



# **Central fatigue after prolonged running**

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## Abstract

### Purpose

The aim of this study was to examine fatigue in the plantar flexor muscle group after a prolonged running exercise.

### Methods

Eight healthy, habitually active male subjects ran on a motorized treadmill during 2 hours at a speed chosen to promote 70-75%  $VO_{2max}$ . To evaluate fatigue the twitch interpolation technique was employed in the plantar flexor muscle group before and immediately after running. To achieve this, the isometric maximal voluntary contraction (MVC) as well as the electrically induced twitch produced during the MVC (IT) and with the muscle at rest (RT) were measured. The level of activation (LOA) during each MVC was calculated as  $LOA (\%) = 100 \cdot (1 - IT \cdot RT^{-1})$ . Fatigue was defined as a decrease in MVC after running. Central fatigue was defined as a decrease in the LOA, and peripheral fatigue as a decrease in the RT.

### Results

MVC decreased significantly from before to after running (from  $148.3 \pm 16$  to  $120.8 \pm 30.7$  Nm;  $-19 \pm 19\%$ ). There was central fatigue with a reduction of  $19 \pm 15\%$  in the LOA (from  $83 \pm 16\%$  to  $68 \pm 20\%$  after running). Peripheral fatigue did not occur as the RT did not change significantly between before and after running ( $61.2 \pm 10.0$  and  $57.4 \pm 9.5$  Nm, respectively). The changes in MVC were correlated to the changes in LOA ( $r = 0.90$ ;  $p = 0.02$ ), and could explain 82% ( $r^2 = 0.82$ ) of the changes in MVC. On the contrary, no significant relationship existed between the changes in MVC and changes in RT ( $r = -0.35$ ;  $p = 0.39$ ). However, when using multiple regression analysis the changes in LOA and RT together were able to explain 83% ( $r^2 = 0.83$ ;  $p = 0.01$ ) of the changes in MVC.

### Conclusion

In contrast to some previous studies using the twitch interpolation technique to investigate fatigue during whole body prolonged exercise, this study employed supramaximal electrical stimulation over a nerve that activates only agonists and no antagonist muscles. The results demonstrates that after 2 h of continuous treadmill running the reduction on isometric maximal voluntary contraction during plantar flexion was caused by central fatigue.

**Key words:** central fatigue, peripheral fatigue, twitch interpolation technique

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# 1 INTRODUCTION

Fatigue has been defined as any exercise-induced reduction in the ability of a muscle to generate force or power<sup>1</sup>. The terminology most commonly used to describe neuromuscular adaptations to fatigue, refers to the factors situated in the central nervous system as being central, whereas the factors situated in the peripheral nervous system, or in the muscle itself, are termed peripheral<sup>2</sup>.

The twitch interpolation technique is commonly used to assess fatigue. It includes electrical stimulation of the motor nerve to a muscle as the subject performs a maximal voluntary contraction (MVC) and when the muscle is relaxed<sup>3</sup>. The amplitude of the interpolated twitch (IT) produced during a voluntary contraction compared with that elicited from the relaxed muscle (RT) provides a means of assessing the relative level of muscle activation (LOA) during any type of voluntary contraction, i.e., how well subjects can drive a muscle to produce force. It allows the extent to which this may change during fatigue to be measured. An increase in the IT/RT with exercise indicates impairment of LOA and thus, central fatigue.

While most studies on central fatigue, using the twitch interpolation technique, have observed effects of isometric exercise<sup>4,5,6</sup>, recent studies have investigated fatigue induced by functional movements, such as running<sup>7,8,9,10</sup>. Contradictory results were found regarding central fatigue during running. While the capacity to voluntarily activate the quadriceps femoris muscle

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<sup>1</sup> Gandevia, S. C., "Spinal and supraspinal factors in human muscle fatigue", *Physiological Reviews*, 81(2001:4), pp. 1725-1789

<sup>2</sup> Bigland-Ritchie, B. & Woods, J. J., "Changes in muscle contractile properties and neural control during human muscular fatigue", *Muscle & Nerve*, 7 (1984), pp. 691-699

<sup>3</sup> Merton P. A., "Voluntary strength and fatigue", *Journal of Physiology*, 123 (1954), pp. 553-564

<sup>4</sup> Bigland-Ritchie, B., Furbush, F. & Woods, J. J., "Fatigue of intermittent submaximal voluntary contractions: central and peripheral factors", *Journal of Applied Physiology*, 61 (1986), pp. 421-429

<sup>5</sup> Löscher W. N., Cresswell, A. G. & Thorstensson, A., "Excitatory drive to  $\alpha$ -motoneuron pool during a fatiguing submaximal contraction in man", *Journal of Physiology*, 491 (1996), pp. 271-280

<sup>6</sup> Nordlund M. M., Thorstensson, A. & Cresswell, A. G., "Central and peripheral contributions to fatigue in relation to level of activation during repeated maximal voluntary isometric plantar flexions", *Journal of Applied Physiology*, 96 (2004), pp. 218-225

<sup>7</sup> Millet G. Y., Leppers, R., Maffiuletti, N. A., Babault, N., Martin, V., Lattier, G., "Alterations of neuromuscular function after an ultramarathon", *Journal of Applied Physiology*, 92 (2002), pp. 486-492

<sup>8</sup> Millet G. Y., Martin, V., Lattier, G., Ballay, Y., "Mechanisms contributing to knee extensor strength loss after prolonged running exercise", *Journal of Applied Physiology*, 94 (2003), pp. 193-198

<sup>9</sup> Place N., Lepers, R., Deley, G., Millet, G. Y., "Time course of neuromuscular alterations during a prolonged running exercise", *Medicine and Science in Sports and Exercise*, 36 (2004:8), pp. 1347-1356

<sup>10</sup> Finni, T., Kyröläinen, H., Avela, J., Komi, P. V., "Maximal but not submaximal performance is reduced by constant-speed 10-km run", *Journal of Sports Medicine and Physical Fitness*, 43 (2003:4), pp. 411-417

group was decreased after 30 km running<sup>11</sup> for the plantar flexor muscle group, such a decrease was not observed after 10 km of running<sup>12</sup>. The divergent results regarding central fatigue can be related to the diverse fatigue protocols adopted as well as to the muscle group under investigation. Furthermore, the twitch interpolation technique originally developed for the adductor pollicis<sup>13</sup>, may work differently when stimulating the tibial nerve for activation of the plantar flexors than when stimulating the femoral nerve to activate the quadriceps femoris (see discussion).

