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The time course of exercise-induced expiratory and inspiratory muscle fatigue

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Time course of exercise-induced respiratory muscle fatigue

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ABSTRACT

Inspiratory muscle fatigue develops during exercise prior to intolerance. The expiratory muscles are less resistant to fatigue compared to the inspiratory muscles, but the time-course of inspiratory and expiratory muscle fatigue during exercise has not been compared. Ten healthy adults (25 ± 5 years; 2 females) cycled on three separate occasions at 25% of the difference between estimated critical power and peak ramp incremental power (severe-intensity domain) for: 1) 100% of time to the limit of tolerance (T_{LIM}; 10.2 ± 2.6 min); 2) 75% T_{LIM} (7.7 ± 1.9 min); and 3) 50% T_{LIM} (5.1 ± 1.3 min). Expiratory and inspiratory muscle fatigue were quantified as the pre- to post-exercise reduction in the gastric (Pga_{tw}) and diaphragm (Pdi_{tw}) twitch pressure response to magnetic stimulation of the thoracic and cervical nerves, respectively. Pga_{tw} and Pdi_{tw} were reduced from baseline values after 50% T_{LIM} (11.9 ± 8.2% and 9.5 ± 9.2%, both $P < 0.05$). The magnitude of expiratory and inspiratory muscle fatigue increased progressively at 75% T_{LIM} (20.0 ± 12.6% and 15.2 ± 10.1%, both $P < 0.05$) and 100% T_{LIM} (30.3 ± 15.6% and 22.4 ± 12.5%, both $P < 0.05$), but there was no difference between muscle groups ($P > 0.05$). Expiratory and inspiratory muscle fatigue develops relatively early during severe intensity exercise and increases progressively in magnitude by exercise intolerance. The onset and progression of respiratory muscle fatigue during exercise is not different between the expiratory and inspiratory muscles.

NEW & NOTEWORTHY

During severe exercise, expiratory and inspiratory muscle fatigue develops by ~50% of tolerable exercise duration. The magnitude of expiratory and inspiratory muscle fatigue increases progressively towards exercise intolerance but is not different between muscle groups; this is despite the expiratory muscles being less fatigue-resistant. Inspecting esophageal and gastric twitches via cervical stimulation, we speculate that the progressive magnitude of exercise-induced inspiratory muscle fatigue is a function of recruitment and fatigue of the accessory inspiratory muscles.

INTRODUCTION

The development of inspiratory and expiratory muscle fatigue in response to heavy-to-severe intensity constant power exercise is well established. Indeed, a pre- to post-exercise reduction in the diaphragm twitch pressure (Pdi_{tw}) and gastric twitch pressure (Pga_{tw}) response to cervical and thoracic nerve stimulation, respectively, has been reported consistently across a range of populations (1-6). The development of respiratory muscle fatigue with exercise may play a role in limiting exercise performance, potentially via an increased perception of dyspnea and the activation of a respiratory muscle metaboreflex (7). The factors responsible for the development of exercise-induced respiratory muscle fatigue are now relatively well understood. The most consistent evidence of respiratory muscle fatigue occurs in response to exercise incurring a high and sustained power of breathing (Pb), under conditions of limited cardiac output to meet the requirements of the respiratory and locomotor muscles (4, 7-9). Indeed, it has been shown that diaphragm fatigue does not occur when the magnitude and duration of diaphragmatic work incurred during exercise is mimicked at rest (9). Moreover, such fatigue does not appear to occur until the pressures developed by the diaphragm are voluntarily increased twofold greater than required during severe intensity whole-body exercise (9). These data suggest the ‘optimal’ conditions for exercise-induced diaphragm fatigue are when increases in diaphragmatic work occur at a time when the diaphragm must compete with locomotor muscles for its share of the available cardiac output. However, few studies have examined the time-course of exercise-induced respiratory muscle fatigue *during* exercise.

In a seminal study by Johnson et al. (4) in 1993, it was speculated that diaphragm fatigue may occur relatively early during high intensity constant power exercise, and that such fatigue may contribute to the pattern of respiratory muscle recruitment. For example, the plateau in diaphragm force output during the mid-to-late phase of exercise, when ventilation and esophageal force output are increasing, suggests that the accessory respiratory muscles may increasingly contribute to the hyperventilatory response as exercise duration proceeds (4). Indeed, the authors reported a lower magnitude of diaphragm fatigue after exercise in individuals that minimized the contribution of the diaphragm to ventilatory work. Since then, further studies that have sought to measure inspiratory muscle fatigue during exercise have presented mixed findings. For example, it has been reported that diaphragm fatigue: 1) does *not* occur and instead its function actually *progressively increases* during exercise (10); 2) does occur at two-thirds of time to the limit of tolerance (T_{LIM}) and is not progressive in magnitude (11); and that 3) diaphragm fatigue occurs relatively late during exercise (75% T_{LIM}) and increases in magnitude by exercise intolerance (100% T_{LIM}) (1). The inconsistent findings of these aforementioned studies may, in part, be due to methodological limitations in the assessment of diaphragm fatigue during exercise. These limitations include not performing exercise to the point of intolerance, failing to account for muscle potentiation (10), and frequent pausing of the exercise trial which likely compromised exercise economy and the measurement of respiratory muscle function (10, 11).

In contrast, the time-course of exercise-induced expiratory muscle fatigue has not been investigated. The expiratory muscles are phenotypically and functionally less fatigue-resistant in comparison to the diaphragm, exhibiting a lower but more varied proportion of type I muscle fibers (12, 13), a decreased oxidative capacity (14), and a reduced metabolic efficiency (15). In contrast to the diaphragm, the magnitude of expiratory muscle fatigue is similar in response to intolerable heavy intensity exercise and short (5 min) or long duration (10 min) severe intensity exercise (3). Thus, it can be argued that this greater ‘fatigability’ of expiratory compared with inspiratory muscles may lead to an earlier onset of expiratory muscle fatigue during severe intensity exercise. However, to date, this hypothesis has not been investigated. Further understanding the time-course of exercise-induced respiratory muscle fatigue will enable identification of the relative time point or ‘phase’ of exercise during which the inspiratory and expiratory muscles may begin to limit exercise performance. This knowledge may be important for informing the design, timing, and targeting of therapeutic interventions, such as respiratory muscle training, by identifying when and in which muscles respiratory muscle fatigue is most likely to emerge.

The aim of this study was to compare the time-course or ‘temporality’ of exercise-induced inspiratory and expiratory muscle fatigue during severe intensity constant-power exercise performed until volitional intolerance. It was hypothesized that: 1) exercise-induced expiratory muscle fatigue would occur at an earlier time-point than inspiratory muscle fatigue; and 2) inspiratory and expiratory muscle contractility would decrease with increasing durations of exercise. An exploratory aim was to examine the relative contribution of the diaphragm and accessory inspiratory muscles to global inspiratory muscle fatigue over time during severe intensity exercise.

METHODS

Participants

Ten healthy participants (sex, 8 males; age, 25 ± 5 years; stature, 1.77 ± 0.07 m; body mass, 72 ± 10 kg) with resting pulmonary function values within normal limits (forced vital capacity, 103 ± 12% of predicted; forced expiratory volume in 1 s, 98 ± 10% of predicted; maximum voluntary ventilation, 113 ± 18% predicted) participated in the study after providing written informed consent. All participants were physically active and free from respiratory, cardiovascular, or metabolic disease. The experimental procedures were approved by the University of Leeds Faculty of Biological Sciences Research Ethics Committee and conformed to the Declaration of Helsinki (approval REF: BIOSCI 17-016). Ten of the subjects participated in our previous study investigating the differential effects of exercise intensity and tolerable duration on exercise-induced diaphragm and expiratory muscle fatigue (3); the hypotheses tested, key comparisons, and primary outcomes in the present study do not overlap with previous analyses.

Experimental Overview

All experimental procedures were completed over the course of four visits to the laboratory, each separated by a minimum of 48 h (Figure 1). The participants abstained from food for 3 h, caffeine for 12 h, and alcohol and exercise for 24 h before each laboratory visit. During the first visit, resting pulmonary function was assessed according to standard procedures (16) and a ramp incremental sprint test (RIST) was performed (3, 17) on an electromagnetically braked cycle ergometer (Excalibur, Lode, Groningen, The Netherlands) for the determination of maximal oxygen uptake ($\dot{V}O_{2max}$), peak ramp power (P_{peak}), and estimated critical power (CP). At the second visit, the participants performed constant-power cycle exercise to the limit of tolerance at ~25% of the difference (Δ) between CP and P_{peak} (*i.e. severe intensity domain;* Δ25). The order of visits 3 and 4 was randomized between the participants. During these visits, the participants performed constant-power cycling exercise at the same power output as in visit 2, for 75% of T_{LIM} and 50% of T_{LIM}. Inspiratory and expiratory abdominal muscle contractility were assessed before and up to 30 min after each constant-power exercise test by measuring Pdi_{tw} and Pga_{tw} in response to magnetic stimulation of the phrenic and thoracic nerve roots, respectively. Thus, this experimental design allowed for the determination of the time-course of the development of inspiratory and expiratory muscle fatigue during severe intensity constant-power exercise.

