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ORIGINAL ARTICLE

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Neuromuscular changes after long-lasting mechanically and electrically elicited fatigue

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Abstract Central fatigue was investigated under an isolated active condition whereby the possible effects of supraspinal fatigue were minimized. Therefore, ten subjects were fatigued by simultaneously and repeatedly mechanically stretching and electrically stimulating their calf muscles for 1 h. This was performed using an ankle ergometer. The active fatigue task included a total of 2400 muscle stretches with an intensity of 10% of the maximal voluntary contraction (MVC). This protocol clearly impaired neuromuscular function, as revealed by a significant reduction in MVC ($P < 0.01$) and the neural input to the muscle (average EMG) ($P < 0.01$–0.001). The interpolated nerve stimulation compensated for this force loss by 4.28% ($P < 0.05$). Stretch-reflex recordings revealed a notable post-fatigue reduction in the peak-to-peak amplitude (59.1%, $P < 0.01$) and stretch-resisting force of the muscle (14.1%, $P < 0.01$). The maximal H-reflex declined by 50.5% ($P < 0.001$) and did not recover while the leg was kept ischemic. It is suggested that the existing protocol with minor metabolic loading can induce central fatigue, which seems to be of reflex origin from the fatigued muscle. Although the role of presynaptic inhibition of Ia terminals is possibly reinforced, disfacilitation via reduced spindle sensitivity cannot be excluded.

Keywords Electromyography · Low-frequency fatigue · Neuromuscular fatigue · Stretch-reflex

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Introduction

Bigland-Ritchie and Woods (1984) proposed that one of the most important signs of fatigue is a decline in maximal force. Such a reduction has been reported to occur after sustained isometric contractions (Fellows et al. 1993; Woods et al. 1987) and after stretch-shortening cycle (SSC) exercises involving exhaustive and intensive effort (Horita et al. 1996; Nicol et al. 1996), as well as long-lasting low-intensity effort (Avela et al. 1999a; Nicol et al. 1991; Sherman et al. 1984). The fatigue processes leading to the impaired force output can develop in different places along the activation-contraction chain (Bigland-Ritchie 1981). These processes can be divided into two categories. Central fatigue (Gandevia 1992), which includes insufficient neural drive to the muscle, and peripheral fatigue (Fitts 1994), which includes all the changes beyond the neuromuscular junction.

It has been suggested that fatigue in voluntary contractions is most probably caused by peripheral fatigue, the reduction in muscle activation by the central nervous system (CNS) being less important (Beelen et al. 1995). This argument also receives support from the earlier studies by Merton (1954) and Bigland-Ritchie (1981), where it did not prove possible to overcome the decline in maximal force by supramaximally stimulating the motor nerve or muscle itself. However, some alternative results have also been presented: McKenzie and Gandevia (1991) demonstrated, by means of twitch interpolation, a small degree of central fatigue that developed progressively during a series of limb muscle contractions. Thus, in several studies in which fatigue was induced by prolonged SSC exercise (Avela and Komi 1998), repeated eccentric and concentric exercises (Komi and Rusko 1974; Komi and Viitasalo 1977) and sustained isometric contraction (Bongiovanni and Hagbarth 1990), some reduction in neural input to muscle has been observed. This has been confirmed by a decline in either the maximal average EMG (aEMG) or the discharge frequencies of the motor units.

In many studies the decline in motor unit activation has been associated with a reduction in reflex sensitivity (Avela and Komi 1998; Avela et al. 1999a; Horita et al. 1996; Nicol et al. 1996). This is in accordance with the suggestion of Asmussen and Mazin (1978), namely that the decline in motor unit activation is reflexly dependent on the signals from the contracting muscle. Two hypotheses have been proposed to explain this mechanism. The first of these relies on the presynaptic inhibition of the Ia terminals and/or inhibition of the interneurones in the oligosynaptic pathways. This may result from metabolically induced activity of the small muscle afferents, such as those belonging to groups III and IV (Biglard-Ritchie and Woods 1984; Garland and McComas 1990). The other hypothesis depends on disfacilitation of the α-motoneurone pool. This could be due to the progressive withdrawal of spindle-mediated fusimotor support to the muscle spindles and/or fatigue of the intrafusal fibers of the muscle spindle itself (Hagbarth et al. 1986; Macefield et al. 1991).

In our recent studies (Avela et al. 1999a, 1999b), we were able to demonstrate that long-lasting and repeated stretching of an active or passive muscle decreases the stretch-resisting force of the muscle, and reduces the reflex sensitivity. Therefore, we concluded that disfacilitation of the α-motoneurone pool could also happen because of a weakened mechanical response of the muscle spindle to stretch, possibly due to impaired mechanical transduction and/or increased spindle compliance.

The purpose of the present study was to test the two central fatigue hypotheses under an isolated active condition, whereby the possible effects of fatigue caused by impairments of supraspinal processes (supraspinal fatigue) (Brasil-Neto et al. 1994) are minimized. It is hypothesized that while muscle activation is induced without voluntary effort, supraspinal processes are not likely to be involved in fatigue as a mechanism. Hence, special interest was in the peripheral reflex mechanisms and especially the possible interactions of the changes in the muscle's stretch-resisting force in response to these mechanisms. Some attempts were also made to characterize the possible peripheral fatigue induced by the present fatigue protocol.

