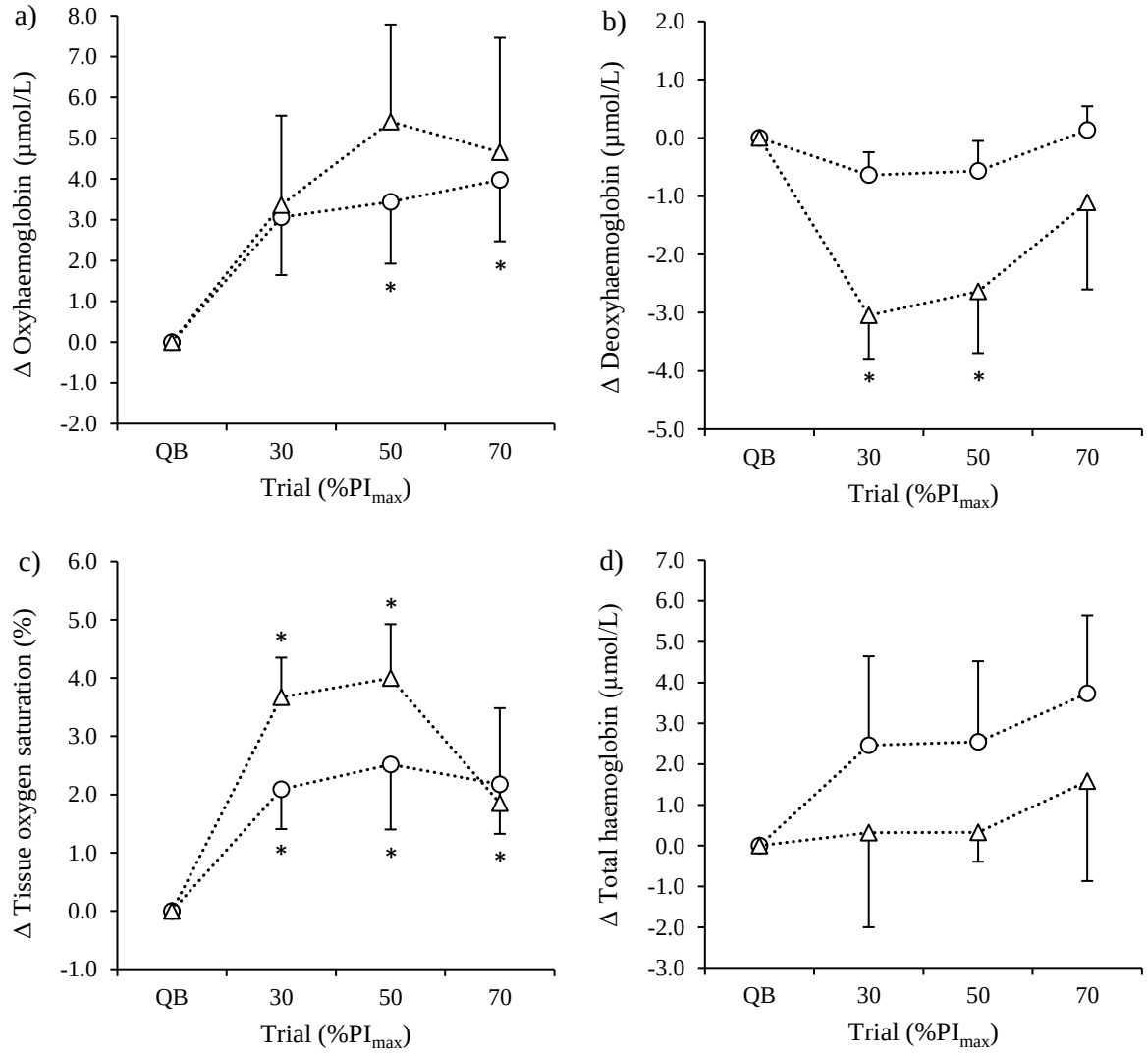

a)
Partial pressure end-tidal carbon dioxide (mmHg)
40
35
30
25
20
**
**
*
*
*
QB
30
50
70
Trial (%PImax)
b)
Partial pressure end-tidal oxygen (mmHg)
130
125
120
115
110
105
100
*
*
*
QB
30
50
70
Trial (%PImax)

Figure 6.


a)
Δ Oxyhaemoglobin (µmol/L)
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
-2.0
QB
30
50
70
Trial (%PI$_{max}$)
b)
Δ Deoxyhaemoglobin (µmol/L)
2.0
1.0
0.0
-1.0
-2.0
-3.0
-4.0
-5.0
QB
30
50
70
Trial (%PI$_{max}$)
c)
Δ Tissue oxygen saturation (%)
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
QB
30
50
70
Trial (%PI$_{max}$)
d)
Δ Total haemoglobin (µmol/L)
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
-2.0
-3.0
QB
30
50
70
Trial (%PI$_{max}$)