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What is the central question of this study? Does the work done above critical power (W') or muscle activation determine the degree of peripheral fatigue induced by cycling time-trials performed in the severe intensity domain?

What is the main finding and its importance? We found that peripheral fatigue increased when power output and muscle activation increased whereas W' did not change between the time-trials. Therefore, no relationship was found between W' and exercise-induced peripheral fatigue such as previously postulated in the literature. In contrast, we found a significant association between EMG amplitude during exercise and exercise-induced reduction in the potentiated quadriceps twitch, suggesting that muscle activation plays a key role in determining peripheral fatigue during severe intensity exercise.

Abstract: In order to determine the relationship between peripheral fatigue, muscle activation and the total work done above critical power (W'), ten men and four women performed, on separated days, self-paced cycling time-trials of 3, 6, 10, and 15 min. Exercise-induced quadriceps fatigue was quantified using pre- to post-exercise (15 s through 15 min recovery) changes in maximal voluntary contraction peak force (MVC), voluntary activation (VA) and potentiated twitch force (QT). VA was measured using the interpolated twitch technique, and QT was evoked by electrical stimulations of the femoral nerve. Quadriceps muscle activation was determined using the root mean square of surface electromyography of vastus lateralis (VL_{RMS}), vastus medialis (VM_{RMS}) and rectus femoris (RF_{RMS}). Critical power and W' were calculated from the power/duration relationship from the four time-trials. Mean power output and mean VL_{RMS}, VM_{RMS} and RF_{RMS} were greater during shorter compared to longer exercises (P<0.05) whereas no significant between-trials change in W' was found. The magnitude of exercise-induced reductions in QT increased with the increase in power output (P<0.001) and were associated with mean VL_{RMS} and VM_{RMS} (P<0.001, r^2>0.369) but not W' (P>0.150, r^2<0.044). Reduction in VA tended (P=0.067) to be more pronounced with the lengthening in time-trial duration while no significant between-trials change in MVC were found. Our data suggest that peripheral fatigue is not related to the amount of work done above the critical power but rather to the level of muscle activation during exercise the severe intensity domain.

***Key words**: critical power, neuromuscular fatigue, recovery from fatigue, muscle activation, exercise performance*

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INTRODUCTION

During severe-intensity endurance exercise accurate prediction of performance can be obtained using the hyperbolic relationship between exercise duration and work rate (Monod & Scherrer, 1965; Moritani *et al.*, 1981; Poole *et al.*, 1988; Jenkins & Quigley, 1991; Hill *et al.*, 2002; Chidnok *et al.*, 2012; 2013; Black *et al.*, 2014). In cycling, this relationship is mathematically determined by two parameters: the critical power which represents the asymptote of the hyperbolic relationship and corresponds to the limit between the heavy and severe intensity domains, and the curvature constant (W') which represents a fixed amount of work that can be performed above the critical power (Poole *et al.*, 1988; Burnley & Jones, 2016; Black *et al.*, 2017). Because task failure in the severe intensity domain (i.e. above the critical power) coincides with the complete use of W', it is proposed that exercise tolerance is determined by the rate of expenditure of W' (Moritani *et al.*, 1981; Chidnok *et al.*, 2012; 2013; Black *et al.*, 2014).

Recent studies using muscle biopsies and ^{31}P-MRS found that the complete utilization of W' coincided with the attainment of a constant and high concentration of intramuscular metabolites (i.e., H^+ and inorganic phosphate) (Hogan *et al.*, 1999; Jones *et al.*, 2008; Vanhatalo *et al.*, 2010; Burnley *et al.*, 2010; Black *et al.*, 2017). The intramuscular accumulation of such metabolic by-products has been associated with the progressive loss of muscle function and efficiency, known as neuromuscular fatigue (Allen *et al.*, 2008). Neuromuscular fatigue involves the impairment of the muscle's ability to produce force in response to a neural input (i.e. peripheral fatigue, Allen *et al.*, 2008) and/or the failure (or compromised willingness) of the central nervous system to fully activate the exercising muscle (i.e. central fatigue, Gandevia, 2001). Given the above-mentioned relationship between W' and intramuscular metabolic disturbances, some authors speculated that W' utilization determines the degree of exercise-induced peripheral fatigue (Broxterman *et al.*, 2015; Schäfer *et al.*, 2018; Broxterman *et al.*, 2019; Zarzissi *et al.*, 2020*a*). This hypothesis is supported by findings showing that, within the severe intensity domain, the magnitude of peripheral fatigue induced by single-leg or cycling exercise remained constant between exercises of various intensity/duration (Burnley *et al.*, 2012; Pethick *et al.*,

2016; Schäfer *et al.*, 2018). In addition, between-subjects level of exercise-induced peripheral fatigue was found to be correlated with W', such as the subjects with the greatest W' had the greatest degree of fatigue (Broxterman *et al.*, 2015; Schäfer *et al.*, 2018; Zarzissi *et al.*, 2020*b*; 2020*a*). However, experiments during which W' was improved using creatine or caffeine intake showed that the increase in W' did not produce a proportional increase in peripheral fatigue (Felippe *et al.*, 2018; Schäfer *et al.*, 2019). In addition, recent findings showed that exercise-induced peripheral fatigue increased with the increase in power output following cycling exercises of various duration / distance within the severe intensity domain, despite presumably similar W' expenditure during the various exercises (Thomas *et al.*, 2016; Ducrocq *et al.*, 2021).

Difference in fatigue measurement methodology and/or exercise modality might explain, at least in part, these discrepancies. In particular, the 1-min delay to the first neuromuscular fatigue measurement after the end of exercise (Schäfer *et al.*, 2018) might have led to an underestimation of exercise-induced fatigue, especially after the shortest / fastest exercise tests, and might account for the absence of statistical difference in peripheral fatigue levels between trials. Alternatively, critical power and W' were not determined in the studies showing an increase in peripheral fatigue with the shortening of exercise duration (Thomas *et al.*, 2016; Ducrocq *et al.*, 2021). Small variations in W' expenditure might have occurred and could have explained the observed difference in peripheral fatigue (Thomas *et al.*, 2016; Ducrocq *et al.*, 2021). Finally, findings from our group (Ducrocq *et al.*, 2021) showed that the increase in peripheral fatigue with the increase in exercise intensity was correlated to the EMG amplitude during exercise (Ducrocq *et al.*, 2021). From these findings, it could be hypothesized that peripheral fatigue would be rather related to the level of muscle activation than to W'. An experimental protocol manipulating exercise intensity within the severe intensity domain and combining measurements of W', muscle activation and neuromuscular fatigue right at exercise termination is needed to elucidate the contribution of W' and muscle activation to neuromuscular fatigue during severe intensity exercise.

Consequently, the main objective of the present study was to determine the relationship between W', muscle activation and peripheral fatigue induced by four cycling time-trials of various durations performed within the severe intensity domain. We hypothesized that peripheral fatigue increases when exercise intensity increases and exercise duration shortens due to a higher level of muscle activation. Accordingly, we hypothesized that peripheral fatigue is associated with the level of muscle activation but not W'.

METHOD

Ethical approval

The study conformed to the standards set by the latest revision of the Declaration of Helsinki except for registration in a data base and was approved by the local ethic committee. Written informed consent was obtained from each participant before the beginning of the study.

Participants

Fourteen participants (four women; mean ± SD; age, 23 ± 3 years; height, 175 ± 10 cm; weight, 71 ± 11 kg; body fat, 15 ± 5 %) participated in the present study. All participants were sports students and were familiar with intense physical activity. All participants were non-smoker and were non-medicated.

Experimental design

During the first preliminary visits, anthropometric measurements were collected. Participants were familiarized with neuromuscular measurements (detailed in "*Data collection and analysis*" section) and cycling exercise. After a 10 minutes warm-up at 1.5 W/kg, participants performed a maximal 8 minutes cycling time-trial on a stationary cycle ergometer (Velotron, Elite Model; Racer Mate, Inc., Seattle, WA). This exercise duration has been chosen as it is the average duration between the shortest (3 minutes) and the longest (15 minutes) cycling time-trial duration of the experimental protocol. Participants were asked to perform as much work as possible and were allowed to freely alter power output by changing the resistance and/or the pedaling frequency. The time elapsed during the time-trial was the only information displayed on a monitor placed directly in front of the participant. Participants were given strong vocal encouragement and were instructed to remain seated throughout exercise.