Methods

Subjects

Ten healthy male subjects, aged 23–48 years (mean 34 years) participated in the study. None of the subjects had any history of neuromuscular or vascular disease. They were fully informed of the procedures and the risks involved in this study and they gave their informed consent (code of Ethics of the World Medical Association, Declaration of Helsinki). They were also allowed to withdraw from the study at will.

Experimental protocol

All of the ten subjects performed the fatigue protocol (protocol 1), in which the right calf muscles were mechanically and electrically stimulated simultaneously for 1 h. The subjects were then randomized into two groups of five subjects and tested for the recovery of reflex excitability 2 weeks after protocol 1. Two weeks was considered as sufficient time for total recovery from the possible training/habitation effects of protocol 1. Non-significant differences between the post-exercise data of these different testing sessions verify this assumption. In this second testing session recovery of the maximal H-reflex (Hoffmann reflex) was followed for 10 min either with (protocol 2) or without (protocol 3) a 5-min period of ischemia. The rather complex experimental protocols are summarized in Fig. 1.

In the fatigue protocol (protocol 1), pre-fatigue measurements were performed in the following sequence: isometric maximal voluntary plantarflexion (MVC) (two measurements), 50% MVC, MVC with superimposed double twitch, maximal H-reflexes (five measurements) with maximal M-responses (maximal compound action potential, M-wave) (three measurements) and, finally, the response of the relaxed triceps surae muscle to electrical stimulation (ES) at frequencies of 20 Hz and 80 Hz. These measurements were performed on the right leg, which served as the experimental leg. Prior to these measurements MVC and maximal H- and M-responses were measured from the non-fatigued left leg, which served for these selected parameters as the control leg.

The post-fatigue measurements were made using the same protocol, except that the immediate measurements were performed

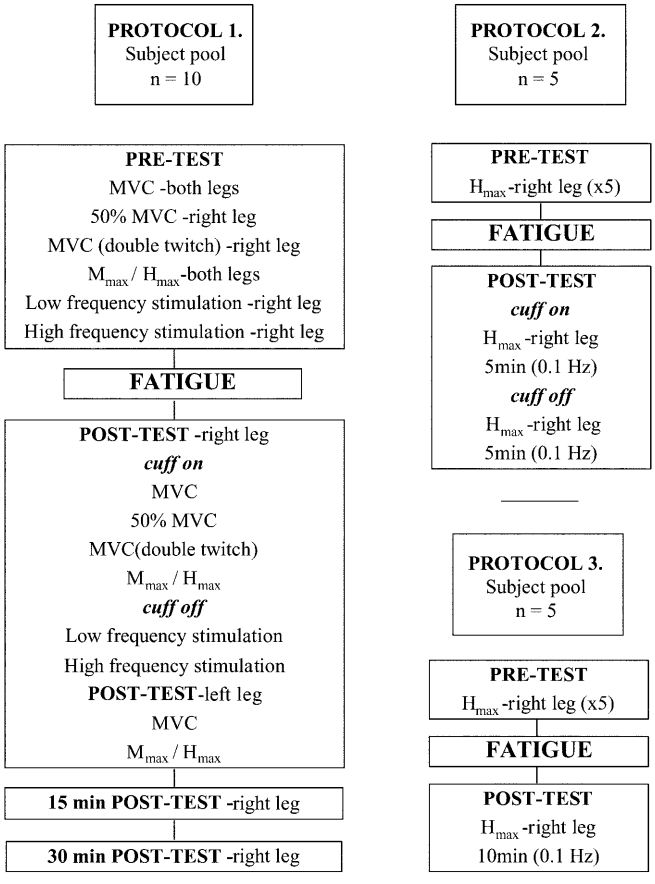

Fig. 1 Experimental protocol illustrating the fatigue protocol (*protocol 1*) on the left and recovery tests with ischemia (*protocol 2*) and without ischemia (*protocol 3*) on the right. [H_{max} Maximum H-reflex, *low- and high- frequency stimulation* electrical stimulation of the passive muscle at 20 Hz and 80 Hz frequencies, respectively, *MVC* maximal voluntary contraction, *MVC (double twitch)* MVC with superimposed double-twitch stimulation of the motor nerve, M_{max} maximum M-wave]

with ischemia and on the right leg only. Ischemia was induced by a blood pressure cuff, which was wrapped around the middle portion of the right thigh and inflated to at least 200 mmHg. This pressure was maintained while the immediate post-fatigue measurements were performed (3–5 min). In our earlier study (Avela et al. 1999b), we show that ischemia of this duration does not affect the Ia afferent fibers. This procedure allows possible metabolic fatigue substances to be retained in the fatigued muscles throughout the measurements. Each complete sequence of post-test measurements took approximately 240 s. Within this period, at least 30 s was allowed to elapse between the MVCs and H-reflex recordings, to avoid the problem of post-contraction depression of the H-reflex (Schieppati and Crenna 1984).

The stretch reflexes were measured as a bout of ten consecutive stretches of the right leg at the very beginning, after 30 min, and at the very end of the fatigue stimulation. Recovery was tested 15 min (15 min+) and 30 min (30 min+) after the end of the fatigue task.

