Central and Peripheral Fatigue in Male Cyclists after 4-, 20-, and 40-km Time Trials

KEVIN THOMAS[1], STUART GOODALL[1], MARK STONE[2], GLYN HOWATSON[1,3], ALAN ST CLAIR GIBSON[4], and LES ANSLEY[1]

[1]Department of Sport, Exercise and Rehabilitation, Faculty of Health and Life Sciences, Northumbria University, Newcastle-upon-Tyne, UNITED KINGDOM; [2]Department of Sport Management, School of Applied Management and Law, Buckinghamshire New University, High Wycombe, UNITED KINGDOM; [3]Water Research Group, School of Environmental Sciences and Development, Northwest University, Potchefstroom, SOUTH AFRICA; and [4]School of Medicine, University of the Free State, Bloemfontein, SOUTH AFRICA

ABSTRACT

THOMAS, K., S. GOODALL, M. STONE, G. HOWATSON, A. ST CLAIR GIBSON, and L. ANSLEY. Central and Peripheral Fatigue in Male Cyclists after 4-, 20-, and 40-km Time Trials. *Med. Sci. Sports Exerc.*, Vol. 47, No. 3, pp. 537–546, 2015. **Purpose**: Few studies have assessed neuromuscular fatigue after self-paced locomotor exercise; moreover, none have assessed the degree of supraspinal fatigue. This study assessed central and peripheral fatigue after self-paced exercise of different durations. **Methods**: Thirteen well-trained male cyclists completed 4-, 20-, and 40-km simulated time trials (TTs). Pre- and immediately post-TT (<2.5 min), twitch responses from the knee extensors to electrical stimulation of the femoral nerve and transcranial magnetic stimulation of the motor cortex were recorded to assess neuromuscular and corticospinal function. **Results**: Time to complete 4-, 20-, and 40-km TTs was 6.0 ± 0.2, 31.8 ± 1.0, and 65.8 ± 2.2 min at average exercise intensities of 96%, 92%, and 87% of maximum oxygen uptake, respectively. Exercise resulted in significant reductions in maximum voluntary contraction, with no difference between TTs (−18%, −15%, and −16% for 4-, 20-, and 40-km TTs, respectively). Greater peripheral fatigue was evident after 4-km (40% reduction in potentiated twitch) compared with that after 20-km (31%) and 40-km TTs (29%). In contrast, longer TTs were characterized by more central fatigue, with greater reductions in voluntary activation measured by motor nerve (−11% and −10% for 20- and 40-km TTs vs –7% for 4-km TTs) and cortical stimulation (−12% and −10% for 20- and 40-km vs –6% for 4-km). **Conclusions**: These data demonstrate that fatigue after self-paced exercise is task dependent, with a greater degree of peripheral fatigue after shorter higher-intensity (6 min) TTs and more central fatigue after longer lower-intensity TTs (>30 min). **Key Words:** FATIGUE, LOCOMOTOR EXERCISE, SELF-PACED, NEUROMUSCULAR, TRANSCRANIAL MAGNETIC STIMULATION

BASIC SCIENCES

In exercise science, fatigue is commonly defined as an exercise-induced impairment in the ability to produce muscular force (17) in the presence of increased perception of effort (14). Fatigue can be attributed to various processes along the motor pathway that are broadly split into central and peripheral origins. Peripheral fatigue attributes the decline in force to processes at, or distal to, the neuromuscular junction (17). Central fatigue attributes the decline in force to processes residing within the CNS (17), commonly assessed by supramaximally stimulating the peripheral motor nerve during an isometric maximum voluntary contraction (MVC) (28). A subset of central fatigue is supraspinal fatigue, which attributes the decline in force to a suboptimal output from the motor cortex (48,49). Transcranial magnetic stimulation (TMS) has been successfully used to demonstrate the presence of supraspinal fatigue across a range of exercise paradigms (18–20,32,37,38). Used in concert, motor nerve and motor cortical stimulation methods can develop deeper understanding of the processes underpinning fatigue.

The extent to which peripheral and central processes contribute to fatigue is dependent on the nature of the exercise task, and hence, task dependency remains a central theme in the study of fatigue. During sustained isometric maximal contractions of a single muscle group, peripheral fatigue is dominant particularly during the early (<60 s) portion of the exercise bout, with central mechanisms increasing in influence as the exercise bout is prolonged (9,36). During submaximal contractions (sustained or intermittent) at low intensities (<30% MVC), the contribution of central fatigue is higher than that observed during higher-intensity submaximal contractions (>30% MVC), where peripheral fatigue predominates and central fatigue is modest or absent (8,41,42). Although less data are available, these patterns of central and peripheral fatigue can also be extended to locomotor exercise. Peripheral fatigue develops early during fatiguing locomotor exercise (13), and reductions in voluntary activation (VA) are evident when the exercise bout is prolonged (23,31). Although

Address for correspondence: Glyn Howatson, Ph.D., Faculty of Health and Life Sciences, Northumbria University, Newcastle-upon-Tyne, NE1 8ST, United Kingdom; E-mail: glyn.howatson@northumbria.ac.uk.
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the available literature suggests that higher-intensity, shorter-duration exercise is primarily limited by peripheral fatigue and central fatigue is exacerbated as the exercise bout lengthens, direct comparison of the contribution of central and peripheral processes to fatigue after locomotor exercise tasks of different durations is not available.

Previous studies investigating fatigue during whole body locomotor exercise have largely used constant-load exercise protocols; a small number of studies have used locomotor exercise paradigms that allow self-selected pacing strategies in response to sensations of fatigue and effort (3,5,6,32). A series of recent studies by Amann et al. (3,5,6) has demonstrated the potential for studying fatigue using self-paced whole body locomotor exercise modes. The authors proposed that the magnitude of exercise-induced peripheral fatigue is regulated to an individual "critical threshold," as evidenced by a remarkably similar end-exercise peripheral fatigue after self-paced 5-km cycling time trial (TT) exercise in conditions of altered inspired air concentrations (4), pre-fatiguing exercise (3), and impaired afferent feedback (5). This centrally mediated restriction is proposed to be regulated by inhibitory afferent feedback to prevent excessive homeostatic disruption (1), perhaps to protect or maintain a muscular reserve capacity (7), and coincides with attainment of an individual "sensory tolerance limit" (17).

