REVIEW ARTICLE

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Alterations of Neuromuscular Function After Prolonged Running, Cycling and Skiing Exercises

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Abstract

It is well known that impairment of performance resulting from muscle fatigue differs according to the types of contraction involved, the muscular groups tested and the exercise duration/intensity. Depending on these variables, strength loss with fatigue can originate from several sites from the motor cortex through to contractile elements. This has been termed 'task dependency of muscle fatigue'.

Only recently have studies focused on the origin of muscle fatigue after prolonged exercise lasting 30 minutes to several hours. Central fatigue has been shown to contribute to muscle fatigue during long-distance running by using different methods such as the twitch interpolation technique, the ratio of the electromyogram (EMG) signal during maximal voluntary contraction normalised to the M-wave amplitude or the comparison of the forces achieved with voluntary- and electrically-evoked contractions. Some central activation deficit has also been observed for knee extensor muscles in cycling but central fatigue after activities inducing low muscular damage was attenuated compared with running. While supraspinal fatigue cannot be ruled out, it can be suggested that spinal adaptation, such as inhibition from type III and IV group afferents or disfacilitation from muscle spindles, contributes to the reduced neural drive after prolonged exercise. It has been shown that after a 30km run, individuals with the greatest knee extensor muscle strength loss experienced a significant activation deficit. How-

ever, central fatigue alone cannot explain the entire strength loss after prolonged exercise. Alterations of neuromuscular propagation, excitation-contraction coupling failure and modifications of the intrinsic capability of force production may also be involved. Electrically-evoked contractions and associated EMG can help to characterise peripheral fatigue. The purpose of this review is to further examine the central and peripheral mechanisms contributing to strength loss after prolonged running, cycling and skiing exercises.

Muscle fatigue is a complex phenomenon that can be appreciated through the inability to sustain further exercise at a required power[1] or through the reduction in the maximum force that a muscle can exert.[2] Muscle fatigue may develop during high- as well as low-intensity exercise and the origin depends on the intensity and duration of exercise. In the literature, there is a lack of integrative studies involving human study participants for exercises of duration equal to or longer than 30 minutes. In addition, most studies examining this type of fatigue have focused on inflammation[3] or endocrine/energetic aspects,[4,5] therefore, little is known about the origin of fatigue after prolonged exercises in running, cycling or skiing. Fatigue can originate from several potential sites that are usually divided in sites located proximal (central fatigue) or distal (peripheral fatigue) to the neuromuscular junction. This distinction is not new as it was considered in 1931 by Brainbridge[6] but has not been applied for prolonged exercise until recently.

It is generally accepted that fatigue due to short-term exercise is mainly caused by metabolic factors or muscular damage if eccentric contractions are involved. During prolonged exercise, the aetiology of muscle fatigue is more multifaceted. It has been suggested that central fatigue may develop during prolonged exercise[7,8] and that metabolic (e.g. glycogen depletion or intracellular Ca^{2+} accumulation) as well as structural changes[3,9-11] may be involved in muscle fatigue after long-duration exercise. No studies had demonstrated the existence of central fatigue for prolonged exercise until the end of the last decade; however, recent works have shown lower central activation after cycling[12,13] or running[14,15] for 30 minutes to several hours duration. Muscle fatigue, especially peripheral fatigue, also depends on the type of muscular contraction. For example, it is well known that muscular damage can exist after eccentric contractions are performed. It has been suggested that the excitation-contraction (E-C) coupling failure is due, at least partly, to physical disruption of the membrane systems involved in the E-C coupling process.[16] Since low-frequency fatigue (LFF, also called long-lasting muscle fatigue) is connected to E-C coupling failure, it has been related to mechanical damage.[17] Only a few studies have focused on the force-frequency relationship after prolonged exercise for the quadriceps muscles.[15,18,19] Surprisingly, no LFF has been observed in these experiments despite the existence of muscular damage after long-distance running.[3,10,11,20]

The aims of this review are: (i) to analyse the lower limbs extensor strength loss after a bout of exercise from 30 minutes to several hours in three different cyclic activities, namely cycling, running and cross-country skiing; and (ii) to examine the origin of neuromuscular fatigue after these prolonged exercises. For clarity, the origins of strength loss after long-duration exercise were divided in central and peripheral components.

