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Inspiratory muscle training enhances pulmonary O_2 uptake kinetics and high-intensity exercise tolerance in humans

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Bailey SJ, Romer LM, Kelly J, Wilkerson DP, DiMenna FJ, Jones AM. Inspiratory muscle training enhances pulmonary O_2 uptake kinetics and high-intensity exercise tolerance in humans. *J Appl Physiol* 109: 457–468, 2010. First published May 27, 2010; doi:10.1152/japplphysiol.00077.2010.—Fatigue of the respiratory muscles during intense exercise might compromise leg blood flow, thereby constraining oxygen uptake ($\dot{V}O_2$) and limiting exercise tolerance. We tested the hypothesis that inspiratory muscle training (IMT) would reduce inspiratory muscle fatigue, speed $\dot{V}O_2$ kinetics and enhance exercise tolerance. Sixteen recreationally active subjects (mean ± SD, age 22 ± 4 yr) were randomly assigned to receive 4 wk of either pressure threshold IMT [30 breaths twice daily at ~50% of maximum inspiratory pressure (MIP)] or sham treatment (60 breaths once daily at ~15% of MIP). The subjects completed moderate-, severe- and maximal-intensity "step" exercise transitions on a cycle ergometer before (Pre) and after (Post) the 4-wk intervention period for determination of $\dot{V}O_2$ kinetics and exercise tolerance. There were no significant changes in the physiological variables of interest after Sham. After IMT, baseline MIP was significantly increased (Pre vs. Post: 155 ± 22 vs. 181 ± 21 cmH_2O; $P < 0.001$), and the degree of inspiratory muscle fatigue was reduced after severe- and maximal-intensity exercise. During severe exercise, the $\dot{V}O_2$ slow component was reduced (Pre vs. Post: 0.60 ± 0.20 vs. 0.53 ± 0.24 l/min; $P < 0.05$) and exercise tolerance was enhanced (Pre vs. Post: 765 ± 249 vs. 1,061 ± 304 s; $P < 0.01$). Similarly, during maximal exercise, the $\dot{V}O_2$ slow component was reduced (Pre vs. Post: 0.28 ± 0.14 vs. 0.18 ± 0.07 l/min; $P < 0.05$) and exercise tolerance was enhanced (Pre vs. Post: 177 ± 24 vs. 208 ± 37 s; $P < 0.01$). Four weeks of IMT, which reduced inspiratory muscle fatigue, resulted in a reduced $\dot{V}O_2$ slow-component amplitude and an improved exercise tolerance during severe- and maximal-intensity exercise. The results indicate that the enhanced exercise tolerance observed after IMT might be related, at least in part, to improved $\dot{V}O_2$ dynamics, presumably as a consequence of increased blood flow to the exercising limbs.

inspiratory muscle fatigue; $\dot{V}O_2$ slow component; pulmonary ventilation; dyspnea; exercise performance

THE INCREASED ACTIVATION OF the muscle contractile machinery at the onset of exercise results in an immediate increase in the rate of ATP turnover. However, oxygen uptake ($\dot{V}O_2$) rises exponentially following the start of exercise, with the energy equivalent of the "O_2 deficit" compensated through an increased energy yield from phosphocreatine (PCr) degradation and "anaerobic" glycolysis (36, 45). After the onset of moderate-intensity exercise below the gas-exchange threshold (GET), pulmonary $\dot{V}O_2$ reaches a "steady state" within 2–3 min (68, 69). In contrast, during supra-GET exercise, the development of the so-called $\dot{V}O_2$ slow component delays the attainment of steady state during heavy-intensity exercise (below the critical power) or results in a continued increase in $\dot{V}O_2$ until the maximal O_2 uptake ($\dot{V}O_{2max}$) is reached during severe-intensity exercise (above the critical power) (47, 69, 71). The $\dot{V}O_2$ slow component reflects an increased muscle energy turnover as constant-work-rate exercise proceeds (8, 57) and is associated with a concomitant depletion of the finite PCr stores (57) and greater glycogen utilization (38). Therefore, interventions that speed the overall $\dot{V}O_2$ kinetics, reduce the $\dot{V}O_2$ slow-component amplitude, and/or increase the $\dot{V}O_{2max}$ would be expected to enhance exercise tolerance by reducing the utilization of the finite anaerobic reserves and the accumulation of metabolites associated with the fatigue process (4, 5, 14, 30).

Classically, the respiratory system has been considered to be overbuilt relative to the other components of the O_2 delivery system and was therefore not deemed as rate limiting to limb O_2 delivery or utilization (18, 58, 66). During high-intensity exercise, however, the respiratory muscles consume ~10–15% of the total $\dot{V}O_2$ (1), require up to 14–16% of the cardiac output (25), and are susceptible to fatigue (3, 28). These data suggest that the respiratory system has the potential to limit leg O_2 delivery and thus $\dot{V}O_2$. Fatigue of the inspiratory muscles results in a sympathetically mediated metaboreflex that increases sympathetic efferent discharge (63), thereby reducing limb blood flow both at rest (60, 61) and during exercise (24, 51). Alleviating respiratory muscle work during severe exercise via a proportional assist ventilator prevents diaphragmatic fatigue (2) and increases leg blood flow and the proportional contribution of leg $\dot{V}O_2$ to pulmonary $\dot{V}O_2$ (24). Moreover, reducing the work of breathing with HeO_2 results in a reduction of the $\dot{V}O_2$ slow-component amplitude during severe exercise (17). Conversely, increasing the work of breathing reduces leg blood flow and the proportional contribution of leg $\dot{V}O_2$ to pulmonary $\dot{V}O_2$ (24) and also increases the amplitude of the $\dot{V}O_2$ slow component (16). Importantly, unloading the respiratory muscles increases the tolerance to severe exercise (26, 27, 48), consequent to reductions in peripheral limb muscle fatigue (53) and the sensations of limb discomfort and dyspnea (26, 53). In contrast, loading the respiratory muscles reduces severe exercise tolerance (26, 53), exacerbates limb muscle fatigue (53), and heightens the sensations of limb discomfort and dyspnea (26, 53). Collectively, these data suggest that fatigue of the inspiratory muscles, which is consistently observed in response to high-intensity exercise, compromises leg blood flow, $\dot{V}O_2$, and exercise tolerance, whereas interventions that reduce inspiratory muscle fatigue have the opposite effects.

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One practical intervention that may reduce exercise-induced inspiratory muscle fatigue is inspiratory muscle training (IMT) (44, 54, 65). IMT has been hypothesized to increase leg blood flow and O_2 delivery (43, 56, 74) and has often been associated with improved exercise performance (e.g., 23, 40, 44, 54, 65). A period of IMT has also been shown to reduce peripheral limb muscle fatigue after prior inspiratory muscle fatigue (43), blood lactate accumulation (11, 12, 40, 62), dyspnea (23, 54, 65), limb discomfort (54), and occasionally minute ventilation ($\dot{V}E$) (11, 40). Reducing $\dot{V}E$ at a given work rate post-IMT would be expected to reduce the blood flow requirements of the respiratory muscles to such that a greater proportion of cardiac output would be available to distribute to the exercising limbs. Moreover, IMT has the potential to reduce lactate accumulation in the contracting inspiratory muscles (12), which might reduce the stimulation of diaphragm metaboreceptors (51, 61) and vasoconstrictor outflow (63) and thereby increase limb blood flow and O_2 delivery.

It is known that interventions that might increase muscle O_2 delivery, including the performance of priming exercise (4, 13, 32) and the inspiration of a hyperoxic gas mixture (41, 49, 52, 70), result in a reduced $\dot{V}O_2$ slow-component amplitude, faster "overall" $\dot{V}O_2$ kinetics, and an increased tolerance of high-intensity exercise (4, 70). It is therefore possible that IMT might reduce the metabolic requirements of the inspiratory muscles during intense exercise, delaying inspiratory muscle fatigue, facilitating increased limb O_2 availability, and resulting in a reduced $\dot{V}O_2$ slow-component amplitude and improved exercise tolerance. The purpose of the present study was therefore to assess the influence of a 4-wk period of either IMT or a placebo intervention (Sham) on pulmonary $\dot{V}O_2$ kinetics, $\dot{V}E$, blood lactate accumulation, and exercise tolerance during moderate-, severe-, and maximal-intensity exercise. We hypothesized that IMT, but not Sham, would be expected to reduce the $\dot{V}O_2$ slow-component amplitude and improve exercise tolerance during severe- and maximal-intensity exercise. We also hypothesized that these adaptations in the IMT group would be accompanied by reductions in blood lactate accumulation, $\dot{V}E$, and the sensations of limb and respiratory discomfort at the same absolute work rates posttraining.