Amann and Secher (7) were careful to emphasize the critical threshold might be specific to the exercise task, and further work from the same group has demonstrated differences in the magnitude of peripheral fatigue after constant-load, single- and double-leg knee extensor exercise modes (34,35). Some support for a universal critical threshold of muscle fatigue during the same exercise mode has been provided for intermittent submaximal isometric contractions to exhaustion at intensities between 38% and 55% MVC (11). Interestingly, Burnley et al. (11) also observed a lower degree of peripheral fatigue at lower exercise intensities (<31% MVC), suggesting that the critical threshold might not be attained in longer-duration lower-intensity exercise, although the exercise was capped at 60 min and task failure only occurred in one of nine participants. No study has directly compared the contribution of central and peripheral processes to fatigue after locomotor exercise tasks of different durations, and the existence of a critical threshold for peripheral fatigue after locomotor exercise warrants further investigation. Self-paced exercise offers an interesting test of this question, as the ability to modulate exercise intensity would theoretically permit the athlete to exhaust the available muscular reserve to maximize performance and attain such a threshold of muscle fatigue. In addition, the contribution of central processes to the fatigue observed after self-paced exercise of different durations and the contribution of supraspinal fatigue have yet to be investigated. Accordingly, the aim of the present study was to examine the degree of central and peripheral fatigue induced by self-paced cycling exercise of different durations. We hypothesized the existence of a consistent critical level of peripheral fatigue between TTs of different durations, whereas the degree of central fatigue would increase as the length of the exercise bout is extended.

METHODS

Participants

After institutional ethical approval, 13 well-trained male cyclists (mean ± SD: age, 31 ± 8 yr; stature, 1.80 ± 0.07 m; body mass, 72.9 ± 9.1 kg; maximum oxygen uptake ($\dot{V}O_{2max}$), 4.26 ± 0.38 $L \cdot min^{-1}$; power at $\dot{V}O_{2max}$ (W_{peak}), 383 ± 29 W) gave a written informed consent to take part in the study. All participants were regularly competing in cycling TT events similar in duration to those used in the study.

Experimental Design

Using a repeated-measures design, each participant visited the laboratory on five separate occasions to complete a preliminary assessment, a practice TT, and three experimental TTs of 4, 20, and 40 km. Trials were separated by a minimum of 2 days and a maximum of 7 days and were conducted at the same time of the day (±1 h). The order of experimental trials was randomized and counterbalanced. Before each visit, participants were required to refrain from caffeine (for at least 12 h) and strenuous exercise (for at least 24 h) and to arrive in a fully rested, hydrated state. Before the first experimental trial, participants completed a 48-h food and activity diary and were instructed to replicate their exercise and nutrition as closely as possible for each subsequent trial. Cardiorespiratory, blood lactate, and perceptual responses were recorded during each TT, and measures of central and peripheral fatigue were assessed before the trial and within 2.5 min after the trial.

Procedures

Preliminary visit. Participants attended the laboratory to complete an incremental assessment to measure $\dot{V}O_{2max}$ and W_{peak}. The test started at 200 W and incremented by 5 W every 15 s. Participants cycled to the limit of tolerance and were given strong verbal encouragement in the latter stages. The test was terminated when participants were unable to maintain a cadence within 20 rpm of their self-selected cadence for the test. $\dot{V}O_{2max}$ ($L \cdot min^{-1}$) was calculated as the highest 30-s mean value; W_{peak} (W) was recorded as the end-test power output.

Practice trial. Participants completed a practice trial to habituate to the measurement tools of the study, particularly electrical stimulation of the femoral nerve and magnetic stimulation of the motor cortex. A 4-km TT was chosen as the distance for the practice trial, as the participant groups were regularly competing in trials of distances approximating 20 and 40 km but were less practiced in shorter-duration TTs. In addition, previous data from our laboratory have shown evidence of a learning effect in well-trained cyclists for 4-km (44) but not 20-km (47) simulated TT. The reproducibility of TT performance across the distances used is good (coefficient of variation, 1.6%–2.3%) (44,47). The procedures adopted during the practice trial rep-licated that of the experimental trials (described in the following section).

Experimental trials. Participants completed 4-, 20-, and 40-km TT on separate occasions with instructions to "complete the distance as fast as possible." All exercises were completed on an electromagnetically braked cycle ergometer (Velotron Pro; RacerMate Inc., Seattle, WA). Participants adjusted the ergometer to mimic their racing position (replicated for each trial) and wore their own cycling shoes and cleats. Visual feedback of distance covered, power output (W), and cadence (rpm) were available to view on a computer screen through the ergometer software (Velotron CS 2008; RacerMate, Inc., Seattle, WA). Participants were able to adjust their power output through variations in cadence and use of an electronic gearing system and were instructed to remain seated for the duration of the trial. An electric fan was positioned 0.5 m in front of the ergometer for cooling during each trial.

Neuromuscular function. Measures of neuromuscular function for the assessment of central and peripheral fatigue were evaluated before and after the trial (within <2.5 min of exercise cessation) using TMS of the motor cortex and electrical stimulation of the femoral nerve, with evoked responses recorded with surface EMG. Pre-TT exercise participants completed six isometric MVC separated by 60-s rest. The first three contractions ensured adequate potentiation of the knee extensors. Femoral nerve stimulation was delivered during and 2-s after MVC to assess VA and potentiated quadriceps twitch force ($Q_{tw,pot}$), respectively. Subsequently, TMS was delivered during brief (approximately 3–5 s) contractions at 100%, 75%, and 50% MVC separated by approximately 5 s of rest for determination of VA from cortical stimulation (VA_{TMS}). This procedure was repeated three times with 15-s rest between each set. Post-TT exercise participants completed three MVC with femoral nerve stimulation and three sets of contractions at 100%, 75%, and 50% MVC with TMS; in line with other investigations that have assessed exercise-induced fatigue of the knee extensors, these measurements were completed within 2.5 min of exercise cessation (18,35,38). The rapid nature of this procedure is necessary to capture the magnitude of fatigue induced by the exercise before it dissipates (16), and the duration (2–2.5 min) was consistent between trials. Resting motor-evoked potentials (MEP) (eight stimuli) were recorded before these baseline measures of fatigue and immediately after the final TMS set after the trial. Further details on these procedures follow.