1. Strength Loss After Prolonged Exercise

Over the past years, several studies have measured knee extensor muscle strength loss after prolonged exercise. After running exercise of longer than 2 hours, the isometric strength loss increased in a non-linear way with the exercise duration (figure 1) and a similar trend can be noted after cross-country skiing events (table I). Of note is the fact that in these running and cross-country skiing studies, exercise intensity was based on the best per-

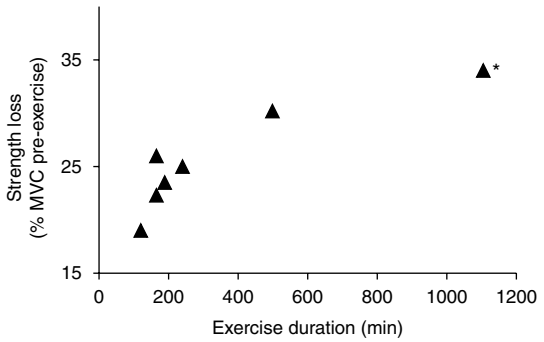

Fig. 1. Relationship between the knee extensor muscle strength loss expressed as a percentage of maximal voluntary contraction (MVC) at rest and the duration of running exercise.[14,15,19,21-23] * indicates value is from unpublished observations.

formance on the considered distance/duration.[14,15,18,19,21-24] However, the same relationship between exercise duration and strength loss does not exist in cycling (table I). The discrepancy is probably not related to differences between activities (e.g. type of contraction) but linked to the type of fatiguing exercise. In fact, in the two studies[25,26] where large strength losses were measured, the intensity (75% maximal oxygen uptake [$\dot{V}O_{2max}$]) was lower than in the experiments of Lepers et al.[12] and Bentley et al.[27] (80% $\dot{V}O_{2max}$) but the study participants were requested to pedal until exhaustion.

The type of muscular contraction performed during the evaluation will determine the reduction in strength. Generally, the strength loss seems to be lower in concentric than in isometric contractions. Table I illustrates this trend for cycling and cross-country skiing. A similar result was found for running since the maximal voluntary contraction decrease was found to amount to 19%, 14%, 13% and 11% at 0 °/sec, +60 °/sec, +120 °/sec, +180 °/sec, respectively.[21] The reasons for this lower strength loss for the concentric contraction are unclear.

The majority of experiments dedicated to fatigue after prolonged exercise have focused on knee extensor muscle strength loss but we are aware of two studies that have measured deterioration of muscle function for plantar flexor muscles. Avela and coworkers reported that maximal voluntary contraction (MVC) for this muscular group decreased by almost 30% immediately after a marathon.[30] An 8.5% triceps surae strength loss was also found by Davies and White after 1 hour of treadmill running at 80% $\dot{V}O_{2max}$.[31] Whatever the muscular group considered, MVC decrease can originated from several potential sites that are usually divided in central and peripheral fatigue. In the definition of central fatigue used in the present paper, both supraspinal and spinal mechanisms are considered, with the latter including positive (facilitations) or negative (inhibitions) influence from peripheral sensors.

Table I. Mean values of knee extensor muscle strength loss after different types of cycling and cross-country (X-C) skiing exercise

Study	Exercise	Duration and intensity	Strength loss (%)				
			isometric	concentric (°/sec)			eccentric (°/sec)
			0	60	120	180	−60
Lepers et al.[13]	Cycling	5h, 55% $\dot{V}O_{2max}$	18		9		
Lepers et al.[28]	Cycling	2h, 70% $\dot{V}O_{2max}$	13	12	15		12
Sahlin and Seger[25]	Cycling	1h 25 min, 75% $\dot{V}O_{2max}$[a]	34	26			20
Booth et al.[26]	Cycling	1h 12 min, 75% $\dot{V}O_{2max}$[a]	28				
Lepers et al.[12]	Cycling	30 min, 80% $\dot{V}O_{2max}$	13		9		
Bentley et al.[27]	Cycling	30 min, 80% $\dot{V}O_{2max}$	13	12	NS	NS	
Viitasalo et al.[24]	X-C skiing	5h 30 min race[b]	10			7	
Forsberg et al.[29]	X-C skiing	4–8h race				12	
Millet et al.[15]	X-C skiing	2h 40 min race	8				

a Exercise performed until exhaustion.

b Strength measured 1–2h after the end of the race.

NS = not significant; **$\dot{V}O_{2max}$** = maximal oxygen uptake.

