Locomotor muscle fatigue is not critically regulated after prior upper body exercise

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1Sport, Health and Performance Enhancement (SHAPE) Research Group, Department of Sports Science, School of Science and Technology, Nottingham Trent University, Nottingham, United Kingdom; and 2Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College London, London, United Kingdom

Submitted 26 January 2015; accepted in final form 6 August 2015

Johnson MA, Sharpe GR, Williams NC, Hannah R. Locomotor muscle fatigue is not critically regulated after prior upper body exercise. J Appl Physiol 119: 840–850, 2015. First published August 13, 2015; doi:10.1152/japplphysiol.00072.2015.—This study examined the effects of prior upper body exercise on subsequent high-intensity cycling exercise tolerance and associated changes in neuromuscular function and perceptual responses. Eight men performed three fixed work-rate (85% peak power) cycling tests: 1) to the limit of tolerance (CYC); 2) to the limit of tolerance after prior high-intensity arm-cranking exercise (ARM-CYC); and 3) without prior exercise and for an equal duration as ARM-CYC (ISOTIME). Peripheral fatigue was assessed via changes in potentiated quadriceps twitch force during supramaximal electrical femoral nerve stimulation. Voluntary activation was assessed using twitch interpolation during maximal voluntary contractions. Cycling time during ARM-CYC and ISOTIME (4.33 ± 1.10 min) was 38% shorter than during CYC (7.46 ± 2.79 min) (P < 0.001). Twitch force decreased more after CYC (−38 ± 13%) than ARM-CYC (−26 ± 10%) (P = 0.004) and ISOTIME (−24 ± 10%) (P = 0.003). Voluntary activation was 94 ± 5% at rest and decreased after CYC (89 ± 9%, P = 0.012) and ARM-CYC (91 ± 8%, P = 0.047). Rating of perceived exertion for limb discomfort increased more quickly during cycling in ARM-CYC [1.83 ± 0.46 arbitrary units (AU/min)] than CYC (1.10 ± 0.38 AU/min, P = 0.003) and ISOTIME (1.05 ± 0.43 AU/min, P = 0.002), and this was correlated with the reduced cycling time in ARM-CYC (r = −0.72, P = 0.045). In conclusion, cycling exercise tolerance after prior upper body exercise is potentially mediated by central fatigue and intolerable levels of sensory perception rather than a critical peripheral fatigue limit.

A consistent reduction (~35%) in the potentiated quadriceps twitch force is observed after high-intensity cycling (4–6, 66, 73, 79). It is proposed that this reduction represents an “individual critical threshold” of peripheral locomotor muscle fatigue beyond which the degree of associated sensory perception would not be tolerable (3). The observation of similar intramuscular metabolic perturbation at the end of exhaustive exercise, irrespective of the work rate (20, 77), supports the notion that it is probably not peripheral fatigue per se that is monitored/regulated, but the associated fatigue-inducing biochemical changes within the muscle (3). The critical limit of peripheral fatigue observed under “normal” conditions is also unchanged when exercise tolerance is reduced (i.e., the critical limit is reached more quickly) due to moderate hypoxia [inspired O2 fraction (FiO2) 0.13–0.15] (7, 66), superimposed inspiratory muscle loading (67), volitionally induced inspiratory or expiratory muscle fatigue (73, 80), prior high-intensity cycling exercise (5), and prior electrically induced quadriceps muscle fatigue (34). Conversely, the degree of peripheral fatigue observed after cycling exercise in severe hypoxia (FiO2 0.10) is about two-thirds of that observed in normoxia, suggesting that the major determinant of exercise tolerance switches from a peripheral to central origin, possibly due to brain hypoxia (8). Individual critical limits to peripheral fatigue are thought to be mediated by thin-fiber group III/IV muscle afferents (3, 31), which may influence central motor drive, and thereby exercise tolerance, by providing inhibitory feedback to the central nervous system in response to intramuscular metabolic perturbation (1, 10, 25, 51). However, despite growing support for an important role of peripheral fatigue in determining exercise tolerance, this notion has been challenged (53, 54). Marcera (53) has proposed a psychobiological model of endurance exercise tolerance, which primarily attributes exercise intolerance to a conscious decision to stop exercise due to perception of effort, mediated exclusively by feed-forward mechanisms (i.e., corollary discharge), reaching a level that the individual is unwilling to tolerate. A pivotal role for the rating of perceived exertion (RPE) in limiting exercise tolerance is also depicted in the “flush model” proposed by Millet (57). However, this model differs from the psychobiological model because it attributes RPE to both feed-forward and feedback (i.e., peripheral) mechanisms, thereby also emphasizing the importance of intramuscular metabolic perturbation and peripheral fatigue. The importance of sensory perception in influencing exercise tolerance is also evident in the striking ability of the RPE to predict the tolerable duration of exercise after prior fatiguing exercise (32), and at various exercise intensities (64), muscle glycogen concentrations (59), and ambient temperatures (24). Thus the rate of increase in RPE (ΔRPE/Δtime), and possibly dyspnea (Δdyspnea/Δtime) may be considered major contributors to the attainment of a “critical sensory tolerance limit” (35, 57) and subsequent cessation of exercise.

Several studies have also shed light on the determinants of exercise tolerance by showing reduced lower body exercise tolerance after prior high-intensity upper body exercise (12, 17, 24, 43, 46, 47, 61). This has been attributed to an accelerated development of peripheral locomotor muscle fatigue secondary to faster intramuscular metabolite (i.e., K+, H+, and La−) accumulation, resulting from the prior upper body exercise. However, this explanation remains conjecture, because peripheral fatigue was not evaluated in these studies. An alternative explanation is that, rather than accelerating the development of

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840 8750-7587/15 Copyright © 2015 the American Physiological Society http://www.jappl.org
peripheral fatigue, prior upper body exercise might reduce lower body exercise tolerance by accelerating the attainment of an intolerable level of sensory perception that is mediated, in part, by the ensemble input of group III/IV muscle afferents. Specifically, since group III/IV muscle afferent input may remain elevated for up to 15 min after high-intensity upper body exercise (25, 45), the ensemble group III/IV muscle afferent input would be elevated during subsequent high-intensity lower body exercise. Subsequently, increases in \( \Delta \text{RPE}/\Delta \text{time} \) and/or \( \Delta \text{dyspnea}/\Delta \text{time} \) may reduce exercise tolerance with less lower body peripheral fatigue incurred. This notion is supported by the observation of increased RPE and dyspnea during single-leg knee extensor exercise, preceded by fatiguing knee extensor exercise using the contralateral leg (10).