Ramp Incremental Sprint & Constant Power Exercise Tests

Ramp Incremental Sprint Test

After 4-6 min of cycling at 20 W, power output was increased linearly at a rate of 25-30 $W \cdot min^{-1}$. Each participant increased their pedal cadence progressively as a smooth function of time until they reached their preferred target cadence between 80-100 rpm; this was maintained until the limit of tolerance, defined as the point at which cadence dropped below 60 rpm despite strong verbal encouragement. Immediately following exercise intolerance, the cycle ergometer was switched to linear (cadence-dependent) mode and each participant accelerated their pedal cadence rapidly and cycled at a maximum effort for 3 min; a duration sufficient to evoke a stable power output that closely approximates CP (Burnley et al., 2006, Vanhatalo et al., 2007). The linear factor (i.e., power/cadence^2) for the sprint phase was set prior to exercise for each participant, assuming a power output of 2.5-3.5 times body mass and a pedal cadence of 80 rpm (3). Sprint power (SP) was calculated as the mean power output after a plateau in cadence had occurred between consecutive 30 s time bins (Murgatroyd et al., 2014).

Constant Power Exercise Tests

Each participant performed a warm-up of cycling at 20 W for 2 min and 30% P_{peak} for 2 min. Immediately following the warm-up, power output was increased to Δ25 and the participants maintained their target cadence (± 5 rpm) until: 1) intolerance, defined as the point at which pedal cadence fell below 60 rpm despite strong verbal encouragement; 2) 75% of T_{LIM}; or 3) 50% of T_{LIM}. Inspiratory and expiratory gas flow was measured using a non-heated linear pneumotachometer (model 4813, Hans Rudolph, Kansas City, MO, USA), and the flow signal was used to determine periods of inspiration and expiration for subsequent pressure time product (PTP) analyses only. Ventilatory and pulmonary gas exchange indices (breath by breath) were measured using a calibrated bidirectional Pitot tube sensor, connected in series with the linear pneumotachometer, for volume measurement and galvanic (O_2) and non-dispersive infrared (CO_2) sensors for gas analysis (Ultima Cardio 2, MGC Diagnostics, St Paul, MN, USA). Heart rate (HR) was measured via 12-lead electrocardiogram (X12, Montara Instrument; Milwaukee, WI, USA). Capillary blood was sampled from an earlobe to determine blood lactate concentration ($[La^-]_B$) at rest, every 2.5 min during exercise, and within 15 s of exercise termination (Lactate Pro 2, Arkray Factory Inc., Shiga, Japan). Ratings of perceived leg discomfort and dyspnea were obtained using a modified Borg CR10 scale at rest, at the end of the 'warm-up', every 2 min during exercise, and within 15 s of exercise termination.

Respiratory Pressures

Esophageal (Pes) and gastric (Pga) pressure were measured using two balloon-tipped catheters (47-9005; Akrad Laboratories, Cooper Surgical, CT, USA) passed intranasally into the stomach and lower one-third of the esophagus, respectively. To ease discomfort during catheter placement, a topical anaesthetic gel (2% lidocaine hydrochloride) was applied to the naris. Each catheter was connected to a calibrated differential pressure transducer (DP15; Validyne, Northridge, CA, USA). After filling with 1 ml of air, the esophageal catheter was positioned in accordance with the occlusion technique (18). The gastric catheter was filled with 2 ml of air to prevent collapse under high expiratory pressures and inserted to a length eliciting a positive end-expiratory Pga throughout eupneic breathing with the participant in the seated position. Diaphragm pressure (Pdi) was obtained by subtracting Pes from Pga. Diaphragm (PTP_{di}) and esophageal pressure time product (PTP_{es}) were calculated by integrating Pdi and Pes, respectively, over periods of inspiratory flow. Expiratory pressure time product (PTP_{ga}) was determined by integrating Pga over periods of expiratory flow. Values of PTP_{di}, PTP_{es}, and PTP_{ga} were calculated per minute as the sum of all breaths within each minute, and cumulative values were calculated as the sum of all breaths in each exercise trial.

Respiratory Muscle Function

Magnetic nerve stimulation

Magnetic stimulation of the nerve roots supplying the respiratory muscles was delivered at 1 Hz via a 90 mm circular coil powered by a magnetic stimulator (Magstim BiStim[2]; The Magstim Company Ltd, Whitland, UK). Inspiratory muscle stimulation was delivered with the coil positioned between the 3rd and 7th cervical vertebrae, with the participants sat upright with the neck flexed (19). Expiratory muscle stimulation was delivered with the coil positioned between the 8th and 11th thoracic vertebrae, with the participants sat forwards on an inclined bench (~30° past vertical) with their chest and abdomen supported (20). Final coil positioning was determined each the location that evoked the greatest twitch pressure amplitude and was marked using indelible ink for all subsequent stimulations. Each stimulation was delivered at functional residual capacity as judged via a stable end-expiratory Pes. Electromyograms (EMG) were recorded from the right hemi-diaphragm (EMG_{DI}) and rectus abdominis (RA; EMG_{RA}) using bipolar surface electrodes (Trigno Avanti, Delsys Inc.; Natick, MA, USA) for the measurement of M-wave responses as described previously (3). To determine if the inspiratory and expiratory muscles were maximally activated, Pdi_{tw} and Pga_{tw} were assessed in response to progressively increasing intensities of stimulation. Three single twitch stimulations were delivered at 50%, 60%, 70%, 80%, 85%, 90%, 95%, and 100% of the maximum power output of the magnetic stimulator for the inspiratory and expiratory muscles, on separate occasions. A plateau was observed in Pdi_{tw} in all participants between 95% and 100% of maximum power output, and in 8/10 participants between 90% and 100% of maximum power output, indicative of maximal activation (Figure 2). In contrast, Pga_{tw} increased in accordance with maximal stimulator power, indicating that the expiratory muscles were not maximally activated (Figure 2).

Neuromuscular function

Assessment of inspiratory and expiratory neuromuscular function was performed ~10 min prior to, and ~5 min and ~30 min after, each of the constant power exercise tests (Figure 1). The order of assessment of inspiratory and expiratory neuromuscular function was randomized and counterbalanced between the participants but remained constant within participants across repeated visits. To account for twitch potentiation, Pdi_{tw} was measured ~5 s after a 5 s maximal Müeller maneuver that was initiated from residual volume. Similarly, Pga_{tw} was assessed ~5 s after a 5 s maximal expulsive maneuver initiated from total lung capacity. This procedure was repeated six times for Pdi_{tw} and Pga_{tw} at each measurement point. The mean value of the highest 2-4 valid twitches for Pdi_{tw} and Pga_{tw} at each measurement point was reported. Twitches that met any of the following criteria were excluded from the analysis: 1) the participant was not resting at a stable end-expiratory Pes prior to stimulation; 2) esophageal peristalsis was evident during a stimulation; 3) there was a rise in Pdi, Pga or EMG activity immediately preceding a stimulation (indicative of a lack of muscle relaxation).

The within-day between occasion test-retest coefficient of variation was <4% for Pdi_{tw} and Pga_{tw} amplitude, and <6.2% for all secondary twitch parameters, including contraction time (CT), maximal rate of pressure development (MRPD), one-half relaxation time ($RT_{0.5}$), maximal relaxation rate (MRR), and end-expiratory Pes (Supplemental Table S1; see https://doi.org/10.6084/m9.figshare.22069094). At the individual participant level, the presence of respiratory muscle fatigue was defined as a reduction in Pdi_{tw} or Pga_{tw} from pre-exercise values of 8% (i.e., twice the within-day between occasion CV).

Data Collection

The raw pressure signals (Pes and Pga) were passed through a carrier demodulator (Validyne model CD15, Northridge, CA, USA). EMG signals were recorded at a band-width of 10-850 Hz (Trigno Avanti, Delsys Inc., Natick, MA). The pressure and airflow signals were digitised at sampling rates of 150 Hz, and EMG signals were digitised at sampling rates of 2kHz (Micro 1401-3, Cambridge Electronic Design, Cambridge, UK), captured using commercially available software (Spike 2 version 8.0, Cambridge Electronic Design, Cambridge, UK).

Additional Twitch Analyses

In addition to activation of the diaphragm, cervical magnetic stimulation (CMS) evokes a contraction of several accessory inspiratory muscles that act to stiffen the ribcage, resulting in an increased Pes_{tw} amplitude in comparison to anterior bilateral phrenic nerve stimulation (21). As such, CMS allows for discrimination between the relative contributions of diaphragm and ribcage muscle fatigue to global inspiratory muscle fatigue (22). Briefly, 1-Hz CMS evokes a measurable gastric (Pga_{twCMS}), esophageal (Pes_{twCMS}), and as such diaphragm (Pdi_{tw}) twitch pressure response. A reduction in Pdi_{tw} and Pga_{twCMS} without a decrease in the

Pes_{twCMS}/Pga_{twCMS} ratio is suggestive of predominant diaphragm fatigue. Alternatively, a reduction in Pdi_{tw} and the Pes_{twCMS}/Pga_{twCMS} ratio with preserved Pga_{twCMS} is indicative of predominant ribcage muscle fatigue (22). In the present study, the fatigue ratio (i.e. the pre- to post-exercise change in: Pes_{twCMS}/Pga_{twCMS}) was used to determine the predominance of diaphragm or inspiratory accessory ribcage muscle fatigue; a fatigue ratio of <1 was indicative of predominant diaphragm fatigue whereas a fatigue ratio of ≥1 was indicative of predominant inspiratory ribcage muscle fatigue. To be clear, however, predominant diaphragm fatigue across trials *does not* preclude an increasing contribution from the accessory ribcage muscles to the overall reduction in Pdi_{tw}. As such, the relative change in Pes_{twCMS} and Pga_{twCMS} were also compared across exercise trials.