2. Central Fatigue

2.1 Electromyogram and Central Activation Deficit

While the development of central fatigue during prolonged exercise has been suggested for several years,[7] no evidence for central origin of fatigue after prolonged exercise has been published until recently. A decrease in integrated electromyography (iEMG) activity during MVC was recorded for quadriceps muscles after marathon running[22] and long-distance cross-country skiing.[24] However, since the sarcolemmal excitability can be modified as well,[32] it was not known if decreases of iEMG were entirely explained by changes of maximum compound motor unit action potential (M-wave) amplitude after these long-term exercises or if central fatigue really occurred. In fact, when an electromyogram (EMG) value during MVC is used to evaluate the existence of central fatigue, this value needs to be normalised by the maximal M-wave for the muscle. The ratio of the root mean square (RMS) of the EMG signal during MVC divided by the M-wave amplitude (RMS/M) is generally used in the literature. A large difference between changes in RMS and changes in RMS/M can be observed with fatigue, showing that RMS or iEMG during MVC are not good evidences of central fatigue. For instance, Viitasalo et al.[24] found a 30–35% lower iEMG activity for vastus lateralis and vastus medialis muscles during maximal isometric contraction after an 85km ski race. However, this result does not conclude that neural input reaching the neuromuscular junction was decreased. In fact, in a recent study examining the effects of marathon skiing, we measured similar decrease of RMS for vastus lateralis muscle,[18] but the M-wave amplitude also declined to about 30% so that the ratio RMS/M was not modified (figure 2). Similarly, Lepers et al.[28] found that RMS of vastus lateralis and vastus medialis muscles decreased by about 10% after a 2-hour cycling exercise but the M-wave amplitude declined by a similar extent indicating that central fatigue did not contribute to the reduction in force. In contrast, the RMS/M value was found to be lower post-exercise after a 30km running race compared with pre-exercise evaluation.[15]

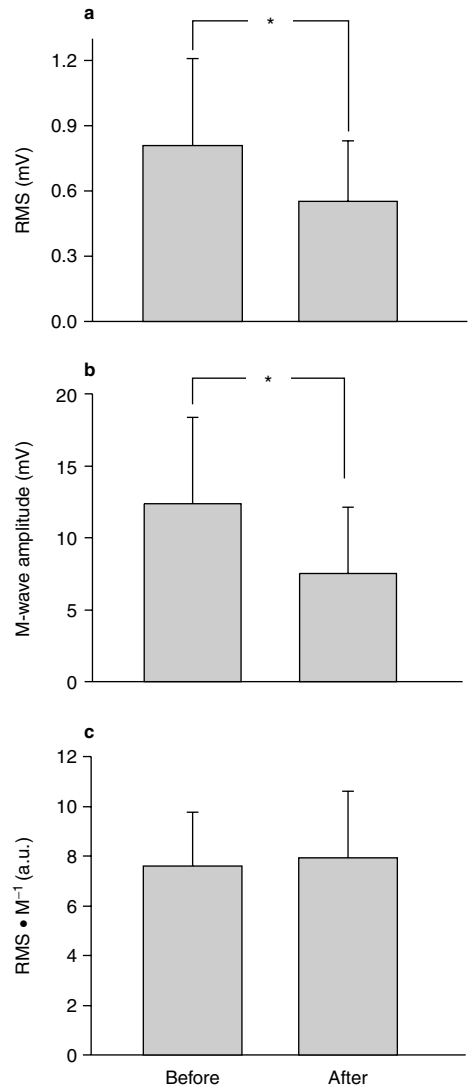

Fig. 2. Mean (± standard deviation) values of (**a**) root mean square (RMS); (**b**) peak-to-peak amplitude of the compound muscle action potential (M-wave amplitude); and (**c**) the ratio of theses two factors (RMS/M) for the vastus lateralis before and after a marathon skiing competition. There is a significant difference between the non-fatigued (before) and the fatigued condition (after). * $p < 0.01$.

There are other techniques that quantify central fatigue and at least two of them have been used after prolonged exercise. The first method consists of a comparison of the forces achieved with voluntary-

and electrically-evoked contractions. According to Duchateau and Enoka,[33] this method is the preferred one for assessing changes in muscle activation. In that sense, it was found that the ratio between knee extensor muscle MVC and mechanical response to a stimulation at 80Hz decreased after a 30km run from 101.9 ± 7.7% to 85.3 ± 18.3% ($p < 0.01$).[15] However, by far the most popular method used in the literature to reveal an activation deficit is the twitch superposition (or interpolation) technique.[34] Central fatigue can be measured by comparing the twitch superimposed to a MVC (see figure 3, panel b) and the twitch evoked on the muscle relaxed. Using this technique, the development of central fatigue after a 30km and a 65km race was demonstrated.[14,15] Interestingly, the strength loss was only slightly higher after the longer than after the shorter race (−30.2% vs −23.5%) while the activation deficit was almost four times greater after the 65km race (−27.7% vs −7.6%). It has been suggested that the reduced maximal voluntary activation in the fatigued state could protect the neuromuscular system because continuing to drive to the muscle would put the muscle fibres into a catastrophic state, one from which the recovery was delayed or impossible.[35] Alternatively, it has been argued that a reduced central activation may be necessary to protect the body under specific conditions.[36] For instance, it could prevent glucopaenic brain damage during prolonged exercise when hypoglycaemia results from liver glycogen depletion.

