Failed Excitability of Spinal Motoneurons Induced by Prolonged Running Exercise

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1Motor Efficiency and Deficiency Laboratory, Equipe d’Accueil 2991, Unité de Formation et de Recherche des Sciences et Techniques des Activités Physiques et Sportives and 2Institut National de la Santé et de la Recherche Médicale, Administration Déleguée Régionale 08, Montpellier, France

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Racinais S, Girard O, Micallef JP, Perrey S. Failed excitability of spinal motoneurons induced by prolonged running exercise. J Neurophysiol 97: 596–603, 2007. First published November 8, 2006; doi:10.1152/jn.00903.2006. The main purpose of this study was to investigate the modulations in H-reflex and V-wave responses (spinal loop properties) induced by prolonged locomotion activities. The second purpose was to compare the development of central fatigue between continuous and intermittent running modes. Eleven males randomly performed two 90-min running exercises either continuously (CONT, first ventilatory threshold) or intermittently (INT, 150 s at a velocity 20% higher than that during CONT/30 s of recovery). Neuromuscular tests of the plantar flexors [including M-wave and H-reflex at rest and M-wave and V-wave during maximal voluntary contraction (MVC)] were performed before and 5 and 30 min after the running exercises. During MVC, the torque significantly decreased (P < 0.05) from preexercise to 5 and 30 min postexercise (−11 and −9%, respectively), as did the RMS/M ratio (−11 and −13%, respectively) and the V/M ratio (−19 and −37%, respectively) for the soleus muscle. At rest, the H/M ratio also decreased significantly (P < 0.001) from preexercise to 5 and 30 min postexercise (−61 and −55%, respectively). Last, no difference in the alteration of spinal loop properties was noted between CONT and INT. In conclusion, the results regarding H-reflex and V-wave suggest for the first time a modulation in spinal loop properties after prolonged running.

INTRODUCTION

Central fatigue induced by exercise is manifested by a decline in muscle activation and this is usually assessed with the twitch interpolation technique (i.e., Gandevia et al. 1996; Lloyd et al. 1991). Electrical stimulation of the motor axon to supramaximal intensity reveals the components of fatigue distally (i.e., neuromuscular junction, sarcolemmal excitability, contractile properties) and proximally (i.e., motivation, physiological capacity of the motor cortex to adequately drive the muscle, descending pathway, spinal synapses, motoneuron pool excitability) to the stimulation point (termed “peripheral” and “central,” respectively). However, this technique cannot determine whether an impairment in central drive occurs at the spinal and/or the supraspinal level (for a review see Gandevia 2001).

At a spinal level, central drive impairment may be partly linked to a depression in the excitability of the α-motoneuron pool (Garland and McComas 1990). A common tool used to evaluate this modulation of the spinal loop is the Hoffmann reflex (H-reflex) recording. Recently, V-wave amplitude was also used to estimate the adaptations of the spinal loop properties during a muscular contraction after training (Aagaard et al. 2002), although this tool has never been used to investigate exercise-induced fatigue. Previous reports showed a decline in H-reflex amplitude after an isometric contraction maintained until exhaustion (Duchateau and Hainaut 1993; Duchateau et al. 2002; Kuchinad et al. 2004), suggesting the occurrence of neural adaptations induced by fatiguing exercise. Furthermore, using transcranial magnetic stimulation, Andersen et al. (2003) observed that a large proportion of the spinal motoneuron pool becomes inaccessible to descending drives when the force-generating capability of a muscle group is depressed. Although these investigations focused on isometric contractions maintained until exhaustion, far less is known about the changes in spinal loop properties after a common task like human locomotion.

To date, only two studies have reported a decrease in H-reflex amplitude after submaximal running exercise (Bulbulian and Bowles 1992; Bulbulian and Darabos 1986). However, these experiments were conducted with short-duration exercises (i.e., 20 min) and a restricted number of subjects (i.e., six subjects). In addition, these studies investigated H-reflex amplitudes at rest only, although there is no evidence that data recording on a relaxed muscle is transferable to an exercising muscle. These limits prevented the authors from drawing any conclusions about fatigue-induced adaptations at both spinal and supraspinal levels after a prolonged (i.e., >30 min) locomotion task.

Increasing evidence suggests that the development of central fatigue as exercise progresses may vary according to the continuous/intermittent nature of the exercise task. From this perspective, Nybo and Nielsen (2001) observed that voluntary activation during repeated intermittent contractions of a few seconds was not impaired by an exhaustive exercise, whereas muscle activation failed when the voluntary contraction was continuously prolonged for about 10 s or so. This suggests that the capacity of the CNS to maximally activate the muscle may be altered only in cases of continuous exercise mode. Bilodeau (2006) recently confirmed this hypothesis by showing an earlier and larger central activation deficit during a continuous elbow extension task than during the same task performed intermittently.