Statistical Analysis

To determine the sample size required to detect a change in Pga_{tw} and Pdi_{tw} from before to after exercise, we used previously reported values of within participant test-retest CV for Pga_{tw} (3.6%) and Pdi_{tw} (5.6%) from our group (23). A meaningful change in Pga_{tw} and Pdi_{tw} was considered as approximately twice the within-participant test-retest CV; we estimated that a sample size of 8 was required to detect a 6% change in Pga_{tw} and an 8% change in Pdi_{tw}, at a statistical power of 0.8 and an alpha level of 0.05 (24). All data are means ± SD. Statistical analysis was performed in IBM SPSS Statistics version 29. One-way repeated measures ANOVA were performed to assess differences in end-exercise responses between each trial (i.e. 50% vs. 75% vs. 100% of T_{LIM}). Changes in respiratory muscle contractility in response to the constant power exercise trials were assessed using two-way repeated measures ANOVA (exercise trial x time). Pairwise comparisons were adjusted using the Holm-Sidak correction. One-way repeated-measures ANOVA with a Holm-Sidak correction was used to compare the change in respiratory muscle contractility from pre-exercise to 5 min post-exercise (i.e., the magnitude of exercise-induced respiratory muscle fatigue) between the exercise trials. Paired samples t-tests were used to compare the pre- to post-exercise change in Pdi_{tw} and Pga_{tw} at 50%, 75%, and 100% of T_{LIM}, and Cohens D effect sizes were reported as small (0.2-0.5), medium (0.5-0.8) and large (>0.8) effects. Differences in the pre- to post-exercise change in Pes_{twCMS} and Pga_{twCMS} between trials were assessed using a one-way repeated measures ANOVA with a Holm-Sidak adjustment. Pearson product-moment correlations were performed to examine relationships between the magnitude of inspiratory muscle fatigue and cumulative and final min PTP_{di} and PTP_{es}, and the magnitude of expiratory muscle fatigue and cumulative and final min PTP_{ga}. The acceptable type I error was set at $P < 0.05$.

RESULTS

Physiological Responses to the Ramp Incremental Sprint Test

Peak values for $\dot{V}_E$, $\dot{V}O_2$, respiratory exchange ratio, HR, and power output during the ramp incremental phase of the RIST were 157 ± 36 $L{\cdot}min^{-1}$, 4.15 ± 0.92 $L{\cdot}min^{-1}$ (57.1 ± 8.8 $ml{\cdot}kg^{-1}{\cdot}min^{-1}$), 1.20 ± 0.09, 184 ± 11 $beats{\cdot}min^{-1}$, and 321 ± 57 W, respectively. CP was estimated as 202 ± 55 W from the sprint phase of the RIST. During the sprint phase, mean $\dot{V}O_2$ was 96 ± 3% of $\dot{V}O_{2peak}$, indicating that a maximal cardiometabolic effort was maintained.

Physiological Responses to Constant Power Exercise Tests

Cardiopulmonary, metabolic, and perceptual responses

The ventilatory, metabolic and perceptual responses to the exercise trials are presented in Table 1. Participants cycled at 234 ± 53 W (Δ25) for 10.2 ± 2.6 min (100% T_{LIM}), 7.7 ± 1.9 min (75% T_{LIM}), and 5.1 ± 1.3 min (50% T_{LIM}). Both end-exercise $\dot{V}_E$ and $\dot{V}O_2$ were significantly higher during 75% and 100% vs. 50% T_{LIM} (all $P < 0.05$) but were not different between 75% and 100% T_{LIM} ($P > 0.05$) (Table 1). There was a significant increase in end-exercise f_R as a function of exercise duration ($P < 0.01$) (Table 1). In contrast, end-exercise V_T was significantly lower at end-exercise of 100% vs. 50% and 75% T_{LIM} trials (both $P < 0.01$) (Table 1). End-exercise T_I and T_E decreased progressively as a function of exercise duration (both $P < 0.01$) (Table 1). At end-exercise, peak HR was greater in 100% vs. 50%

T_{LIM} (P = 0.030) but not different between 100% and 75% T_{LIM} (P = 0.167) (Table 1). Similarly, peak $[La^{-}]_B$ was greater in 100% vs. 50% T_{LIM} (*P* = 0.006) but not different in 100% compared to 75% T_{LIM} (*P* = 1.000) (Table 1). End-exercise breathing discomfort increased significantly in line with exercise duration (P < 0.01) (Table 1). End-exercise leg discomfort was maximal in all participants at 100% T_{LIM}, but values were significantly lower at 75% and 50% T_{LIM} (both P < 0.01) (Table 1).

Respiratory muscle pressure generation

End-exercise PTP_{di} was not different between trials (P > 0.05) (Table 1). In contrast, PTP_{es} increased significantly and progressively in line with exercise duration (P < 0.05) (Table 1). End-exercise PTP_{ga} was greater during 100% vs. 50% T_{LIM}, (P = 0.036), but not different to 75% T_{LIM} (P = 0.400) (Table 1). There was a significant and progressive increase in cumulative PTP_{di} and PTP_{ga} in line with exercise duration (both P < 0.01) (Figure 3).

Exercise-induced Respiratory Muscle Fatigue

The mechanical and electrical responses to magnetic stimulation of the cervical and thoracic nerve roots before and after exercise performed to 100%, 75%, and 50% of T_{LIM} in a representative participant are shown in Figure 4.

Inspiratory Muscle Fatigue

Magnetically evoked M-wave amplitude, duration, and area for the diaphragm were not different before versus after exercise in 50%, 75% and 100% T_{LIM} (Table 2). From before to after exercise, there was a reduction in group mean Pdi_{tw} for 100%, 75%, and 50% T_{LIM} (all *P* < 0.05) (Figure 5). The magnitude of exercise-induced inspiratory muscle fatigue was greater after 100% (−22.4 ± 12.5%) vs. 50% (−9.5 ± 9.2%; *P* = 0.037) and 75% T_{LIM} (−15.2 ± 10.1%; *P* = 0.044) (Figure 5). Inspiratory muscle fatigue on an individual participant basis was present in 4 participants in 50% T_{LIM} (40%), 8 participants in 75% T_{LIM} (80%), and in all participants in 100% T_{LIM} (100%) (Figure 5). At 30 min after exercise, Pdi_{tw} had recovered to near baseline values in 50% T_{LIM} (−1.5 ± 6.1%; P = 0.864), but remained significantly lower than baseline in 75% T_{LIM} (−10.0 ± 9.0%; P = 0.043) and 100% T_{LIM} (−13.5 ± 8.6%; P = 0.008). Secondary diaphragm twitch characteristics (CT, MRPD/Pdi_{tw}, $RT_{0.5}$, MRR/Pdi_{tw}, end-expiratory Pes) from before to after exercise are presented in Table 2. There was a negative correlation between the magnitude of inspiratory muscle fatigue and final min PTP_{di} (r = −0.36, *P* = 0.025) and PTP_{es} (r = −0.48, *P* = 0.004) across all trials. There was no correlation between the magnitude of inspiratory muscle fatigue and cumulative PTP_{di} (r = −0.19, *P* = 0.157) and PTP_{es} (r = −0.25, *P* = 0.088) across all trials.

In response to all exercise trials, there was a greater decrease in Pga_{twCMS} compared to Pes_{twCMS} (as reflected by a Pes_{twCMS}/Pga_{twCMS} fatigue index of <1) suggesting that diaphragm fatigue contributed predominately to the reduction in global inspiratory contractility. However, the pre- to post-exercise change in Pga_{twCMS} was not different in response to 50% T_{LIM} (−20.5 ± 31.1%), 75% T_{LIM} (−37.8 ± 20.2%) and 100% T_{LIM} (−35.4 ± 12.5%) (P = 0.218). In contrast, the pre- to post-exercise reduction in Pes_{twCMS} was greater in magnitude at 100% T_{LIM} (−16.0 ± 15.7%) vs 50% T_{LIM} (−3.5 ± 11.7%) (*P* = 0.047), but was not different vs 75% T_{LIM} (−8.9 ± 10.4%) (*P* = 0.405). Therefore, although the diaphragmatic contribution to inspiratory muscle fatigue remained 'predominant', these data suggest that the accessory inspiratory ribcage muscles increasingly contributed to the reduction in global inspiratory muscle fatigue as exercise duration progressed.

Expiratory muscle fatigue

Due to unacceptable gastric twitch variability in one participant, analyses of Pga_{tw} and associated variables pertains to 9 of the 10 participants. Magnetically evoked M-wave amplitude, duration, and area for the rectus abdominis were not different before versus after exercise in 50%, 75% and 100% T_{LIM} (Table 2). From before to after exercise, there was a reduction in Pga_{tw} in response to 50%, 75%, and 100% T_{LIM} (all *P* < 0.05) (Figure 5). The magnitude of exercise-induced expiratory abdominal muscle fatigue was greater after 100% T_{LIM} (−30.3 ± 15.6%) vs. 50% (−11.9 ± 8.2%; P = 0.008) and 75% T_{LIM} (−20.0 ± 12.6%; P = 0.024) (Figure 5). Expiratory muscle fatigue on an individual participant basis was present in 6 participants in 50% T_{LIM} (67%), 8 participants in 75% T_{LIM} (89%), and in all 9 participants in 100% T_{LIM} (100%) (Figure 5). At 30 min after exercise, Pga_{tw} had recovered to near baseline values in 50% T_{LIM} (−6.7 ± 8.3%; P = 0.166), but remained significantly lower than baseline in 75% T_{LIM} (−12.2 ± 7.0%; P = 0.009) and 100% T_{LIM} (−17.6 ± 14.0%; P = 0.008). Secondary expiratory muscle twitch characteristics (CT, MRPD/Pga_{tw}, $RT_{0.5}$, MRR/Pga_{tw}, end-expiratory Pes) from before to after exercise are presented in Table 2. There was no correlation between the magnitude of expiratory muscle fatigue and final min PTP_{ga} (r = −0.14, P = 0.473) or cumulative PTP_{ga} (r = −0.22, P = 0.130) across all trials.