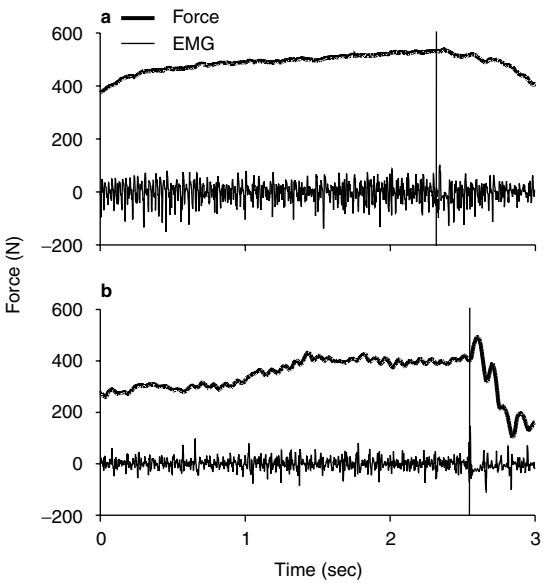

Fig. 3. Typical force trace during knee extensor muscle maximal voluntary contraction (MVC) and maximal activation determination before (**a**) and after (**b**) an ultra-marathon. An electromyogram (EMG) of the vastus medialis is represented to visualise the time of the superimposed twitch.

2.2 Spinal and Supraspinal Factors

By measuring an activation deficit with the twitch interpolation technique at the peripheral nerve or muscle or with other techniques described in section 2.1, it was not possible to determine if the central fatigue originates from a supraspinal site and/or from the spinal level.[35] In a recent study, we measured the changes in strength of a muscle not involved in the fatiguing exercise to further explore the origin of the lower central drive post-exercise. We hypothesised that a grip strength loss after running would be a good revealer of supraspinal fatigue. No changes were observed in grip strength in this study but this measurement did not conclude the absence of supraspinal fatigue after a 30km run because selective supraspinal fatigue may have occurred. However, we believe that it is worthwhile to perform this type of simple measurement to further explore the potential existence of supraspinal fatigue after longer exercise, e.g. an ultra-marathon.[8] One hypothesis to explain supraspinal fatigue, namely the serotoninergic hypothesis,[37,38] is based on the increased concentration of free tryptophan (the serotonin precursor) in the brain during prolonged exercise. The increase of free tryptophan could occur for two reasons. Firstly, a lower plasmatic branched-chain amino acid concentration since these amino acids are oxidised for energy in contracting skeletal muscles with low glycogen stores. In fact, the theoretical consequence of this lower plasmatic branched-chain amino acid concentration is a higher concentration of brain tryptophan because this amino acid shares the same blood/brain barrier mechanism with branched-chain amino acids. Secondly, an increase in plasma free fatty acid concentration during prolonged exercise.[8,35] This

may cause a parallel increase in free tryptophan since free fatty acids displace tryptophan from the usual binding sites on albumin molecules. Regarding this latter point, it is worthy to report our findings showing that the respiratory exchange ratio of study participants running an ultra-marathon decreased from 0.92 ± 0.06 to 0.79 ± 0.04 at a given submaximal intensity, suggesting a higher oxidation of free fatty acids.[39]

Cycling exercise involves mainly concentric contractions and therefore induces lower muscular damage compared with running. For cycling exercises where intensity and duration are similar to the running studies quoted in section 2.1,[14,15] central fatigue was not detected[28,40] or was lower[13] compared with running. The results of another study from our group[18] agree with these observations. We have previously shown that ski skating involves a stretch-shortening cycle type of contraction for lower limb extensor muscles.[41,42] However, running and skiing are different in that no shock waves exist in ski skating, thus muscular damage is considerably lower. When comparing marathon skiing[18] and 30km running[15] of similar duration with both performed in racing conditions, there is a large difference in strength loss (−8.4 ± 8.7% vs −23.5 ± 14.9%, respectively) and, more importantly, there is a large difference in activation deficit between the two exercises (figure 4). This confirms that fatigue is task dependent.[2] Also, this allows speculation about the relative influence of supraspinal or spinal factors for exercise of that duration (2–3 hours). In fact, changes in cortical excitability *per se* are not necessarily the only cause of central fatigue. It has been suggested that neurally mediated afferent feedback from the muscle (i.e. presynaptic inhibition and fusimotor system disfacilitation) plays a part in the inhibition of motoneuron excitability. Since two exercises with similar duration in racing conditions but where muscle damage was not the same have different consequences in terms of central fatigue, these results favour spinal modulation rather than supraspinal alterations after the running exercise.[15] This conclusion is consistent with an experiment suggesting that marathon running induced disfacilitation and presynaptic inhibition of motoneuron α.[30] Particularly, the role of fatigue of intrafusal fibres themselves has been emphasised in this study.