In the second testing session (protocols 2 and 3) fatigue stimulation was preceded just by maximal H-reflex measurement (five measurements). Therefore, only the recovery of the maximal H-reflex peak-to-peak amplitude, which was measured at a stimulus frequency of 0.1 Hz, was measured post-fatigue. In the first of these tests (protocol 2) the first 5 min of recovery was measured with ischemia.

Throughout all the reflex measurements background EMG activity was monitored on an oscilloscope to ensure that it was silent. This precaution was important since the H-reflex is known to change if the soleus (SOL) muscle is not fully relaxed (Verrier 1985).

Throughout the experimental procedure, the legs were warmed with an infra-red lamp, and the skin temperature was measured during every test unit. Thus, a constant skin temperature could be ensured by adjusting the distance of the lamp according to the skin temperature reading.

Blood samples were drawn from the ulnar vein before, 5 min after and 1 day after the fatigue task to determine possible markers of muscle damage (serum creatine kinase activity, S-CK). Furthermore, capillary blood samples were taken from the fingertip for blood lactate (B-La) determination before and 5 min after the fatigue. S-CK was analyzed using a CK ultraviolet test kit (Boehringer Mannheim, Germany) and B-LA was analyzed enzymatically using a commercial kit (Biochemica Boeringer, Germany).

The recording electrodes for the H-reflexes, M-waves, stretch reflexes, and the EMGs associated with MVC and 50% MVC were bipolar surface electrodes (Beckman miniature skin electrodes 650437, Illinois, USA) fixed at a constant inter-electrode distance of 20 mm. The electrodes were placed on both legs 6 cm above the superior aspect of the calcaneus on the SOL muscle and between the center of the innervation zone and distal end of the lateral head of the gastrocnemius (GA) muscle. The ground electrodes (textile band dipped in a physiological saline solution) were wrapped around the shank between the stimulating and recording electrodes. All the EMG activity associated with voluntary contractions and stretch reflexes was amplified (10 Hz to 1 kHz) by an evoked-potential measuring system (MEB-5304 K, Nihon Kohden, Japan) and then transferred through an AD converter (1 kHz), to a microcomputer for further analysis. All the signals were also stored simultaneously on a magnetic tape recorder (Racal, England).

Fatigue task

Fatigue was induced in the calf muscles of the right leg by simultaneous ES and mechanical perturbation for 1 h. This was performed using an ankle ergometer (Avela et al. 1999b). In this procedure, the subjects sat in an ergometer chair with the thigh of their right leg clamped and the foot mounted on the rotation platform so that the rotation axes of the ankle joint and motor drive coincided, thus only allowing motion around the ankle joint. The initial ankle position was 90° and the knee angle was set at 140°. The mechanical stimulus was generated by the servo motor system of the ankle ergometer, which was controlled by a microcomputer (A). The mechanical stimulus was set to produce a 10° ankle joint dorsiflexion with an average stretching velocity of 3.5 rad·s^{-1} and a frequency of 1.5 Hz. The evoked-potential measuring system (MEB-5304K, Nihon Kohden, Japan), including a precision impulse generator, was used to electrically stimulate the right calf muscles simultaneously. The stimulator was controlled by a second microcomputer (B), which was synchronized to the mechanical stimuli by computer A. The stimulation intensity was set to a level that would induce 10% of the MVC. The stimulation frequency was 30 Hz (duration 0.2 ms) (Löscher et al. 1996), which has been found to be less painful to the subjects as compared to higher or lower frequencies. The ES covered each mechanical perturbation unit with a pre-stimulation of 75 ms (Fig. 2). Self-adhering medical electrodes (5 cm × 5 cm) (StimTrode, Axelgaard, California, USA) were used for the fatigue stimulation, as well as in the low-high frequency fatigue test, which is a test to identify forms of peripheral fatigue (Jones 1996). The electrodes were placed percutaneously on the right GA muscle so that two cathodes were attached on the proximal head of the lateral and medial GA muscles and one anode was located distally on the muscle-tendon region.

Recording procedures

All the torque measurements in the present protocol were measured with a torque-transducer (Kistler, Switzerland) mounted between the servomotor of the ankle ergometer and the foot platform. The angular movement of the ankle joint with respect to the foot platform was monitored by a linear potentiometer. For visual feedback, the torque signal was displayed on an oscilloscope, so that the subjects could, when necessary, produce 50% MVC.

The standard methodology was used to record the H-reflex. After preparing the skin, stimulation electrodes (pregelled Ag/AgCl electrodes, Niko, Denmark) were positioned bilaterally for H-reflex and M-wave testing. The position of the stimulating electrodes was tested first in the upright stance, and then again in the experimental position to ensure constant recording conditions. The intensity of the electrical stimulus was set in every testing unit to elicit the maximal H-response (H_{max}) and M-response (M_{max}). For both legs the cathode (1.5×1.5 cm) was placed over the tibial nerve in the popliteal fossa and the anode (5×8 cm) was placed superior to the patella. For H-reflex and M-wave testing, single rectangular pulses of 1 ms duration were delivered from the signal generator of the evoked-potential measuring system. H-reflex and M-wave recording signals were also amplified, stored and analyzed by the evoked-potential measuring system. The maximal H-reflex peak-to-peak amplitudes were expressed in relation to the maximal M-wave peak-to-peak amplitudes. Theoretically H:M ratios, so determined, should not be affected by any fatigue-induced changes in the peripheral excitability of the muscle fibers. All latencies were analyzed as well.