At velocities ranging from 1.0 to 9.0 m · s<sup>-1</sup>, Nilsson and collaborators<sup>14</sup> demonstrated that gastrocnemius was activated after the touch down, at about 13-18% and 75 and 85% of the stride cycle. Kyröläinen and collaborators<sup>15</sup> showed that the activity of the gastrocnemius was higher during all phases of running, at maximal speed, than during MVC. Millet and collaborators<sup>16</sup> found central fatigue in the quadriceps femoris and no evidence of peripheral fatigue in the plantar flexors after an ultramarathon. Surprisingly though, despite the importance of the plantar flexor muscle group during running its central and peripheral contributions to fatigue after long distance running have not been investigated concomitantly.

The aim of this study was to examine fatigue in the plantar flexor muscle group after a prolonged running exercise. To accomplish this, the twitch interpolation technique was employed in this muscle group before and after two hours of continuous treadmill running.

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<sup>11</sup> Millet *et al.*, 2003

<sup>12</sup> Finni *et al.*, 2003

<sup>13</sup> Merton, 1954

<sup>14</sup> Nilsson, J., Thorstensson, A. & Halbertsma, J., "Changes in leg movements and muscle activity with speed of locomotion and mode of progression in humans", *Acta Physiologica Scandinavica*, 123 (1985:4), pp. 457-475

<sup>15</sup> Kyröläinen, H., Avela, J. & Komi, P. V., "Changes in muscle activity with increasing running speed", *Journal of Sports Sciences*, 23 (2005:10), pp. 1101-1109

<sup>16</sup> Millet *et al.*, 2002

## 2 METHODS

### 2.1 Subjects

Eight healthy, habitually active male subjects [age  $27.1 \pm 2.7$  (SD) yr, height  $1.80 \pm 0.10$  m, body mass  $73.7 \pm 10$  kg] gave their written informed consent to participate in the study. The investigation was conducted in compliance with the Declaration of Helsinki and was approved by the Regional Ethics Committee in Stockholm (2005/295-31/1). The subjects were asked to perform no intense physical activities within 24h before each session.

### 2.2 First session

During the first session that took place at least one week before the main experiment, the subjects ran 5 min on a motorized treadmill at a self-selected speed as warm-up and were then familiarized with the strength measurement and the electrical stimulation procedures. At the end of this familiarization the measurements were recorded to be used for test-retest comparisons. Subsequently, the subjects underwent an incremental treadmill exercise with a rise in the inclination of 1 degree uphill every minute until volitional exhaustion ( $10 \pm 1$  min). Expired air was analysed continuously (Amis 2001 Innovision, Denmark, Respicare) and heart rate was recorded (Polar, Finland). From the results of the incremental exercise the maximal oxygen uptake ( $VO_{2max}$ ) was defined and a regression of  $VO_{2max}$  against heart rate was used to find the heart rate range that corresponded to 70-75%  $VO_{2max}$ .

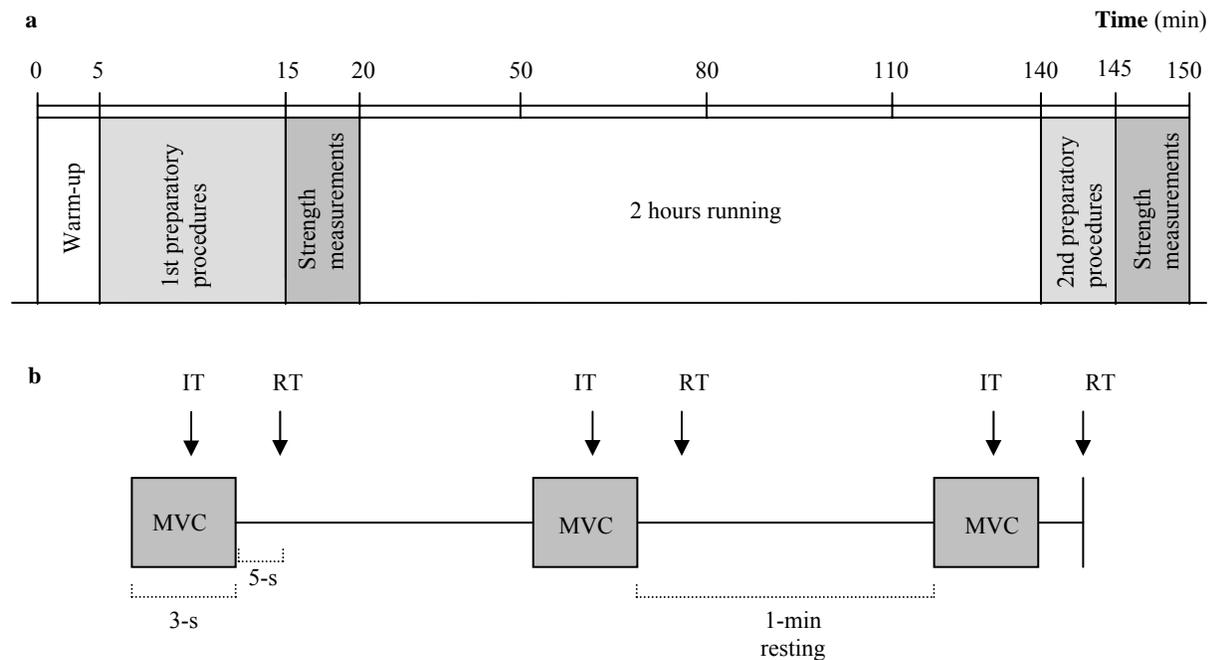
### 2.3 Main session

A schematic representation of the main session is shown in Fig 1. The fatigue protocol consisted of 2 hours of continuous treadmill running. The heart rate monitor was attached around the chest of the subject. Heart rate was recorded and the subjects expressed their rating of perceived exertion on the Borg Scale of 6-20<sup>17</sup> every 15<sup>th</sup> and 30<sup>th</sup> min, respectively. During the first 15 min of running the treadmill inclination was set at 1 degree uphill and the speed was gradually increased until the heart rate reached the stipulated range of 70-75%  $VO_{2max}$  determined in the first session for each subject. In the remaining period, small adjustments in the speed of the

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<sup>17</sup> Borg, G., *Borg's Perceived exertion and pain scales* (Champaign, Ill.: Human Kinetics, 1998)

treadmill were made individually, in order to provide a high running velocity that the subjects could tolerate for 2 h. The heart rate range stipulated and the rating of perceived exertion on the Borg Scale were taken into account to set the running velocity. Fluid in form of water was available to the subjects on demand during the experiments, and intake was recorded.



