© 2019. Published by The Company of Biologists Ltd | Journal of Experimental Biology (2019) 222, jeb197483. doi:10.1242/jeb.197483

RESEARCH ARTICLE

Fatigue and recovery measured with dynamic properties versus isometric force: effects of exercise intensity

Renata L. Krüger[1], Saied Jalal Aboodarda[1], Libia Marcela Jaimes[1], Brian R. MacIntosh[1], Pierre Samozino[2] and Guillaume Y. Millet[1,*]

ABSTRACT

Although fatigue can be defined as an exercise-related decrease in maximal power or isometric force, most studies have assessed only isometric force. The main purpose of this experiment was to compare dynamic measures of fatigue [maximal torque (T_{max}), maximal velocity (V_{max}) and maximal power (P_{max})] with measures associated with maximal isometric force [isometric maximal voluntary contraction (IMVC) and maximal rate of force development (MRFD)] 10 s after different fatiguing exercises and during the recovery period (1–8 min after). Ten young men completed six experimental sessions (3 fatiguing exercises×2 types of fatigue measurements). The fatiguing exercises were: 30 s all-out intensity (AI), 10 min at severe intensity (SI) and 90 min at moderate intensity (MI). Relative P_{max} decreased more than IMVC after AI exercise (P=0.005) while the opposite was found after SI (P=0.005) and MI tasks (P<0.001). There was no difference between the decrease in IMVC and T_{max} after the AI exercise, but IMVC decreased more than T_{max} immediately following and during the recovery from the SI (P=0.042) and MI exercises (P<0.001). Depression of MRFD was greater than V_{max} after all fatiguing exercises and during recovery (all P<0.05). Despite the general definition of fatigue, isometric assessment of fatigue is not interchangeable with dynamic assessment following dynamic exercises with large muscle mass of different intensities, i.e. the results from isometric function cannot be used to estimate dynamic function and vice versa. This implies different physiological mechanisms for the various measures of fatigue.

KEY WORDS: Maximal power output, Maximal isometric voluntary contraction, Neuromuscular fatigue assessment

INTRODUCTION

One of the most common definitions of neuromuscular (NM) fatigue is an exercise-related decrease in the maximal voluntary force or power output (Bigland-Ritchie et al., 1986; Enoka, 2012). The vast majority of fatigue investigations, including our own studies, have only considered the decrement in isometric maximal voluntary contraction (IMVC) as a fatigue index (e.g. Behm and St-Pierre, 1997; Bigland-Ritchie and Woods, 1984; Doyle-Baker et al., 2018; Froyd et al., 2016; Gandevia et al., 1996; Kennedy et al., 2016; MacIntosh et al., 1994; Morris et al., 2012; Temesi et al., 2014; Thomas et al., 2016; Wüthrich et al., 2014). In fact, in our recently published meta-analysis (Kruger et al., 2018), we were able to identify 29 experimental studies that have examined the effects of age on IMVC loss after NM fatigue versus only 11 studies that have measured power output decrements. One reason for using almost exclusively IMVC as an index of fatigue is probably the simplicity of this measurement, as isometric transducers are more accessible and less expensive than dynamic ergometers. Another reason is that isometric contractions in combination with peripheral nerve/transcranial magnetic stimulation allow investigation of central (voluntary activation) and peripheral (electrically evoked force responses on relaxed muscles) fatigue (Millet et al., 2011). Yet, the assessment of changes in the maximal power output may be equally critical to quantify the impact of a fatiguing task, particularly after dynamic exercise, because of task specificity. Some experimental studies have shown that NM function changes with fatigue can be accompanied by a greater reduction in maximum power output and/or dynamic force production at high velocity than is typically seen for isometric force (Cheng and Rice, 2005, 2009; Westerblad et al., 1998). For instance, Cheng and Rice (2005) reported a ∼46% drop in power output following isotonic single-limb contractions, while isometric force decreased by ∼26%. This apparent discrepancy was related to the fact that power is dependent on both force and velocity, both of which can change with fatigue. Therefore, the assessment of isometric force alone can give an incomplete or misleading interpretation of the overall consequences of fatigue.