During the following four experimental visits, participants repeated, in random order, the same protocol but with different cycling exercise durations, namely 3 min (3_{min}TT), 6 min (6_{min}TT), 10 min (10_{min}TT), and 15 min (15_{min}TT). Neuromuscular function was evaluated before and after each exercise. We chose closed-loop exercises (i.e. time-trial) *vs*. open-loop exercises (i.e. time to task failure) because it is a validated method to determine critical power and W' (Black *et al.*, 2015) and it is less affected by day-to-day variability in performance (Laursen *et al.*, 2007). We chose exercise durations ranging from 3 min to 15 min, because it allows an optimal quantification of participants' critical power and W' (Mattioni Maturana *et al.*, 2018) and allows us to study the effect of a very broad spectrum of exercise intensities in the severe intensity domain (i.e. above the critical power) on neuromuscular fatigue and recovery.

Data collection and analysis

Determination of critical power and work done above critical power

For each cycling time-trial, exercise duration (s), mean power output (W) and the total amount of work done

during exercise (J) were calculated. Three different models were used to determine CP and (Poole *et al.*, 1988; Black *et al.*, 2015).

(1) the linear work-time model expressed as

$$W\ (J) = CP(w)\ \times\ t(s) + W'(J)$$

(2) the linear inverse-of-time model

$$P(w) = W'(J)\ \times \left(\frac{1}{t(s)}\right) +\ CP(w)$$

(3) the non-linear power-time model

$$t(s) = \frac{W'(J)}{P(w) - CP(w)}$$

where W is the total amount of work done during exercise, P is the mean power output, CP is the critical power, t is exercise duration and W' is the total amount of work done above critical power.

The averaged standard errors for critical power and work done above the critical power were calculated from the data measured during each cycling time-trial and expressed as coefficient of variation. For every participant, the model providing the lowest coefficient of variation in the determination of CP and W' was used for further analysis (linear work-time model: n=13; linear inverse-of-time model: n=1).

Neuromuscular function

Contractile function and voluntary activation of the quadriceps. For the assessment of the contractile function, subjects were seated on a custom-made bench, arms folded across the chest, with a trunk/thigh angle of 90° and the right knee joint angle at 90°. A non-compliant strap attached to a calibrated load cell (model SM-2000N, Interface, Scottsdale, AZ, USA) was fixed to the subject's right ankle, just superior to the malleoli. The cathode, a self-adhesive electrode (3 x 3 cm, Ag-AgCl, Mini-KR, Contrôle-Graphique, Brie-Comte-Robert, France), was placed on the femoral triangle, at the stimulation site that resulted in both maximal force output and maximal amplitude of the compound muscle action potential (M_{MAX}) for the *vastus lateralis* (VL), *vastus medialis* (VM) and *rectus femoris* (RF). The anode, a carbon-impregnated electrode (70 x 50 mm), was rubbed with conductive gel and placed mid-way between the great trochanter and superior iliac crest. The position of these electrodes was marked with indelible ink to ensure a reproducible stimulation site across visits. A constant-current stimulator (DS7A, Digitimer, Hertfordshire, United-Kingdom) delivered a square wave stimulus (1 ms) at a maximum of 400V. To assure maximal spatial recruitment of motor units during the neuromuscular tests, the stimulation intensity (98 ± 20 mA) was set to 120% of the stimulation intensity eliciting maximal quadriceps twitch and M_{MAX} with increasing stimulus intensities (Neyroud *et al.*, 2014). No electrical activity of the *biceps femoris* (BF) was observed during stimulations.

Neuromuscular assessment of the quadriceps muscle was conducted prior and immediately after every cycling time-trials using a standardized set of contractions. In each set, participants performed a 3 s maximal voluntary contraction (MVC) during which superimposed paired stimuli at 100 Hz ($QT_{100,\ superimposed}$) were delivered at the peak force of the MVC to determine voluntary activation of the quadriceps (VA, Merton, 1954). Then, potentiated quadriceps twitch evoked by paired [100 Hz (QT_{100}) and 10 Hz (QT_{10})] and single (QT_{single}) electrical stimulations of the femoral nerve were elicited 2 s, 4 s, and 6 s after each MVC, respectively. At baseline (i.e. before the cycling time-trial), six standardized set of contractions, separated by 1min, were performed. Following exercise, in order to capture the rapid recovery from fatigue that occurs within the first minutes following exercise termination, the same standardized set of contractions were performed at exactly 10s and 1, 2, 4, 6 and 15 min post-exercise. Quantifying neuromuscular fatigue indices during recovery allows 1) to determine the contribution of the different fatigue mechanisms to exercise-induced fatigue (Carroll *et al.*, 2017), such as prolonged low frequency force depression and 2) to monitor the recovery of the neuromuscular function from fatiguing exercise trials of various duration and intensity. For all QT_{10}, QT_{100}, and MVCs, we determined peak force. For all QT_{single}, we assessed peak force, contraction time to peak force, maximal rate of force development (maximal value of the first derivative of the force signal), and half relaxation time (time to obtain half the decline in maximal force). The QT_{10}/QT_{100} ($QT_{10:100}$) ratio was calculated, as a decrease in this ratio is commonly interpreted as an index of prolonged low-frequency force depression (Martin *et al.*, 2004). Quadriceps VA was calculated according to the following formula: VA (%) = (1 - $QT_{100,superimposed}/QT_{100}$) × 100. Baseline values for MVC peak force, maximal rate of force development, VA, $QT_{10:100}$, QT_{single}, QT_{10} and QT_{100} peak force were calculated by averaging the three highest values from the pre-exercise standardized sets of contractions. Baseline values for twitch contraction time and twitch half-relaxation time were calculated by averaging the three lowest values from the pre-exercise standardized sets of contractions. Pre- to post-exercise difference in MVC, VA, QT_{single}, QT_{10}, QT_{100} and $QT_{10:100}$ (expressed as a percent change from pre-exercise) were calculated to quantify and characterize the origin of exercise-induced neuromuscular fatigue.

To quantify the rate of recovery over time, the time-course of recovery was divided into three periods: I) from 15 s to 2 min, II) from 2 min to 4 min, and III) from 4 min to 15 min. The recovery rate for each period was calculated as follows: Recovery (in % / min) = 100 × $[(Xt_1 - Xt_2)/X_{Fat}]/T_{recovery}$, with Xt_1 and Xt_2 corresponding to the exercise-induced reduction in the index (in %) measured at the beginning (t_1) and end (t_2) of the recovery period, X_{Fat} corresponding to the highest level of exercise-induced fatigue (i.e. maximal pre- to post-reduction in a given fatigue index; in %), and $T_{recovery}$ the duration of the recovery period (1.75, 2, 11 min for the first, second and third recovery period, respectively).

Surface electromyography

Electrical activity of the VL, VM, RF and BF of the right leg was recorded by four pairs of Ag/AgCl surface electrodes (diameter = 10 mm; inter-electrode distance = 20 mm) placed on the muscle belly connected to an EMG system (Octal Bio-Amp, ML138, AdInstrument, Bella-Vista, Australia). A reference electrode was placed on the lateral condyle of the right tibia. The skin was shaved, abraded with emery paper and cleaned with alcohol to reduce skin impedance below 3kΩ. The position of the electrodes optimizing M_{MAX} was marked with indelible ink to ensure identical placement at subsequent visits. EMG signals were amplified (gain = 20mV), filtered (bandwidth frequency, 10 Hz – 500 Hz), and recorded (sampling frequency, 4 kHz) using a commercially available software (Labchart 7, ADInstruments, Bella-Vista, Australia). Each burst onset and offset of the rectified EMG signal recorded during exercise was determined using a custom-made algorithm in Matlab (Matlab 7.12, MathWorks, Natick, MA, USA). The root mean square (RMS) of each burst from the EMG signal was then calculated, normalized to the RMS recorded during pre-exercise MVC ($RMS_{\%MVC}$), and averaged over intervals corresponding to 10% of the total exercise duration. RMS during each MVC (RMS_{MVC}) was calculated over a 0.5 s interval during the plateau phase of the MVC in order to determine the maximal level of muscle activation during the MVC.

