

Effect of expiratory muscle fatigue on exercise tolerance and locomotor muscle fatigue in healthy humans

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Taylor BJ, Romer LM. Effect of expiratory muscle fatigue on exercise tolerance and locomotor muscle fatigue in healthy humans. *J Appl Physiol* 104: 1442–1451, 2008. First published March 6, 2008; doi:10.1152/jappphysiol.00428.2007.—High-intensity exercise ($\geq 90\%$ of maximal O_2 uptake) sustained to the limit of tolerance elicits expiratory muscle fatigue (EMF). We asked whether prior EMF affects subsequent exercise tolerance. Eight male subjects (means \pm SD; maximal O_2 uptake = 53.5 ± 5.2 ml \cdot kg $^{-1}\cdot$ min $^{-1}$) cycled at 90% of peak power output to the limit of tolerance with (EMF-EX) and without (CON-EX) prior induction of EMF and for a time equal to that achieved in EMF-EX but without prior induction of EMF (ISO-EX). To induce EMF, subjects breathed against an expiratory flow resistor until task failure (15 breaths/min, 0.7 expiratory duty cycle, 40% of maximal expiratory gastric pressure). Fatigue of abdominal and quadriceps muscles was assessed by measuring the reduction relative to prior baseline values in magnetically evoked gastric twitch pressure ($P_{ga_{tw}}$) and quadriceps twitch force (Q_{tw}), respectively. The reduction in $P_{ga_{tw}}$ was not different after resistive breathing vs. after CON-EX (-27 ± 5 vs. $-26 \pm 6\%$; $P = 0.127$). Exercise time was reduced by $33 \pm 10\%$ in EMF-EX vs. CON-EX (6.85 ± 2.88 vs. 9.90 ± 2.94 min; $P < 0.001$). Exercise-induced abdominal and quadriceps muscle fatigue was greater after EMF-EX than after ISO-EX (-28 ± 9 vs. $-12 \pm 5\%$ for $P_{ga_{tw}}$, $P = 0.001$; -28 ± 7 vs. $-14 \pm 6\%$ for Q_{tw} , $P = 0.015$). Perceptual ratings of dyspnea and leg discomfort (Borg CR10) were higher at 1 and 3 min and at end exercise during EMF-EX vs. during ISO-EX ($P < 0.05$). Percent changes in limb fatigue and leg discomfort (EMF-EX vs. ISO-EX) correlated significantly with the change in exercise time. We propose that EMF impaired subsequent exercise tolerance primarily through an increased severity of limb locomotor muscle fatigue and a heightened perception of leg discomfort.

abdominal muscle fatigue; quadriceps muscle fatigue; dyspnea; leg discomfort; exercise performance

HIGH-INTENSITY EXERCISE [$\geq 90\%$ of maximum O_2 uptake ($\dot{V}_{O_{2max}}$)] sustained to the limit of tolerance elicits diaphragm fatigue in healthy humans, as demonstrated by a significant reduction relative to prior baseline values in the transdiaphragmatic pressure (P_{di}) response to bilateral phrenic nerve stimulation (10, 18). More recently, our group and others (42, 44) have shown that the expiratory abdominal muscles fatigue in response to high-intensity exercise, as demonstrated by a significant reduction in the gastric pressure (P_{ga}) response to thoracic nerve stimulation. Prior loading of the respiratory muscles, using either inspiratory resistive loading (17, 36) or voluntary isocapnic hyperpnea (7, 19, 37), has been shown to impair (17, 19) or to not affect (7, 36, 37) subsequent high-intensity, whole body exercise tolerance.

Recent evidence suggests that prior loading of the expiratory muscles can also impair subsequent exercise tolerance (45), although the precise mechanisms for such an effect are unclear. Fatiguing contractions of the expiratory muscles carried out to task failure have been shown to elicit a time-dependent increase in sympathetic vasoconstrictor outflow in resting limb musculature (6). In resting and exercising canines, a bolus injection of lactic acid into the deep circumflex iliac artery elicits a reduction in both hindlimb blood flow and vascular conductance (32). A reduction in blood flow to the working limb muscles would be expected to limit exercise tolerance via an increased severity of limb muscle fatigue and heightened perceptions of limb discomfort, as has been shown to occur when the inspiratory muscles are loaded before (21) or during exercise (33). In addition, expiratory muscle fatigue (EMF) would be expected to increase central respiratory drive to maintain expiratory muscle force production (8), as has been shown to occur when the inspiratory muscles are fatigued (39). Such an increase in central drive would likely be perceived as an increased sense of effort (12), which might impair exercise tolerance.

Based on the aforementioned considerations, we investigated the effect of prior EMF on subsequent exercise tolerance. To quantify the magnitude of EMF induced by expiratory resistive loading or exercise, we measured the reduction in magnetically evoked twitch P_{ga} ($P_{ga_{tw}}$) relative to prior baseline values. In addition, we assessed the severity of exercise-induced limb locomotor muscle fatigue by measuring the reduction in the quadriceps twitch force (Q_{tw}) response to direct femoral nerve stimulation from pre- to postexercise and the increase in the integrated electromyographic response of the quadriceps during the exercise. We hypothesized that prior EMF would impair subsequent exercise tolerance through an exacerbation of exercise-induced limb muscle fatigue and heightened perceptions of dyspnea and leg discomfort.

METHODS

Subjects

Eight healthy, nonsmoking male subjects participated in the study (means \pm SD: age = 28 ± 5 years, stature = 183 ± 9 cm, body mass = 82.9 ± 8.6 kg). The subjects were physically active and had normal forced vital capacity ($105 \pm 3\%$ of predicted), forced expiratory volume in 1 s ($116 \pm 3\%$), and maximal voluntary ventilation ($108 \pm 7\%$). The study was approved by the local Research Ethics Committee, and each subject provided written informed consent.

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Experimental Procedures

The experimental procedures were conducted during four laboratory sessions that were each separated by at least 48 h. For each subject, exercise trials were performed at a similar time of day to minimize diurnal biological variation. The subjects abstained from caffeine for 12 h and exercise for 48 h before each session. During the first session, the subjects were familiarized with the magnetic stimulation procedures and the volitional maneuvers. Pulmonary function was assessed using an on-line spirometer (Oxycon Pro; Jaeger, Höchberg, Germany) according to standard procedures (26). Subjects performed a maximal incremental exercise test (35 W every 3 min starting at 95 W) on an electromagnetically braked cycle ergometer (Excalibur; Lode, Groningen, The Netherlands). Peak power output (\dot{W}_{peak}) was calculated as the sum of the final completed work rate plus the fraction of the partially completed work rate performed before exhaustion. $\dot{V}O_{2\text{max}}$ was the highest mean value recorded over 30 s. During the next two sessions, the subjects performed constant-load cycle exercise at 90% of \dot{W}_{peak} either with (EMF-EX) or without (CON-EX) prior induction of EMF (Fig. 1). Exercise time to the limit of tolerance (T_{LIM}) was recorded for each trial. To induce EMF, subjects breathed against an expiratory flow resistor until task failure. The order of the two trials was randomized and counterbalanced such that four subjects performed CON-EX first and four subjects performed EMF-EX first. During the fourth session, subjects exercised for a time equal to that achieved in EMF-EX but without prior induction of EMF (ISO-EX) (Fig. 1). Abdominal and quadriceps muscle contractilities were assessed before and up to 30 min after each of the exercise trials by measuring the $P_{\text{ga,tw}}$ and Q_{tw} response to magnetic stimulation of the nerve roots supplying these muscles (14, 29). In addition, abdominal muscle contractility was assessed immediately after expiratory resistive loading during EMF-EX

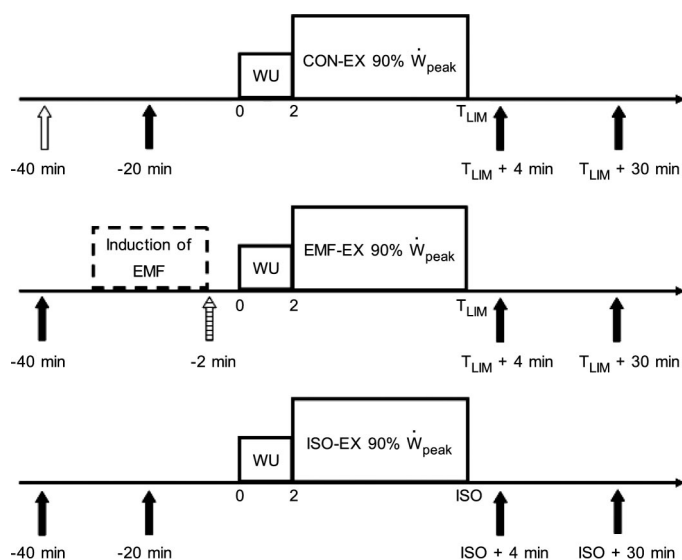


Fig. 1. Testing protocols for constant-load exercise trials. Subjects cycled at 40% of peak power output (\dot{W}_{peak}) for 2 min [warm-up (WU)] and then at 90% \dot{W}_{peak} to the limit of tolerance (T_{LIM}) either without (CON-EX) or with (EMF-EX) prior induction of expiratory muscle fatigue (EMF) and for a time equal to that achieved in EMF-EX but without prior induction of EMF (ISO-EX). To induce EMF, subjects breathed against an expiratory flow resistor until task failure (15 breaths/min, 0.7 expiratory duty cycle, 40% of maximal expiratory gastric pressure). Abdominal and quadriceps muscle contractilities in response to magnetic nerve stimulation (1 Hz) were assessed before and up to 30 min after exercise at each session (closed arrow). In addition, abdominal muscle contractility only (dashed arrow) was assessed immediately after induction of EMF during EMF-EX. Abdominal and quadriceps muscle supramaximalities (open arrow) were assessed 20 min before the first assessment of muscle function during CON-EX.