Although the assessment of power can give rise to additional insights into NM function that would not be discerned with the measurement of isometric force alone, most of the published studies considering dynamic measures of fatigue have used an isotonic or isokinetic dynamometer to measure power during single-limb tasks (Cheng and Rice, 2005, 2009; Dalton et al., 2015; Wallace et al., 2016). Investigating power responses during dynamic exercises with large muscle mass (e.g. cycling) is relevant because of its functional association with daily activities. For this reason, we recently developed an innovative cycling ergometer that can measure NM fatigue in both dynamic and isometric mode immediately after the cessation of exercise (Doyle-Baker et al., 2018). From evaluation of a single all-out acceleration, torque–velocity (T–V) and power–velocity (P–V) relationships can be obtained. These relationships allow calculation of the maximal theoretical torque (T_{max}, representing maximal force production capability) and angular velocity (V_{max}, representing maximal angular velocity until force can be produced), as well as the maximal power output (P_{max}), which combines both measurements (Samozino et al., 2007). These theoretical values represent the two extremes of the T–V spectrum and well characterize the dynamic force production capabilities at low (T_{max}) and high (V_{max}) velocities. They give a better estimation of the maximal dynamic

[1]Human Performance Laboratory, Faculty of Kinesiology, University of Calgary, 2500 University Drive NW, Calgary, AB, Canada T2N 1N4. [2]Univ Savoie Mont Blanc, Laboratoire Interuniversitaire de Biologie de la Motricité, EA 7424, F-73000 Chambéry, France.

*Author for correspondence (gmillet@ucalgary.ca)

R.L.K., 0000-0001-7816-8127; S.J.A., 0000-0001-5108-2235; B.R.M., 0000-0002-7475-9939; P.S., 0000-0002-1665-870X; G.Y.M., 0000-0002-6395-0762

Received 6 December 2018; Accepted 13 March 2019

Journal of Experimental Biology (2019) 222, jeb197483. doi:10.1242/jeb.197483

List of symbols and abbreviations

AI	all-out intensity
IMVC	isometric maximal voluntary contraction
MI	moderate intensity
MRFD	maximal rate of force development
NM	neuromuscular
P_{max}	maximal power
P–V	power–velocity
RPE	rating of perceived exertion
SI	severe intensity
$\dot{V}_E/\dot{V}_{O_2}$	ventilatory equivalent ratio for oxygen
$\dot{V}_E/\dot{V}_{CO_2}$	ventilatory equivalent ratio for carbon dioxide
V_{max}	maximal velocity
$\dot{V}_{O_2,max}$	maximal oxygen uptake
$\dot{V}_{O_2}$	oxygen uptake
VT1	first ventilatory threshold
VT2	second ventilatory threshold
T–V	torque–velocity
T_{max}	maximal torque

force production capabilities than the instantaneous torques measured during a cycling test as the instantaneous torques largely depend on the resistance set during the sprints, which is not the case for T_{max} and V_{max}. Moreover, our cycle ergometer has lockable pedals that allow switching from cycling to isometric contraction modes within seconds (Doyle-Baker et al., 2018).

As stated above, only a few studies have considered both isometric force and power responses after fatiguing tasks (Cheng and Rice, 2005, 2009) and, to the best of our knowledge, no study has examined both IMVC and power output following dynamic exercises with a large muscle mass performed at different intensities/durations. In addition, no study has yet compared the responses of dynamic assessment – P_{max}, T_{max} and V_{max} – with isometric measures of fatigue – IMVC and maximal rate of force development (MRFD) – following different fatiguing cycling exercises. Therefore, the aim of this study was to compare dynamic (T_{max}, V_{max} and P_{max}) with isometric (IMVC and MRFD) measures of fatigue immediately after various intensities of dynamic fatiguing exercise and during the subsequent recovery period.