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Therefore the main purpose of this study was to use H-reflex (at rest) and V-wave (during contraction) responses to examine whether prolonged (90 min) running would induce a modulation in spinal loop properties. We hypothesized that central fatigue would be linked to an alteration in spinal loop properties, as evidenced by a decrease in evoked reflex waves.

A secondary hypothesis was that resting periods during the submaximal running exercise (intermittent mode) would minimize the occurrence of central fatigue compared with continuous running mode. Last, handgrip contractions were performed to examine the effect of fatigue on an inactive muscle group (Nybo and Nielsen 2001) during the prolonged running exercises. The rationale for the different protocols was to elucidate which component (spinal vs. supraspinal) of neuromuscular activation is affected by fatigue during a common locomotion task.

METHODS

Subjects

Eleven healthy males (age range, 19 to 30 yr; mean age, 23 yr) gave informed written consent to participate in this study. The procedures complied with the Declaration of Helsinki regarding human experimentation and were approved by the local Ethics Committee. None of the subjects suffered from muscle soreness or ankle injuries. Subjects were asked to refrain from caffeine intake for the 8 h preceding the test and to avoid all vigorous activity for the 24 h preceding the test.

Experimental procedures

The subjects visited our laboratory on three occasions, with at least 7 days between visits. After an initial familiarization session, they participated in two experimental sessions of continuous (CONT) or intermittent (INT) running exercise.

FAMILIARIZATION SESSION. The subjects were first introduced to and familiarized with the experimental procedure. They performed maximal voluntary contractions (MVCs) of the plantar flexors until they felt accustomed to the equipment; the coefficient of variation in three successive trials was <5%. This session was also used to accustom the subjects to the electrical stimulation of the tibial nerve. After a 15-min resting period, during which they were allowed to drink without restriction, the subjects were then asked to perform an incremental test on a motorized treadmill (S2500, HEF Techmachine, Andrézieux–Bouthéon, France). During the run, expired gases were collected breath by breath (ZAN 680, ZAN Messgerate, Oberthulba, France). During the run, expired gases were collected breath by breath (ZAN 680, ZAN Messgerate, Oberthulba, Germany). The test consisted of an initial 3-min workload of 8 km·h⁻¹ followed by increases of 0.5 km·h⁻¹ every minute (0% incline). This procedure determines the intensity at which a nonlinear increase in pulmonary ventilation occurs (first ventilatory threshold). Specifically, the ventilatory threshold was determined using the criteria of an increase in VE/VO₂ with no increase in VE/VCO₂ and the departure from linearity of VE (Davis 1985).

CONT AND INT TEST SESSIONS. The CONT and INT sessions each lasted for 210 min and were conducted as follows: preparation of the subject’s leg (i.e., electrode placement), neuromuscular pretests (see following text), preparation of the subject for running (i.e., placement of the mask for expired gas collection, fixation of the EMG cable with strap and muff net to prevent movement artifacts during running), 90 min of running exercise (either continuous or intermittent in randomized order), and neuromuscular posttests performed 5 and 30 min after the end of the fatiguing exercise bout. The subjects were allowed to drink throughout the experimental session.

RUNNING EXERCISES. The CONT exercise consisted of 90 min of running on the same treadmill as in the first session at a constant velocity corresponding to the first ventilatory threshold determined during the first session. The INT exercise consisted of 90 min of running with a 30-s passive recovery period every 150 s of running. The running velocity imposed for intermittent running was 20% higher than that for CONT running to ensure that subjects covered exactly the same distance in the two sessions. During these sessions, heart rate (HR; Polar S610, Electro OY, Kempele, Finland), oxygen consumption (VO₂; ZAN 680, ZAN Messgerate), and EMG activity of the soleus (SOL) (see electromyography) were recorded continuously and averaged over eight periods of 30 s every 12 min (i.e., after 1, 13, 25, 37, 49, 61, 73, and 85 min of running). At the same time intervals, dominant handgrip force was measured using a handgrip dynamometer (Captels, St Mathieu de Treviers, France). Subjects were instructed to perform a maximal isometric contraction for a 4-s duration with the arm held straight down against the body. During the handgrip tasks, EMG activity of the flexor digitorum was recorded using the system described below (electrodes were placed on the muscle belly).