Systemic response to exercise

Pulmonary ventilation and gas exchange indices were measured breath-by-breath at rest and throughout time-trials using a stationary automatic ergospirometer (MS-CPX, Viasys, San Diego, California, USA). Before each test, gas analyzers were calibrated using a certified gas preparation (O_2: 16% - CO_2: 5%) and an accurate volume of ambient air (2 L) was used to adjust the pneumotachograph. Heart rate was calculated from R-R intervals recorded by a heart rate monitor (M400, Polar Electro, Kempele, Finland). Oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), $\dot{V}CO_2.\dot{V}O_2^{-1}$, minute ventilation ($\dot{V}_E$), $\dot{V}_E.\dot{V}O_2^{-1}$, $\dot{V}_E.\dot{V}CO_2^{-1}$, breathing frequency ($f_B$), tidal volume ($V_T$) and heart rate (HR) measured during exercise were averaged over the entire duration of the time-trial. Capillary blood samples (5µl) were collected from a fingertip at rest and 3 min post-exercise. Samples were analyzed by an electrochemical method (LactatePro2, Arkray, Kyoto, Japan) immediately after sampling to determine blood lactate concentration ($[La]_b$).

Rate of perceived exertion

To evaluate rate of perceived exertion (RPE), participants were asked to rate on the centiMax scale (CR100) (Borg & Kaijser, 2006) how hard, heavy and strenuous was the exercise during the period that followed the preceding measure. This scale ranged from 0, "nothing at all" to 100, "maximal". The total time-trial distance was split in 20% sections for each time-trial and participants reported RPE at the end of every section.

Statistical analysis

Data presented in the results section are expressed as mean ± SD. Normality of every dependent variable and homogeneity of the variance of the distributions (equal variance) were confirmed using Kolmogorov-Smirnov test and the Levene test, respectively. To protect against the risk of type I error arising from multiple comparisons (Tabachnick & Fidell, 2007), a multivariate analysis (MANOVA) was conducted on the dependent variables recorded during exercise (i.e. power output, $RMS_{\%MVC}$ and cardio-metabolic data) or during post-exercise recovery (i.e. neuromuscular fatigue indices). A significant ($P < 0.001$) *trial × time* effect was found for both the exercise and post-exercise recovery dataset. We determined the effect of time-trials duration on the dependent variables recorded during exercise and during post-exercise recovery (i.e. power output, $RMS_{\%MVC}$, cardio-metabolic, rate of perceived exertion data and neuromuscular fatigue indices) using two-ways ANOVAs with repeated measures (*trial × time*). The effect of time-trials duration on [La]b was determined using a one-way ANOVA with repeated measures. When a significant difference was found, multiple comparisons analysis was performed using the Tukey's HSD test. Effect size was assessed using partial eta-squared (η^2). An η^2 index for effect size was considered as small when η^2 was lower than 0.07, medium when η^2 was comprised between 0.07 and 0.20, and large when η^2 was greater

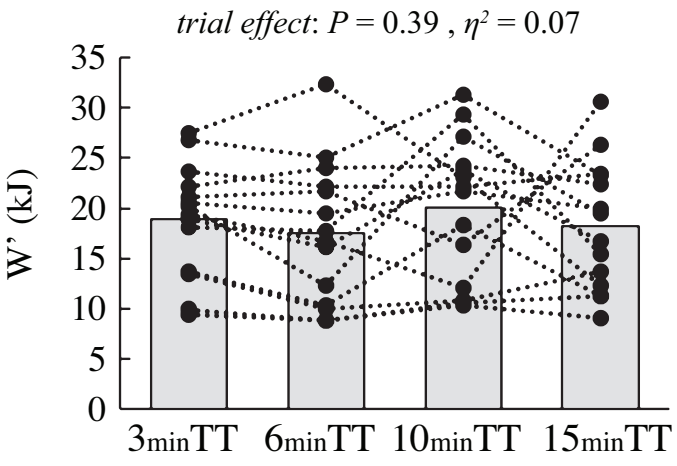

Figure 1. The total work done above critical power during cycling time-trials of different exercise duration

Group mean (bars) and individual (black circles & dotted lines) data are presented for each condition. Data were analyzed using one-way ANOVA (n = 14). No difference was found between conditions. 3minTT, three minutes cycling time-trial; 6minTT, six minutes cycling time-trial; 10minTT, ten minutes cycling time-trial; 15minTT, fifteen minutes cycling time-trial.

than 0.20 (Cohen, 1977). Association between peripheral fatigue indices and muscle activation or W' (i.e. predictors) was tested using linear multilevel models with random intercept. The regression coefficients (β) were computed with 95% confident intervals (95% CI) and goodness of the fit from the predictor effect was computed using r^2 coefficient. Statistical analyses were conducted using Statistica 8.0 (StatSoft, Inc., Tulsa, OK, US), except for the multilevel models analysis which was conducted using R (4.1.2, https://www.R-project.org/) with the packages *lme4, lmerTest and modelsummary*. Statistical significance was set at $P < 0.05$.

RESULTS

Determination of critical power and work done above critical power

Critical power and W' were 175 ± 45 W and 19.0 ± 5.6 kJ with an averaged standard error of 5.7 ± 4.3 W and 2.5 ± 1.9 kJ, respectively. No significant difference was found in W' estimated from each cycling time-trials ($P = 0.39$, $\eta^2 = 0.07$, Fig. 1).

Exercise performance and quadriceps muscle activation during cycling time-trials

As presented in Figure 2, mean power output significantly decreased as exercise duration increased. During exercise, mean VL, VM and RF $RMS_{\%MVC}$ decreased from 3_{min}TT to 6_{min}TT and from 6_{min}TT and 10_{min}TT to 15_{min}TT (Table 1, Fig. 2). No significant change was found in VL, VM and RF $RMS_{\%MVC}$ between 6_{min}TT and 10_{min}TT. No pre- to post-exercise difference was found in VL, VM and RF M_{max} ($P > 0.20$), showing that membrane excitability was unchanged following the cycling time-trials.

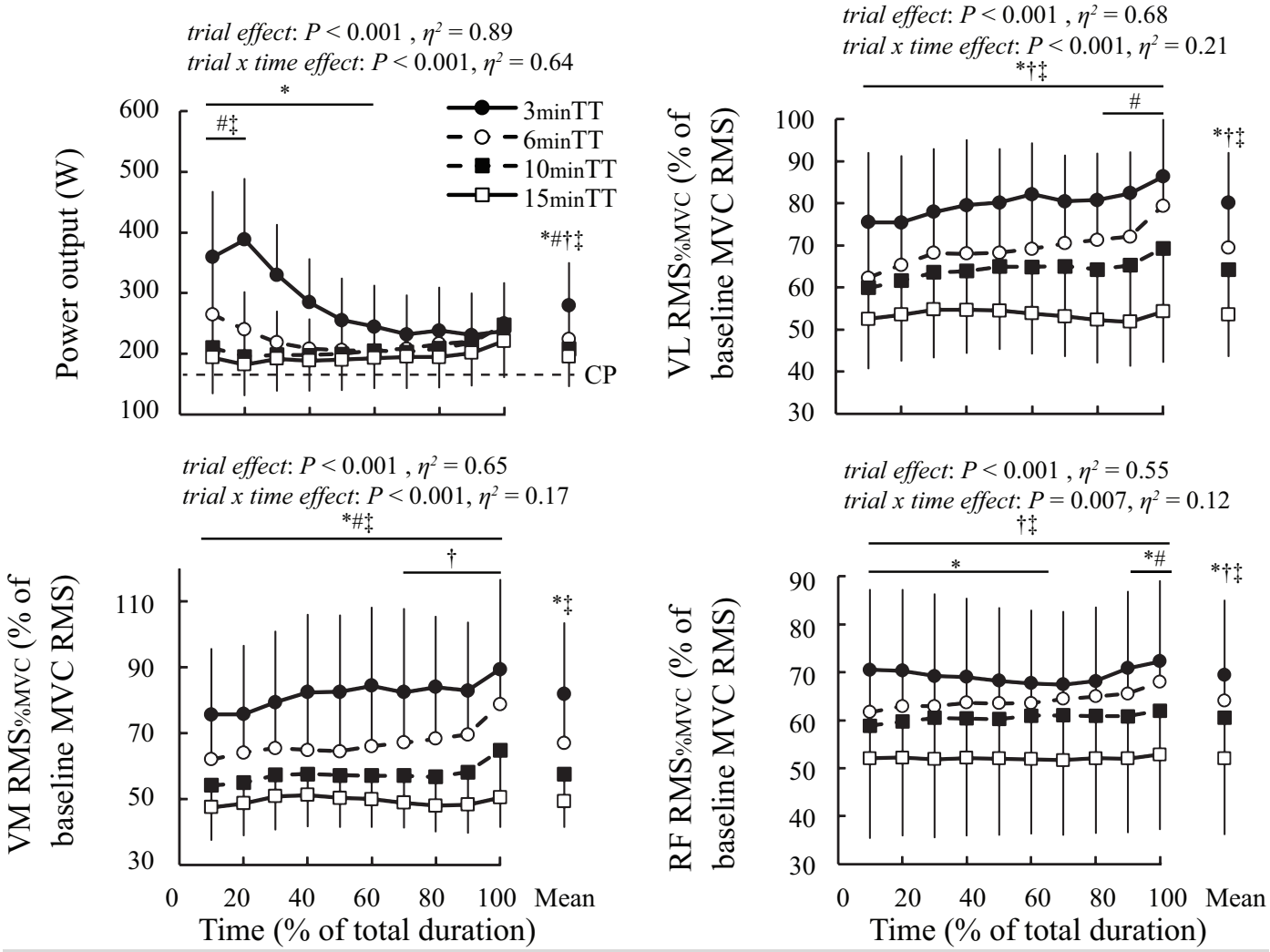

Figure 2. Power output and muscle activation during severe-intensity cycling time-trials

