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# Mechanisms contributing to knee extensor strength loss after prolonged running exercise

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**Millet, G. Y., V. Martin, G. Lattier, and Y. Ballay.** Mechanisms contributing to knee extensors strength loss after prolonged running exercise. *J Appl Physiol* 94: 193–198, 2003. First published September 20, 2002; 10.1152/japplphysiol.00600.2002.—The aim of this study was to identify the mechanisms that contribute to the decline in knee extensor (KE) muscles strength after a prolonged running exercise. During the 2 days preceding a 30-km running race [duration 188.7 ± 27.0 (SD) min] and immediately after the race, maximal percutaneous electrical stimulations (single twitch, 0.5-s tetanus at 20 and 80 Hz) were applied to the femoral nerve of 12 trained runners. Superimposed twitches were also delivered during isometric maximal voluntary contraction (MVC) to determine the level of voluntary activation (%VA). The vastus lateralis electromyogram was recorded. KE MVC decreased from pre- to postexercise (from 188.1 ± 25.2 to 142.7 ± 29.7 N·m; $P < 0.001$) as did %VA (from 98.8 ± 1.8 to 91.3 ± 10.7%; $P < 0.05$). The changes from pre- to postexercise in these two variables were highly correlated ($R = 0.88$; $P < 0.001$). The modifications in the mechanical response after the 80-Hz stimulation and M-wave peak-to-peak amplitude were also significant ($P < 0.001$ and $P < 0.05$, respectively). It can be concluded that *1*) central fatigue, neuromuscular propagation, and muscular factors are involved in the 23.5 ± 14.9% reduction in MVC after a prolonged running bout at racing pace and *2*) runners with the greatest KE strength loss experience large activation deficit.

low- and high-frequency electrical stimulation; central activation; M wave; electromyogram

SEVERAL HOURS OF RUNNING, highly strenuous stretch-shortening cycle exercise has large deleterious effects on the neuromuscular function. Muscle fatigue is often quantified as a reduction in the maximum force that a muscle can exert (8). The etiology of muscle fatigue is complex, especially under conditions of prolonged moderate-intensity exercise (4). In humans, integrative studies of such exercise are limited, so little is known about the origin of strength loss after prolonged exercise, especially for exercise using eccentric or stretch-shortening cycle contractions. For instance, it is established that muscular damage in lower limb extensor muscles occurred after 2–3 h of running (e.g., Ref. 13), but no experiment has been designed to determine whether the origin of strength loss (6, 15, 20, 27) is entirely due to these damages. In fact, muscle fatigue can be due to changes in a number of sites from the supraspinal level to subcellular damage of muscle fibers.

Several experiments have studied the effects of intense stretch-shortening cycle exercise lasting 1–8 min (e.g., Refs. 30, 31), and our laboratory recently examined the effects of an ultramarathon on muscular function (18, 19); however, to the best of our knowledge, no studies allow for an estimate of the relative roles of central and peripheral factors for fatigue induced by intermediate-duration running exercise. Nicol et al. (20) observed a decrease in integrated electromyography (iEMG) activity during maximal contractions after a marathon run; however, because the sarcolemmal excitability can be modified as well (25), it is not known whether decreases of iEMG are entirely explained by changes of M-wave amplitude after such long-term exercise or whether central fatigue really occurs for prolonged but not ultralong running exercise. Also, one experiment (6) has used electrical stimulation at different frequencies to better understand the underlying mechanisms of this type of fatigue. However, because the intensities of stimulation were submaximal in this study, complete recruitment of the muscle group was not ensured so that possible heterogeneity in damage may have compromised the validity of the approach (33). In addition, no data about the absolute changes in electrically evoked strength were given in that experiment (6). Thus the aim of the present experiment was to identify the mechanisms that contribute to the decline in muscle strength after several hours of running. For that purpose, voluntary and electrically induced (superimposed and on the relaxed muscle) contractions of knee extensor (KE) muscles were measured before and after a 30-km running race.

## METHODS

*Subjects.* Twelve trained male runners [age 37.8 ± 7.9 (SD) yr, mass 71.5 ± 5.5 kg, height 175.8 ± 3.9 cm], who competed on the regional to national level, completed the study. The event used in the study as a fatiguing exercise was 30-km-long trail race. The course started and finished at the same

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altitude, and the total amount of uphill throughout the entire course was 800 m. Written informed consent was obtained from the subjects. The study was conducted according to the Declaration of Helsinki. Approval for the project was obtained from the local Committee on Human Research.