**Figure 1** Schematic representation of the experiment in the main session. The first preparatory procedures consisted of strapping the foot of the subject appropriately, applying the electrodes and conducting the electrical stimulation process; for more details see text. In the second preparatory procedures the foot was strapped and the electrodes were applied to the marked positions (a). The strength measurements indicated in a) are magnified (b). The grey boxes indicate an isometric maximal voluntary contraction (MVC). Arrows indicate when supramaximal electrical stimulations were applied to the tibial nerve. During the MVC electric stimulation induced an interpolated twitch (IT), and at rest electric stimulation evoked a twitch (RT) 5 s after the end of each MVC.

## 2.4 Measurement and experimental procedures

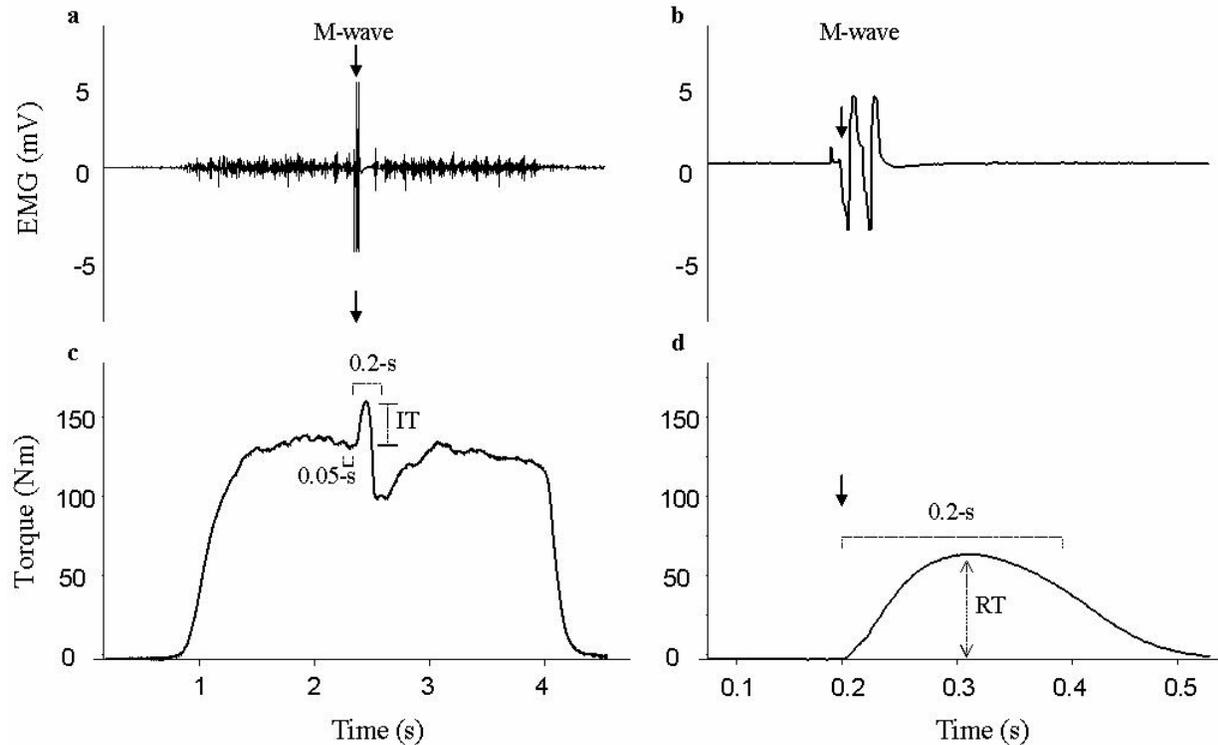
### 2.4.1 Strength measurements

The strength measurements were conducted on the right plantar flexor muscles with the subjects lying prone on a bench with their right ankle at 90° and their right foot strapped tightly to a

vertical footplate, instrumented with a force transducer (Nobel, KRG-4)<sup>18</sup>. The axis of rotation of the footplate was aligned with the lateral malleolus. Subjects were asked to perform submaximal contractions preceding the strength measurements to optimise the strapping. They were instructed not to perform extraneous movement of the upper body during the trials, i.e. not to grasp the bench or elevate the pelvis. The force signal was analog-to-digital converted and sampled at 1 kHz. The force measured by the transducer was multiplied by its lever arm (0.3 m) to achieve the plantar flexor torque (strength) value. The strength measurements included isometric maximal voluntary contraction (MVC) and electrically evoked twitches. Subjects were asked to perform three 3-s-MVCs with a 1-min-rest between the trials. During the MVCs electric stimulation induced an interpolated twitch (IT) on the plateau reached during each MVC (Fig 1b and 2c). An electrical evoked twitch was also performed at rest (RT) after 5 s of the end of each MVC (Fig 1b and 2d). Subjects were verbally encouraged during MVCs. The strength measurements before running were accomplished succeeding a similar warm-up to the first session. The strength measurements after running started within 5 min after the end of running and lasted no longer than 10 min.

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<sup>18</sup> Nordlund, M. M., Thorstensson, A. & Cresswell, A. G., "Variations in the soleus H-reflex as a function of activation during controlled lengthening and shortening actions", *Brain Research*, 952 (2002:2), pp. 301-307



**Figure 2** Typical trace of the electromyogram (EMG) from one subject during isometric maximal voluntary contraction (MVC) with transcutaneous electrical stimulation applied to the tibial nerve indicated by the M-wave (a), typical EMG from the stimulation applied at rest indicated by the M-wave (b), typical trace of torque produced during MVC with interpolated twitch (IT) caused by the stimulation (c), and typical trace of torque produced by the stimulation applied at rest (resting twitch) (RT) (d). To achieve the IT during MVC (c), the mean torque measured during the 0.05 s preceding the transcutaneous electrical stimulation was subtracted from the peak torque within 0.2 s from when the electrical stimulation was applied, both based on the M-wave marked by the solid arrow (a and c). The RT (d) was measured as the peak torque occurring within 0.2 s from when the electrical stimulation was applied also based on the M-wave (d) indicated by the solid arrow.