(Fig. 1). The participants could not be blinded to the EMF, but they were unaware of the experimental hypotheses and naive to the purpose of the study.

Respiratory Pressure Measurements

P_{ga} and esophageal pressure (P_{es}) were measured by using two balloon-tipped catheters (Ackrad Labs, Cooper Surgical, Berlin, Germany) that were placed as described previously (42). Each catheter was connected to a differential pressure transducer (Validyne DP45, Northridge, CA; range of ± 229 cmH₂O), calibrated across the physiological range with an electromanometer (model M14; Mercury, Glasgow, Scotland). The esophageal balloon was filled with 1 ml of air. The gastric balloon was filled with 2 ml of air to ensure that it did not collapse under high expiratory pressure (23, 30).

Magnetic Stimulation

Abdominal muscles. The subjects sat facing an inclined bench with their hips flexed and chest supported. Magnetic stimuli were delivered to the thoracic nerve roots supplying the abdominal muscles via a circular 90-mm coil powered by a magnetic stimulator (Magstim 200; Magstim, Whitland, Wales). The coil was positioned over the vertebral column between the 8th (T_8) and 11th (T_{11}) thoracic vertebrae. The optimal coil position was defined as the vertebral level that when stimulated evoked the highest $P_{\text{ga,tw}}$ and was marked with indelible ink to ensure the coil position was identical for subsequent stimulations. The stimulations were performed at end-expiratory P_{es} against a semi-occluded airway. End-expiratory P_{es} and P_{ga} results were not different across time for any of the trials (see Table 2), indicating that all stimulations were delivered at the same lung volume and at the same abdominal muscle length.

Quadriceps muscles. The subjects lay semi-recumbent on a strength-testing chair (Techno Gym, Cesena, Italy) with the right knee at 1.57 rads (90°) of flexion and arms folded across the chest. A noncompliant strap was fastened just superior to the malleoli of the right ankle joint. The strap was attached via a swivel link to a calibrated load cell (model ABA Ergo Meter, Globus Italia, Codogne, Italy), which was fixed to the chair and adjusted to a height that was in the direct line of applied force for each subject. Magnetic stimuli were delivered to the femoral nerve via a double 70-mm coil powered by another magnetic stimulator (Magstim 200). The area of stimulation that evoked the greatest quadriceps Q_{tw} was located and marked with indelible ink.

Electromyography

Electromyograms (EMG) were recorded from the rectus abdominis (RA), vastus lateralis (VL), and rectus femoris (RF) as described previously (2, 42). The electrodes were positioned according to the optimal M-wave response to magnetic stimulation. The position of the EMG electrodes was marked with indelible ink to ensure that they were placed in the same location at subsequent visits.

Supramaximal Stimulation

To determine whether nerve stimulation of the abdominal and quadriceps muscles was supramaximal, three single twitches were delivered to each muscle group at 50, 60, 70, 80, 85, 90, 95, and 100% of the stimulator's maximum power output. The incremental protocol was applied after 10 min of rest and 20 min before the preexercise assessment of neuromuscular function during session 2. There was a plateau in RA M-wave amplitude [i.e., no significant increase in amplitude with increasing stimulation intensity (paired *t*-tests with Bonferroni adjustment)] but no plateau in $P_{\text{ga,tw}}$, indicating that only the RA was stimulated supramaximally (Fig. 2). The technical considerations associated with submaximal nerve stimulation have been discussed previously (14, 42, 44). There was a plateau in Q_{tw} and VL

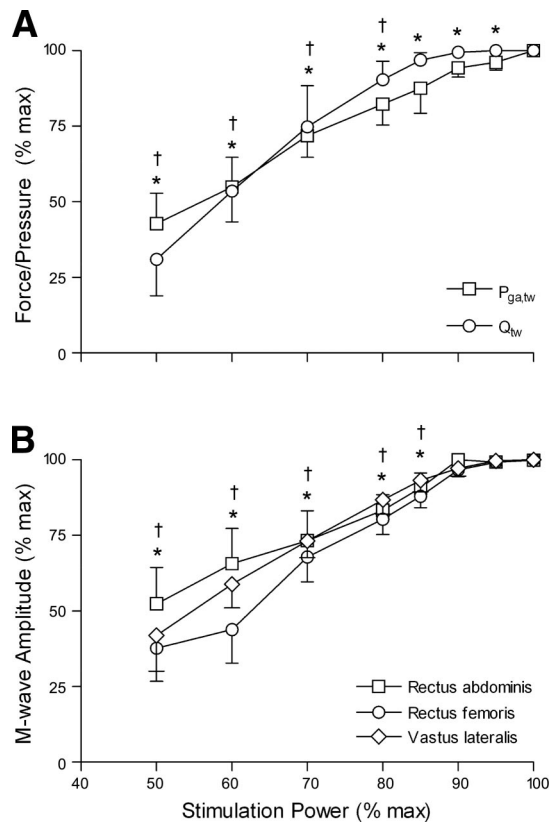


Fig. 2. A: gastric twitch pressure ($P_{ga,tw}$) and quadriceps twitch force (Q_{tw}) in response to 1-Hz magnetic stimulation of the thoracic nerves and the femoral nerve, respectively. B: M-wave amplitudes in response to 1-Hz magnetic stimulation of the thoracic nerves (rectus abdominis) and the femoral nerve (rectus femoris and vastus lateralis). The incremental protocol was applied after 10 min of rest and completed 20 min before the preexercise assessment of neuromuscular function at *visit 1*. Values are group means \pm SD for 8 subjects. * $P < 0.05$, values significantly different from those at 100% of the stimulator's power output for $P_{ga,tw}$ (A) and rectus abdominis (B); † $P < 0.05$, values significantly different from those at 100% of the stimulator's power output for Q_{tw} (A) and rectus femoris and vastus lateralis (B).

and RF M-wave amplitudes with increasing stimulation intensity, indicating maximum depolarization of the femoral nerve (Fig. 2).

Neuromuscular Function

Abdominal and quadriceps muscle functions were assessed before (~ 20 min) and after (4 and 30 min) each of the exercise trials. In addition, abdominal muscle function was assessed immediately after (1 min) expiratory resistive loading during EMF-EX (Fig. 1). The stimulations were administered at 100% of the stimulator's power output and were each separated by 30 s. Four 1-Hz stimulations were delivered to the nerve roots supplying the abdominal muscles such that four nonpotentiated twitches were obtained. The potentiated twitch is a more sensitive measure of muscle fatigue than the nonpotentiated twitch, particularly when the degree of fatigue is small (13, 15). Furthermore, the potentiated twitch is a more valid measure for comparing differences in fatigue when the levels of postactivation potentiation are unequal (31), as we expected to occur in the present study because of different exercise durations. Accordingly, $P_{ga,tw}$ was measured ~ 5 s after a maximal expulsive maneuver against a semi-occluded airway. The maneuver was initiated from total lung capacity and maintained for ~ 5 s. This procedure was repeated six times such that six potentiated $P_{ga,tw}$ results were obtained. The degree of potentiation was slightly smaller after the first and, to a lesser extent,

after the second voluntary effort; therefore, we discarded the first two measurements.

Four 1-Hz stimulations were also delivered to the right femoral nerve. The stimulations were delivered at 100% of the stimulator's power output and were separated by 30 s. In accordance with our abdominal muscle assessment procedures, we measured peak Q_{tw} elicited by a 1-Hz stimulation ~ 5 s after a maximal voluntary isometric contraction of the right quadriceps that was maintained for ~ 5 s. This procedure was repeated six times such that six potentiated Q_{tw} measurements were obtained; again, the first two measurements were discarded. Although the potentiated twitches were reduced more than the nonpotentiated twitches after each trial (CON-EX, EMF-EX, ISO-EX), the percent changes between each of the trials were not different. Thus only changes in potentiated $P_{ga,tw}$ and potentiated Q_{tw} are reported. The order of abdominal and quadriceps muscle assessment was randomized and balanced between subjects but remained constant within subjects for each of the trials.