NEUROMUSCULAR TESTS. All the neuromuscular tests began by evoking three maximal H-reflexes (Hmax) interspaced by 20 s and three maximal M-wave amplitudes (Mmax) interspaced by 8 s. The amplitudes of the three twitches evoked at the Hmax and Mmax intensities were averaged for subsequent analysis. Afterward, subjects were instructed to perform a plantar flexor MVC for 5 s. Subjects were vigorously encouraged to perform maximally. A superimposed stimulus (Mmax intensity) was evoked during the MVC plateau to obtain a superimposed twitch and both superimposed M-wave (Msup) and V-wave (Vsup; see following text). The ratio of the amplitude of the superimposed twitch torque to the amplitude of the twitch evoked at rest 4 s after the MVC was used to assess the level of voluntary activation (VA) (Allen et al. 1995). According to the twitch interpolation method (Allen et al. 1995), the percentage of VA was calculated as follows: VA (%) = [1 – (superimposed twitch/potentiated twitch)] × 100. The Msup amplitude was used to normalize the root mean square (RMS) activity during MVC.

Measurement and calculations

ELECTROMYOGRAPHY. Electromyographic activity (EMG) of the SOL and flexor digitorum was recorded by means of bipolar Ag/AgCl electrodes (Contrôle Graphique Medical, Brie-Comte-Robert, France) with a diameter of 9 mm and an interelectrode distance of 25 mm. The reference electrode was placed on the left wrist. Low impedance between the two electrodes (<5 kΩ) was obtained by abrading and washing the skin with emery paper and cleaning with alcohol. EMG signals were amplified and filtered (band-pass 30–500 Hz, gain = 1,000). Muscle electrical activity was determined by measuring the mean value of the RMS. During running, the RMS was determined between the onset and offset of the burst. During isometric MVCs, the RMS values of SOL and flexor digitorum were calculated over 1 s when the MVC had reached a plateau. The force signal and EMG data were recorded at a sampling frequency of 2,000 Hz using MP30 hardware (Biopac Systems, Santa Barbara, CA) and dedicated software (BSL Pro Version 3.6.7, Biopac Systems).

TORQUE MEASUREMENT. MVC torque of the right plantar flexor muscles was recorded by a dynamometric pedal (Captels, St Mathieu de Treviers, France). The subject’s position was standardized with pelvis, knee and ankle angulations of 90°, the foot securely strapped on the pedal, and a motionless head (Zehr 2002).

EVOKE POTENTIALS. The tibial nerve was stimulated using a cathode electrode with a diameter of 9 mm stuck in the popliteal cavity (Contrôle Graphique Medical, Brie-Comte-Robert, France) with constant compression supplied by a strap. The anode (10 × 5 cm,
Medicompex, Ecublens, Switzerland) was positioned beneath the patella. Electrical stimulations (400 V, rectangular pulse of 0.2 ms) were delivered by a high-voltage stimulator (Digitimer DS7AH, Digitimer, Hertfordshire, UK). The amperage was adjusted for each subject during the familiarization session. During this first session, amperage was raised progressively (10 mA increment) until a plateau in twitch mechanical response [peak torque (Pt)] and \( M_{\text{max}} \) was observed. During the increase in stimulation intensity, the H-reflex response increased progressively, then decreased progressively and disappeared. Thereafter, the intensity needed to obtain \( H_{\text{max}} \) was adjusted by 1 mA. The stimulation intensity needed to evoke \( H_{\text{max}} \) was determined at rest (mean of 47 ± 27 mA) and was held constant throughout the test session.

**Calculation.** Pt may be considered as an index of excitation–contraction coupling and \( M_{\text{max}} \) amplitude represents an index of muscle excitability, whereas \( H_{\text{max}} \) amplitude is dependent on presynaptic inhibition and spinal loop properties (i.e., transmission efficacy in Ia afferent synapses and motoneuron excitability) (Andersen et al. 2003; Bongiovanni and Hagbarth 1990; Bulbulian and Bowles 1992; Duchateau et al. 2002; Macefield et al. 1991). At rest, maximal intensity stimulation eliciting \( M_{\text{max}} \) is followed by a refractory period. However, during voluntary contraction, the antidromic action potential will collide with the orthodromic action potential from the central axon and neuromuscular junction (Cupido et al. 1996), we normalized these recordings to the M-wave amplitude recorded in the same testing conditions (i.e., \( H_{\text{max}}/M_{\text{max}} \) and \( V_{\text{sup}}/M_{\text{sup}} \) ratios).