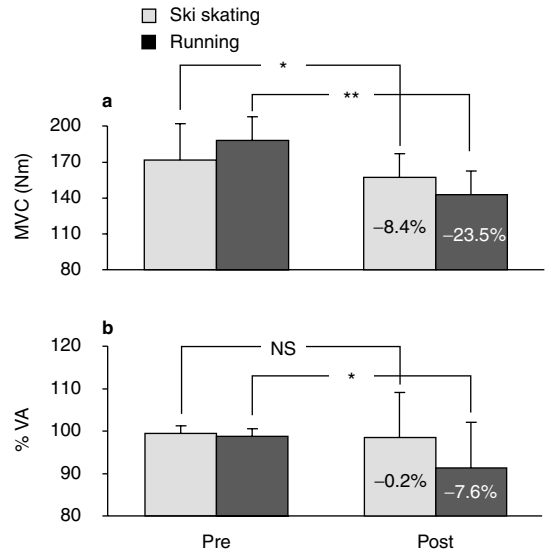

Fig. 4. Mean (± standard deviation) values of knee extensor muscle maximal voluntary contraction (MVC) and maximal voluntary activation (%VA) before (pre) and after (post) a 30km run (running) and a marathon ski (ski skating) of similar duration performed in racing conditions. **NS** = not significant; * $p < 0.05$; ** $p < 0.001$.

Paradoxically, a significant activation deficit after a cycling exercise, i.e. an exercise inducing much less damage than running,[12] has also been observed. However, this result, which is in line with the work of Bentley et al.,[27] does not necessarily contradict the above conclusion because the intensity requested in these two studies[12,27] was 80% of the study participants' maximal aerobic power. Therefore, it is possible that the higher activation deficit in the fatigued state was also due to muscle afferent inputs because it is known that among the factors that cause an increase of the group III and IV afferents discharge are metabolite accumulation and ischaemia.[35] These two conditions probably occur at a high mechanical power in cycling.

A significant relationship was found between MVC decrease and alterations in the level of voluntary activation after a prolonged running exercise.[15] The authors concluded that runners with the greatest knee extensor muscle strength loss experienced a

Table II. Mean (± standard deviation) values of pre-exercise, post-exercise and changes between pre- and post-exercise for M-wave PPA and PPD in different exercises lasting 30 minutes to several hours

Study	Duration (min)	Activity	PPA			PPD		
			pre (mV)	post (mV)	ΔPPA (%)	pre (ms)	post (ms)	ΔPPD (%)
Lepers et al.[12]	30	Cycling	10 ± 1	10 ± 1	−3 ± 7	9 ± 2	9 ± 3	1 ± 15
Lepers et al.[28]	120	Cycling	13 ± 5	11 ± 4	−13 ± 10	9 ± 1	11 ± 3	24 ± 15*
Millet et al.[18]	160	Ski skating	12 ± 6	7 ± 5	−29 ± 24**	7 ± 1	7 ± 3	4 ± 26
Millet et al.[15]	190	Running	10 ± 5	9 ± 5	−9 ± 18*	9 ± 3	9 ± 2	2 ± 19
Lepers et al.[13]	300	Cycling	9 ± 1	8 ± 2	−9 ± 14	9 ± 2	10 ± 2	5 ± 20
Millet et al.[14]	510	Running	12 ± 4	11 ± 4	1 ± 36	8 ± 2	9 ± 3	16 ± 22

PPA = peak-to-peak amplitude; **PPD** = peak-to-peak duration; Δ**PPA** = change in PPA; Δ**PPD** = change in PPD; * $p < 0.05$; ** $p < 0.01$.

large activation deficit. However, central fatigue alone cannot totally explain strength loss after prolonged exercise. Alterations of neuromuscular propagation, E-C coupling failure and modifications of the contractile apparatus may also be involved.

3. Characterisation of Peripheral Fatigue

3.1 Neuromuscular Propagation

Surface EMG recordings during evoked contractions have been used to explore neuromuscular propagation alteration after prolonged exercise. In particular, muscle compound action potential (M-wave) has been considered. M-wave characteristics can be affected by the synchronisation of muscle fibre action potentials or the degree of dispersion in the release of transmitters from motor nerve terminals.[43] According to some authors, changes of M-wave characteristics do not reflect modifications of intracellular action potential.[44] During prolonged exercise, muscular oedema and sweat can complicate interpretation of the EMG signal. Nevertheless, M-wave is commonly used in human fatigue experiments as an index of neuromuscular transmission and action potential propagation in muscle fibres.[45]

Table II summarises the changes in the maximal M-wave peak-to-peak amplitude and duration for the vastus lateralis muscle in six studies recently conducted by our group after prolonged exercise.[12-15,18,28] When significant changes were observed, there was: (i) a decrease in amplitude; and (ii) a moderate increase of duration. However, table II shows that M-wave is not always significantly altered by prolonged exercise. Also, there were large differences in the M-wave alterations between study participants after exercise.

