

# Individualized mental fatigue does not impact neuromuscular function and exercise performance

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## **Abstract**

### **Introduction**

Recent studies have questioned previous empirical evidence that mental fatigue negatively impacts physical performance. The purpose of this study is to investigate the critical role of individual differences in mental fatigue susceptibility by analyzing the neurophysiological and physical responses to an individualized mental fatigue task.

### **Methods:**

In a pre-registered (<https://osf.io/xc8nr/>), randomized, within-participant design experiment, twenty-two recreational athletes completed a time to failure test at 80% of their peak power output under mental fatigue (individual mental effort) or control (low mental effort). Before and after the cognitive tasks, subjective feeling of mental fatigue, neuromuscular function of the knee extensors, and corticospinal excitability were measured. Sequential Bayesian analysis until it reached strong evidence in favor of the alternative hypothesis ( $BF_{10} > 6$ ) or the null hypothesis ( $BF_{10} < 1/6$ ) were conducted.

### **Results:**

The individualized mental effort task resulted in a higher subjective feeling of mental fatigue in the mental fatigue condition: 0.50 (95%CI 0.39 - 0.62) AU compared to control: 0.19 (95%CI 0.06 - 0.339) AU. However, exercise performance was similar in both conditions (control; 410 (95%CI 357 – 463) vs. mental fatigue 422 (95%CI 367 – 477) seconds,  $BF_{10} = 0.15$ ). Likewise, mental fatigue did not impair knee extensor maximal force generating capacity ( $BF_{10} = 0.928$ ) and did not change the extent of fatigability or its origin after the cycling exercise.

### **Conclusions:**

There is no evidence that mental fatigue adversely affects neuromuscular function or physical exercise, even if mental fatigue is individualized, computerized tasks seem not to affect physical performance.

### **Keywords:**

cognitive load, maximal voluntary contraction, motor evoked potential, evoked force, NIRS, perceived exertion

## INTRODUCTION

Over the course of the last decade, a growing body of research has shown that the performance of a standard cognitively demanding (or long) task induces a subjective feeling of mental fatigue<sup>1</sup>, impairs objective performance<sup>2</sup> in a subsequent physical exercise (2–4). However, recent studies have cast some doubt on this assertion and meta-analytical evidence has also suggested a bias in the literature (6, 7). Absence of evidence of an effect is not evidence of the absence of an effect, and we cannot yet discard that mental fatigue might have a negative effect on fatigability, given the high interindividual variability response to mental fatigue (7).

In contrast to physical exercise, where the load is typically tailored to each individual, in the studies investigating the effect of mental fatigue, the cognitive load of the task has not been systematically individualized (8). However, individualization of the mental load seems entirely necessary, since, by individualizing the mental load, we could determine whether a comparable level of mental load could actually affect performance in a subsequent physical exercise. Here, we propose an original approach where we impose high demands on mental processes (executive functions) by adapting the mental load to individual characteristics. In doing so, we assess the hypothesis that the mental load has a negative effect on exercise performance.

Exerting an individualized and demanding mental effort would likely lead to an increased perceptual fatigue, which can be captured in different ways. Subjective self-reported feeling of fatigue with a visual analog scale (VAS) has been the most common indicator (9), but subjective pre-post measurements may be driven by initial effects related to the adjustment to the experimental situation and only provide two snapshots of a continuum (10). Because individual differences can also be reflected at brain level, we advocate for monitoring cerebral oxygenation via near-infrared spectroscopy (NIRS) to study the adjustments of individual cerebral activation that occur during mentally fatiguing tasks and in order to assess whether brain oxygenation could be used as an objective biomarker of mental fatigue. For example, it has been recently suggested that brain oxygenation increases in frontal areas throughout the course of mental effort tasks and it is followed by a sharp drop (11, 12), which might contribute to the subsequent reduced exercise performance.

In line with this framework, it has been suggested that corticospinal excitability assessed with transcranial magnetic stimulation (TMS) is reduced as a consequence of mental fatigue (13), but these

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<sup>1</sup> We refer to mental fatigue as a mental activity over time leading to feeling the need for mental rest or a mismatch between mental effort expended and actual mental performance (1).

<sup>2</sup> We refer to objective performance as performance fatigability, i.e, a change in performance in a given task and involves disturbances at the level of the central nervous system and/or beyond the neuromuscular junction (5).

findings are difficult to generalize as there was no control condition without a cognitive task, and there was no measure of performance after the cognitive task. Similarly, reports suggest that in response to mental fatigue there is a need to increase the neural drive to pursue a submaximal exercise at a constant intensity (14). Furthermore, the perception of effort has been suggested to correlate with central motor command during the execution of the movement (15). Therefore, it is plausible that a mental fatigue-induced reduction in corticospinal excitability together with an increased perception of effort could explain the reduced performance in a subsequent exercise.

To summarize, there are open questions regarding the relationship between mental fatigue, perception of fatigue and objective performance that needs further consideration. The present pre-registered research aims at analyzing neurophysiological, perceptual and physical responses to an individualized mental fatigue task on performance. The hypotheses driving this research are summarized in supplementary table 1.

## **Methods**

### **Compliance with ethical regulations**

All experimental procedures were designed to comply with the Declaration of Helsinki. Before being recruited, participants provided written informed consent having previously read a participant information sheet and health questionnaire. All data were entered in a case report form, and subsequently in a computerized database and stored at the Institute of sport sciences, University of Lausanne. The study was approved by the Cantonal Commission for Ethics in Human Research in Vaud, Switzerland (project number 2022-00442).

### **Design**

The study is a pre-registered (<https://osf.io/xc8nr/>), within-participant and counterbalanced design. Before the familiarization visit, participants were randomly assigned to start the experimental protocol with one of the two experimental sessions (individualized mental effort protocol or control) based on balanced permutations generated by a web-based computer program ([www.randomization.com](http://www.randomization.com)). Due to the heterogeneity of effect sizes reported in this literature and publication bias (6), previous studies did not allow us to establish a clear effect size to calculate the sample size. Then, the sample size was determined using sequential tests with one-sided Bayes factor with a minimum of 20 participants and controlling the Bayes factor for the main index of physical performance (i.e., average time in the cycling task would be reduced in the mental fatigue condition) until it reaches strong evidence in favor of the alternative hypothesis ( $BF_{10} > 6$ ) or the null hypothesis ( $BF_{10} < 1/6$ ). If the Bayes factor did not reach the criteria, we planned to collect participants in batches of two (to keep the randomization and counterbalancing) until it fulfills the criteria. If not, we also planned to stop the experiment when we

reached the maximum number of participants we would be able to recruit (40 participants) or 8 months after the beginning of the data collection. Finally, we decided to stop the experiment when we reached 22 participants (18 males and 4 females with an age  $26.4 \pm 4.46$  years,  $70.8 \pm 8.4$  Kg,  $178.2 \pm 8.0$  cm and peak power output  $371 \pm 53$  watts). For some variables, we do not have the full dataset, e.g., technical issues during the electromyographic (EMG) or NIRS data collection. Therefore, the sample size for each variable is indicated in the results.