METHODS

Subjects. Sixteen healthy subjects (12 men, mean ± SD age = 22 ± 4 yr, stature = 1.79 ± 0.06 m, body mass = 77 ± 8 kg; and 4 women, age = 20 ± 1 yr, stature = 1.63 ± 0.05 m, body mass = 65 ± 6 kg) volunteered to participate in this study. All subjects were nonsmokers, free from asthma and other respiratory impairments, and had normal pulmonary function (forced vital capacity = 5.21 ± 0.99 liters; forced expiratory volume in 1 s = 4.44 ± 0.86 liters; forced expiratory volume in 1 s/forced vital capacity = 85 ± 7%). The subjects participated in exercise at a recreational level but were not highly trained and were familiar with laboratory exercise testing procedures, having previously participated in studies employing cycle ergometry in our laboratory. The procedures employed in this study were approved by the University of Exeter Research Ethics Committee, and all subjects were required to give their written informed consent before the commencement of the study after the experimental procedures, associated risks, and potential benefits of participation had been explained. Subjects were instructed to arrive at the laboratory in a rested and fully hydrated state, at least 3 h postprandial, and to avoid strenuous exercise in the 24 h preceding each testing session. Each subject was also asked to refrain from caffeine and alcohol 6 and 24 h before each test, respectively. All tests were performed at the same time of day (±2 h).

Experimental design. The subjects were required to report to the laboratory on five occasions over a 2-wk period prior to the intervention period, with all tests separated by at least 24 h. During these five laboratory visits, subjects underwent a number of preliminary tests for the determination of maximum inspiratory pressure (MIP), $\dot{V}O_{2max}$ and GET, $\dot{V}O_2$ kinetics, and exercise tolerance. After completion of the preliminary tests, subjects were randomly assigned to either the IMT or Sham group. After completion of the training protocols, subjects returned to the laboratory on five occasions and repeated all the baseline tests at the same absolute work rates to determine the effect of the respective training interventions on the physiological and performance parameters.

Incremental test. Both before and after the intervention period, the subjects completed a ramp incremental exercise test for determination of the $\dot{V}O_{2max}$ and GET (67). All exercise tests were performed on an electrically braked cycle ergometer (Lode Excalibur Sport, Groningen, The Netherlands). Initially, subjects performed 3 min of baseline cycling at 0 W, after which the work rate was increased by 30 W/min for male subjects and by 25 W/min for female subjects until the limit of tolerance. The subjects cycled at a self-selected pedal rate (70–90 rpm), and this pedal rate, along with saddle and handle bar height and configuration, was recorded and reproduced in subsequent tests. Breath-by-breath pulmonary gas-exchange data were collected continuously during the incremental tests and averaged over consecutive 10-s periods. The $\dot{V}O_{2max}$ was taken as the highest 30 s average value attained before the subject's volitional exhaustion in the test. The GET was determined from a cluster of measurements including *1*) the first disproportionate increase in CO_2 production ($\dot{V}CO_2$) from visual inspection of individual plots of $\dot{V}CO_2$ vs. $\dot{V}O_2$, *2*) an increase in expired ventilation ($\dot{V}E$)/$\dot{V}O_2$ with no increase in $\dot{V}E/\dot{V}CO_2$, and *3*) an increase in end-tidal O_2 tension with no fall in end-tidal CO_2 tension. The data collected during the incremental test were used to calculate the work rates that were employed during the subsequent step tests. Specifically, the work rates that would require 80% of the GET (termed "moderate" exercise), 60% of the difference between the work rate at the GET and $\dot{V}O_{2max}$ (60%Δ; termed "severe" exercise), and 100% $\dot{V}O_{2max}$ (termed "maximal" exercise) were subsequently calculated, with account taken of the mean response time for $\dot{V}O_2$ during ramp exercise (i.e., two-thirds of the ramp rate was deducted from the work rate at GET and peak) (67).

Step tests. Both before and after the intervention period, the subjects completed two step tests on four occasions for the determination of pulmonary $\dot{V}O_2$ kinetics. The protocol comprised one moderate-intensity followed by either one severe-intensity or one maximal-intensity cycle transition. Therefore, all subjects performed a total of four bouts of moderate-intensity exercise, two bouts of severe-intensity exercise, and two bouts of maximal-intensity exercise both before and after the intervention period. The order of the administered step test combinations was randomly assigned and counterbalanced, and each subject completed the same order of step tests following the intervention period. Each transition began with 3 min of baseline cycling at 20 W before an abrupt transition to the target work rate. A passive recovery of 15 min separated the transitions. The four moderate-intensity steps were each of 6-min duration both before and after the intervention period. Of the two severe-intensity transitions performed before and after the intervention period, one was of 6-min duration, whereas the other was continued to the limit of tolerance. The two maximal-intensity transitions performed before the intervention period were both continued to the limit of tolerance. After the intervention period, one of the maximal transitions was continued to the limit of tolerance, whereas the remaining transition was terminated at the preintervention task failure iso-time (defined as the mean limit of tolerance recorded in the two maximal transitions completed before the intervention period). The time to task failure was used as a

measure of exercise tolerance and was recorded when the pedal rate fell more than 10 rpm below the required pedal rate.

Training interventions. After the initial stage of experimental testing, the male and female subjects were ranked separately by baseline MIP and then assigned to either the IMT group (age 20 ± 2 yr, stature 1.75 ± 0.10 m, body mass 74 ± 10 kg) or the Sham group (age 22 ± 4 yr, stature 1.75 ± 0.09 m, body mass 74 ± 9 kg). Both groups contained six male and two female subjects. Each subject performed a total of 1,680 inspiratory maneuvers over a 4-wk period. The IMT group completed 30 dynamic inspiratory efforts twice daily for a 4-wk period against a pressure-threshold load equivalent to ~50% of the MIP, as employed previously (e.g., Refs. 64, 65). The Sham group completed 60 slow protracted breaths once daily for 4 wk at ~15% of the MIP, a protocol known to elicit negligible changes in inspiratory muscle function (54, 65). Subjects were instructed to initiate each breath from residual volume and to continue the inspiratory effort until the maximal lung volume was attained. A nose clip was worn during all breaths, and, to avoid hyperventilation, subjects were instructed to maintain a low breathing frequency. The initial training loads were set by the investigators, and all of the inspiratory efforts were performed using a pressure-threshold device (Powerbreathe, HaB International, Southam, UK). The subjects in the IMT group were instructed to periodically increase the resistive load, such that the completion of 30 breaths approximated the limit of inspiratory muscle tolerance, whereas the subjects in the placebo group were instructed to retain the resistive load set by the investigators for the duration of the training intervention. To ensure that subjects adhered to the specific training requirements of the respective training interventions, subjects reported to the laboratory on a twice weekly basis to ensure that the pressure-threshold load was increasing as expected for the IMT group and was unchanged for the Sham group and to observe that the correct breathing technique was upheld. To ensure that the subjects were naive to the purpose and hypotheses of the investigation, the IMT group was told they were undertaking an inspiratory strength training intervention, and the Sham group was informed that they were undertaking an inspiratory endurance training intervention. All subjects ceased training 48 h before the posttraining exercise tests.

Measurements. During all exercise tests, pulmonary gas exchange and ventilation were measured continuously using a portable metabolic cart (MetaMax 3B, Cortex Biophysik, Leipzig, Germany), as described previously (4–6). A DVT turbine digital transducer measured inspired and expired airflow, and an electrochemical cell O_2 analyzer and infrared CO_2 analyzer simultaneously measured expired gases. Subjects wore nose clips and breathed through a low-dead-space, low-resistance mouthpiece that was securely attached to the volume transducer. The inspired and expired gas volume and gas concentration signals were continuously sampled via a capillary line connected to the mouthpiece. The gas analyzers were calibrated before each test with gases of known concentration, and the turbine volume transducer was calibrated using a 3-liter syringe (Hans Rudolph, Kansas City, MO). Pulmonary gas exchange and ventilation were calculated and displayed breath-by-breath. Heart rate (HR) was measured during all tests using short-range radiotelemetry (Polar S610, Polar Electro Oy, Kempele, Finland).

During one of the transitions to moderate-, severe-, and maximal-intensity exercise, pre- and posttraining, a blood sample was collected from a fingertip into a capillary tube over the 20 s preceding the step transition in work rate and within the last 20 s of exercise. A capillary blood sample was also collected at the limit of tolerance for the severe- and maximal-intensity bouts. These whole blood samples were subsequently analyzed to determine blood lactate concentration (YSI 1500, Yellow Springs Instruments, Yellow Springs, OH) within 30 s of collection. Blood lactate accumulation was calculated as the difference between blood lactate concentration at the end of exercise and blood lactate concentration at baseline. Ratings of perceived exertion (RPE; respiratory and leg discomfort) were also obtained every 2 min using Borg's 6–20 scale.

MIP was assessed in a standing position using a handheld mouth pressure meter (Micro Medical, Kent, UK) as described previously (22). Each MIP was initiated at residual volume, and subjects wore nose clips during the inspiratory maneuvers. A minimum of five well-executed MIP measurements were conducted, and the highest of three measurements within 5 cmH_2O difference was defined as the maximum (22). MIP was assessed pre- and postintervention in the IMT and Sham groups at baseline and at 2 and 10 min following the completion of all exercise bouts. In addition, MIP was assessed after the preintervention task failure iso-time during maximal exercise following the intervention period, where appropriate. The baseline MIP was taken as the mean of the five measurements made at baseline on the testing day in question.