Therefore, the present study aimed to elucidate the mechanism(s) by which prior high-intensity upper body exercise reduces subsequent leg cycling exercise tolerance. Specifically, we tested the hypothesis that prior upper body exercise reduces subsequent leg cycling exercise tolerance, and that this is associated with less peripheral fatigue, but an accelerated rise in \( \Delta \text{RPE}/\Delta \text{time} \) and \( \Delta \text{dyspnea}/\Delta \text{time} \).

METHODS

Participants

Eight healthy, nonsmoking, moderately trained men (age: 26 ± 4 yr; height: 182 ± 4 cm; body mass: 83 ± 4 kg; peak oxygen uptake: 50 ± 10 ml·kg\(^{-1}\)·min\(^{-1}\)) provided written, informed consent to participate in the study. Five of the participants had previously taken part in investigations that included assessment of neuromuscular function using the methods described in the present study (38–41). Participants refrained from strenuous exercise and alcohol the day preceding and the day of an exercise test, abstained from caffeine on test days, and reported to the laboratory at least 2 h postprandially. The study was approved by the Nottingham Trent University Human Ethics Committee, and all procedures were conducted in accordance with the Declaration of Helsinki.

Experimental Design

Participants attended the laboratory on five separate occasions, at a similar time of day, separated by at least 48 h. The initial visit comprised a maximal incremental cycling test for the determination of peak oxygen uptake and peak cycling power (\( W_{\text{peak}} \)). The second visit comprised familiarization with the knee extensor neuromuscular function assessments and arm-cranking protocol. The subsequent three visits comprised the experimental trials. The first two experimental trials were performed in a randomized order and comprised a fixed work-rate cycling test at 85% \( W_{\text{peak}} \), and exercise was performed to the limit of tolerance. These two cycling tests were performed without (hereafter termed CYC) and with (hereafter termed ARM-CYC) prior high-intensity arm-cranking exercise. For the third experimental trial, the CYC protocol was repeated, except that the cycling test was terminated after an identical duration to that achieved during ARM-CYC (hereafter termed ISOTIME). Knee extensor force and surface electromyographic (EMG) signals were recorded during a series of electrically evoked and voluntary isometric contractions of the dominant leg to quantify the presence and magnitude of central and peripheral locomotor muscle fatigue. For an illustration of the protocol for the experimental trials, please refer to Fig. 1.

Neuromuscular Function

Dynamometer. Participants were seated in a rigid, custom-built dynamometer adapted from Hannah et al. (40), with hip and knee joint angles of 100° and 95° (180° = full extension), respectively. Adjustable strapping across the pelvis and shoulders prevented extraneous movement during muscle activation. A noncompliant strap was attached to the dominant leg of the participant ~2 cm proximal to the medial malleolus and was in series with a linear strain gauge (615, Tedea-Huntleigh, Herzliya, Israel) oriented perpendicular to the tibia. The dynamometer configuration was established during the familiarization session and replicated thereafter. The force signal was amplified (×1,000) in the frequency range 0–500 Hz, and sampled at 2,000 Hz using an external A/D converter (1401; CED, Cambridge, UK), interfaced with a personal computer using Spike 2 software (CED). Force data were low-pass filtered in both directions at 450 Hz using a fourth-order zero-lag Butterworth filter before analysis. Baseline resisting force was subtracted from all force recordings to correct for the effect of gravity.

EMG. EMG signals were recorded from the superficial quadriceps (rectus femoris, vastus medialis, and vastus lateralis) and hamstring (biceps femoris) muscles, as described previously (40). After preparation of the skin by shaving, light abrasion, and cleaning with alcohol, bipolar surface electrodes (2.5-cm interelectrode distance; silver/silver chloride, 95 mm\(^2\) area, Ambu Blue Sensor; Ambu, Ballerup, Denmark) were attached over each muscle at standardized

Fig. 1. Experimental protocol. Arrows denote timing of measurement. Note that blood lactate concentration ([La\(^{-}\)-B]), heart rate, rating of perceived exertion (RPE), and dyspnea were measured immediately before the start of leg cycling exercise. NMF, neuromuscular function.
percentages of thigh length measured from the knee joint space to the greater trochanter (rectus femoris, 55%; vastus medialis, 25%; vastus lateralis and biceps femoris, 45%). These sites were selected to avoid the innervation zones of each muscle (65). Electrodes were positioned parallel to the presumed orientation of the muscle fibers. EMG signals were preamplified by active EMG leads (input impedance 100 MΩ, common mode rejection ratio > 100 dB, base gain 500, first-order high-pass filter set to 10 Hz; Noraxon, Scottsdale, AZ) connected in series to a custom-built junction box and subsequently to the same A/D converter and computer software that enabled synchronization with the force data. The signals were sampled at 2,000 Hz. Before analysis, EMG data were band-pass filtered in both directions between 20 and 450 Hz using a fourth-order zero-lag Butterworth filter (26, 27, 55).

Electrical stimulation. Equipment and procedures for electrical stimulation have been described previously (41). A constant-current variable voltage stimulator (DSTAH; Digitimer, Welwyn Garden City, UK) was used to assess knee extensor contractile properties while the participant was voluntarily passive. Square-wave pulses (0.2-ms duration) were delivered via supramaximal femoral nerve stimulation to evoke maximal potentiated twitch and triplet (3 pulses at 300 Hz) contractions (24, 41). Stimulation of the femoral nerve was achieved via a 1-cm-diameter cathode stimulation probe (Electro Medical Supplies, Wantage, UK) pressed into the femoral triangle. The surface of the anode, a 4 × 7-cm carbon rubber electrode (Electro Medical Supplies), was coated in electrode gel and located over the greater trochanter. The precise location of the cathode was determined as the position that evoked the greatest twitch response for a particular submaximal electrical current (typically 30–50 mA) and was marked on the skin using indelible ink to ensure accurate repositioning within each trial.