The superimposed MVC was induced by two interpolated peripheral nerve stimuli (frequency was 100 Hz) (McKenzie and Gandevia 1991). The purpose of this test was to determine the

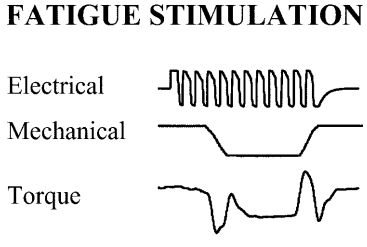

Fig. 2 An example of one repetition of simultaneous mechanical and electrical stimulation during the fatigue task

relative levels of central activation in the different testing conditions. The degree of failure of voluntary muscle activation was quantitated as the ratio of the superimposed twitch response to the maximal voluntary effort before the twitch, expressed as a percentage increment. The same electrode arrangement was used as in the H-reflex testing. The stimulus intensity was set approximately 25% higher than that of the maximal M-wave to ensure a maximal response in every testing condition. Special care was taken to ensure that the double twitch was applied during the maximum torque level.

In the low-high frequency torque test, the arrangement of the stimulating electrodes was the same as that in the fatigue task. The relaxed triceps surae muscle was stimulated by two consecutive trains of impulses at frequencies of 20 Hz and 80 Hz (square pulses of 0.2 ms duration in both, respectively). The stimulation amplitude was set to three times the motor threshold and was kept the same for both frequencies, thus allowing the mean value for the leveled torque (500-ms window) to be calculated.

The stretch-reflexes were measured with the same mechanical stimulation as used in the fatigue task. However, during the stretch-reflex recordings the electrical stimulation was turned-off and the subjects were instructed to fully relax the calf muscles. Ten consecutive stretch-reflexes were averaged and peak-to-peak amplitudes were analyzed together with latency times, resisting torques, and displacement of the ankle joint angle.

The active and passive stretch resisting torques were measured from the fatigue stimulation (active) and stretch reflex tests (passive) and analyzed as an average plantar flexion torque for the first 40 ms of the stretch, before any possible contribution of the stretch reflex responses. The empty pedal torque was subtracted from that of the stretch-resisting torque. In all the cases torque was divided by the lever arm to obtain force.

EMG activity during 50% MVC was also recorded with fine wire electrodes in all subjects. In preparing the wire electrodes the electrode area was kept constant and clean by removing 2 mm of Teflon insulation from a 50-μm diameter Evanohm wire (Wilbur B. Driver, New Jersey, USA). The bipolar wire electrode was inserted into the SOL muscle laterally 10 cm above the muscle-tendon region. Achieving the all-important connection between the electrode and the amplifier conductor was achieved with a spring-wire coil connector. The EMG signal was amplified (bandwidth 20 Hz to 1 kHz) through a Nihon Kohden measuring system and stored in a microcomputer for zero crossing rate (ZCR) analysis (1024-ms window).

Statistical analysis

Mean and standard deviation values were calculated for the various parameters in all the different tests. In the fatigue protocol (protocol 1) ($n = 10$), the inter-test statistical significance for the different parameters was determined by double multivariate analysis of variance (MANOVA). When a significant F-ratio occurred for the main effects, the paired Student's t-test was used to locate the source of difference. For protocols 2 and 3 ($n = 5$) only descriptive statistical methods were applied.

Results

Fatigue stimulation

The 1-h fatigue stimulation of the calf muscles was characterized by a clear reduction in most of the parameters measured. Figure 3 presents the analogue signals of one subject in the different test conditions. The contractile output of the muscle is clearly impaired. The MVC torque of all subjects decreased on average by 18.5 (7.0)% ($P < 0.01$). This was also true for the maximal neural input to the GA and SOL muscles, as expressed by the relative reduction in the average EMG values of 11.9 (6.9)% ($P < 0.001$) and 14.8 (11.7)% ($P < 0.01$),