Force and EMG recordings. Knee extensor force (N) during voluntary and evoked contractions was measured using a calibrated load cell (MuscleLab force sensor 300; Ergotest Technology, Norway) fixed to a custom-built chair and connected to a noncompliant strap attached around the participant's right leg superior to the ankle malleoli. The height of the load cell was individually adjusted to ensure a direct line with the applied force. During all measurements, participants sat upright, with the hips and knees at 90° flexion, and were given specific instruction to remain seated. EMG of the knee extensors and flexors was recorded from the vastus lateralis (VL) and the lateral head of the biceps femoris, respectively. After the skin was shaved and cleaned, surface electrodes (Ag/AgCl; Kendall H87PG/F, Covidien, Mansfield, MA) were placed 2 cm apart over the belly of each muscle. A reference electrode was placed on the patella. The positions of the electrodes were marked with indelible ink to ensure consistent placement on repeat trials. The electrodes were used to record the root mean square amplitude for maximal voluntary contractions (MVC_{RMS}), the compound muscle action potential (M-wave) from the electrical stimulation of the femoral nerve, and the MEP elicited by TMS. Surface electrode signals were amplified (×1000; 1902, Cambridge Electronic Design, Cambridge, United Kingdom), band-pass–filtered (EMG only, 20–2000 Hz), digitized (4 kHz, micro 1401; Cambridge Electronic Design), and acquired for offline analysis (Spike 2 version 7.01; Cambridge Electronic Design).

Femoral nerve stimulation. Single electrical stimuli (200-μs duration) were delivered to the right femoral nerve via surface electrodes (CF3200; Nidd Valley Medical Ltd., Harrogate, United Kingdom) using a constant-current stimulator (DS7AH; Digitimer Ltd., Welwyn Garden City, United Kingdom) at rest and during MVC. The cathode was placed over the nerve high in the femoral triangle; the anode was positioned midway between the greater trochanter and the iliac crest (20). The exact positioning was determined by the response that elicited the maximum quadriceps twitch amplitude (Q_{tw}) and M-wave (M_{max}) at rest. To determine stimulation intensity, single stimuli were delivered in 20-mA stepwise increments from 100 mA until a plateau in Q_{tw} and M-wave was observed. To ensure a supramaximal stimulus, the final intensity was increased by 30% (mean ± SD current, 194 ± 101 mA). The peak-to-peak amplitude and area of the electrically evoked M_{max} were used as a measure of membrane excitability (15). Measures of muscle contractility were derived for each resting twitch, as follows: twitch amplitude, maximum rate of force development (MRFD), maximum relaxation rate (MRR), contraction time (CT), and one-half relaxation time ($RT_{0.5}$).

TMS. Using a concave double cone coil (110-mm diameter; maximum output, 1.4 T), single-pulse magnetic stimuli 1 ms in duration were delivered to the left motor cortex, powered by a monopulse magnetic stimulator (Magstim 200; The Magstim Company Ltd., Whitland, United Kingdom). The coil was held and tilted lateral to the vertex (1.5 ± 0.6 cm) to stimulate the left hemisphere (posteroanterior intracranial current flow) over the area relating to Brodmann area 4, the primary motor cortex. The coil position elicited a large MEP in the vastus lateralis and a concurrent small MEP in the biceps femoris and was marked on the scalp using indelible ink to ensure consistent placement on repeat trials. Resting motor threshold (rMT) was determined before each experimental trial and was not different between trials ($P = 0.49$). Starting at subthreshold intensity (35% of stimulator output), single-pulse TMS was delivered over the optimal site of stimulation in 5% increments until the peak-to-peak amplitude of the evoked MEP consistently exceeded 50 μV. Subsequently, the stimulus intensity was reduced in 1% decrements until MEP response was below 50 μV in more than half of 10 stimuli

(33). rMT for the knee extensors occurred at 49% ± 12% of maximum stimulator output, and subsequently during experimental trials, TMS was delivered at 130% of rMT. This intensity elicited a large MEP in the vastus lateralis (area on average 80% of M_{max} during knee extensor MVC) and a small MEP in the biceps femoris (area on average 6% of the raw quadriceps MEP during MVC).

Cardiorespiratory, blood [lactate], and perceptual measures. During each trial, expired air was analyzed breath by breath using an online system (Cortex Metalyser 3b; Biophysik, Leipzig, Germany) and HR was measured with short-wave telemetry (Polar Electro, Finland). Blood [lactate] was determined from 20-μL samples of fingertip capillary blood immediately analyzed using an automated analyzer (Biosen C-Line; EKF Diagnostics, Barleben, Germany) that was calibrated before use with a 12-mM standard. Blood sampling was aligned between trials, such that samples occurred at the same distance covered in each, on the basis of sampling blood at 20% of the distance covered in each trial—at 0.8, 1.6, 2.4, 3.2, and 4 km for the 4-km TT, at the same intervals plus 8, 12, 16, and 20 km for the 20-km TT, and then at all of the previously outlined intervals plus 24, 32, and 40 km for the 40-km TT. RPE were obtained every 20% of the trial distance covered using the Borg 6–20 scale. Participants were asked to provide a subjective assessment of RPE, taking into account all sensations of physical stress, effort, and fatigue (10). After assessment of neuromuscular function and a timed 5-min standardized cooldown, participants were asked for a session RPE score that best represented the effort over the entire TT.

Data Analysis

VA measured through stimulation of the motor nerve was quantified using the twitch interpolation method (28). Briefly, the amplitude of the superimposed twitch force (SIT) measured during MVC was compared with the amplitude of the potentiated twitch force assessed 2 s after MVC at rest. VA (%) = (1 − [SIT/$Q_{tw,pot}$] × 100). For cortical stimulation, VA_{TMS} was assessed by measurement of the force responses to TMS at 100%, 75%, and 50% MVC (for an illustration of these methods, see Figure, Supplemental Digital Content 1, http://links.lww.com/MSS/A428, Raw traces of twitch forces and EMG responses to TMS and peripheral motor nerve stimulation from a representative participant). Corticospinal excitability increases during voluntary contraction; therefore, it is necessary to estimate, rather than directly measure, the amplitude of the resting twitch in response to motor cortex stimulation. The amplitude of the estimated resting twitch (ERT) was calculated as the *y*-intercept of the linear regression between the mean amplitude of the superimposed twitches evoked by TMS at 100%, 75%, and 50% MVC and voluntary force (19,48,49); regression analyses confirmed the existence of a linear relation both before and after exercise (r^2 = 0.96 ± 0.03 and 0.94 ± 0.05, respectively). VA (%) was subsequently calculated as (1 − [SIT/ERT] × 100). The reproducibility and validity of this procedure for the knee extensors has been previously established (19,37). For pre- and postmeasures of VA, the median score was used for analysis (17). The peak-to-peak amplitude and area of the evoked M_{max} and MEP responses were quantified offline. The peak-to-peak amplitude was measured as the absolute difference between the maximum and minimum points of the biphasic M-wave or MEP (15). The area was calculated as the integral of the reflected value of the entire M-wave or MEP (15). The area of vastus lateralis MEP was normalized to the M_{max} measured during the MVC to ensure that the magnetic stimulus was activating a high proportion of the knee extensor motor units and to quantify corticospinal excitability during contraction. Resting corticospinal excitability was quantified as the ratio between the resting MEP and resting M_{max}. The cortical silent period (CSP) was quantified during the MVC as the duration between the point of cortical stimulation until the post-stimulus EMG exceeded ±2 SD of the pre-stimulus EMG for >100 ms (20).