**Statistical analysis.** Each variable was tested for normality using the Shapiro–Wilk test. With the assumption of normality confirmed, parametric tests were performed. The effect of the running exercise was analyzed for each variable by a two-way ANOVA for repeated measures (2 types of exercise × 3 times of test). Statistical analyses were performed with R software (R Foundation, Vienna, Austria). In the case of a significant effect of the running exercise, the Bonferroni post hoc test was applied to determine any differences between the data obtained after 5 and 30 min of recovery. Data are reported as means ± SD and the statistical significance was set at \( P < 0.05 \).

**RESULTS**

**Running exercise.**

Running velocity during INT (12 ± 1 km h\(^{-1}\)) was higher than that during CONT (10 ± 1 km h\(^{-1}\)). HR (168 ± 11 vs. 172 ± 9 bpm for CONT and INT, respectively) and SOL RMS activity (215 ± 42 vs. 226 ± 49 \( \mu \)V for CONT and INT, respectively) tended to be higher during INT than during CONT [both \( F_{(1,10)} = 4.62; 0.05 < P < 0.07 \)]. Cardiorespiratory variables (\( V_{\text{O2}} \) and HR) increased significantly from the onset of exercise [both \( F_{(7,70)} > 6, P < 0.001 \)] to the 13th minute and remained stable until the end of exercise (mean \( V_{\text{O2}} \) of 2.6 ± 0.3 L min\(^{-1}\) during CONT and 2.6 ± 0.3 L min\(^{-1}\) during INT), confirming the exercise as a submaximal intensity locomotion task.

Handgrip force did not change significantly during CONT and INT [mean: 48.5 ± 0.6 kg, \( F_{(7,70)} = 0.79 \), NS] but the RMS activity of the flexor digitorum decreased significantly [\( F_{(7,70)} = 2.79, P < 0.02 \)] over the course of the two exercises (from 878 ± 471 \( \mu \)V after 1 min of running to 764 ± 418 \( \mu \)V after 85 min of running; –13%).

**MVC torque and muscle activation.**

All the data presented hereafter were independent of the running mode (CONT vs. INT, NS). The effect of the locomotion task was never dependent on the running mode (no significant interaction effect) and thus the variations presented below correspond to an effect of the locomotion task over time (i.e., fatigue). Furthermore, no significant difference was noted in any of the parameters measured at 5 and 30 min postexercise, indicating that 30 min did not permit a significant recovery (posttests 5 and 30 min after the end of exercise, NS for all parameters).

The MVC torque significantly decreased from 85.2 ± 19 N m at rest to 75.6 ± 21 N m 5 min postexercise and 78.6 ± 23 N m 30 min postexercise [\( F_{(2,20)} = 10.2, P < 0.001 \)]. From preexercise to postexercise, a tendency toward a lower VA level at rest, maximal 30 min was noted [from 96 ± 11% at rest to 93 ± 10% 5 min postexercise and 93 ± 13% 30 min postexercise, \( F_{(2,20)} = 3.04, P = 0.07 \)]. A significant decrease in SOL RMS activity expressed both in absolute units [from 303 ± 129 \( \mu \)V at rest to 241 ± 140 \( \mu \)V 5 min postexercise and 247 ± 103 \( \mu \)V 30 min postexercise, \( F_{(2,20)} = 7.62, P < 0.005 \)] and normalized to the M-wave amplitude [from 0.042 ± 0.023 at rest to 0.033 ± 0.019 5 min postexercise and 0.032 ± 0.014 30 min postexercise, \( F_{(2,20)} = 3.76, P < 0.05 \)] was observed. The detailed data are given in Table 1. Furthermore, because the data were independent of the running mode, the mean of the two conditions is displayed in Fig. 1.

**Evoked potentials.**

The running exercises induced significant changes in evoked potentials, Pt, and EMG activity parameters, independently of mode (Table 1). Furthermore, the subjects did not recover after a 30-min rest period (Fig. 1). The small M-wave associated with the \( H_{\text{max}} \) intensity remained constant throughout the test sessions [mean of 2.4 mV, corresponding to 35% of \( M_{\text{max}} \), \( F_{(2,20)} = 2.36, P > 0.05 \)], suggesting that the stimulus conditions were stable.

The \( M_{\text{max}} \) [\( F_{(2,20)} = 9.60, P < 0.001 \)], \( H_{\text{max}} \) [\( F_{(2,20)} = 23.26, P < 0.001 \]), and \( V_{\text{sup}} \) [\( F_{(2,20)} = 5.42, P < 0.02 \)] amplitudes decreased significantly after running exercise (Table 1). At rest, the \( H_{\text{max}}/M_{\text{max}} \) ratio was significantly reduced [\( F_{(2,20)} = 22.4, P < 0.001 \)] from 0.44 ± 0.26 preexercise to 0.14 ± 0.17 and 0.16 ± 0.16, respectively, 5 min and 30 min postexercise. During MVC, the \( V_{\text{sup}}/M_{\text{sup}} \) ratio also displayed a significant decrease [\( F_{(2,20)} = 4.20, P < 0.05 \)] from 0.56 ± 0.53 preexercise to 0.44 ± 0.35 and 0.35 ± 0.24, respectively, 5 and 30 min postexercise. Examples of evoked potentials recorded before and 5 min after the fatiguing running exercise are shown in Fig. 2.