Two testing sessions were conducted. The first one was performed during the 2 days preceding the race and started with a 10-min warm-up of running at a self-selected pace. Because the testing site was located nearby the finish line, the second session started <3 min after the race, i.e., the time taken for the experimental setup. The testing session postexercise lasted 7–10 min. Because the fatiguing exercise was a race, each subject was well motivated to perform maximally over the distance. This type of intensity normalization (see also Ref. 19) was chosen because subjects are not always motivated to perform near their maximal individual aptitudes during experimental procedures when long-duration exercise is required in the laboratory. It also takes into account the fact that selecting a percentage of maximal oxygen uptake has been questioned as a normalizing independent variable (10).

*Measurements of muscle contractile function.* All muscle contractile measurements were conducted on the right KE muscles with the subjects seated in a strength-training device (leg-extension machine). The knee angle was fixed at 90° (0° = knee fully extended). Velcro straps were used to stabilize the subject, and the mechanical response was recorded by a strain gauge (SBB 200 kg, Tempo Technologies, Taipei, Taiwan). The isometric contractions performed during the experiment included maximal voluntary contraction (MVC) and electrically evoked torque measurements.

MVC testing involved two trials. The subjects were strongly encouraged, and the best result was used for further analysis. KE maximal voluntary activation (%VA) was estimated by using a technique based on the interpolated-twitch method. Briefly, an electrically evoked twitch was superimposed to the isometric plateau. The ratio of the amplitude of the superimposed twitch over the size of the twitch in the relaxed muscle (control twitch) was then calculated to obtain %VA as follows

$$\%\,\mathrm{VA} = (1 - \text{superimposed twitch/mean control twitch}^{-1}) \cdot 100$$

The mean control twitch was a potentiated twitch (tw3; see Fig. 1) that was measured as explained below.

Electrical stimulations were delivered by using a high-voltage stimulator (model DS-7 stimulator, Digitimer, Herthfordshire, UK). During the preexercise tests, the amperage of a maximal 400-V rectangular pulse (500 μs) was progressively increased. It was considered that the optimal intensity, i.e., that which recruited all KE motor units, was reached when an increase in intensity did not induce a further increase in the twitch response and in the peak-to-peak amplitude (PPA) of the vastus lateralis compound muscle action potential (M wave; see *Electromyogram recording*).

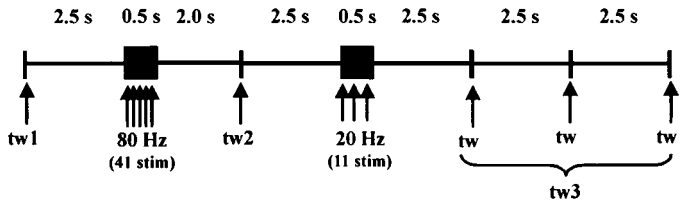


Fig. 1. Schematic view of the electrically induced contractions. tw1, First twitch; tw2, second twitch; tw3, third twitch [mean of last 3 twitches (tw)].

This individual optimal intensity was also used during the postexercise tests. The femoral nerve was stimulated by using a monopolar cathodal electrode (0.5-cm diameter) situated over the femoral triangle. The anode was a 10 by 5-cm rectangular electrode (Compex, Ecublens, Switzerland) located in the gluteal fold opposite the cathode. The electrically evoked torque measurements comprised five single twitches and two 0.5-s tetanic stimulations at frequencies of 80 and 20 Hz (i.e., 41 and 11 stimuli, respectively). Preexperimentation showed that 0.5 s was long enough to induce a plateau in the mechanical response. For the high-frequency stimulation, the torque corresponded to nearly 100% of MVC. The stimulations were delivered in the order presented in Fig. 1. The posttetanic potentiation was calculated as peak twitch torque ($P_t$) of the second twitch (tw2) divided by $P_t$ of first twitch (tw1) (see Fig. 1). The last three twitches were averaged, and this mean twitch (tw3) was considered as the control twitch for the calculation of %VA and for the comparison before and after the race.