Data analysis procedures. The breath-by-breath $\dot{V}O_2$ data from each test were initially examined to exclude errant breaths caused by coughing, swallowing, sighing, and so forth, and those values that were more than four standard deviations from the local mean were removed. The breath-by-breath data were subsequently linearly interpolated to provide second-by-second values, and, for each individual, like transitions were time aligned to the start of exercise and ensemble averaged to enhance the signal-to-noise ratio and improve confidence in the parameters derived from the model fits (39). The first 20 s of data after the onset of exercise (i.e., the phase I response) were deleted (68), and a nonlinear least-squares algorithm was used to fit the data thereafter. A single-exponential model was used to characterize the $\dot{V}O_2$ responses to moderate exercise, and a biexponential model was used for severe exercise as described in *Eqs. 1* and *2*, respectively.

$$\dot{V}O_2(t) = \dot{V}O_{2baseline} + A_p[1 - e^{-(t-TD_p/\tau_p)}] \quad (1)$$

$$\dot{V}O_2(t) = \dot{V}O_{2baseline} + A_p[1 - e^{-(t-TD_p/\tau_p)}] + A_s[1 - e^{-(t-TD_s/\tau_s)}] \quad (2)$$

where $\dot{V}O_2(t)$ represents the absolute $\dot{V}O_2$ at a given time t; $\dot{V}O_{2baseline}$ represents the mean $\dot{V}O_2$ in the baseline period; A_p, TD_p, and τ_p represent the amplitude, time delay, and time constant, respectively, describing the phase II increase in $\dot{V}O_2$ above baseline; and A_s, TD_s, and τ_s represent the amplitude of, time delay before the onset of, and time constant describing the development of the $\dot{V}O_2$ slow component, respectively. We also fit the severe exercise data with a monoexponential model to characterize the overall response dynamics. To quantify the $\dot{V}O_2$ response dynamics during maximal exercise, we first fit the data with a mono- and biexponential model with the fitting window constrained to 120 s to determine the goodness of fit, as determined by the mean squared error. Once the appropriate model fit was identified, we compared the pre- and postintervention maximal exercise $\dot{V}O_2$ response dynamics by *1*) fitting both the pre- and postintervention data to 120 s (*fit 1*); *2*) fitting the preintervention data to task failure and the postintervention data to the preintervention task failure iso-time (*fit 2*); and *3*) fitting the pre- and postintervention data both to task failure (*fit 3*).

An iterative process was used to minimize the sum of the squared errors between the fitted function and the observed values. $\dot{V}O_{2baseline}$ was defined as the mean $\dot{V}O_2$ measured over the final 90 s of baseline pedaling. The end-exercise $\dot{V}O_2$ was defined as the mean $\dot{V}O_2$ measured over the final 30 s of exercise. Because the asymptotic value (A_s) of the exponential term describing the $\dot{V}O_2$ slow component may represent a higher value than is actually reached at the end of the exercise, the amplitude of the $\dot{V}O_2$ slow component at the end of exercise was defined as A'_s. The A'_s parameter was compared at the same iso-time (360 s) pre- and posttraining for severe exercise. During maximal exercise, A'_s was compared according to *fits 1–3* as described above. The amplitude of the $\dot{V}O_2$ slow component was also described relative to the entire $\dot{V}O_2$ response.

Table 1. *MIP at baseline and following moderate-intensity, severe-intensity, and maximal-intensity exercise in the IMT and Sham groups pre- and postintervention*

	MIP, cmH_2O			
	IMT Pre	IMT Post	Sham Pre	Sham Post
Baseline MIP	155 ± 22	181 ± 21†	153 ± 34	159 ± 30
		Moderate-intensity exercise		
MIP at 2 min	151 ± 26	175 ± 27†	149 ± 26	155 ± 24
MIP at 10 min	150 ± 27	177 ± 24†	148 ± 27	157 ± 26
		Severe-intensity exercise		
MIP at 2 min	124 ± 28*	168 ± 29*†	143 ± 31*	142 ± 37*
MIP at 10 min	120 ± 23*	173 ± 28†	140 ± 33*	146 ± 27*
MIP at 2 min Tlim	120 ± 28*	165 ± 33*†	138 ± 32*	143 ± 28*
MIP at 10 min Tlim	118 ± 16*	167 ± 31*†	138 ± 36*	141 ± 29*
		Maximal-intensity exercise		
MIP at 2 min ISO	128 ± 21*	160 ± 33*†	140 ± 34*	143 ± 28*
MIP at 10 min ISO	132 ± 20*	164 ± 33*†	145 ± 32*	144 ± 28*
MIP at 2 min Tlim	128 ± 21*	167 ± 36†	140 ± 34*	142 ± 29*
MIP at 10 min Tlim	132 ± 20*	171 ± 35†	145 ± 32*	143 ± 25*

Values are means ± SD. IMT, inspiratory muscle training; ISO, preintervention task failure iso-time; MIP, maximum inspiratory pressure; Pre, preintervention; Post, postintervention; Sham, placebo intervention; Tlim, limit of tolerance. *Significantly different from baseline ($P < 0.05$); †significantly different from Pre ($P < 0.05$).

We also modeled the HR response to exercise in each condition. For this analysis, HR data were linearly interpolated to provide second-by-second values, and, for each individual, identical repetitions from like transitions were time aligned to the start of exercise and ensemble averaged. A nonlinear least-square monoexponential model without time delay was used to fit the data to moderate-, severe-, and maximal-intensity exercise, with the fitting window commencing at $t = 0$ s. The derived HR mean response time provides an insight into the overall rate of adjustment of HR dynamics. To determine whether $\dot{V}E$ was influenced by the IMT or Sham intervention, we compared $\dot{V}E$ at baseline (90 s preceding step transition) and at 120 s, at 360 s, and at exhaustion (average response over the final 30 s) during moderate-, severe-, and maximal-intensity exercise before and after the intervention period, as appropriate.

Statistics. A two-way (time-by-group) ANOVA with repeated measures for time was employed to determine the effects on the relevant physiological variables elicited by the different interventions. Where the analysis revealed a significant main or interaction effect, simple follow-up contrasts were employed to determine the origin of such effects. The relationship between changes in MIP and changes in $\dot{V}O_2$ kinetics and exercise tolerance were assessed with Pearson product moment correlation coefficients. All data are presented as means ± SD unless otherwise indicated. Statistical significance was accepted at $P < 0.05$.

RESULTS

All subjects were recreationally active on recruitment to the study, and the physiological parameters of interest (i.e., MIP, $\dot{V}O_{2max}$, $\dot{V}O_2$ at GET, $\dot{V}O_2$ phase II τ_p, $\dot{V}O_2$ slow-component amplitude) were not significantly different between the IMT and Sham groups before the commencement of the study (Tables 1–3). Each subject self reported 100% compliance to the prescribed training and also self-reported that they did not alter their physical activity for the duration of the study.

Incremental test. The $\dot{V}O_{2max}$ preintervention was 47 ± 5 $ml \cdot kg^{-1} \cdot min^{-1}$ in the IMT group and 48 ± 8 $ml \cdot kg^{-1} \cdot min^{-1}$ in the Sham group, with the GET occurring at ~50% $\dot{V}O_{2max}$ in both groups. There were no significant changes in the $\dot{V}O_2$, $\dot{V}E$, or work rate attained at the GET or at peak exercise during the incremental test following either the IMT or Sham interventions.

Maximum inspiratory pressure. The MIP at baseline and after moderate-, severe-, and maximal-intensity exercise for the IMT and Sham groups, pre- (Pre) and postintervention (Post), are presented in Table 1. There was a significant interaction effect between the IMT and Sham groups ($P < 0.01$) such that baseline MIP was significantly increased (17%) after IMT (155 ± 22 Pre vs. 181 ± 21 cmH_2O Post; $P < 0.01$) but not changed with Sham (153 ± 34 Pre vs. 159 ± 30 cmH_2O Post).