Data were analyzed using two-way ANOVA (n = 14) and are presented as mean ± SD. The dotted line in the first panel represents the mean critical power (CP) from all participants. $RMS_{\%MVC}$, root mean square of each burst from the EMG signal, normalized by the root mean square calculated during pre-exercise maximal voluntary contractions (MVC); VL, vastus lateralis; VM, vastus medialis; RF, rectus femoris; 3_{min}TT, three minutes cycling time-trial; 6_{min}TT, six minutes cycling time-trials; 10_{min}TT, ten minutes cycling time-trials; 15_{min}TT, fifteen minutes cycling time-trials; *, indicates significant difference between 3_{min}TT and the other time-trials ($P < 0.05$); #, indicates significant difference between 6_{min}TT and 10_{min}TT ($P < 0.05$); †, indicates significant difference between 6_{min}TT and 15_{min}TT ($P < 0.05$), ‡, indicates significant difference between 10_{min}TT and 15_{min}TT ($P < 0.05$).

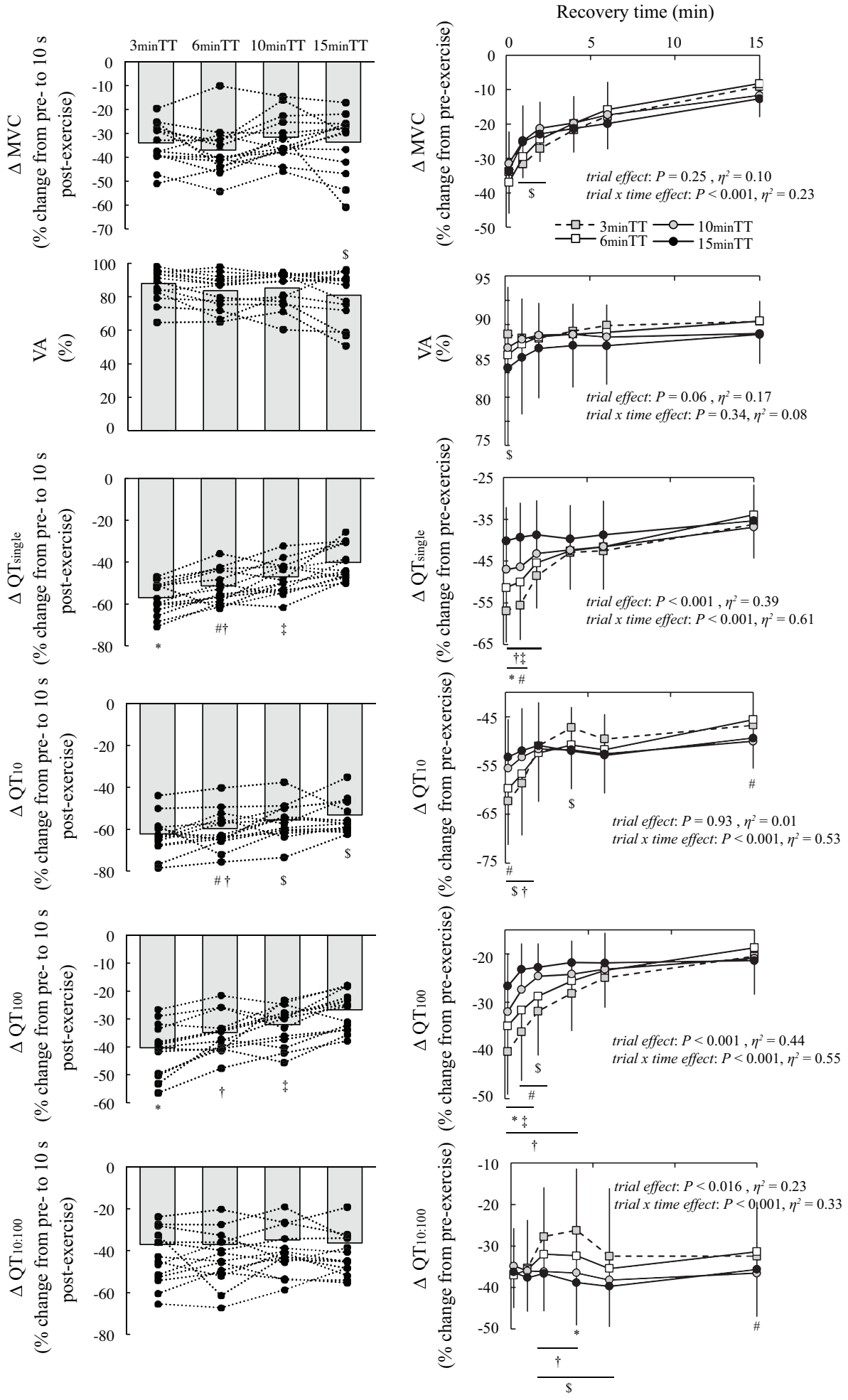
3minTT
6minTT
10minTT
15minTT
Recovery time (min)
Δ MVC (% change from pre- to 10 s post-exercise)
Δ MVC (% change from pre-exercise)
trial effect: P = 0.25 , η² = 0.10
trial x time effect: P < 0.001, η² = 0.23
VA (%)
trial effect: P = 0.06 , η² = 0.17
trial x time effect: P = 0.34, η² = 0.08
Δ QTsingle (% change from pre- to 10 s post-exercise)
Δ QTsingle (% change from pre-exercise)
trial effect: P < 0.001 , η² = 0.39
trial x time effect: P < 0.001, η² = 0.61
Δ QT10 (% change from pre- to 10 s post-exercise)
Δ QT10 (% change from pre-exercise)
trial effect: P = 0.93 , η² = 0.01
trial x time effect: P < 0.001, η² = 0.53
Δ QT100 (% change from pre- to 10 s post-exercise)
Δ QT100 (% change from pre-exercise)
trial effect: P < 0.001 , η² = 0.44
trial x time effect: P < 0.001, η² = 0.55
Δ QT10:100 (% change from pre- to 10 s post-exercise)
Δ QT10:100 (% change from pre-exercise)
trial effect: P < 0.016 , η² = 0.23
trial x time effect: P < 0.001, η² = 0.33

Figure 3 (previous page). Neuromuscular fatigue and recovery following severe-intensity cycling time-trials
Group mean (bars) and individual (black circles & dotted lines) data for neuromuscular fatigue indices at exercise termination (left panels) are presented as percent change from pre- to 10 s post-exercise (except for VA which remains in %). Group mean ± SD data for recovery from fatigue (right panel) are presented as percent change from pre-exercise (except for VA which remains in %). All data were analyzed using two-way ANOVA (n = 14). MVC, maximal voluntary contraction; VA, voluntary activation; QTsingle, potentiated twitch peak force evoked by single electrical stimulation of the femoral nerve; 3_{min}TT, three minutes cycling time-trial; 6_{min}TT, six minutes cycling time-trials; 10_{min}TT, ten minutes cycling time-trials; 15_{min}TT, fifteen minutes cycling time-trials. *, indicates significant difference between 3_{min}TT and other time-trials ($P < 0.05$); $, indicates significant differences between 3_{min}TT and 10_{min}TT or 15_{min}TT ($P < 0.05$); #, indicates significant difference between 6_{min}TT and 10_{min}TT ($P < 0.05$); †, indicates significant difference between 6_{min}TT and 15_{min}TT ($P < 0.05$); ‡, indicates significant difference between 10_{min}TT and 15_{min}TT ($P < 0.05$).

