Central Fatigue after Cycling Evaluated Using Peripheral Magnetic Stimulation

IAN J. KREMENIC[1], BETH W. GLACE[1], S. SIMON BEN-AVI[2], STEPHEN J. NICHOLAS[1], and MALACHY P. MCHUGH[1]

[1]*Nicholas Institute of Sports Medicine and Athletic Trauma, Lenox Hill Hospital, New York, NY; and* [2]*The Cooper Union for the Advancement of Science and Art Albert Nerken School of Engineering, New York, NY*

ABSTRACT

KREMENIC, I. J., B. W. GLACE, S. S. BEN-AVI, S. J. NICHOLAS, and M. P. MCHUGH. Central Fatigue after Cycling Evaluated Using Peripheral Magnetic Stimulation. *Med. Sci. Sports Exerc.*, Vol. 41, No. 7, pp. 1461–1466, 2009. Central and peripheral mechanisms contribute to fatigue during exercise. Electrical and transcranial magnetic stimulation have been used to assess these fatigue mechanisms. Peripheral magnetic stimulation (PMS) of the femoral nerve is associated with very little subject discomfort and has been shown to elicit quadriceps contractions of >70% maximal voluntary contraction (MVC). **Purpose**: To examine peripheral versus central mechanisms of fatigue in men during prolonged cycling using a peripheral nerve magnetic stimulation-based technique. **Methods**: Eleven men (aged 41 ± 3 yr) cycled for 2 h at approximately 66% of $\dot{V}O_{2peak}$ (55 ± 2 $mL \cdot kg^{-1} \cdot min^{-1}$) with five 1-min sprints interspersed, followed by a 3-km time trial. Oxygen consumption was measured every 20 min to verify a constant workload. RPE were measured simultaneously and during each sprint using a Borg scale. Quadriceps isometric strength testing was performed in a seated position before and after cycling: 1) MVC, 2) MVC with superimposed magnetic stimulation to measure central activation ratio (CAR), 3) femoral nerve stimulation alone. One-minute recoveries were allowed between contractions. Changes in metabolic measurements over time were analyzed with repeated-measures ANOVA, and strength changes before to after with Student's paired *t*-tests. **Results**: HR ($P = 0.03$) and RPE ($P < 0.001$) increased over time during the 2 h, and MVC declined by 22% ($P = 0.001$) indicating fatigue. Force elicited by PMS alone decreased 17% ($P < 0.001$). CAR decreased from 83% before exercise to 71% ($P = 0.005$) after exercise indicating a loss of central drive. PMS-induced force was ≥90% of MVC. **Conclusions**: Results clearly demonstrate that trained cyclists experience significant central fatigue during prolonged cycling. PMS may be a better technique for identifying central fatigue than the traditionally used interpolated twitch technique. **Key Words:** ENDURANCE, EXERCISE, MUSCLE, CENTRAL ACTIVATION

BASIC SCIENCES

Fatigue can be defined as any exercise-induced loss of ability to produce force and power. Many factors contribute to the fatigue process during exercise, including fiber-type composition, the intensity of exercise, and the type and duration of the contraction. Both central and peripheral mechanisms contribute to fatigue. Central fatigue represents the failure of the nervous system to drive the muscle or a reduction in voluntary activation (VA) or neural drive to the muscle. Peripheral fatigue is a loss of force-generating capacity of the muscle itself (25).

Both magnetic and electrical stimulations have been used to assess fatigue (13,29). Transcranial magnetic stimulation (TMS) has been used to evaluate central fatigue during short-duration, high-intensity exercise (see Taylor and Gandevia [28] for review); more recently, Ross et al. (24) used TMS and peripheral magnetic stimulation (PMS) to evaluate central fatigue in the tibialis anterior after a marathon. However, TMS is not FDA-approved for use in the United States. Similarly, electrical stimulation has been used to examine central fatigue during prolonged exercise (13). Subject discomfort often limits the use of electrical stimulation, and maximal contractions may be difficult to induce. Previously, we have used PMS of the femoral nerve to elicit quadriceps contractions of more than 70% of maximal voluntary contraction (MVC); because this was well tolerated by subjects, the limiting factor in force generation was not subject discomfort but the power available to the device (10).