#### 2.4.2 Electrical stimulation

Supramaximal transcutaneous electrical stimulation was applied to the tibial nerve through a cathode (Ag-AgCl, Neuroline 725-01-K, 7 mm of diameter) placed in the popliteal fossa and an anode (Coal-rubber electrode, Cefar Medical AB, 100 × 50 mm) placed on the anterior aspect of the thigh, just proximal to the knee (Nordlund et al., 2002). Stimulations consisting of two 0.5 ms supramaximal pulses with a 0.02 s interval were delivered by a Grass constant-voltage somatosensory stimulator (S10DSCM A, Grass Instruments) and a stimulus isolation unit (SIU8T B, Grass Instruments) to induce twitches in the force signal and M-waves in the EMG. Firstly, the optimal placement of the stimulating electrode was determined at rest based on the size of the

twitch produced by moving a stimulator probe. The placement was marked on the skin to enable fixing the stimulating electrode at the same place before and after running. The electrical stimulus intensity was then adjusted and considered maximal when increasing the intensity no longer induced a higher twitch. This intensity was further increased to reach the supramaximal value to be used throughout the protocol with attention to not cause a reduction in the twitch due to antagonist activation.

#### 2.4.3 *Electromyographic recordings*

Surface electromyographic recordings (EMG) were collected from the soleus muscle with the purpose to use the compound motor action potential (M-wave) induced by the electric stimulation as the reference for the strength analyses, i.e. timing for the twitch. A pair of electrodes (Ag-AgCl, Grass F-E9M-40-5 Reusable, 11 mm) was placed in a belly-tendon configuration over the soleus muscle and Achilles tendon. A ground electrode (Ag-AgCl, Bluesensor M-00-5, 10 mm) was placed on the fibular head. The EMG signal was amplified 1000 times (AD Instruments Dual Bio Amp), band-pass filtered between 3 Hz and 1 kHz (NL 125, Digitimer) and analog-to-digital converted at a sampling frequency of 1 kHz. Both strength and EMG were sampled using the Powerlab SP data collection system with the Chart (version 4.0) software.

#### 2.4.4 *Level of activation*

The level of activation (LOA) was assessed by means of the twitch interpolation technique<sup>19</sup>. To achieve the IT during MVC, the mean torque measured during the 0.05 s preceding the electrical stimulation (M-wave, Fig 2a and c) was subtracted from the peak torque within 0.2 s from when the electrical stimulation was applied (Fig 2b and d). RT was measured as the peak torque occurring within 200 ms from when the electrical stimulation was applied (Fig 2b and d). The LOA during each MVC was calculated as  $LOA (\%) = 100 \cdot (1 - IT \cdot RT^{-1})$  induced after the same MVC). The trial with the highest LOA was chosen for further analyses.

#### 2.4.5 *Definitions of fatigue*

Fatigue was defined as a decrease in MVC after running. Central fatigue was defined as a decrease in the LOA, and peripheral fatigue as a decrease in the RT.

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<sup>19</sup> Merton, 1954

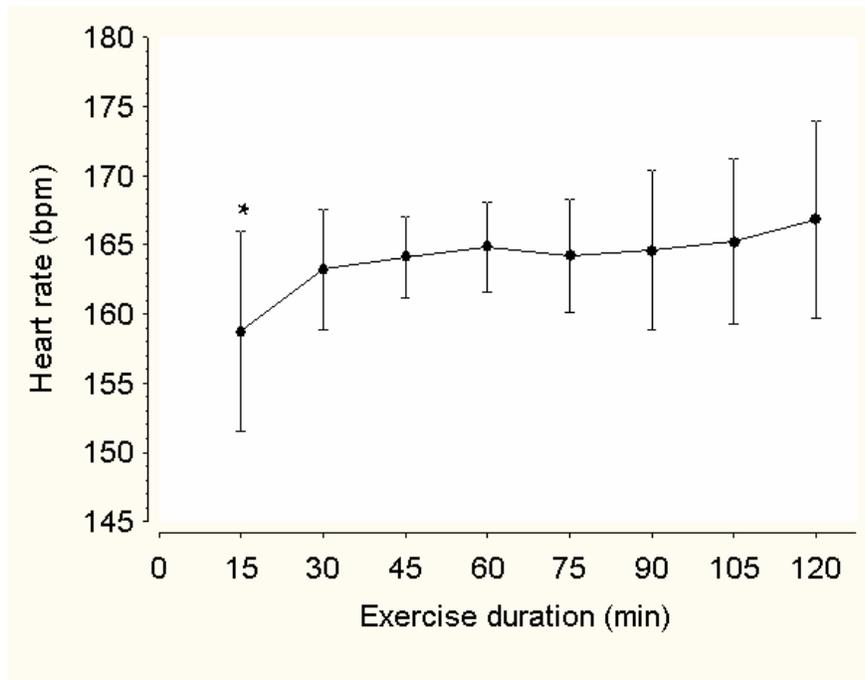
## 2.5 Statistics

Normality of the data was confirmed by using the Shapiro-Wilk  $W$  test. To test the reliability of the measurements for MVC, RT, and LOA done in the first session and before running the coefficient of variation (CV), the Intra Class Coefficient ( $ICC_{2,1}$ ), and a paired  $t$ -test were applied. A paired  $t$ -test was also used to identify differences in MVC, LOA and RT between before and after running. Correlation and multiple regression analyses were employed to investigate to what extent the changes in MVC could be explained by the changes in LOA and RT. Correlation was also used to investigate the relation between the water intake and MVC, RT, and LOA after running. Friedman and repeated-measures ANOVA were used to detect alteration during the exercise period in RPE and heart rate, respectively. Spearman was used to assess the correlation between RPE and central fatigue. The analyses were performed using Statistica 6 (StatSoft). The level of significance was set to  $p < 0.05$ . Unless elsewhere stated, all data are presented as means  $\pm 1$  SD.