Reproducibility Coefficients

Typical error (TE) and intraclass correlation coefficients (ICC) between the pretrial scores were calculated to quantify reproducibility of the outcome measures of interest. Reproducibility was high for MVC (ICC, 0.98; TE, 4.0%), $Q_{tw,pot}$ (ICC, 0.98; TE, 6.6%), motor nerve VA (ICC, 0.96; TE, 3.0%), VA_{TMS} (ICC, 0.98; TE, 1.7%), and moderate for ERT (ICC, 0.91; TE, 10.8%), CSP (ICC, 0.95; TE, 12.8%), M_{max} (ICC, 0.86; TE, 29.1%), and MEP/M_{max} ratio (ICC, 0.74; TE, 12.6%).

Statistical Analysis

Statistical procedures were planned *a priori*. For all neuromuscular measures, paired-samples *t*-tests were used to assess the expected effect of each TT on measures of fatigue (comparison of before vs after trial). The effect of TT length on all measures of fatigue and neuromuscular function was assessed using one-way repeated-measures ANOVA on the pre- to post-trial change scores, with Tukey pairwise *post hoc* comparisons calculated in the event of a significant main effect. The same procedure was used to analyze differences between trials for TT performance (power output (W)), cardiorespiratory, and blood lactate responses. Where a significant main effect was detected, selected effect sizes for three group comparisons were computed as eta squared (η^2) and for two group comparisons as Cohen *D*. Friedman ANOVA with *post hoc* Wilcoxon signed-rank tests were used for nonparametric data (i.e., RPE). To assess for differences in pacing strategy, mean power output covered was computed in bins representing 10% of the distance covered for each trial and expressed relative to the trial mean. These data were then analyzed using 3 × 10 repeated-measures ANOVA, with a focus on the interaction effect to determine whether pacing strategy differed between trials. Previous data have demonstrated association between the degree of peripheral fatigue and capillary blood [lactate] accumulation (38); thus, Pearson product moment

correlations were used to determine the relation between these variables. The assumptions underpinning these statistical procedures were verified as per the guidelines outlined by Newell et al. (30), and all data were considered normal. Descriptive data are presented as means ± SD in the text, tables, and figures, unless otherwise indicated. Statistical analysis was conducted using SPSS (version 19.0; IBM SPSS, Chicago, IL). Statistical significance was assumed at $P < 0.05$.

RESULTS

Exercise Responses

Mean power output was significantly higher in the 4-km (340 ± 30 W) compared with that in the 20-km (279 ± 22 W, $D = 0.98$, $P < 0.05$) and in the 20-km compared with that in the 40-km (255 ± 21 W, $D = 0.97$, $P < 0.05$) (Fig. 1A). The pacing strategy adopted was not different between trials ($P = 0.57$) (Fig. 1A). The mean power output during 4, 20, and 40 km corresponded to relative exercise intensities of 89%, 73%, and 67% of W_{peak} and 96%, 92%, and 87% of $\dot{V}O_{2max}$, respectively. Mean whole trial values for $\dot{V}O_2$, minute ventilation ($\dot{V}_E$), tidal volume, ventilatory equivalent for oxygen ($\dot{V}_E/\dot{V}O_2$), and RER were higher in the 4-km compared with that in both the 20- and 40-km ($P < 0.01$), and RER was higher ($P < 0.01$) in the 20-km compared with that in the 40-km (Table 1). HR was higher in both the 4 and 20 km in comparison with that in the 40 km ($P < 0.01$) (Table 1). Both mean and peak blood lactate were higher in the 4-km (mean, 9.6 ± 1.9 mM; peak, 14.5 ± 2.8 mM) compared with those in both the 20- and 40-km ($P < 0.05$) and higher in the 20-km (mean, 7.8 ± 0.9 mM; peak, 11.5 ± 1.8 mM) compared with those in the 40-km (mean, 5.1 ± 1.3 mM; peak, 8.1 ± 2.2 mM; $P < 0.05$) (Fig. 2). The evolution of RPE across each trial was similar, independent of distance (Fig. 1B), but participants perceived the 4-km to be harder than both the 20- and 40-km, with differences between both the average RPE and the session RPE ($P < 0.05$) (Table 1).

TABLE 1. Performance, cardiorespiratory, and perceptual responses to 4-, 20-, and 40-km cycling TTs.

	4-km	20-km	40-km
Exercise time (min)	5.96 ± 0.20*,**	31.84 ± 1.04**	65.76 ± 2.18
Mean power (W)	340 ± 30*,**	279 ± 22**	255 ± 21
Cadence (rpm)	100 ± 7**	97 ± 3**	92 ± 5
$\dot{V}O_2$ (L·min^{-1})	4.10 ± 0.36*,**	3.92 ± 0.38**	3.70 ± 0.31
$\dot{V}CO_2$ (L·min^{-1})	4.45 ± 0.54*,**	3.79 ± 0.36**	3.41 ± 0.29
RER	1.08 ± 0.06*,**	0.96 ± 0.03**	0.92 ± 0.03
$\dot{V}_E$ (L·min^{-1})	152 ± 25*,**	130 ± 16**	111 ± 16
f_R	55 ± 7**	52 ± 7	48 ± 9
V_T (L)	2.78 ± 0.54*,**	2.56 ± 0.46**	2.34 ± 0.46
$\dot{V}_E/\dot{V}O_2$	36.8 ± 4.1*,**	33.2 ± 2.6**	30.0 ± 2.9
$\dot{V}_E/\dot{V}CO_2$	34.1 ± 3.6	34.4 ± 2.6	32.4 ± 2.7
HR (bpm)	178 ± 14**	177 ± 13**	172 ± 14
RPE (mean)	17 ± 1*,**	15 ± 1	15 ± 1
RPE (peak)	19 ± 1*,**	18 ± 2	18 ± 1
RPE (session)	17 ± 2*,**	16 ± 1	16 ± 1