Compared to baseline, the MIP was not significantly reduced at 2 or 10 min after the completion of moderate exercise either before or after the intervention in either group (Table 1). However, a significant interaction effect was observed for the absolute MIP at both time points after moderate exercise ($P < 0.05$), with MIP being significantly increased in the IMT group ($P < 0.05$) but not in the Sham group ($P > 0.05$). After 6 min of severe exercise and severe exercise to exhaustion, MIP was reduced compared with baseline in the IMT and Sham groups both before and after the intervention period (Table 1). However, after the intervention period, the absolute MIP after severe exercise manifested a significant interaction effect ($P < 0.01$), with the MIP increased in the IMT group ($P < 0.05$) but not in the Sham group ($P > 0.05$; Table 1). Ten minutes after the completion of 6 min of severe exercise, MIP was not significantly different from the baseline value in the IMT group but remained significantly below the baseline value at all time points after Sham (Table 1). Similar to results with severe exercise, MIP was significantly reduced below the baseline following maximal exercise in both the IMT and Sham groups prior to the intervention period (Table 1). After the intervention period, there was a significant interaction effect between the IMT and Sham groups for the MIP after maximal exercise ($P < 0.05$), with the absolute MIP being significantly increased at the preintervention exhaustion time (iso-time) and also after

Table 2. *$\dot{V}E$ during moderate-intensity, severe-intensity, and maximal-intensity exercise in the IMT and Sham groups pre- and postintervention*

	$\dot{V}E$, l/min			
	IMT Pre	IMT Post	SHAM Pre	SHAM Post
		Moderate-intensity exercise		
Baseline $\dot{V}E$	23 ± 3	24 ± 4	21 ± 2	22 ± 2
$\dot{V}E$ at 120 s	33 ± 7	33 ± 7	29 ± 3	29 ± 2
$\dot{V}E$ at 360 s	34 ± 7	35 ± 7	30 ± 3	30 ± 2
		Severe-intensity exercise		
Baseline $\dot{V}E$	23 ± 4	24 ± 5	23 ± 3	22 ± 2
$\dot{V}E$ at 120 s	78 ± 17	78 ± 17	73 ± 14	73 ± 14
$\dot{V}E$ at 360 s	106 ± 35	102 ± 29	88 ± 15	73 ± 14
$\dot{V}E$ at exhaustion	135 ± 47	138 ± 45	120 ± 26	118 ± 13
		Maximal-intensity exercise		
Baseline $\dot{V}E$	25 ± 5	25 ± 4	23 ± 2	24 ± 3
$\dot{V}E$ at 120 s	126 ± 33	119 ± 32*	124 ± 29	120 ± 29
$\dot{V}E$ at exhaustion	148 ± 46	148 ± 45	139 ± 27	140 ± 22

Values are means ± SD. $\dot{V}E$, minute ventilation. *Significantly different from Pre ($P < 0.05$).

maximal exercise to exhaustion in the IMT ($P < 0.05$) group but not in the Sham group ($P > 0.05$). Moreover, the MIP was not significantly different from the baseline after exhaustive maximal exercise post-IMT, whereas it remained significantly below baseline following Sham (Table 1).

Pulmonary ventilation. The $\dot{V}E$ results at baseline and during moderate-, severe-, and maximal-intensity exercise in the IMT and Sham groups for Pre and Post are presented in Table 2. There was no significant difference in the absolute $\dot{V}E$ during moderate and severe exercise after either the IMT or Sham interventions. During maximal exercise, however, there was a significant main effect for time for the $\dot{V}E$ at 120 s ($P < 0.05$). Follow-up analyses revealed that the $\dot{V}E$ at 120-s was significantly reduced after IMT ($P < 0.05$) but was not significantly different after Sham ($P > 0.05$; Table 2).

$\dot{V}O_2$ kinetics. The parameters of $\dot{V}O_2$ dynamics before and after the IMT and Sham interventions during moderate-, severe-, and maximal-intensity exercise are presented in Table 3 and illustrated in Figs. 1, 2, and 3, respectively. The dynamics of $\dot{V}O_2$ during moderate exercise were unaffected by the IMT and Sham interventions (Table 3, Fig. 1).

There was a significant interaction effect between the IMT and Sham groups for the overall $\dot{V}O_2$ kinetics during severe exercise ($P < 0.01$; as assessed with a monoexponential function), with follow-up analyses revealing that the overall $\dot{V}O_2$ kinetics was 21% faster after IMT (99 ± 18 s Pre vs. 78 ± 13 s Post; $P < 0.01$) but was not different after Sham. The phase II $\dot{V}O_2$ time constant was not significantly altered by IMT or Sham. However, there was a significant main effect for time for the fundamental and slow-component $\dot{V}O_2$ amplitudes ($P < 0.05$). Subsequent analyses revealed that the fundamental component $\dot{V}O_2$ amplitude was significantly increased (1.77 ± 0.41 l/min Pre vs. 1.92 ± 0.49 l/min Post; $P < 0.05$) and the $\dot{V}O_2$ slow-component amplitude was significantly reduced (0.60 ± 0.20 l/min Pre vs. 0.53 ± 0.24 l/min Post; $P < 0.05$) during severe exercise after IMT, whereas these parameters were not significantly different after Sham (Table 3, Fig. 2). The $\dot{V}O_2$ at exhaustion was not significantly different from the $\dot{V}O_{2max}$ measured in the initial incremental test either before or after the interventions.

During maximal exercise, there was a significant interaction effect between the IMT and Sham groups for the $\dot{V}O_2$ at 120 s

Table 3. *Pulmonary $\dot{V}O_2$ dynamics during moderate-intensity, severe-intensity, and maximal-intensity exercise in the IMT and Sham groups pre- and postintervention*

	IMT Pre	IMT Post	SHAM Pre	SHAM Post
		Moderate-intensity exercise		
Baseline $\dot{V}O_2$, l/min	0.93 ± 0.11	0.94 ± 0.11	0.93 ± 0.08	0.92 ± 0.09
End-exercise $\dot{V}O_2$, l/min	1.50 ± 0.27	1.56 ± 0.28	1.44 ± 0.20	1.43 ± 0.16
Phase II time constant, s	22 ± 7	23 ± 7	21 ± 5	21 ± 8
Fundamental amplitude, l/min	0.58 ± 0.19	0.60 ± 0.20	0.51 ± 0.18	0.51 ± 0.17
Mean response time, s	37 ± 5	38 ± 7	38 ± 5	40 ± 11
		Severe-intensity exercise		
Baseline $\dot{V}O_2$, l/min	0.96 ± 0.12	0.94 ± 0.11	0.95 ± 0.08	0.97 ± 0.09
$\dot{V}O_2$ at 360 s, l/min	3.32 ± 0.69	3.37 ± 0.74	3.17 ± 0.49	3.20 ± 0.44
$\dot{V}O_2$ at exhaustion, l/min	3.42 ± 0.73	3.47 ± 0.74	3.25 ± 0.42	3.28 ± 0.41
Phase II time constant, s	26 ± 7	27 ± 6	27 ± 7	29 ± 7
Fundamental amplitude, l/min	1.77 ± 0.41	1.92 ± 0.49*	1.77 ± 0.26	1.81 ± 0.33
Slow-component amplitude, l/min	0.60 ± 0.20	0.53 ± 0.24*	0.46 ± 0.20	0.43 ± 0.16
Slow-component amplitude, %end	25 ± 3	21 ± 4†	20 ± 6	19 ± 6
Overall time constant, s	99 ± 18	78 ± 13†	74 ± 19	74 ± 12
		Maximal-intensity exercise		
Baseline $\dot{V}O_2$, l/min	0.98 ± 0.12	1.03 ± 0.17	1.01 ± 0.10	0.99 ± 0.12
$\dot{V}O_2$ at 120 s, l/min	3.31 ± 0.63	3.41 ± 0.64†	3.34 ± 0.43	3.35 ± 0.48
$\dot{V}O_2$ at exhaustion, l/min	3.42 ± 0.65	3.61 ± 0.68†	3.44 ± 0.44	3.48 ± 0.48
Biexponential *fit 1* (120 s vs. 120 s)				
Phase II time constant, s	20 ± 6	23 ± 7	20 ± 6	19 ± 5
Fundamental amplitude, l/min	2.07 ± 0.45	2.23 ± 0.52*	2.16 ± 0.43	2.19 ± 0.45
Mean response time, s	30 ± 5	32 ± 5	30 ± 3	29 ± 3
Slow-component amplitude, l/min	0.28 ± 0.14	0.18 ± 0.07*	0.19 ± 0.10	0.18 ± 0.14
Slow-component amplitude, %end	12 ± 4	7 ± 2*	9 ± 5	8 ± 7
Biexponential *fit 2* (Tlim vs. ISO)				
Phase II time constant, s	20 ± 6	24 ± 7	21 ± 6	19 ± 6
Fundamental amplitude, l/min	2.08 ± 0.46	2.23 ± 0.50	2.17 ± 0.41	2.19 ± 0.44
Mean response time, s	31 ± 5	32 ± 4	30 ± 5	29 ± 3
Slow-component amplitude, l/min	0.41 ± 0.21	0.35 ± 0.18	0.28 ± 0.14	0.30 ± 0.18
Slow-component amplitude, %end	16 ± 6	13 ± 6†	12 ± 6	12 ± 8
Biexponential *fit 3* (Tlim vs. Tlim)				
Phase II time constant, s	20 ± 6	23 ± 7	21 ± 6	19 ± 6
Fundamental amplitude, l/min	2.08 ± 0.46	2.21 ± 0.51	2.17 ± 0.41	2.19 ± 0.44
Mean response time, s	31 ± 5	32 ± 5	30 ± 5	29 ± 3
Slow-component amplitude, l/min	0.41 ± 0.21	0.41 ± 0.21	0.28 ± 0.14	0.33 ± 0.17
Slow-component amplitude, %end	16 ± 6	16 ± 7	12 ± 6	13 ± 7

Values are means ± SD. $\dot{V}O_2$, oxygen uptake. *Significantly different from Pre ($P < 0.05$); †significantly different from Pre ($P < 0.01$).