The purposes of this study were 1) to examine mechanisms of fatigue (central vs peripheral) in men during prolonged submaximal, concentric exercise, of the type commonly experienced by endurance cyclists and 2) to explore the novel use of a PMS-based technique. Elucidating the source of fatigue during exercise may allow development of interventions meant to delay fatigue and thereby improve performance. We hypothesized that there would be a significant central component to fatigue after prolonged submaximal cycling.

METHODS

Eleven healthy, New York metropolitan area, male cyclists or triathletes who had been cycling at least 100

Address for correspondence: Ian J. Kremenic, M.Eng., Nicholas Institute of Sports Medicine and Athletic Trauma, Lenox Hill Hospital, 130 E 77th St, 10th Floor New York, NY 10075; E-mail: ian@nismat.org.
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miles·wk^{-1} during the previous 3 months, reported to the physiology laboratory on two separate days, no less than 3 d apart and no more than 2 wk apart. Each subject served as his own control. Before testing, subjects gave written informed consent to participate in the protocol, which had been approved by the Institutional Review Board of Lenox Hill Hospital. Subjects were instructed to eat before the testing as they normally do before racing. On the first day, subjects underwent a maximal exercise test to volitional exhaustion on a cycle ergometer. EKGs and oxygen consumption were measured throughout the testing using the Sensor Medics Vmax system (Sensor Medics, Yorba Linda, CA). Data were collected using the breath-by-breath mode, and values were reported as means per minute. Before each test, the flowmeter was calibrated using a 3-L volumetric syringe and the gas analyzer was calibrated using standardized gases. The protocol was performed on a Monark 834 Ergomedic cycle ergometer (Monark Exercise AB, Vansbro, Sweden) using an incremental protocol. Pedal frequency was maintained at 90 rpm, and work was increased by 30 W·min^{-1}. Maximal oxygen consumption and anaerobic threshold were determined from the data.

The ventilatory threshold [V_T] was determined through visual inspection of the graphs of the ventilatory equivalents for oxygen and for carbon dioxide according to the method of Caiozzo et al. (4). Respiratory gas measures are plotted graphically, and the V_T is determined by identifying the interval before the increase in the ventilatory equivalent for oxygen [ventilation/$\dot{V}O_2$], without an increase in the ventilatory equivalent for carbon dioxide [ventilation/CO_2]. Caiozzo et al. (4) have found that this method agrees well with venous lactate estimates of the anaerobic threshold.

On the second day of testing, subjects' body mass was determined after voiding. Subjects were allowed a brief (5–10 min) bike warm-up at self-selected low resistance. A timeline of the test protocol is shown in Figure 1. Subjects' isometric quadriceps strength was assessed while seated in a chair in a slightly reclined position (approximately 30° hip extension to facilitate magnetic stimulation), with the knee flexed 60°. Subjects were secured to the chair using crossover shoulder straps and a belt across the abdomen. The ankle was attached to a chain that was attached to a force transducer (Kistler, Inc., Amherst, NY). Subjects then performed quadriceps strength testing, consisting of two 5-s MVC (primarily as a warm-up and for familiarization), two 5-s MVC with superimposed PMS pulse trains, and two contractions using PMS pulse trains alone. Subjects performed all voluntary contractions with their arms folded across their chests while receiving strong verbal encouragement. All magnetic stimulation pulse trains were at a frequency of 40 Hz, using a MagStim Rapid Stimulator (MagStim, Corp, Wales, United Kingdom) with eight booster units and a double-circular 90-mm (inside diameter) coil. The intensity of the stimulus was set at 100% of the output of the unit. Before administration of the pulse trains, optimal location for the stimulating coil over the femoral nerve was determined by identifying the position giving the greatest twitch response to stimulation with single pulses. Central activation ratio (CAR) was measured using the contractions with PMS superimposed to differentiate central from peripheral sources of fatigue. CAR was defined as the ratio of maximal voluntary force produced to that produced by maximum volitional effort with PMS superimposed (Fig. 2). For the superimposed stimuli, a 3-s stimulus at 100% of the power output of the stimulator was superimposed on a 5-s voluntary MVC, approximately 2 s into the contraction. For PMS alone, the magnetic stimulator ramped in intensity from 50% to 100% for 1 s followed by 3 s of 100% intensity stimulation. Force was recorded continuously at 1000 Hz into a computer using AcqKnowledge 3.2 (Biopac, Santa Barbara, CA).