Values are mean ± SD for the whole trial ($n = 13$).
*Indicates a statistically significant difference from 20 km, $P < 0.05$.
**Indicates a statistically significant difference from 40 km, $P < 0.05$.
$\dot{V}CO_2$, carbon dioxide output; f_R; respiratory frequency; V_T, tidal volume; $\dot{V}_E/\dot{V}O_2$, ventilatory equivalent for oxygen; $\dot{V}_E/\dot{V}CO_2$, ventilatory equivalent for carbon dioxide.

Pre- and Post-exercise Responses

Peripheral responses. Exercise resulted in significant peripheral fatigue in all TTs ($\Delta Q_{tw,pot}$), along with alterations in muscle contractility (Table 2). Conversely, there were no differences in MVC_{RMS} or measures of membrane excitability between the pre- and post-trial (M_{max} amplitude and area) (Table 2). The reduction in MVC was not different between trials (102 ± 85, 84 ± 62, and 84 ± 41 N drop for the 4-, 20-, and 40-km TTs, respectively; $P = 0.56$, $\eta^2 = 0.04$) (Fig. 3A). The drop in $Q_{tw,pot}$ was different between trials ($P = 0.03$, $\eta^2 = 0.25$). There was evidence of greater reduction in

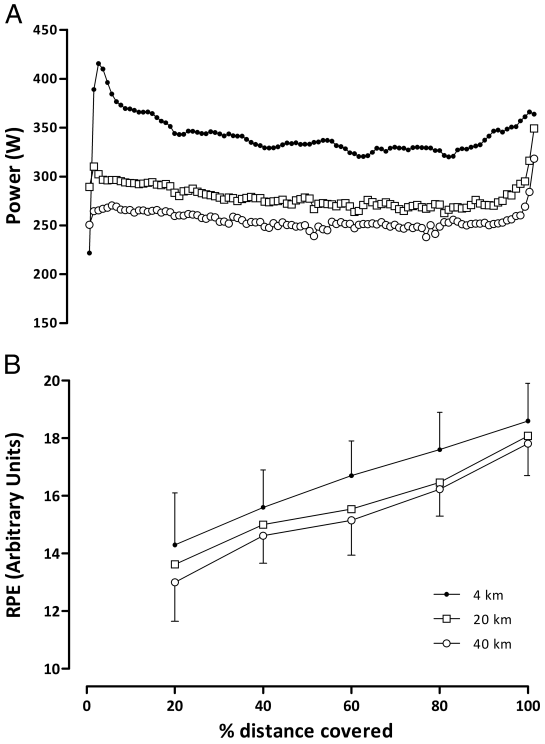

FIGURE 1—Time course of power output (A) and RPE (B) during 4-, 20-, and 40-km cycling TTs expressed relative to the distance covered in each trial. Values for power output are 1% means of the total distance covered. Values for RPE are mean ± SD; error bars are omitted for clarity.

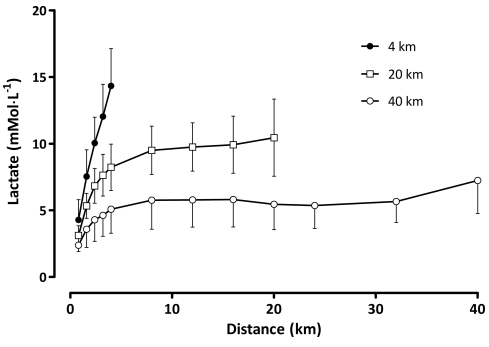

FIGURE 2—Time-course of blood [lactate] (mM) response to 4-, 20-, and 40-km cycling TT (values are mean ± SD). Capillary blood sampling was aligned between trials, such that samples occurred at the same distance covered in each, on the basis of sampling blood at 20% of the distance covered in each trial.

$Q_{tw,pot}$ after the 4-km trial (61 ± 37 N) compared with both the 20-km (46 ± 28 N, $P = 0.03$, $D = 0.46$) and the 40-km trial (44 ± 28 N, $P = 0.049$, $D = 0.52$), with no difference between 20 and 40 km (Fig. 3B). Greater decrements in MRFD of the potentiated twitch were observed after the 4-km trial compared with those observed after both 20- and 40-km trials ($P < 0.05$), whereas MRR, CT, and $RT_{0.5}$ changed similarly, independent of TT length (Table 2). End-trial peak [lactate] was correlated with the reduction in potentiated twitch force for the 4-km trial ($r = -0.76$, $P < 0.01$) but not for 20 ($r = -0.37$, $P = 0.22$) or 40 km ($r = 0.17$, $P = 0.66$).

Central responses. Two participants exhibited small responses to TMS (MEP/M_{max} ratio in VL, <60%). Low MEP/M_{max} ratios are indicative of incomplete activation of the available motoneuron pool by the magnetic stimulus, which could invalidate the measurement of VA (37). These participants were subsequently excluded from analysis of data elicited by TMS (Table 3). VA at baseline was similar for both motor nerve and motor cortical stimulation methods (93% ± 6% vs 93% ± 4%, $P > 0.05$). Exercise resulted in significant reductions in both motor nerve VA (Table 2) and VA_{TMS} (Table 3). The change in motor nerve VA was different between trials ($P = 0.02$, $\eta^2 = 0.37$). Specifically, the drop in motor nerve VA was less after the 4 km (−7%) compared with that in both the 20 (−11%, $P = 0.03$, $D = 0.47$) and the 40 km (Δ10%, $P = 0.02$, $D = 0.59$) (Fig. 3C). The reduction in VA_{TMS} was also different between trials ($P = 0.02$, $\eta^2 = 0.34$) and mirrored the pattern observed for motor nerve VA. The decline in VA_{TMS} was less after the 4 km (−6%) compared with that after both 20 (−12%, $P = 0.01$, $D = 1.00$) and 40 km (−10%, $P = 0.04$, $D = 0.55$) (Fig. 3D). Corticospinal excitability during contraction (MEP expressed relative to M_{max} during MVC) was unchanged after exercise (Table 3). At rest, corticospinal excitability was reduced after the 20 ($P = 0.004$) and 40 km ($P = 0.04$), but not after the 4 km, compared with that at baseline (Table 3), although analysis of the relative and absolute change revealed no significant effect of TT length ($P < 0.05$). The CSP was unchanged in all trials (Table 3).