Plasmatic [K+] increases after long-duration exercise.[11,46] Since the rise in [K+] in the interstitium surrounding the fibres may be larger than in the blood,[47] the muscle fibres undergo a more pronounced reduction in chemical gradient than estimated from the plasmatic [K+]. The consequence is alteration of sarcolemmal excitability[48] or tubular system excitability[49] so that large alterations of sarcolemmal excitability were anticipated after prolonged exercise. However, the moderate changes of M-wave characteristics shown in table II and also found in the study of Avela et al.[30] suggest that sarcolemmal excitability does not play a fundamental role in fatigue for such exercise, as it could be during high-intensity contractions.[50] Interestingly, it has been shown that the concentration of muscle Na^+-K^+ pumps increased after a 100km run.[11] In addition, it has been recently suggested that elevated [K+] is of less importance for fatigue than indicated by previous studies on isolated muscles.[51] However, the individuals participating in the studies described above[12-15,18,28] were endurance-trained athletes. Since training increases the concentration of Na^+-K^+ pumps,[47,52] it is possible that a different conclusion would have been reached with sedentary study participants. The influence of sarcolemmal excitability changes on performance deterioration is likely dependent on the training status of the study participants.

3.2 Twitch Mechanical Response

It has been shown that stiffness of the series elastic component can be altered with training[53] and also with fatigue.[54] Despite the influence of stiffness alteration on the evoked twitch mechanical response (Pt), it has been proposed to use Pt to measure fatigue of the quadriceps group.[55] Recent observations did not support this assertion. While Pt was found to decrease after prolonged cycling exercise,[12,13] we measured a 22–35% Pt increase after an ultra-marathon.[14] This latter result was unexpected because it has been shown that glycogen depletion was associated with depressed force, lower Ca^{2+} release and inhibited contractile protein,[56] and because of muscle damage after such a long-distance run.[9] Also, Pt increased by 8% after a ski skating marathon while there was a slight and non significant decrease of force evoked by a train of stimulation at 80Hz.[18] Pt can be affected by a modification of series elastic component stiffness and the net twitch tension also depends on potentiation- and fatigue-associated effects. In particular, we hypothesised that phosphorylation of myosin light chain, which is known to induce a higher Ca^{+} sensitivity and ATPase activity, could explain the higher Pt in the fatigued state after these two long-distance exercises. Thus, an increase in peak twitch tension is not necessarily associated with enhanced neuromuscular function.

To further examine the significance of the twitch modification with fatigue, we compiled the results from studies of our group where voluntary and evoked torques at 20 and 80Hz (figure 5) were measured before and after a fatiguing exercise. These exercises were as follows: a 30km run;[15] a marathon ski skating;[18] an intermittent running exercise at 120% of $\dot{V}O_{2max}$;[57] and intermittent one-legged downhill running exercise on an inclined treadmill.[57] As shown in figure 6 (panels a and b), there were no significant relationships between the changes of torque evoked by a twitch (ΔPt) and the changes in MVC or torque evoked by a high-frequency tetanus. In contrast, significant correlations were found between ΔPt and: (i) the changes of torque evoked by a low-frequency tetanus (figure 6, panel c); or (ii) the modifications of the ratio of the torque evoked by a low-frequency tetanus divided by the torque evoked by a high-frequency tetanus (figure 6, panel d). It can be concluded that Pt alterations cannot be considered as a general index of peripheral fatigue as previously suggested but only reflects the low-frequency stimulation evolution that is thought to be primarily the result of an impairment of E-C coupling. These conclusions are consistent with those of Binder-MacLeod et al.[58] after fatigue induced by electrical stimulation.

