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Prolonged mental exertion does not alter neuromuscular function of the knee extensors

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Running Head: Mental fatigue and neuromuscular function

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ABSTRACT

Purpose: The aim of this study was to test the hypotheses that prolonged mental exertion i) reduces maximal muscle activation and ii) increases the extent of central fatigue induced by subsequent endurance exercise. **Methods:** Neuromuscular function of the knee extensor muscles was assessed in 10 male subjects in two different conditions: i) before and after prolonged mental exertion leading to mental fatigue; ii) before and after an easy cognitive task (control). Both cognitive tasks lasted 90 min and were followed by submaximal isometric knee extensor exercise until exhaustion (endurance task), and a third assessment of neuromuscular function. **Results:** Time to exhaustion was $13 \pm 4\%$ shorter in the mental fatigue condition (230 ± 22 s) compared to the control condition (266 ± 26 s) ($P < 0.01$). Prolonged mental exertion did not have any significant effect on maximal voluntary contraction (MVC) torque, voluntary activation level (VAL) and peripheral parameters of neuromuscular function. A similar significant decrease in MVC torque (mental fatigue condition: $-26.7 \pm 5.7\%$; control condition: $-27.6 \pm 3.3\%$, $P < 0.001$), VAL (mental fatigue: $-10.6 \pm 4.3\%$; control condition: $-11.2 \pm 5.2\%$, $P < 0.05$) and peripheral parameters of neuromuscular function occurred in both conditions following the endurance task. However, mentally fatigued subjects rated perceived exertion significantly higher during the endurance task compared to the control condition ($P < 0.05$). **Conclusion:** These findings provide the first experimental evidence that i) prolonged mental exertion does not reduce maximal muscle activation and ii) does not increase the extent of central fatigue induced by subsequent endurance exercise. The negative effect of mental fatigue on endurance performance seems to be mediated by higher perception of effort rather than impaired neuromuscular function.

Keywords: Perception of effort, muscle activation, mental fatigue, peripheral fatigue, central fatigue, endurance performance.

INTRODUCTION

Paragraph 1

Prolonged mental exertion is well known to induce mental fatigue, a psychobiological state characterized by subjective feelings of “tiredness” and “lack of energy” (3). The negative effects of mental fatigue on cognitive performance are well established and include impairments in attention, action monitoring, and cognitive control (e.g. 3, 37). On the contrary, the effects of mental fatigue on physical performance have been scarcely investigated. In 1906, Mosso (25) reported that two of his colleagues did poorly in a muscle fatigue test performed after delivering long physiology lectures and viva examinations. More recently, Bray et al. (5, 6) showed that performing a demanding cognitive task before or between isometric contractions significantly reduces the endurance and strength of isolated upper limb muscles. However, in these studies, mental exertion was not prolonged enough to induce subjective feelings of mental fatigue. Furthermore, neuromuscular function was assessed with EMG, a method that does not provide a valid measure of maximal voluntary activation of muscle (15). Therefore, the link between prolonged mental exertion and the central component of muscle fatigue is still unclear. Marcora et al. (21) conducted the first experimental study on the effect of prolonged mental exertion on endurance performance during dynamic whole-body exercise. These investigators induced mental fatigue in a group of healthy and fit subjects using a prolonged demanding cognitive task performed for 90 min, and found a significant reduction in time to exhaustion during subsequent high-intensity cycling exercise. However, the physiological mechanisms underlying the negative effect of prolonged mental exertion on endurance performance are currently unknown. Marcora et al. (21) did not find any effect of mental fatigue on the cardiovascular, respiratory and metabolic responses to high-intensity cycling exercise. Motivation related to the time to exhaustion test was also unaffected by mental fatigue. In this

study, the only factor that could explain a premature exhaustion was the higher perception of effort experienced by mentally fatigued subjects during high-intensity cycling exercise. According to the psychobiological model of endurance performance, exhaustion is not caused by muscle fatigue (20), i.e. by the failure of the fatigued neuromuscular system to produce the force/power required by the endurance task despite a maximal voluntary effort. On the contrary, it is proposed that exhaustion results from a conscious decision to disengage from the endurance task. In highly motivated subjects this effort-based decision is taken when perception of effort is maximal and continuation of the endurance task seems impossible.

Paragraph 2

Although this explanation is plausible, Marcora et al. (21) did not measure neuromuscular function. Therefore, a reduction in maximal muscle activation or an increase in the extent of central fatigue induced by endurance exercise may also explain the negative effect of mental fatigue on endurance performance. Central fatigue is an exercise-induced reduction in the capacity of the central nervous system (CNS) to fully recruit the active muscles (muscle activation) during a maximal voluntary contraction (MVC), and occurs at both spinal and/or supraspinal level (15). Central fatigue is thought to negatively affect endurance performance (1) and several authors have proposed a strong link between mental and central fatigue (e.g. 5, 11, 26). Because supraspinal fatigue seems to occur in brain areas upstream of the primary motor cortex (34), it is plausible that prolonged mental exertion can alter maximal muscle activation and, thus, impair endurance performance.

Paragraph 3

The main aim of the present study was to test experimentally this hypothetical link between mental fatigue, maximal muscle activation and central fatigue. Specifically, we hypothesized that prolonged mental exertion leading to mental fatigue i) would reduce maximal muscle activation and ii) would increase the extent of central fatigue induced by

subsequent endurance exercise. We tested these two main hypotheses by measuring maximal muscle activation of the knee extensor muscles before and after prolonged mental exertion, and immediately after subsequent submaximal isometric contraction of the knee extensor muscles until exhaustion (endurance task). Additionally, we hypothesized that prolonged mental exertion would reduce endurance performance via a higher perception of effort during the endurance task.

METHODS

Paragraph 4

Subjects and Ethical Approval. Ten physically active male adults (age: 22 ± 2 yr, height: 177 ± 6 cm, weight: 70 ± 8 kg) volunteered to participate in this study. None of the subjects had any known mental or somatic disorder. Each subject gave written informed consent prior to the study. Experimental protocol and procedures were approved by the local Ethics Committee of the Faculty of Sport Sciences, University of Burgundy in Dijon. All subjects were given written instructions describing all procedures related to the study but were naive of its aims and hypotheses. Participants believed that the study was on the effects of two different cognitive activities (a computerized task and watching a movie) on the neuromuscular responses to an endurance task. To ensure high motivation during the cognitive and endurance tasks, a reward (ticket to a professional sport event) was given to the best performances in both the cognitive and endurance tasks. At the end of the last session, subjects were debriefed and asked not to discuss the real aims of the study with other participants. The study conformed to the standards set by the World Medical Association Declaration of Helsinki “Ethical Principles for Medical Research Involving Human Subjects” (2008).