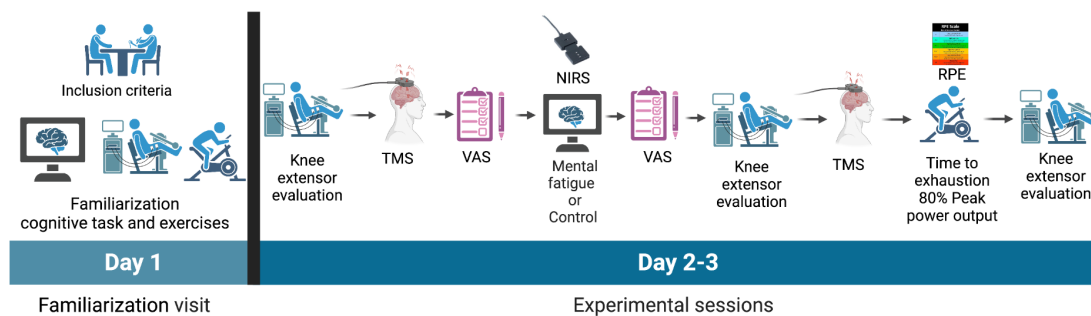
We recruited participants from the Lausanne area population in Switzerland and experimental sessions took place in the Institute of Sport Science at the University of Lausanne. We recruited male and female recreationally healthy active adults involved in regular training (4-8 h/week), with ages between 18 and 50 years old. Exclusion criteria were the presence of symptomatic cardiomyopathy, metal implants, metabolic disorders such as obesity or diabetes, chronic obstructive pulmonary disease, epilepsy, neurological disorders, and hormonal therapy. Data collection and analysis was not performed blind to the conditions of the experiments, but participants were naïve to the real aim of the study in order to avoid expectation effects. Once they completed their participation, they were debriefed with the purpose of the study. Participation in this study was compensated by a gift voucher.

### **Experimental Procedure**

Participants came to the laboratory on three different occasions, with each session separated at least for 48 h and completed at the same time ( $\pm 1$  hours) of the day to avoid fluctuations due to circadian rhythm. Participants were asked to refrain from eating or drinking anything for the 2 h prior to each session and to refrain from heavy exercise during the 24 h preceding each session. They were asked to keep a similar diet for each experimental session. On the first visit, all participants had a familiarization session to set the individual threshold of the cognitive task (see mental effort task). After a short break, they were familiarized with voluntary and electrically evoked muscle contractions and they performed an incremental exercise on a cycle ergometer (Lode Excalibur, Cosmed Quark, Rome, Italy) to determine their peak power output for the experimental sessions. The test began with a load of 30W and then the load increased progressively by 30 W every 1 minute (i.e., 2 W/sec) until volitional exhaustion (i.e., a pedal frequency of less than 60 rpm for more than 5 seconds despite strong verbal encouragement). The familiarization session lasted approximately 1 hour.

At least 48 h after the familiarization session, participants attended the laboratory on two separate sessions to perform either the individualized mental effort protocol or the control condition. Upon arrival, first, we carried out the neuromuscular evaluation of knee extensors adapted from a previous experiment (16, 17). Then, TMS was used to evoke MEPs from the first dorsal interosseous muscle (FDI) muscle to evaluate corticospinal excitability. Then, participants completed a Visual Analog Scale (VAS) to rate their subjective feeling of mental fatigue and activation status. After that, they completed

the cognitive tasks for approximately 30 minutes in a dimly illuminated room, while NIRS was recording. After completion of the task, participants completed the VAS again and were resubmitted to the neuromuscular and corticospinal excitability evaluation. They were then positioned on the cycle ergometer to start the time to exhaustion cycling test. The cycling test consists of a 5-min warmup at 40% of peak power output followed by a rectangular workload corresponding to 80% of peak power output achieved in the familiarization visit. Participants rated their perceived exertion every minute. The third session was exactly the same except for the mental task, which was that corresponding to the counterbalanced assignment (see figure 1 for a schematic representation of the procedure).



**Figure 1.** Experimental procedure for the experiment. Created with BioRender.com

### **Mental fatigue protocol**

We used the Time Load Dual-back task (TloadDback (18)) to individualize the cognitive effort for each participant. The TloadDback task allows to adapt the specific parameters of the task for each participant by pre-assessing the minimum time needed to perform the task properly, thus providing an individual rate of maximum cognitive load. Importantly, the TloadDback assesses the variations in performance within time of task characteristic of fatigue research (19)), by limiting the time allocated to respond. This dual task features an N-back task (the participant must decide whether the current stimulus matches the one displayed n trials ago) and a second interference task (odd/even decision task). The mental load of the task is calculated as the shortest stimulus duration to maintain accuracy performance > 85 %. In the control condition, participants completed a 0-back task adapted to individual characteristics by increasing 50% (respect to the TloadDback) the available time to process the requested demands. A set of letters appeared on the screen and participants had to press the keyboard when the letter “X” appeared. The control condition was designed so that participants engaged in a similar cognitive task, but keeping the mental effort low. The duration of both tasks was approximately 30 minutes. For the analysis, the task was divided into 8 blocks of approximately 4 minutes each to study the time on task effect and the first block was discarded to control for the familiarization effect with the task. The tasks were programmed in Psychtoolbox-3 in Matlab 2021b presented in a 21-inch screen Windows PC.

## **Subjective scales**

VAS: We used a VAS in an excel form, ranging from 0 to 100 (7), to check the task demands of the individualized mental effort and control condition to the following questions: (1) “What is your perception of mental fatigue now?” (2) “What is your activation level now?” (7). Activation is defined as the state of being physiologically alert, awake and attentive. Data was analyzed by (normalized) rating change: post-test rating minus pre-test divided by post-test rating plus pre-test.

Rate of perceived exertion: we asked participants to rate their perceived exertion to the physical task with the modified Borg CR-10 scale (20) on a scale of 0-10 (0 - not at all, 10 - extremely tired) every minute. They were asked to rate “How effortful is the cycling task?” (21) and participants were familiarized with the scale in the screening visit.

## **MEP recording**

In order to measure the changes in corticospinal excitability in response to the mental effort task, we used TMS and record evoked potentials from the FDI muscle, as large MEP can be elicited as compared with lower limb muscles. The method was close to that reported in the recent study of Latella et al. (22). Briefly, single-pulse TMS was delivered over the M1 representation of the right FDI with the muscle at rest. A 90-mm round coil attached to a BiStim 200<sup>2</sup> magnetic stimulator (Magstim, United Kingdom) was held with the handle in a postero-lateral orientation at ~45° laterally away from the midsagittal line. The “hot spot” was determined as the site that elicited the largest MEPs recorded from the FDI and marked on the swim scalp worn by the participant. The resting motor threshold (RMT) was defined by determining the lowest TMS intensity at which an MEP could be visually detected in at least 3 out of 5 stimuli. Single-pulse stimuli was delivered at 120% of RMT and one series of 20 MEP was recorded with stimulations delivered at every ~5 sec. MEP were recorded and stored before analysis (AcqKnowledge software 5.0; BIOPAC Systems, Goleta, CA). EMG signals were amplified (gain: 1000), filtered through a 10-500 Hz band-pass filter, and digitized at a sampling frequency of 2 kHz using an AD conversion system (MP150, BIOPAC, Goleta, CA).

## **NIRS measurement**

We used a 3-transmitter NIRS system (PortaLite, Artinis) that emits continuous wavelengths of 780 and 850 nm light and it was placed over the left prefrontal cortex (PFC). The position was standardized as approximately 1 cm above the eyebrow and 2 cm from the midline of the forehead in the Brodmann area Fp1 according to the international 10–20 System. Sampling rate was set at 10 Hz and exported at 1 Hz. The NIRS was registered with the lights off and the device was secured in position using a headband and the swim cap in order to minimize ambient light interference and movement artifacts. For the cerebral cortex, an age-dependent differential optical path length factor was used. Measurements

were normalized as changes from an initial value arbitrarily defined as 0  $\mu\text{m}$ . Data was processed following the company's recommendations with a low pass filter at 0.1 Hz in all datasets in the Oxysoft Software (Artinis, Medical Systems) and then exported and processed with custom scripts in R Studio (<https://osf.io/xc8nr/>). Changes in oxygenated (O<sub>2</sub>Hb), deoxygenated (HHb), and total hemoglobin (tHb; calculated as the sum of O<sub>2</sub>Hb and HHb) were measured using the modified Beer-Lambert law from the average of the 3 transmitters.