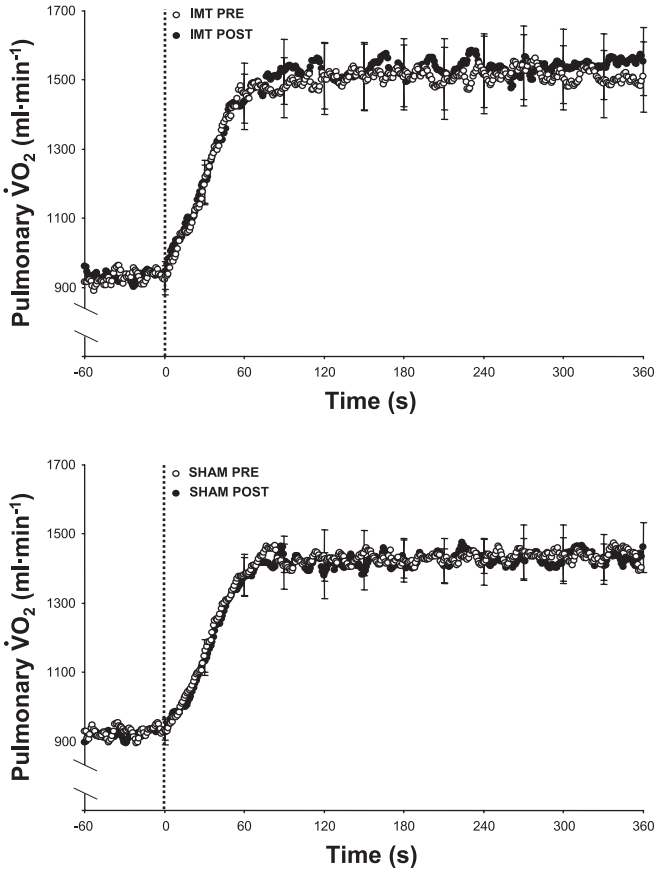

Fig. 1. Group mean ± SE pulmonary oxygen uptake ($\dot{V}O_2$) responses to a step increment from an unloaded baseline to a moderate-intensity work rate in the inspiratory muscle training (IMT) group (*top*) and the sham intervention (Sham) group (*bottom*). ○, Preintervention (Pre) responses; ●, postintervention (Post) responses. The vertical line represents the abrupt transition to the higher work rate. Note that pulmonary $\dot{V}O_2$ kinetics was unaffected by both IMT and Sham.

($P < 0.05$), with a significantly greater $\dot{V}O_2$ at 120 s after IMT (3.31 ± 0.63 l/min Pre vs. 3.41 ± 0.64 l/min Post; $P < 0.01$) but not after Sham. During maximal exercise, the $\dot{V}O_2$ phase II time constant and the mean response time were unaffected after the IMT and Sham interventions regardless of the fitting procedure employed (Table 3). However, using *fit 1*, the $\dot{V}O_2$ fundamental component amplitude was significantly increased (2.07 ± 0.45 l/min Pre vs. 2.23 ± 0.52 l/min Post; $P < 0.05$), and the $\dot{V}O_2$ slow-component amplitude was significantly reduced after IMT (0.28 ± 0.14 l/min Pre vs. 0.18 ± 0.07 l/min Post; $P < 0.05$), whereas these parameters were not significantly different after Sham (Fig. 3). There was a significant main effect for time ($P < 0.05$) with no interaction effect ($P > 0.05$) for the peak value of $\dot{V}O_2$ attained during maximal exercise. The follow-up *t*-test revealed that $\dot{V}O_2$ at exhaustion was significantly greater after IMT than before IMT ($P < 0.01$). The $\dot{V}O_2$ at exhaustion was significantly lower ($P < 0.05$) than the $\dot{V}O_{2max}$ measured in the initial incremental test before, but not after, the IMT intervention.

HR dynamics and blood lactate concentration. HR was not significantly different during moderate-, severe-, and maximal-intensity exercise after the IMT and Sham intervention periods (Table 4). Blood lactate accumulation was unaffected after the IMT and Sham interventions during moderate exercise. However, there was a significant interaction effect for the blood lactate accumulation over the first 360 s of severe exercise ($P < 0.05$), whereby blood lactate accumulation was significantly reduced after IMT (6.0 ± 1.2 mM Pre vs. 5.0 ± 1.0 mM Post; $P < 0.01$) but was not significantly altered after Sham (Table 4). During maximal exercise, the blood lactate concentration at exhaustion was significantly greater after IMT (7.2 ± 1.8 mM Pre vs. 9.0 ± 1.2 mM Post; $P < 0.01$) but was not significantly different after Sham.

Ratings of dyspnea and limb discomfort. Ratings of dyspnea and limb discomfort were not significantly different during moderate exercise following either the IMT or Sham interventions (Table 5). During severe exercise, however, ratings of dyspnea ($P < 0.01$) and limb discomfort ($P < 0.05$) were significantly reduced at 2, 4, and 6 min of exercise following IMT, whereas only limb RPE at 2 min was reduced after the sham intervention ($P < 0.05$). During maximal exercise, dyspnea, but not limb discomfort, was significantly reduced at 2 min of exercise after IMT, but neither dyspnea nor limb discomfort was affected by the Sham intervention.

Exercise tolerance. A significant main effect for time ($P < 0.01$) was observed for severe-intensity exercise tolerance. Four weeks of IMT resulted in a 39% improvement in severe-

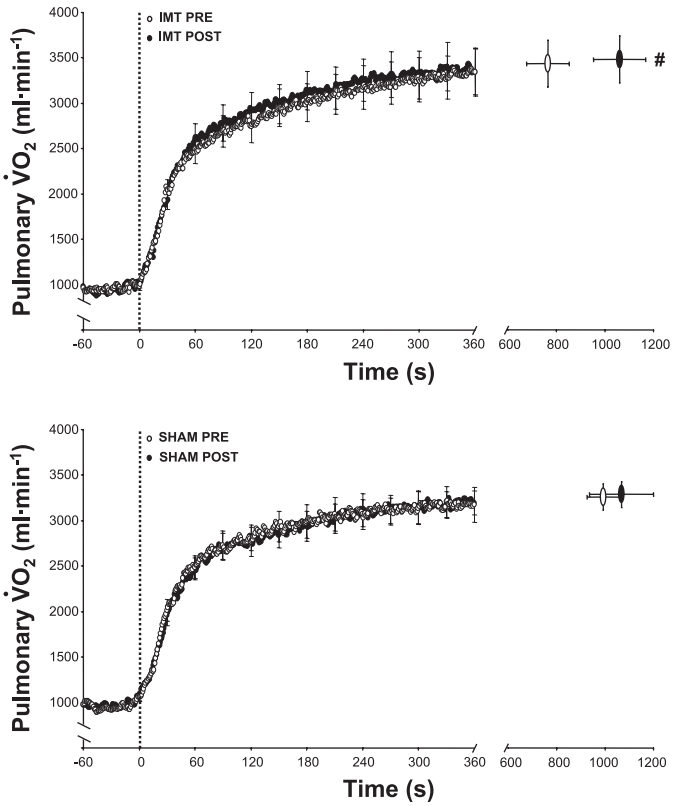

Fig. 2. Group mean ± SE pulmonary $\dot{V}O_2$ responses to a step increment from an unloaded baseline to a severe-intensity work rate in the IMT group (*top*) and Sham group (*bottom*). ○, Pre responses; ●, Post responses. The vertical line represents the abrupt transition to the higher work rate. Note that the overall pulmonary $\dot{V}O_2$ kinetics was significantly faster post-IMT consequent to an increased fundamental and reduced slow-component amplitude, whereas these parameters were not affected by Sham intervention. Exercise tolerance was significantly enhanced post-IMT but not post-Sham. #Significantly different from Pre ($P < 0.01$).

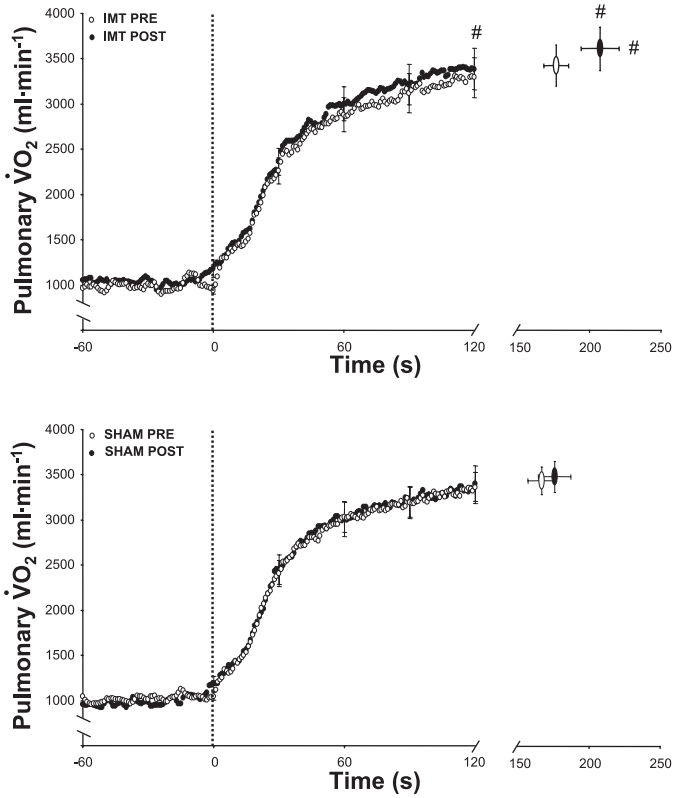

Fig. 3. Group mean ± SE pulmonary $\dot{V}O_2$ response to a step increment from an unloaded baseline to a maximal work rate in the IMT group (*top*) and Sham group (*bottom*). ○, Pre responses; ●, Post responses. The vertical line represents the abrupt transition to the higher work rate. The pulmonary $\dot{V}O_2$ was significantly greater at 120 s and at exhaustion post-IMT but not post-Sham. Exercise tolerance was significantly enhanced post-IMT but not post-Sham. #Significantly different from Pre ($P < 0.01$).