Paragraph 5

Experimental Protocol. Subjects visited the laboratory on three different occasions. During the first visit, subjects were familiarised with the laboratory and the experimental procedures. During the second and third visit, subjects performed either a mental fatigue task or a control task (see *Cognitive Tasks* for more details) in a randomized and counterbalanced order. After the cognitive task, subjects performed submaximal isometric knee extensor exercise until exhaustion (see *Endurance Task* for more details). Neuromuscular function of the knee extensor muscles was tested before and after the cognitive task, and after the subsequent endurance task. Mood was assessed before and after the cognitive task, whilst motivation was measured before the subsequent endurance task (Fig. 1). For more details see *Neuromuscular Function Tests* and *Psychological Questionnaires*.

Paragraph 6

Each participant completed all three visits over a period of 3 weeks with a minimum of 72 hours recovery period between visits. All participants were given instructions to sleep for at least 7 hours, refrain from the consumption of alcohol, and not to practise vigorous physical activity the day before each visit. Participants were also instructed not to consume caffeine and nicotine at least 3 hours before testing, and were asked to declare if they had taken any medication or had any acute illness, injury or infection.

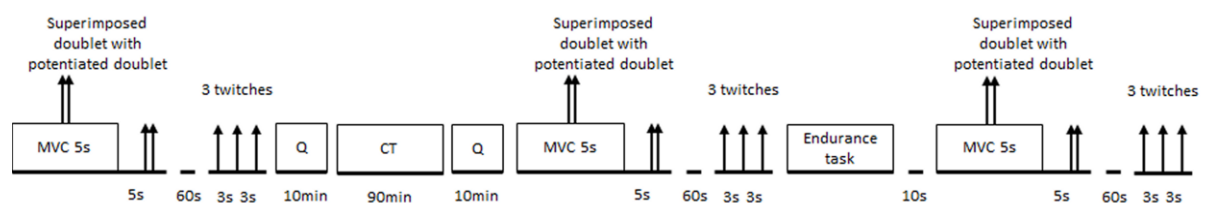


Figure 1. Graphical overview of the protocol for one session.

Order and timing was the same for each subject and each session. Q = psychological questionnaires, CT = cognitive task, MVC = maximal voluntary contraction

Paragraph 7

Cognitive Tasks

Mental Fatigue Task. Mental fatigue was induced by asking the subject to perform the AX-Continuous Performance Test (AX-CPT) (8) for 90 min on a personal computer. In this cognitive task, sequences of letters were visually presented one at time in a continuous fashion on a computer screen with black background. All letters were presented centrally, for duration of 300 ms in 24-point uppercase Helvetica font. Each letter was followed by a 1200 ms interval, for a total of a 4500 ms delay between the presentation of cue and probe stimuli. Participants sat in front of the computer screen and were instructed to press the keyboard space bar on target trials and the control button otherwise. Any missed or incorrect response activated a beep sound from two speakers as a prompt to increase speed and accuracy. To further increase engagement in the mental fatigue task, a ticket for a professional sporting event was given as a prize for the best performance. Feedback on performance was presented on the computer screen every 30 minutes as a percentage of the maximum possible score. Performance was scored automatically by the computer on the basis of correct responses and response time. Target trials were defined as a cue-probe sequence in which the letter A (in red) appeared as a cue and the letter X (in red) as the probe. To increase task difficulty, two white distractor letters (except A, K, X or Y) were presented between the cue and probe (in white). All other cue-probe sequences served as invalid cues and non-target probes. Letter sequences were presented in pseudorandom order, such that target (AX) trials occurred with 70 % and non-target trials occurred with 30 % frequency.

Paragraph 8

Control Task. The non-fatiguing cognitive task consisted of watching “Earth”, a documentary following the migration paths of four animal families (Alastair Fothergill and Mark Linfield, 2007), for 90 min on the same computer. During both cognitive tasks, heart rate (HR) was

recorded continuously using a HR monitor (Polar RS400, Polar Electro Oy, Kempele, Finland).

Paragraph 9

Endurance Task. To evaluate endurance performance, subjects performed one prolonged submaximal isometric contraction of the knee extensor muscles until exhaustion. Equipment and subject position was similar to that used for mechanical recordings during the neuromuscular function tests. A target value of 20% MVC torque was chosen. The MVC before the cognitive task was used to calculate the target torque. Visual feedback of the torque exerted during the endurance task was clearly displayed on a computer screen located one meter in front of the subject. Torque feedback was represented as a horizontal line and subjects were required to reach an upper target line fixed at the target level. The endurance task terminated when torque fell below the required target value for more than 3 s despite strong verbal encouragement (exhaustion) given by a research assistant blind to the nature of the cognitive task previously performed by the subject. Endurance performance was measured as time to exhaustion. Subjects were not aware of time during the endurance task, and they were made aware of their times to exhaustion after the study was completed. Perception of effort defined as “the conscious sensation of how hard, heavy, and strenuous exercise is” (18) was measured using the 15 points rating of perceived exertion (RPE) scale (4). Standardized explanations of the scale were given to each subject before the warm-up. Briefly subjects were asked to rate how hard they were driving their leg during the endurance task. Leg RPE was assessed every 20 s. HR and electromyographic (EMG) signal (see *Electromyographic recordings*) for the knee extensor muscles were continuously recorded during the endurance task. HR was calculated for consecutive sampling intervals of 20 s.

Paragraph 10

Neuromuscular Function Tests

Electrical stimulation. Both single and double (100 Hz frequency) stimulation were used for assessment of neuromuscular function. Transcutaneous electrically-evoked contractions of the knee extensor muscles were induced by using a high-voltage (maximal voltage 400 V) constant-current stimulator (model DS7 modified, Digitimer, Hertfordshire, UK). The femoral nerve was stimulated using a monopolar cathode ball electrode (0.5 cm diameter) pressed into the femoral triangle by the same experimenter during all tests. The site of stimulation producing the largest resting twitch amplitude and compound muscle action potential (M-Wave) was located and was marked on the skin so that it could be repeated reliably before and after the cognitive task, and after the endurance task. The anode was a 50 cm² (10 × 5 cm) rectangular electrode (Compex SA, Ecublens, Switzerland) located in the gluteal fold opposite the cathode. The optimal intensity of stimulation (i.e. that which recruited all knee extensors motor unit) was considered to be reached when an increase in the stimulation intensity did not induce a further increase in the amplitude of the twitch torque and of the peak-to-peak amplitude of the knee extensors compound muscle action potentials (M-waves). The stimulus duration was 1 ms and the interval of the stimuli in the doublet was 10 ms. Once the optimal intensity was found, 130% of this intensity was used and kept constant throughout the session for each subject. The supramaximal intensities ranged from 60 to 140 mA. Methodology and supramaximal intensities are according to previous studies (e.g. 29, 30).