The amplitudes (baseline to peak) of the abdominal muscle pressure response and the quadriceps muscle force response were analyzed for each stimulation. In addition, the maximal rate of pressure and force development, maximal relaxation rate, contraction time, and one-half relaxation time were assessed for the abdominal and quadriceps muscles (42). Membrane excitability was determined by measuring the magnetically evoked peak-to-peak amplitude (mV), duration (ms), and area (mV/ms) of the RA, VL, and RF M waves (42). To quantify the progression of limb muscle fatigue throughout the constant-load exercise tests, EMG was recorded from VL and the integral of the EMG burst (iEMG) during each contraction was calculated as described previously (2).

Reproducibility

To determine the within-day, between-occasion reproducibility of neuromuscular measurements, abdominal and quadriceps muscle functions were assessed before and after 20 min of rest (Fig. 1), during which time the subjects were removed from the testing apparatus and sat quietly in a chair. There were no systematic differences in either evoked pressure or evoked force measurements before vs. after the 20-min rest period. In addition, reproducibility coefficients were all $< 11\%$ for coefficients of variation and > 0.61 for intraclass correlation coefficients (Table 1).

Expiratory Resistive Loading

EMF was induced with a protocol that we have previously shown to elicit significant abdominal muscle fatigue yet minimizes fatigue of the diaphragm and inspiratory rib cage muscles (43). Subjects exhaled against a flow-resistive load provided by a variable aperture (MicroRMA; Micro Medical, Kent, UK); inspiration was unimpeded. Subjects maintained a respiratory frequency (f_R) of 15 breaths/min and an expiratory duty cycle [expiratory time (T_E)/total breath time (T_{TOT})] of 0.7 while targeting 40% of maximal expiratory Pga. The target expiratory pressure was displayed on a computer screen, and the subjects maintained f_R and T_E/T_{TOT} by following a computer-generated audio signal. Subjects were instructed to maintain a constant Pga at the target level throughout each expiration. End-tidal PCO_2 (P_{ETCO_2}) was measured using the on-line gas-analysis system (Oxycon Pro). The inspired fraction of CO_2 was manually adjusted to prevent P_{ETCO_2} from dropping below eupneic values. Task failure was defined as an inability to generate the target pressure for three consecutive expiratory efforts despite verbal encouragement.

Exercise Responses

Subjects cycled for 2 min at 40% of \dot{W}_{peak} before work rate was increased to 90% of \dot{W}_{peak} . Each subject pedaled at a self-selected cadence and maintained this cadence during all subsequent trials. Subjects pedaled until they were unable to maintain pedal cadence

Table 1. Within-day reproducibility of neuromuscular function measurements

| Variable | Trial 1 | Trial 2 | CV, % | ICC |
|--|-------------|-------------|-------|------|
| <i>Abdominals</i> | | | | |
| Pga _{tw} , cmH ₂ O | 34.5±7.1 | 34.7±8.8 | 2.8 | 0.92 |
| CT, ms | 325±122 | 328±144 | 6.0 | 0.65 |
| MRPD/Pga _{tw} , s | 9.8±2.3 | 10.6±1.7 | 5.7 | 0.71 |
| RT _{0.5} , ms | 107±45 | 116±68 | 3.6 | 0.83 |
| MRR/P _{ga, tw} , s | -8.1±2.3 | -8.6±2.5 | 7.2 | 0.61 |
| RA M-wave amplitude, mV | 1.3±0.6 | 1.2±1.1 | 9.8 | 0.74 |
| RA M-wave duration, ms | 24.1±5.9 | 22.3±6.8 | 5.3 | 0.83 |
| RA M-wave area, mV/ms | 0.010±0.008 | 0.009±0.001 | 5.0 | 0.73 |
| PE _{max} , cmH ₂ O | 191±34 | 186±28 | 5.1 | 0.74 |
| <i>Quadriceps</i> | | | | |
| Q _{tw} , N | 173±54 | 174±68 | 3.8 | 0.84 |
| CT, ms | 349±102 | 361±124 | 6.3 | 0.64 |
| MRFD/Q _{tw, tw} , s | 18.4±6.2 | 17.4±9.6 | 4.9 | 0.69 |
| RT _{0.5} , ms | 109±31 | 106±34 | 4.9 | 0.72 |
| MRR/Q _{tw} , s | -7.4±3.1 | -7.3±5.4 | 6.0 | 0.70 |
| VL/RF M-wave amplitude, mV | 1.2±0.6 | 1.3±1.1 | 8.3 | 0.76 |
| VL/RF M-wave duration, ms | 43.5±9.3 | 45.0±13.0 | 6.5 | 0.84 |
| VL/RF M-wave area, mV/ms | 0.012±0.014 | 0.012±0.011 | 8.0 | 0.73 |
| MVC, N | 553±161 | 534±144 | 4.6 | 0.76 |

Values are group means ± SD for 8 subjects. Trial 1 and trial 2 represent measurements taken before and after 30 min of quiet rest, respectively. CV, coefficient of variation; ICC, intraclass correlation coefficient; Pga_{tw}, gastric twitch pressure; CT, contraction time; MRPD, maximal rate of pressure development; RT_{0.5}, relaxation time from peak twitch to one-half peak twitch; MRR, maximal relaxation rate; RA, rectus abdominis; PE_{max}, expiratory gastric pressure during maximal expulsive maneuver; Q_{tw}, quadriceps twitch force; MRFD, maximal rate of force development; VL, vastus lateralis; RF, rectus femoris; MVC, maximal voluntary contraction force.

above 60 rpm. The subjects received no information on either exercise time or heart rate, and verbal encouragement was not provided to prevent bias due to potential intertrial inconsistency. Inspiratory and expiratory air flows were measured breath-by-breath using an ultrasonic phase-shift flow meter (Birmingham Flowmetrics, Birmingham, UK). Ventilatory and pulmonary gas exchange indexes were also measured with the on-line gas-analysis system (Oxycon Pro) with a calibrated turbine for volume measurement and paramagnetic (O₂) and infrared absorption (CO₂) gas sensors for gas analysis. The resistance and dead space provided by the ultrasonic flow meter and turbine in combination were 0.074 cmH₂O·l·s⁻¹ and 200 ml, respectively. Cardiac frequency was measured beat by beat via telemetry (Polar Vantage NV, Polar Electro Oy). Arterial oxygen saturation (SpO₂) was estimated with the use of a pulse oximeter (Ohmeda Biox 3700e; BOC Healthcare, Louisville, CO) and earlobe sensor. Mean values for each of the aforementioned physiological variables were calculated for each minute of exercise. Capillary blood was sampled from an earlobe before and every 2 min during exercise for the subsequent determination of hemolyzed blood lactate concentration (Biosen C-line Sport; EKF Diagnostics, Barleben, Germany). Ratings of perceived exertion (dyspnea and leg discomfort) were obtained at rest, at 1 min of exercise, and every 2 min thereafter with Borg's modified CR10 scale (4). Pga and Pes were measured throughout exercise and aligned to the airflow signal via predetermined delays. Pdi was obtained online by subtracting Pes from Pga. The cumulative force outputs of the abdominal muscles and the diaphragm were calculated by integrating Pga and Pdi over the periods of expiratory flow and inspiratory flow, respectively, for the entire duration of exercise. In addition, peak Pga during expiration was averaged for the final minute of exercise. End-expiratory and end-inspiratory lung volumes were measured using inspiratory capacity maneuvers (11).

Data Capture

The pressure, force, flow, SaO₂, and EMG signals were passed through an amplifier (model 1902; Cambridge Electronic Design, Cambridge, UK), digitized at sampling rates of 150 Hz and 3 kHz (EMG only) with an analog-to-digital converter (micro 1401 mkII; Cambridge Electronic Design), and acquired on a personal computer running commercially available software (Spike 2 version 5.12; Cambridge Electronic Design).

Statistical Analyses

Repeated-measures ANOVA was used to compare absolute pressure and force measurements across time (preexercise, 4 min postexercise, and 30 min postexercise) and percent changes in these measurements between trials (EMF-EX, CON-EX, ISO-EX). When significant main effects were shown, planned pair-wise comparisons were made with the Bonferroni method. Repeated-measures ANOVA with Bonferroni adjustment was also used to compare the absolute physiological responses at equivalent time points between the three trials. Pearson's product-moment correlation coefficients (*r*) were computed to assess the relationship between the percent changes in selected physiological variables at the end of exercise (EMF-EX vs. ISO-EX) and the percent changes in T_{LIM} (CON-EX vs. EMF-EX). The acceptable type I error was set at *P* < 0.05. Results are expressed as means ± SD. Statistical analyses were performed using SPSS version 13 for Windows (SPSS, Chicago, IL).

RESULTS

Preliminary Exercise

During maximal incremental exercise, \dot{W}_{peak} was 325 ± 27 W and $\dot{V}_{\text{O}_{2\text{max}}}$ was 4.36 ± 0.56 l/min (53.5 ± 5.2 ml·kg⁻¹·min⁻¹).