Procedure. Initially, discrete electrical stimuli were delivered via percutaneous stimulation of the femoral nerve in the femoral triangle to elicit twitch contractions of the quadriceps. Stepwise increments in the current were delivered and separated by 10 s to allow for neuromuscular recovery, until plateaus were reached in the amplitude of twitch force and compound muscle action potentials (M-waves). The stimulus intensity was then increased by 25% above the value required to elicit a plateau to ensure supramaximal stimulation. Participants subsequently performed submaximal voluntary contractions of the knee extensors, lasting ~3 s and interspersed by ~30-s rest, at ~50, 75, and 90% of their perceived maximal force. Thereafter, and following baseline measurements for heart rate and blood lactate concentration ([La]B), participants performed four maximum voluntary contractions (MVCs) lasting 3–4 s and interspersed by ~30-s rest. Participants were instructed to extend the knee “as hard and as fast as possible.” During and after each contraction, participants received strong verbal encouragement. Online feedback of the force signal was provided, and a marker showing maximum force during that session was displayed onscreen to assist participants in attempting to maintain a high and stable force level. Each MVC was followed within 1–2 s by two supramaximal electrical stimuli, separated by 1 s, delivered to the femoral nerve to elicit maximal potentiated twitches (49). Single electrically evoked triplet contractions (3 supramaximal stimuli delivered at 300 Hz) were superimposed on the third and fourth MVC, and at rest ~1–2 s after the two potentiated twitch contractions (29, 48). Triplets were used in the calculation of voluntary activation (see below), because the detection of single superimposed twitches becomes increasingly difficult at high forces as a result of the decreasing signal-to-noise ratio. This may lead to the erroneous conclusion that voluntary activation is maximal (i.e., 100%). Consequently, some studies have suggested the use of multiple stimuli (48, 63, 72). Furthermore, triplets may offer advantages over potentiated twitches as an indicator of peripheral fatigue, since pilot data from our laboratory and that of de Ruiter et al. (28, 29) has found the force evoked by 300-Hz bursts (3–8 pulses) to be insensitive to potentiation, and, because they evoke much greater force than potentiated twitches, they may better reflect the functional changes observed during MVCs.

The maximum voluntary force (MVF) of the quadriceps was defined as the greatest instantaneous force produced during the relevant series of MVCs. The root mean square (RMS) amplitude of the EMG signal for each agonist muscle (vastus medialis, vastus lateralis, and rectus femoris) was calculated over a 500-ms epoch surrounding MVF (250 ms either side) (19). Agonist EMG RMS values were averaged to calculate a mean quadriceps (QEMGmax) value and normalized to the peak-to-peak amplitude of the M-wave (see below) to provide a measure of neuromuscular activation. Potentiated twitches were measured for peak force and the amplitude of M-wave response for the three quadriceps electrodes, which were then averaged across the three sites to provide a mean quadriceps value. Mean quadriceps M-wave amplitude and potentiated peak twitch force were averaged across the latter four twitch contractions (i.e., after the 3rd and 4th MVC) within each time period because it typically takes three MVCs to fully potentiate twitches (49). The mean quadriceps M-wave amplitude across the four potentiated twitches was defined as the maximal M-wave amplitude (Mmax) and was used for normalization of voluntary quadriceps EMG RMS (19). Measures of triplet peak force were averaged across the two contractions within each time period. To evaluate the presence and magnitude of central fatigue, voluntary activation was evaluated for the third and fourth MVC using the formula for the twitch interpolation technique (56), as described previously (29, 48):

\[
\text{Voluntary activation (\%)} = 100 - \frac{\text{triplet force increment/resting triplet force}}{100}
\]

where the triplet force increment refers to that produced by superimposed triplet stimulation. The highest voluntary activation of the two MVCs was retained for analysis. Assessment of neuromuscular function (from the first MVC to the last triplet) took ~2 min.

Maximal Incremental Cycling Test

Participants initially performed a maximal incremental cycling test using an electromagnetically braked cycle ergometer (Excalibur Sport; Lode, Groningen, The Netherlands). Tests began at 0 W, power was increased by discrete 20-W increments every 60 s, and exercise was performed to the limit of volitional tolerance or task failure (i.e., cycling cadence below 60 rpm) (46). Participants wore a facemask (model 7940; Hans Rudolph) connected to a flow sensor (ZAN variable orifice pneumotach; Nspire Health, Oberthulba, Germany) that was calibrated using a 3-liter syringe. Gas concentrations were measured using fast-responding laser diode absorption spectroscopy sensors, which were calibrated using gases of known concentration (5% CO2, 15% O2, balance N2; BOC, Guildford, UK), and ventilatory and pulmonary gas exchange variables were measured breath by breath (ZAN 600USB; Nspire Health), as described previously (46). Peak oxygen uptake was defined as the highest recorded value over any 30-s period, and \( W_{\text{peak}} \) was calculated as the sum of the power output in the last completed stage plus the product of ramp increment (20 W) and the fraction of the final stage actually completed.

Experimental Trials

During the experimental trials (CYC, ARM-CYC, and ISOTIME), heart rate was measured using short-range telemetry (Polar S610; Polar, Kempele, Finland), and fingertip capillary blood samples were taken and analyzed for [La]B using an automated analyzer (Bösen C-line Sport; EKF Diagnostics, Barleben, Germany).

An illustration of the timing of measurements taken during the experimental trials is shown in Fig. 1. Each experimental trial comprised a fixed work-rate cycling test at 85% \( W_{\text{peak}} \) preceded by a standardized 23.5-min period. During the first 6 min of this period, baseline measures of heart rate, [La]B, and neuromuscular function were taken.

\[ \text{J Appl Physiol • doi:10.1152/japplphysiol.00072.2015 • www.jappl.org} \]
After baseline measurements, participants remained seated in the dynamometer and then either rested (CYC and ISOTIME) or performed intense intermittent arm-cranking exercise (ARM-CYC) using an electromagnetically braked arm-cranking ergometer (Angio; Lode). The arm-cranking protocol comprised 8 × 1-min arm-cranking bouts, interspersed with 30-s rest, at a fixed work rate of 1.0–1.5 W/kg body mass (mean: 1.2 ± 0.2 W/kg body mass, 100 ± 15 W) (46). As in our laboratory’s previous study (46), the arm-cranking work rate for each individual was selected based on their habitual upper body exercise regimen. This work rate was trialed during the familiarization session and, based on successful completion by all participants, was deemed suitable for subsequent testing. Cadence was maintained between 90 and 110 rpm. Heart rate was measured at the end of each arm-cranking bout during ARM-CYC, and [La−]b was also measured after the final arm-cranking bout. These measurements were taken at equivalent time points while participants rested during CYC and ISOTIME. Quadriceps and hamstring muscle EMG was recorded throughout the arm-cranking protocol and displayed online with a high gain to aid visual detection of EMG activity. Participants received verbal feedback regarding EMG activity to ensure minimal activation of the leg muscles.