The following parameters were obtained from the mechanical response of the evoked twitch: *1*) $P_t$ (see Fig. 2), i.e., the highest value of twitch torque production; *2*) twitch contraction time (CT), i.e., the time from the origin of the mechanical response to $P_t$; *3*) maximal rate of twitch torque development (MRTD), i.e., the maximal value of the first derivative of the torque signal; *4*) average rate of twitch torque development ($P_t$/CT); and *5*) maximal rate of twitch torque relaxation (MRTR), i.e., the most negative value of the first derivative of the torque signal. The highest value of tetanus torque production for the two frequencies investigated [80 Hz (P80) and 20 Hz (P20); see Fig. 2] and the P20/P80 ratio were considered. The maximal rates of tetanus torque development i.e., the maximal value of the first derivative of the torque signal, were also quantified for the two tetanic stimulations.

Right handgrip force was measured with a transducer (SBB 200 kg, Tempo Technologies, Taipei, Taiwan). Special attention was paid to the position of the fingers on the transducer. The subjects were instructed to produce two maximal isometric contractions for 2 s with a resting interval of ~10 s. The best result was retained.

*Electromyogram recording.* The electromyogram (EMG) signals of the right vastus lateralis were recorded by using bipolar silver chloride surface electrodes during MVC and percutaneous electrical stimulation. The recording electrodes were fixed lengthwise over the middle of the muscle belly with an interelectrode distance of 20 mm. The position of the electrodes was marked on the skin to fix them at the same place postexercise. The reference electrode was attached to the wrist of the opposite arm. Low impedance at the skin-electrode surface was obtained (<5 kΩ) by abrading the skin with emery paper and cleaning with alcohol. Myoelectrical signals were amplified with a bandwidth frequency ranging from 1.5 Hz to 2 kHz and simultaneously digitized on-line (sampling frequency 2,000 Hz). PPA and peak-to-peak duration of the M wave were determined during the maximal twitches. In addition, the root mean square (RMS) value was calculated during the MVC trials over a 0.5-s period after the torque had reached a plateau and before the superimposed stimulation was evoked. All mechanical and EMG data were stored with commercially available software (Tida, Heka Elektronik, Lambrecht/Pfalz, Germany).

*Statistical analysis.* All data presented are means ± SD. Each study variable was compared between pre- and postexercise with a Student's paired *t*-test (single-tailed). Correlation coefficients were calculated to determine the relationships between selected parameters. For all statistical