intensity exercise tolerance (765 ± 249 s Pre vs. 1,061 ± 304 s Post; $P < 0.01$), whereas the 8% increase after Sham was not significant (992 ± 188 s Pre vs. 1,068 ± 374 s Post; Fig. 4). A significant interaction effect between groups was observed for maximal-intensity exercise tolerance ($P < 0.01$), with maximal exercise tolerance being significantly enhanced (by 18%) after IMT (177 ± 24 s Pre vs. 208 ± 37 s Post; $P < 0.01$) but not significantly different (5%) after Sham (167 ± 28 s Pre vs. 176 ± 32 s Post; Fig. 4).

Relationships between changes in MIP and changes in $\dot{V}O_2$ kinetics and exercise tolerance. Although IMT resulted in improvements in baseline MIP and in $\dot{V}O_2$ kinetics and exercise tolerance during severe- and maximal-intensity exercise, the changes in these variables were not significantly correlated. For example, changes in baseline MIP were not significantly correlated with changes in overall $\dot{V}O_2$ kinetics (severe: $r = 0.20$, $P = 0.63$; maximal: $r = -0.62$, $P = 0.10$) or the $\dot{V}O_2$ slow-component amplitude (severe: $r = 0.20$, $P = 0.63$; maximal: $r = -0.62$, $P = 0.10$). Changes in baseline MIP were also not significantly correlated with changes in exercise tolerance during severe-intensity ($r = 0.60$, $P = 0.12$) or maximal-intensity ($r = 0.29$, $P = 0.48$) exercise.

DISCUSSION

This is the first investigation to comprehensively assess the influence of IMT on $\dot{V}O_2$ kinetics and exercise tolerance across a range of exercise intensities. The principal original finding was that, compared with Sham training, 4 wk of pressure threshold IMT resulted in significant changes in several features of the dynamic $\dot{V}O_2$ response to severe- and maximal-intensity (but not moderate-intensity) exercise in young healthy adults. For severe exercise, the faster overall $\dot{V}O_2$ dynamics was accompanied by reductions in blood lactate accumulation and the perceptions of dyspnea and limb discomfort at the same absolute work rate posttraining and improved exercise tolerance. Similarly, during maximal exercise, the $\dot{V}O_2$ slow-component amplitude was reduced, and end-exercise $\dot{V}O_2$ and exercise tolerance were increased after IMT. These results demonstrate that IMT, presumably through reducing the extent of fatigue and therefore the metabolic requirements of the inspiratory muscles during high-intensity exercise, enhanced $\dot{V}O_2$ dynamics and exercise tolerance. The improvements in exercise tolerance after IMT that have been reported previously (e.g., 23, 40, 44, 54, 65) might therefore be linked, at least in part, to changes in $\dot{V}O_2$ kinetics.

MIP and pulmonary ventilation. We observed a 17% increase in baseline MIP following IMT, indicating that the maximum force-generating capacity of the inspiratory muscles was substantially increased post-IMT, consistent with earlier studies (44). Moderate exercise did not cause significant changes in MIP. However, after severe exercise before the intervention period, the MIP was significantly reduced (by ~23%) below the baseline value, suggestive of the development of inspiratory muscle fatigue. After IMT, the extent of this fatigue was reduced, with the MIP being within 9% of the baseline, consistent with previous studies (54, 65). Furthermore, 10 min after 6 min of severe-intensity exercise, the MIP was not significantly different from the baseline value, indicating that the inspiratory muscles recovered more rapidly after IMT than after Sham. Short-duration maximal-intensity exercise also resulted in a significant reduction (by ~18%) of MIP below the baseline value. The extent of this reduction was reduced after IMT (MIP was 8% lower than baseline).

The absolute $\dot{V}E$ during moderate- and severe-intensity exercise was not different after IMT or Sham. However, $\dot{V}E$ was slightly but significantly reduced at 2 min during maximal-intensity exercise after IMT. Some previous studies have also reported reductions in $\dot{V}E$ after IMT (10, 11, 40), although others have found no change (62, 64, 73). This reduction in $\dot{V}E$ during maximal-intensity exercise might have contributed to the reduced degree of inspiratory muscle fatigue that was measured and the reduced perception of dyspnea. A reduction in $\dot{V}E$ for the same work rate after IMT might also reduce the metabolic requirements of, and thus blood flow commandeered by, the respiratory muscles.

Fatigue of the inspiratory muscles stimulates diaphragm innervating metaboreceptors (7), invoking sympathetically mediated vasoconstrictor outflow (63) and a reduction in limb blood flow (60). It is known that the metaboreflex is activated once a threshold of fatiguing inspiratory work has been exceeded (61) and in response to the accumulation of fatigue-related metabolites, including lactic acid (51). We observed a reduced blood lactate accumulation during the first 6 min of severe exercise after IMT, which may be, in part, due to the reduced inspiratory muscle fatigue (12). Therefore, the reduced blood lactate accumulation and inspiratory muscle fatigue might have reduced the magnitude of the metaboreflex (74)

Table 4. *Heart rate and blood lactate concentration dynamics during moderate-intensity, severe-intensity, and maximal-intensity exercise in the IMT and Sham groups pre- and postintervention*

	IMT Pre	IMT Post	SHAM Pre	SHAM Post
Moderate-intensity exercise				
Baseline HR, beats/min	90 ± 8	91 ± 6	100 ± 13	99 ± 12
End-exercise HR, beats/min	109 ± 8	110 ± 7	113 ± 14	111 ± 13
HR Fundamental time constant, s	32 ± 10	29 ± 9	27 ± 16	28 ± 15
Baseline blood [lactate], mM	1.0 ± 0.1	1.1 ± 0.3	0.9 ± 0.4	0.9 ± 0.3
End-exercise blood [lactate], mM	1.2 ± 0.4	1.3 ± 0.6	0.9 ± 0.4	1.0 ± 0.3
ΔBlood [lactate], mM	0.2 ± 0.5	0.3 ± 0.4	0.0 ± 0.3	0.1 ± 0.5
Severe-intensity exercise				
Baseline HR, beats/min	93 ± 7	92 ± 7	101 ± 15	99 ± 14
HR at 120 s, beats/min	151 ± 9	151 ± 8	155 ± 13	153 ± 11
HR at 360 s, beats/min	168 ± 8	168 ± 9	170 ± 11	169 ± 9
HR mean response time, s	63 ± 18	58 ± 18	58 ± 17	61 ± 18
Baseline blood [lactate], mM	0.9 ± 0.2	1.0 ± 0.2	0.8 ± 0.3	0.9 ± 0.2
Blood [lactate] at 360 s, mM	6.9 ± 1.3	6.0 ± 1.1*	5.0 ± 1.0	4.8 ± 1.0
Blood [lactate] at exhaustion, mM	8.8 ± 2.2	8.5 ± 1.8	6.9 ± 1.2	6.5 ± 1.3
ΔBlood [lactate] 360 s-baseline, mM	6.0 ± 1.2	5.0 ± 1.0†	4.1 ± 0.8	3.9 ± 1.0
ΔBlood [lactate] exhaustion-baseline, mM	7.9 ± 2.1	7.5 ± 1.7	6.1 ± 1.1	5.7 ± 1.4
Maximal-intensity exercise				
Baseline HR, beats/min	91 ± 6	92 ± 6	102 ± 10	102 ± 14
HR at 120 s, beats/min	164 ± 7	164 ± 8	170 ± 9	169 ± 9
HR mean response time, s	38 ± 20	34 ± 10	27 ± 7	26 ± 4
Baseline blood [lactate], mM	0.9 ± 0.2	1.0 ± 0.2	0.9 ± 0.2	0.9 ± 0.1
Blood [lactate] at ISO, mM	7.2 ± 1.8	7.4 ± 1.5	7.5 ± 1.0	7.8 ± 1.5
Blood [lactate] at exhaustion, mM	7.2 ± 1.8	9.0 ± 1.2†	7.5 ± 1.0	8.6 ± 1.6
Δ blood [lactate] ISO-baseline, mM	6.3 ± 1.7	6.4 ± 1.6	6.6 ± 1.1	6.9 ± 1.4
Δ blood [lactate] exhaustion-baseline, mM	6.3 ± 1.7	8.0 ± 1.2†	6.6 ± 1.1	7.7 ± 1.5

Values are means ± SD. HR, heart rate; [lactate], lactate concentration; Δ, difference. *Significantly different from Pre ($P < 0.05$); †significantly different from Pre ($P < 0.01$).

and, subsequently, increased blood flow to the exercising limbs. The reduced $\dot{V}_E$ during maximal-intensity exercise would also reduce the $\dot{V}O_2$ requirements of the respiratory muscles (1) such that leg blood flow might be greater. Although empirical evidence that IMT increases leg blood flow during whole-body exercise is currently lacking, it is clear that reducing the work of breathing via proportional assist ventilator prevents diaphragm fatigue (2) and increases leg blood flow (24), whereas increasing the work of breathing reduces leg blood flow (24).