Subjects cycled for 2 h at their previously determined V_T (approximately 65%–70% of maximal oxygen consumption). They pedaled on their own bicycles, which were set up on a cycle trainer (Kurt Kinetic Road Machine; Kurt Kinetic, Jordan, MN). Respiratory gas measurements were made periodically for 5 min, every 20 min of cycling. Workload was adjusted to maintain oxygen consumption. The Borg scale was used to assess RPE at each measurement period (2). Immediately after the gas measurements, the cyclists sprinted for 1 min, after which measurements of RPE for the sprint were obtained. HR was determined using a Polar Heart Rate Monitor (Polar CIC, Port Washington, NY). Water was provided at a rate of 1% of body weight each hour.

After cycling for 2 h, they performed a 3-km time trial. Subjects were allowed to perform a 5-min cool-down on

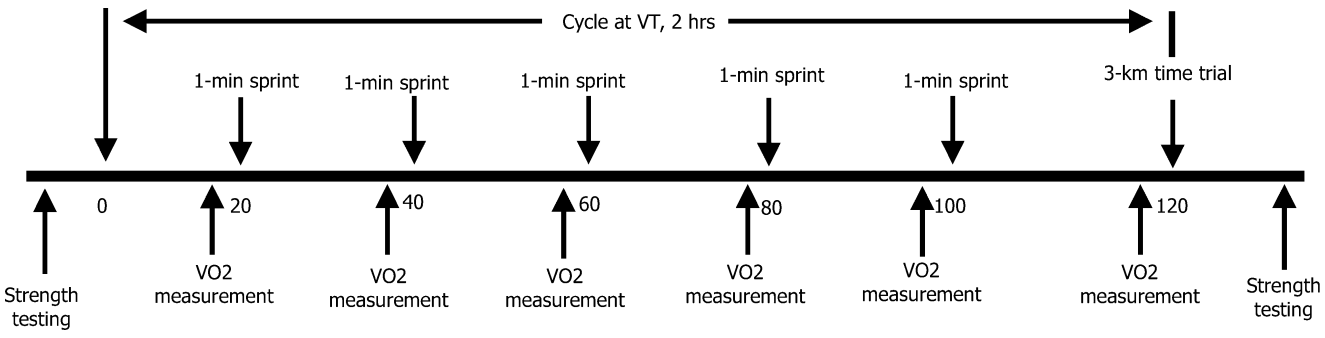

FIGURE 1—Timeline of the experimental protocol.

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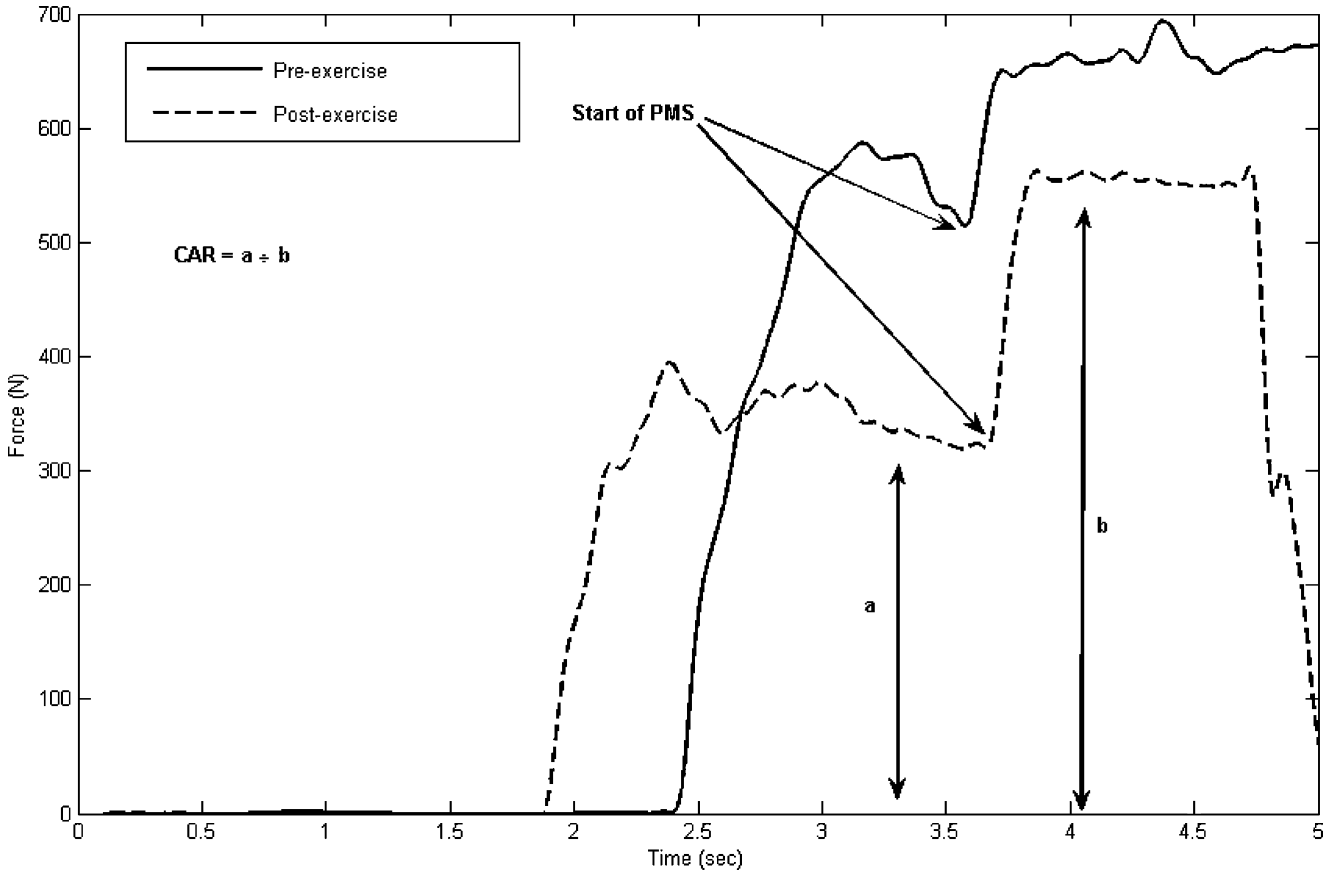