### **Neuromuscular evaluation**

Knee extensor neuromuscular function was assessed with the techniques routinely used in the laboratory and previously described (17). The participant sat comfortably in an isometric chair and the strain gauge is attached to the chair on one end and securely strapped above the ankle with a custom-made mold. Participants seated with a knee angle of 90° and a trunk-thigh angle of 100° (180° = full extension). Extraneous movements of the upper body were limited by two crossover shoulder harnesses and a belt across the lower abdomen. Participants received visual feedback of the force they produced during the MVCs. These evaluations consist of voluntary and evoked contractions through the use of transcutaneous electrical stimulation of the femoral nerve, while force and surface electromyography (EMG) from the *vastus lateralis* (VL), *vastus medialis* (VM) and *rectus femoris* (RF) muscles were recorded and stored before analysis as previously described for the MEP. A high-voltage (maximum 400 V) constant-current stimulator (DS7AH, Digitimer, Hertfordshire, UK) was used to deliver single and paired electrical stimuli (pulse width: 1ms). The cathode (5 cm diameter, Dermatode, American Imex, Irvine, CA) and the anode (5 × 10 cm, Compex, Ecublens, Switzerland) were placed over the femoral nerve at the femoral triangle level beneath the inguinal ligament and on the lower part of the gluteal fold opposite to the cathode, respectively. Silver chloride (Ag/AgCl) circular (recording diameter of 1 cm) surface electrodes were positioned lengthwise over the middle part of the muscle belly with an inter-electrode (center-to-center) distance of 2 cm and the reference electrode was placed over the patella. The maximal stimulation intensity was determined by evoking single electrical stimulations every 5 s with an increasing intensity until a plateau twitch and M-wave amplitude responses were obtained. We used a supramaximal intensity, i.e., 120% of the minimal intensity used to obtain the plateau. Then, knee extensor warm-up (8 to 10 contractions at 20-80% of estimated maximal voluntary contraction (MVC) force) was performed. We performed a sequence comprised of a 5 s MVC with a superimposed 100 Hz doublet evoked via supramaximal electrical stimulation of the femoral nerve (twitch interpolation technique) and followed by supramaximal stimulation evoked at 2 s intervals: a paired stimuli at 100 Hz, 10 Hz, and a single stimulus to obtain the M wave. The same sequence was repeated before the mental fatigue protocol, after the mental fatigue protocol and after exercise for both experimental sessions (see figure 5A). From these measurements, the following dependent variables were determined: MVC force, voluntary activation level (1 – superimposed



twitch/resting twitch)  $\times 100$ ), potentiated doublet amplitude, M-wave amplitude, 10 Hz / 100 Hz ratio and the maximal EMG root mean square / M-wave ratio.

### **Statistical analysis**

We calculated Bayes factors for the individualized mental effort vs control using the open-source JASP (version 0.16) statistical package (23). As prior distribution of the sample effect size ( $\delta$ ), we used a zero-truncated Cauchy distribution with 0.707 width for the Bayesian t-test and a default uniform for the repeated measures. To ensure that this arbitrary choice did not affect the results, we conducted robustness checks with a wide range of alternative scaling factors (provide it in the supplementary material). Data is reported as mean and 95% credible intervals.

We calculated one-sided Bayes factors for paired samples t-tests for the subjective scales and the cycling time-to-exhaustion performance. We calculated Bayesian repeated measures ANOVA for the following measures and we report the results as the model-averaged inclusion Bayes Factor supporting the alternative hypothesis across all models<sup>3</sup>: 1) Cognitive task performance (2 condition -effort vs control- x 8 blocks -4 minutes-); 2) MEP amplitude (2 conditions -effort vs control- x 2 times -pre-mental task, post-mental task-) and 3) for the knee extensor neuromuscular evaluation (2 conditions -effort vs control- x 3 times pre-mental task, post-mental task and post-exercise), and 4) NIRS variables (2 conditions -effort vs control- x 8 blocks -4 minutes-).

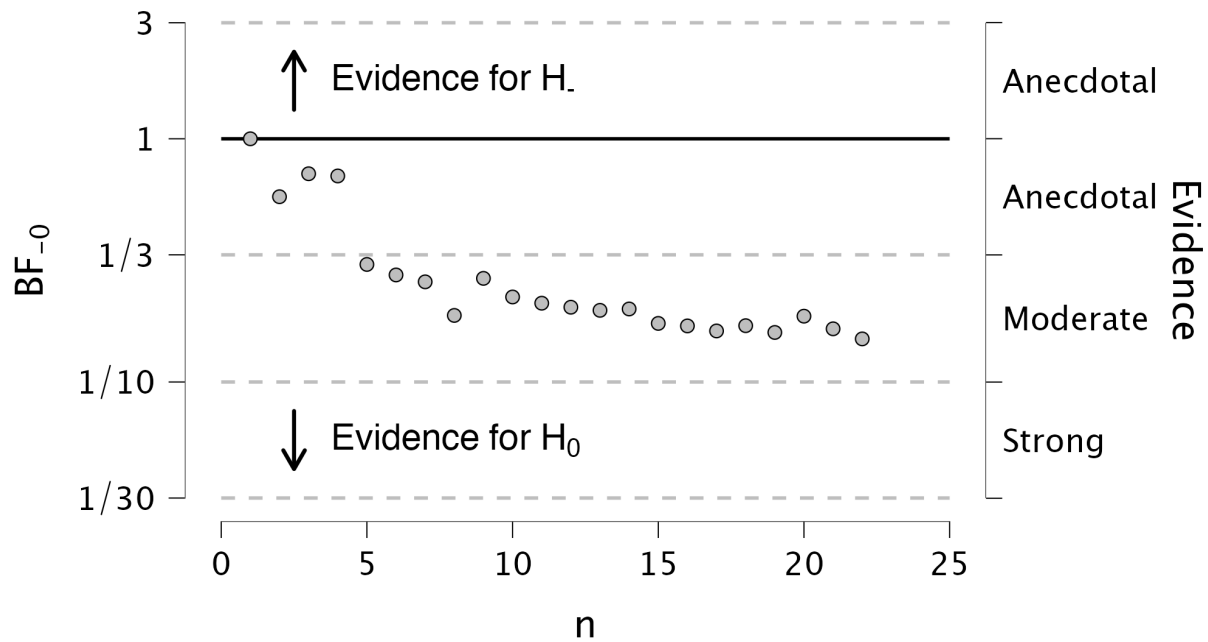
### **Deviation from pre-registration**

Our protocol and analysis stayed consistent with the preregistration, but some updates were performed.

We established a Bayes factor for the cycling task of  $BF_{10} > 10$  in favor of the alternative hypothesis or  $BF_{10} < 1/10$  in favor of the null hypothesis to stop the experiment. However, we finally set a less strict bayes factor of  $BF_{10} > 6$  or  $BF_{10} < 1/6$ , since according to sequential analysis, evidence toward the null hypothesis was increasing with each increment in sample size (Figure 2) and due to resource constraints.

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<sup>3</sup> For being consistent with the repeated comparison, we always report the  $BF_{10}$  considering the alternative hypothesis. However, note that  $BF_{10} < 1$  indeed represents evidence toward the null hypothesis, and therefore it represents no evidence toward the alternative hypothesis (see (24)).



**Figure 2.** Bayes sequential analysis for the alternative hypothesis that individualized mental effort negatively influences performance in the cycling task. The figure clearly illustrates the increasing evidence for the null hypothesis as sample size increased.

We indicated that we would measure paired stimulation to assess short intracortical inhibition and intracortical facilitation with the TMS, but after pilot studies we decided not to include this measure because of a high relative variability in the responses. Moreover, we mentioned that we would normalize the average MEP by the M-wave amplitude obtained by supramaximal single stimulation of the ulnar nerve ( $M_{max}$ ). We obtained the ratio from a subset of 8 participants and the conclusions were similar to the non-normalized data.