Paragraph 11

Mechanical recordings. Mechanical parameters were recorded using a Biodex isokinetic dynamometer (Biodex Medical Systems Inc., New York, USA). The axis of the dynamometer was aligned with the knee axis, and the lever arm was attached to the shank with a strap. Extraneous movement of the upper body was limited by two crossover shoulder harnesses and a belt across the abdomen. Neuromuscular function tests were performed with the right

leg at a knee joint angle of 90° of flexion (0° = knee fully extended) and a hip angle of 90°. The following parameters were analysed from the twitch response (average of 3 single stimulation interspaced by 3 s): peak twitch (Tw), time to peak twitch (contraction time, Ct) and half-relaxation time. The peak torque of the doublet (potentiated doublet, 5 s after the MVC) was also analysed. MVC torque was considered as the peak torque attained during the MVC. Voluntary activation level (VAL) during the MVC was estimated according to the following formula:

$$VAL = \frac{\frac{\text{superimposed doublet amplitude}}{\text{potentiated doublet amplitude}}}{1} \cdot 100$$

$\left(\frac{\text{MVC at stimulation}}{\text{MVC}}\right)$ corresponding to Strojnik and Komi correction (4) was used if the stimulation appears not at the MVC torque value. All VAL calculations were performed for a $\text{MVC}_{\text{at stimulation}}$ between 95 and 100% MVC in order to ensure reliability of measurement. Mechanical signals were digitized on-line at a sampling frequency of 1 kHz using a computer, and stored for analysis with commercially available software (Acqnowledge 4.1 for MP Systems, Biopac Systems Inc., Goleta, USA). Timing of stimulation could be found in Figure 1.

Paragraph 12

Electromyographic recordings. EMG of the vastus lateralis (VL) and rectus femoris (RF) muscles was recorded with pairs of silver chloride circular (recording diameter of 10 mm) surface electrodes (Swaromed, Nessler Medizintechnik, ref 1066, Innsbruck, Austria) with an interelectrode (centre-to-centre) distance of 20 mm. Recording sites were then carefully adjusted by eliciting the greatest M-wave amplitude for each muscle at a given intensity via femoral nerve stimulation at the beginning of each testing session. Low resistance between the two electrodes (< 5kΩ) was obtained by shaving the skin, and dirt were removed from the skin using alcohol swabs. The reference electrode was attached to the patella of the left knee.

Myoelectrical signals were amplified with a bandwidth frequency ranging from 1 Hz to 5 kHz (common mode rejection ratio = 110 dB; impedance input = 1000 M Ω ; gain = 1000 for RF and 500 for VL), digitized on-line at a sampling frequency of 2 kHz using a computer, and stored for analysis with commercially available software (Acqnowledge 4.1 for MP Systems, Biopac Systems Inc., Goleta, USA). The root mean square (RMS), a measure of EMG amplitude, was automatically calculated with the software.

Paragraph 13

Peak-to-peak amplitude and duration of the M-waves were analysed for VL and RF muscles with the average of the three trials used for analysis. EMG amplitude of VL and RF muscles during the knee extensors MVC was quantified as the RMS for a 0.5 s interval at peak torque (250 ms interval either side of the peak torque). Maximal RMS values for VL and RF muscles were then normalized by the M-wave peak-to-peak amplitude for the respective muscles, in order to obtain RMS/M-wave ratio. This normalization procedure accounted for peripheral influences including neuromuscular propagation failure and changes in impedance from the EMG recordings. RMS EMG was calculated for consecutive sampling intervals of 20 s during the endurance task for both VL and RF. The RMS EMG during endurance task was normalized to the RMS EMG determined during the MVC precognitive task.

Paragraph 14

Psychological Questionnaires

Mood. The Brunel Mood Scale (BRUMS) developed by Terry et al. (36) was used to quantify current mood (“How do you feel right now?”) before and after the cognitive tasks. This questionnaire contains 24 items (e.g., “angry, uncertain, miserable, tired, nervous, energetic”) divided into six respective subscales: anger, confusion, depression, fatigue, tension, and vigor. The items are answered on a 5 point scale (0 = not at all, 1 = a little, 2 = moderately, 3

= quite a bit, 4 = extremely), and each subscales, with four relevant items, can achieve a raw score in the range of 0 to 16. Only scores for the Fatigue and Vigour subscales were considered in this study as subjective markers of mental fatigue.

Paragraph 15

Motivation. Motivation related to the endurance task was measured using the success motivation and intrinsic motivation scales developed and validated by Matthews et al. (23). Each scale consists of 7 items (e.g., “I want to succeed on the task” and “I am concerned about not doing as well as I can”) scored on a 5-point scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = very much, 4 = extremely). Therefore, total scores for these motivation scales range between 0 and 28.

Paragraph 16

Statistics. All data are presented as means \pm standard error of the means (SEM). Assumptions of statistical tests such as normal distribution and sphericity of data were checked as appropriate. Greenhouse-Geisser correction to the degrees of freedom was applied when violations to sphericity were present. Paired t-tests were used to assess the effect of condition (mental fatigue vs control) on time to exhaustion, motivation scores, HR at exhaustion, leg RPE at exhaustion, and RMS at exhaustion. One-way repeated measure ANOVA was used to test the effect of time (15-min blocks) on the number of incorrect answers, reaction time and HR during the AX-CPT task. Fully repeated measure 2 x 2 ANOVAs were used to test the effect of condition and time on mood before and after the cognitive tasks. Fully repeated measure 2 x 3 ANOVAs were used to test the effect of condition and time on MVC torque, VAL, M-wave parameters for each muscle, RMS/M-wave ratio, twitch properties, and peak doublet torque before and after the cognitive tasks, and after the endurance task. Fully repeated measure 2 x 7 ANOVAs were used to test the effect of condition and time on HR, leg RPE, and RMS at isotime (time elapsed from the beginning of the endurance task to the

last measurement before exhaustion of the shortest performance). Significant main effects of time and significant interactions were followed up with Bonferonni tests as appropriate. Significance was set at 0.05 (2-tailed) for all analyses, which were conducted using the Statistical Package for the Social Sciences, version 19 for Mac OS X (SPSS Inc., Chicago, IL, USA).