DISCUSSION

This study assessed the contribution of central and peripheral processes to fatigue after self-paced locomotor exercise of different durations. The main findings demonstrate that the magnitude of peripheral fatigue after high-intensity,

TABLE 2. Neuromuscular function and surface EMG responses to electrical stimulation of the motor nerve at rest and during MVC before and after 4-, 20-, and 40-km cycling TTs.

		4 km	20 km	40 km
Global fatigue				
MVC (N)	Before	548 ± 144	536 ± 143	535 ± 137
	After	445 ± 137*	452 ± 121*	451 ± 120*
	Percent change	18 ± 13	15 ± 10	16 ± 7
Peripheral fatigue				
$Q_{tw,pot}$ (N)	Before	147 ± 34	143 ± 33	145 ± 37
	After	85 ± 25*	97 ± 25*	101 ± 28*
	Percent change	40 ± 20**,***	31 ± 17	29 ± 18
MRFD ($N \cdot ms^{-1}$)	Before	4.40 ± 3.32	4.62 ± 3.07	4.72 ± 1.82
	After	2.22 ± 1.27*	3.06 ± 1.71*	3.67 ± 1.52*
	Percent change	42 ± 22**,***	27 ± 20	22 ± 18
CT (ms)	Before	86 ± 13	89 ± 15	84 ± 12
	After	81 ± 11	78 ± 13*	76 ± 13*
	Percent change	5 ± 13	10 ± 15	9 ± 10
MRR ($N \cdot ms^{-1}$)	Before	−1.47 ± 0.85	−1.96 ± 1.13	−1.67 ± 0.72
	After	−1.15 ± 0.49	−1.60 ± 0.98	−1.59 ± 0.57
	Percent change	10 ± 37	17 ± 29	1 ± 23
$RT_{0.5}$ (ms)	Before	87 ± 26	75 ± 25	82 ± 25
	After	65 ± 22*	61 ± 26*	60 ± 16*
	Percent change	24 ± 21	18 ± 22	23 ± 22
Central fatigue				
Motor nerve VA (%)	Before	92 ± 8	92 ± 8	92 ± 6
	After	85 ± 13*	81 ± 15*	82 ± 15*
	Change	7 ± 7**,***	10 ± 10	11 ± 10
Surface EMG				
Resting responses				
M_{max} amplitude (mV)	Before	4.53 ± 2.63	5.21 ± 1.99	5.67 ± 2.98
	After	4.86 ± 2.36	4.89 ± 1.82	5.17 ± 3.21
M_{max} area ($\mu V \cdot s^{-1}$)	Before	36.2 ± 18.2	40.9 ± 15.7	48.0 ± 19.6
	After	42.0 ± 17.9	36.8 ± 11.3	41.5 ± 22.9
During MVC				
MVC_{RMS} (mV)	Before	0.29 ± 0.13	0.28 ± 0.11	0.34 ± 0.17
	After	0.27 ± 0.15	0.26 ± 0.14	0.32 ± 0.17
M_{max} amplitude (mV)	Before	3.96 ± 2.28	4.56 ± 2.10	4.94 ± 2.01
	After	3.79 ± 2.16	4.24 ± 1.64	4.84 ± 2.37
M_{max} area ($\mu V \cdot s^{-1}$)	Before	25.5 ± 16.0	26.8 ± 10.5	35.6 ± 15.5
	After	27.4 ± 16.9	23.8 ± 8.7	30.3 ± 15.4

Values are mean ± SD, $n = 13$.
*Indicates a statistically significant difference from values before the trial, $P < 0.05$.
**Indicates a statistically significant difference from 20 km, $P < 0.05$.
***Indicates a statistically significant difference from 40 km, $P < 0.05$.
MVC_{RMS}; root mean square of EMG during MVC; $Q_{tw,pot}$, potentiated twitch.

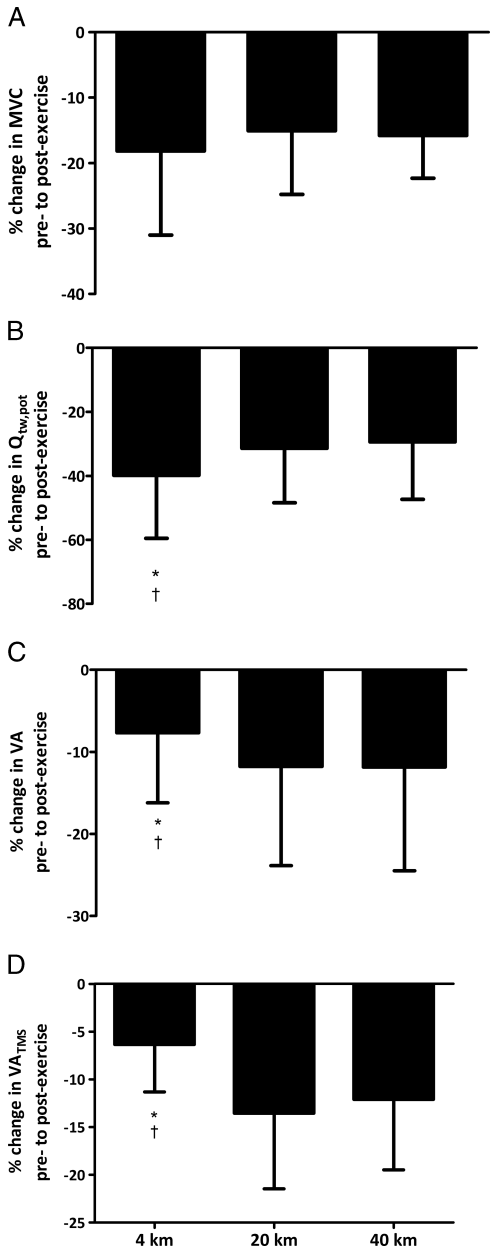

FIGURE 3—Pre- to post-trial percentage change in MVC (A), potentiated twitch (B), VA measured with motor nerve stimulation (C), and VA measured with cortical stimulation (VA_{TMS}) (D) after 4-, 20-, and 40-km cycling TTs. Values are mean + SD. *Different from 20 km, $P < 0.05$; †Different from 40 km, $P < 0.05$.

short-duration (approximately 6 min), self-paced locomotor exercise is greater than that after lower-intensity longer exercise bouts (>30 min), where central fatigue is exacerbated. These data are the first to demonstrate that the contributions of central and peripheral processes to the fatigue observed after self-paced locomotor exercise are dependent on the duration and intensity of the exercise task.