FIGURE 2—Representative strength data. *Solid line* indicates maximal isometric force before fatiguing exercise. *Dashed line* indicates maximal isometric force after fatiguing exercise. *Arrows* indicate start of PMS imposed on voluntary contraction. CAR computed from ratio of voluntary contraction force (a) to force from contraction augmented with PMS (b).

the bike at self-selected low resistance. Within 10 min of finishing the time trial, strength testing with magnetic stimulation was repeated as described above.

Changes in metabolic parameters were analyzed with repeated-measures ANOVA. Voluntary (VOL) and stimulated (PMS) strength, voluntary contraction with superimposed magnetic stimulation (VOL + AUG), augmentation from superimposed magnetic stimulation (AUG), and CAR were compared within subjects using paired *t*-tests. Previous testing of PMS of the quadriceps in our laboratory (10) has shown that we can detect a force decrement of 19% with 80% power using 12 subjects with PMS of the femoral nerve. Fatigue has been shown to produce force decrements of 23.5% using similar techniques to those described above with endurance athletes (18). *Post hoc* power testing of the strength testing data (voluntary and elicited contractions) demonstrated 85% power to detect a significant difference at $P < 0.05$ with 11 subjects.

RESULTS

Subjects' descriptions are listed in Table 1. The subjects ranged from well-trained triathletes to Category 2 competitive cyclists, with a mean age of 41 yr. Their mean peak oxygen consumption ($\dot{V}O_{2peak}$) of 55.7 mL·kg^{-1}·min^{-1} was typical of well-trained recreational cyclists, and their V_T occurred at 65% of their $\dot{V}O_{2peak}$.

Water was provided throughout exercise. Although there was a significant decline in body mass during cycling ($P = 0.003$), it represented only 0.65 kg or 0.9% of initial mass. Oxygen consumption did not change during the prolonged cycling bout (effect of time, $P = 0.22$). However, during the 2-h period, RER declined from 0.93 to 0.85 (effect of time, $P < 0.001$). RPE while pedaling at their own V_T increased during the 2-h period, from a mean of 11.4 at 20 min to 12.9 at 2 h ($P = 0.001$). RPE during the five 1-min sprints remained unchanged over time, ranging from 16.5 to 17.3 (effect of time, $P = 0.3$). HR increased over time, from a mean of 128 bpm at 20 min to 138 bpm at 2 h ($P = 0.3$).