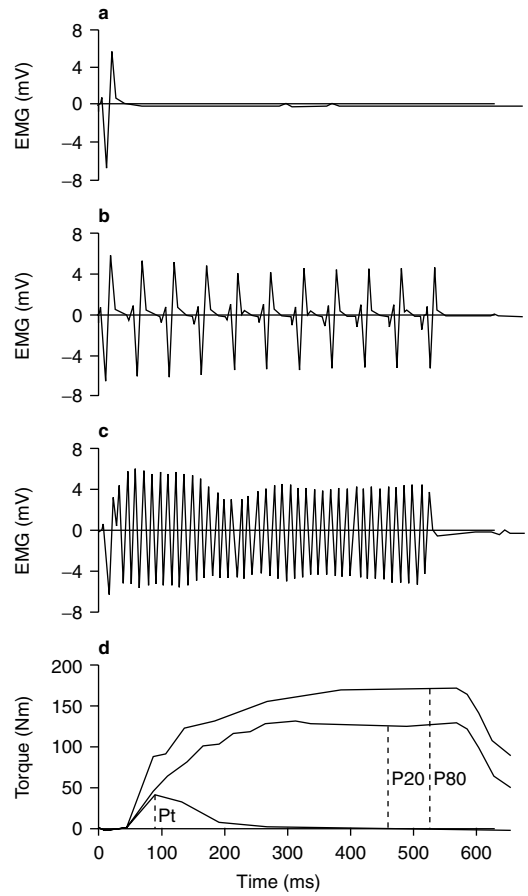

Fig. 5. Typical trace of the vastus lateralis electromyogram (EMG) for a single twitch (**a**) and two tetanus twitches at 20Hz (**b**) and 80Hz (**c**). (**d**) represents a typical trace of a single twitch torque (Pt) for the knee extensor muscle and the torque evoked with a 20Hz and 80Hz stimulation (P20 and P80, respectively).

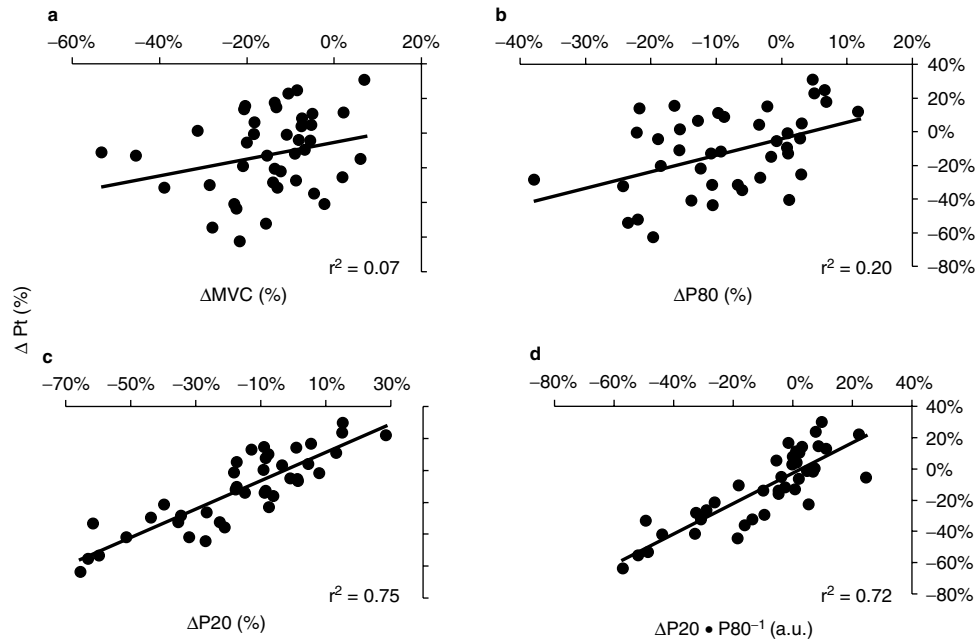

Fig. 6. Relationships between the changes due to fatigue in twitch mechanical response (ΔPt) and the changes in (**a**) maximal voluntary contraction (ΔMVC), (**b**) mechanical response to a 0.5-second tetanus at 80Hz (ΔP80), (**c**) mechanical response to a 0.5-second tetanus at 20Hz (ΔP20) and (**d**) P20 • P80^{-1} ratio.

3.3 High- and Low-Frequency Fatigue

No changes in torque evoked by a high-frequency (80Hz) torque have been observed after prolonged cycling or skiing exercise.[18,40] In contrast, a significant decrease of the high-frequency evoked torque ($-9.0 \pm 6.9\%$, $p < 0.001$) was observed after a 30km run.[15] Then, it appears that for prolonged exercise, failure of the myofibrillar apparatus is explained by muscle damage due to eccentric contractions and shock wave rather than metabolic changes.