Arm-cranking (ARM-CYC) or seated rest (CYC and ISOTIME) was followed by another 6-min period before the start of the fixed work-rate cycling test. During this period, measures of neuromuscular function were taken, and participants then transferred to the cycle ergometer (positioned ~2 m from the dynamometer). Immediately before the start of the cycling test, heart rate and [La−]b were measured along with dyspnea (defined as “breathing effort”) and RPE for leg discomfort using Borg’s modified CR10 scale (18).

Participants adopted a self-selected cadence between 80 and 100 rpm during the first cycling test, and this was replicated during subsequent tests. Quadriceps and hamstring muscle EMG was synchronized with the cycle ergometer crank position via a reed switch attached to the crank and ergometer. The RMS amplitude of the EMG signal of the quadriceps muscle was measured at the start and end of each minute during each arm-cranking exercise bout and normalized to QEMGmax to quantify quadriceps neuromuscular activation. EMG RMS amplitude of the quadriceps and hamstring muscles was also measured over 10 consecutive pedal revolutions at the end of the first, third, and final minute of cycling exercise and normalized to Mmax (quadriceps only) to quantify changes in neuromuscular activation during cycling. Onsets and offsets of EMG bursts were determined visually by the same investigator, according to a previously published method (22, 23). Threshold methods for determining EMG onsets and offsets are sensitive to changes in background EMG (42) and are unsuitable for this type of analysis, because bursts of EMG activity occur with background activity already present in the muscles, and the amplitude of background activity varies between muscles (22, 23). Heart rate, RPE, and dyspnea were measured after 3 min of cycling. During CYC and ARM-CYC, cycling exercise was performed to the limit of volitional tolerance. An additional criterion for terminating a cycling test was a fall in cadence below 60 rpm. During ISOTIME, cycling exercise was terminated by the investigators after an identical duration to that achieved during ARM-CYC.

On cessation of cycling exercise heart rate, [La−]b, RPE, and dyspnea were measured immediately, and participants were assisted to the dynamometer for neuromuscular function evaluation with the first MVC initiated after 2 min (±9 s).

### Statistical Analyses

Data were analyzed using SPSS for Windows (IBM, Chicago, IL). Trial-to-trial variation in baseline neuromuscular function was calculated as the within-participant coefficient of variation. Measurement error and reproducibility of baseline neuromuscular function were calculated, and the smallest meaningful change was subsequently determined (16, 43). A one-way repeated-measures ANOVA followed by Tukey’s post hoc test was used to analyze differences between trials for cycling exercise duration and rates of change in perceptual responses expressed relative to absolute exercise time (∆RPE/∆time and ∆dyspnea/∆time) and when normalized to total cycling exercise duration (∆RPE/%time and ∆dyspnea/%time). All other data were analyzed using a two-way (trial × time) repeated-measures ANOVA. Significant interactions were further explored by performing one-way repeated-measures ANOVA: 1) within each trial and 2) across trials at individual time points, followed by Tukey’s post hoc test. When differences were observed within or between trials, 95% confidence intervals (CI) for the difference were calculated (2). Pearson’s correlation coefficient was used to determine the relationship between selected variables. Statistical significance was set at *P* < 0.05. Results are presented as means ± SD.

### RESULTS

#### Cycling Exercise Tolerance

There was an effect of trial on cycling exercise duration at 85% \( W_{\text{peak}} (273 ± 26 \text{ W}) \) [F(2,14) = 16.8, *P* < 0.001], which was, as expected, identical (4.33 ± 1.10 min) during ARM-CYC and ISOTIME and 38 ± 17% shorter than CYC (7.46 ± 2.79 min) (mean difference = 3.13 ± 2.15 min, 95% CI = 1.50–4.75 min, *P* < 0.001). Cycling cadence at the termination of cycling exercise in CYC (68 ± 6 rpm, range: 61–78 rpm), ARM-CYC (66 ± 5 rpm, range: 60–74 rpm), and ISOTIME (92 ± 10 rpm, range: 85–104 rpm) was always ≥60 rpm. Therefore, cycling exercise during CYC and ARM-CYC was always performed to the limit of volitional tolerance rather than being terminated by the investigators.

#### Neuromuscular Function

Baseline measures of neuromuscular function are shown in Table 1, and these were highly reproducible between trials. Raw traces of force from a representative participant at baseline performing a MVC with superimposed triplet, followed by twitch and triplet contractions, are shown in Fig. 2. In all trials, measures of neuromuscular function were unchanged from baseline measures are shown as means ± SD. CYC, cycling test to the limit of tolerance; ARM-CYC, cycling test to the limit of tolerance after prior high-intensity arm-cranking exercise; ISOTIME, cycling test without prior exercise and for an equal duration as ARM-CYC; CV, coefficient of variation; SMC, smallest meaningful change; MVC, maximal voluntary force; EMG, electromyography; RMS, root mean square; Mmax, maximal M-wave amplitude.

### Table 1. Baseline neuromuscular function and between-trial reproducibility

<table>
<thead>
<tr>
<th></th>
<th>CYC</th>
<th>ARM-CYC</th>
<th>ISOTIME</th>
<th>Within-participant CV, %</th>
<th>Measurement Error</th>
<th>Reproducibility</th>
<th>SMC</th>
</tr>
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<tbody>
<tr>
<td>MVF, N</td>
<td>616 ± 75</td>
<td>602 ± 84</td>
<td>616 ± 73</td>
<td>4</td>
<td>19</td>
<td>53</td>
<td>27</td>
</tr>
<tr>
<td>Potentiated twitch force, N</td>
<td>201 ± 33</td>
<td>200 ± 20</td>
<td>203 ± 22</td>
<td>3</td>
<td>11</td>
<td>29</td>
<td>15</td>
</tr>
<tr>
<td>Potentiated triplet force, N</td>
<td>339 ± 35</td>
<td>328 ± 37</td>
<td>337 ± 33</td>
<td>3</td>
<td>10</td>
<td>28</td>
<td>14</td>
</tr>
<tr>
<td>Voluntary activation, %</td>
<td>94 ± 7</td>
<td>95 ± 6</td>
<td>94 ± 6</td>
<td>2</td>
<td>1.8</td>
<td>5.1</td>
<td>2.6</td>
</tr>
<tr>
<td>Quadriceps M-wave amplitude, mV</td>
<td>6.3 ± 2.1</td>
<td>6.1 ± 1.9</td>
<td>5.8 ± 2.5</td>
<td>10</td>
<td>0.6</td>
<td>1.7</td>
<td>0.8</td>
</tr>
<tr>
<td>Quadriceps EMG RMS at MVF, %Mmax amplitude</td>
<td>8.8 ± 2.9</td>
<td>8.5 ± 2.9</td>
<td>8.9 ± 2.5</td>
<td>11</td>
<td>1.0</td>
<td>2.7</td>
<td>1.3</td>
</tr>
</tbody>
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baseline to precycling (data not shown). Thus arm-cranking per se did not result in central or peripheral locomotor muscle fatigue.