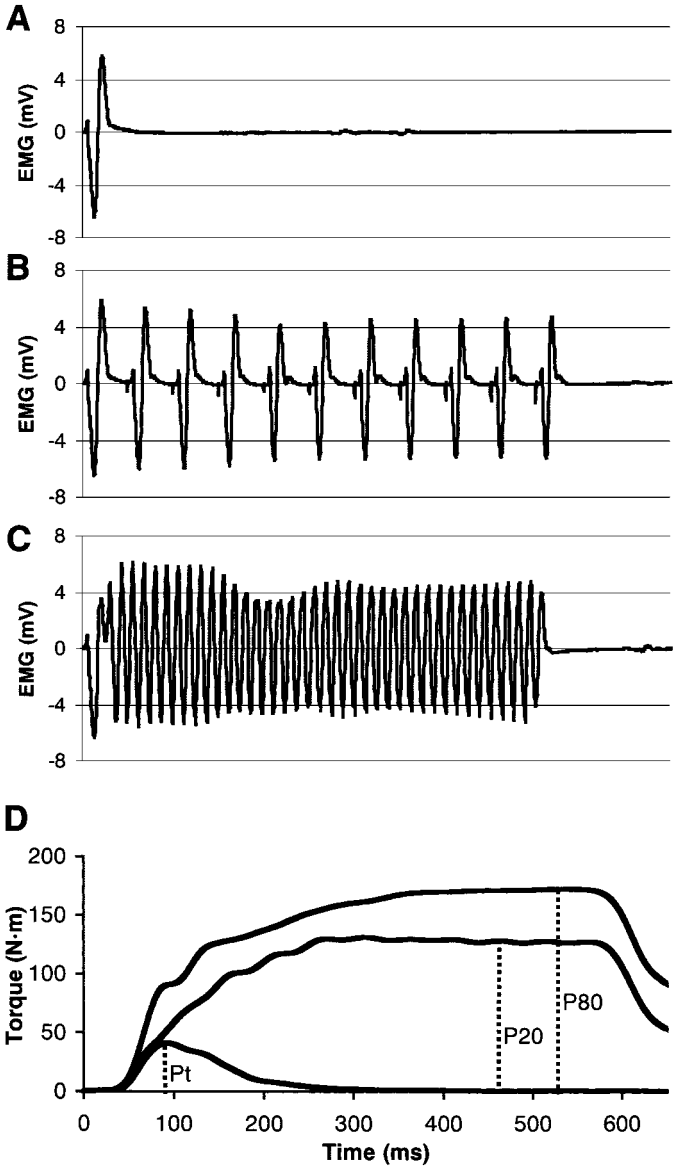


Fig. 2. Typical trace of the electromyogram (EMG) for a single twitch (*A*) and the 2 tetanic stimulations at 20 Hz (*B*) and 80 Hz (*C*). *D*: typical trace of a single twitch torque ($P_t$) and the torque evoked with the 20- and 80-Hz stimulation (P20 and P80, respectively).

analyses, a $P$ value of 0.05 was accepted as the level of significance.

## RESULTS

The time of the winner of the race, a national level runner, was 145.2 min, and the average time of the subjects participating to the study was 188.7 ± 27.0 min, i.e., 129.9 ± 18.6% of the winning time.

*MVC and maximal voluntary activation.* MVC decreased significantly from pre- to postexercise (from 188.1 ± 25.2 to 142.7 ± 29.7 N·m, −23.5 ± 14.9%; $P < 0.001$). Similarly, maximal voluntary activation was significantly higher before the race than after (from 98.8 ± 1.8 and 91.3 ± 10.7%, respectively; $P < 0.05$). RMS of the vastus lateralis during MVC decreased significantly from 0.60 ± 0.24 to 0.46 ± 0.18 mV (−20.9 ± 18.4%; $P < 0.01$) after the running exercise. In contrast, the handgrip force stayed at the same level before and after the race (149.3 ± 20.9 and 148.4 ± 13.1 N, respectively).

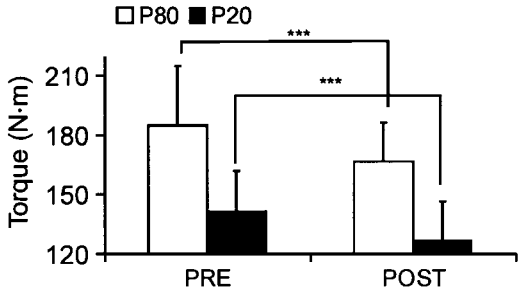


Fig. 3. Maximal mechanical response of the 80-Hz tetanus (P80) and the 20-Hz tetanus (P20) before (pre) and after (post) the running exercise. Values are means ± SD. ***Significant difference between pre- and postexercise, $P < 0.001$.

*Electrically evoked stimulation.* Preexercise, the torque evoked with 80-Hz stimulation (P80) reached 98.7 ± 8.1% MVC torque, showing that almost all motor units were recruited by the electrical stimulation. P80 and P20 decreased to a similar extent from pre- to postexercise (−9.0 ± 6.8 and −10.4 ± 7.1%, respectively; $P < 0.001$; Fig. 3) so that the P20/P80 ratio did not change significantly (77.0 ± 2.3 vs. 75.8 ± 4.4%).

The MVC/P80 ratio decreased from pre- to postexercise (from 101.9 ± 7.7 to 85.3 ± 18.3%, −16.4 ± 15.4%; $P < 0.01$). No changes were detected in maximal rates of contraction (2,836 ± 450 vs. 2,780 ± 657 $N \cdot m \cdot s^{-1}$ and 1,674 ± 348 vs. 1,757 ± 393 $N \cdot m \cdot s^{-1}$ for the 80- and 20-Hz tetanic stimulations, respectively; see Table 1 for MRTD).

The changes in MVC were correlated with the alterations in the level of voluntary activation ($R = 0.88$; $P < 0.001$; Fig. 4, *top*). A highly significant correlation was also found between the changes in MVC and the sum of the changes of %VA and P80 ($R = 0.89$; $P < 0.001$; Fig. 4, *bottom*). On the contrary, no relationship existed between MVC changes and P80 changes ($R = 0.53$; not significant).