Strength data (VOL, PMS, VOL + AUG, AUG, CAR) are shown in Table 2. After the cycling exercise, subjects showed a 22% loss in strength ($P = 0.001$). Absolute force elicited by PMS alone also showed a decrease (17%, $P < 0.001$). PMS alone elicited 89.6 ± 9.6% MVC

TABLE 1. Subjects' descriptions.

Body Mass (kg)	Height (cm)	Age (yr)	$\dot{V}O_{2peak}$ (mL·kg^{-1}·min^{-1})	V_T (% $\dot{V}O_{2peak}$)
76.0 ± 2.3	180.3 ± 2.3	41.0 ± 3.0	55.7 ± 1.7	65.1 ± 0.8

Results are reported as mean ± SE.

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TABLE 2. Results of precycling and postcycling strength testing.

	Precycling	Postcycling	P
VOL (N)	536.7 ± 19.7	419.6 ± 34.0	0.001*
PMS (N)	475.2 ± 44.8	392.3 ± 36.0	<0.001*
VOL + AUG (N)	651.9 ± 16.2	595.6 ± 28.6	0.060
AUG (N)	115.2 ± 26.6	176.0 ± 38.7	0.035*
CAR	0.83 ± 0.04	0.71 ± 0.05	0.005*

Results are reported as mean ± SE.
* Statistically significant, $P < 0.05$.

before exercise and 104.4 ± 18.0% MVC after exercise ($P = 0.184$); alternately, expressed as a percentage of VOL + AUG, PMS elicited contractions of 72 ± 6% before exercise and 66 ± 5% after exercise ($P = 0.164$). Voluntary strength augmented with PMS tended to decrease by 8% (VOL + AUG, $P = 0.06$) before to after exercise. The force augmentation with PMS increased after fatigue (AUG, $P = 0.035$); CAR decreased 15% after the cycling protocol ($P = 0.005$).

DISCUSSION

The objective of this study was to characterize neuromuscular fatigue in knee extensor muscles after prolonged cycling exercise which mimicked racing demands using a novel PMS-based method. We found that our cycling protocol induced fatigue (22% decrease in VOL) and that this fatigue had both peripheral (17% decrease in PMS, nonsignificant 8% decrease in VOL + AUG) and central (15% decrease in CAR) components, in accordance with our hypothesis (representative data for one subject are shown in Fig. 2). Central fatigue has been well demonstrated in endurance running (16,18,19). Some (1,13,20) but not all (17) studies of cycling have shown evidence for central fatigue, but generally, these studies have used longer duration or more intense exercise protocols than the one presented here. This is the first study to our knowledge that has used PMS for this application (for cycling or any other activity).

Most protocols designed to investigate the effect of exercise on fatigue during cycling have been performed at a constant workload (12,21). In this study, we used a protocol meant to more closely mimic the fatigue developed in "real-world" racing situations, where multiple sprints are interspersed with sustained, steady-state cycling, and where a maximal effort is exerted during the final stages of the ride. This protocol is similar to those used by others (e.g., Cureton et al. [5]) to induce fatigue.

Studies that have evaluated fatigue using TMS have largely been limited to muscles of the upper extremity (e.g., [3,7,26,27,29]). Although some works have examined fatigue in the lower extremity using TMS (8,11,23), these studies have usually been limited to examining electrical manifestations of fatigue via magnetic evoked potentials (MEP). The work of Ross et al. (24) is the only example of which we are currently aware which has used TMS to examine lower extremity fatigue after endurance exercise using force measurements of VA. This is because of the relative ease of activating the arm and hand musculature via cortical stimulation, as the regions of the cortex controlling these are superficial. TMS of the lower extremity is a much more difficult task because the portion of the motor cortex controlling the lower extremity is much deeper in the brain. Thus, we used PMS to elicit contraction of large muscle groups in the lower extremity.

Effects on metabolic parameters. We controlled $\dot{V}O_2$ during the 2-h period to maintain energy expenditure at the V_T. Despite this control, HR increased over time. This "cardiac drift" may be attributable to the slight (0.8%) loss in body mass and due to cumulative thermoregulatory stresses (31). The subjects did rate their effort as greater as cycling progressed, as would be expected with fatigue.