Neuromuscular quadriceps function after cycling time-trials

Neuromuscular fatigue indices are presented in Figures 3 and 4, and in Table 1 and 2. Except for contraction time ($P = 0.66$, $\eta^2 = 0.05$), all neuromuscular fatigue indices were significantly reduced (Fig. 3, Table 1; $P < 0.001$, $\eta^2 > 0.44$) from pre- to 10-s post-exercise after every cycling time-trial. At 10-s after the end of exercise, the exercise-induced reductions in QT_{single}, QT_{10} and QT_{100} were gradually more pronounced with the increase in exercise intensity / shortening in exercise duration (Fig. 3). Conversely, VA tended to gradually decrease with the reduction in exercise intensity / lengthening in exercise duration, but differences did not reach statistical significance (Fig. 3; $P = 0.06$). Finally, exercise-induced reductions in MVC and $QT_{10:100}$ were not different between conditions (Fig. 3).

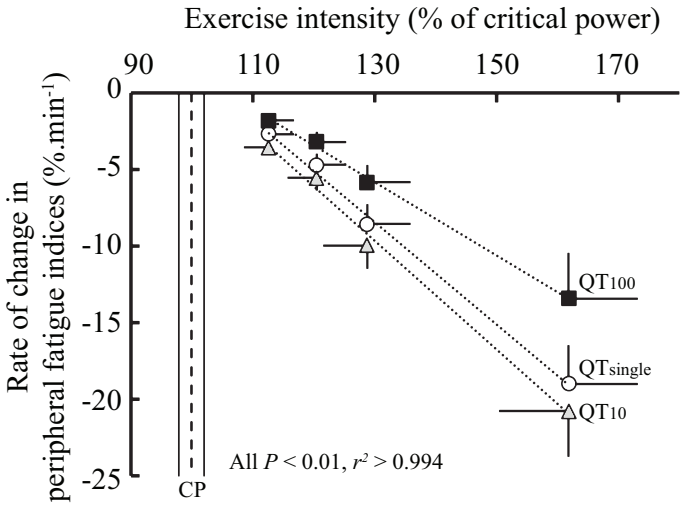

Figure 4. Effect of exercise intensity above the critical power on the rate of peripheral fatigue development
Data are presented as mean ± SD and were analyzed using Pearson product moment correlation (n = 4). The rate of peripheral fatigue development for every fatigue index was calculated by the percent force reduction measured at 10-s post-exercise in peak potentiated single twitch (QT_{single}), low-frequency doublet (QT_{10}) or high frequency doublet (QT_{100}) divided by exercise time. Critical power ± SD are represented by the discontinuous and continuous lines, respectively. Significant difference was found for every fatigue index between every cycling time-trial intensity ($P < 0.001$, $\eta^2 > 0.87$).

The rate of fatigue development (in $\%.min^{-1}$, Fig. 4), calculated as the ratio between percent reduction in twitch force pre- to 10 s post-exercise and time trial duration, linearly increased ($P < 0.01$, $r^2 > 0.99$) with the increase in exercise intensity (expressed as % of CP). A significant negative association was found between ΔQT_{single} (see Fig. 5), ΔQT_{10} and ΔQT_{100} with mean VL (QT_{10}: $\beta = -0.32$, 95% CI = [-0.42 -0.22], $P < 0.0001$, $r^2 = 0.576$; QT_{100}: $\beta = -0.42$, 95% CI = [-0.52 -0.33], $P < 0.0001$, $r^2 = 0.735$), VM (QT_{10}: $\beta = -0.23$, 95% CI = [-0.31 -0.15], $P < 0.0001$, $r^2 = 0.461$; QT_{100}: $\beta = -0.30$, 95% CI = [-0.38 -0.22], $P < 0.0001$, $r^2 = 0.393$) and RF $RMS_{\%MVC}$ (QT_{10}: $\beta = -0.36$, 95% CI = [-0.50 -0.20], $P < 0.0001$, $r^2 = 0.603$; QT_{100}: $\beta = -0.55$, 95% CI = [-0.68 -0.41], $P < 0.0001$, $r^2 = 0.369$) but not with W' (QT_{10}: $\beta = -0.23$, 95% CI = [-0.61 -0.15], $P = 0.220$, $r^2 = 0.029$; QT_{100}: $\beta = -0.12$, 95% CI = [-0.52 -0.28], $P = 0.541$, $r^2 = 0.008$).

During recovery, all neuromuscular fatigue indices but VA ($P = 0.073$) remained significantly reduced compared with baseline up to 15 min after exercise (Fig. 3). The recovery from fatigue for all QT indices was on averaged significantly faster after 3_{min}TT compared to 10_{min}TT and 15_{min}TT and after 6_{min}TT compared to 15_{min}TT ($P < 0.001$, $\eta^2 = 0.49$). During the different phases of the recovery period, recovery from fatigue (Table 2) during R1 (i.e. 15 s to 2 min post-exercise) for QT_{single} ($P = 0.010$, $\eta^2 = 0.18$), QT_{10} ($P < 0.01$, $\eta^2 = 0.28$) and $QT_{10:100}$ ($P < 0.001$, $\eta^2 = 0.36$) was accelerated from the 15_{min}TT to the 3_{min}TT. The recovery for QT_{single} and QT_{10} were also faster during R2 (i.e. 2 min to 4 min post-exercise) following the 3_{min}TT compared to the 15_{min}TT ($P < 0.05$). For QT_{100}, recovery during R1 tended to be faster following the 3_{min}TT compared to the 15_{min}TT but did not reach statistical significance ($P = 0.066$, $\eta^2 = 0.14$).