Table 1 reports the changes in the evoked twitch torque. The posttetanic potentiation decreased signifi-

Table 1. *Main mechanical characteristics of the evoked twitch before and after the fatiguing exercise*

| | Before | After | Change % |
|---|---|---|---|
| $P_t$, N·m | 51.1 ± 8.4 | 46.3 ± 7.6 | −8.3 ± 14.6* |
| CT, ms | 94.3 ± 5.6 | 89.9 ± 6.4 | −4.6 ± 6.6* |
| RTD, $N \cdot m \cdot s^{-1}$ | 536 ± 94 | 516 ± 94 | −1.9 ± 19.6 |
| MRTD, $N \cdot m \cdot s^{-1}$ | 1,767 ± 335 | 1,729 ± 452 | −1.9 ± 18.2 |
| MRTR, $N \cdot m \cdot s^{-1}$ | 825 ± 203 | 746 ± 236 | −8.2 ± 22.0 |

Values are means ± SD. Pt; twitch peak torque; CT; contraction time; RTD, average rate of torque development; MRTD; peak rate of torque development; MRTR; peak rate of torque relaxation. Evoked twitch is mean of last 3 twitches (tw3) in Fig. 1. *Significant difference between the nonfatigued (before) and the fatigued condition (after), $P < 0.05$.

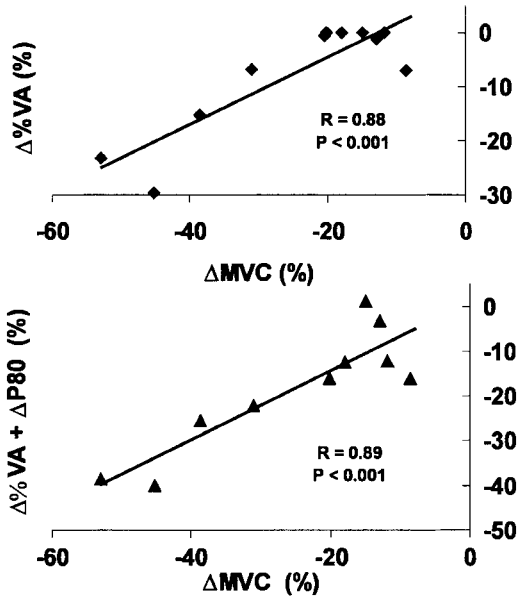


Fig. 4. Relationship between the changes in maximal voluntary contraction (ΔMVC) and *1*) the alterations in the level of voluntary activation (Δ%VA; *top*) and *2*) the sum Δ%VA plus the changes of maximal mechanical response of the 80-Hz tetanus (ΔP80; *bottom*).

cantly from pre- to postexercise (from 110.9 ± 10.4 to 103.9 ± 5.2%; $P < 0.01$; Fig. 5).

The M-wave PPA was lower after the race (8.9 ± 4.6 mV) than before (9.9 ± 4.9 mV; $P < 0.05$), but no relationship existed between MVC changes and M-wave PPA changes. The RMS/PPA ratio decreased from pre- to postexercise (0.068 ± 0.028 to 0.059 ± 0.022, −11.7 ± 24.8%; $P = 0.05$). Thus this ratio decreased to a lower extent compared with RMS but it still reached the level of significance. The M-wave peak-to-peak duration was not affected by the type of fatigue induced in this experiment (9.0 ± 2.5 vs. 8.9 ± 4.6 ms).

## DISCUSSION

The main results of the present study are that *1*) central fatigue, neuromuscular propagation, and muscular factors are involved in the 23.5 ± 14.9% reduction in MVC after a prolonged running bout at racing pace; *2*) subjects with the greatest KE strength loss after a prolonged running exercise experience large central fatigue; and *3*) when measured <10 min after the race, low-frequency fatigue (LFF) of the KE muscles is not detected despite muscular damage previously suggested for these muscles after prolonged running.