We compared dynamic properties and isometric force in response to three distinct cycling fatiguing exercises [30 s all-out intensity (AI), 10 min at severe intensity (SI) and 90 min at moderate intensity (MI)] to examine whether the differences and/or similarities between isometric and dynamic properties vary according to the intensity/duration of the protocol. As previously discussed and shown in the literature (Cheng and Rice, 2005, 2009; Dalton et al., 2015; de Haan et al., 1989), we expected that IMVC and P_{max} would decrease differently after the fatiguing exercises, but the effects of different exercise intensity on the diversity of responses still required investigation. As both IMVC and T_{max} represent the capacity to produce maximal force and both V_{max} and MRFD are measures of explosiveness, we would expect a similar magnitude of changes of these properties in response to fatigue. Again, whether this is true following exercise at different intensities is not known. However, studies that have assessed either dynamic or isometric measures of fatigue have shown that these assessments are affected differently, according to the exercise intensity–duration relationship (Black et al., 2017; Hureau et al., 2014; Morris et al., 2012; O'Bryan et al., 2017; Thomas et al., 2016, 2015). Thus, we expected changes in fatigue outcome of different amplitude after the different exercise intensities/durations. For example, fatigue induced by AI exercise may cause a greater decrease in V_{max} and, by consequence, P_{max} than the other fatiguing exercises because of an enhancement in [ADP], which has been associated with a reduction in maximal velocity (Westerblad et al., 1998).

MATERIALS AND METHODS

Ethical approval

Written informed consent was obtained from each participant before beginning the study. This study was approved by the Conjoint Health Research Ethics Board of the University of Calgary (REB #15-2430) and it was conducted according to the guidelines of the Declaration of Helsinki, except for registration in a database.

Participants

Ten young adult males volunteered to participate in this study [mean±s.d. age: 27±4 years; height: 181±6 cm; body mass: 79±9 kg; maximal oxygen uptake ($\dot{V}_{O_2,max}$): 49±7 ml kg^{-1} min^{-1}]. To be included in this study, participants needed to be healthy, non-smokers, non-obese and without chronic metabolic disease. All participants were healthy according to the Physical Activity Readiness Questionnaire (PAR-Q). Physical activity status was assessed with the Godin Leisure Time Exercise Questionnaire. The participants were classified as physically active (exercise duration >150 min per week of moderate to vigorous intensity exercise) consistent with the Canadian Physical Activity Guidelines (https://csepguidelines.ca). The participants were instructed to refrain from consuming caffeine and alcohol for 12 h prior to testing sessions and from participating in any strenuous exercise the day before testing. The characteristics of the participants are presented in Table 1.

Experimental protocol

Participants visited the laboratory on seven different occasions. During the first visit, participants performed an incremental exercise test on a recumbent cycle ergometer to volitional exhaustion while their oxygen uptake was measured by open circuit spirometry (Quark CPET, COSMED, Rome, Italy). The initial power output was 90 W with 15 W increments every minute. The Quark CPET metabolic cart was used to determine first ventilatory threshold (VT1), second ventilatory threshold (VT2), and $\dot{V}_{O_2,max}$. $\dot{V}_{O_2,max}$ was determined to have been achieved when a $\dot{V}_{O_2}$ plateau was observed (when the $\dot{V}_{O_2}$ varied by less than 1.5 ml kg^{-1} min^{-1} with an increase in workload) (Cunha et al., 2011). If there was no plateau, the $\dot{V}_{O_2}$ peak was considered as the highest $\dot{V}_{O_2}$ over 30 s. VT1 was identified as the minimum workload at which the ventilatory equivalent ratio for oxygen ($\dot{V}_E/\dot{V}_{O_2}$) systematically increased