For MVF, there was a trial × time interaction \( F(4,28) = 6.2, P < 0.001 \) and an effect of time in CYC \( F(2,14) = 14.3, P < 0.001 \), ARM-CYC \( F(2,14) = 11.5, P = 0.001 \), and ISOTIME \( F(2,14) = 8.5, P = 0.003 \). MVF decreased from baseline to postcycling in CYC (mean difference = 95 ± 70 N, 95% CI = 45–145 N, \( P < 0.001 \), ARM-CYC (mean difference = 56 ± 39 N, 95% CI = 22–89 N, \( P = 0.002 \), and ISOTIME (mean difference = 49 ± 48 N, 95% CI = 13–85 N, \( P = 0.008 \)). Furthermore, there was an effect of trial on the decrease in MVF \( F(2,14) = 8.3, P = 0.004 \), which was greater in CYC than ARM-CYC (mean difference = 39 ± 38 N, 95% CI = 7–71 N, \( P = 0.02 \)) and ISOTIME (mean difference = 46 ± 43 N, 95% CI = 14–78 N, \( P = 0.005 \)) (Fig. 3A).

For voluntary activation, there was a trial × time interaction \( F(4,28) = 3.8, P = 0.013 \) and an effect of time in CYC \( F(2,14) = 8.0, P = 0.005 \) and ARM-CYC \( F(2,14) = 4.7, P = 0.027 \), but not ISOTIME \( F(2,14) = 0.8, P = 0.46 \). Voluntary activation decreased from baseline (see Table 1) to postcycling in CYC (89 ± 9%, mean difference = 5.0 ± 4.8%, 95% CI = 1.4–8.7%, \( P = 0.012 \)) and ARM-CYC (91 ± 8%, mean difference = 3.8 ± 4.7%, 95% CI = 0.1–7.4%, \( P = 0.047 \)). Furthermore, there was an effect of trial on the decrease in voluntary activation \( F(2,14) = 5.2, P = 0.021 \), which was greater in CYC than ISOTIME (mean difference = 4.4 ± 4.9%, 95% CI = 0.7–8.0%, \( P = 0.019 \)) (Fig. 3B).

For potentiated twitch force, there was a trial × time interaction \( F(4,28) = 8.8, P < 0.001 \) and an effect of time in CYC \( F(2,14) = 49.4, P < 0.001 \), ARM-CYC \( F(2,14) = 48.3, P < 0.001 \), and ISOTIME \( F(2,14) = 22.7, P < 0.001 \).
Potentiated twitch force decreased from baseline to postcycling in CYC (mean difference = 77 ± 30 N, 95% CI = 55–98 N, P < 0.001), ARM-CYC (mean difference = 52 ± 21 N, 95% CI = 38–66 N, P < 0.001), and ISOTIME (mean difference = 50 ± 24 N, 95% CI = 30–70 N, P < 0.001). Furthermore, there was an effect of trial on the decrease in potentiated twitch force [F(2,14) = 10.9, P = 0.001], which was greater in CYC than ARM-CYC (mean difference = 25 ± 17 N, 95% CI = 8–41 N, P = 0.004) and ISOTIME (mean difference = 27 ± 22 N, 95% CI = 10–43 N, P = 0.003) (Fig. 3C).

For potentiated triplet force, there was a trial × time interaction [F(4,28) = 9.1, P < 0.001] and an effect of time in CYC [F(2,14) = 11.1, P = 0.001], ARM-CYC [F(2,14) = 5.4, P = 0.018], and ISOTIME [F(2,14) = 7.2, P = 0.007]. Potentiated triplet force decreased from baseline to postcycling in CYC (mean difference = 63 ± 50 N, 95% CI = 26–100 N, P = 0.001), ARM-CYC (mean difference = 37 ± 40 N, 95% CI = 7–66 N, P = 0.014) and ISOTIME (mean difference = 31 ± 26 N, 95% CI = 9–52 N, P < 0.001). Furthermore, there was an effect of trial on the decrease in potentiated triplet force [F(2,14) = 9.0, P = 0.003], which was greater in CYC than ARM-CYC (mean difference = 27 ± 18 N, 95% CI = 5–48 N, P = 0.015) and ISOTIME (mean difference = 33 ± 28 N, 95% CI = 11–54 N, P = 0.004) (Fig. 3D).

Quadriiceps M_max and neuromuscular activation (i.e., RMS EMG normalized to M_max) at MVF remained unchanged in all trials.

Leg Muscle EMG During Cycling

Quadriiceps EMG RMS during arm-cranking was ≤3% of the QEMG_max during an MVC (data not shown), thus demonstrating minimal leg activation. For quadriiceps neuromuscular activation (EMG RMS normalized to M_max) during cycling, there was a trial × time interaction [F(4,28) = 6.1, P = 0.001] and an effect of time in CYC [F(2,14) = 36.3, P < 0.001], ARM-CYC [F(2,14) = 11.6, P = 0.001], and ISOTIME [F(2,14) = 36.3, P = 0.012]. There was also an effect of trial on neuromuscular activation in the final minute of cycling [F(2,14) = 6.2, P = 0.012], which was greater in CYC than ARM-CYC (mean difference = 0.76 ± 0.84% M_max, 95% CI = 0.03–1.5% M_max, P = 0.040) and ISOTIME (mean difference = 0.91 ± 0.87% M_max, 95% CI = 0.18–1.64% M_max, P = 0.014) (Fig. 4). The absolute hamstrings EMG RMS remained constant during cycling and was not different between trials (pooled data: 0.08 ± 0.05 mV).