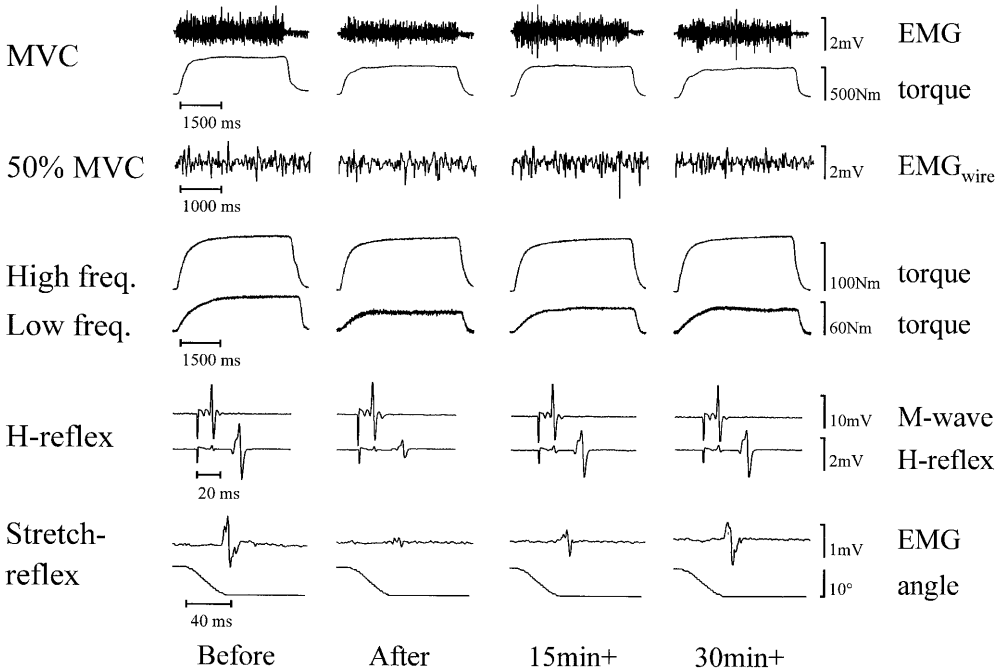

Fig. 3 Data from one subject illustrating the effectiveness of the fatigue stimulation and the following recovery. All signals are from the experimental leg and all EMG signals represent soleus muscle activity. From *top* to the *bottom*: soleus EMG and isometric plantarflexion torque from the maximal voluntary contraction (*MVC*), soleus EMG recorded with fine wire electrodes from the 50% MVC (*50% MVC*), plantarflexion torque due to low- and high-frequency stimulation (*High freq.* and *Low freq.*), maximal M-waves and H-reflexes and soleus EMG (*H-reflex*), plantarflexion torque and ankle angle displacement from the stretch-reflex recordings (*stretch-reflex*). The time window of the different measurements is different

respectively (Fig. 4). These reductions resulted in non-significant changes in the EMG/force ratio. The decreased amplitude of the maximal EMG was accompanied by reduced frequency properties of the 50% MVC EMG signal. This was demonstrated by a 8.0 (7.4)% ($P < 0.01$) decrement in the ZCR value immediately after fatigue.

In the pre-fatigue measurements, the MVC was affected by only a 0.5 (1.6)% increment following twitch interpolation with twin stimuli. This difference was slightly elevated immediately after fatigue, at 4.3 (3.1)% ($P < 0.05$). The values during the follow-up were 1.6 (1.1)% and 1.5 (1.9)% for the 15 and 30 min post-fatigue, respectively.

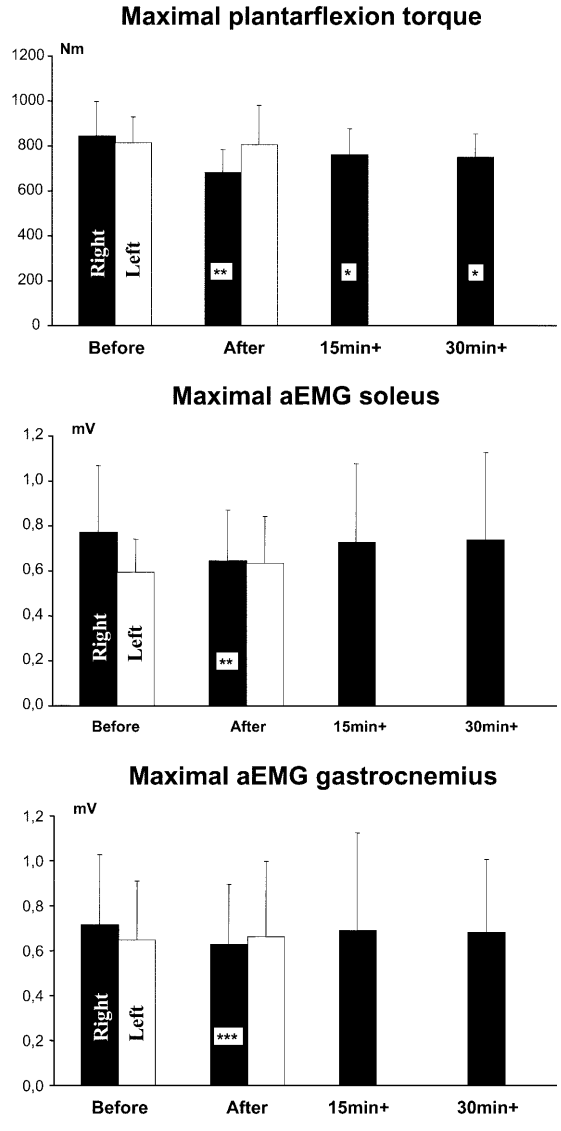

Fig. 4 Mean values (±SD) of maximal plantarflexion torque and corresponding average EMGs (*aEMGs*) of the soleus and gastrocnemius muscles. Right leg represents the experimental leg. $***P < 0.001$, $**P < 0.01$ and $*P < 0.05$ refer to the statistical significances between the values compared before, and after stimulation

In the low-high frequency stimulation test only the low-frequency torque was significantly reduced from 205 (89) Nm to 179 (94) Nm ($P < 0.01$). This reduction was even more pronounced in the 15-min follow-up test (Fig. 5).

The recordings of the stretch reflexes showed that the peak-to-peak amplitude had reduced dramatically as early as 30 min after the fatigue stimulation had started. As the fatigue stimulation continued, the peak-to-peak amplitude carried on reducing, but not by much more (Fig. 6). The passive stretch-resisting force showed a very similar pattern during the fatigue stimulation. The immediate after-fatigue reduction was 14.1 (10.4)% ($P < 0.01$). However, in this case a full recovery was observed during the follow-up period (Fig. 7). A marked reduction [34.9 (12.4)%, $P < 0.001$] of the active stretch-resisting force was detected 30 min after the fatigue stimulation began. Only a slight recovery was seen during the follow-up.