LFF, i.e. a large decrease of force evoked by a stimulation at low frequency with fatigue together with no or smaller change in force evoked by a stimulation at high frequency, is generally considered to reflect E-C coupling failure. For example, a recent experiment has established a correlation between the depressed calcium release and a decreased ratio of torques generated at 20 **:** 50Hz.[59] By evoking tetanus at maximal intensity to the femoral nerve, we did not find evidence of any LFF after prolonged skiing,[18] cycling[40] or running.[15] This last result was not anticipated since muscular damage occurs after prolonged running.[3,10] In fact, it has been suggested that E-C coupling failure is due, at least in part, to physical disruption of the membrane systems involved in Ca^{2+} release[16] so that muscular damage and LFF are usually connected.[17] The lack of LFF after a 30km run[15] is in line with a previous study examining the effect of 4 hours of treadmill running on the muscular function.[19] This is also consistent with an experiment showing that 90 minutes of intermittent downhill running did not induce LFF in the rat soleus muscle.[60]

Since the measurements in the fatigued state were performed less than 10 minutes after the end of the exercise in these three studies,[15,19,60] the exercise may have potentiated the low-frequency evoked torque and thus may have hidden LFF. As a consequence, the lack of LFF does not allow for complete certainty that a failure of the E-C coupling did not occur. Additional measurements of force at low and high frequency still have to be performed 20–30 minutes after the exercise when potentiation caused

by the exercise would have dissipated. In that sense, it has been shown that 1 hour of running at 70% $\dot{V}O_{2max}$ slightly but significantly decreased the 20 : 50Hz ratio evoked on triceps surae.[31] Interestingly, the post-exercise measurements were performed 15 minutes after the cessation of the running bout in this study.

While stimulation was applied over the femoral nerve at maximal intensity in some studies,[15,18,40] tetanus was evoked at submaximal intensity of stimulation by electrodes placed over the muscle in others.[19,31] Thus, no LFF was observed in both experiments despite the utilisation of two different methods. However, further studies are needed to test the hypothesis that the submaximal stimulation, used in several studies[19,31,61,62] probably because it is less painful, is always comparable to the maximal stimulation when the aim is to characterise peripheral fatigue. In fact, because it has been suggested that: (i) motor units are recruited in reverse sequence when electrically stimulated as compared with voluntary contractions,[63,64] and (ii) type II fibres are predominantly located at the muscle surface,[65] it can be considered that electrical stimulation at submaximal intensity preferentially recruits type II fibres. This may affect the submaximal method. Similar questions about the influence of the intensity of stimulation have been previously raised.[31]

4. Conclusion

Despite the systematic implication of knee extensor muscle in locomotion, only few experiments have been dedicated to studying fatigue of this muscular group after prolonged exercise. Recent studies have explored fatigue after prolonged exercise in different locomotions. The presence of central fatigue has been identified after prolonged running exercise but central fatigue does not exist or is of lower amplitude for cycling or skiing, i.e. locomotion inducing less muscular stress. This creates speculation about the role of spinal inhibition and/or disfacilitation in central fatigue. Regarding peripheral fatigue, single stimulation may give information about neuromuscular propagation if EMG is associated. However, the twitch mechanical response cannot be considered as a general index of alterations of phenomena below the neuromuscular junction since peak twitch can be increased after several hours of running. Instead, it only reflects the changes of low-frequency stimulation. Thus, tetanus evoked at different frequencies are needed to characterise peripheral fatigue. To date, no evidence of knee extensor muscle LFF has been demonstrated after prolonged exercise, including after prolonged running bouts.

5. Further Research Directions

It has been shown that during progressive fatigue of knee extensor muscle in isometric conditions, antagonist activation increases and contributes to the loss of extensor force-producing capacity.[66] It is not known whether coactivation is higher in the fatigued state following prolonged exercise; however, since the increase in coactivation during fatigue is centrally mediated,[67] this hypothesis requires testing in the future. Also, the majority of studies dedicated to that type of fatigue have used the twitch interpolation technique to evidence central fatigue. It has been suggested that high-frequency maximal trains of stimuli, rather than single stimulation, may improve the detection of central activation failure.[68] Therefore, even though the conventional twitch superimposition technique indicates no central fatigue, a difference of a few percent in voluntary activation may be present. Future experiments should consider this factor and should also involve new techniques of central fatigue investigation such as transcranial magnetic stimulation.[69-71]

To explore peripheral fatigue, both sub-maximal and maximal electrical stimulation have been used in the literature. However, it is not known whether both methods are comparable when investigating the presence of high- or low-frequency fatigue. This question probably deserves more examination because maximal stimulation of the femoral nerve may be painful and not tolerated by some study participants. Also, while no LFF was detected after prolonged exercise, this result still has to be verified by repeating stimulations at low and high frequency

when the effects of potentiation have disappeared. Finally, most of the experiments have examined neuromuscular alteration by looking at the difference between pre- and post-exercise but little is known about the evolution of fatigue during the exercise. Thus, future studies should also focus on fatigue kinetics during prolonged exercise.

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