Pt was significantly decreased postexercise [from 13.9 ± 2.6 N m at rest to 12.5 ± 3.2 N m 5 min postexercise and 12.6 ± 3.0 N m 30 min postexercise, \( F_{(2,20)} = 4.67, P < 0.05 \)].
observation, a significant decrease in the RMS/M_{sup} ratio was confirmed by two different methods. First, our results showed a significant decrease in SOL RMS activity concomitant with central alteration after the prolonged (90 min) running was an exhausting exercise, given that the subjects were not asked to perform a locomotion task rather a competitive event leading to exhaustion, but the development of a large decrease observed in the H-reflex modulation could be because of the large difference in the fatigue protocols. The pool excitability probably occurs after this type of task. The reciprocal inhibition and recurrent Renshaw inhibitions, H-wave inhibition, and the spinal loop modulation (motoneuron excitability in vivo) can enhance calculation of VA, the single twitch was chosen in some studies to obtain V_{sup} measurements (Aagaard et al. 2002; Duclay and Martin 2005; Pensini and Martin 2004; Upton et al. 2001).

**DISCUSSION**

It seems important to first specify that, although the locomotion task performed in this study induced fatigue (i.e., maximal torque decreased by 11% after the run), it was not an exhausting exercise, given that the subjects were not asked to continue until exhaustion or to increase their velocity with an endpoint. We focused on a locomotion task rather a competitive event leading to exhaustion, but the development of a central alteration after the prolonged (90 min) running was confirmed by two different methods. First, our results showed a significant decrease in SOL RMS activity concomitant with a decrement in plantar flexor MVC torque. In line with this observation, a significant decrease in the RMS/M_{sup} ratio was observed after the two prolonged running exercises (INT and CONT), but it was not possible to distinguish between the alterations occurring at the spinal and supraspinal levels. Second, in line with previous reports on prolonged (>2 h) running exercise (Millet et al. 2003), the VA level (estimated by the twitch interpolation method; Allen et al. 1995) was reduced—although not significantly—after both prolonged running exercises in the present study. It should be noted that although some studies have suggested that eliciting a doublet or triplet can enhance calculation of VA, the single twitch was chosen in this study to obtain V_{sup} measurements (Aagaard et al. 2002; Duclay and Martin 2005; Pensini and Martin 2004; Upton et al. 2001).

**Spinal loop modulation**

Despite the fact that H-reflex is likely to be influenced by reciprocal inhibition and recurrent Renshaw inhibitions, H-reflex amplitude is classically used as a tool to evaluate the modulation of the spinal loop (motoneuron excitability in vivo) (Aagaard et al. 2002; Schieppati 1987). In the present study, significant decreases in the evoked reflex-wave amplitudes (i.e., both H_{max} and H_{max}/M_{max}) were observed after a 90-min running exercise performed continuously or intermittently. This indicates for the first time that a decrease in motoneuron pool excitability probably occurs after this type of task. The postexercise amplitude of the normalized H-reflex declined by 61%. This decline seems to be slightly greater than the previously reported declines ranging from 28 to 52% after isometric localized contractions (i.e., Duchateau and Hainaut 1993; Duchateau et al. 2002; Garland and McComas 1990; Kuchinad et al. 2004). However, comparison between studies is difficult because of the large difference in the fatigue protocols. The large decrease observed in the H-reflex modulation could be linked to the task duration (i.e., 90 min) and/or to the task specificity (i.e., muscle damage induced by running). Further studies involving different locomotion modalities are needed to determine more precisely the role of spinal adaptations with fatigue.