Table 1. Characteristics of the participants

	Mean±s.d.
Age (years)	27±4
Height (cm)	181±6
Mass (kg)	79±9
$\dot{V}_{O_2,max}$ or $\dot{V}_{O_2,peak}$ (ml kg^{-1} min^{-1})	49±7
P_{max} output (W)	304±53
P output at the plateau (W)	268±40
VT1	
$\dot{V}_{O_2}$ (ml kg^{-1} min^{-1})	32±4
P output (W)	155±10
VT2	
$\dot{V}_{O_2}$ (ml kg^{-1} min^{-1})	42±7
P output (W)	226±30

$\dot{V}_{O_2,max}$, maximal oxygen uptake; $\dot{V}_{O_2,peak}$, peak oxygen uptake; $\dot{V}_{O_2}$, oxygen uptake; P_{max}, maximal power; *P*, power; VT1, first ventilatory threshold; VT2, second ventilatory threshold. *n*=10 participants.

without an increase in the ventilatory equivalent ratio for carbon dioxide ($\dot{V}_E/\dot{V}_{CO_2}$) and VT2 as the lowest workload where $\dot{V}_E/\dot{V}_{O_2}$ and $\dot{V}_E/\dot{V}_{CO_2}$ both increased. VT1, VT2 and $\dot{V}_{O_2,max}$ were obtained by visual inspection of graphs by two independent observers (R.L.K. and L.M.J.). Disagreements were resolved by a third author (G.Y.M.). After the incremental cycling test, the participants were familiarized with the isometric NM function assessment and the *T–V* cycling sprint test.

Subsequently, participants randomly completed the six experimental sessions separated by at least 3 days. The responses to three durations of cycling exercises (30 s all-out intensity, 10 min at severe intensity and 90 min at moderate intensity) were assessed by either isometric or dynamic measures of fatigue. The measurements were performed before (Pre), after (Post) and at +1, +2, +4 and +8 min after each cycling task.

Fatiguing exercises

Participants performed three different durations of exercise on a recumbent cycling ergometer adapted from a Velotron ergometer (Racer Mate, Seattle, WA, USA). For the AI exercise trial, participants were instructed to cycle as fast and as hard as possible against the same resistance previously determined for the *T–V* sprint test for 30 s. The SI cycling task was performed at a power output corresponding to 5% above VT2. Participants were instructed to keep the cadence constant between 60 and 80 rpm. If they were not able to keep the cadence above 60 rpm (n=3), power output was slightly reduced (by 10 W) so that they could finish the task. When this happened, the same power output reduction was applied during the other SI session. For the MI session, intensity was determined as the power output corresponding to 20% below VT1. Participants were also instructed to keep the cadence constant at their preferred rate (between 60 and 80 rpm). In the SI and MI conditions, participants were instructed to choose a cadence between 60 and 80 rpm and to keep it constant during the exercise. The average cadence sustained during the SI and MI tasks was 76±5 and 76±6 rpm, respectively. Rating of perceived exertion (RPE) was again assessed within the first revolutions and within the last 30 s of exercise. For the AI exercise, RPE was assessed before and immediately after cessation of the task.