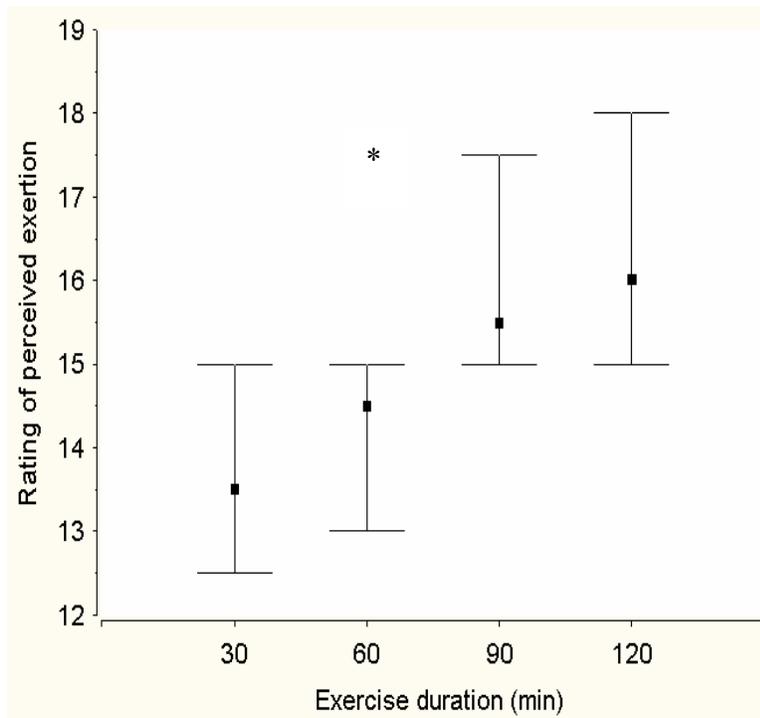
### 3 RESULTS

The coefficient of variation (CV) and intra class correlation ( $ICC_{2,1}$ ) between the values obtained during the first session and before running for MVC, RT and LOA were 6.4%, 0.48 ( $ICC_{2,1}$ ), 6.8%, 0.82 ( $ICC_{2,1}$ ), and 4.8%, 0.89 ( $ICC_{2,1}$ ), respectively. A paired  $t$ -test confirmed no difference for MVC, RT and LOA between the first session and before running.

The mean  $VO_{2max}$ , velocity during the 2 h running and total distance covered were  $67.01 \pm 5.9 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ,  $13.4 \pm 1.1 \text{ km} \cdot \text{h}^{-1}$  and  $26.8 \pm 2.0 \text{ km}$ , respectively. Heart rate gradually increased from  $159 \pm 9 \text{ bpm}$  at 15 min to  $167 \pm 8 \text{ bpm}$  at the end of 120 min running, but the rise became significant ( $p < 0.05$ ) only from 60 min of exercise differing from the value at 15 min (Fig 3). At the termination of running the mean rating of perceived exertion was 16.2 (between hard and very hard) (Fig 4).



**Figure 3** Heart rate during 2 h treadmill running. Data are presented as means  $\pm$  SE of means. \* denotes a significantly lower HR at 15 min compared to the HR measurements performed at 60 min through 120 min.

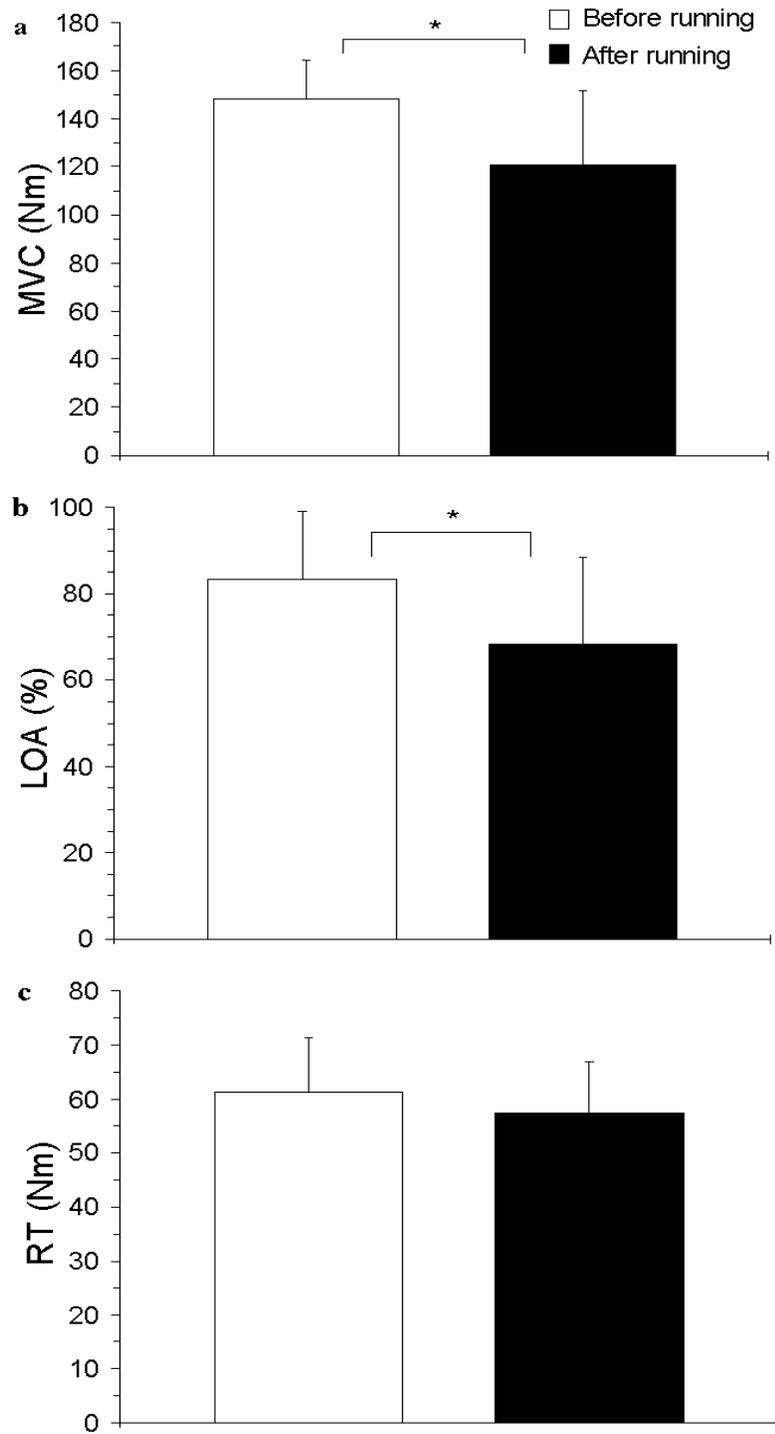


**Figure 4** Rating of perceived exertion during 2 h treadmill running. \* There is a significant increase in the rating of perceived exertion detected by using Friedman ANOVA ( $p < 0.05$ ). Data are presented as median, maximum, and minimum values.

MVC decreased significantly from before to after running (from  $148.3 \pm 16$  to  $120.8 \pm 30.7$  Nm;  $-19 \pm 19\%$ ) (Fig 5a). LOA was significantly higher before ( $83 \pm 16\%$ ) the running than after ( $68 \pm 20\%$ ), with a reduction of  $19 \pm 15\%$  (Fig 5b). RT did not change significantly between before and after running ( $61.2 \pm 10.0$  and  $57.4 \pm 9.5$  Nm, respectively; Fig 5c).