*MVC and maximal voluntary activation.* Maximal isometric knee extension force has been shown to decrease after a marathon on average by 26% (20). Similar strength loss has been observed after 4 h of treadmill running in another study (6). Our results are in good agreement with the findings of these two experiments. It is accepted that long-distance events reduce neuromuscular activity (e.g., Ref. 29), but, to the best of our knowledge, the present study is the first to demonstrate the occurrence of central fatigue after 2–3 h of running. In fact, Nicol et al. (20) observed a decrease in iEMG activity during maximal contractions after a marathon running, but a decrease in iEMG or RMS during MVC does not necessarily imply a higher central activation deficit with fatigue. For instance, we found that both the RMS of vastus lateralis and M-wave amplitude decrease by ~30% after a skiing marathon (19a), so that their ratio was unchanged. In the present study, three indexes of central fatigue demonstrate that part of the 23.5% strength loss measured can be explained by a lower activation of the KE during maximal contractions: *1*) the change in %VA measured with the interpolated-twitch method, *2*) the lower ratio of vastus lateralis RMS during MVC divided by the M-wave PPA, and *3*) the significant decrease of MVC/P80.

As recently reviewed by Gandevia (9), this central fatigue can originate from a supraspinal site and/or from the spinal level. Supraspinal fatigue after prolonged exercise has been linked to various hormones circulating in the cerebrospinal fluid (8). Particularly, the negative influence of serotonin has been previously suggested during prolonged exercises to explain the decrease in the corticospinal impulses (7, 16). In the present study, we measured the changes in strength of a muscle not implicated in the fatiguing exercise to further explore the origin of the lower central drive after the race. We hypothesized that a grip strength loss after running would be a good revealer of supraspinal fatigue. Because no changes were observed for grip force, this measurement did not allow us to conclude in any way regarding the existence of this fatigue after long-duration running exercise because selective supraspinal fatigue may have occurred. Because EMG of the knee flexors was not recorded, it is not known whether coactivation increased from pre- to postexercise. However, it is likely that feedback transmitted by small-diameter muscle afferents, known to alter descending drive and to inhibit group Ia input and thus to depress the excitability of motoneurons (8, 9), can ex-

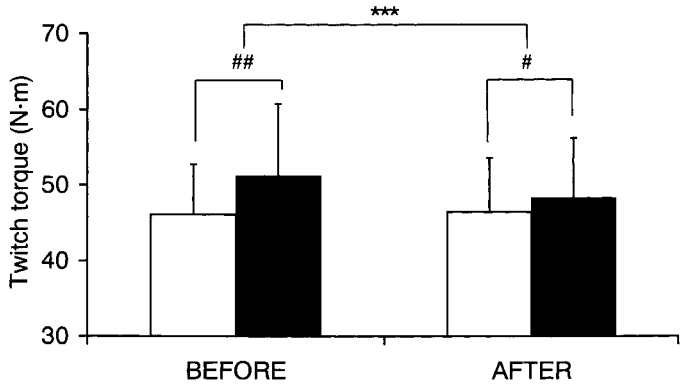


Fig. 5. Maximal mechanical response of the nonpotentiated (tw1; open bars) and the potentiated twitch (tw2; solid bars) before and after the running exercise. Values are means ± SD. ***Significant difference of the ratio $P_t$ tw2/$P_t$ tw1 between pre- and postexercise, $P < 0.001$. Significant difference of $P_t$ between tw1 and tw2: #$P < 0.05$, ##$P < 0.01$.

plain a large part of the central fatigue observed in the present study. The cytokines and other metabolic products such as extracellular $K^+$ (e.g., Ref. 5) can stimulate the group III and IV afferents. Because it has been shown that interleukin-6 can be observed in plasma as early as 30 min after the beginning of a running exercise (22) and that extracellular $K^+$ was increased after marathon running (26), these small-diameter afferents are probably implicated in the decrease of central activation. Finally, the role of the fusimotor system in the decreased %VA must be considered because Avela et al. (3) have recently shown that prolonged passive muscle stretching induced stretch-reflex disfacilitation.

*Electrically evoked stimulation.* In addition to central activation, force is controlled by neuromuscular propagation and cellular mechanisms. Several potential impairments such as depletion of neurotransmitter or reduction of the sensitivity of the postsynaptic receptors can explain the alteration of the neuromuscular propagation (8). However, the lower M-wave amplitude found after running in the present study is likely due, at least partly, to the depressed conduction of the action potential along the sarcolemma (17). In fact, the lower muscle fiber excitability could originate from a reduced chemical gradient for $Na^+$ and $K^+$ across the membrane. Particularly, it has been shown that prolonged exercise can lead to loss of $K^+$ from working muscles as reflected by the increased concentration of plasma $K^+$ after marathon running (26). Recent studies on humans have shown that in the interstitium surrounding the fibers, the rise in extracellular $K^+$ concentration may be larger than in the plasma, indicating that the muscle fibers undergo a more pronounced reduction in the chemical gradient for $K^+$ than estimated from the rise in plasma (21). It is known that the ability to sustain action potentials at high frequency primarily depends on the ability to resequester $K^+$ back to the cell (11).