For the VAS measure, we said that we would normalize the score as post-test rating minus pre-test rating divided by pre-test rating x 100, but in order to be consistent with our previous studies (7) we normalized the rating change as: post-test rating minus pre-test divided by post-test rating plus pre-test.

For the RPE, we said that we would calculate: 2 conditions (effort vs control) x n times points (i.e, depending on the individual duration of the cycling task), but in order to simplify the analysis for the different number of data point and given that there were not differences in physical performance between conditions, we calculated the average RPE for each participant in each condition and performed an one sided bayes t-test.

For the NIRS measure, we do not present tissue saturation index calculation, as this variable does not add value to our study.

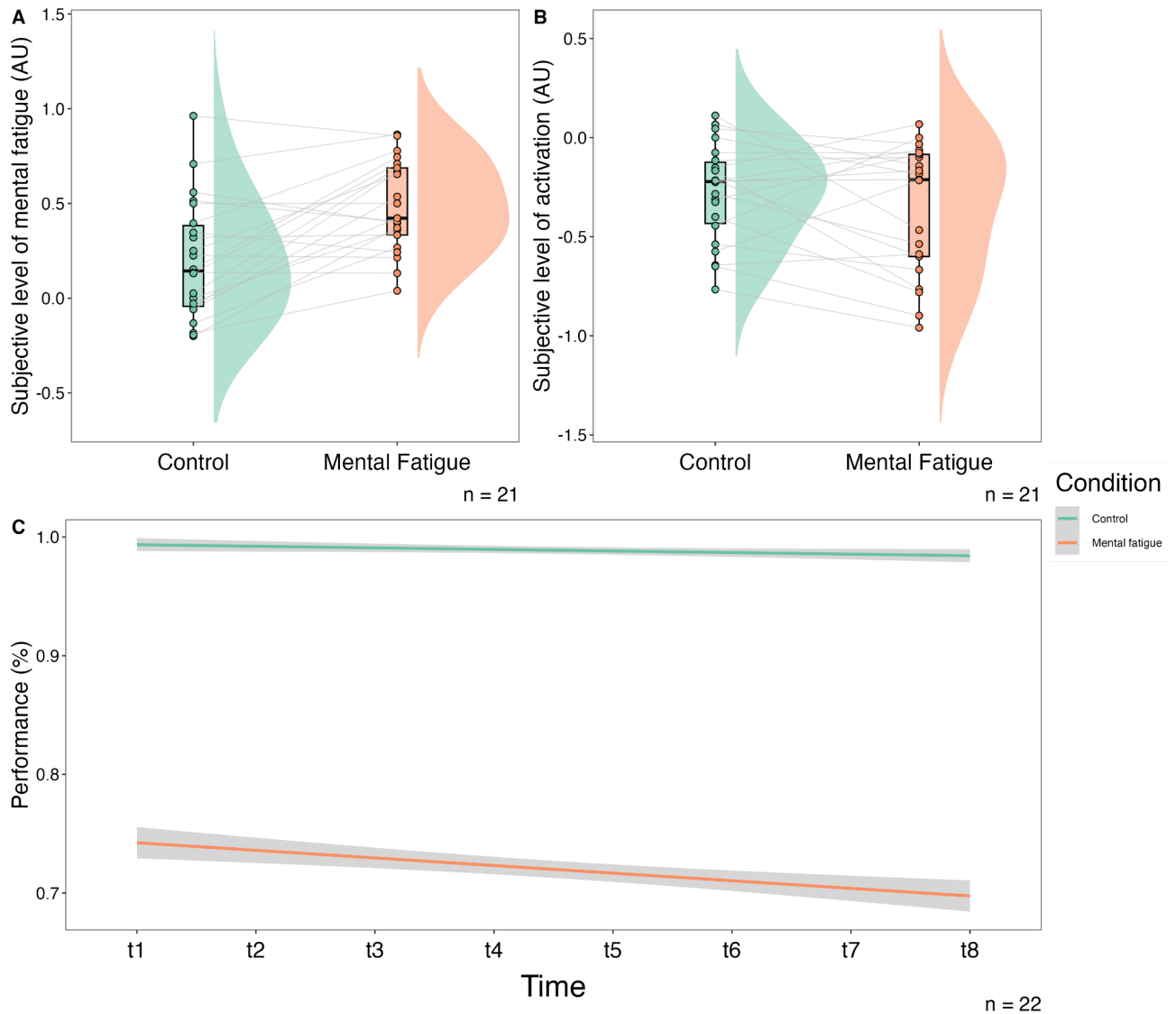
## Results

All dataset and scripts to wrangle the data and create figures, as well as the statistical outputs generated can be found in OSF: <https://osf.io/xc8nr/>.

### Confirmatory analysis

#### *Subjective scales*

The normalized VAS scores for “What is your mental fatigue level now?” for both conditions were: 0.199 (95%CI 0.06 - 0.339) arbitrary unit (AU) and 0.507 (95%CI 0.392 - 0.623) AU for the control and mental fatigue conditions, respectively (Figure 3A). The one-sided Bayes factor for the normalized score was  $BF_{10} = 134.239$ , which represents extreme evidence in favor of the alternative hypothesis, i.e., that the mental fatigue task was more mentally fatiguing than the control task. The normalized VAS scores for “What is your activation level now?” were: -0.275 (95%CI -0.390 - -0.16) AU and -0.356 (95%CI -0.504 - -0.207) AU, for the control and mental fatigue conditions, respectively. The two-sided Bayes factor for the normalized was  $BF_{10} = 0.227$ , which represents moderate evidence in favor of the null hypothesis, i.e., both tasks kept a similar arousal level (Figure 3B).



**Figure 3.** Manipulation check. Panel A) and B) depict a rain Cloud plot for the VAS questions. The raincloud plot (25) shows the cloud of points (i.e., individual raw data) connected by lines between each condition, a box plot and a one-sided violin plot (showing the probability density of the data at different values). A) Subjective level of mental fatigue. The shape of distribution indicates that in both conditions the observed values were located around the median, but the subjective level of mental fatigue was twice higher after the individualized mental fatigue task compared to the control condition. Furthermore, individual data shows that most of the participants were more mentally fatigued after completing the mental fatigue task. B) Subjective level of arousal. Subjective arousal level was similar across conditions, which shows that performing a task with low cognitive load (control task) did not reduce the arousal level. C) Performance in the cognitive task for each condition and across time. Shaded areas represent the 95% confidence interval.