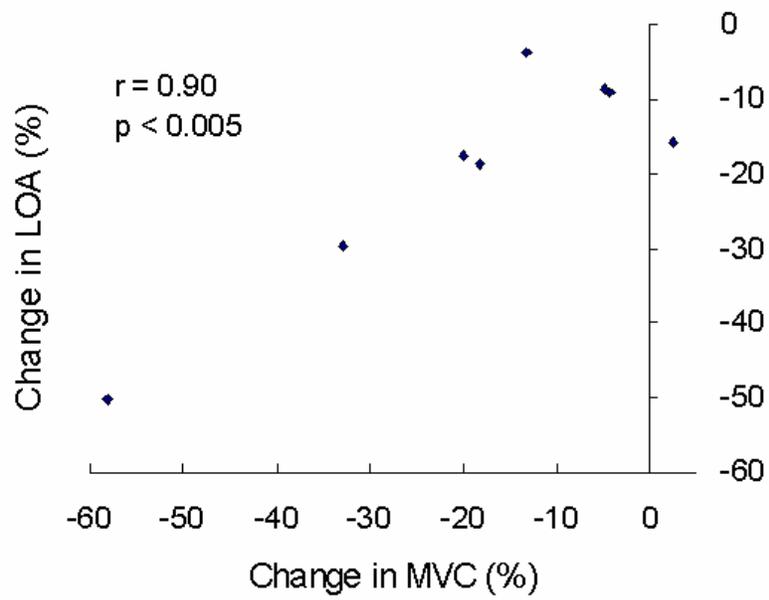
The changes in MVC were correlated to the changes in LOA ( $r = 0.90$ ;  $p = 0.02$ ; Fig 6), and could explain 82% ( $r^2 = 0.82$ ) of the changes in MVC. On the contrary, no relationship existed between the changes in MVC and changes in RT ( $r = -0.35$ ;  $p = 0.39$ ). However, when using multiple regression analysis the changes in LOA and RT together were responsible for 83% ( $r^2 = 0.83$ ;  $p = 0.01$ ) of the changes in MVC. The rating of perceived exertion at the termination of running was not related to the decrement in LOA ( $r = 0.33$   $p = 0.43$ ).

There was a considerable variability in the volume of water intake during running, ranging from 600 to 2400 ml (mean  $1200 \pm 600$  ml) but it was not correlated with any variable after running: MVC ( $r = -0.52$ ,  $p = 0.23$ ), RT ( $r = -0.02$ ,  $p = 0.96$ ) and LOA ( $r = -0.44$ ,  $p = 0.32$ ).



**Figure 5** Isometric maximal voluntary contraction (MVC) (a), level of activation (LOA) (b), and resting twitch (RT) (c) before and after 2 h treadmill running. Data are presented as means  $\pm$  SD for eight subjects.

\* Significantly different between before and after running.



**Figure 6** Correlation between the change in the level of activation (LOA) and the change in the isometric maximal voluntary contraction (MVC) after 2 h treadmill running where  $y = -6.403 + 0.6889 * x$  and  $r^2 = 0.82$ .

## 4 DISCUSSION

The aim of this study was to examine the fatigue after 2 h treadmill running using the twitch interpolation technique in the plantar flexor muscles. The main findings were that central fatigue, i.e. decrement in LOA, was involved in the reduction of MVC after 2 h treadmill running, subjects with the greatest plantar flexor strength loss after running experienced the largest central fatigue and there was no peripheral fatigue, i.e. no difference in the RT.

The most important finding of the present study was that central fatigue could be demonstrated during maximal voluntary isometric plantar flexion after two hours of running. One criticism against previous studies on central fatigue induced by prolonged exercise has been that electrical stimulation of the femoral nerve does not recruit the whole muscle group<sup>20</sup>. Furthermore, through electrical stimulation of the femoral nerve, both quadriceps femoris (agonist) and sartorius (antagonist) can be activated which can make it difficult to distinguish the force increments, produced by the electrical stimulation, during maximal voluntary contractions. This fact can give the impression that the agonist muscles are fully activated even if they are only submaximally activated<sup>21</sup>. Also, an increased antagonist coactivation with fatigue might reduce the antagonist contribution to the interpolated twitch during MVC and thus increase the net interpolated twitch which will be interpreted as a reduced LOA. On the other hand, transcutaneous electrical stimulation of the tibial nerve activates almost all plantar flexor muscles (medial and lateral gastrocnemius, soleus, plantaris, tibialis posterior, flexor digitorum longus, and flexor hallucis longus), with exception only for peroneus brevis and longus, without activating any antagonist muscle. Further, it has been reported, that during electrical stimulation of the tibial nerve, the subjects tolerate the use of supramaximal intensities<sup>22</sup>. Consequently, even if the threshold of the motor axons increases during a fatiguing exercise, by using supramaximal intensity the muscle can still be fully activated. In the present study, the maximal electrical stimulus intensity was further increased to reach the supramaximal value with attention to not cause a reduction in the twitch due to antagonist activation.

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<sup>20</sup> Nybo, L. & Nielsen, B., "Hyperthermia and central fatigue during prolonged exercise in humans", *Journal of Applied Physiology*, 91(2001:3), pp. 1055-1060 (b)

<sup>21</sup> Shield, A. & Zhou, S., "Assessing voluntary muscle activation with the twitch interpolation technique", *Sports Medicine*, 34 (2004:4), pp. 253-267

<sup>22</sup> Nordlund *et al.*, 2004

In the present investigation, the central fatigue induced by running could explain 82% of the reduction in the MVC. Millet and others<sup>23</sup> also observed decreased MVC and LOA, in the quadriceps, after 30 km race running. It is difficult to compare the exercise intensity current used with the one used by Millet and collaborators<sup>24</sup> since their subjects ran outdoors at approximately  $9.5 \text{ km} \cdot \text{h}^{-1}$  with 800 m uphill. Whether these two distinct exercise protocols induce central fatigue in both the quadriceps and the plantar flexor muscle groups remains to be established. Even so, the mechanisms involved in the central fatigue in both studies may be similar as they were both caused by whole body prolonged exercise.

In contrast to our study, Finni and collaborators<sup>25</sup> looking at the plantar flexor muscles did not observe central fatigue after 10 km running even though the MVC, RT and the 20 m sprint speed were reduced. This different result may be related to the duration and intensity of the exercise, as in their study the running lasted for less than one hour and the mean velocity was  $12.6 \text{ km} \cdot \text{h}^{-1}$  while in ours the subjects ran for 2 h with the mean velocity of  $13.4 \text{ km} \cdot \text{h}^{-1}$ .