Peripheral fatigue after self-paced cycling exercise. Previous research has demonstrated the existence of an individual critical threshold of peripheral fatigue and associated sensory tolerance limit that is never voluntarily exceeded after high-intensity endurance cycling (3–5). These authors were careful, however, to emphasize that this threshold might be task dependent and have recently demonstrated differences in the sensory tolerance limit between different modes of exercise requiring small versus large muscle mass (35). Some support for the concept of a universal critical threshold has, however, been provided during isolated knee extensor exercise at intensities between 38% and 55% MVC by Burnley et al. (11). On the basis of this work, we hypothesized that such a threshold might exist across self-paced cycling TT of different durations. Self-pacing would theoretically allow participants to modulate power output in response to sensations of fatigue to maximize performance, which would presumably coincide with attainment of the aforementioned critical threshold of peripheral fatigue. However, contrary to our hypothesis, we observed a greater degree of peripheral fatigue after the 4 km (40% reduction in $Q_{tw,pot}$) compared with that observed after both the 20- and 40-km TT (31% and 29% reduction, respectively). The reduction in potentiated twitch force after the 4-km TT was similar in magnitude to that in previous studies that have proposed the existence of a critical threshold of peripheral fatigue after high-intensity locomotor exercise (approximately 35% (3–5)), and it is plausible that this degree of peripheral fatigue represents such a threshold. However, our data indicate that this threshold is not attained after longer-duration, lower-intensity, self-paced exercise.

The most likely explanation for the greater magnitude of peripheral fatigue observed after the 4 km is the higher intensity of this trial. The concept of a critical threshold of peripheral fatigue is currently limited to studies of high-intensity locomotor (2–6) and isolated muscle (11) exercise. During these trials, the high exercise intensity elicited responses consistent with non–steady-state exercise, including high and rising blood lactate response (Fig. 2), attainment of near-maximal values for $\dot{V}O_2$ (Table 1), and, in other work, progressive recruitment of higher threshold motor units (11). The critical intensity (i.e., torque, speed, and power) for a given task demarcates the boundary between sustainable and unsustainable exercise, and exercise above and below this intensity is characterized by distinct physiological responses (11,22). High-intensity exercise is associated with significant disruption to intramuscular homeostasis (22) and a disproportionate increase in the rate of peripheral fatigue development (11). The greater degree of peripheral fatigue observed in the 4 km might reflect the distinct physiological responses observed during high-intensity exercise. In contrast, the elevated but stable blood lactate response in the longer TT indicates that the exercise intensity in these trials was sustainable for the majority of the bout (Fig. 2). During lower-intensity, longer-duration exercise, peripheral fatigue occurs without significant metabolic disturbance (22) and exercise terminates with substantial motor unit reserve (11). The smaller but significant degree of peripheral fatigue observed after the longer TT is probably specific to the lower threshold motor units responsible for the exercise task (27) and likely explained by the lower average intensity of the longer trials.

TABLE 3. Neuromuscular function and surface EMG responses to magnetic stimulation of the motor cortex at rest and during MVC before and after 4-, 20-, and 40-km cycling TTs.

		4 km	20 km	40 km
VA_{TMS} (%)	Before	94 ± 5	93 ± 7	93 ± 7
	After	88 ± 8*	81 ± 11*	83 ± 12*
	Change	6 ± 5**,***	12 ± 6	10 ± 6
ERT (N)	Before	154 ± 46	137 ± 34	142 ± 46
	After	92 ± 41*	93 ± 39*	93 ± 47*
	Percent change	41 ± 20	32 ± 18	36 ± 20
Surface EMG				
Resting responses				
MEP amplitude (mV)	Before	0.32 ± 0.21	0.32 ± 0.25	0.37 ± 0.32
	After	0.24 ± 0.17	0.10 ± 0.09	0.09 ± 0.06
MEP/M_{max} (%)	Before	7.4 ± 5.7	6.2 ± 5.4	6.3 ± 6.8
	After	6.8 ± 6.1	2.8 ± 3.9*	2.1 ± 1.6*
During MVC				
CSP (ms)	Before	165 ± 51	176 ± 57	167 ± 47
	After	175 ± 50	162 ± 49	173 ± 50
MEP amplitude (mV)	Before	1.91 ± 0.91	2.11 ± 1.05	2.86 ± 1.68
	After	2.09 ± 1.02	2.19 ± 0.84	2.75 ± 1.75
MEP area ($\mu V \cdot s^{-1}$)	Before	17.4 ± 7.4	18.7 ± 6.8	24.4 ± 11.8
	After	18.9 ± 6.2	17.4 ± 5.5	21.4 ± 11.1
MEP/M_{max} amplitude (%)	Before	59 ± 16	58 ± 27	55 ± 18
	After	64 ± 16	55 ± 26	57 ± 15
MEP/M_{max} area (%)	Before	79 ± 18	76 ± 24	78 ± 27
	After	84 ± 24	79 ± 32	80 ± 29

Values are mean ± SD, $n = 11$.
*Indicates a statistically significant difference from values before the trial, $P < 0.05$.
**Indicates a statistically significant difference from 20 km, $P < 0.05$.
***Indicates a statistically significant difference from 40 km, $P < 0.05$.
VA_{TMS}, VA measured using TMS.