RESULTS

Paragraph 17

Manipulation Checks. Heart rate decreased over time in both conditions ($P < 0.001$) but it was significantly higher in the mental fatigue condition (73 ± 1 beat/min) compared to the control condition (69 ± 1 beat/min) ($P = 0.004$) (Fig. 2B). The number of incorrect responses (Fig. 2C) and reaction time (Fig. 2D) did not change significantly over time during the AX-CPT task.

Paragraph 18

The mood questionnaire revealed a significant decrease in Vigour after both the AX-CPT task (9.0 ± 0.9 to 6.5 ± 0.9) and the control task (9.7 ± 0.6 to 7.1 ± 0.7) ($P = 0.003$) with no significant difference between conditions. However, there was a significant interaction for the subjective fatigue ($P = 0.033$). Follow-up tests demonstrated that Fatigue increased significantly only after the AX-CPT task ($P = 0.007$) with no significant change after the control task (Fig. 2A).

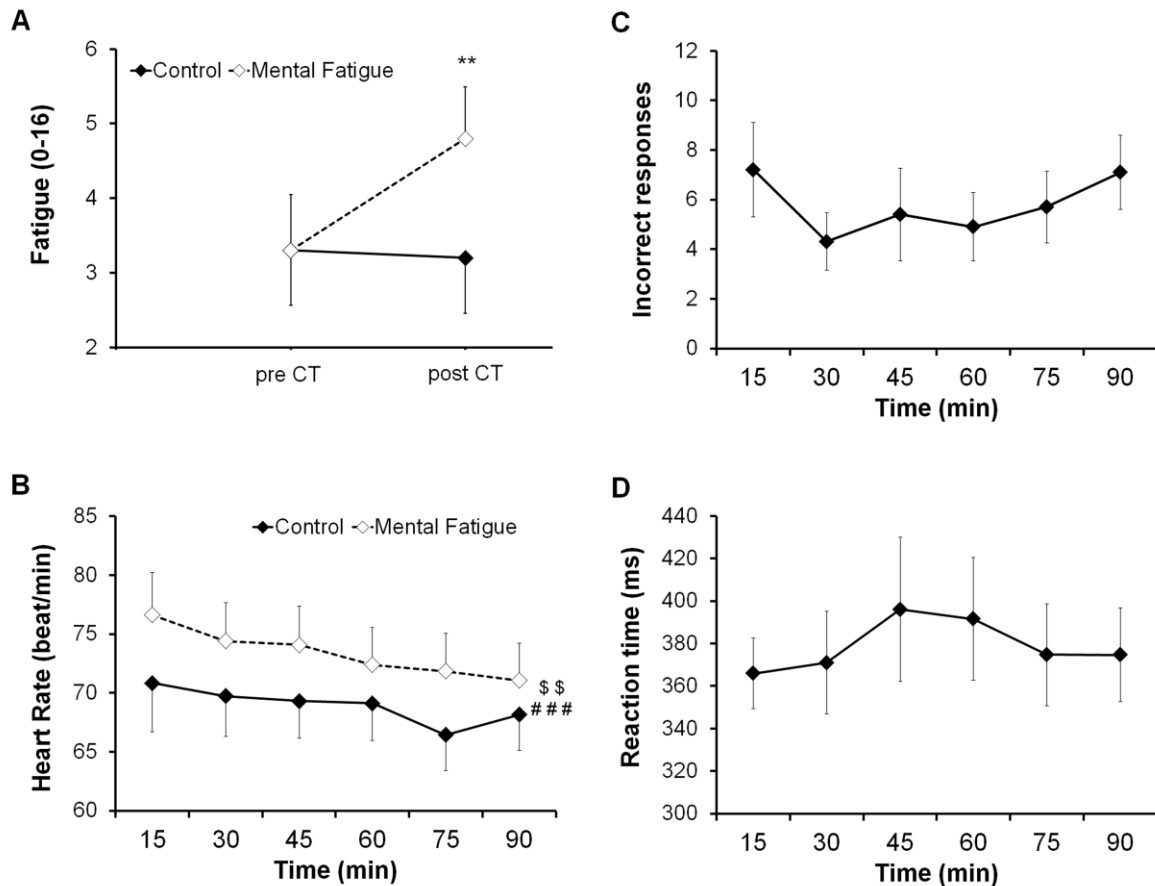


Figure 2. Markers of mental fatigue.

A. Effect of cognitive tasks on self-reported fatigue. B. Heart rate during both cognitive tasks. C. Number of incorrect responses during the mental fatigue task. D. Reaction time during the mental fatigue tasks. CT = cognitive task. \$\$ Significant main effect of condition ($P < 0.01$). ** Significant condition x time interaction ($P < 0.01$).). ### Significant main effect of time ($P < 0.001$). Data are presented as means \pm SEM

Paragraph 19

Effects of Mental Fatigue on Intrinsic and Success Motivation. There were no significant differences between conditions in intrinsic motivation (mental fatigue condition 16.5 ± 1.3 , control condition 16.5 ± 1.1 , $P=1.000$) and success motivation (mental fatigue condition 18.8 ± 1.6 , control condition 15.8 ± 1.8 , $P=0.111$).

Paragraph 20

Effects of Mental Fatigue on Time to exhaustion, HR, EMG amplitude, and Perception of Effort during the Endurance Task. Time to exhaustion (Fig. 3A) was 13 ± 4 % shorter in the mental fatigue condition compared to the control condition ($P=0.008$). Individual times to exhaustion were shorter in the mental fatigue condition compared to the control condition in 8 out of 10 subjects (Fig. 3B). Heart rate (Fig. 3D) increased significantly during the endurance task ($P<0.001$) with no significant differences between conditions at both isotime and exhaustion. EMG amplitude (RMS/RMS pre-cognitive task MVC) of the VL muscle (Fig 3C) increased significantly during the endurance task ($P=0.003$) with no significant difference between conditions at isotime. At exhaustion, however, VL EMG amplitude tended to be higher in the control condition (52.8 ± 6.8 %) compared to the mental fatigue condition (41.5 ± 5.9 %) ($P = 0.095$). Leg RPE (Fig. 3E) increased significantly during the endurance task ($P<0.001$) and it was significantly higher in the mental fatigue condition compared to the control condition ($P = 0.045$), without interaction effect ($P = 0.353$). Leg RPE at exhaustion was not significantly different between conditions.