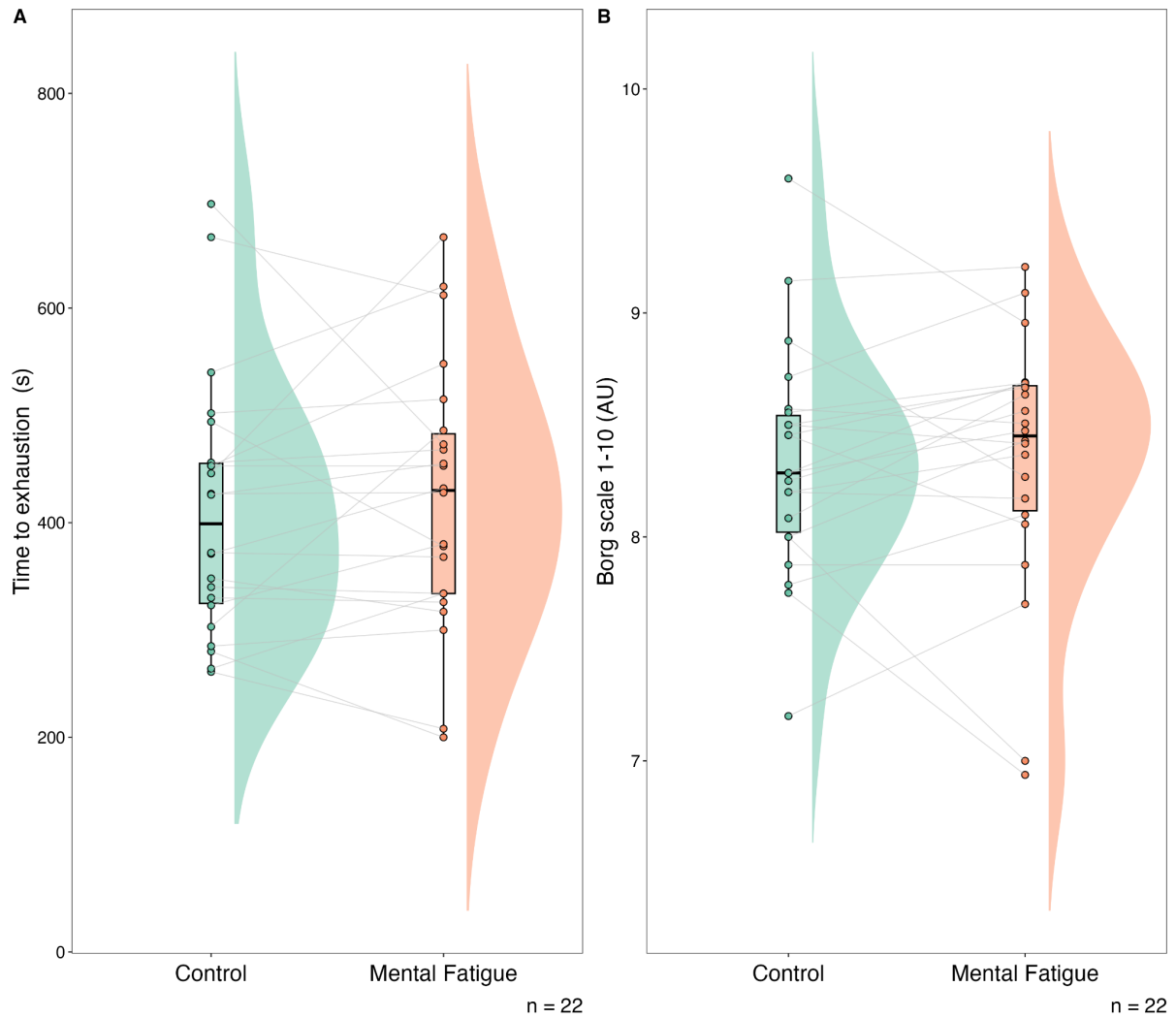
#### *Cognitive effort task*

For the cognitive tasks (n = 22), the average performance was: 0.98 (95%CI 0.97 - 0.99) and 0.72 (95%CI 0.68 - 0.76), for the control and mental fatigue conditions, respectively (Figure 3C).

Bayesian repeated measures ANOVA indicated extreme evidence in favor of the alternative hypothesis regarding the effect of condition  $BF_{10} = 2.568 \times 10^7$ . Post hoc comparison revealed that there was extreme evidence for a reduced performance in the individualized mental fatigue task compared to the control ( $BF_{10} = 4.440 \times 10^{61}$ ). However, the results indicated strong evidence in favor of the null hypothesis of time  $BF_{10} = 0.10$  and very strong for the interaction between condition and time  $BF_{10} = 0.039$ .

### *Performance*

The average time completed for both conditions was: 410 (95%CI 357 - 463) and 422 (95%CI 367 - 477) seconds for the control and mental fatigue conditions, respectively (Figure 4A). The one-sided Bayes factor for the time-to-exhaustion test measure was  $BF_{10} = 0.15$ , indicating that the observed data moderately to strongly support the null hypothesis that the individualized mental fatigue did not have a detrimental effect on physical performance. Likewise, the average RPE for both conditions were: 8.3 (95%CI 8.1 - 8.5) AU and 8.3 (95%CI 8 - 8.5) AU for the control and mental fatigue conditions, respectively (Figure 4B). The one-sided Bayes factor for the RPE was  $BF_{10} = 0.239$ , which indicates moderate evidence in favor of the null hypothesis that the mental effort task did not increase perception of fatigue.

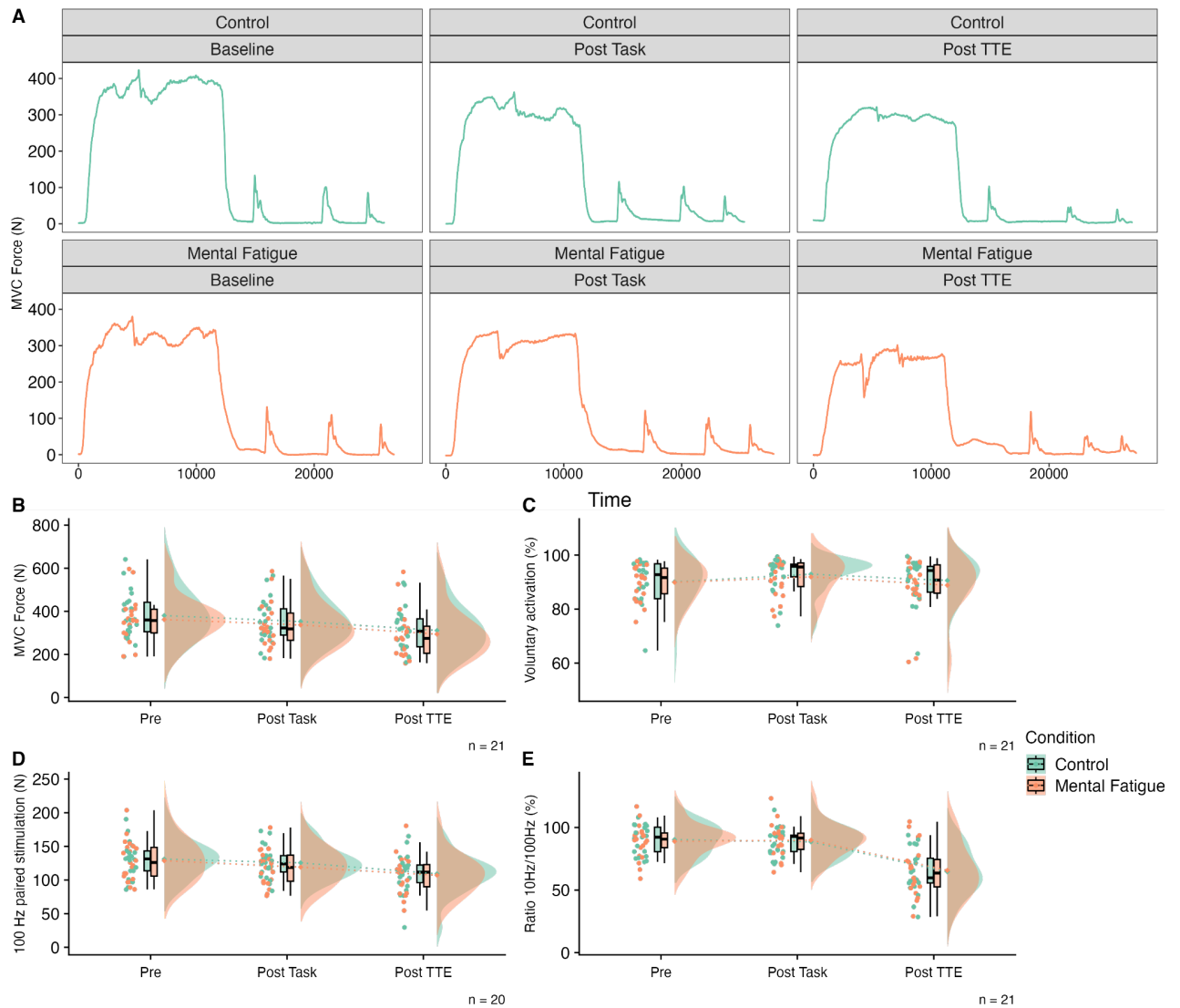


**Figure 4.** Rain Cloud plot for (A) physical performance in the cycling time-to-exhaustion test at 80% of peak power output and (B) average rate of perceived exertion during the time-to-exhaustion test. The shape of distribution indicates that in both conditions, values were located around the median and there were no differences between conditions. Individual data shows that 12 out 22 participants performed better in the mental fatigue condition, 9 performed better in the control condition and 1 performed equally. Similarly, the distribution of the RPE values were around the median and there were no differences between both conditions.