Heart Rate and [La−]_B

For heart rate, there was a trial × time interaction [F(24,168) = 81.7, P < 0.001] and an effect of trial on the mean of the eight heart rate measurements taken during the 11.5-min period of arm-cranking in ARM-CYC or seated rest in CYC and ISOTIME (see Fig. 1) [F(2,24) = 144.3, P < 0.001]. The mean heart rate during this period was higher in ARM-CYC (153 ± 19 beats/min) than CYC (72 ± 14 beats/min) (mean difference = 81 ± 20 beats/min, 95% CI = 67–96 beats/min, P < 0.001) and ISOTIME (73 ± 11 beats/min) (mean difference = 80 ± 16 beats/min, 95% CI = 66–95 beats/min, P < 0.001). There was also an effect of trial on heart rate measured precycling [F(2,14) = 21.7, P < 0.001], after 3 min of cycling [F(2,14) = 17.8, P < 0.001], and postcycling [F(2,14) = 12.3, P < 0.001]. Precycling, heart rate was higher in ARM-CYC than CYC (mean difference = 34 ± 21 beats/min, 95% CI = 18–49 beats/min, P < 0.001) and ISOTIME (mean difference = 34 ± 15 beats/min, 95% CI = 18–49 beats/min, P < 0.001). After 3 min of cycling, heart rate was higher in ARM-CYC than CYC and ISOTIME (mean difference from both trials = 10 ± 6 beats/min, 95% CI = 5–15 beats/min, P < 0.001). Postcycling, heart rate was lower in ISOTIME than CYC (mean difference = 10 ± 6 beats/min, 95% CI = 3–16 beats/min, P = 0.005) and ARM-CYC (mean difference = 12 ± 8 beats/min, 95% CI = 5–18 beats/min, P = 0.001) (Fig. 5A).

For [La−]_B, there was a trial × time interaction [F(6,42) = 79.7, P < 0.001] and an effect of trial on [La−]_B measured immediately after the period of arm-cranking in ARM-CYC or seated rest in CYC and ISOTIME [F(2,14) = 167.2, P < 0.001]. Immediately after this period, [La−]_B was higher in ARM-CYC than CYC and ISOTIME (mean difference from both trials = 10.3 ± 2.2 mmol/l, 95% CI = 8.6–12.0 mmol/l, P < 0.001). There was also an effect of trial on [La−]_B measured precycling [F(2,14) = 158.2, P < 0.001], which was higher in ARM-CYC than CYC (mean difference = 8.5 ± 2.0 mmol/l, 95% CI = 7.0–10.0 mmol/l, P < 0.001) and ISOTIME (mean difference = 8.6 ± 1.8 mmol/l, 95% CI = 7.2–10.1 mmol/l, P < 0.001). Furthermore, there was an effect of trial on [La−]_B measured postcycling [F(2,14) = 31.9, P < 0.001], which was higher in ARM-CYC than CYC (mean difference = 2.3 ± 1.0 mmol/l, 95% CI = 0.8–3.9 mmol/l, P = 0.003) and ISOTIME (mean difference = 4.6 ± 1.8 mmol/l, 95% CI = 3.1–6.1 mmol/l, P < 0.001). Postcycling, [La−]_B was also higher in CYC than ISOTIME (mean difference = 2.3 ± 2.0 mmol/l, 95% CI = 0.8–3.8 mmol/l, P = 0.004) (Fig. 5B).

RPE and Dyspnea

There was a trial × time interaction for RPE [F(4,28) = 14.7, P < 0.001] and an effect of trial on RPE measured after 3 min of cycling [F(2,14) = 11.7, P = 0.001], which was
higher in ARM-CYC than CYC [mean difference = 2.4 ± 1.7 arbitrary units (AU), 95% CI = 1.0–3.9 AU, P = 0.002] and ISOTIME (mean difference = 2.3 ± 1.9 AU, 95% CI = 0.8–3.8 AU, P = 0.003). There was also an effect of trial on RPE measured postcycling [F(2,14) = 18.4, P < 0.001], which was lower in ISOTIME than CYC (mean difference = 3.3 ± 1.9 AU, 95% CI = 1.4–5.2 AU, P = 0.001) and ARM-CYC (mean difference = 4.1 ± 2.6 AU, 95% CI = 2.2–5.9 AU, P < 0.001) (Fig. 6A).

There was a trial × time interaction for dyspnea [F(4,28) = 5.8, P < 0.001] and an effect of trial on dyspnea measured after 3 min of cycling [F(2,14) = 16.3, P < 0.001], which was

Fig. 5. Heart rate (A) and \([\text{La}^-]_B\) (B) during CYC (●), ARM-CYC (○), and ISOTIME (△). Values are means ± SD, and x-error bars are omitted at the end of cycling exercise to improve clarity. Measurements at 0 min were taken immediately before the start of cycling exercise. bpm, Beats/min. Significant difference between trials (P < 0.01): **ARM-CYC vs. CYC and ISOTIME; †CYC and ARM-CYC vs. ISOTIME at the end of cycling; #all trials at the end of cycling.

Fig. 6. RPE (A and C) and dyspnea (B and D) during cycling exercise in CYC (●), ARM-CYC (○), and ISOTIME (△). Values are means ± SD and expressed relative to absolute exercise time (A and B) and when normalized to total cycling exercise duration (C and D). Measurements at 0 min and 0% time were taken immediately before the start of cycling exercise. X-error bars in A and B are omitted at the end of cycling exercise to improve clarity. Significant difference (P < 0.01): **ARM-CYC vs. CYC and ISOTIME; †CYC and ARM-CYC vs. ISOTIME at the end of cycling.
higher in ARM-CYC than CYC (mean difference = 1.9 ± 1.4 AU, 95% CI = 0.9–3.0 AU, \( P < 0.001 \)) and ISOTIME (mean difference = 2.1 ± 1.1 AU, 95% CI = 1.0–3.2 AU, \( P < 0.001 \)). There was also a main effect of trial on dyspnea measured postcycling [\( F(2,14) = 11.8, \ P = 0.001 \)], which was lower in ISOTIME than CYC (mean difference = 2.8 ± 2.4 AU, 95% CI = 0.9–4.6 AU, \( P = 0.004 \)) and ARM-CYC (mean difference = 3.1 ± 2.6 AU, 95% CI = 1.3–5.0 AU, \( P = 0.002 \)) (Fig. 6B).