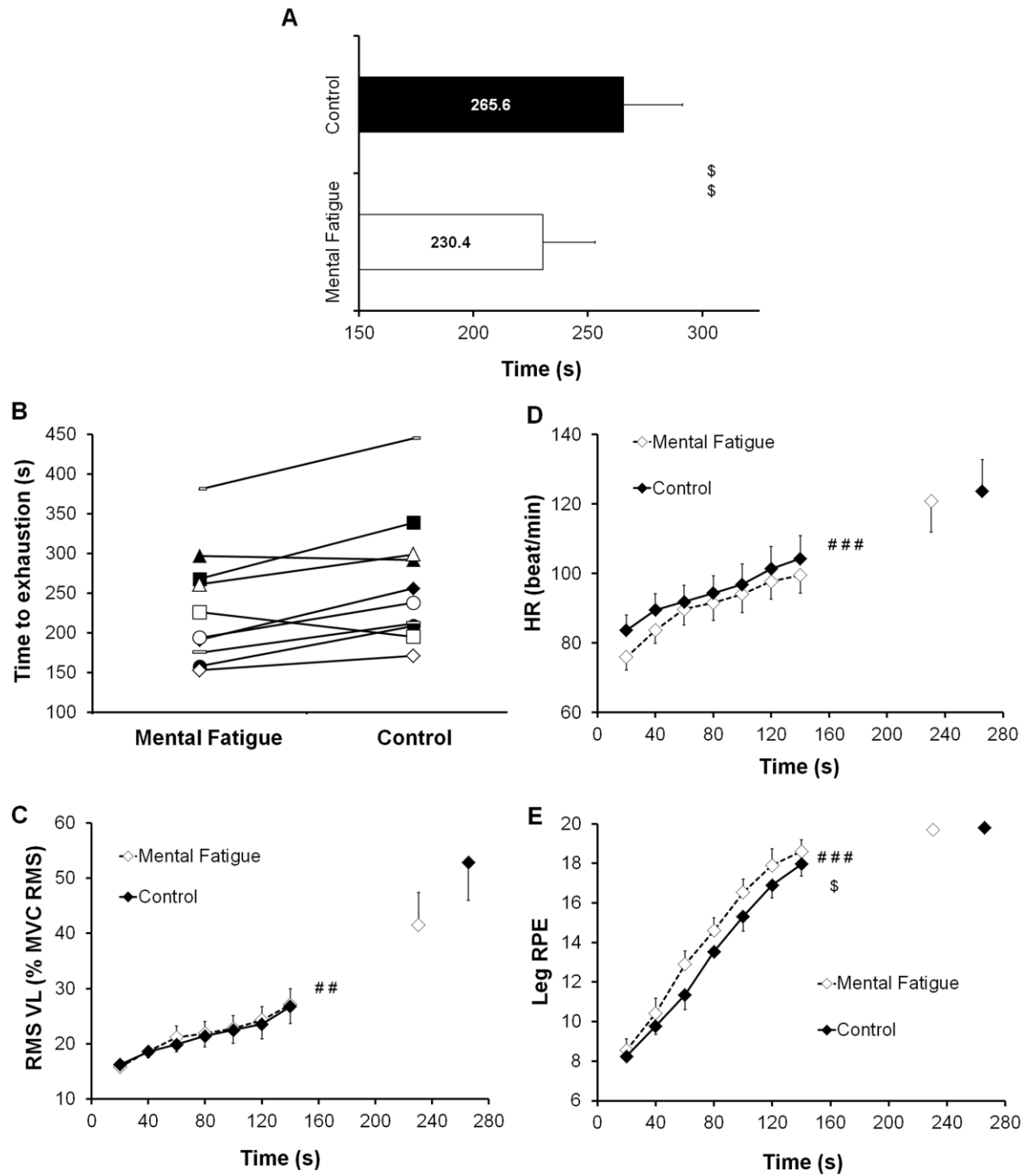


Figure 3. Effects of cognitive tasks on time to exhaustion, and physiological and perceptual responses during the endurance task.

A. Mean effect of mental fatigue on time to exhaustion. B. Individual effect of mental fatigue on time to exhaustion. C. Root mean square (RMS) EMG of the vastus lateralis (VL) muscle during the endurance task. Values are expressed as a percentage of the maximal value before the cognitive task. D. Heart rate (HR) during the endurance task. E. Leg rating of perceived exertion (RPE) during the endurance task

\$ Significant main effect of condition ($P < 0.05$). \$\$ Significant main effect of condition ($P < 0.01$). ## significant main effect of time ($P < 0.01$). ### Significant main effect of time ($P < 0.001$). Data are presented as means \pm

SEM

Paragraph 21

Effects of Mental Fatigue and the Endurance Task on Neuromuscular Function

MVC. There was no significant main effect of condition or interaction on knee extensors MVC (Fig. 4A). Follow-up tests of the significant main effect of time ($P < 0.001$) revealed that the cognitive tasks did not affect MVC torque. The endurance task caused a significant reduction in MVC torque in both the mental fatigue and control condition (mental fatigue condition -26.7 ± 5.7 %, control condition -27.6 ± 3.3 %) ($P < 0.001$). The MVC torque of the knee flexors was not significantly affected by the cognitive tasks and the endurance task (pre-cognitive task: mental fatigue condition 94 ± 5 Nm, control condition 91 ± 6 Nm ; post-cognitive task: mental fatigue condition 86 ± 5 Nm, control condition 93 ± 6 Nm ; post endurance task : mental fatigue condition 89 ± 6 Nm, control condition 93 ± 7 Nm).