#### *Knee extensor neuromuscular evaluation*

For the MVC force, the results ( $n = 21$ ) revealed that MVC was reduced (see Figure 5B), indicating extreme evidence for the main effect of time in favor of the alternative hypothesis,  $BF_{10} = 1.373 \times 10^9$ . The MVC was reduced 8% between baseline and post-task ( $BF_{10} = 27417.681$ ), 19% between baseline and post TTE ( $BF_{10} = 1.05 \times 10^{10}$ ) and 12% between post task and post TTE ( $BF_{10} = 1.837 \times 10^7$ ). However, the results indicated no evidence regarding the effect of condition  $BF_{10} = 0.928$  and moderate effect in favor of the null hypothesis for the interaction between condition and time  $BF_{10} = 0.292$ . However, for the voluntary activation level (see Figure 5C), the results indicated moderate evidence in

favor of the null hypothesis regarding the effect of condition  $BF_{10} = 0.268$ , anecdotal evidence for the effect of time  $BF_{10} = 0.884$  and very strong for interaction between condition and time  $BF_{10} = 0.103$ . For the RMS/M-ratio and M-wave amplitude, table 3 summarizes the physiological data for each variable and muscle. The results indicated weak evidence for effect of condition, time and the interaction of condition and time (table 1). The potentiated doublet amplitude (100Hz), was reduced across time, the results indicated extreme evidence for the main effect of time in favor of the alternative hypothesis,  $BF_{10} = 6539.065$  (see Figure 5D). Post hoc comparison revealed that there was extreme evidence less potentiation between baseline and post task ( $BF_{10} = 97136.061$ ), between baseline and post TTE ( $BF_{10} = 637154.365$ ) and very strong between post task and post TTE ( $BF_{10} = 71.71$ ). However, there were no differences between the conditions, as the results indicated anecdotal evidence in favor of the null hypothesis regarding the effect of condition  $BF_{10} = 0.547$ , and anecdotal for the interaction between condition and time  $BF_{10} = 0.395$ . Similarly, the 10Hz/100Hz ratio (see Figure 5E), was reduced across time and the results indicated extreme evidence for the main effect of time in favor of the alternative hypothesis,  $BF_{10} = 3.793 \times 10^8$ . Post hoc comparison revealed that there was extreme evidence for a reduction of the ratio 10/100Hz from baseline to post TTE ( $BF_{10} = 7.490 \times 10^8$ ) and from post task to post TTE ( $BF_{10} = 3.337 \times 10^9$ ). However, there were no differences between conditions. The results indicated moderate evidence regarding the effect of condition  $BF_{10} = 0.296$ , and anecdotal for the interaction between condition and time  $BF_{10} = 0.332$ .



**Figure 5.** A) Original recordings of knee extensor neuromuscular function evaluation in a representative participant. The MVC was conducted with a superimposed 100 Hz doublet, followed by supramaximal stimulation evoked at intervals of 2 seconds with paired pulses at 100 Hz, 10 Hz, and a single pulse. Rain Cloud plot for knee extensors evaluation outcome: B) Maximal voluntary contraction (MVC). C) Voluntary activation level. D) Potentiated doublet amplitude. E) Ratio 10 Hz/ 100 Hz.

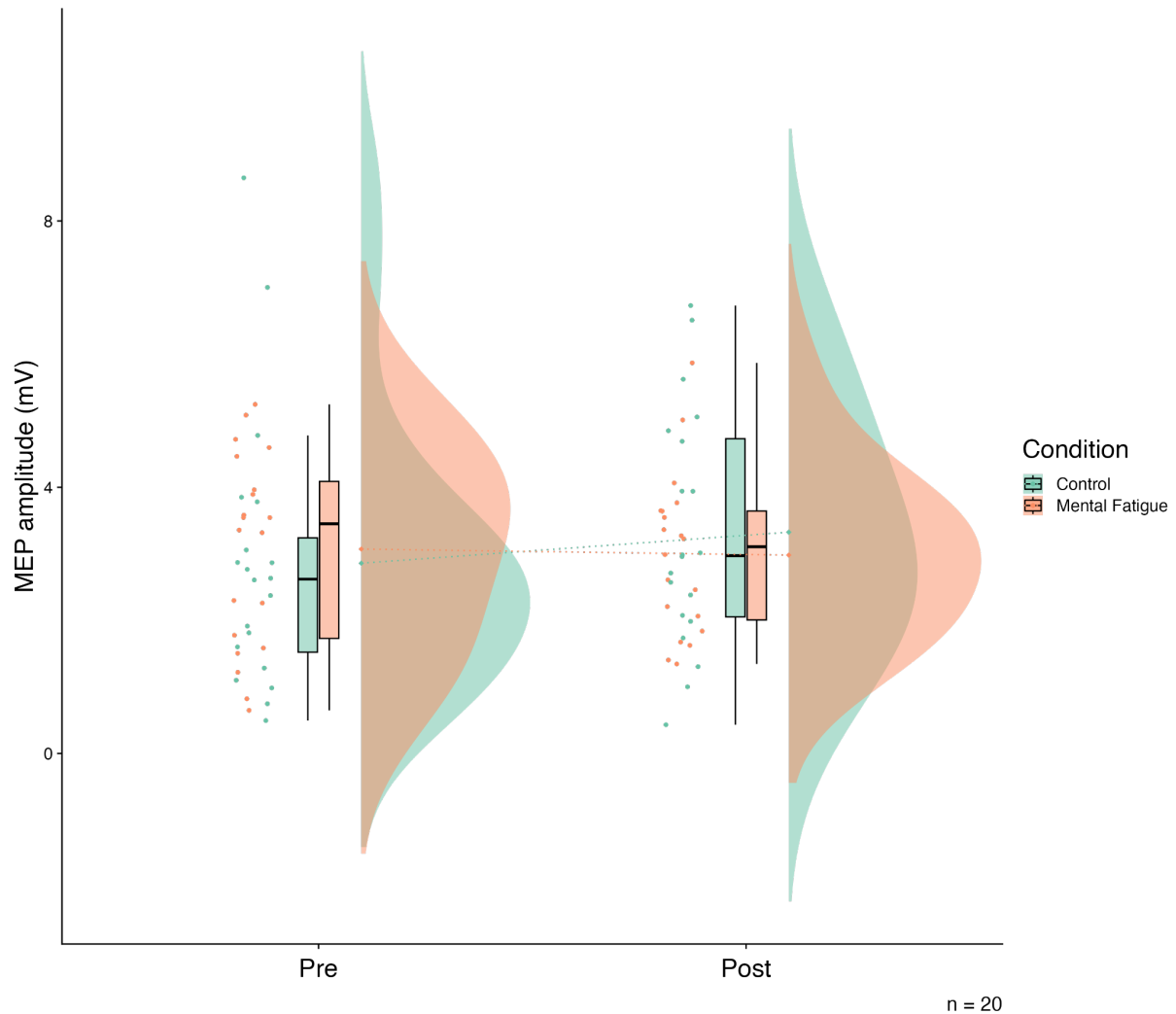


**Table 1.** Mean and 95%CI for the M-Wave amplitude and RMS/M-Ratio for both conditions and time points at the *vastus medialis (VM)*, *vastus lateralis (VL)* and *rectus femoris (RF)* and analysis of effects.