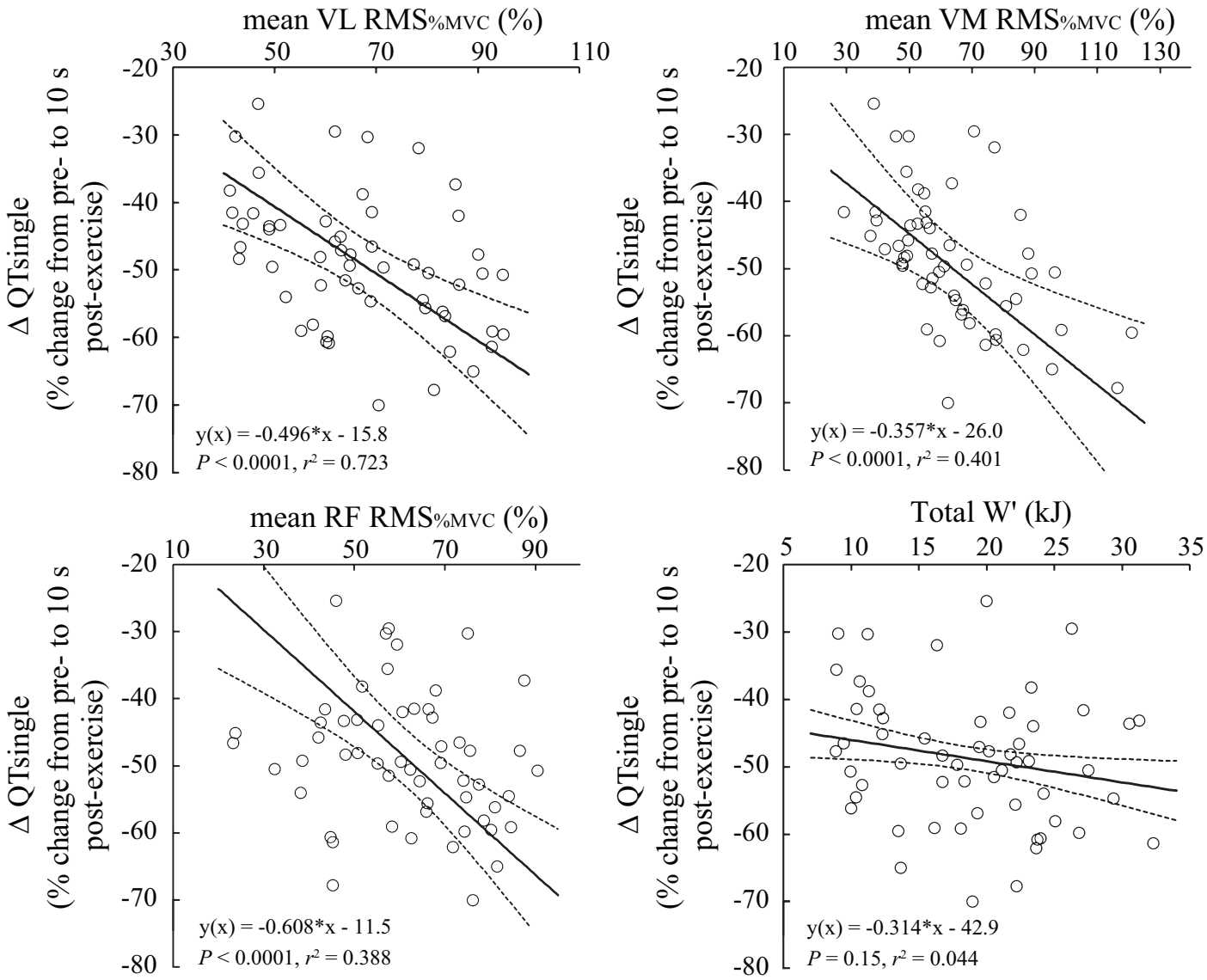

Figure 5. Association between peripheral fatigue, mean quadriceps muscle activity and W' during severe-intensity cycling time-trials.
Individual data (open circles) from every condition were pooled together for every variable. Association between variables were analyzed using linear multilevel models with random intercept (n = 56). Regression line (black line) was computed using the intercept and β coefficient calculated from the models. Dotted lines represent the 95% confident interval of the regression. QTsingle, potentiated twitch peak force evoked by single electrical stimulation of the femoral nerve; RMS%MVC, root mean square of EMG bursts activity, normalized by the root mean square calculated during pre-exercise maximal voluntary contraction; VL, vastus lateralis; VM, vastus medialis; RF, rectus femoris; W', Work done above critical power.

Systemic response to exercise during cycling time-trials
Significant *trial* ($P < 0.05$, $\eta^2 > 0.18$) and *trial × time* ($P < 0.001$, $\eta^2 > 0.30$) effects were found for $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$, V_T, fB and HR. More specifically, our data showed that mean $\dot{V}O_2$ was significantly greater during 3_{min}TT and 6_{min}TT compared to 15_{min}TT ($P = 0.024$). No difference was however found in $\dot{V}O_{2peak}$ between the various time-trials ($P = 0.21$, $\eta^2 = 0.11$). Moreover, mean $\dot{V}CO_2$, $\dot{V}_E$ and fB were significantly higher during 3_{min}TT compared to the other time-trials (Table 3, $P < 0.012$). Mean HR was significantly lower during 3_{min}TT and 6_{min}TT compared to 15_{min}TT. Significant *trial effect* was found for $[La]_b$ ($P < 0.001$, $\eta^2 = 0.55$) and *post-hoc* analysis revealed that $[La]_b$ decreased from 3_{min}TT to 10_{min}TT and 15_{min}TT and from 6_{min}TT to 15_{min}TT ($P < 0.01$). No significant *trial* ($P = 0.16$, $\eta^2 = 0.15$) or *trial × time* ($P = 0.19$, $\eta^2 = 0.11$) effects was found for rate of perceived exertion (Fig. 6).

DISCUSSION

We sought to determine the link between the work done above critical power (W'), muscle activation and the degree of exercise-induced peripheral fatigue. When participant performed exercises of different durations / intensities to exhaustion within the severe intensity domain (i.e. above critical power), the magnitude of peripheral fatigue increased with the increase in power output and the decrease in exercise duration. Our

Table 1. Effects of different cycling time-trial durations on neuromuscular function indices

		3_{min}TT			6_{min}TT			10_{min}TT			15_{min}TT		
Index		Pré	10 s	15 min	Pré	10 s	15 min	Pré	10 s	15 min	Pré	10 s	15 min
MVC	N	555 ± 39	377 ± 29*	518 ± 36*	554 ± 150	354 ± 30*†	514 ± 36*	583 ± 150	398 ± 29*	517 ± 37*	551 ± 39	379 ± 34*	495 ± 33*
VA	%	93 ± 1	88 ± 3*	91 ± 4	94 ± 1	84 ± 3*	91 ± 1	94 ± 1	85 ± 3*	88 ± 2	93 ± 1	81 ± 4*	88 ± 5
QT_{single}	N	165 ± 9	72 ± 6*#†‡	107 ± 8*	163 ± 9	80 ± 23*†‡	109 ± 8*	165 ± 10	88 ± 23*‡	105 ± 7*	160 ± 9	96 ± 7*	104 ± 8*
QT_{10}	N	239 ± 14	91 ± 8*†‡	130 ± 11*	247 ± 14	97 ± 9*†‡	132 ± 11*	241 ± 17	111 ± 10*	125 = 10*	235 ± 16	111 ± 8*	121 ± 10*
QT_{100}	N	249 ± 14	147 ± 9*#†‡	197 ± 11*	240 ± 13†	157 ± 8*†‡	197 ± 11*	252 ± 14	170 ± 9*	199 ± 11*	242 ± 14	179 ± 35*	192 ± 10*
$QT_{10:100}$	Ø	.97 ± .02	.61 ± .03*	.66 ± .04*	.97 ± .04	.61 ± .03*	.67 ± .03*	.97 ± .03	.64 ± .03*	.62 ± .03*	.98 ± .03	.62 ± .02*	.63 ± .04*
CT	ms	69 ± 7	70 ± 3	71 ± 7	70 ± 7	67 ± 2	65 ± 2	68 ± 7	66 ± 2	69 ± 5	71 ± 7	66 ± 2	66 ± 3
MRFD	N/ms	2.5 ± 0.3	1.1 ± 0.2*†‡	1.5 ± 0.2*	2.4 ± 0.4	1.2 ± 0.2*‡	1.7 ± 0.3*	2.5 ± 0.4	1.4 ± 0.2*	1.5 ± 0.2*	2.3 ± 0.3	1.5 ± 0.2*	1.6 ± 0.2*
HRT	ms	71 ± 6	49 ± 13*	43 ± 6*	73 ± 7	46 ± 12*	41 ± 8*	75 ± 7	48 ± 12*	38 ± 5*	72 ± 6	42 ± 8*	39 ± 8*
VL M_{max}	mV	11.4 ± 1.6	11.5 ± 1.7	11.3 ± 1.7†‡	11.6 ± 1.8	12.1 ± 1.9	11.2 ± 1.7†‡	11.1 ± 1.5	11.5 ± 1.7	10.4 + 1.6*	11.2 ± 1.7	11.5 ± 1.9	10.3 ± 1.7*
VM M_{max}	mV	16.0 ± 2.0	16.1 ± 4.1	16.0 ± 2.1#†‡	15.1 ± 2.7#	15.7 ± 2.6	15.3 ± 2.4	15.3 ± 2.2	15.6 ± 2.3	15.0 ± 2.2	15.6 ± 2.3	15.7 ± 2.1	15.0 ± 2.3
RF M_{max}	mV	5.5 ± 1.1	5.3 ± 0.9	5.2 ± 1.0	5.6 ± 1.0	5.2 ± 0.8	5.3 ± 0.8	5.3 ± 0.9	4.9 ± 0.7	5.0 ± 0.8	6.0 ± 0.9	5.8 ± 0.8	5.7 ± 0.8

Results are presented as mean ± SD and were analyzed using two-way ANOVA (n = 14). No significant difference was found for baseline measurement between conditions. MVC, maximal voluntary contraction; VA, voluntary activation; QT_{single}, QT_{10} and QT_{100}, potentiated twitch peak force evoked by single, 10 Hz paired and 100 Hz paired electrical stimulation of the femoral nerve, respectively; $QT_{10:100}$, low-frequency fatigue ratio (QT_{10}/QT_{100}); CT, contraction time; MRFD, maximal rate of force development; HRT, half relaxation time; VL, *vastus lateralis*; VM, *vastus medialis*; RF, *rectus femoris*; Mmax, M-wave maximal amplitude; 3_{min}TT, three minutes cycling time-trial; 6_{min}TT, six minutes cycling time-trials; 10_{min}TT, ten minutes cycling time-trials; 15_{min}TT, fifteen minutes cycling time-trials; *, Significant difference compared to pre-exercise value ($P < 0.05$); #, Significant difference compared to 6_{min}TT ($P < 0.05$); †, Significant difference compared to 10_{min}TT ($P < 0.05$); ‡, Significant difference compared to 15_{min}TT ($P < 0.05$).

Table 2. Recovery of neuromuscular fatigue indices after cycling time-trials of different exercise durations.