**Origin of spinal fatigue**

The decline in the H_{max}/M_{max} ratio observed in this study could be linked to both a presynaptic inhibition leading to a decrement in excitatory inputs from Ia afferences (Bongiovanni and Hagbarth 1990; Macefield et al. 1991) and a decre-

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**TABLE 1. Torque, EMG activity, and evoked potentials before and 5 and 30 min after the continuous (CONT) and intermittent (INT) running exercises**

<table>
<thead>
<tr>
<th></th>
<th>CONT</th>
<th>INT</th>
<th></th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Pre-exercise</td>
<td>5 min</td>
<td>30 min</td>
<td>Pre-exercise</td>
</tr>
<tr>
<td>Force, N · m</td>
<td>83.5 ± 18.9</td>
<td>72.7 ± 19.7</td>
<td>77.4 ± 22.2</td>
<td>86.9 ± 20.9</td>
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<td>Voluntary activation, %</td>
<td>94.7 ± 13.3</td>
<td>92.6 ± 10.8</td>
<td>93.0 ± 13.6</td>
<td>96.6 ± 8.4</td>
</tr>
<tr>
<td>RMS activity, μV</td>
<td>301 ± 137</td>
<td>247 ± 119</td>
<td>261 ± 122</td>
<td>304 ± 127</td>
</tr>
<tr>
<td>RMS/M_{sup}</td>
<td>0.039 ± 0.022</td>
<td>0.034 ± 0.017</td>
<td>0.032 ± 0.016</td>
<td>0.044 ± 0.025</td>
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<tr>
<td>Pt, N · m</td>
<td>14.0 ± 2.8</td>
<td>12.4 ± 3.1</td>
<td>12.3 ± 3.2</td>
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<td>M_{max}, mV</td>
<td>8.9 ± 1.4</td>
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<td>8.8 ± 1.7</td>
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<td>H_{max}, mV</td>
<td>3.87 ± 2.72</td>
<td>0.79 ± 0.69</td>
<td>0.69 ± 0.65</td>
<td>4.20 ± 2.57</td>
</tr>
<tr>
<td>V_{sup}, mV</td>
<td>3.88 ± 2.73</td>
<td>3.43 ± 3.60</td>
<td>3.01 ± 2.29</td>
<td>4.04 ± 3.53</td>
</tr>
<tr>
<td>H_{max}/M_{max}</td>
<td>0.41 ± 0.28</td>
<td>0.11 ± 0.10</td>
<td>0.09 ± 0.08</td>
<td>0.46 ± 0.24</td>
</tr>
<tr>
<td>V_{sup}/M_{sup}</td>
<td>0.50 ± 0.38</td>
<td>0.42 ± 0.31</td>
<td>0.35 ± 0.19</td>
<td>0.62 ± 0.67</td>
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Values are means ± SD; n = 11. All the data displayed a significant effect of the exercise (P < 0.05) independently of the task modality (CONT vs. INT) and without difference between the data recorded 5 or 30 min after the exercise.

**FIG. 1.** Changes in plantar flexors maximal isometric voluntary contraction (MVC), peak twitch torque (Pt), electromyographic activity of the soleus muscle recorded during the MVC expressed in absolute units (RMS) and normalized by the M-wave amplitude (RMS/M_{sup}), and voluntary activation (VA) level estimated by the twitch interpolated method. Data are expressed as percentage from preexercise values and are averaged within the 2 running modalities. All the data displayed a significant effect of the exercise (P < 0.05) independently of the task modality [continuously vs. intermittently (CONT vs. INT)] and without difference between the data recorded 5 or 30 min after the exercise.
ment in motoneuron pool excitability (Andersen et al. 2003; Bulbulian and Bowles 1992; Duchateau et al. 2002). Concerning the level of excitatory inputs from Ia afferences, Gandevia (2001) suggested that changes in the H–M recruitment curve are likely to occur, whereas Kuchinad et al. (2004) showed no significant changes in the shape of the H–M recruitment curves after a fatiguing exercise. In this context, it is important to note that our results failed to show any changes in the M-wave patterns associated with the H_max wave.

Theoretically, the decrement in excitatory input from Ia afferences to α-motoneurons could arise from primary afferent depolarization (PAD) by GABAergic synapses under both local and descending control (for a review, see Rudomin and Schmidt 1999). However, PDA is known to last about 200 ms (Rudomin and Schmidt 1999) and is probably unable to explain the decline in H_max/M_max ratio observed several minutes after the two prolonged running exercises. Previous studies suggested that the depression in H_max/M_max ratio could be explained by a homosynaptic postactivation depression (HPAD) of the Ia terminal (Hultborn et al. 1996; Nordlund et al. 2004; Pinniger et al. 2001). This HPAD is believed to be caused by an intrinsic mechanism within the Ia terminal itself and occurs only when the muscle spindle is, or has recently been, discharging (Hultborn et al. 1996; Nordlund et al. 2004; Trimble et al. 2000; Wood et al. 1996). Because HPAD is known to last ≤15 s, it might offer a valuable explanation for the H-reflex depression measured immediately after an isometric fatiguing exercise (i.e., Duchateau and Hainaut 1993). Although previous authors reported a quick recovery of spinal loop properties within a few minutes (Andersen et al. 2003; Kuchinad et al. 2004) of an isometric contraction of one muscle group, it is interesting to note that in the present study, the H_max/M_max ratio was still depressed after a 30-min recovery period. This suggests that factors other than PAD or HPAD were probably involved in the postexercise decline of H_max/M_max.