Variable/Muscle	Control			Mental Fatigue		
	Baseline	Post Task	Post TTE	Baseline	Post Task	Post TTE
<b>M-Wave amplitude VM (mV)</b>	7.1 (5.9 - 8.7)	6.9 (5.2 - 8.5)	6.7 (4.8 - 8.6)	5.6 (4.0 - 7.1)	5.7 (3.9 - 7.4)	5.6 (4.0 - 7.1)
<b>M-Wave amplitude VL (mV)</b>	4.7 (3.7 - 5.7)	4.5 (3.5 - 5.6)	4.5 (3.5 - 5.6)	5.6 (4.6 - 6.6)	5.5 (4.4 - 6.5)	5.3 (4.0 - 6.5)
<b>M-Wave amplitude RF (mV)</b>	3.5 (2.8 - 4.3)	3.6 (2.9 - 4.3)	3.7 (2.8 - 4.5)	3.0 (2.1 - 3.9)	3.0 (2.3 - 3.8)	3.0 (2.1 - 2.9)
<b>RMS/M ratio VM</b>	0.051 (0.042 - 0.060)	0.061 (0.051 - 0.071)	0.063 (0.047 - 0.079)	0.082 (0.024 - 0.139)	0.095 (0.038 - 0.153)	0.115 (0.016 - 0.214)
<b>RMS/M ratio VL</b>	0.051 (0.040 - 0.062)	0.057 (0.045 - 0.069)	0.057 (0.041 - 0.072)	0.042 (0.034 - 0.049)	0.051 (0.041 - 0.061)	0.091 (0.012 - 0.171)
<b>RMS/M ratio RF</b>	0.062 (0.053 - 0.071)	0.067 (0.056 - 0.079)	0.059 (0.051 - 0.067)	0.069 (0.048 - 0.090)	0.086 (0.059 - 0.113)	0.085 (0.054 - 0.117)
<b>Analysis of Effects</b>	<b>M-wave amplitude</b>			<b>RMS/M-ratio</b>		
<b>Effects (BF10)</b>	<b>VM (n = 18)</b>	<b>VL (n=20)</b>	<b>RF (n=21)</b>	<b>VM (n = 18)</b>	<b>VL (n=20)</b>	<b>RF (n=21)</b>
Condition	0.688	0.825	0.720	0.533	0.210	1.215
Time	0.119	0.097	0.080	0.236	0.250	0.699
Condition *						
Time	0.069	0.036	0.026	0.096	0.108	0.954

*Corticospinal excitability*

Figure 6 shows that the FDI MEP amplitude ( $n = 20$ ) did not vary between condition or time. The results indicated anecdotal evidence in favor of the null hypothesis regarding the effect of condition  $BF_{10} = 0.286$ , for the effect of time  $BF_{10} = 0.279$  and moderate evidence for the interaction between condition and time  $BF_{10} = 0.198$ .

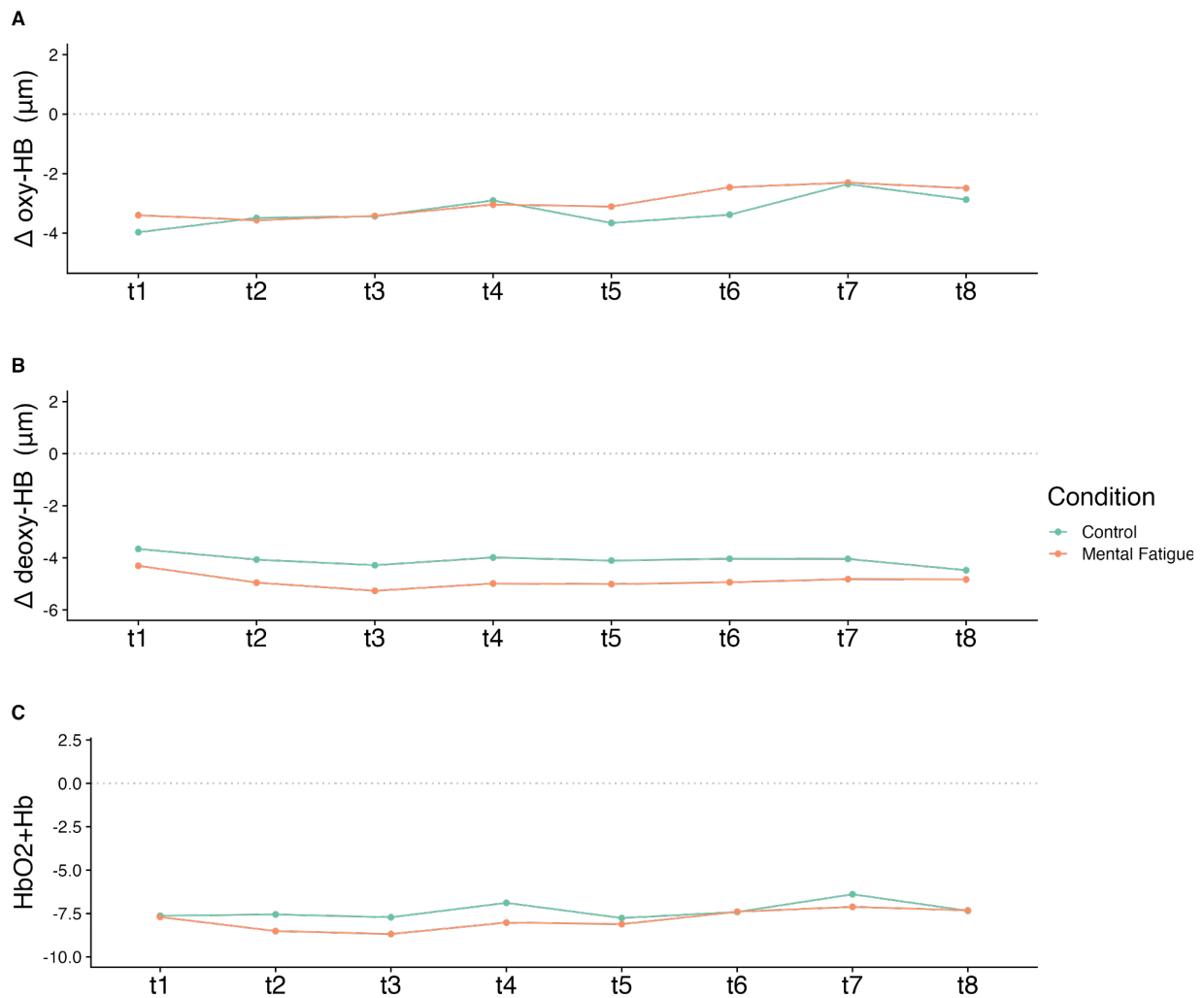


**Figure 6.** Rain cloud for the FDI MEP amplitude (average of 20 MEPs) for each condition and time point.

### *NIRS measures*

Oxygenated hemoglobin (O2Hb) and deoxygenated hemoglobin (HHb) did not change between conditions or across time (figure 7). The results ( $n = 21$ ) indicated moderate evidence in favor of the null hypothesis of the effect of condition  $BF_{10} = 0.374$ , strong for the effect of time  $BF_{10} = 0.07$  and extreme for interaction between condition and time  $BF_{10} = 0.003$ . For the HHb, the results indicated anecdotal evidence in favor of the null hypothesis of the effect of condition  $BF_{10} = 0.32$ , very strong for the effect of time  $BF_{10} = 0.016$  and extreme for interaction between condition and time  $BF_{10} = 0.001$ . Likewise, for the total hemoglobin (tHb) the results indicated moderate evidence in favor of the null

hypothesis of the effect of condition  $BF_{10} = 0.27$ , very strong for the effect of time  $BF_{10} = 0.012$  and extreme for interaction between condition and time  $BF_{10} = 0.001$ .