Expiratory Resistive Loading and EMF

Task failure during expiratory resistive loading occurred at 24 ± 5 min. There was a 27 ± 5% reduction in Pga_{tw} pre- vs. postexpiratory loading (34.9 ± 6.3 vs. 24.9 ± 5.7 cmH₂O; *P* = 0.009). Similarly, Pga in response to maximal voluntary expulsive maneuvers decreased by 21 ± 8% pre- vs. postexpiratory loading (193 ± 27 vs. 154 ± 30 cmH₂O; *P* < 0.001).

EMF and Exercise Tolerance

Individual subject changes in exercise tolerance (T_{LIM}) in response to prior EMF are shown in Fig. 3. T_{LIM} was reduced by 33 ± 10% in EMF-EX vs. CON-EX (6.85 ± 2.88 vs. 9.90 ± 2.94 min; *P* < 0.001). All of the individual subject data points

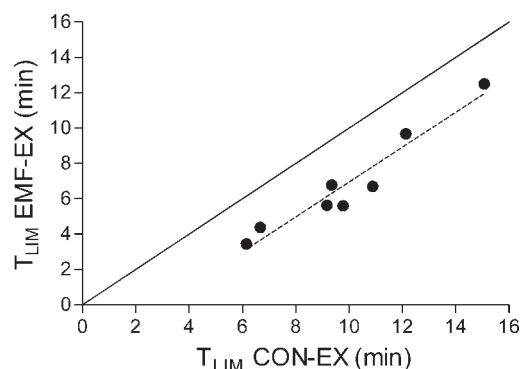


Fig. 3. An identity plot showing individual subject T_{LIM} for control exercise (CON-EX) and after induction of EMF (EMF-EX). The dotted line represents the regression line of CON-EX vs. EMF-EX.

are below the line of identity, indicating that EMF induced a reduction in exercise tolerance in all subjects. The regression line of CON-EX vs. EMF-EX is parallel to the line of identity, indicating that the effect of prior EMF on subsequent exercise tolerance was similar across all of the exercise times.

Exercise-Induced Muscle Fatigue

Magnetic stimulation. Evoked M-wave amplitude, duration, and area for RA, VL, and RF did not differ before vs. after exercise in CON-EX, EMF-EX, or ISO-EX (Table 2). Immediately after exercise in CON-EX, EMF-EX, and ISO-EX, $P_{ga_{tw}}$ and Q_{tw} were reduced below preexercise baseline values, despite some recovery and remained below baseline at 30 min postexercise (Fig. 4). The percent decreases in $P_{ga_{tw}}$ and Q_{tw} immediately after exercise did not differ for CON-EX vs. EMF-EX. However, the decreases in $P_{ga_{tw}}$ and Q_{tw} were greater after EMF-EX vs. ISO-EX (-28 ± 9 vs. $-12 \pm 5\%$ for $P_{ga_{tw}}$, $P = 0.001$; -28 ± 7 vs. $-14 \pm 6\%$ for Q_{tw} , $P = 0.015$). The severity of abdominal muscle fatigue was not different after expiratory resistive loading vs. after CON-EX (-27 ± 5 vs. $-26 \pm 6\%$ for $P_{ga_{tw}}$; $P > 0.05$).

Maximal rates of pressure/force development and relaxation were reduced below baseline after each of the exercise trials. When the decreases in $P_{ga_{tw}}$ and Q_{tw} were taken into account, however, neither maximal rate of pressure/force development nor maximal relaxation rate was altered (Table 2). Furthermore, there were no pre- vs. postexercise differences in contraction time or one-half relaxation time (Table 2). The pressure and force responses to maximal volitional efforts were reduced below baseline immediately after CON-EX and

EMF-EX, but these responses were blunted after ISO-EX (Table 2).

iEMG. From the first minute to the last minute, iEMG of VL increased significantly in CON-EX, EMF-EX, and ISO-EX (Fig. 5). The percent increase in iEMG was significantly higher at end exercise in EMF-EX than in ISO-EX ($119 \pm 9\%$ vs. $110 \pm 6\%$; $P = 0.021$).

Exercise Responses

Heart rate, oxygen saturation, and blood lactate concentration. In CON-EX, cardiac frequency at end exercise was $98 \pm 5\%$ of maximum and was not different between EMF-EX, CON-EX, and ISO-EX. No change was found in Sp_{O_2} during CON-EX, EMF-EX, or ISO-EX. Blood lactate concentration was not different at end exercise during EMF-EX vs. CON-EX but was significantly higher at end exercise in EMF-EX vs. ISO-EX (Table 3).

Pulmonary gas exchange and breathing pattern. In CON-EX, O_2 consumption rose steadily throughout exercise, reaching $98 \pm 6\%$ of $\dot{V}_{O_{2max}}$. At end exercise, O_2 consumption was not different between EMF-EX, CON-EX, and ISO-EX. In CON-EX, minute ventilation (\dot{V}_E) rose throughout exercise, reaching $97 \pm 5\%$ of maximum. In EMF-EX, \dot{V}_E at end exercise was significantly greater than that in CON-EX and ISO-EX. This increase in \dot{V}_E was due primarily to an increase in f_R because tidal volume did not differ between trials. The increase in f_R was due to a decrease in both T_E and inspiratory time. The increased ventilatory response to exercise after induction of EMF was reflected by a lower P_{ETCO_2} at end exercise in EMF-EX than in CON-EX and ISO-EX. Neither

Table 2. Neuromuscular function measurements before and immediately (4 min) after exercise

| | CON-EX | | EMF-EX | | ISO-EX | |
|--|-------------------|-----------------------|-------------------|-----------------------|-------------------|-------------------|
| | Preexercise | Postexercise | Preexercise | Postexercise | Preexercise | Postexercise |
| <i>Abdominals</i> | | | | | | |
| End-expiratory Pes, cmH ₂ O | -2.4 ± 1.8 | -2.1 ± 2.1 | -2.7 ± 1.1 | -2.6 ± 1.7 | -2.2 ± 1.6 | -2.5 ± 1.4 |
| End-expiratory Pga, cmH ₂ O | 10.8 ± 3.1 | 10.4 ± 3.7 | 11.3 ± 2.8 | 10.9 ± 4.8 | 11.7 ± 4.2 | 11.6 ± 4.0 |
| CT, ms | 325 ± 65 | 317 ± 68 | 362 ± 82 | 351 ± 74 | 325 ± 122 | 330 ± 71 |
| MRPD/ $P_{ga_{tw}}$, s | 10.6 ± 1.9 | 11.8 ± 3.7 | 9.7 ± 1.1 | 10.5 ± 1.1 | 9.8 ± 2.3 | 10.5 ± 2.5 |
| RT _{0.5} , ms | 109 ± 40 | 108 ± 48 | 116 ± 42 | 114 ± 59 | 107 ± 45 | 110 ± 45 |
| MRR/ $P_{ga_{tw}}$, s | -8.1 ± 1.4 | -8.1 ± 1.7 | -8.3 ± 2.0 | -8.6 ± 1.7 | -8.1 ± 2.3 | -8.2 ± 2.0 |
| RA M-wave amplitude, mV | 1.1 ± 0.6 | 1.1 ± 0.8 | 1.1 ± 0.6 | 1.0 ± 0.6 | 1.3 ± 0.6 | 1.1 ± 0.8 |
| RA M-wave duration, ms | 24.2 ± 7.4 | 23.8 ± 7.6 | 24.1 ± 7.4 | 22.8 ± 7.6 | 24.1 ± 5.9 | 23.0 ± 8.2 |
| RA M-wave area, mV/ms | 0.009 ± 0.006 | 0.009 ± 0.008 | 0.010 ± 0.006 | 0.009 ± 0.008 | 0.010 ± 0.008 | 0.011 ± 0.008 |
| PE_{max} , cmH ₂ O | 190 ± 22 | $156 \pm 31^\dagger$ | 193 ± 28 | $151 \pm 31^\dagger$ | 191 ± 34 | 178 ± 28 |
| <i>Quadriceps</i> | | | | | | |
| CT, ms | 381 ± 88 | 394 ± 62 | 378 ± 82 | 382 ± 65 | 349 ± 102 | 358 ± 79 |
| MRFD/ Q_{tw} , s | 18.2 ± 3.7 | 18.9 ± 2.5 | 17.8 ± 4.2 | 17.9 ± 3.4 | 18.4 ± 6.2 | 18.8 ± 5.7 |
| RT _{0.5} , ms | 111 ± 40 | 116 ± 54 | 107 ± 40 | 110 ± 42 | 109 ± 31 | 111 ± 57 |
| MRR/ Q_{tw} , s | -8.5 ± 2.8 | -8.8 ± 1.7 | -7.6 ± 2.5 | -8.0 ± 2.0 | -7.4 ± 3.1 | -7.5 ± 2.0 |
| VL M-wave amplitude, mV | 1.2 ± 1.1 | 1.1 ± 0.8 | 1.4 ± 0.8 | 1.4 ± 0.6 | 1.0 ± 0.3 | 1.2 ± 1.1 |
| VL M-wave duration, ms | 39.1 ± 6.2 | 40.7 ± 8.2 | 37.9 ± 6.8 | 40.1 ± 9.3 | 41.3 ± 4.5 | 40.7 ± 8.8 |
| VL M-wave area, mV/ms | 0.010 ± 0.008 | 0.012 ± 0.011 | 0.011 ± 0.005 | 0.015 ± 0.010 | 0.012 ± 0.011 | 0.011 ± 0.006 |
| RF M-wave amplitude, mV | 1.1 ± 1.0 | 1.4 ± 1.1 | 1.2 ± 0.9 | 1.4 ± 1.1 | 1.1 ± 0.6 | 1.0 ± 1.4 |
| RF M-wave duration, ms | 41.9 ± 7.9 | 43.8 ± 5.7 | 40.2 ± 8.8 | 40.8 ± 8.2 | 42.8 ± 7.1 | 43.9 ± 8.5 |
| RF M-wave area, mV/ms | 0.011 ± 0.010 | 0.010 ± 0.006 | 0.012 ± 0.009 | 0.014 ± 0.008 | 0.009 ± 0.002 | 0.010 ± 0.008 |
| MVC, N | 537 ± 169 | $453 \pm 150^\dagger$ | 554 ± 170 | $433 \pm 110^\dagger$ | 553 ± 161 | $522 \pm 181^*$ |