The decline in transmission from the Ia afferent stimulation to α-motoneuron excitation was also proposed to be a consequence of a presynaptic inhibition mediated by group III and group IV afferents (Avela et al. 2006; Bigland-Ritchie et al. 1986; Duchateau et al. 2002; Garland 1991; Garland and McComas 1990; Woods et al. 1987). The duration of this presynaptic inhibition will depend on whether the input that is producing the inhibition is ongoing or has ceased. Thus the persistence of the H-reflex depression 30 min postexercise in our study could be explained by delayed input of group III and group IV muscle afferents in relation to muscle damage (Avela et al. 1999). However, it is still unknown whether these sensitive, small-diameter muscle afferents are directly responsible for the exercise-induced presynaptic inhibition of motoneurons in healthy humans (Taylor et al. 2000b). Indeed, the data of the literature seem contradictory. Some studies observed that when the firing of group III and group IV muscle afferents was maintained after fatiguing exercise by muscle ischemia, the recovery of the discharge rates of motoneurons was prevented (Bigland-Ritchie et al. 1986; Woods et al. 1987). This suggests that feedback from the fatiguing muscle to group III and group IV muscle afferents can reflexively depress or inhibit motoneuronal firing rates. Other studies reported that maintaining the muscle in an ischemic state did not affect the altered responses to transcranial stimulation (Andersen et al. 2003; Gandevia et al. 1996; Taylor et al. 2000b). This suggests that during fatigue, group III and group IV muscle afferents do not directly inhibit motoneurons but instead act upstream of the motor cortex to impair voluntary descending drive (Taylor et al. 2006). It was thus proposed that these phenomena may have only a minor influence on the
spinal motoneuronal output after a fatiguing contraction in healthy humans (Andersen et al. 2003). The discrepancies between these studies may be partly explained by recent data showing that elbow flexors, but not extensors, are able to recover when ischemia is maintained after fatiguing contractions (Martin et al. 2006), a finding that suggests differential influences of group III and group IV muscle afferents on different motoneuron pools (Martin et al. 2006).

In summary, a presynaptic inhibition of the motoneuron pool mediated by group III and group IV muscle afferents seems to explain the decreased amplitude of the reflex waves observed in this study. However, the possibility of changes in the intrinsic properties of human motoneurons has not yet been addressed (Johnson et al. 2004), although intrinsic adaptation of the motoneuron firing frequency to a constant excitatory drive was observed in the cat (Kernell and Monster 1982a,b). Thus because our data cannot be unequivocally explained by reflex inhibition of the motoneuron pool, we suggest that the intrinsic properties of α-motoneurons should also be considered in humans.

Although the H/M ratio was observed to be similar at rest and during MVC (Pensini and Martin 2004), there is no evidence that the adaptations observed in a relaxed muscle reflect the functional adaptations that occur during voluntary contraction. Furthermore, the stimulation intensity used to evoke the H-reflex is known to recruit only small-diameter motoneurons (Aagaard et al. 2002). We thus decided to investigate the effect of fatigue-induced changes after prolonged exercise on V-wave responses. The V-wave, or the first volitional wave, reaches the muscle only during voluntary contraction and recruits a larger pool of motor units. Our results showed a significant decrease in the Vsup/Msup ratio after exercise. This decrement confirms our first hypothesis of a decrease in motoneuron pool excitability after prolonged running.

Other sources of the modulation in force production

Recent studies recorded changes in the force of a muscle (i.e., flexor digitorum) not implicated in a fatiguing exercise (i.e., a prolonged period of running) to explore whether supraspinal fatigue occurs after the exercise (Millet et al. 2003; Place et al. 2004). None of these studies observed a loss in handgrip force, leading the authors to conclude that supraspinal fatigue did not occur in this type of exercise (Millet et al. 2003; Place et al. 2004). Although these studies recorded only the handgrip force signal (Millet et al. 2003; Place et al. 2004), our EMG data showed for the first time a decrease in RMS activity over the course of the running exercise. When RMS activity decreases in parallel with a force loss, it is generally assumed that a decrement in neural drive is partly responsible for the force loss and this has been termed “central fatigue” (i.e., Millet and Lepers 2004). However, our results showed that the maximal voluntary force remained stable during the two running exercises, suggesting an absence of fatigue in the flexor digitorum neuromuscular system. Indeed, our results showed that the force/RMS ratio significantly increased [F(7,70) = 2.93, P < 0.02] during exercise (+22% from the first minute of running to the 85th minute), suggesting a reduced quantity of neural drive needed to produce a given level of force. This can be explained by the warm-up effect of running and the previous demonstration increase in the force/RMS ratio with an increase in temperature (Racinais et al. 2005). It thus seems that the altered RMS activity was not the direct result of a failure in motor-unit recruitment but instead may be viewed as part of a regulatory process (Tucker et al. 2006). In summary, the decline in RMS activity can be considered as a supraspinal adaptation of a complex system with feedback rather than the supraspinal fatigue of a system unable to maximally drive the muscle.