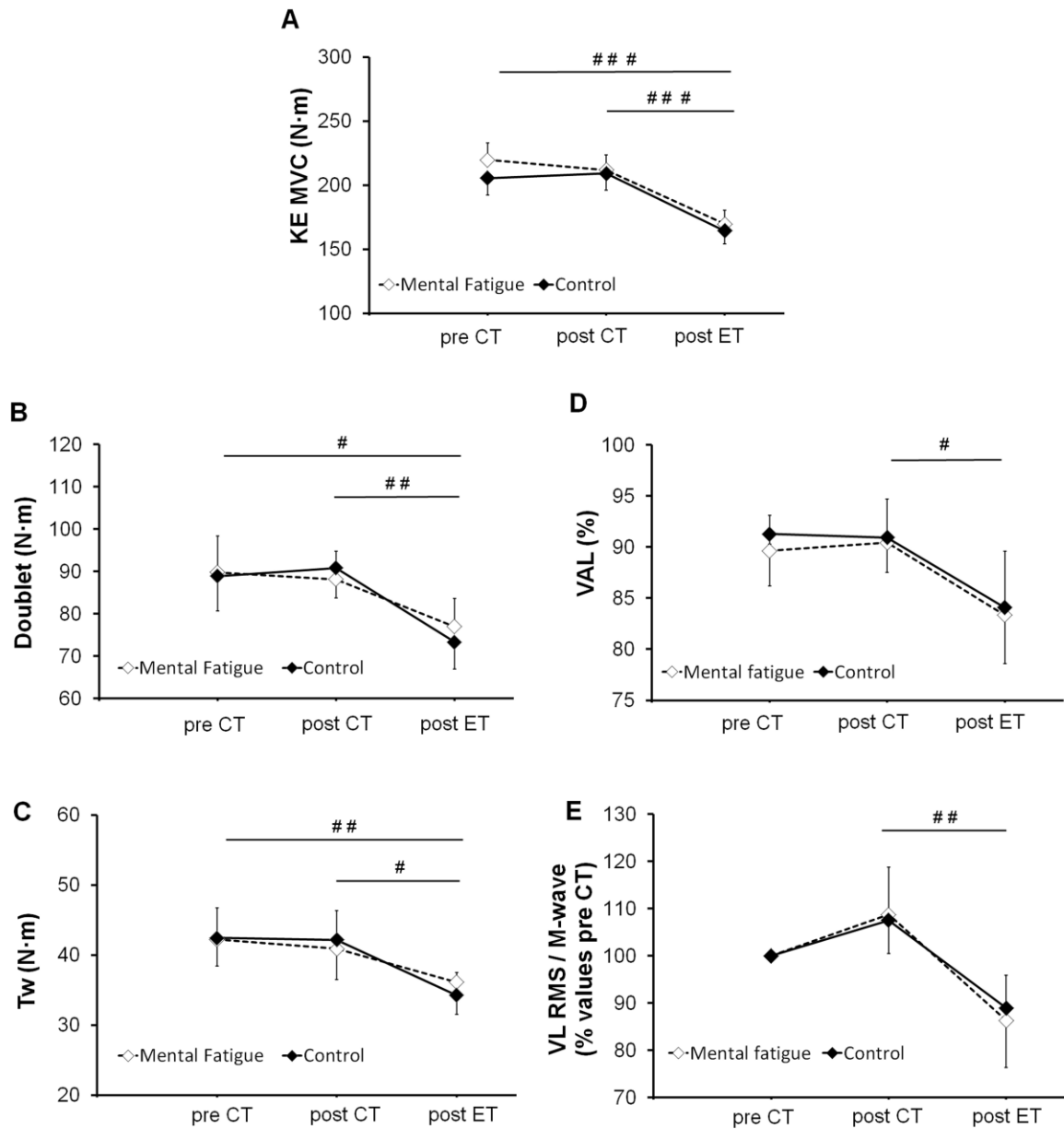


Figure 4. Effects of cognitive tasks and endurance task on central and peripheral parameters of neuromuscular function.

A. Maximal voluntary contraction (MVC) torque of the knee extensors (KE). B. Peak torque of the doublet. C. Peak twitch (Tw). D. Voluntary activation level (VAL). E. Root mean square (RMS)/Mmax (M-wave) ratio of the vastus lateralis (VL) muscle. Values are expressed as a percentage of baseline values (pre cognitive task values). CT = cognitive task, ET = endurance task. # Significant main effect of time ($P < 0.05$). ## Significant main effect of time ($P < 0.01$). ### Significant main effect of time ($P < 0.001$). Data are presented as means \pm

SEM

Paragraph 22

Peripheral Fatigue. There were no significant main effects of condition or interactions on all twitch parameters. Follow-up tests of the significant main effects of time (all $P < \text{or} = 0.010$) revealed that the cognitive tasks did not affect Tw (Fig. 4C), Ct, and doublets (Fig. 4B). Half relaxation time of the twitch peak force was significantly higher after the cognitive tasks ($P=0.047$). The endurance task significantly affected Tw ($P=0.021$) (Fig. 4C), Ct ($P=0.021$), Half relaxation time of the twitch peak force ($P=0.034$), and doublet ($P=0.035$) (Fig. 4B). M-wave amplitude and duration for VL and RF (Table 1) muscles were not significantly affected by the cognitive tasks and the endurance task (amplitude: $P=0.352$ and $P=0.444$, duration: $P=0.488$ and $P=0.792$). M-wave amplitude and duration for VL and RF muscles did not change between condition (amplitude: $P=0.177$ and $P=0.740$, duration: $P=0.088$ and $P=0.177$) and did not show any interaction effect (amplitude: $P=0.804$ and $P=0.972$, duration: $P=0.804$ and $P=0.360$).

	Mental fatigue			Control		
	Pre CT	Post CT	Post ET	Pre CT	Post CT	Post ET
Amplitude VL (mV)	12.19 ± 2.52	11.81 ± 2.37	12.5 ± 2.47	13.30 ± 2.13	13.38 ± 1.95	13.89 ± 2.07
Duration VL (ms)	8.85 ± 0.48	9.08 ± 0.47	9.22 ± 0.47	10.63 ± 0.67	11.11 ± 0.66	10.78 ± 0.73
Amplitude RF mV)	7.70 ± 1.35	7.46 ± 1.22	7.79 ± 1.24	7.44 ± 1.04	7.11 ± 1.09	7.43 ± 1.00
Duration RF (ms)	8.03 ± 0.57	8.68 ± 0.86	8.53 ± 1.07	9.88 ± 0.85	9.67 ± 0.89	9.70 ± 0.98

Table 1. Peak-to-peak amplitude and duration of the maximal M-wave associated with the single twitch.

CT = cognitive task, ET = endurance task, VL = vastus lateralis and RF = rectus femoris.