Values are group means \pm SD. CON-EX, without prior induction of expiratory muscle fatigue (EMF); EMF-EX, with prior induction of EMF; ISO-EX, with exercise for a time equal to that achieved in EMF-EX but without prior induction of EMF; Pes, esophageal pressure; Pga, gastric pressure. * $P < 0.05$ and $^\dagger P < 0.01$, significantly different from preexercise values.

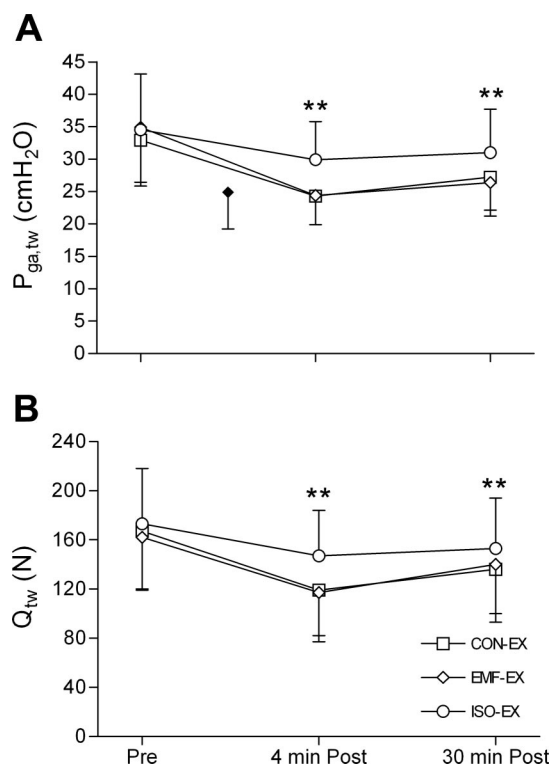


Fig. 4. $P_{ga,tw}$ (A) and Q_{tw} (B) responses to magnetic stimulation before (Pre), 4 min postexercise (post), and 30 min postexercise during CON-EX, EMF-EX, and ISO-EX [$P_{ga,tw}$ immediately after expiratory resistive loading (24.9 ± 5.7 cmH₂O) shown in A]. Values are group means \pm SD for 8 subjects. $**P < 0.01$, values significantly different from preexercise values for CON-EX, EMF-EX, and ISO-EX.

end-expiratory lung volume nor end-inspiratory lung volume was different at end exercise in CON-EX vs. that shown in EMF-EX and ISO-EX (Fig. 6 and Table 3).

Respiratory pressures. The cumulative force output of the abdominal muscles ($\int P_{ga}/dt$) and the diaphragm ($\int P_{di}/dt$) was significantly greater in EMF-EX than in ISO-EX ($4,721 \pm 956$ vs. $3,984 \pm 1,216$ cmH₂O/s, $P = 0.002$, and $3,348 \pm 825$ vs. $3,067 \pm 953$ cmH₂O/s, $P = 0.013$, respectively). In addition, peak expiratory P_{ga} was significantly elevated in EMF-EX vs. ISO-EX at end exercise (Table 3). This was likely a result of

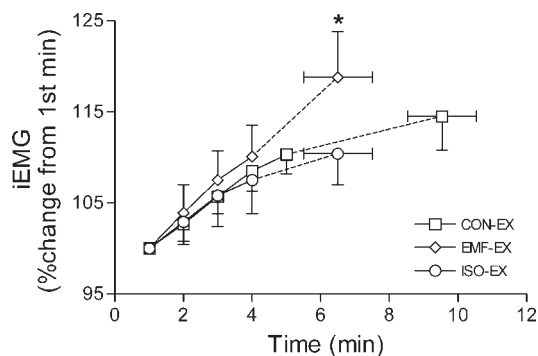


Fig. 5. Myoelectrical activity [integrated EMG (iEMG)] of vastus lateralis for CON-EX, EMF-EX, and ISO-EX. Values are group means \pm SD for 6 subjects. $*P < 0.05$, EMF-EX significantly different from ISO-EX at the same time.

Table 3. Exercise responses for the final minute of exercise

| | CON-EX | EMF-EX | ISO-EX |
|--|-------------------|-------------------|-------------------------------|
| Work rate, W | 298 \pm 37 | 298 \pm 32 | 298 \pm 32 |
| T _{LIM} , min | 9.9 \pm 2.88 | 6.9 \pm 2.94 | 6.9 \pm 2.94 |
| f _c , beats/min | 174 \pm 9 | 169 \pm 11 | 170 \pm 11 |
| SpO ₂ , % | 96.6 \pm 3.7 | 96.3 \pm 2.3 | 96.6 \pm 2.5 |
| [Lac ⁻] _B , mmol/l | 10.3 \pm 1.7 | 9.8 \pm 2.0 | 7.8 \pm 1.7 [†] |
| \dot{V}_E , l/min | 138 \pm 23 | 147 \pm 23* | 131 \pm 20* [†] |
| VT, liters | 3.27 \pm 0.48 | 3.31 \pm 0.54 | 3.23 \pm 0.62 |
| f _R , breaths/min | 45 \pm 9 | 49 \pm 8* | 40 \pm 11* [†] |
| Ti, s | 0.65 \pm 0.14 | 0.62 \pm 0.11 | 0.73 \pm 0.17 |
| Te, s | 0.70 \pm 0.14 | 0.66 \pm 0.11* | 0.76 \pm 0.17* [†] |
| Ti/T _{TOT} | 0.481 \pm 0.011 | 0.485 \pm 0.019 | 0.481 \pm 0.013 |
| Te/T _{TOT} | 0.519 \pm 0.011 | 0.515 \pm 0.019 | 0.519 \pm 0.013 |
| VT/TE, l/s | 4.51 \pm 1.04 | 4.99 \pm 0.82* | 4.30 \pm 0.88 [†] |
| EELV, %FVC | 21 \pm 11 | 20 \pm 8 | 22 \pm 8 |
| EILV, %FVC | 92 \pm 11 | 93 \pm 17 | 90 \pm 11 |
| $\dot{V}O_2$, l/min | 4.17 \pm 1.21 | 4.08 \pm 1.35 | 4.08 \pm 1.24 |
| $\dot{V}CO_2$, l/min | 4.61 \pm 1.58 | 4.63 \pm 1.49 | 4.39 \pm 1.67 |
| $\dot{V}_E/\dot{V}O_2$ | 26.6 \pm 9.1 | 35.9 \pm 9.1 | 32.0 \pm 4.8 |
| $\dot{V}_E/\dot{V}CO_2$ | 30.1 \pm 7.1 | 31.1 \pm 6.2 | 29.9 \pm 6.5 |
| PETCO ₂ , Torr | 34.9 \pm 4.0 | 33.6 \pm 4.2 | 38.3 \pm 6.2* [†] |
| Peak expiratory P _{ga} , cmH ₂ O | 33.5 \pm 13.0 | 35.9 \pm 14.1 | 26.6 \pm 12.2* [†] |

Values are group means \pm SD for 8 subjects. T_{LIM}, exercise time to the limit of tolerance; f_c, cardiac frequency; SaO₂, arterial oxygen saturation; [Lac⁻]_B, blood lactate concentration; \dot{V}_E , minute ventilation; VT, tidal volume; f_R, respiratory frequency; Ti, inspiratory time; Te, expiratory time; Ti/T_{TOT}, fractional inspiratory time; Te/T_{TOT}, fractional expiratory time; EELV, end-expiratory lung volume; EILV, end-inspiratory lung volume; FVC, forced vital capacity; $\dot{V}O_2$, oxygen uptake; $\dot{V}CO_2$, carbon dioxide output; PETCO₂, end-tidal PCO₂. $*P < 0.05$ values significantly different from CON-EX; $^{\dagger}P < 0.05$, values significantly different from EMF-EX.

the shortened Te and increased expiratory flow associated with the tachypnic breathing pattern after EMF.