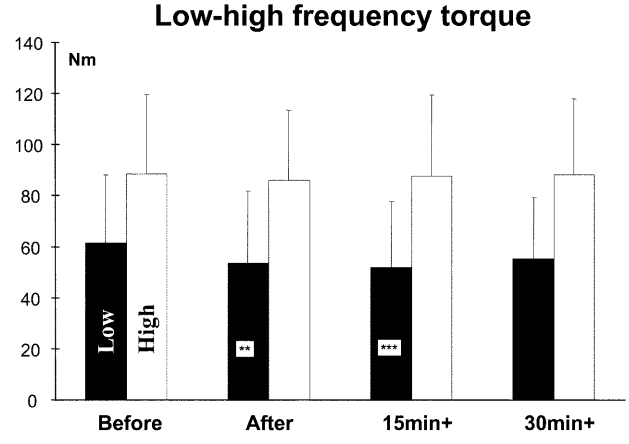

Fig. 5 The relative changes in the torques induced by the low- and high-frequency stimulation (mean and SD). $***P < 0.001$ and $**P < 0.01$ refer to the statistical significances between the values compared before, and after stimulation

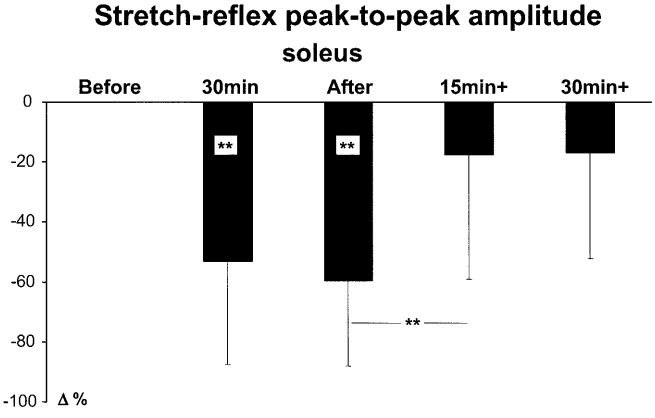

Fig. 6 The relative changes in the stretch-reflex peak-to-peak amplitude of the soleus muscle (mean and SD). $**P < 0.01$ refers to the statistical significances before, during and after stimulation or within the post-stimulation period

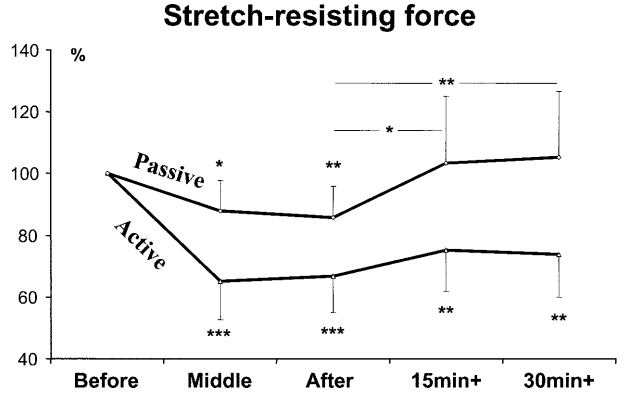

Fig. 7 The relative values of passive and active stretch-resisting forces between different conditions (mean and SD). ***$P < 0.001$, **$P < 0.01$ and *$P < 0.05$ refer to the statistical differences before, during and after stimulation or within the post-stimulation period, as marked by *bars*

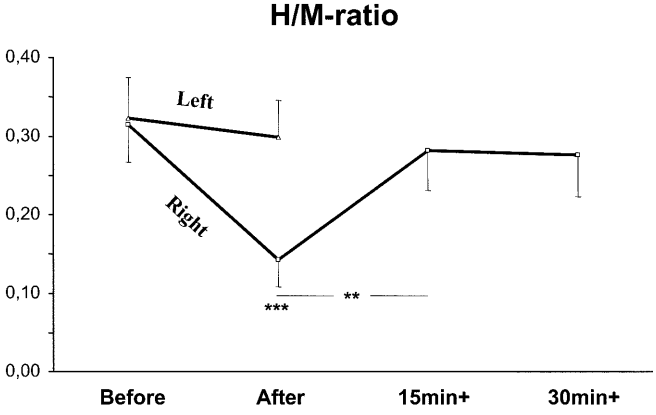

Fig. 8 Mean values (±SD) of the maximal H/M ratio. Right leg represents the experimental leg. ***$P < 0.001$ and **$P < 0.01$ refer to the statistical differences before, and after stimulation and within the post-stimulation period, as marked by the *bars*

The maximal H-reflex declined by 55.3 (21.2)% ($P < 0.001$) immediately after the fatigue. While this reduction was not associated with any decrease in the maximal M-wave, the maximal H/M ratio was also depressed [mean decline 50.5 (37.6)%] (Fig. 8). The before and after comparison of control leg data revealed that no significant changes occurred. This was also the case for all the latencies measured during the reflex tests.