Paragraph 23

Central Fatigue. There was no significant main effect of condition or interaction on VAL (Fig. 4D). Follow-up tests of the significant main effect of time ($P = 0.027$) revealed that the cognitive tasks did not significantly affect VAL. However, the endurance task significantly

reduced VAL ($P=0.024$). Similarly, there was no significant main effect of condition or interaction on RMS/M-wave ratio of the RF and VL (Fig. 4E) muscles. Follow-up tests of the significant main effects of time (all $P < 0.009$) revealed that the cognitive tasks did not affect RMS/M of the RF and VL muscles. However, RMS/M decreased significantly after the endurance task for both the RF ($P < 0.001$) and VL ($P=0.010$) muscles.

DISCUSSION

Paragraph 24

The main aim of the present study was to test the hypotheses that prolonged mental exertion leading to mental fatigue i) would reduce maximal muscle activation and ii) would increase the extent of central fatigue induced by subsequent endurance exercise. Contrary to our hypotheses, this study demonstrates that prolonged mental exertion does not lead to any impairment in neuromuscular function. In accordance with previous findings (21), the negative effect of prolonged mental exertion on endurance performance seems to be mediated by the higher perception of effort experienced by mentally fatigued subjects during the endurance task.

Paragraph 25

Prolonged Mental Exertion and Mental Fatigue

The higher HR observed during the AX-CPT task compared to watching a movie confirms the demanding nature of this cognitive task. In fact, an increase in HR and other cardiovascular changes are associated with exertion of effort during cognitive tasks (32). Given its demanding nature, it is not surprising that 90-min of the AX-CPT task induced a significant increase in subjective feelings of fatigue. This effect is in accordance with

previous studies (21, 38), and demonstrates we were successful in experimentally inducing a state of mental fatigue in our subjects. However, we did not observe any significant decrease in cognitive performance during the AX-CPT task. It is possible that the reward we gave for best performance in the AX-CPT task made our subjects able to overcome the negative effects of mental fatigue on cognitive performance (2).

Paragraph 26

Prolonged Mental Exertion Does Not Reduce Maximal Muscle Activation

Our first hypothesis was that prolonged mental exertion would reduce maximal muscle activation. It is well known that endurance exercise can reduce maximal muscle activation (15); but until now, it was not known whether prolonged mental exertion could also reduce the capacity of the CNS to maximally recruit the active muscles. We tested this hypothesis by examining neuromuscular function before and after the two cognitive tasks. Because small changes in maximal muscle activation may be hard to detect using the twitch interpolation technique (33), careful consideration of numerous experimental details was taken (e.g. use of pair stimuli or high resolution measurement of torque). Contrary to our hypothesis, the present study failed to show a decrease in knee extensors muscles MVC torque following the fatiguing cognitive task (90 min AX-CPT). Furthermore, VAL and RMS/M-wave ratio during MVC were not affected by mental fatigue. These novel results suggest that, unlike endurance exercise, prolonged mental exertion does not reduce maximal muscle activation. However, in the present study, the 90 min AX-CPT induced a relatively moderate level of mental fatigue. Therefore, we cannot exclude that cognitive tasks leading to higher levels of mental fatigue may reduce maximal muscle activation.

Paragraph 27

Interestingly, some literature suggests that mental fatigue can have systemic effects such as alterations of amino acids concentration in the blood (24, 27). These and other

unknown systemic effects of mental fatigue could theoretically cause some peripheral fatigue. Our experimental study, however, failed to find any significant effect of prolonged mental exertion on twitches and M-waves properties.

Paragraph 28

Our findings are in contrast with those of Bray et al. (5) who found a negative effect of a demanding cognitive task on MVC of the hand flexor muscles. These authors suggested an interaction between the demanding cognitive task and an alteration of the ability of the CNS to maximally recruit the active muscles. However, no valid measure of maximal muscle activation was included in their study. The discrepancy between our results and those of Bray et al. (5) may also be explained by the difference in muscle group tested to measure neuromuscular function (hand flexor muscles vs knee extensor muscles). Furthermore, the increase in MVC observed by Bray et al. (5) in the control condition suggests that their subject did not exert a maximal voluntary effort during all tests of neuromuscular function. Lack of maximal voluntary effort is well known to negatively affect measures of neuromuscular function (12). Further research is required to get better insights on the possible effect of prolonged mental exertion on maximal muscle activation in different muscle groups.

Paragraph 29

Prolonged Mental Exertion Does Not Increase the Extent of Central Fatigue Induced by Subsequent Endurance Exercise

Although prolonged mental exertion did not reduce maximal muscle activation, it may be possible that exercising in a mental fatigue state would increase the extent of central fatigue measured at exhaustion. In order to investigate the hypothetical interaction between mental and central fatigue, we chose a submaximal isometric knee extensor exercise protocol known to induce a reduction in VAL, i.e. to induce central fatigue (e.g. 30). Moreover

because timing for neuromuscular assessment is crucial (13), submaximal isometric exercise immediately followed by an MVC of the same muscle group provides us with the fastest way to accurately quantify the extent of central fatigue at exhaustion. As expected, the endurance task induced significant central and peripheral fatigue in both the mental fatigue and control conditions. However the similar reduction in VAL at exhaustion in both conditions is against our hypothesis that prolonged mental exertion would increase the extent of central fatigue induced by subsequent endurance exercise. Because time to exhaustion was significantly different between the mental fatigue and control conditions, further investigations on the effect of prolonged mental exertion on the time course of central fatigue during endurance exercise are required. However, it should be pointed that any small difference in voluntary activation between mental fatigue and control conditions may be hard to detect. Further research is also needed to investigate whether higher levels of mental fatigue or different endurance tasks (e.g., dynamic whole-body exercise) are associated with an increase in the extent of central fatigue induced by subsequent endurance exercise.

Paragraph 30

Prolonged Mental Exertion versus Endurance Exercise

Our findings demonstrate for the first time that prolonged mental exertion and endurance exercise have different effects on neuromuscular function. The fact that prolonged mental exertion, unlike endurance exercise, does not alter peripheral muscle function is not surprising because the fatiguing cognitive task (90 min AX-CPT) does not involve the knee extensor muscles. However, we expected that prolonged mental exertion would reduce maximal muscle activation of the knee extensors. As in previous studies (30), our submaximal isometric knee extensor exercise protocol induced a significant reduction in maximal muscle activation, a phenomenon called central fatigue (15). However, the 90 min AX-CPT did not reduce maximal muscle activation of the knee extensors despite leading to a

significant level of mental fatigue. The different effects of prolonged mental exertion and endurance exercise on maximal muscle activation suggest that different mechanisms are involved. One possibility is that prolonged mental exertion and endurance exercise are associated with different neurochemical changes in the brain. However, both prolonged mental exertion (14, 17) and endurance exercise (9, 22) have been associated with an increase in brain adenosine and a reduction in brain glycogen. Therefore, at present, the most likely explanation for the different effects of prolonged mental exertion and endurance exercise on maximal muscle activation is that the neurochemical changes associated with both phenomena occurs in different areas of the CNS.