Perceptual ratings. Perceptions of leg discomfort and dyspnea were rated higher at 1 and 3 min and at end-exercise during EMF-EX vs. ISO-EX but were not different at end exercise between EMF-EX and CON-EX (Fig. 7).

Correlations Between Variables

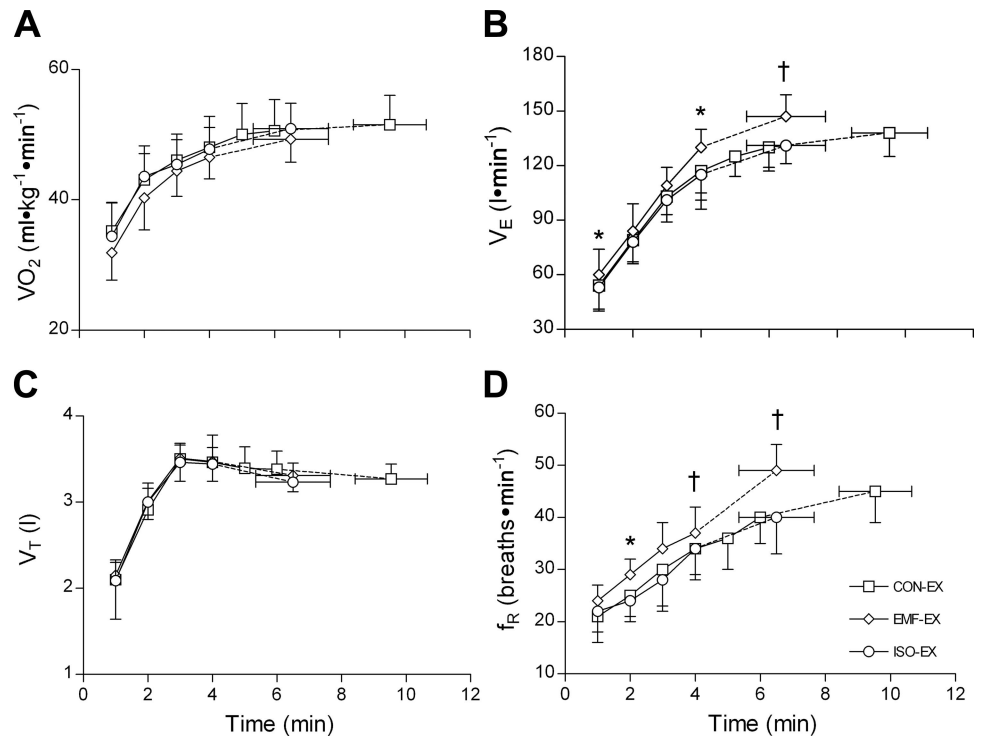
The correlations between the percent changes in selected variables for EMF-EX vs. ISO-EX at end exercise are shown in Fig. 8. The changes in leg fatigue and leg discomfort correlated significantly with the changes in T_{LIM} ($r = 0.67$, $P = 0.025$ and $r = 0.72$, $P = 0.001$, respectively). In addition, the change in dyspnea tended to correlate with the change in T_{LIM} ($r = 0.66$, $P = 0.085$). Neither the increase in the cumulative abdominal force output nor the cumulative diaphragm force output correlated significantly with the change in T_{LIM} ($r = 0.47$, $P = 0.133$ and $r = 0.41$, $P = 0.218$).

DISCUSSION

Main Findings

The major findings were that acute induction of EMF resulted in 1) a decrease in exercise time (T_{LIM}), 2) an exacerbation of exercise-induced abdominal and quadriceps muscle fatigue at exercise isotime, 3) elevated perceptions of dyspnea and leg discomfort, and 4) relative tachypnea during high-intensity exercise.

Fig. 6. Oxygen consumption ($\dot{V}O_2$; A), minute ventilation (\dot{V}_E ; B), tidal volume (V_T ; C), and respiratory frequency (f_R ; D) for CON-EX, EMF-EX, and ISO-EX. Values are group means \pm SD for 8 subjects. * $P < 0.05$, EMF-EX significantly different from ISO-EX at the same time. † $P < 0.05$, EMF-EX significantly different from both ISO-EX and CON-EX at the same time.



Technical Considerations

Performance measure. One concern about using T_{LIM} as a measure of exercise tolerance is the relatively large variability of this measure (28). Day-to-day differences in subject motivation, effort perceptions, learning effects, and biological variability can lead to variations in this performance measure. We randomized and balanced the order of CON-EX and EMF-EX trials to avoid any potential learning effect, and the subjects performed exercise at similar times of day to minimize diurnal biological variation. Although we acknowledge that time trials are more reproducible than fixed work-rate tests (28), a time-trial test was not feasible in the present study because of the need to measure physiological variables during exercise at identical times and work rates. Nevertheless, the expected changes in time-trial performance are of a much smaller magnitude than the expected changes in T_{LIM} . In the present study, we found a significant 33% reduction in T_{LIM} and the likely range of the true effect of EMF on the average subject (95% confidence interval) included changes (−22% to −37%) more than twice the variation previously reported for an exercise trial of similar duration (~15%) (22). Furthermore, we observed a reduction in T_{LIM} in every subject. We are therefore confident that the change in T_{LIM} represents a true effect of EMF on exercise performance.

Subject expectation. A potential problem with assessing the effects of prior EMF on subsequent exercise tolerance is that subject expectations may have contributed an unknown amount to the observed changes. That is, if the subjects believed that the expiratory loading protocol would induce EMF, then it is perhaps not surprising that exercise tolerance was reduced. Although the subjects could not be blinded to EMF, we ensured that they remained unaware of the experimental hypotheses and naive to the purpose of the study. Subjects

received no information on exercise time or physiological cues such as heart rate, and no verbal encouragement was given to the subjects at any point during the exercise trials. Thus, although we cannot rule out an effect of subject expectation on exercise tolerance, we propose that any such effect was likely minimal.

EMF: expiratory resistive loading vs. whole-body exercise. One concern is that the demands placed on the expiratory muscles during expiratory resistive loading may not be representative of the normally occurring demands placed on these muscles during exercise. Any such discrepancy may lead to a subsequent overestimation or underestimation of the effect of the normally occurring level of EMF on exercise tolerance. The degree of EMF induced by expiratory loading and whole body exercise (CON-EX), however, was remarkably similar (−27 vs. −26%, respectively). We therefore conclude that the reduction in expiratory muscle function induced by expiratory loading was representative of the magnitude of EMF induced by the breathing requirements of high-intensity exercise.

Inspiratory muscle fatigue. We and others have shown that expiratory resistive loading can elicit inspiratory muscle fatigue and EMF (40, 43). This is important because prior fatiguing contractions of the inspiratory muscles have been shown to impair subsequent exercise tolerance (17). To circumvent this potential problem, we used an expiratory loading protocol that elicits a level of abdominal muscle fatigue similar to that found after whole body exercise yet minimizes the severity of diaphragm and rib cage muscle fatigue (43). Thus, although we cannot rule out an effect of inspiratory muscle fatigue on exercise tolerance, we are confident that any inspiratory muscle fatigue induced would have had only a minor effect on subsequent exercise tolerance.

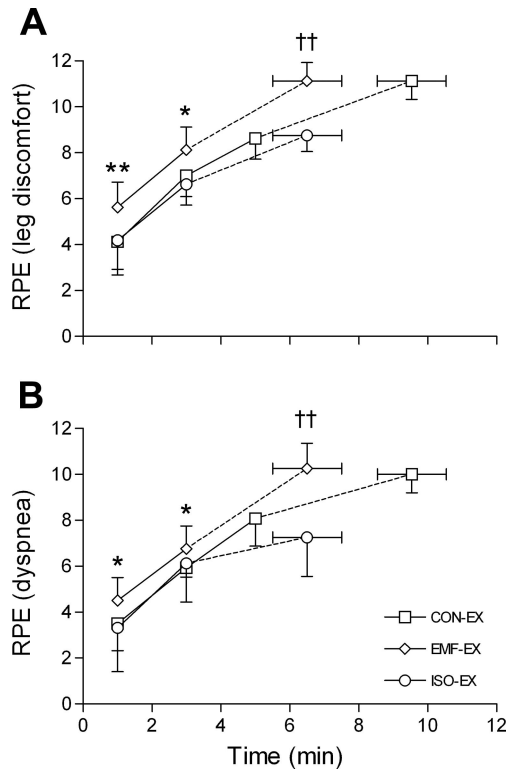


Fig. 7. Ratings of perceived exertion (RPE) for leg discomfort (A) and dyspnea (B) for CON-EX, EMF-EX, and ISO-EX. Values are group means \pm SD for 8 subjects. * $P < 0.05$ and ** $P < 0.01$, EMF-EX significantly different from both CON-EX and ISO-EX at the same time. †† $P < 0.01$, EMF-EX significantly different from ISO-EX at the same time only.