The B-La measurement revealed that the fatigue stimulation caused a slight metabolic loading. The mean peak lactate concentration increased from 1.44 (0.33) mmol·l^{-1} to 2.41 (0.58) mmol·l^{-1} ($P < 0.001$). For S-CK this increment rose from 196 (98) U·l^{-1} to 283 (84) U·l^{-1} ($P < 0.001$) 5 min post-fatigue and to 450 (92) U·l^{-1} ($P < 0.001$) 1 day after the fatigue stimulation.

H-reflex recovery

The recovery of reflex excitability was measured more precisely by the maximal H-reflex stimulation (Fig. 9). The recovery pattern showed two different shapes depending on the test situation. Under normal blood supply conditions (protocol 3), recovery of the H-reflex occurred within 3–4 min and then leveled off to the post-exercise level. When the leg was kept ischemic (protocol 2) for the first 5 min of the recovery period, no recovery was observed. However, the H-reflex recovered immediately to the post-exercise level when the blood was once again allowed to circulate freely.

Discussion

As expected, the fatigue protocol of the present study induced a considerable reduction in the force output of the investigated muscles. The MVC was reduced by 18.5% immediately after the fatigue with concomitant changes in the neural input to the muscle (aEMG and ZCR). The other major findings in the present study were reduced reflex sensitivity, including the stretch reflex as well as the H-reflex, a lower low-frequency stimulation torque and a significant but small increase in torque development following superimposed double-twitch stimulation. The metabolic parameters demonstrated a small significant increase in B-La immediately after fatigue as well as an immediate and delayed increase in S-CK activity.

The major aims of the present study were first to examine the overall nature of central fatigue and, secondly, to clarify the mechanisms that might be involved. Several studies have suggested that fatigue in voluntary contractions is most probably due to peripheral fatigue only (Beelen et al. 1995; Bigland-Ritchie 1981; Merton 1954). This argument is based on the fact that in these studies single shocks were not able to induce any superimposed twitches during sustained MVC. The problem with the single-twitch technique is that its sensitivity is not high enough to reveal whether more than 95% of the optimal force has been achieved voluntarily (Gandevia et al. 1995). Therefore, a superimposed double-

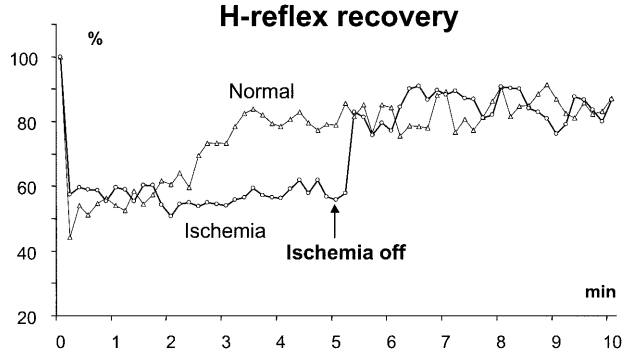

Fig. 9 The mean recovery curve of the H-reflex peak-to-peak amplitude measured either in the presence of ischemia or with normal blood circulation. *Arrow* indicates ischemia cuff removal. No changes were statistically significant

twitch technique was used in the present study to increase the sensitivity of the method. Our results demonstrated that with our well-trained and motivated subjects torque production increased with interpolated double stimulation by 4.3% ($P < 0.05$) immediately after fatigue. This result permits the speculation that part of the force decline in the present study could have been caused by the decreased neural drive to the muscle. This possibility in central fatigue has also been presented by other researchers using a variety of fatigue protocols (Lloyd et al. 1991; McKenzie and Gandevia 1991; Thomas et al. 1989). This is also in line with the suggestion by Bigland-Ritchie and Woods (1984) that the declining motor drive may well limit force production in exercise carried out for more than 60 s.

According to the literature, central fatigue can be divided into three different mechanisms:

1. Supraspinal fatigue (Brasil-Neto et al. 1994),
2. Disfacilitation of the α-motoneurone pool (Bongiovanni and Hagbarth 1990),
3. Reflex inhibition (Garland 1991).

The present experiment did not include any direct methods for quantifying supraspinal fatigue. The difficulty of accomplishing this task was one of the reasons why the muscle activity during our fatigue protocol was induced by external electrical stimulation. Thus, we feel that the effect of supraspinal fatigue is negligible in the present case and, therefore, the remaining discussion concentrates on the two latter hypotheses.

These hypotheses are based on the suggestion of Assmusen and Mazin (1978), later supported by Bigland-Ritchie et al. (1986), that the decline in motor unit activation during fatigue depends on some reflex response from the contracting muscle itself, resulting in decreased α-motoneurone pool excitability. More direct evidence for reduced reflex sensitivity due to fatigue has since been presented by Nicol et al. (1996) and Horita et al. (1996). The decreased H/M ratio (50.5%) and stretch reflex peak-to-peak amplitude (59.1%) in the present study is clearly in line with these suggestions and findings and, therefore, we believe that some forms of the reflex mechanism are responsible for the observed changes in neural drive.