Why was peripheral fatigue different between trials? The differing degree of peripheral fatigue observed after self-paced locomotor exercise of different durations is therefore likely explained by differences in exercise intensity, and further work is warranted to explicitly test this postulate. However, this proposal does not explain why peripheral fatigue was lower in the longer-duration trials where participants were afforded the ability to self-pace. The pacing strategy adopted was also consistent between trials (Fig. 1A), suggesting no influence of this on the observed differences in fatigue. For longer-duration TTs, our data suggest that factors other than muscle fatigue might play a larger role in limiting performance. Greater demands on temperature regulation, glycogen use, and additional central fatigue occur during submaximal exercise (22), which might have limited the attainment of a greater magnitude of peripheral fatigue after the longer TTs. Alternatively, the longer duration of the trials might have negatively affected motivation, and the observed difference in peripheral fatigue could reflect a psychological rather than a physiological limit to performance. Both mean and peak RPE were higher in the 4 km compared with those in the 20 and 40 km (Table 1 and Fig. 1B). In the present study, the RPE scale was used as originally defined to measure the total physical and psychological strain of the exercise (10). In this respect, the RPE does not distinguish between the perception of effort, defined as the conscious awareness of the central motor command to the active muscles (29) and the perception of exertion or sensation of fatigue that arises because of afferent feedback from the working muscle (43). Consequently, it is unknown whether the higher RPE in the 4 km reflects higher perception of effort (because of greater power output) or higher perception of exertion (because of stronger afferent signal). Both concepts are limiting factors to self-paced exercise performance (1,26) but will be balanced against the desire to perform, knowledge of the endpoint, and previous experience of similar exertion (24). The shorter duration of the 4-km trial, where the endpoint of exercise is within reach for much of the bout, might permit higher sensory tolerance limit than could be reached during longer-duration trials. In contrast, the substantial degree of both central and peripheral fatigue in the latter stages of the longer TTs might act collectively to negatively affect motivation, and the effort required to sustain a higher power output might have been perceived as unattainable (25).

Greater central fatigue after longer TTs. While the degree of peripheral fatigue was lower after longer TTs, central fatigue (defined as a reduction in the VA of muscle) was exacerbated. This pattern supports previous research in both single-limb and locomotor exercise models that has demonstrated a duration-dependent contribution of central fatigue to reductions in the voluntary force-producing capability of the skeletal muscle (11,23,31). For single-limb exercise, Burnley et al. (11) demonstrated that central fatigue decreased as exercise intensities increased above critical torque in the knee extensors. The present study is the first to explicitly compare different durations of locomotor exercise, but the available literature also suggests a duration-dependent contribution of central processes to fatigue, at least for constant-load exercise. For example, reductions in VA have been observed after 4 h of cycling (23) and 5 h of running (31) at 55% of aerobic maximum. For higher-intensity constant-load cycling, significant central fatigue has been observed after 30–40 min of repeated 5-min intervals at 80% of aerobic maximum (38) that only manifests after 80% of the exercise bout is

completed (13). For a continuous bout of constant-load cycling to exhaustion at a similar intensity, reductions in VA have been observed after only 8 min of exercise (18). Collectively, the current data and the available literature suggest that central fatigue is exacerbated in a duration-dependent manner but the intensity of exercise also seems to be of influence. This is further supported by the present data, as central fatigue was similar in the 20 km compared with that in the 40 km despite the longer duration of the 40 km. Further work that explicitly compares different durations of exercise, both self-paced and constant-load exercise, is warranted to better understand the contribution of central and peripheral processes to the fatigue induced by locomotor exercise.

The reduction in VA measured using TMS followed a similar pattern to that measured using stimulation of the motor nerve, with greater reductions after the 20 and 40 km compared with that after the 4 km. This reduction implicates a potential contribution of supraspinal processes to fatigue or suboptimal output from motor cortical cells (17). The resting excitability of the corticospinal pathway was also significantly depressed after the 20 and 40 km, with no apparent depression after the 4 km (Table 3). Whether this depression could have contributed to the observed central fatigue is not clear, particularly considering that corticospinal excitability was unchanged when measured during contraction (Table 3), a finding that has previously been reported after prolonged constant-load locomotor exercise (38). In addition, without a concomitant measure of motoneuron excitability (i.e., via stimulation at the cervicomedullary junction), it is not possible to distinguish between changes in cortical versus motoneuron excitability. Further work is warranted to better understand the functional consequences of fatigue-induced changes at all levels of the motor pathway.

The measurement of fatigue after exercise in this study was completed within 2.5 min of exercise cessation. Considering that significant recovery of muscle function can occur 2 min after exercise (16), it is likely that the magnitude of central and peripheral fatigue was underestimated. This limitation is common in the majority of literature studying fatigue incurred by locomotor exercise modes and assumes that the fatigue observed after exercise is also present during the bout. This notwithstanding, the time taken to assess fatigue was consistent between trials; significant central and peripheral fatigue was observed after all TTs, and the magnitude of central and peripheral fatigue was influenced by TT length. These observations suggest that the methods used were suitable to detect differences in the central and peripheral contributions to fatigue after TT exercise of different durations. The time delay might also have masked changes in processes relating to fatigue that could recover quickly on exercise cessation. For example, membrane excitability in the VL was unchanged after the trial in this study but has recently been shown to be depressed during, but not after, a 30-min bout of locomotor exercise (39). In addition, the CSP has consistently been shown to lengthen during sustained isolated muscle exercise, including knee extensor contractions (21), but recovery on exercise cessation is rapid (12,45,46). The lack of difference observed in these variables after exercise, which have been reported in other similar studies (18,38), could be due to the time delay between the end of exercise and the assessment of neuromuscular function. Assessing the development of central and peripheral fatigue during exercise is an area warranting further research (40).

In conclusion, the contribution of central and peripheral processes to fatigue after self-paced TT cycling exercise is task dependent, with a greater degree of peripheral fatigue evident after shorter high-intensity (approximately 6 min) TTs and increased contribution of central fatigue after longer lower-intensity TTs (>30 min). These findings suggest an intensity- and duration-dependent influence on the neuromuscular underpinning to fatigue after self-paced exercise, and further research that explicitly compares the central and peripheral contributions to fatigue after locomotor exercise tasks of different demands is warranted.

All experiments were performed within the Sport Central Laboratory facilities at Northumbria University. K. T. and S. G. contributed to the conception and design of the experiments, data collection, data analysis, data interpretation, manuscript drafting, and editorial process. M. S. contributed to the conception and design of the experiments, data collection, and manuscript drafting. G. H., A. S. G., and L. A. contributed to the conception and design of the experiments, data interpretation, and manuscript drafting. All authors approved the final version of the manuscript.

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