Inspiratory vs. Expiratory Muscle Fatigue

Due to unacceptable Pga_{tw} variability in one participant, differences in the magnitude of inspiratory vs. expiratory muscle fatigue were compared in n = 9. There was no significant difference in the magnitude of inspiratory vs. expiratory muscle fatigue at 50%, 75%, or 100% T_{LIM} (all P > 0.14). Cohens D effect sizes were 0.27, 0.33, and 0.55 for 50, 75 and 100% T_{LIM} respectively.

DISCUSSION

Main Findings

The present study investigated the time-course of exercise-induced inspiratory and expiratory abdominal muscle fatigue. The major findings were that: 1) inspiratory and expiratory muscle fatigue developed early during exercise and was evident at 50% T_{LIM}; 2) the group mean magnitude and frequency of inspiratory and expiratory muscle fatigue increased as a function of exercise time (i.e. percentage of T_{LIM}); 3) there was no difference in the magnitude of inspiratory vs. expiratory muscle fatigue at any time point; and 4) the diaphragm component of global inspiratory muscle fatigue remained stable over time, whereas the magnitude of accessory ribcage muscle fatigue increased progressively with exercise time.

Time-course of Exercise-induced Inspiratory Muscle Fatigue

Exercise-induced inspiratory muscle fatigue appears to be a function of both an elevation in the inspiratory Pb and a limitation in the availability of blood flow. Indeed, voluntarily mimicking the diaphragmatic 'work' incurred during exercise in otherwise resting individuals does not result in diaphragm fatigue (9), and it has been suggested that the reserve in cardiac output was a contributing factor to the absence or lower frequency of diaphragm fatigue in response to heavy-intensity exercise protocols (4, 25, 26). Importantly, both the intensity of diaphragm work and the time for which such work is sustained (i.e. cumulative force history) also appear to be important determinants of the magnitude of exercise-induced diaphragm fatigue. For example, diaphragm fatigue is abolished in comparison to time-matched control conditions when the inspiratory muscle Pb is reduced via proportional assist ventilation (8). Additionally, the absence of diaphragm fatigue in response to exercise protocols that engender a high inspiratory Pb for only a short time period (i.e. >90% of $\dot{V}O_{2max}$ for <~4 min) (27, 28). Perhaps unsurprisingly, the magnitude of diaphragm fatigue is greater in response to prolonged severe intensity exercise, in comparison to short-duration severe intensity or heavy intensity exercise (3).

The present findings that the magnitude and frequency of inspiratory muscle fatigue increased in association with the percentage of T_{LIM} (Figure 5) further highlight the importance of the duration of a high inspiratory Pb. Indeed, although the magnitude of PTP_{di} during the final minute of exercise was not different between trials, cumulative PTP_{di} increased substantially in relation to exercise time (Figure 3). The time-course of exercise-induced inspiratory muscle fatigue was also similar to previous findings for severe intensity constant power exercise. For example, Archiza et al. (1) reported a progressive impairment in inspiratory muscle contractility during high-intensity constant power cycling, characterized by a reduction in Pdi_{tw} of −24 ± 6% after 75% of T_{LIM} (~6 min) and −35 ± 12% by exercise intolerance (~7.5 min). Similarly, in the present study the magnitude of global inspiratory muscle fatigue increased from −15 ± 10% at 75% of T_{LIM} (~7.5 min) to −22 ± 12% at exercise intolerance (~10 min) (Figure 5). In combination, the present findings provide further evidence that contrasts to the original suggestion that diaphragm 'strength' progressively increases during high-intensity exercise, and that impairments in diaphragm contractility are only evident during recovery (10, 29).

In a study by Walker et al. (11) that prescribed exhaustive constant-power exercise at >85% $\dot{V}O_{2max}$ and corrected for changing lung volumes during exercise, a decline in Pdi_{tw} was reported within the initial two thirds of the exercise bout, but there was no further decrease by exercise intolerance (i.e. fatigue was not progressive). Due to the utilization of anterior bilateral stimulation of the phrenic nerves in the aforementioned study, which avoids co-contraction of the accessory inspiratory ribcage muscles (30), it was suggested that the magnitude of diaphragm fatigue does not increase from relatively early during exercise to intolerance. In the present study we were able to estimate the contribution of the accessory inspiratory ribcage muscles and the diaphragm to the progressive reduction in Pdi_{tw} by measuring the relative change across trials in the pre- to post-exercise change in Pes_{twCMS}, Pga_{twCMS}, and the Pes_{twCMS}/Pga_{twCMS} fatigue index (22). There was a similar reduction in Pga_{twCMS} in response to all exercise trials. In contrast, the pre- to post-exercise reduction in Pes_{twCMS} increased progressively as a function of exercise time. These data are speculatively interpreted as evidence of an early reduction in diaphragm contractility followed by a progressive recruitment and fatigue of the accessory inspiratory ribcage muscles, which would support the potential link between the development of diaphragm fatigue and its decreased contribution to the hyperventilatory response to exercise as time proceeds. Indeed, previous data suggests that during exercise the relative contribution of the diaphragm to ventilation decreases over time, and that the diaphragm increasingly functions as a flow- rather than a pressure-generator (31). Moreover, pre-fatigue of the diaphragm elicits an increase in sternocleidomastoid EMG activity during subsequent constant-power exercise, but no change in diaphragm EMG activity in comparison to control conditions (32). From 50% to 100% of T_{LIM} in the present study, PTP_{di} was not different whereas PTP_{es} increased progressively (Table 1). An early but consistent impairment in diaphragm contractility during exercise is also consistent with the relatively rapid decrease and plateau in Pdi_{tw} exhibited in response to volitional hyperpnea and inspiratory resistive breathing that precedes task failure (33-36) and the suggestion that cumulative diaphragm work is not well correlated to the magnitude of diaphragm fatigue during maximal exercise (4).

Time-course of Exercise-induced Expiratory Muscle Fatigue

The development of expiratory abdominal muscle fatigue in response to severe intensity whole-body exercise is relatively well established (5, 6, 37); however, to the authors' knowledge no previous study has measured the time course of its development. In the present study, the magnitude and frequency of expiratory muscle fatigue increased as a function of exercise time (Figure 5). Similarly to the inspiratory muscles, these data demonstrate the importance of the duration of elevated expiratory muscle work (i.e. cumulative force history) in determining the magnitude of exercise-induced expiratory muscle fatigue. Indeed, concomitant with the progressive decrease in Pga_{tw}, cumulative PTP_{ga} increased substantially from 50% to 75% to 100% of T_{LIM} (Figure 3). Similarly, previous studies have reported a significant relationship between the cumulative force output of the expiratory muscles and the magnitude of exercise-induced expiratory muscle fatigue ($r = -0.73$) (5). Although we are unaware of any previous data investigating the time-course of expiratory muscle fatigue during exercise, previous studies have measured the progression of expiratory muscle fatigue during submaximal isocapnic hyperpnea. Indeed, in response to volitional hyperpnea at ~70% of maximal voluntary ventilation, Renggli et al. (33) reported a decrease in Pga_{tw} of ~20% after 8 min, that did not further decline by task failure (~25 min). However, unlike submaximal isocapnic hyperpnea, the expiratory abdominal muscles contribute progressively to the increased demands for ventilation during exercise. Indeed, in the present study end-exercise PTP_{ga} increased by ~200 $cmH_2O \cdot s \cdot min^{-1}$ from 50% to 100% of T_{LIM} and previous data show that EMG activity of the expiratory muscles increases in association with ventilation during progressive intensity exercise (38). Increased expiratory muscle recruitment in combination with a limited supply of cardiac output during exercise likely explains the difference in the 'progression' of expiratory muscle fatigue in comparison to rested isocapnic hyperpnea.

Differences in Exercise-induced Inspiratory vs. Expiratory Muscle Fatigue

In the present study, it was hypothesized that based on a lower resistance to fatigue and the additional non-ventilatory functions performed during exercise (39, 40), the expiratory abdominal muscles would fatigue earlier and to a greater extent during exercise than in comparison to the inspiratory muscles. Despite the absence of a significant difference in the magnitude of expiratory vs. inspiratory muscle fatigue between trials, expiratory muscle contractility was impaired in the majority of participants (n = 6/9; 67%) after only ~5 min of submaximal exercise (50% T_{LIM}) whereas inspiratory muscle fatigue was only present in 40% (n = 4/10) of individuals at 50% T_{LIM} (Figure 5). Therefore, these data are suggestive of an increased susceptibility to fatigue of the expiratory muscles compared to the inspiratory muscles early during constant power exercise. These findings are highly similar to fatiguing resistive loading protocols, whereby the ability to generate maximal pressure falls at a substantially faster rate for the expiratory vs. inspiratory muscles (39).