$\dot{V}O_2$ kinetics. The phase II $\dot{V}O_2$ time constant, which reflects the rate at which $\dot{V}O_2$ in the contracting muscles increases toward the required metabolic rate (21, 37), was not altered by IMT during moderate-, severe-, or maximal-intensity exercise. This is consistent with previous reports that indicate that the phase II $\dot{V}O_2$ time constant is insensitive to interventions which might enhance muscle O_2 delivery, at least in young healthy subjects performing large muscle group exercise (4, 13, 41, 45, 70, 72). The results for moderate-intensity exercise are also consistent with a previous report that IMT did not alter $\dot{V}O_2$ kinetics (20). However, the amplitudes of the fundamental and slow components of $\dot{V}O_2$ were increased and decreased, respectively, during both severe- and maximal-intensity exercise. It has been suggested that the fundamental and slow-component $\dot{V}O_2$ response amplitudes might be sensitive to muscle O_2 availability (32, 35). Interventions that likely result in an acute increase in muscle O_2 delivery during exercise, such as the performance of prior exercise and the inspiration of hyperoxic gas, result in an increased $\dot{V}O_2$ fundamental component amplitude and/or a reduced $\dot{V}O_2$ slow-component amplitude (4, 13, 41, 70), whereas interventions that might compromise muscle O_2 delivery have the opposite effects (34, 35). That IMT altered $\dot{V}O_2$ dynamics during severe- and maximal-intensity exercise in which inspiratory muscle fatigue was reduced, but not during moderate-intensity exercise, which did not fatigue the inspiratory muscles, suggests that a redistribution of blood flow from the respiratory muscles to the exercising limbs might have facilitated the altered $\dot{V}O_2$ response. However, it is noteworthy that the effects of IMT on $\dot{V}O_2$ kinetics during severe exercise (i.e., ~12% reduction in the $\dot{V}O_2$ slow-component amplitude and ~21% speeding of the overall $\dot{V}O_2$ dynamics) are somewhat less impressive than the effects of interventions such as training and prior exercise, both of which can result in 40–50% reductions in the $\dot{V}O_2$ slow-component amplitude and $\dot{V}O_2$ mean response time. This is likely because, in addition to enhancing muscle O_2 delivery, these other interventions also alter factors such as motor unit recruitment patterns and muscle oxidative enzyme activity (and thus O_2 utilization) (4, 5, 31, 32).

Measurements of pulmonary $\dot{V}O_2$ predominantly reflect leg muscle $\dot{V}O_2$ over both the fundamental (21, 37) and slow phases (37, 46) of the $\dot{V}O_2$ response to exercise. It has been reported that loading the inspiratory muscles during intense cycle exercise reduces leg blood flow and leg $\dot{V}O_2$ as a percentage of pulmonary $\dot{V}O_2$, whereas unloading the inspiratory muscles increases leg blood flow and leg $\dot{V}O_2$ as a percentage of pulmonary $\dot{V}O_2$ (24). In the present study, IMT increased the $\dot{V}O_2$ fundamental component amplitude during severe- and maximal-intensity exercise, presumably by en-

Table 5. *Ratings of perceived exertion for limb and respiratory discomfort during moderate-intensity, severe-intensity, and maximal-intensity exercise in the IMT and Sham groups pre- and postintervention*

	IMT Pre	IMT Post	SHAM Pre	SHAM Post
Moderate-intensity exercise				
Limb RPE at baseline	7 ± 1	7 ± 1	7 ± 1	7 ± 2
Limb RPE at 2 min	9 ± 1	9 ± 1	9 ± 1	8 ± 1
Limb RPE at 4 min	9 ± 1	9 ± 2	10 ± 1	9 ± 1
Limb RPE at 6 min	10 ± 1	10 ± 2	10 ± 1	9 ± 1
Respiratory RPE at baseline	7 ± 1	6 ± 1	7 ± 1	7 ± 2
Respiratory RPE at 2 min	9 ± 1	9 ± 1	10 ± 1	9 ± 2
Respiratory RPE at 4 min	9 ± 1	9 ± 2	10 ± 1	9 ± 2
Respiratory RPE at 6 min	10 ± 1	10 ± 2	10 ± 1	9 ± 2
Severe-intensity exercise				
Limb RPE at baseline	8 ± 2	7 ± 1	8 ± 2	7 ± 2
Limb RPE at 2 min	13 ± 2	12 ± 2*	15 ± 2	13 ± 2*
Limb RPE at 4 min	15 ± 2	13 ± 1*	16 ± 2	15 ± 2
Limb RPE at 6 min	16 ± 2	14 ± 2*	16 ± 2	15 ± 1
Respiratory RPE at baseline	7 ± 2	7 ± 1	8 ± 2	8 ± 2
Respiratory RPE at 2 min	13 ± 1	11 ± 1†	13 ± 1	12 ± 1
Respiratory RPE at 4 min	14 ± 2	12 ± 1†	14 ± 1	13 ± 2
Respiratory RPE at 6 min	15 ± 2	13 ± 1†	15 ± 1	14 ± 2
Maximal-intensity exercise				
Limb RPE at baseline	8 ± 1	7 ± 1	8 ± 1	7 ± 1
Limb RPE at 2 min	16 ± 1	16 ± 2	18 ± 1	17 ± 2
Respiratory RPE at baseline	7 ± 1	7 ± 1	8 ± 1	7 ± 1
Respiratory RPE at 2 min	16 ± 1	15 ± 1†	17 ± 2	16 ± 2

Values are means ± SD. RPE, rating of perceived exertion. *Significantly different from Pre ($P < 0.05$); †significantly different from Pre ($P < 0.01$).

abling a greater leg blood flow. This suggests that muscle O_2 delivery might play an important role in setting the $\dot{V}O_2$ fundamental component amplitude during high-intensity exercise and that IMT, through reducing inspiratory muscle fatigue and thus the onset of the metaboreflex, increased muscle O_2 delivery and thus $\dot{V}O_2$ in the early minutes of such exercise.

The increased $\dot{V}E$ during high-intensity exercise has been estimated to account for up to 24% of the $\dot{V}O_2$ slow-component amplitude (15). In keeping with this, loading the inspiratory muscles increases the $\dot{V}O_2$ slow-component amplitude (16), whereas changing lung mechanics by breathing HeO_2 reduces the $\dot{V}O_2$ slow-component amplitude (17). A reduction in absolute $\dot{V}E$ (as was observed at 2 min into maximal-intensity exercise) or in the $\dot{V}O_2$ requirement for a given $\dot{V}E$ (i.e., improved efficiency) might therefore contribute to the reduced $\dot{V}O_2$ slow component that we observed after IMT. Specific training of the respiratory muscles has been reported to increase the proportion of type I fibers in the external intercostal muscles (50), which would be expected to result in improved contractile efficiency (9). Another explanation for the reduced $\dot{V}O_2$ slow component after IMT is that an enhanced leg blood flow across the initial exercise transient reduced the rate of limb muscle fatigue development (24, 53) and thus the requirement to recruit lower-efficiency type II muscle fibers to support power production as exercise continued. This delayed-onset recruitment of type II muscle fibers has been proposed to be a key determinant of the $\dot{V}O_2$ slow component (9, 38, 46, 57).

The $\dot{V}O_2$ at exhaustion during maximal-intensity exercise was significantly greater after IMT. This observation is somewhat surprising given that previous studies have shown no effect of IMT on $\dot{V}O_{2max}$, at least during incremental exercise (e.g., 42, 44, 59, 64). It is possible that high-intensity exercise is terminated when the energy available from substrate-level phosphorylation has been exhausted and/or fatigue-related muscle metabolites have accumulated to intolerable levels (33, 47). During maximal-intensity (or "extreme") exercise (71), the duration of exercise might be so short (≤3 min) that the limit of tolerance is reached before the $\dot{V}O_{2max}$ is attained. Consistent with this, the $\dot{V}O_2$ attained at the termination of maximal-intensity exercise in the present study was slightly but significantly lower than the $\dot{V}O_{2max}$ measured in the initial incremental test before, but not after, the IMT intervention. It is possible that the higher $\dot{V}O_2$ (and thus oxidative contribution to energy turnover) over the first 2 min of maximal-intensity exercise after IMT spared the energetic contribution from substrate-level phosphorylation, thereby extending the duration of exercise and permitting the $\dot{V}O_{2max}$ to be attained.