Strength loss and central fatigue. We noted a 22% decrease in voluntary strength after prolonged exercise, consistent with the reports of others (6,12,13,16–18,20,21). Using PMS, we were able to demonstrate significant central and peripheral components to this strength loss. Force elicited by PMS alone decreased by 17%. This is largely an indicator of peripheral fatigue, as stimulation alone bypasses the central drive from the motor cortex. This decrease may also reflect changes in the motor threshold of the femoral nerve (30). The 13% decrease in CAR from 0.84 to 0.73 is largely indicative of central fatigue. Whereas a significant component of central fatigue in knee extensors has been found after an ultramarathon race (16,18), Millet et al. (17) did not detect central fatigue after a cycling race using electrical twitch interpolation. Our results using PMS demonstrate significant peripheral and central components of fatigue after prolonged cycling that simulated racing conditions.

We feel that this PMS-based technique is superior for evaluating fatigue and CAR for several reasons. Many authors (12,13,16) investigate fatigue using a single- or double-twitch interpolation technique. Although this has long been used (originally proposed by Merton [14]), this technique often leads to data with large variability (13). Miller et al. (15) found stimulus trains better able than single pulses in augmenting voluntary contractions of the quadriceps and recommended their use in determining central activation failure. Some (1,14,18,20,21) have used trains of stimuli superimposed on voluntary contractions. Although we agree that this approach will likely lead to greater augmentation, electrical stimulation at this intensity is often painful to subjects, with this pain being the limiting factor of the intensity/frequency of stimulation. PMS is much better tolerated than electrical stimulation (10,12), which should allow for greater intensity/frequency of stimulation and less variable data as the stimulus is more likely to be supramaximal. In fact, Ross et al. (24) used PMS of the peroneal nerve to achieve supramaximal stimulation of the tibialis anterior (as documented by MEP recruitment curves) before and after a treadmill marathon. Polkey et al. (22) also demonstrated supramaximal activation

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of the quadriceps via PMS of the femoral nerve. We were able to induce contractions of greater than 90% MVC in the prefatigued state and greater than MVC after fatigue; expressed as a percentage of VOL + AUG rather than MVC (as subjects demonstrated incomplete activation), PMS was able to induce contractions of 72% before fatigue and 66% after fatigue. All of these exceed the recommendation of at least 65% MVC proposed by Kent-Braun (9).

The initial CAR of 0.84 indicates that these cyclists did not maximally activate their knee extensor muscles before fatigue. Similar results have been reported elsewhere (16,24) in endurance runners. This is perhaps not surprising given the unfamiliar nature of the task (maximal isometric contraction) and unusual posture (slightly reclined in hip extension) for subjects whose usual training modality is endurance cycling, which by nature is very submaximal and is performed in an upright posture with the hip flexed.

This PMS-based technique lends itself to exploration of many different facets of fatigue. For example, women have been shown to be more resistant to fatigue than men (6,9), although the mechanisms responsible for this difference are unclear. Magnetic stimulation of superficial nerves may be a useful technique to clarify if this difference is of peripheral or central origin. Magnetic stimulation may also be used to explore the mechanism of known ergogenic aids such as caffeine and carbohydrates. For example, Kalmar and Cafarelli (7,8) have used TMS to demonstrate that caffeine increases central excitability. PMS, however, is not without limitations. Its usefulness depends on the accessibility of a superficial nerve, and better contractions may be induced in lean subjects than in those with a significant amount of subcutaneous fat. The cost of the equipment is also substantially greater than the traditionally used electrical stimulation units. On the basis of measurements of magnetically elicited force as a percentage of VOL + AUG (72% and 66% before and after exercise, respectively), our technique did not provide supramaximal stimulation, so quantification of peripheral fatigue may be limited. In addition, our protocol was limited in that neither did we provide exogenous carbohydrate nor did we measure blood glucose levels. Nybo (20) demonstrated centrally mediated fatigue after 3 h of cycling with no carbohydrate supplementation. Although this could have contributed to the fatigue our subjects experienced, none reported any symptoms associated with low blood sugar (e.g., shakiness, dizziness, confusion, difficulty speaking). We plan to investigate the effect of carbohydrate supplementation in future studies.

In conclusion, these results clearly demonstrate that trained male cyclists experience significant central fatigue during prolonged cycling. PMS may be a better technique for identifying central fatigue than the traditionally used interpolated twitch technique. Used in combination with TMS, PMS can be used to pinpoint the locus of fatigue. Further work in this area should explore this technique to examine differences in fatigue between men and women and to examine central versus peripheral effects of ergogenic aids.

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