The theory concerning the disfacilitation of the α-motoneurone pool has been presented in several studies (Hagbarth et al. 1986; Hayward et al. 1988; Macefield et al. 1991). It is based on direct and indirect evidence of decreased Ia-afferent activity during fatigue. This reduction can be caused either by withdrawal of fusimotor support to the muscle spindle or by direct fatigue processes in the intrafusal fibers of the muscle spindle itself, as proposed by Bongiovanni and Hagbarth (1990). Methodologically it is very difficult to separate these two mechanisms. In our earlier study (Avela et al. 1999b) we managed to induce similar changes in reflex sensitivity by inducing muscle fatigue with long-lasting and repeated passive stretches. Our assumption was that during the fatigue protocol the intrafusal fibers were affected by the external force only and, therefore, the Ia-afferent activity was induced without fusimotor-driven background activity. We took this as possible evidence that the muscle spindle itself is an individual mechanism that can induce disfacilitation. However, in that case the reason for the reduced spindle sensitivity would seem to be mechanical modification of the extrafusal and/or intrafusal fibers. Along those lines Komi and Nicol (2000) have proposed the possibility of direct mechanical damage in the intrafusal fibers themselves, a mechanism that could also reduce muscle spindle sensitivity and should not therefore be underestimated. In the present fatigue protocol fusimotor support to the muscle spindles was also minimized by using external electrical stimulation. In addition, we observed a similar reduction in the passive stretch-resisting force of the muscle (14.1%) immediately after fatigue, as we did in our earlier study with the passive muscle (16.0%) (Avela et al. 1999b). Hence, this result allows the interesting possibility that the mechanical modification (possibly slackening) of the muscle (decreased mechanical response of the muscle spindle) in the present study could have acutely reduced the Ia-afferent activity, leading to disfacilitation of the α-motoneurone pool. This mechanical modification of the muscle might also have impaired the direct force transfer from the muscle fibers to the tendon. The reduced active stretch-resisting force (34.9%) supports this theory. Part of this large decrement in the active resisting force can be explained by events related to the low-frequency fatigue (18.0%) (discussed later). However, the remaining force deficit seems to fit within the range of a reduced passive component. Interestingly, we have observed a similar reduction in the passive stretch-resisting force (12.4%) after marathon running (Avela et al. 1999a).

The hypothesis concerning reflex inhibition relies on metabolically induced activity of the small myelinated and unmyelinated afferents (group III and IV) (Bigland-Ritchie et al. 1986; Garland 1991), activation of which might lead to presynaptic inhibition of the Ia-terminals (Duchateau and Hainaut 1993). This would result in reduced excitability of the α-motoneurone pool, as was the case in the present study. Our metabolic parameters demonstrated that the fatigue stimulation induced some level of metabolic loading and muscle damage; therefore, there is indeed a strong possibility that the activity of the III and IV afferents was increased. This interaction between muscle damage and reduced reflex sensitivity was more clearly demonstrated by Nicol et al. (1996) in their study of shorter and more intensive SSC exercise. However, the most convincing evidence for the reflex inhibition hypothesis in the present study was the recovery pattern of the maximal H-reflex peak-to-peak amplitude. When the blood supply was not restricted, the recovery of the H-reflex took place in about 3–4 min, similarly to the period reported by Bigland-Ritchie et al. (1986). However, no recovery was observed while the fatigue-induced metabolic accumulation was retained throughout ischemia. The same phenomenon was also demonstrated by Duchateau and Hainaut (1993).

The neuromuscular block was assumed to be one of the causes of fatigue during voluntary contractions (Krnjevic and Miledi 1958). This phenomenon has been associated with the effectiveness of electrical propagation across the neuromuscular junction and along the muscle surface membrane (Bigland-Ritchie and Woods 1984). However, neither a decline in the mass action potential (M-wave) nor force loss during high-frequency stimulation, which has been connected with the above mechanisms (Edwards et al. 1977), was observed after the present fatigue protocol. The force impairment must therefore be caused by some failure in the contractile properties of the muscle. This possibility is discussed only briefly in respect to low-frequency fatigue.

The present study demonstrated a significant reduction (18.0%) in the low-frequency stimulation torque. This decline has been defined as low-frequency fatigue, which is known to be pronounced during fatigue induced by eccentric muscle action (Newham et al. 1983). Low-frequency fatigue is thought to signify an impairment of excitation–contraction coupling, a process linking the action potential in the surface membrane with the activation of actomyosin by calcium (formation of cross-bridges) (Warren et al. 1993). This type of fatigue has been found to exist even after the muscle metabolites have recovered (Edwards et al. 1977), and it has also been described as long-lasting fatigue (Jones 1996). It has therefore been suggested that low-frequency fatigue is not simply a consequence of an impaired excitation–contraction coupling mechanism, but is also due to muscle damage caused by the exercise (Jones 1996). In the present study this was supported by a significant immediate and then delayed increase in S-CK activity after fatigue. Increased CK has been proposed as an indirect indicator of muscle damage (Newham et al. 1987).

In conclusion, the artificial fatigue stimulation of the calf muscles induced a clear impairment in neuromuscular function. The principal causes of the reduced force output seem to be related to an impaired excitation–contraction coupling mechanism or muscle damage. The possibility of central fatigue is also apparent, as shown by the increased enhancement in force immediately after fatigue due to the interpolated double stimuli. The origin of the decreased neural input seems to be the fatigued muscle itself via certain reflex pathways. The results of the H-reflex recovery appear to verify the importance of presynaptic inhibition of the Ia terminals through the activation of group III and IV afferents. However, the possibility of reduced spindle sensitivity, which leads to disfacilitation of the α-motoneurone pool, cannot be excluded.

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