	3_{min}TT			6_{min}TT			10_{min}TT			15_{min}TT		
Index (%/min)	R1	R2	R3	R1	R2	R3	R1	R2	R3	R1	R2	R3
QT_{Single}	8.5 ± 4.3‡	4.9 ± 3.6‡	1.1 ± 1.0*	7.0 ± 5.4‡	2.5 ± 3.9*	1.4 ± 1.0*	4.7 ± 4.9	0.8 ± 3.0	0.9 ± 1.3	2.0 ± 5.7	-1.3 ± 3.0	1.0 ± 0.9
QT_{10}	10.4 ± 5.2†‡	2.9 ± 4.0*‡	0.0 ± 0.9*	7.2 ± 3.5‡	1.1 ± 3.2*	0.8 ± 1.0*	4.1 ± 5.6	-0.3 ± 2.4*	0.2 ± 1.0*	2.4 ± 5.5	-1.0 ± 2.2	0.5 ± 0.6
QT_{100}	12.4 ± 7.4	4.4 ± 3.9*	1.8 ± 1.4*	10.8 ± 7.9	4.1 ± 3.3*	1.8 ± 1.6*	13.0 ± 7.9‡	0.3 ± 4.3*	0.9 ± 1.8*	7.2 ± 8.2	1.7 ± 3.8*	0.3 ± 1.1*
$QT_{10:100}$	15.0 ± 16.9#†‡	3.0 ± 11.3*	-1.6 ± 2.4*	7.4 ± 7.5†‡	-0.1 ± 6.9*	0.2 ± 1.1*	-1.7 ± 9.3	-0.2 ± 4.2	-0.1 ± 1.2	0.0 ± 7.6	-2.4 ± 4.0	0.8 ± 0.8

Results are presented as mean ± SD and were analyzed using two-way ANOVA (n = 14). QT_{single}, QT_{10} and QT_{100}, potentiated twitch peak force evoked by single, 10 Hz paired and 100 Hz paired electrical stimulation of the femoral nerve, respectively; 3_{min}TT, three minutes cycling time-trial; 6_{min}TT, six minutes cycling time-trials; 10_{min}TT, ten minutes cycling time-trials; 15_{min}TT, fifteen minutes cycling time-trials; *, Significant difference compared to R1 ($P < 0.05$); #, Significant difference compared to 6_{min}TT ($P < 0.05$); †, Significant difference compared to 10_{min}TT ($P < 0.05$); ‡, Significant difference compared to 15_{min}TT ($P < 0.05$).

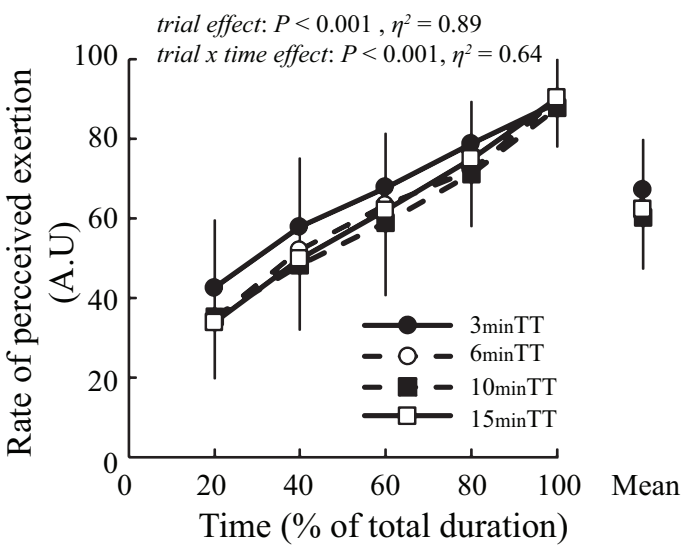

Figure 6. Rate of perceived exertion during cycling time-trials in the severe intensity domain.
Data are presented as mean ± SD and were analyzed using two-way ANOVA (n = 14). The total time-trial distance was split in 20% sections for every trial and participants reported RPE at the end of every section. 3_{min}TT, three minutes cycling time-trial; 6_{min}TT, six minutes cycling time-trials; 10_{min}TT, ten minutes cycling time-trials; 15_{min}TT, fifteen minutes cycling time-trials.

correlative findings suggest that this increase in peripheral fatigue with exercise intensity was not dependent upon W' - which remained constant between the various time-trials - but was rather linked to an increase in quadriceps muscle activation. Our findings also showed that the recovery from fatigue was accelerated in its early phase (10 s to 4 min post-exercise) from the 15 min to the 3 min cycling time-trial such as the greater degree of peripheral fatigue was associated with the faster rate of recovery.

Neuromuscular fatigue and W'

Consistent with our hypothesis, we found that reductions in potentiated twitch force evoked by single or paired stimuli – indicative of peripheral fatigue – were larger when power output increased and exercise duration was shortened (Fig. 3). Considering that similar amounts of W' were depleted at the end of every cycling time-trial and that no association was found between end-exercise peripheral fatigue and W', our findings also showed that peripheral fatigue following exhaustive cycling time-trials within the severe intensity domain was not determined by W'. These findings extend results from two studies showing that exercise-induced reduction in potentiated twitch force was larger following shorter compared to longer constant workload cycling exercise (Thomas *et al.*, 2016) or cycling time-trials (Ducrocq *et al.*, 2021), presumably performed within the severe intensity domain (i.e. exercise duration < 12 min). They are also consistent with findings from experiments that improved W' using creatine or caffeine intake and failed to find a relation between peripheral fatigue and W' (Felippe *et al.*, 2018; Schäfer *et al.*, 2019). Together these findings do not support the previously suggested hypothesis that exercise-induced peripheral fatigue in the severe intensity domain is determined by W' (Broxterman *et al.*, 2015; Schäfer *et al.*, 2018; Zarzissi *et al.*, 2020*b*).

Table 3. Cardioventilatory and metabolic response to cycling time-trials of different exercise durations

Index	Units	3_{min}TT	6_{min}TT	10_{min}TT	15_{min}TT
$\dot{V}O_2$	L/min	2.9 ± 0.8‡	3.0 ± 0.8‡	2.8 ± 0.7	2.7 ± 0.7
$\dot{V}CO_2$	L/min	3.6 ± 1.0#†‡	3.3 ± 0.9‡	2.9 ± 0.8	2.7 ± 0.7
$\dot{V}_E$	L/min	124 ± 28#†‡	109 ± 27	100 ± 24	97 ± 23
V_T	L	2.3 ± 0.6	2.5 ± 0.7	2.4 ± 0.7	2.3 ± 0.6
f_B	breaths/min	53 ± 7#†‡	43 ± 6	42 ± 8	43 ± 8
HR	beats/min	169 ± 10†‡	173 ± 9‡	174 ± 9	177 ± 11
$[La]_b$	mmol/L	16.5 ± 3.4†‡	14.8 ± 3.3‡	13.3 ± 1.9	12.0 ± 1.9

Data were averaged over the entire duration of the time-trial and results are presented as mean ± SD. Data were analyzed using one-way ANOVA (n = 14). $\dot{V}O_2$, oxygen uptake; $\dot{V}CO_2$, carbon dioxide output; $\dot{V}_E$, minute ventilation; V_T, tidal volume; f_B, breathing frequency; HR, heart rate; $[La]_b$, capillary blood lactate concentration. 3_{min}TT, three minutes cycling time-trial; 6_{min}TT, six minutes cycling time-trials; 10_{min}TT, ten minutes cycling time-trials; 15_{min}TT, fifteen minutes cycling time-trials; #, Significant difference compared to 6minTT ($P < 0.05$); †, Significant difference compared to 10_{min}TT ($P < 0.05$); ‡, Significant difference compared to 15_{min}TT ($P < 0.05$).