**Figure 7.** Changes in oxyhaemoglobin (A) deoxyhaemoglobin (B) and (C) total haemoglobin during the performance of the cognitive tasks.

## Discussion

The goal of this study was to shed light on the controversial topic of the effect of mental fatigue on exercise performance by individualizing cognitive effort among participants. Even if the data showed extreme evidence in favor of individualized mental effort to increase perception of mental fatigue, we did not find evidence of an impaired performance in the cycling task under this state. In addition, the higher subjective feeling of mental fatigue did not influence perception of effort during the exercise or any other neurophysiological variables compared to the control condition. In summary, our results do

not support the idea that performing an effortful cognitive task has a negative influence on objective performance or perception of effort, in line with previous replication attempts (7).

Even though several studies initially suggested that mental fatigue induced by cognitive tasks could negatively affect exercise performance (4, 26), currently, the literature in this field is unclear, with overestimated effects, low statistical power and possible publication bias (6, 27). The negative effects of mental fatigue on performance have been challenged by several research studies in recent years (7, 28). For example, O’Keeffe et al. (28) also employed the individualized mental fatigue task for 16 minutes before a 15-min, self-paced, arm-bike physical performance test and they did not find that mental fatigue had a detrimental effect on exercise performance compared to the control condition. With a protocol similar to the present study, Holgado et al., (7) failed to replicate the mental fatigue effect previously reported by Marcora et al., (4), testing one of the largest samples in this topic (n=30). Therefore, taking into account that the study of the impact of mental fatigue on exercise performance has grown exponentially in the last decade without much self-criticism, its replicability should be evaluated independently, ideally through a multi-lab study testing larger samples (29).

Transcranial magnetic stimulation has been used in some studies to establish a potential link between reduced corticospinal excitability (one of the potential contributors of central fatigue) and mental fatigue as a mechanism by which mental fatigue might reduce exercise performance. In our study, we did not observe that MEP amplitude of the FDI was affected after performing a cognitive task with high demands. Indeed, there are limited studies examining how corticospinal excitability changes as one performs a cognitive fatigue task, and the relationship between these two components is unclear. For example, Bailey et al., (13) also measured the MEP amplitude on FDI as an index of corticospinal excitability. MEP amplitude was reduced by 16% after performing a Stroop color word task for 60 min. However, the authors did not include a condition without a cognitive task and there was not any physical measurement after the cognitive task, so it is difficult to determine whether the reduction in cortical excitability impacts subsequent physical exercise based on these findings. Derosière et al. (30) found that MEP amplitude of the abductor pollicis brevis increased during the performance of a 30 min mentally fatiguing task. They suggested that in order to cope with the increasing task demands, the corticospinal tract and M1 area are recruited as complementary regions to the attention-related areas. In contrast, Morris and Christie (31) did not find that performing a 20 min Psychomotor Vigilance task reduced MEP amplitude of the tibialis anterior. Alternatively, Nakashima et al., (32) found reduced MEP amplitude in the abductor pollicis brevis after participants completed a prolonged (approximately 40 min) motor imagery task. Indeed, repeated simulation of a motor task resulted in deteriorating physical performance for the participants and therefore the reduced motor evoked amplitude could be partially explained by the decrease in excitability of the corticospinal tract (32). It is possible, however, that the conclusions drawn from these studies may be due to differences in task nature and demands (i.e., a computerized cognitive task versus a motor imagery task). Considering the disparities in the

tasks and the location-based assessment of MEP, it is unlikely to be an effective marker of corticospinal excitability in response to a mental fatigue task.

Although we hypothesized that with this new individualization approach, mental fatigue could alter maximal force generating capacity and neuromuscular parameters, the absence of evidence in favor of the alternative hypothesis is in line with most of the studies on this topic (33, 34). For example, Pageaux et al. (34) did not find any change in MVC force or other neuromuscular parameters after a 90 min cognitive task, despite an increased subjective feeling of mental fatigue. Likewise, Silva-Cavalcante et al., (33) did not find that despite a higher level of mental fatigue, performance in a time trial was not affected, nor was MVC force, voluntary activation or twitch force after the cycling exercise. Hence, even if there is an elevated subjective level of mental fatigue, the possible impairment in exercise performance is not a result of altered neuromuscular parameters, since neither the extent of central and peripheral fatigue is altered after performing the cognitive task nor after performing the exercise in a state of mental fatigue.

Regarding brain oxygenation, although the cognitive demands of both tasks were well differentiated (and the level of perceived mental fatigue was higher in mental effort task), no different patterns in brain activation were observed. It is possible that we did not observe differences because of the limited NIRS set up available for this study. NIRS measures were limited to a specific location in the present study (frontal areas) and included only one channel by hemisphere. The majority of the studies reporting variations in oxygenation levels following different cognitive demands find these changes in prefrontal areas (35, 36) or fronto-parietal areas (37, 38). fNIRS with more channels has shown more reliable results in detecting linear changes and functional connectivity during the completion of similar tasks to the ones we performed in the study (36). However, the explanation of brain oxygenation during a cognitive task is not often straightforward. For example, it is possible that brain oxygenation does not change across time if the performance is maintained (39). Whereas it is also possible that cerebral oxygenation increases/decreases across time, but without changes in performance (40). Literature often alludes to the idea that more resources have been invested to maintain the same level of performance, even if that level of performance remains unchanged (41). The modification done here to the TloadDbadk paradigm, a task designed to trigger mental fatigue by considering interindividual differences, intended to double the task default time during which continuous demands occupy attentional resources. This manipulation allows creating a longer time window to investigate the allocation of resources during this situation of constant demands. In line with other studies in the topic (39), we hypothesized that increased oxygenation levels would be necessary to maintain performance. Although performance scores showed the previously described (8, 18) stabilization of performance after the first block, NIRS results did not disclose changes in brain oxygenation.

Studies on mental fatigue generally involve artificially induced fatigue through computerized tasks that are unlikely to mimic normal day-to-day tasks which could potentially affect performance and perception of effort. Future studies will probably benefit from the study of the factors and causes that people identify as mentally draining, so that we can better understand whether mental fatigue impacts performance (42). Mental fatigue is likely to arise by long-term exposure to stressors rather than by acute manipulations used to date. The mechanism underlying this phenomenon may vary according to the prevailing circumstances and the mental fatigue task used. Thus, to understand whether mental fatigue might negatively affect physical performance, people need to experience similar stressors to those encountered in their daily lives. This literature will probably benefit from longitudinal studies identifying the causal link between mental fatigue fluctuations across different periods of the year and performance outcomes (43). Furthermore, there are other factors which can potentially reduce the possible negative effect of mental fatigue. For example, some studies have pointed out that providing adequate feedback to participants can counteract the possible effects of performing a cognitive task and therefore reduce the fatigability (44, 45).

In conclusion, our data challenge the notion that mental fatigue negatively impacts exercise performance. However, the results of our study do not provide a definitive answer regarding the effects of mental fatigue on physical exercise, as we do not yet know whether the accumulation of mental fatigue over time in a real-world context impacts fatigability. It would be helpful to conduct future research on the fluctuations in mental fatigue over different periods, as well as their effects on training and performance in different populations.

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### **Data availability statement**

All data and materials will be publicly shared on OSF at <https://osf.io/xc8nr/>.

### **Code Availability**

All codes and materials utilized for the analysis of the present manuscript will be available at <https://osf.io/xc8nr/>.

## Author contributions

All authors have made substantial contributions to various elements of the study.

Conceptualization: DH, GB, DS, NP

Data collection: DH, LJ

Data curation: DH, LJ

Formal analysis: DH, GB, LJ

Methodology: DH, GB, DS, NP

Project administration: DH, NP

Resources: NP

Supervision: NP, DS

Writing – original draft: DH

Writing – review & editing: DS, NP, GB

## Competing interests

The authors have declared that no competing interests exist.

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