There was an effect of trial on \( \Delta \text{RPE}/\Delta \text{time} \) [\( F(2,14) = 11.7, P = 0.001 \)], which was higher in ARM-CYC than CYC (mean difference = 0.72 ± 0.63 AU/min, 95% CI = 0.25–1.21 AU/min, \( P = 0.003 \)) and ISOTIME (mean difference = 0.79 ± 0.55 AU/min, 95% CI = 0.31–1.27 AU/min, \( P = 0.002 \)) (Table 2). There was also an effect of trial on \( \Delta \text{dyspnea}/\Delta \text{time} \) [\( F(2,14) = 4.5, P = 0.031 \)], which was higher in ARM-CYC than ISOTIME (mean difference = 0.46 ± 0.58 AU/min, 95% CI = 0.02–0.90 AU/min, \( P = 0.038 \)) (Table 2).

There was an effect of trial on \( \Delta \text{RPE}/\Delta \text{time} \) [\( F(2,14) = 19.1, P < 0.001 \)] (Fig. 6C and Table 2), which was lower in ISOTIME than CYC (mean difference = 0.03 ± 0.01 AU/%time, 95% CI = 0.01–0.05 AU/%time, \( P < 0.001 \)) and ARM-CYC (mean difference = 0.04 ± 0.02 AU/%time, 95% CI = 0.02–0.05 AU/%time, \( P < 0.001 \)). There was also an effect of trial on \( \Delta \text{dyspnea}/\Delta \text{time} \) [\( F(2,14) = 7.5, P = 0.006 \)] (Fig. 6D and Table 2), which was lower in ISOTIME than CYC (mean difference = 0.03 ± 0.01 AU/%time, 95% CI = 0.01–0.05 AU/%time, \( P = 0.006 \)) and ARM-CYC (mean difference = 0.02 ± 0.01 AU/%time, 95% CI = 0.001–0.04 AU/%time, \( P = 0.036 \)).

When data from CYC and ARM-CYC were pooled, \( \Delta \text{RPE}/\Delta \text{time} \) was negatively correlated with the time to the limit of voluntary activation in CYC and ARM-CYC (correlation coefficient = -0.79, 95% CI = -0.63–0.93 AU/min, \( P < 0.001 \)). There was also an effect of trial on \( \Delta \text{dyspnea}/\Delta \text{time} \) (correlation coefficient = -0.038) (Table 2).

**DISCUSSION**

The present study examined the effects of prior high-intensity upper body exercise on subsequent high-intensity leg cycling exercise tolerance and associated changes in neurovascular function and perceptual responses. Our main findings were threefold: 1) prior upper body exercise in ARM-CYC reduced subsequent cycling exercise tolerance by 38%; 2) the reduced cycling exercise tolerance in ARM-CYC was associated with less peripheral muscle fatigue incurred but a similar reduction in voluntary activation compared with CYC; and 3) the reduced cycling exercise tolerance in ARM-CYC was related to increases in \( \Delta \text{RPE}/\Delta \text{time} \) and \( \Delta \text{dyspnea}/\Delta \text{time} \). These findings suggest that exercise tolerance is not regulated by a critical level of peripheral fatigue. Instead, central fatigue and an exacerbation of perceptual responses are the potential mechanisms underlying the reduced cycling exercise tolerance after prior upper body exercise.

Our laboratory recently showed that high-intensity cycling exercise tolerance was reduced by a strikingly similar extent after an identical upper body exercise protocol (46). Several authors suggest that reduced lower limb exercise tolerance after prior upper body exercise occurs because of accelerated development of peripheral fatigue caused by greater intramuscular metabolic perturbation (12, 17, 36, 44, 46, 61). This notion is supported, indirectly, by the observation that prior high-intensity upper body exercise elevated leg muscle [La\(^{-}\)] and [H\(^{+}\)] at the onset of isolated knee extensor exercise (11, 12), accelerated the exercise-induced increase in interstitial [K\(^{+}\)] (61), and reduced exercise tolerance (12, 61). However, although such metabolite accumulation has been implicated in the etiology of peripheral fatigue (21, 33), previous prior upper body exercise studies did not measure peripheral fatigue or neuromuscular activation. Comparisons of our work with isolated knee extensor exercise studies are also complicated by the task-specificity of fatigue etiology (13, 74). Two observations from the present study suggest that peripheral fatigue during cycling exercise was not accelerated by prior upper body exercise. First, the extent of peripheral fatigue in ARM-CYC and ISOTIME was the same, even though there was considerable systemic metabolic perturbation in ARM-CYC. Indeed, in our previous study, the same upper body exercise protocol reduced the strong ion difference by 15%, increased plasma [H\(^{+}\)] by 33%, reduced \( \text{W}_{\text{peak}} \) by 29%, and accelerated the increase in plasma [K\(^{+}\)] during subsequent cycling exercise by 56% (46). Second, if peripheral fatigue during cycling exercise was accelerated, this would be expected to result in greater neuromuscular activation (i.e., increased motor unit recruitment and/or firing frequency) to compensate for the reduced force-generating capacity (14, 30); however, this was not observed. Collectively, these observations, therefore, suggest that systemic metabolite perturbation plays a minor role in peripheral fatigue generation.

Our findings contrast previous cycling exercise studies in which moderate hypoxia (7, 66), superimposed inspiratory muscle loading (67), volitionally induced inspiratory or expiratory muscle fatigue (73, 80), prior high-intensity cycling exercise (5), and prior electrically induced quadriceps muscle fatigue (34) reduced exercise tolerance but resulted in the same degree of peripheral fatigue incurred compared with control conditions. These observations are taken as evidence for inhibitory group III/IV muscle afferent feedback to the central nervous system regulating central motor drive to confine the development of peripheral fatigue to a critical threshold (3, 31). However, although the 38% reduction in twitch force after CYC is comparable to the proposed critical threshold of pe-
Peripheral fatigue previously reported after high-intensity fixed work-rate cycling exercise (4, 5, 66, 73, 80), this degree of peripheral fatigue was not reached during ARM-CYC (26% reduction in twitch force). This finding is similar to the observation of less peripheral fatigue incurred after high-intensity cycling exercise in severe hypoxia (FIO2 0.10) compared with normoxia (8). The notion that peripheral fatigue is not critically regulated is also supported by two recent isolated muscle studies: Rossmann et al. (68) observed greater quadriceps muscle fatigue during single-leg compared with double-leg knee extensor exercise, whereas Amann et al. (10) observed less quadriceps muscle fatigue during single-leg knee extensor exercise after fatiguing knee extensor exercise with the contralateral leg. The present study thus extends these observations to whole body exercise by providing novel evidence that peripheral fatigue is not independently regulated during high-intensity fixed work-rate cycling exercise to volitional tolerance.