Finally, our data displayed a significant decrease in Mmax amplitude, indicating a failure in neuromuscular propagation properties at the sarcolemmal level (Avela et al. 2006). This result agrees with previous findings concerning prolonged running (Millet and Lepers 2004). The decline might be linked to reduced sarcoplasmic excitability (Avela et al. 2006; Millet et al. 2003) and suggests the occurrence of ionic disturbances at a peripheral level concomitant with neural modulations at both spinal and supraspinal levels. Nevertheless, results obtained with the surface EMG technique must be analyzed with caution. Indeed, Mmax represents the numerical sum of the synchronization of many muscle fiber action potentials (Avela et al. 2006) and the amplitude of surface EMG data may be complicated by amplitude cancellation (Weir et al. 2006). Thus in the present study, the significant decrement in twitch contractile properties (Pt), which suggests altered excitation–contraction coupling, supports the notion that peripheral modulations are also likely to occur in this type of exercise. However, even with all these changes, our subjects would have been able to speed up (at least for the last minutes) in a context of self-paced velocity, such as a competitive running event. This suggests that these changes can be functionally overridden by central drive to the muscle in cases of submaximal exercise or specific motivation (i.e., a competitive event or emergency situation).

Effect of running modality

A secondary aim of this study was to determine whether the same exercise (equivalent in distance covered) performed with recovery periods (intermittent) would minimize central fatigue compared with a continuous mode. Although our results showed evidence of central fatigue (based on VA and the RMS/Msup ratio), they failed to display any significant effect of the mode of exercise. This lack of difference may be explained by two opposite mechanisms. First, it has been suggested that the CNS is able to partly recover within a few seconds (Nybo and Nielsen 2001) and one thus may argue that the successive recovery periods (30 s) of the intermittent task reduced central fatigue. However, brief rest periods may be not sufficient to fully prevent the development of central fatigue (Bilodeau 2006). Second, because the alteration in motoneuron pool excitability is dependent on exercise intensity (Bulbulian and Darabos 1986), it is possible that the higher velocity imposed during the intermittent task blunted the small effect of the recovery period. Thus the lack of difference in central alteration/spinal modulation between the continuous and intermittent exercise modes was probably the result of the same amount of work performed within the same time in the two locomotion conditions. It is also important to keep in mind that the continuous exercise was not a continuous contraction, as in an isometric task. The individual muscles were not continu-
ously engaged and thus the motoneurons driving each muscle presumably operated in an intermittent fashion. However, the time within of each motor action during running remained very short in comparison of the recovery time allowed during the intermittent activity. Because numerous physical activities (e.g., team and racket sports, physical work) are intermittent in nature and thus differ from laboratory testing (continuous activity), comparison between intermittent and continuous activities remains an interesting topic that should be further investigated.

In conclusion, the main objective of this study was to examine the neural adaptations induced by a prolonged (90-min) running exercise. Our results confirmed the occurrence of central fatigue (according to VA and the RMS/Msup ratio) and, in accordance with our initial hypothesis, the main findings showed for the first time a spinal component to this central fatigue. To assess the effect of running-induced fatigue on the force production capacity of the skeletal muscle in vivo, the following points should be considered.

1) Peripheral alterations (decreased Pt and Msup amplitudes)

2) Spinal modulations leading to a decline in motoneuron pool excitability (decreased amplitudes of Hmax/Mmax and Vsup/Msup ratios)

3) Supraspinal modulations of a system controlled by a feedback loop (decrease in RMS activity of the flexor digitorum)

4) Although not investigated in this study, some factors “upstream” of the motor cortex (Taylor et al. 2000a).

The second purpose of this work was to determine whether an intermittent exercise with brief recovery periods would minimize central fatigue. Our results regarding the H-reflex and V-wave suggest a modulation of spinal loop properties after prolonged running that was independent of the continuous/interruption running mode.

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REFERENCES