Exercise tolerance. After 4 wk of IMT, which significantly increased MIP and reduced the extent of inspiratory muscle fatigue, exercise tolerance was improved by a mean of 39% and 18% during severe- and maximal-intensity exercise, respectively. Improved exercise performance has also been observed previously during constant work-rate tests to exhaustion (10, 11, 20, 42), as well as during time trials (29, 54, 65) and fixed duration exercise (23) after training of the respiratory muscles. Increasing the work of breathing exacerbates peripheral leg fatigue (53), heightens dyspnea and sensations of leg discomfort, and compromises leg blood flow and whole body exercise tolerance (26, 53). However, when the work of breathing is reduced, the extent of peripheral limb muscle fatigue (53), diaphragm fatigue (2), dyspnea, and leg discomfort (53) are reduced, and leg blood flow (24) and exercise tolerance (26, 27, 48) are improved. Collectively, these findings indicate that the increased inspiratory muscle fatigue resistance that we observed post-IMT might have reduced the fraction of total cardiac output required by the respiratory muscles during exercise and blunted the accumulation of fatigue-related metabolites. In this way, any potential reflex vasoconstrictive effects on the locomotor muscle vasculature would be attenuated (61, 74). Leading to an increased limb blood flow (24) and enhanced exercise tolerance (26).

Given that certain aspects of $\dot{V}O_2$ dynamics are sensitive to changes in muscle O_2 availability (41, 45, 70) and IMT has the potential to increase leg O_2 supply, the improved exercise performance often observed after IMT might be ascribed, in part, to an enhanced dynamic $\dot{V}O_2$ response to exercise. A faster adjustment of oxidative phosphorylation in response to the same absolute work rate after IMT would reduce the magnitude of the O_2 deficit and thus the energy contribution from substrate-level phosphorylation (14, 45). Likewise, a reduction in the $\dot{V}O_2$ slow-component amplitude would reduce PCr breakdown (57) and glycogen depletion (38). Interventions that elicit such alterations in the $\dot{V}O_2$ response would therefore spare the finite anaerobic reserves, reduce the accumulation of fatiguing metabolites, and improve exercise tolerance (4–6, 14, 30). Consistent with earlier studies, blood lactate accumulation (10, 11, 40, 62) and the perceptions of dyspnea and limb discomfort (23, 54, 65) were reduced after IMT during severe exercise. The improved $\dot{V}O_2$ dynamics after IMT would be expected to reduce blood lactate accumulation

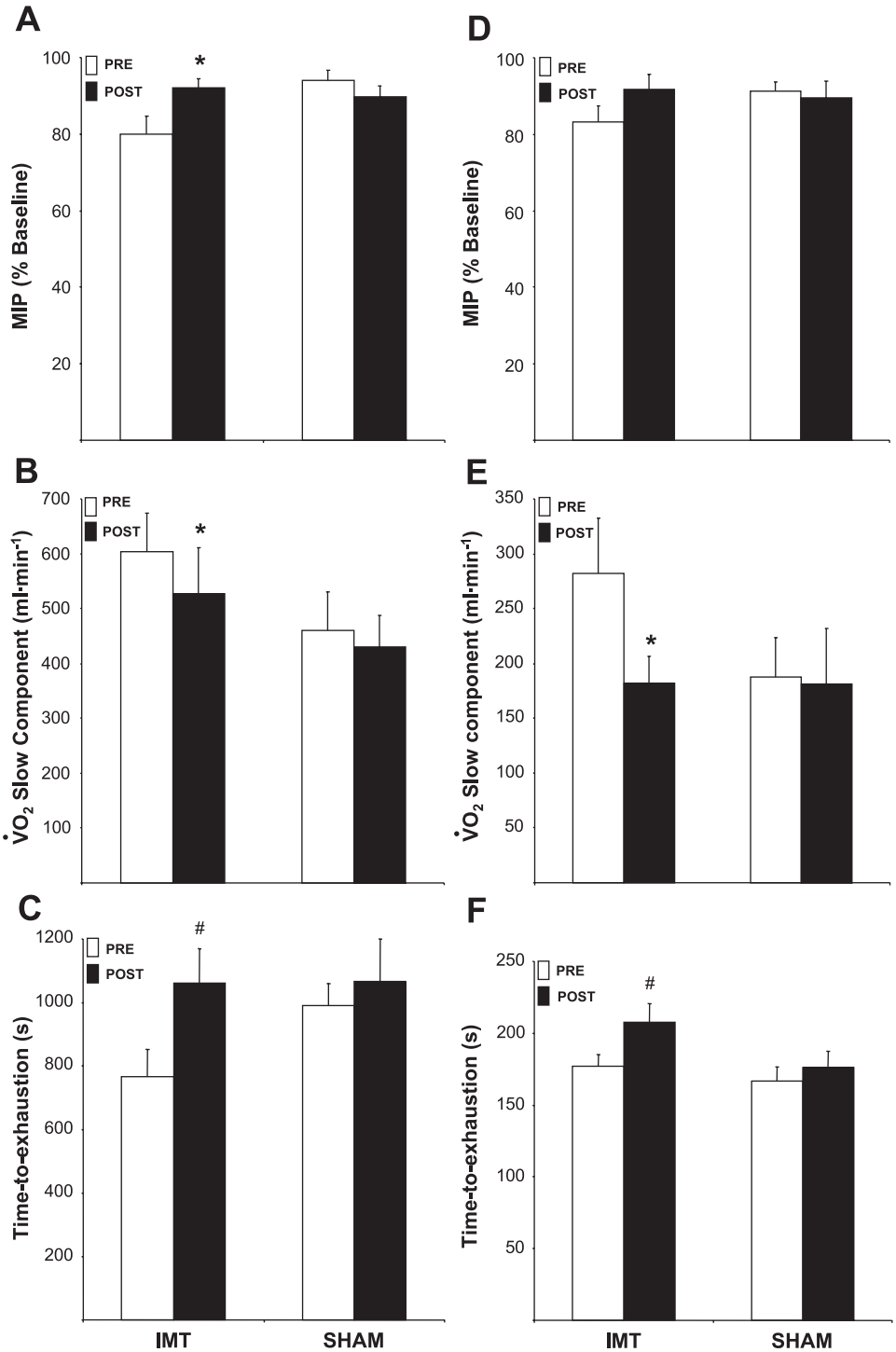

Fig. 4. Severe and maximal exercise inspiratory muscle fatigue, $\dot{V}O_2$ slow-component amplitude, and exercise tolerance in the IMT and Sham groups Pre and Post. *A–C*: severe-intensity exercise inspiratory muscle fatigue, $\dot{V}O_2$ slow-component amplitude, and exercise tolerance, respectively. *D–F*: maximal exercise inspiratory muscle fatigue, $\dot{V}O_2$ slow-component amplitude, and exercise tolerance, respectively. Open bars, Pre data. Solid bars, Post data. MIP, maximum inspiratory pressure. Results are group means ± SE. Note that post-IMT, inspiratory muscle fatigue and $\dot{V}O_2$ slow-component amplitude were reduced and exercise tolerance was significantly enhanced during both severe and maximal exercise. The parameters were not affected by Sham intervention. *Significantly different from Pre ($P < 0.05$); #significantly different from Pre ($P < 0.01$).

(4, 5), which, through reduced group III and IV afferent discharge, may reduce the sensations of respiratory and limb muscle discomfort and improve exercise tolerance (56). It should be noted, however, that despite the concomitant changes in $\dot{V}O_2$ dynamics and exercise tolerance after IMT, the changes in MIP were not significantly correlated with changes in $\dot{V}O_2$ kinetics or the time to task failure. It is possible that this lack of significant relationship was a function of the relatively low sample size ($n = 8$) and interindividual variability in the physiological responses to IMT.

Conclusions. Specific training of the inspiratory muscles increased baseline MIP, reduced inspiratory muscle fatigue and enhanced $\dot{V}O_2$ dynamics and exercise tolerance during severe- and maximal-intensity exercise. We propose that a reduction of inspiratory muscle fatigue after IMT spared the O_2 and blood-flow requirements of ventilation and offset the metaboreflex (61, 74), thereby increasing limb O_2 delivery (24). Increased muscle O_2 availability, in turn, resulted in a speeding of the overall $\dot{V}O_2$ dynamics (perhaps by reducing the rate of fatigue development and delaying the recruitment of low-

efficiency fibers) (9, 38) and enhancement of exercise tolerance (4, 14, 70).

Pressure-threshold IMT appears to present a practical and efficacious means for modulating the $\dot{V}O_2$ response to high-intensity exercise in healthy young people. These changes are likely to be, at least in part, responsible for the enhanced exercise tolerance after IMT that has been reported herein and in previous investigations. IMT therefore appears to have considerable potential as an adjunct to physical training for the enhancement of exercise performance. Further research is required to establish whether similar (or greater) effects on $\dot{V}O_2$ kinetics and exercise tolerance are possible in the elderly or in populations with ventilatory or cardiovascular impairments.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

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