Individual Differences in the Temporality of Exercise-induced Respiratory Muscle Fatigue

In the present study, we observed heterogeneity between participants in the development and temporality of exercise-induced inspiratory and expiratory muscle fatigue (Figure 5). Indeed, visual inspection of our data suggests a 'linear' or progressive increase in exercise-induced inspiratory and expiratory muscle fatigue with increasing exercise time (50% vs. 75% vs. 100% T_{LIM}) in some but not all participants. Although the factors responsible for the development of respiratory muscle fatigue are relatively well understood (i.e., Pb, cumulative work history of the respiratory muscles, and the availability of blood flow), the reason(s) for inter-individual differences in the development of fatigue are less clear. For example, previous studies report a prevalence of respiratory muscle fatigue as low as 42% and 58% of females and males, respectively, in response to exhaustive high intensity cycling, with no discernable between-participant responses to explain the divergence in the presence or absence of fatigue within sexes (2). Aerobic fitness, for example, does not appear to influence the development of respiratory muscle fatigue (41). The two females in the present study did not develop inspiratory muscle fatigue at 50% T_{LIM} and exhibited a smaller reduction in Pdi_{tw} at 100% T_{LIM} (–14.1% and –15.8%) compared to the group mean response (–22.4%). Although we note that this study was underpowered to conduct formal statistical analyses of sex-based differences in the fatigue response to exercise, our observation perhaps lends support to previous reports suggesting a greater resistance to exercise-induced inspiratory muscle fatigue in females (2).

To understand the mechanisms of such response heterogeneity, we performed a series of correlations between key variables implicated in the development of respiratory muscle fatigue. For the inspiratory muscles, a significant relationship was observed between the magnitude of inspiratory muscle fatigue and final min PTP_{di} ($r = -0.36$) and PTP_{es} ($r = -0.48$), but not cumulative PTP_{di} or PTP_{es}. The absence of a relationship between cumulative PTP and fatigue is perhaps unsurprising, as although cumulative PTP_{di} typically increased in line with the magnitude of fatigue on an individual level (Figure 3), there was significant variability between individuals in absolute cumulative PTP_{di}. For example, some participants exhibited higher values of cumulative PTP_{di} at 50% T_{LIM} compared to others at 100% T_{LIM} (Figure 3), likely due to differing absolute exercise durations and fitness status. In contrast, no significant relationships were observed between PTP_{ga} responses and the magnitude of expiratory muscle fatigue at the group level. These findings are also likely to be influenced by variability in total and cumulative PTP_{ga} between individuals (Figure 3).

Implications

The development of inspiratory and expiratory abdominal muscle fatigue may limit exercise tolerance in healthy individuals primarily via an increased perception of dyspnea and/or the activation of a respiratory muscle metaboreflex (7). Our findings that the development of inspiratory and expiratory muscle fatigue occur prior to the point of intolerance, i.e., by 50% of T_{LIM}, have important implications for interventional studies aiming to delay or attenuate the development of respiratory muscle fatigue to improve exercise performance. For example, previous studies suggest that inspiratory muscle training attenuates the cardiovascular response associated with the inspiratory muscle metaboreflex and blunts the impairment in peripheral locomotor fatigue (42, 43). Similarly, improvements in exercise performance following inspiratory muscle training have been associated with a decreased magnitude of inspiratory muscle fatigue at exercise intolerance (44). However, in addition to an attenuation of its magnitude, it remains to be empirically determined whether respiratory muscle training also delays the progression of exercise-induced respiratory muscle fatigue, and thus postpones the occurrence of task-limiting fatigue-induced cardiovascular or dyspnogenic effects. To date, few studies have explored the utility of expiratory muscle training to enhance exercise performance, yet a higher number of individuals reported expiratory vs inspiratory muscle fatigue by 50% T_{LIM} in the present study.

Technical Considerations

Submaximal depolarization of thoracic nerve roots with magnetic stimulation

In contrast to a near-maximal Pdi_{tw} response to incremental cervical nerve stimulation intensity, the Pga_{tw} response to thoracic nerve stimulation at 100% stimulator output was likely submaximal (Figure 2). This is in agreement with previous findings (1, 2, 5, 20). The primary concerns with submaximal activation of motor nerves are: 1) poor stimulus reproducibility; and 2) an altered activation threshold of motor neurons secondary to axonal hyperpolarization. However, we report an excellent between occasion test-retest CV for

Pga_{tw} and Pdi_{tw} of ~4%, demonstrating the consistency of our method (Supplemental Table S1). Moreover, the peak transdiaphragmatic and gastric pressures per breath (typically <20-40% of Pdi_{MAX} and Pga_{MAX}) during exercise are unlikely to be of sufficient magnitude to engender axonal hyperpolarization, as described by us previously (3). We acknowledge that it is theoretically possible that the magnitude of expiratory muscle fatigue may have been overestimated relative to the magnitude of diaphragm fatigue by a small amount in this study, due to the absence of maximal activation of the thoracic nerves.

Constant power exercise testing

One concern is that our participants were not familiarized with the constant power exercise protocol prior to completion of the 100% T_{LIM} trial, and between-occasion reproducibility of constant power exercise T_{LIM} was not established. Theoretically, if a 'learning effect' was present, then the exercise time(s) and thus the magnitude of respiratory muscle fatigue may have been underestimated in the 50% and 75% T_{LIM} trials. However, given that the magnitude of exercise-induced expiratory and inspiratory muscle fatigue progressed from 50% to 75% and to 100% T_{LIM}, any theoretical underestimation of the magnitude of fatigue is unlikely to have impacted the key findings of this study. Moreover, to avoid any systematic learning effect influencing the fatigue responses observed in the 50% and 75% T_{LIM} trials, the order of these visits was randomized between participants. Finally, the physiological responses to 50% and 75% T_{LIM} were also highly consistent with that which would be expected at these timepoints, e.g. $\dot{V}O_2$ was submaximal at end-exercise of 50% T_{LIM}, but not significantly different to peak values by 75% T_{LIM} (Table 1). Therefore, we are highly confident that the lack of familiarization with constant power testing did not influence the responses observed in this study.

Conclusions

Inspiratory and expiratory abdominal muscle fatigue develops relatively early during severe intensity constant power exercise, and the magnitude of fatigue increases progressively towards exercise intolerance. Despite a greater frequency of expiratory muscle fatigue early during exercise, there was no difference in the magnitude of expiratory and inspiratory muscle fatigue at any time point during exercise. From additional analyses of the inspiratory twitch response, we speculate that diaphragm fatigue is present relatively early during exercise, and that the progressive reduction in global inspiratory muscle fatigue is caused by recruitment and consequent fatigue of the accessory inspiratory ribcage muscles.

DATA AVAILABILITY

Data are subject to privacy/ethical restrictions: Source data for this study are not publicly available due to privacy or ethical restrictions. The source data are available to verified researchers upon request by contacting the corresponding author.

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DISCLOSURES

C.F. is involved in contracted clinical research with United Therapeutics, Genentech, Regeneron, Respira Therapeutics and Mezzion. She reports consulting fees from Respira Therapeutics. She had a pending patent application filed by The Lundquist Institute, titled "Testing System to Diagnose Neuromuscular Deconditioning and Pathologic Conditions". She is a visiting Associate Professor at the University of Leeds, UK. B.J.T. is involved in contracted clinical research with United Therapeutics, LungTrainers®, and Prolaio. He is also a paid consultant for Prolaio.

AUTHOR CONTRIBUTIONS

T.A.H. and B.J.T. conceived and designed the research; T.A.H., M.R.C. and B.J.T performed experiments; T.A.H and B.J.T. analyzed data; T.A.H., M.R.C., C.F., T.J.C. and B.J.T. interpreted results of experiments; T.A.H. prepared figures; T.A.H. drafted manuscript; T.A.H., M.R.C., C.F., T.J.C. and B.J.T. edited and revised manuscript; T.A.H., M.R.C., C.F., T.J.C. and B.J.T. approved final version of manuscript.

SUPPLEMENTAL DATA

Supplemental Table S1: https://doi.org/10.6084/m9.figshare.22069094

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FIGURE & TABLE LEGENDS

FIGURE 1. Experimental exercise protocols. RIT, ramp incremental test; TF, task failure; P_{peak}; peak power; CP, critical power; Pga_{tw}, gastric twitch pressure; Pdi_{tw}, diaphragm twitch pressure.

FIGURE 2. Diaphragm and expiratory abdominal muscle supramaximality curves. A, the diaphragm twitch pressure (Pdi_{tw}) response to incremental magnetic stimulation of the phrenic nerve roots; B, the gastric twitch pressure (Pga_{tw}) response to incremental magnetic stimulation of the thoracic nerve roots. Group mean values ± SD (black), and individual responses (grey) are presented in 10 participants. For Pdi_{tw} there was a change of <5% from 90 to 100% stimulator power in 7/10 participants. * $P < 0.05$, significantly different to 100%.