Effect of EMF on breathing pattern. With prior induction of EMF, there were marked increases in \dot{V}_E and f_R compared with that with ISO-EX, whereas tidal volume was unchanged. Thus it appears that EMF, like inspiratory muscle fatigue (16, 17,

36), elicits a pattern of rapid but not shallow breathing. This increase in ventilation resulted in a significant increase in the cumulative force output of the abdominal muscles and the diaphragm, which in turn may have contributed to the observed reduction in exercise tolerance. However, neither the increase in abdominal force output nor diaphragm force output correlated significantly with the change in T_{LIM} . Accordingly, we are confident that the increases in abdominal and diaphragm force production were not primary determinants of the decrease in exercise tolerance.

Comparisons With Previous Studies

Several studies have investigated the effect of prior inspiratory muscle work (17, 36), expiratory muscle work (45), or global respiratory muscle work (7, 19, 37) on subsequent exercise tolerance, with studies reporting either an impairment (17, 19, 45) or no change (7, 36, 37). We propose two main reasons that could account for the divergent findings between studies. First, most of the studies did not assess respiratory muscle fatigue (7, 19, 37) or quantified fatigue using indirect, effort-dependent measures (17, 45). It is therefore possible that some studies either failed to induce significant respiratory muscle fatigue before subsequent exercise or overestimated the normally occurring level of fatigue after whole body exercise. In the present study, the direct evidence that the abdominal muscles were fatigued after expiratory loading. Furthermore, expiratory loading and cycle exercise elicited a similar degree of abdominal muscle fatigue (27 vs. 26% reduction in $P_{ga_{w}}$). Second, the discrepant findings may have been because of differences in exercise protocol. Recent evidence has shown that partially unloading the inspiratory muscles during maximal incremental exercise does not elicit an increase in exercise time (34), likely because other limiting factors reach predominance before any effects of respiratory muscle fatigue are manifest. It is perhaps not surprising, therefore, that acute

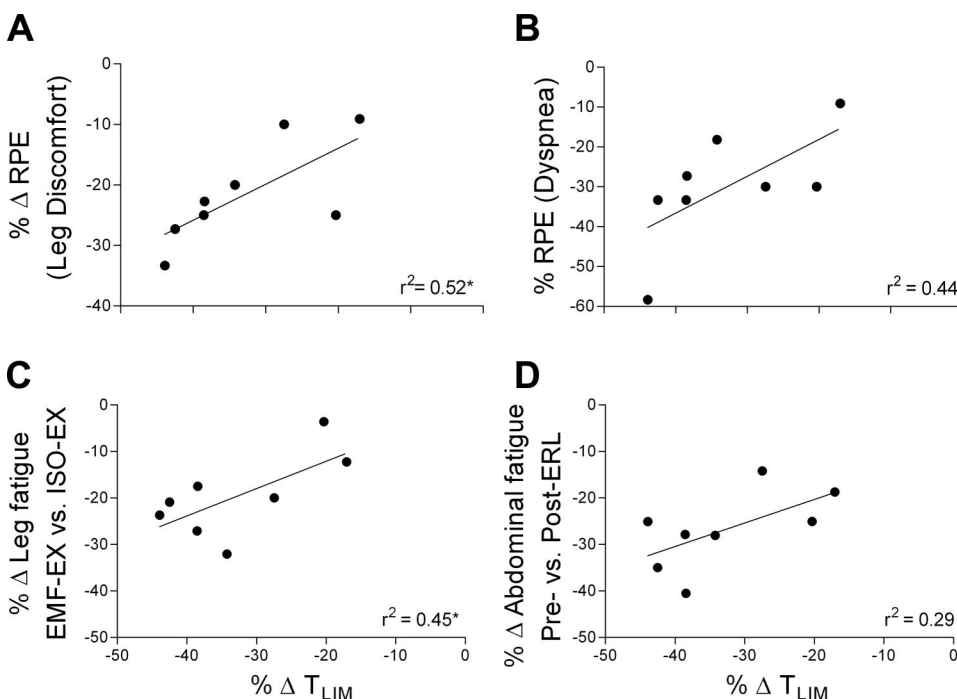


Fig. 8. Scatter plots showing relationships between the individual subject percent change in T_{LIM} (CON-EX vs. EMF-EX) and the percent difference in leg discomfort (A), dyspnea (B), leg fatigue (C) (EMF-EX vs. ISO-EX), and abdominal muscle fatigue elicited by expiratory resistive loading (ERL) (D). * $P < 0.05$, significant correlation.

inspiratory muscle loading also does not affect exercise time during maximal incremental exercise (36).

Why Did EMF Limit Exercise Tolerance?

Locomotor muscle fatigue. The severity of quadriceps muscle fatigue was greater after cycle exercise of the same intensity and duration with prior induction of EMF than without. Furthermore, the exacerbation of quadriceps muscle fatigue accounted for a significant amount of the variation in T_{LIM} , suggesting that the reduction in exercise tolerance was mediated largely by the increased rate of leg muscle fatigue. The exacerbation of exercise-induced quadriceps muscle fatigue was likely a consequence of two mechanisms. First, prior fatigue of the abdominal muscles may have caused a sympathetically mediated vasoconstriction in exercising limb muscles, similar to that described previously for fatiguing inspiratory muscle work (35). Fatiguing abdominal work in the otherwise resting human was shown to elicit a reflex increase in limb muscle sympathetic nerve activity that was likely triggered by an accumulation of metabolites in the fatiguing abdominal muscles (6). In the resting and exercising canine, infusion of lactic acid into the deep circumflex iliac artery resulted in a reduction in hindlimb blood flow, an effect that was prevented via pharmacological sympathetic blockade (32). A reduction in blood flow to working limb muscles would be expected to limit exercise tolerance via an increased severity of leg muscle fatigue, as has been shown to occur when the inspiratory muscles are loaded before (21) or during exercise (33).

Second, an increase in abdominal pressure during active expiration mechanically impedes venous return from the locomotor limb muscles, thereby reducing the steady-state hyperemic response to dynamic exercise (1, 24, 25, 38). For example, Stark-Leyva et al. (38) applied an expiratory load during submaximal cycle exercise that resulted in an additional 7–18 cmH₂O increase in P_{ga} and a consequent decrease in cardiac output in healthy humans. Such elevations in expiratory pressure production are thought to decrease venous return from the legs and, in turn, decrease blood flow through the inferior vena cava via a “Starling resistor” mechanism (41). In the present study, peak expiratory P_{ga} was 9.3 cmH₂O greater in EMF-EX than in ISO-EX, and this increase was of a magnitude similar to that induced by Stark-Leyva et al. (38). It is therefore possible that the increase in abdominal pressure production after induction of EMF resulted in a reduction in cardiac output that contributed to the exacerbation of quadriceps muscle fatigue and the consequent reduction in exercise tolerance.

Perceived exertion. Perceptions of dyspnea and leg discomfort were rated higher at every time point during EMF-EX vs. during ISO-EX. In turn, the changes in exercise tolerance correlated closely with both perceptions, although only leg discomfort correlated significantly. It is therefore possible that our subjects terminated exercise prematurely after induction of EMF due, in part, to heightened perceptions of dyspnea and leg discomfort during exercise. The increases in dyspnea and leg discomfort with prior EMF were likely related to the exacerbation of both exercise-induced abdominal and quadriceps fatigue, respectively. With the onset and development of muscle fatigue, there is an increased central drive to maintain force production in the muscle (8) that is subsequently perceived via

corollary discharge to the primary somatosensory cortex as an increased sense of effort (12), which may provide a critical signal to the central nervous system to curtail exercise. Because prior EMF exacerbated both abdominal and quadriceps muscle fatigue, there was likely an increased central drive to the muscles during EMF-EX with a subsequent increase in effort perception and premature curtailment of exercise. This notion is supported by the finding that both \dot{V}_E and abdominal muscle pressure production were greater at end-exercise in EMF-EX than in ISO-EX. That is, the enhanced ventilatory response to exercise with EMF likely represents an increase in central motor drive. In addition, iEMG from the VL during each pedal stroke was significantly greater at end exercise in EMF-EX than in ISO-EX, indicating a concurrent increase in central motor drive to the fatiguing quadriceps muscles.

Conclusions

Prior EMF limited subsequent exercise tolerance, primarily via an increased severity of limb locomotor muscle fatigue and a heightened perception of leg discomfort. We postulate that the increased severity of limb muscle fatigue arose from impairment in limb muscle blood flow. This impairment may have been caused by a sympathetically mediated vasoconstrictor influence exerted by an exacerbation of abdominal muscle fatigue, combined with a reduction in cardiac output facilitated by an augmented expiratory P_{ga}.