Paragraph 31

The AX-CPT task we used to experimentally induce mental fatigue in our subjects is known to strongly activate the anterior cingulate cortex (ACC) (8), an area of the brain associated with task difficulty and sustained attention in a variety of cognitive tasks (28). Importantly, the ACC has also been linked with perception of effort during endurance exercise (41). It is, therefore, biologically plausible that prolonged mental exertion induces changes in the ACC, which in turn, increase perception of effort and reduce endurance performance. However, our results suggest that prolonged activation of the ACC does not reduce the capacity of the CNS to maximally recruit the active muscles.

Paragraph 32

The reduction in maximal muscle activation induced by exercise (central fatigue) can occur at both spinal and supraspinal level (15). Although it has been proposed that supraspinal fatigue during maximal and submaximal isometric contractions is localised in brain areas upstream of the primary motor cortex (34), there are few neuroimaging studies investigating the brain areas associated with supraspinal fatigue. Some studies have shown progressive increase in activity in several brain areas such as the sensorimotor cortex,

supplementary motor areas, frontal cortex, and the insular cortex during submaximal fatiguing exercise (16, 31, 39, 40). However, it is not clear whether the concept of central fatigue is meaningful during submaximal muscle contractions (35). In fact, these changes in cerebral activity during submaximal fatiguing exercise are likely to reflect brain adaptations to compensate for spinal and/or peripheral muscle fatigue rather than mechanisms of supraspinal fatigue. To the best of our knowledge, only van Duinen et al. (39) have investigated the brain areas associated with supraspinal fatigue by measuring their activity during MVCs performed before and after fatiguing exercise. These authors showed a significant decrease in activity of the supplementary motor areas and, to a lesser extent, in parts of the paracentralgyrus, right putamen, and in a small cluster of the left parietal operculum. The fact that central fatigue was not associated with changes in ACC activity suggests that the brain areas affected by prolonged mental exertion and endurance exercise are different.

Paragraph 33

Furthermore, we have to consider that the neurochemical changes induced by prolonged mental exertion are likely to be confined to the brain, whilst some of the neurochemical changes leading to central fatigue may also occur at spinal level (15). Therefore, the different effects of prolonged mental exertion and endurance exercise on maximal muscle activation could be explained by i) the different brain areas affected by prolonged mental exertion and endurance exercise, and ii) the spinal alterations likely to occur during endurance exercise but not during prolonged mental exertion..

Paragraph 34

Mental Fatigue, Perceived Exertion and the Psychobiological Model of Endurance Performance

Finally, the present results provide experimental evidence that higher perception of effort induced by prolonged mental exertion is not associated with lower muscle activation before exercise. In fact, the higher perception of effort experienced by mentally fatigued subjects occurs despite no reduction of maximal muscle activation before the endurance task, and similar extent of central fatigue at exhaustion in the mental fatigue and control conditions. However, the increase in perception of effort occurring over time during the endurance task in both conditions may be caused, at least in part, by the central and peripheral fatigue induced by endurance exercise. In fact, in the presence of significant muscle fatigue, an increase in central motor command is required to maintain the same submaximal force. Because the sensory signal for perception of effort is the corollary discharge of the central motor command, the increase in central motor command required to overcome muscle fatigue is reflected in a significant increase in perception of effort (10, 19). A previous study (21) suggests that the higher perception of effort experienced by mentally fatigued subjects during the endurance task may be due to altered central processing of sensory signals. However, further research is required to understand the neurophysiological mechanisms underlying the negative effect of mental fatigue on perception of effort during endurance exercise.

Paragraph 35

Similar to previous findings on the effect of mental fatigue on endurance performance during dynamic whole-body exercise (21), we found that mental fatigue significantly reduces time to exhaustion during submaximal isometric knee extensor exercise. These results suggest that mental fatigue has a negative effect on endurance performance regardless of the type of contraction and muscle mass active during endurance exercise.

Paragraph 36

A plausible explanation for the negative effect of mental fatigue on endurance performance is provided by the psychobiological model of endurance performance (20) based on Motivational Intensity Theory (7). This model postulates that exhaustion is a form of task disengagement that occurs when subjects perceive the task as being impossible to complete despite their maximal effort, or when the effort required by the task exceeds the upper limit of what people are willing to do (potential motivation). Accordingly, a reduction in time to exhaustion can occur either because of an increase in perception of effort or a reduction in potential motivation. In accordance to a previous study (21), we did not measure any negative effect of mental fatigue on intrinsic and success motivation related to the endurance task. Therefore, the only mechanism that can explain the negative effect of prolonged mental exertion on time to exhaustion is the higher perception of effort experienced by mentally fatigued subjects during the endurance task. As leg RPE increased similarly over time in both conditions, mentally fatigued subjects reached their maximal level of perceived exertion and disengaged from the endurance task earlier than in the control condition.

*Paragraph 37**Conclusions and Perspectives*

The present study provides the first experimental evidence that prolonged mental exertion does not alter neuromuscular function measured as maximal muscle activation and central fatigue induced by subsequent endurance exercise. These findings suggest that prolonged mental exertion and endurance exercise affect different areas of the CNS. Future studies on brain and endurance performance should investigate the specific mechanisms of mental fatigue and central fatigue without making the wrong assumption that these two phenomena are two different aspects of the same central alterations. Because perception of effort is the most likely mediator of the negative effect of mental fatigue on endurance performance,

further studies are required to investigate the neurophysiological alterations associated with the higher perception of effort experienced by mentally fatigued subjects during endurance exercise. On a more practical perspective, the present study suggests that the negative impact of mental fatigue on physical performance is limited to endurance and may not have a negative impact on performance of short maximal voluntary efforts such as sprint or jump.

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CONFLICT OF INTEREST

The results of the present study do not constitute endorsement by ACSM. No conflict of interest, financial or otherwise is declared by the authors. No funding was received for this study.

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