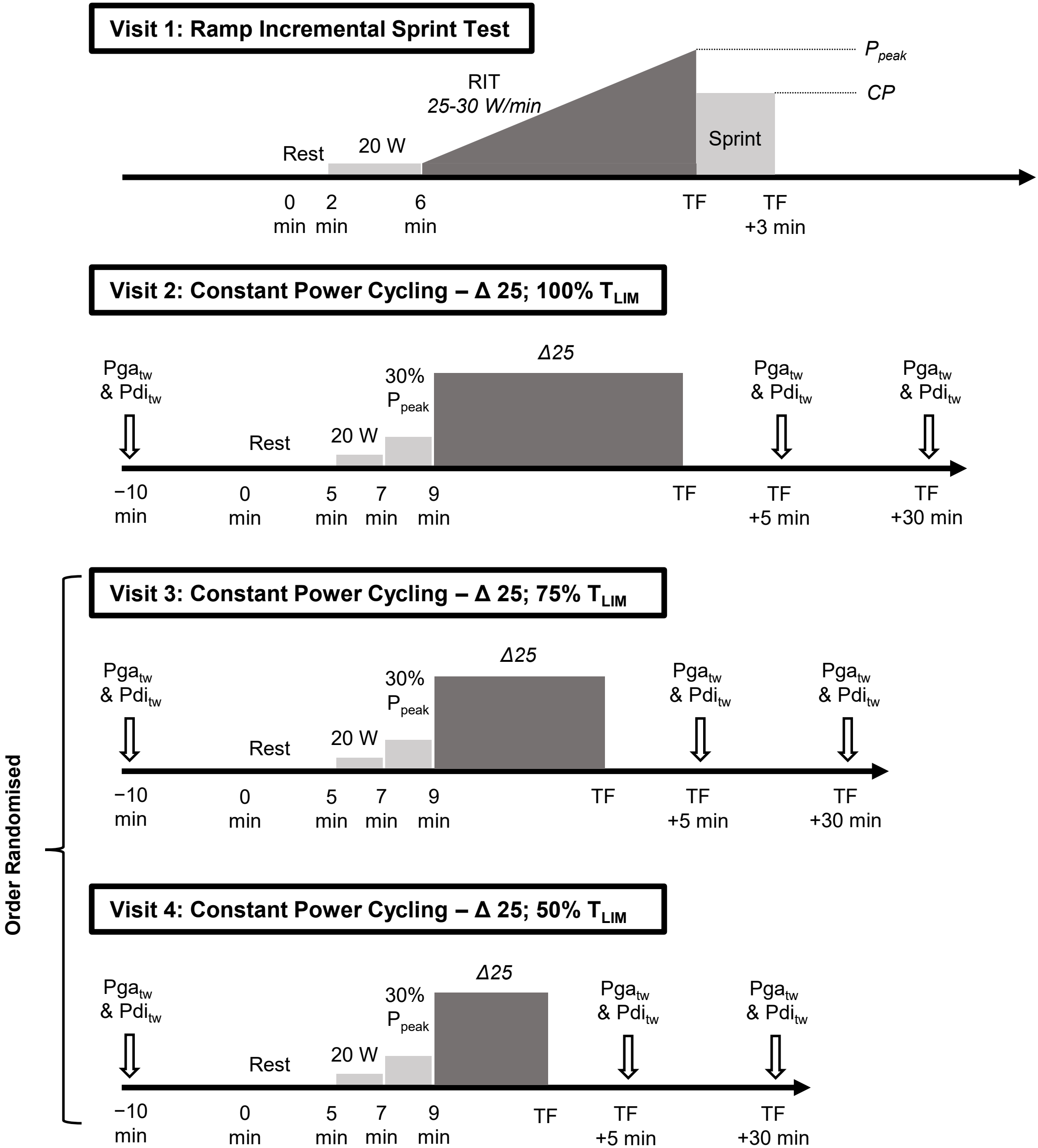
FIGURE 3. Cumulative diaphragm (PTP_{di}) and gastric (PTP_{ga}) pressure time product in response to exercise (50% T_{LIM} vs. 75% T_{LIM} vs. 100% T_{LIM}). A-B, total cumulative PTP_{di} and PTP_{ga} in response to exercise; C-D, individual relationships between cumulative PTP_{di} and PTP_{ga} vs. exercise-induced diaphragm (Pdi_{tw}) and expiratory muscle fatigue (Pga_{tw}) respectively; E-F, the relationship between exercise duration, cumulative PTP_{di} and PTP_{ga}, and diaphragm and expiratory muscle fatigue. A one-way repeated-measures ANOVA with a Holm-Sidak post hoc correction was used to assess differences in cumulative PTP_{di} and PTP_{ga} between trials (50% T_{LIM} vs. 75% T_{LIM} vs. 100% T_{LIM}). *Significant difference to 50% T_{LIM} ($P < 0.05$); † significant difference to 75% T_{LIM} ($P < 0.05$).

FIGURE 4. Individual representative ensemble average traces for diaphragm pressure (Pdi) in response to cervical nerve stimulation (A) and gastric pressure (Pga) in response to thoracic nerve stimulation (B) at baseline (mean value across all time points) and ~5 min after 50%, 75%, and 100% T_{LIM} exercise trials. Electromyographic responses for the diaphragm (EMG_{DI}) and rectus abdominis (EMG_{RA}) are also shown.

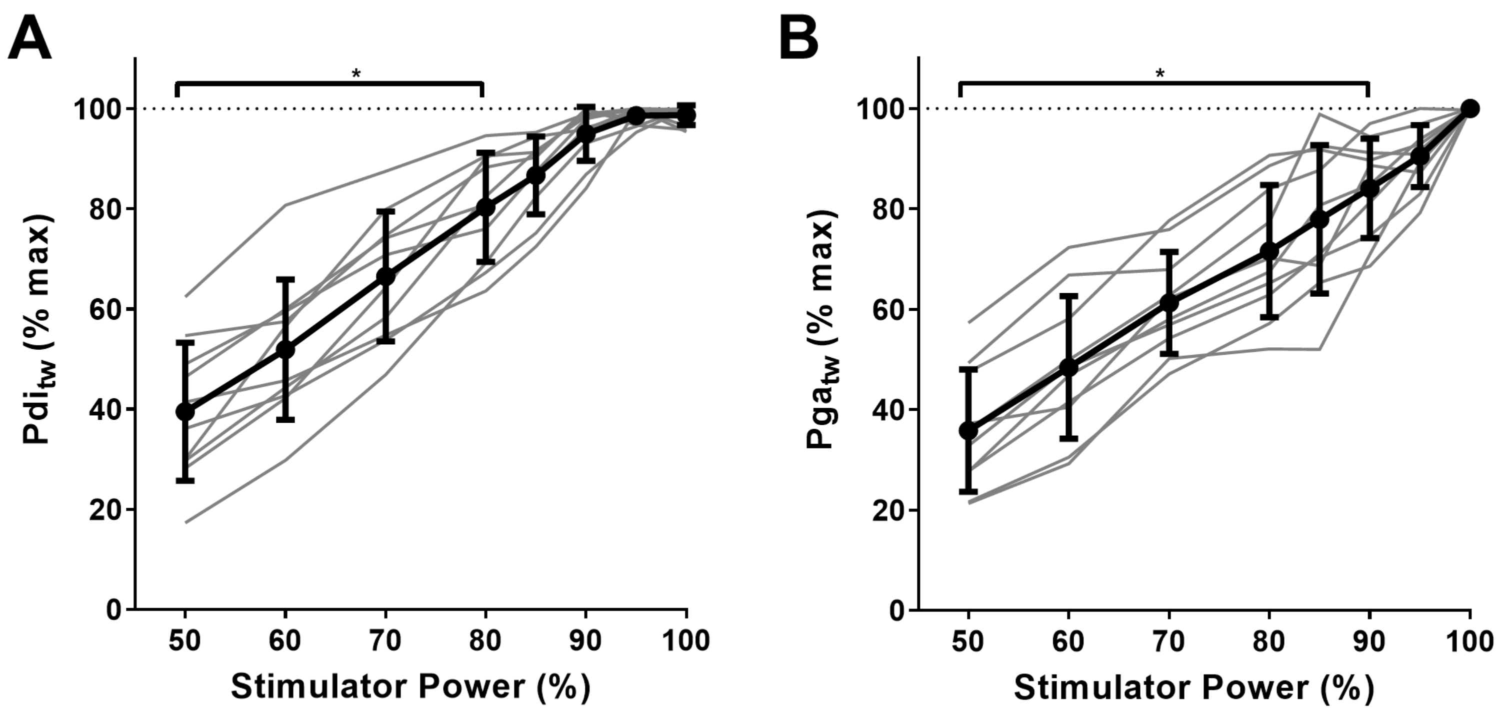
FIGURE 5. The change in diaphragm twitch pressure (Pdi_{tw}; panel A) and gastric twitch pressure (Pga_{tw}, panel B) from before to ~5 min after exercise trials (50% T_{LIM} vs. 75% T_{LIM} vs. 100% T_{LIM}). Symbols represent individual participants (n = 10 for Pdi_{tw}; n = 9 for Pga_{tw}). Data were analyzed by two-way repeated measures ANOVA with Holm-Sidak post hoc correction. One-way repeated measures ANOVA with a Holm-Sidak correction were used to compare the change in respiratory muscle contractility from pre-exercise to 5 min post-exercise (i.e., the magnitude of exercise induced respiratory muscle fatigue) between the exercise trials (50% T_{LIM} vs. 75% T_{LIM} vs. 100% T_{LIM}). *Significant difference between 100% T_{LIM} vs. 50% T_{LIM} ($P < 0.05$); †Significant difference between 100% T_{LIM} and 75% T_{LIM} ($P < 0.05$).