REFERENCES

1. Aliverti A, Dellaca RL, Lotti P, Bertini S, Duranti R, Scano G, Heyman J, Lo Mauro A, Pedotti A, Macklem PT. Influence of expiratory flow-limitation during exercise on systemic oxygen delivery in humans. *Eur J Appl Physiol* 95: 229–242, 2005.
2. Amann M, Romer LM, Subudhi AW, Pegelow DF, Dempsey JA. Severity of arterial hypoxemia affects the relative contributions of peripheral muscle fatigue to exercise performance. *J Physiol* 15: 389–403, 2007.
3. Baydur A, Behrakis PK, Zin WA, Jaeger M, Milic-Emili J. A simple method for assessing the validity of the esophageal balloon technique. *Am Rev Respir Dis* 126: 788–791, 1982.
4. Borg G. *Borg's Perceived Exertion and Pain Scales*. Champaign, IL: Human Kinetics, 1998.
5. Dempsey JA, Adams L, Ainsworth DM, Fregosi RF, Gallagher CG, Guz A, Johnson BD, Powers SK. Airway, lung, and respiratory muscle function during exercise. In: *Handbook of Physiology. Exercise: Regulation and Integration of Multiple Systems*. Bethesda, MD: Am. Physiol. Soc., 1996, sect. 12, chapt. 12, p. 448–514.
6. Derchak PA, Sheel AW, Morgan BJ, Dempsey JA. Effects of expiratory muscle work on muscle sympathetic nerve activity. *J Appl Physiol* 92: 1539–1552, 2002.
7. Dodd SL, Powers SK, Thompson D, Landry G, Lawler J. Exercise performance following intense, short-term ventilatory work. *Int J Sports Med* 10: 48–52, 1989.
8. Enoka RM, Stuart DG. Neurobiology of muscle fatigue. *J Appl Physiol* 72: 1631–1648, 1992.
9. Harms CA, Babcock MA, McClaran SR, Pegelow DF, Nickle GA, Nelson WB, Dempsey JA. Respiratory muscle work compromises leg blood flow during maximal exercise. *J Appl Physiol* 82: 1573–1583, 1997.
10. Johnson BD, Babcock MA, Suman OE, Dempsey JA. Exercise-induced diaphragmatic fatigue in healthy humans. *J Physiol* 460: 385–405, 1993.
11. Johnson BD, Saupe KW, Dempsey JA. Mechanical constraints on exercise hyperpnea in endurance athletes. *J Appl Physiol* 73: 874–886, 1992.
12. Jones LA. The senses of effort and force during fatiguing contractions. *Adv Exp Med Biol* 384: 305–313, 1995.
13. Kufel TJ, Pineda LA, Mador MJ. Comparison of potentiated and unpotentiated twitches as an index of muscle fatigue. *Muscle Nerve* 25: 438–444, 2002.

14. **Kyroussis D, Mills GH, Polkey MI, Hamnegard CH, Koulouris N, Green M, Moxham J.** Abdominal muscle fatigue after maximal ventilation in humans. *J Appl Physiol* 81: 1477–1483, 1996.
15. **Laghi F, D'Alfonso N, Tobin MJ.** Pattern of recovery from diaphragmatic fatigue over 24 hours. *J Appl Physiol* 79: 539–546, 1995.
16. **Mador MJ, Acevedo FA.** Effect of respiratory muscle fatigue on breathing pattern during incremental exercise. *Am Rev Respir Dis* 143: 462–468, 1991.
17. **Mador MJ, Acevedo FA.** Effect of respiratory muscle fatigue on subsequent exercise performance. *J Appl Physiol* 70: 2059–2065, 1991.
18. **Mador MJ, Magalang UJ, Rodis A, Kufel TJ.** Diaphragmatic fatigue after exercise in healthy human subjects. *Am Rev Respir Dis* 148: 1571–1575, 1993.
19. **Martin B, Heintzelman M, Chen HI.** Exercise performance after ventilatory work. *J Appl Physiol* 52: 1581–1585, 1982.
20. **Martin JG, De Troyer A.** The behaviour of the abdominal muscles during inspiratory mechanical loading. *Respir Physiol* 50: 63–73, 1982.
21. **McConnell AK, Lomax M.** The influence of inspiratory muscle work history and specific inspiratory muscle training upon human limb muscle fatigue. *J Physiol* 577: 445–457, 2006.
22. **McLellan TM, Cheung SS, Jacobs I.** Variability of time to exhaustion during submaximal exercise. *Can J Appl Physiol* 20: 39–51, 1995.
23. **Milic-Emili J, Mead J, Turner JM, Glauser EM.** Improved technique for estimating pleural pressure from esophageal balloons. *J Appl Physiol* 19: 207–211, 1964.
24. **Miller JD, Hemauer SJ, Smith CA, Stickland MK, Dempsey JA.** Expiratory threshold loading impairs cardiovascular function in health and chronic heart failure during submaximal exercise. *J Appl Physiol* 101: 213–227, 2006.
25. **Miller JD, Pegelow DF, Jacques AJ, Dempsey JA.** Effects of augmented respiratory muscle pressure production on locomotor limb venous return during calf contraction exercise. *J Appl Physiol* 99: 1802–1815, 2005.
26. **Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CP, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen OF, Pellegrino R, Viegi G, Wanger J.** Standardisation of spirometry. *Eur Respir J* 26: 319–338, 2005.
27. **Ng JK, Kippers V, Richardson CA.** Muscle fibre orientation of abdominal muscles and suggested surface EMG electrode positions. *Electro-myogr Clin Neurophysiol* 38: 51–58, 1998.
28. **Paton CD, Hopkins WG.** Tests of cycling performance. *Sports Med* 31: 489–496, 2001.
29. **Polkey MI, Kyroussis D, Hamnegard CH, Mills GH, Green M, Moxham J.** Quadriceps strength and fatigue assessed by magnetic stimulation of the femoral nerve in man. *Muscle Nerve* 19: 549–555, 1996.
30. **Polkey MI, Luo Y, Guleria R, Hamnegard CH, Green M, Moxham J.** Functional magnetic stimulation of the abdominal muscles in humans. *Am J Respir Crit Care Med* 160: 513–522, 1999.
31. **Rassier DE, Macintosh BR.** Coexistence of potentiation and fatigue in skeletal muscle. *Braz J Med Biol Res* 33: 499–508, 2000.
32. **Rodman JR, Henderson KS, Smith CA, Dempsey JA.** Cardiovascular effects of the respiratory muscle metaboreflexes in dogs: rest and exercise. *J Appl Physiol* 95: 1159–1169, 2003.
33. **Romer LM, Lovering AT, Haverkamp HC, Pegelow DF, Dempsey JA.** Effect of inspiratory muscle work on peripheral fatigue of locomotor muscles in healthy humans. *J Physiol* 571: 425–439, 2006.
34. **Romer LM, Miller JD, Haverkamp HC, Pegelow DF, Dempsey JA.** Inspiratory muscles do not limit maximal incremental exercise performance in healthy subjects. *Respir Physiol Neurobiol* 156: 353–361, 2007.
35. **Sheel AW, Derchak PA, Morgan BJ, Pegelow DF, Jacques AJ, Dempsey JA.** Fatiguing inspiratory muscle work causes reflex reduction in resting leg blood flow in humans. *J Physiol* 537: 277–289, 2001.
36. **Sliwinski P, Yan S, Gauthier AP, Macklem PT.** Influence of global inspiratory muscle fatigue on breathing during exercise. *J Appl Physiol* 80: 1270–1278, 1996.
37. **Spengler CM, Knopfli-Lenzin C, Birchler K, Trapletti A, Boutellier U.** Breathing pattern and exercise endurance time after exhausting cycling or breathing. *Eur J Appl Physiol* 81: 368–374, 2000.
38. **Stark-Leyva KN, Beck KC, Johnson BD.** Influence of expiratory loading and hyperinflation on cardiac output during exercise. *J Appl Physiol* 96: 1920–1927, 2004.
39. **Supinski GS, Clary SJ, Bark H, Kelsen SG.** Effect of inspiratory muscle fatigue on perception of effort during loaded breathing. *J Appl Physiol* 62: 300–307, 1987.
40. **Suzuki S, Suzuki J, Okubo T.** Expiratory muscle fatigue in normal subjects. *J Appl Physiol* 70: 2632–2639, 1991.
41. **Takata M, Wise RA, Robotham JL.** Effects of abdominal pressure on venous return: abdominal vascular zone conditions. *J Appl Physiol* 69: 1961–1972, 1990.
42. **Taylor BJ, How SC, Romer LM.** Exercise-induced abdominal muscle fatigue in healthy humans. *J Appl Physiol* 100: 1554–1562, 2006.
43. **Taylor BJ, Romer LM.** Respiratory muscle fatigue in response to expiratory resistive loading: a magnetic stimulation study (Abstract). *Am J Respir Crit Care Med* 175: A769, 2007.
44. **Verges S, Schulz C, Perret C, Spengler CM.** Impaired abdominal muscle contractility after high-intensity exhaustive exercise assessed by magnetic stimulation. *Muscle Nerve* 34: 423–430, 2006.
45. **Verges S, Sager Y, Erni C, Spengler CM.** Expiratory muscle fatigue impairs exercise performance. *Eur J Appl Physiol* 101: 225–232, 2007.