To the best of our knowledge, this study is the first to apply maximal stimulation to the KE muscles at low and high frequency after prolonged running exercise so that comparisons with other experiment are not possible. The value of P20/P80 at rest is consistent with previous studies conducted on KE muscles (e.g., Ref. 6), but this ratio did not change from pre- to postexercise. LFF, also called long-lasting fatigue, is known to result from eccentric and intense stretch-shortening cycle exercises (e.g., Refs. 28, 31). LFF is generally viewed as involving impaired excitation-contraction coupling and structural damage (1, 17). Despite the existence of muscular damages after marathon running (e.g., Refs. 13, 23), no LFF was detected in the present study. It is worth noting that in the recent study of Kyparos et al. (12), rough recalculation of the decreases in evoked forces immediately after 90 min of intermittent running downhill in the rat soleus muscle does not evidence LFF. Several explanations can be suggested to explain the lack of LFF in the present study, such as the fact that type I fibers, known to be present in high proportion in long distance runners' KE muscles, are less sensitive to mechanical stress than fast-twitch fibers (32). However, the main hypothesis deals with observations of the respective modifications in tw1 and tw2 and the fact that postexercise measurements were performed <10 min after the race. This suggests that exercise may have potentiated the 20-Hz contraction torque and thus may have hidden LFF. Additional measurement of force at 20 and 80 Hz still has to be performed 20–30 min after the race when twitch potentiation caused by the event would be recovered. As a consequence, the lack of LFF does not allow for complete certainty that a failure of the excitation-contraction coupling did not occur.

The intracellular mechanisms also implied the force produced by the cross bridges (2). It is of interest to note that the decrease in %VA and in P80 (−7.5 and −9%, respectively) did not explain totally the 23.5% KE strength loss. In addition, the correlation between MVC changes and the sum of the changes of %VA and P80 (Fig. 4, *bottom*) was $R = 0.89$ showing that the decrease in the level of maximal activation and alteration of intrinsic muscle properties can account for ~80% of strength loss. These two results suggest that other factors played a role in MVC decrease. As discussed above, the sarcolemma excitability probably explains part of this difference, but an increase in cocontraction or a worth synergy between agonist muscles cannot be ruled out.

The lower $P_t$ found postexercise is in line with the lower P20 value and is also consistent with previous experiments studying twitch mechanical response after exercise lasting 1–2 h (e.g., Ref. 14). Single-twitch tension results from potentiation- and fatigue-associated effects, and the net result depends on their sum so that peripheral fatigue cannot be detected from this measure. For that reason, we also measured tetanic torques in the present study. Interestingly, KE torque resulting from a single twitch was not increased in the present study as it was after an ultramarathon, confirming the specificity of the fatigue due to ultralong exercise that we recently suggested (19). When further exploring the differences in adaptations after a 65-km ultramarathon (see Ref. 19) and the present 30-km race performed in similar conditions, it must be noted that the strength loss was only slightly higher after the 65-km than after the 30-km run (−30.2 vs. −23.5%), whereas the activation deficit was almost four times greater postexercise for the ultramarathon (− 27.7 vs. −7.6%). Of importance is the fact that the method used (i.e., the twitch interpolation) and the rest period after the exercise were comparable. Also, the M-wave amplitude was not affected for the vastus lateralis muscle after the 65-km race, which is different from the present study because a minor but significant decrease of M-wave PPA was observed. On the contrary, neither the ultramarathon nor the 30-km race affected the M-wave peak-to-peak duration. Unfortunately, tetanic stimulations and handgrip force were not measured in our laboratory's previous study (19).

In conclusion, central fatigue as well as alteration of neuromuscular propagation and muscular properties

are involved in the 23.5% reduction in KE MVC after a 30-km running bout. The present results also show that runners with the greatest strength loss experience large activation deficit. Finally, a prolonged running exercise at race pace does not induce LFF of the KE muscles when measured <10 min after the event. However, it is possible that postexercise potentiation has hidden the failure of the excitation-contraction coupling that was expected after such long duration exercise.

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