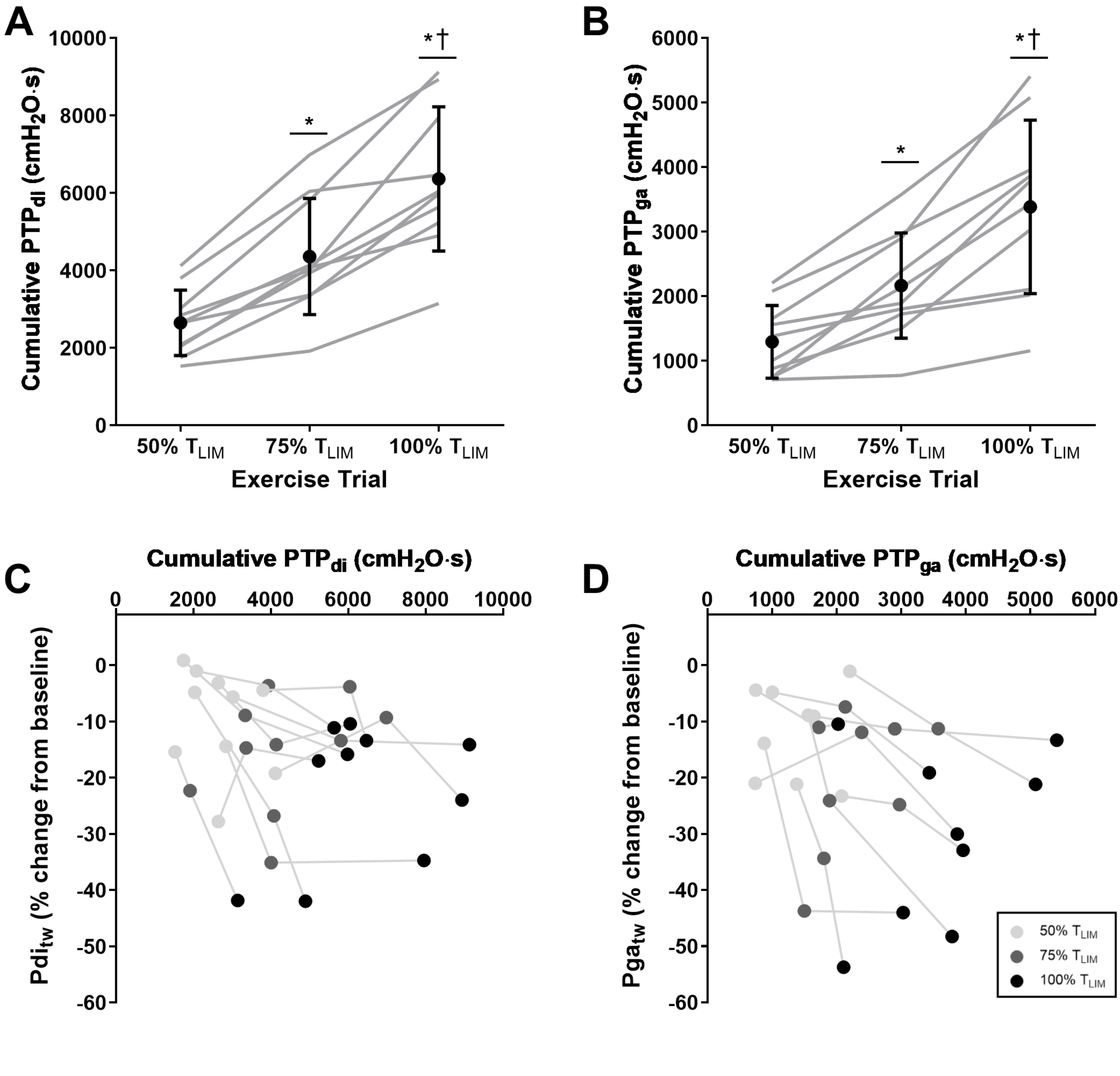
TABLE 1. Ventilatory, metabolic, and perceptual exercise responses during the final minute of exercise.

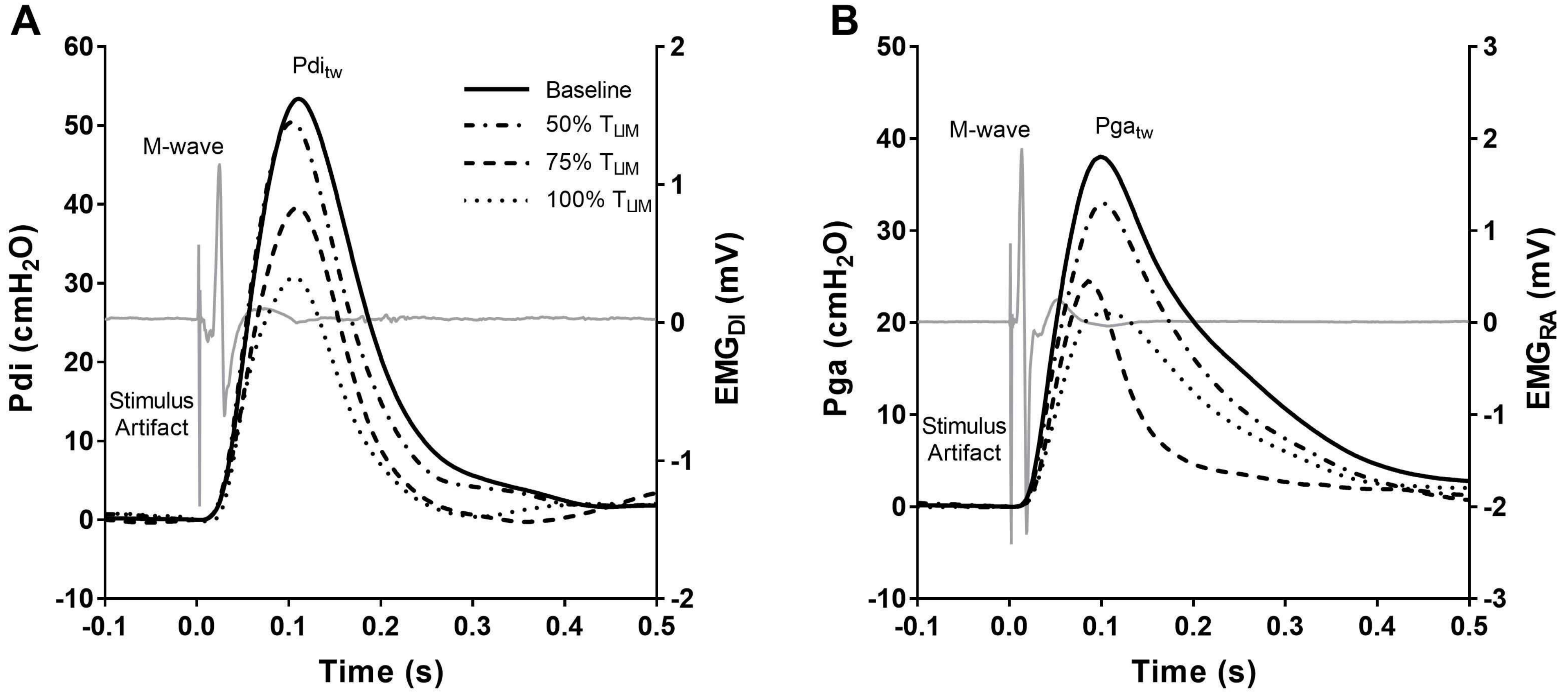
TABLE 2. Inspiratory and expiratory twitch characteristics from before to 5 min post-exercise.



⇩ Assessment of respiratory muscle function (Pga_{tw}, gastric twitch pressure; Pdi_{tw}, transdiaphragmatic twitch pressure).


A
B
*
*
Pdi$_{tw}$ (% max)
Pga$_{tw}$ (% max)
0
20
40
60
80
100
50
60
70
80
90
100
Stimulator Power (%)
Stimulator Power (%)


A
B
C
D
Cumulative PTP$_{di}$ (cmH$_2$O·s)
Cumulative PTP$_{ga}$ (cmH$_2$O·s)
Exercise Trial
50% T$_{LIM}$
75% T$_{LIM}$
100% T$_{LIM}$
*
*†
Pdi$_{tw}$ (% change from baseline)
Pga$_{tw}$ (% change from baseline)



A
B
Pdi (cmH2O)
EMGDI (mV)
Pditw
M-wave
Stimulus Artifact
Baseline
50% TLIM
75% TLIM
100% TLIM
Time (s)
Pga (cmH2O)
EMGRA (mV)
Pgatw
60
50
40
30
20
10
0
-10
2
1
0
-1
-2
-0.1
0.0
0.1
0.2
0.3
0.4
0.5
3
-3