Central fatigue can be related to a variety of mechanisms from supraspinal and spinal sites. Possible mechanisms for the supraspinal fatigue include reduced descending output from the motor cortex and/or reduced efficacy of output from the motor cortex in generating force<sup>26</sup>. It could be hypothesized that central fatigue occurs due to usage within the supraspinal circuits<sup>27</sup>. However, in the present study, there was no such evidence as the subjects with higher ability to voluntarily activate the plantar flexor muscle group before running did not exhibit more central fatigue ( $r = -0.16$ ;  $p = 0.70$ ). On the other hand, the exercise used in the present study consisted of repeated submaximal contractions that probably did not require high levels of activation.

In this study, the fatigue experienced during the 2 h treadmill running was evaluated via RPE on the Borg Scale of 6-20. In agreement with the literature<sup>28,29</sup>, the perceived exertion to exercise at the same intensity increased throughout the running, where the median rate at 30 min

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<sup>23</sup> Millet *et al.*, 2003

<sup>24</sup> Millet *et al.*, 2003

<sup>25</sup> Finni *et al.*, 2003

<sup>26</sup> Taylor, J. L., Todd, G. & Gandevia, S. C., "Evidence for a supraspinal contribution to human muscle fatigue", *Clinical and Experimental Pharmacology & Physiology*, 33 (2006:4), pp. 400-405

<sup>27</sup> Petersen, N. T., Taylor, J. L., Butler, J. E., Gandevia, S. C., "Depression of activity in the corticospinal pathway during human motor behavior after strong voluntary contractions", *The Journal of Neuroscience*, 23 (2003:22), pp. 7974-7980

<sup>28</sup> Saboisky, J., Marino, F. E., Kay, D., Cannon, J., "Exercise heat stress does not reduce central activation to non-exercised human skeletal muscle", *Experimental Physiology*, 88 (2003:6), pp. 783-790

<sup>29</sup> Place *et al.*, 2004

was 13.5 (between somewhat hard and hard) and at 120 min had increased to 16.2 (between hard and very hard). In a study of Jones and Hunter<sup>30</sup> a linear increase in the perceived force during sustained submaximal contractions was found. The change in force sensation was paralleled by an increase in the EMG of the fatiguing muscle. However, the mechanisms behind increased sense of exertion during 2 h running is likely to be different since there was no muscle fatigue and hence no need for increased neural activation during running. Interestingly, Nybo & Nielsen<sup>31</sup> investigating cycling exercise until exhaustion, in a hot environment, did not observe increased activation (EMG) in the vastus lateralis despite a RPE of  $20 \pm 0$  at the point of exhaustion. They instead, described that a cerebral activation over the prefrontal cortex was positively correlated to the RPE ( $r = 0.98$   $p < 0.001$ ). In another study by Nybo & Nielsen<sup>32</sup> the twitch interpolation technique was used during sustained isometric contraction before and after a cycling exercise. Based on these two studies the authors argue that there may be a relation between decreased arousal and hindered ability of the brain to sustain motor activity. Moreover, in the present study, there was no correlation between RPE and central fatigue ( $r = 0.33$ ;  $p = 0.43$ ). However, to the best of our knowledge, no study had correlated RPE to central fatigue measured via the twitch interpolation technique. To investigate such possible relation further, the same subjects should express their rating of perceived exertion while being under different levels of central fatigue. Furthermore, evaluating fatigue only via RPE does not allow for a clear discrimination between peripheral and central factors contributing to fatigue.

Although the current fatigue exercise was performed indoors, the influence of an increased core temperature on central fatigue cannot be ruled out. In the investigation of Davies & Thompson<sup>33</sup> (1986) where the subjects ran indoors ( $21^{\circ}$  C environment) during four hours there was an increase in the core temperature from  $38.43 \pm 0.31^{\circ}$  C at the end of the first hour to  $39.09 \pm 0.50^{\circ}$  C at the fourth hour. Nybo & Nielsen<sup>34</sup> examined the influence of hyperthermia ( $40^{\circ}$  C environment) on central fatigue after cycling exercise. They observed that after exercise both exercised (leg) and non exercised (arm) muscles developed reduction in voluntary strength

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<sup>30</sup> Jones, L. A. & Hunter, I. W., "Effect of fatigue on force sensation", *Experimental Neurology*, 81 (1983:3), pp. 640-650

<sup>31</sup> Nybo, L. & Nielsen, B., "Perceived exertion is associated with an altered brain activity during exercise with progressive hyperthermia", *Journal of Applied Physiology*, 91(2001:5), pp. 2017-2023 (a)

<sup>32</sup> Nybo & Nielsen, 2001 (b)

<sup>33</sup> Davies, C. T. & Thompson, M. W., "Physiological responses to prolonged exercise in ultramarathon athletes", *Journal of Applied Physiology*, 61 (1986:2), pp. 611-617

<sup>34</sup> Nybo & Nielsen, 2001 (b)

during sustained MVC. Furthermore, the LOA at the end of the hyperthermic trial was lower compared to the control trial ( $54 \pm 5\%$  and  $82 \pm 5\%$ , respectively).

Moreover, it has been reported that the motoneurons are affected in fatigued conditions also via spinal mechanisms and peripheral feedback mainly via decreased excitation from Ia afferents<sup>35</sup>, increased activity of group III and IV afferents<sup>36</sup> and increased recurrent inhibition<sup>37</sup>. In fact, decreased stretch reflexes and Hoffman-reflexes have been observed after marathon running and it was suggested to occur due to increased presynaptic inhibition of Ia-afferents. However, there was no measurement of central fatigue and thus it can not be clearly concluded that the decreased reflexes cause central fatigue<sup>38</sup>.

Furthermore, changes in neurotransmitters concentration in the brain can be involved in supraspinal fatigue during prolonged exercise, where 5-HT has received most of the attention as its synthesis is increased in such exercise<sup>39,40</sup>, and increases in brain tryptophan (precursor of 5-HT), via intracerebro-ventricular injection, reduced mechanical efficiency and running performance in rats<sup>41</sup>. So far, in humans, during prolonged exercise, using nutritional factors that affect tryptophan availability to the brain, controversial results have been reported regarding the role of 5-HT on central fatigue<sup>42,43,44,45,46,47</sup>. However, these investigations have been based on

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<sup>35</sup> Nordlund *et al.*, 2004

<sup>36</sup> Garland, S. J., "Role of small diameter afferents in reflex inhibition during human muscle fatigue", *Journal of Physiology*, 435 (1991), pp. 547-558

<sup>37</sup> Löscher *et al.*, 1996

<sup>38</sup> Avela, J., Kyröläinen, H., Komi, P. V., Rama, D., "Reduced reflex sensitivity persists several days after long-lasting stretch-shortening cycle exercise", *Journal of Applied Physiology*, 86 (1999:4), pp. 1292-1300