Whether peripheral fatigue plays an important role in governing exercise tolerance remains controversial (9, 53, 54, 60). Consistent with previous observations (5, 7, 54, 71, 75), submaximal quadriceps muscle recruitment was observed at the limit of exercise tolerance in CYC and ARM-CYC (~55 and 50%, respectively, of the QEMGmax), and Noakes (58) argues that this negates peripheral fatigue as the single limiting factor to exercise tolerance. Furthermore, Decorte et al. (30) have shown that peripheral fatigue during cycling exercise at 80% \( W_{\text{peak}} \) develops mostly during the first half of the test, such that the limit of tolerance approaches without further peripheral fatigue, but with a significant reduction in voluntary activation. The similar reduction in voluntary activation after CYC and ARM-CYC indicates that central fatigue developed more quickly in ARM-CYC, possibly due to a “spill-over” of central fatigue from the exercised upper body muscles to the leg locomotor muscles. In support, it was recently demonstrated that fatiguing leg cycling exercise resulted in a “spill-over” of central fatigue (i.e., reduced voluntary activation) to the remote unexercised elbow flexors (69). This effect was attributed to inhibitory group III/IV muscle afferent feedback originating in fatigued leg muscle, since attenuating this feedback using intrathecal fentanyl abolished the decline in voluntary activation of the elbow flexors. Whether a fall in voluntary activation limits cycling exercise that is characterized by submaximal muscle contractions remains uncertain (74). However, it is also recognized that a limiting influence of central fatigue on exercise tolerance may be manifest by changes in sensory perception (57, 74).

The conscious perception of fatigue is thought to reflect the complex integration and interpretation of central motor drive and an associated corollary discharge, somatosensory feedback (4, 50, 70, 78), and cognitive functions, such as motivation and emotional state (70). After 3 min of cycling, RPE for leg discomfort was greater in ARM-CYC compared with CYC and ISOTIME, despite similar levels of quadriceps neuromuscular activation, which supports observations made during single-leg knee extensor exercise after fatiguing knee extensor exercise with the contralateral leg (10). Furthermore, at the end of cycling, RPE was greater in ARM-CYC compared with ISOTIME, despite similar levels of peripheral fatigue incurred, whereas RPE was similar at the end of cycling in CYC and ARM-CYC, despite less peripheral fatigue incurred during ARM-CYC. Collectively, our findings suggest that the perception of leg discomfort during cycling exercise does not exclusively reflect the extent of quadriceps neuromuscular activation or degree of peripheral fatigue incurred. Similar observations have been made in COPD patients, who sometimes stop exercise because of leg discomfort, and in the absence of quadriceps muscle fatigue (52). These observations suggest that the conscious perception of leg discomfort likely reflects a complex interplay between multiple factors other than peripheral fatigue and neuromuscular activation (70). Minute ventilation was not measured in the present study, and thus it cannot be ruled out that the greater \( \Delta \text{dyspnea}/\Delta \text{time} \) during ARM-CYC resulted, in part, from a greater ventilatory response (10). However, afferents involved in the perception of dyspnea and limb discomfort project to the same sensorimotor brain areas (62), and, therefore, a heightened level of one perception may potentiate the other. In support, quadriceps fatigue induced by sustained contractions increased dyspnea during a subsequent inspiratory loaded breathing challenge without affecting breathing pattern or pleural pressure swings (37). Thus, although we could not elucidate the precise causative mechanism(s), we propose that the greater \( \Delta \text{RPE}/\Delta \text{time} \) and \( \Delta \text{dyspnea}/\Delta \text{time} \) during ARM-CYC reflects, in part, greater ensemble group III/IV afferent projections to integrated sensorimotor brain structures due to cycling, commencing with preexisting afferent input originating from the previously exercised respiratory (50) and upper body musculature (10, 25, 45), lungs (50), and heart (78). During cycling exercise, the preexisting afferent input would have been added to the prevailing inputs related to central motor drive, and locomotor muscle (10) and cardiorespiratory (50, 78) activity, thereby accelerating the increase in perceptual responses and reducing exercise tolerance. The correlation between increased \( \Delta \text{RPE}/\Delta \text{time} \) and \( \Delta \text{dyspnea}/\Delta \text{time} \) during cycling exercise tolerance in ARM-CYC also supports sensory perception as an important mediator of exercise tolerance. Our findings are, therefore, consistent with the “flush model” proposed by Millet (57), which suggests that exercise tolerance is mediated primarily by \( \Delta \text{RPE}/\Delta \text{time} \), which, in turn, depends mainly on feedback (i.e., peripheral) and feed-forward (i.e., central) mechanisms.

The greater \( \Delta \text{RPE}/\Delta \text{time} \) and \( \Delta \text{dyspnea}/\Delta \text{time} \) during ARM-CYC compared with CYC, but similar \( \Delta \text{RPE}/\Delta \text{time} \) and \( \Delta \text{dyspnea}/\Delta \text{time} \), suggests that the preexisting afferent input at the onset of cycling in ARM-CYC affects perceptual responses by increasing their gain. Similar effects on the absolute and normalized RPE are observed when exercise tolerance is reduced by muscle glycogen depletion (59), warm and cold ambient temperatures (24), and prior fatiguing activity using the same muscle groups (32). These observations underpin the notion that perceptual responses are set in anticipation, otherwise known as teleoanticipation (76), so that exercise terminates at a critical sensory tolerance limit (32, 58, 60, 75). By limiting exercise tolerance, the sensory tolerance limit will, therefore, also mediate the degree of peripheral fatigue incurred, which is consistent with the findings of recent studies using the isolated knee extensor exercise model (10, 68). We note, however, that the limit of cycling exercise tolerance during CYC and ARM-CYC was sometimes associated with submaximal RPE and dyspnea, suggesting that ad-

J Appl Physiol • doi:10.1152/japplphysiol.00072.2015 • www.jappl.org
ditional influences, such as psychological factors (15, 54), were also mediating the limit of exercise tolerance.

In conclusion, reductions in cycling exercise tolerance due to prior upper body exercise are associated with an acceleration of central fatigue and greater perceptual responses rather than an accelerated development of peripheral fatigue. These findings suggest that peripheral fatigue is not independently regulated during high-intensity fixed work-rate cycling exercise to volitional tolerance, and that exercise tolerance, and thus the degree of peripheral fatigue incurred, is potentially determined by intolerable levels of sensory perception.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS


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J Appl Physiol • doi:10.1152/japplphysiol.00072.2015 • www.jappl.org


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