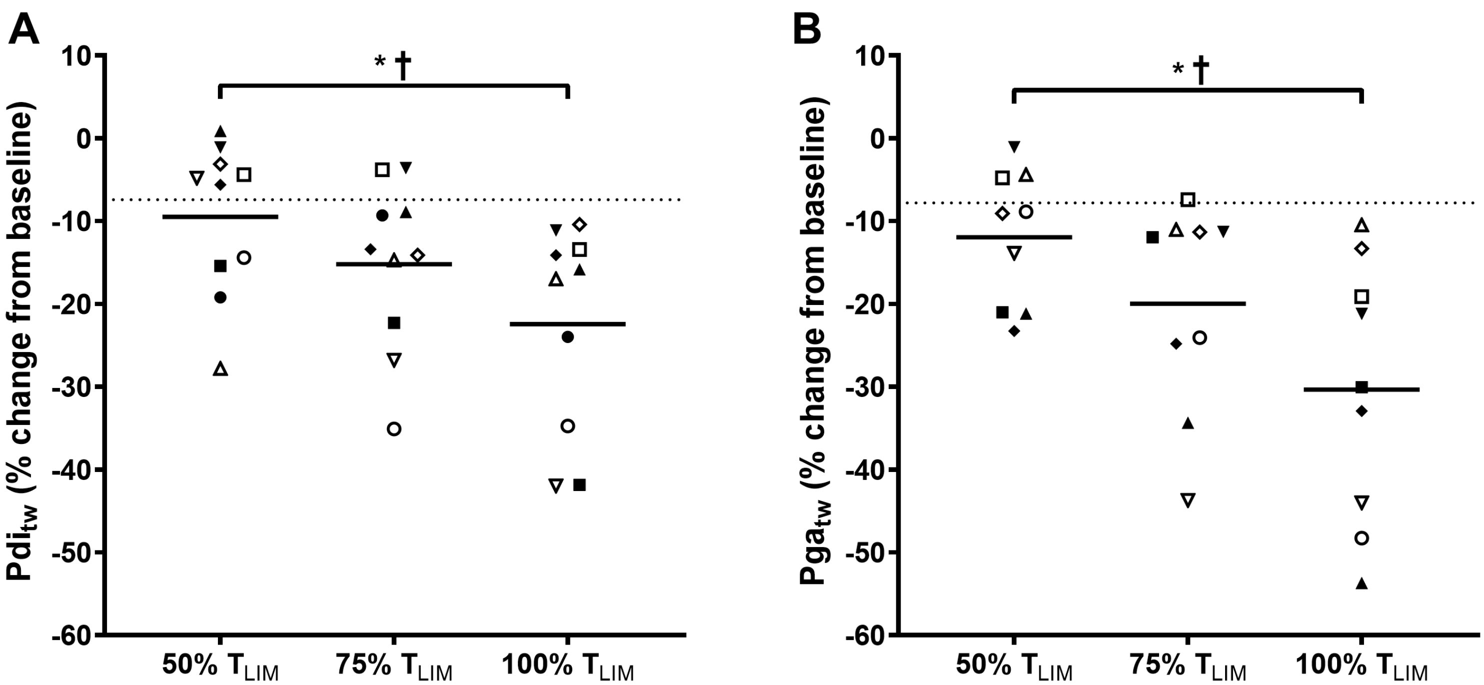

A
B
*†
10
0
-10
-20
-30
-40
-50
-60
Pdi_tw (% change from baseline)
Pga_tw (% change from baseline)
50% T_LIM
75% T_LIM
100% T_LIM

TABLE 1.

	50% T_{LIM}	75% T_{LIM}	100% T_{LIM}
$\dot{V}_E$, L·min^{-1}	118 ± 19	132 ± 24*	142 ± 30*
f_R, breaths·min^{-1}	43 ± 5	50 ± 4*	60 ± 8*†
V_T, L	2.79 ± 0.63	2.70 ± 0.52	2.38 ± 0.42*†
T_I, s	0.56 ± 0.08	0.49 ± 0.06*	0.41 ± 0.07*†
T_E, s	0.88 ± 0.10	0.75 ± 0.07*	0.62 ± 0.08*†
T_I/T_{TOT}, s	0.39 ± 0.02	0.39 ± 0.02	0.39 ± 0.02
T_E/T_{TOT}, s	0.61 ± 0.02	0.61 ± 0.02	0.61 ± 0.02
$\dot{V}O_2$, L·min^{-1}	3.69 ± 0.71	3.91 ± 0.85*	3.94 ± 0.86*
$\dot{V}CO_2$, L·min^{-1}	4.15 ± 0.90	4.31 ± 0.98	4.25 ± 0.90
$P_{ET}CO_2$, mmHg	31.0 ± 4.4	28.0 ± 3.7*	26.7 ± 4.1*
Heart Rate, beats·min^{-1}	174 ± 10	179 ± 8	182 ± 9*
Blood Lactate, mmol·L	8.8 ± 3.0	11.3 ± 3.0*	11.6 ± 3.4*
PTP_{di}, cmH_2O·s·min^{-1}	614 ± 142	724 ± 208	753 ± 169
PTP_{es}, cmH_2O·s·min^{-1}	817 ± 158	966 ± 202*	1189 ± 325*†
PTP_{di}/PTP_{es}	0.76 ± 0.15	0.74 ± 0.18	0.66 ± 0.16
PTP_{ga}, cmH_2O·s·min^{-1}	344 ± 159	446 ± 212	536 ± 247*
Breathing Discomfort, points	6.2 ± 1.3	7.9 ± 1.1*	9.6 ± 0.7*†
Leg Discomfort, points	7.4 ± 1.0	8.5 ± 1.1*	10.0 ± 0.0*†

Values are means ± SD for 10 subjects (blood lactate, n = 8). Cardiorespiratory parameters were averaged during the final 60 s of exercise for all trials. Data were analyzed for between-group differences at end exercise by one-way repeated-measures ANOVA with Holm-Sidak post hoc correction. $\dot{V}_E$, minute ventilation; f_R, respiratory frequency; V_T, tidal volume; T_I, inspiratory time; T_E, expiratory time; T_{TOT}, total respiratory time; $\dot{V}O_2$, pulmonary oxygen uptake; $\dot{V}CO_2$, pulmonary carbon dioxide production; $P_{ET}CO_2$, end-tidal carbon dioxide tenson; PTP_{di}, diaphragm pressure time product; PTP_{es}, esophageal pressure time product; PTP_{ga}, gastric pressure time product. * $P < 0.05$ vs. 50% T_{LIM}; † $P < 0.05$ vs. 75% T_{LIM}.

Table 2.

Twitch Characteristic	50% T_{LIM} Pre-exercise	50% T_{LIM} Post-exercise	75% T_{LIM} Pre-exercise	75% T_{LIM} Post-exercise	100% T_{LIM} Pre-exercise	100% T_{LIM} Post-exercise
Pdi_{tw}, cmH_2O	40.4 ± 11.6	36.9 ± 12.5*	43.1 ± 2.9	36.2 ± 2.3†	44.3 ± 12.6	34.3 ± 12.0†
CT, ms	112 ± 5	106 ± 7†	114 ± 9	106 ± 7†	115 ± 6	105 ± 6†
MRPD/Pdi_{tw}, s/cm	19.0 ± 2.9	19.6 ± 1.9	17.9 ± 0.9	19.9 ± 1.8†	18.0 ± 1.3	20.0 ± 1.4†
$RT_{0.5}$, ms	68 ± 11	58 ± 8†	67 ± 11	57 ± 10†	67 ± 6	56 ± 9†
MRR/Pdi_{tw}, s/cm	10.1 ± 1.7	12.0 ± 1.9†	10.1 ± 1.8	12.2 ± 2.3†	10.2 ± 1.0	12.2 ± 2.2*
End-expiratory Pes, cmH_2O	−4.9 ± 1.9	−5.0 ± 1.7	−4.6 ± 1.7	−5.3 ± 2.0	−4.4 ± 1.5	−5.3 ± 2.0
EMG_{DI} M-Wave Amplitude, mV	2.2 ± 1.0	2.4 ± 1.2	2.1 ± 1.3	2.2 ± 1.3	2.2 ± 1.2	2.2 ± 1.2
EMG_{DI} M-Wave Duration, ms	33.3 ± 6.1	31.0 ± 5.1	30.4 ± 4.5	30.4 ± 4.3	30.7 ± 5.2	30.9 ± 5.2
EMG_{DI} M-Wave Area, mV·ms	14.1 ± 6.1	15.4 ± 7.0	12.7 ± 7.2	13.6 ± 7.5	12.2 ± 5.6	13.0 ± 5.7
Pga_{tw}, cmH_2O	52.1 ± 29.6	45.7 ± 26.8†	51.5 ± 28.0	42.7 ± 27.1†	54.8 ± 36.8	40.7 ± 33.5†
CT, ms	109 ± 14	108 ± 14	108 ± 16	104 ± 15	112 ± 18	108 ± 16
MRPD/Pga_{tw}, s/cm	16.6 ± 3.8	16.7 ± 3.7	16.8 ± 4.2	16.7 ± 3.3	17.1 ± 3.2	16.7 ± 2.4
$RT_{0.5}$, ms	122 ± 17	101 ± 17†	116 ± 23	94 ± 22*	112 ± 26	87 ± 22†
MRR/Pga_{tw}, s/cm	5.4 ± 1.2	6.3 ± 0.8	5.8 ± 1.6	7.0 ± 2.4	5.7 ± 1.1	7.1 ± 1.9*
End-expiratory Pes, cmH_2O	−5.4 ± 1.9	−6.6 ± 2.1	−4.9 ± 1.7	−6.1 ± 2.2†	−4.6 ± 1.6	−6.0 ± 2.6
EMG_{RA} M-Wave Amplitude, mV	3.1 ± 1.7	3.2 ± 1.7	3.1 ± 1.6	3.1 ± 1.7	3.4 ± 2.1	3.3 ± 2.3
EMG_{RA} M-Wave Duration, ms	25.0 ± 5.8	24.5 ± 6.0	23.9 ± 6.8	23.7 ± 5.4	24.5 ± 4.7	24.0 ± 5.6
EMG_{RA} M-Wave Area, mV·ms	15.6 ± 8.1	15.5 ± 8.2	15.2 ± 8.1	15.2 ± 7.8	16.8 ± 10.0	15.4 ± 9.4

Values are means ± SD for 10 participants for inspiratory twitch characteristics and 9 participants for expiratory twitch characteristics. Pdi_{tw}, diaphragm twitch pressure; CT, contraction time; MRPD, maximal rate of pressure development; $RT_{0.5}$, one-half relaxation time; MRR, maximal relaxation rate; Pes, esophageal pressure; EMG_{DI} (n = 7) diaphragm EMG; Pga_{tw}, gastric twitch pressure; EMG_{RA}, rectus abdominis EMG. *$P < 0.05$ and † $P < 0.01$, significantly different to pre-exercise value. Note, statistical analyses include 30 min recovery comparisons (data not shown).