<sup>39</sup> Barchas, J. D. & Freedman, D. X., "Brain Amines: Response to Physiological Stress", *Biochemical Pharmacology*, 12 (1963), pp. 1232-1235

<sup>40</sup> Chaouloff, F., Laude, D. & Elghozi, J. L., "Physical exercise: evidence for differential consequences of tryptophan on 5-HT synthesis and metabolism in central serotonergic cell bodies and terminals", *Journal of Neural Transmission*, 78 (1989:2), pp. 121-130

<sup>41</sup> Soares, D. D., Lima, N. R., Coimbra, C. C., Marubayashi, U., "Evidence that tryptophan reduces mechanical efficiency and running performance in rats", *Pharmacology, Biochemistry and Behaviour*, 74 (2003:2), pp. 357-362

<sup>42</sup> Blomstrand, E., Celsing, F. & Newsholme, E. A., "Changes in plasma concentrations of aromatic and branched-chain amino acids during sustained exercise in man and their possible role in fatigue", *Acta Physiologica Scandinavica*, 133 (1988:1), pp. 115-121

<sup>43</sup> Blomstrand, E., Hassmen, P., Ekblom, B., Newsholme, E. A., "Administration of branched-chain amino acids during sustained exercise--effects on performance and on plasma concentration of some amino acids", *European Journal of Applied Physiology*, 63 (1991:2), pp. 83-88 (a)

<sup>44</sup> Blomstrand, E., Hassmen, P. & Newsholme, E. A., "Effect of branched-chain amino acid supplementation on mental performance", *Acta Physiologica Scandinavica*, 143 (1991:2), pp. 225-226 (b)

<sup>45</sup> Segura, R. & Ventura, J. L., "Effect of L-tryptophan supplementation on exercise performance", *International Journal of Sports Medicine*, 9 (1988:5), pp. 301-305

psychological aspects (perceived exertion scale, word and colour tests) and on physical performance, restricted to time to exhaustion, to judge central fatigue.

Although central fatigue did occur in the present study, it is not possible with the currently applied technique to specify the individual contribution of the mechanisms, cited above, to central fatigue. The test-retest reliability of the RT (CV = 4.8%; ICC<sub>2,1</sub> = 0.89) and LOA (CV = 6.8%; ICC<sub>2,1</sub> = 0.82) suggests that the methods presented here can be used in future studies that concomitantly investigate possible mechanisms of central fatigue after running. For example, the fatigue exercise as well as the twitch interpolation technique, in the plantar flexor muscle group, employed in the present investigation associated to a nutritional supplementation would help to clarify the role of 5-HT on central fatigue. Since, however, there was a large inter individual variability in central fatigue (from 4 to 50%), such investigations would need a large number of subjects or a selection of only subjects who display a relatively large amount of central fatigue. The ICC<sub>2,1</sub> was lower for the MVC measurement (0.48) than for the LOA and the RT. This was most likely due to one subject who produced lower MVC before running than in the first session (202.4 and 151.2 Nm, respectively).

In the present study there was no peripheral fatigue, that is, no significant ( $p > 0.05$ ) reduction in the RT. Potentiation and fatigue combined effects may have occurred impairing the analyses of peripheral fatigue as the strength measurements after running lasted 7-10-min<sup>48</sup>. This result is in agreement with the literature<sup>49,50</sup> where an increase in the RT has been observed after exercise.

Some authors<sup>51,52</sup> have criticized the use of the RT to measure peripheral fatigue and suggest the use of tetanic stimulation with high and low frequencies to avoid the potentiation

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<sup>46</sup> van Hall, G., Raaymakers, J. S., Saris, W. H., Wagenmakers, A. J., "Ingestion of branched-chain amino acids and tryptophan during sustained exercise in man: failure to affect performance", *Journal of Physiology*, 486 (1995), pp. 789-794

<sup>47</sup> Nybo, L., Nielsen, B., Blomstrand, E., Moller, K., Secher, N., "Neurohumoral responses during prolonged exercise in humans", *Journal of Applied Physiology*, 95 (2003:3), pp. 1125-1131

<sup>48</sup> Sale, D. G., "Postactivation potentiation: role in human performance", *Exercise and Sport Sciences Reviews*, 30 (2002:3), pp. 138-143

<sup>49</sup> Millet *et al.*, 2002

<sup>50</sup> Place *et al.*, 2004

<sup>51</sup> Millet *et al.*, 2003

<sup>52</sup> Lattier, G., Millet, G. Y., Martin, A., Martin, V., "Fatigue and recovery after high-intensity exercise part I: neuromuscular fatigue", *International Journal of Sports Medicine*, 25 (2004:6), pp. 450-456

effect. However, even using tetanic stimulation Millet and collaborators<sup>53</sup> reported potentiation using stimulation of 20 Hz after 30 km running. Furthermore, it is well documented in the literature that the discomfort using supramaximal electrical intensity is augmented along with the number of stimuli<sup>54</sup>. Based on the discomfort and that the main purpose of the present study was to examine central fatigue, we choose do not exposure our subjects to a tetanic stimulation, i.e., more than two stimuli.

In conclusion, this investigation demonstrated that after 2 h of continuous treadmill running there was central fatigue during isometric maximal voluntary plantar flexion and subjects with the greatest plantar flexor strength loss after running experienced the largest central fatigue.

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<sup>53</sup> Millet *et al.*, 2003

<sup>54</sup> Sale, D., Quinlan, J., Marsh, E., McComas, A. J., Belanger, A. Y., "Influence of joint position on ankle plantarflexion in humans", *Journal of Applied Physiology*, 52 (1982:6), pp. 1636-1642

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## 6 APPENDIX

### KÄLL- OCH LITTERATURSÖKNING

**Frågeställningar:** *Is there central fatigue after prolonged running?*

#### VAD?

Vilka ämnesord har du sökt på?

Ämnesord	Synonymer
<i>central fatigue prolonged exercise</i>	<i>central fatigue running human</i>

#### VARFÖR?

Varför har du valt just dessa ämnesord?

<i>The main purpose of the present study was to investigate central fatigue caused by prolonged exercise.</i>
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#### HUR?

Hur har du sökt i de olika databaserna?

Databas	Söksträng	Antal träffar	Antal relevanta träffar
Pub Med	<i>central fatigue prolonged exercise</i> <i>central fatigue running human</i>	71 24	12 10

#### KOMMENTARER:

Firstly I followed the references list of some papers I had already read. Then I searched in the Pub Med databases to look for other references and also to find recent publications in the field. I used the “related articles” function to find articles in the same field.
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