Conversely, the further increase in peripheral fatigue with the increase in power output and the reduction in exercise duration might rather be explained, at least in part, by the increase in muscle activation. Indeed, our findings showing that VL, VM and RF $RMS_{\%MVC}$ increased by 39 to 67 % from the 15 min to the 3 min time-trial (Fig. 2) and that the degree of exercise- induced reduction in evoked twitch force was significantly associated with this increase in muscle activation (Fig. 5) suggest that the greater degree of peripheral fatigue found after shorter/ higher intensity exercises was associated with the recruitment and subsequent fatigue of a greater pool of motor units. These findings are consistent with previous results from our laboratory (Ducrocq *et al.*, 2021) and from others (Decorte *et al.*, 2012) showing that reduction in evoked potentiated quadriceps twitch force following various modality of exercise to exhaustion was associated with the level of quadriceps muscle activation. The enhanced muscle activation and power output during the shortest time-trials were likely associated with a greater contribution of fast-twitch, fatigue-sensitive muscle fibers to force production (Henneman, 1957; Duchateau & Enoka, 2011). These motor units are characterized by higher phosphocreatine stores (Karatzaferi *et al.*, 2001), glycolytic enzymes and ATPase activity (Essén *et al.*, 1975; Costill *et al.*, 1976; Bottinelli *et al.*, 1994), and lower oxidative capacity compared to slow twitch muscle fibers (Essén *et al.*, 1975; Howald *et al.*, 1985). During an intense exercise of several minutes, these fibers thus consume high amounts of creatine phosphate and glycogen to account for the high rate of ATP hydrolysis, and consequently large amounts of metabolites associated with fatigue such as inorganic phosphate, adenosine diphosphate and H^+ (Karatzaferi et al., 2001; Allen et al., 2008). The accumulation of these metabolites within the fast twitch fibers likely explain the further reduction in potentiated twitches with the increase in muscle activation.

It is unclear why different levels of muscle activation were reached between exercises. Indeed, despite participants' willingness to sprint during the last ~30 - 60 s of every cycling time-trial, participants were unable to reach similar peak levels of EMG amplitude at the end of the various time-trials (Fig. 2). We interpret these findings as evidence that muscle activation was restrained during exercise, presumably in response to the increase in the inhibitory tonic input from group III-IV muscle afferent feedback (Amann *et al.*, 2009; 2011; Gagnon *et al.*, 2012; Sidhu *et al.*, 2014; Blain *et al.*, 2016; Sidhu *et al.*, 2017; Hureau *et al.*, 2019).

Our findings showing an increase in peripheral fatigue with the increase in cycling time-trial intensity within the severe intensity domain are not consistent with previous results showing no significant difference between the level of peripheral fatigue or the level of intramuscular metabolite concentrations associated with peripheral fatigue (i.e. inorganic phosphate, H^+) reached at the end of constant workload cycling exercises of duration ranging from 2 to 14 min (Black *et al.*, 2017; Schäfer *et al.*, 2018). Difference in exercise modality, fatigue measurement methodology and/or level of muscle activation might explain, at least in part, these discrepancies. For example, the longer delay to the first neuromuscular fatigue measurement following the end of exercise in Schäfer *et al*. (2018) compared to the present study (i.e. 10 s) likely led to an underestimation of exercise-induced fatigue, especially after the shortest / fastest exercise (see Fig. 3). Moreover, while we observed significant increase in muscle activation with the increase in power output, Black *et al.* (2017) did not. Given the linear relationship we found between EMG amplitude and reduction in potentiated twitch force (Fig. 5), these differences in muscle activation between studies might explain, at least in part, the discrepancy between our results showing an increase in peripheral fatigue and findings showing no change in intramuscular metabolites concentrations (Black *et al.*, 2017; Schäfer *et al.*, 2018) with the increase in exercise intensity. Our results showing that $[La]_b$ increased with exercise intensity also indirectly suggest that a greater concentration of intramuscular metabolites might have been reached during the shortest duration exercises in the present study.

In contrast to peripheral fatigue indices, no change in exercise-induced reduction in MVC was found following the various cycling time-trials. This result supports the hypothesis that MVC is relatively insensitive to change in exercise intensity and duration (Baker *et al.*, 1993; Burnley *et al.*, 2012; Wüthrich *et al.*, 2014; Thomas *et al.*, 2015; 2016; O'Leary *et al.*, 2016; Schäfer *et al.*, 2018; Ansdell *et al.*, 2019). In addition, these results suggest neuromuscular fatigue development rely on different mechanisms within the severe intensity domain. Indeed, while the contribution of peripheral fatigue increased with the shortening in exercise duration, the contribution of central fatigue decreased by ~7% from the 15 min to the 3 min cycling time trial. This finding is consistent with recent results from our group showing that exercise-induced reduction in VA following a 10 min time-trial was significantly greater than following a 1 min time-trial (Ducrocq *et al.*, 2021).

Recovery of neuromuscular fatigue indices following exercise within the severe intensity domain

The influence of exercise intensity and duration on recovery from neuromuscular fatigue is poorly documented. Here, we found that exercise intensity and duration have little influence on the recovery of MVC peak force and, to a lesser extent, to VA (Fig. 3). This result contrast with our previous findings showing an accelerated recovery for MVC peak force and VA following a 10 min time-trial compared to a 1 min time-trial (Ducrocq *et al.*, 2021). This discrepancy might be explained by the fact that the 1 min time-trial belong to the extreme intensity domain (Burnley & Jones, 2016)

and might elicit a different fatigue response than exercise tests performed in the severe intensity (such as the ones performed in the present study). For example, the greater reduction in MVC was observed immediately after exercise termination (i.e. 10 s) following the 3_{min}TT while MVC progressively decreased during the first part of the recovery period (i.e. up to 2 min) after the 1 min time trial in our previous experiment (Ducrocq *et al.*, 2021). Further data are however needed to verify this hypothesis.

The time-course of recovery for QT_{single}, QT_{10}, $QT_{10:100}$, was significantly faster following exercises with the highest intensities, shortest durations during the early recovery period (Fig. 3, Table 2). The higher levels of muscle activation and power output with the increase in exercise intensity / shortening in exercise duration (Fig. 2) were likely associated with a greater recruitment of fast-twitch, fatigue-sensitive muscle fibers. During strenuous exercise, the high rates of ATP and phosphocreatine hydrolyses within these fibers lead to the accumulation of metabolites associated with peripheral fatigue, such as inorganic phosphate and adenosine diphosphate (Karatzaferi *et al.*, 2001; Allen *et al.*, 2008). We thus speculate that the faster time course of recovery from peripheral fatigue during the fastest cycling time-trials was linked to the rapid time course of intramuscular phosphagen resynthesis and metabolite clearance (Miller *et al.*, 1987; Newham & Cady, 1990; Baker *et al.*, 1993; Bogdanis *et al.*, 1995; 1998; Mendez-Villanueva *et al.*, 2012; Kennedy *et al.*, 2014; 2015; Carroll *et al.*, 2017).

Moreover, the lack of recovery in $\Delta QT_{10:100}$ following 10_{min}TT and 15_{min}TT indicates that recovery from peripheral fatigue was limited after the longest / lowest intensity cycling time-trials by mechanisms associated with prolonged low-frequency force depression (Edwards *et al.*, 1977; Bruton *et al.*, 2008; Watanabe & Wada, 2016). Prolonged low-frequency force depression after cycling time trials within the severe-intensity domain might be explained, at least in part, by decreased myofibrillar sensitivity to Ca^{2+} and/or decreased amount of Ca^{2+} released from the sarcoplasmic reticulum in response to the intramuscular accumulation of reactive oxygen species during exercise (Bruton *et al.*, 2008; Cheng *et al.*, 2015; Watanabe & Wada, 2016).

CONCLUSION

Our findings showed that, within the severe intensity domain, exercise-induced peripheral fatigue is not determined by the total amount of work done above the critical power. Rather, the significant association between peripheral fatigue indices and EMG amplitude provides evidence that the degree of peripheral fatigue might depend on the level of muscle activation during exercise. Moreover, higher levels of peripheral fatigue and faster rates of peripheral fatigue recovery during its early phase were found following the more intense / shortest cycling time-trials. Together these findings suggest that the combined metabolites accumulation and neuromuscular fatigue during exercise and the consecutive need for metabolite clearance after exercise were much higher with the increase in power output. Conversely, the time course of recovery from peripheral fatigue following longer / less intense cycling time-trials was more influenced by the long-lasting effects of prolonged low-frequency force depression. The findings of this study enhance our understanding of the etiology of exercise-induced neuromuscular fatigue and the subsequent recovery from fatigue when exercise is performed in the severe intensity domain. They therefore provide important insights into the neuromuscular limits of human performance and have applications in the management of exercise intensity and duration in the exercising human.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

COMPETING INTEREST

The authors have no conflicting interests

AUTHOR CONTRIBUTIONS

G. P. D. and G. M. B. conceived the study, interpreted the data, and prepared the manuscript. G. P. D. analyzed the data. All authors executed the study and edited, revised, and approved the final version of the manuscript. All authors agree to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part are appropriately investigated and resolved. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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