NM function test

The NM function assessment was performed on the same recently validated recumbent cycling ergometer (Doyle-Baker et al., 2018). This ergometer includes instrumented pedals (Model PF1.0.0, Radlabor GmbH, Freiburg, Germany) that measure bilateral force applied to the crank in two directions (radial and tangential). The pedals can be locked at the 90 deg knee position to allow the subject to perform a unilateral isometric contraction similar to that which can be performed in an isometric chair (Doyle-Baker et al., 2018). In this study, the NM function test was conducted with the right leg only. To perform IMVCs with the right knee extensors, the left pedal needs to be locked at a fixed leg position, allowing the right knee and ankle to be at the 90 deg position. During the IMVC, the individuals were secured by non-compliant straps at the hip and chest and were instructed to place their hands across their chest. The participants performed a 5 min standard warm-up, which consisted of cycling for 3 min at 30%, 1 min at 45% and 1 min at 60% of the power output corresponding to the beginning of the $\dot{V}_{O_2,max}$ plateau. Following the warm-up, the first NM evaluation was carried out (Fig. 1A), without moving from the ergometer. First, an explosive IMVC was performed as fast and as hard as possible (<1 s) to measure MRFD. Participants were instructed to contract as fast as possible and to quickly relax right after reaching the maximal force. One second after full relaxation, participants performed a 5 s IMVC during which they attempted to contract as hard as possible and to maintain this level for ∼5 s while receiving strong verbal encouragement. MRFD and IMVC were not measured during the same contraction because many subjects have difficulty maintaining a force plateau when contracting as fast as possible. Therefore, the assessment of both outcomes in the same contraction could jeopardize the voluntary activation measurement (data not shown) by reducing the possibility of reaching a plateau during the IMVC. The pre-assessment was performed twice with 2 min of rest between repeats. If there was a noticeable difference (∼5–10%) in the IMVC, we asked the participant to repeat the sequence. The participants then performed one of the three fatiguing cycling exercises. At 10 s (Post) and 1, 2, 4 and 8 min after the end of the exercise, the participants repeated the same NM function assessments as prior to the trial. The 10 s delay between exercise cessation and the beginning of the post-exercise measurement was intentionally chosen to match the timeline of the 'Post' time point for the *T–V* sprint test. Force data were collected from the crank sensors at 500 Hz during the experiment using Imago Record (v.8.50; Radlabor GmbH). These data were saved and exported to Labchart 8 software (ADInstruments, Bella Vista, Australia) for later analysis.

T–V sprint test

All-out 7 s sprints (Fig. 1B) were performed on the same electronically braked recumbent cycling ergometer (Velotron) equipped with an eddy current braking system, which allows control of the resistance directly from the software. The participants performed two 7 s sprints against a resistance which was equivalent to 5% or 7% of body weight. The individual resistance was chosen based on the goodness of fit of the *T–V* and *P–V* relationships: highest coefficient of determination (R^2), a greater range of velocities covered by experimental points (i.e. pedal downstrokes), and points distributed as equally as possible to both sides of the *P–V* relationship curve. This individual resistance would allow the subjects to achieve maximal power at about 50% of the sprint duration. Sprints were separated by 2 min rest. During the 7 s sprints, the participants were vigorously encouraged to pedal as fast as possible, remaining seated on the saddle and secured by chest and hip straps. The sprints were recorded with a video camera (Fujifilm FinePix XP80 Waterproof Digital Camera with 2.7 inch LCD, Tokyo, Japan) with a 240 Hz sampling frequency. Reflective markers were placed on the crank and on the pedal to measure angular displacement during the sprint. The camera was synchronized with the Labchart 8 software with a light signal. After 3 min of rest, one of the three cycling exercises was performed. At 10 s (Post) and +1, +2, +4 and +8 min after the end of the exercise, the 7 s sprint was repeated. This 10 s delay was necessary to bring the flywheel to a complete stop from which the subsequent acceleration was initiated. During the 7 s sprint cycling tests, the instantaneous torque at the pedal crank was obtained from the instrumented pedals (sum of the tangential force of both pedals multiplied by the crank length) and recorded at 240 Hz in the Imago software, and the instantaneous angular velocity was calculated from the camera and Kinovea software after tracking the crank angular displacement at each 4.17 ms (240 Hz). Power was then calculated as the product of instantaneous torque and angular velocity.

After the MI condition, one individual could not achieve optimal velocity during the *T–V* relationship tests. The lower ability to rapidly overcome the flywheel resistance after NM fatigue

Journal of Experimental Biology (2019) 222, jeb197483. doi:10.1242/jeb.197483

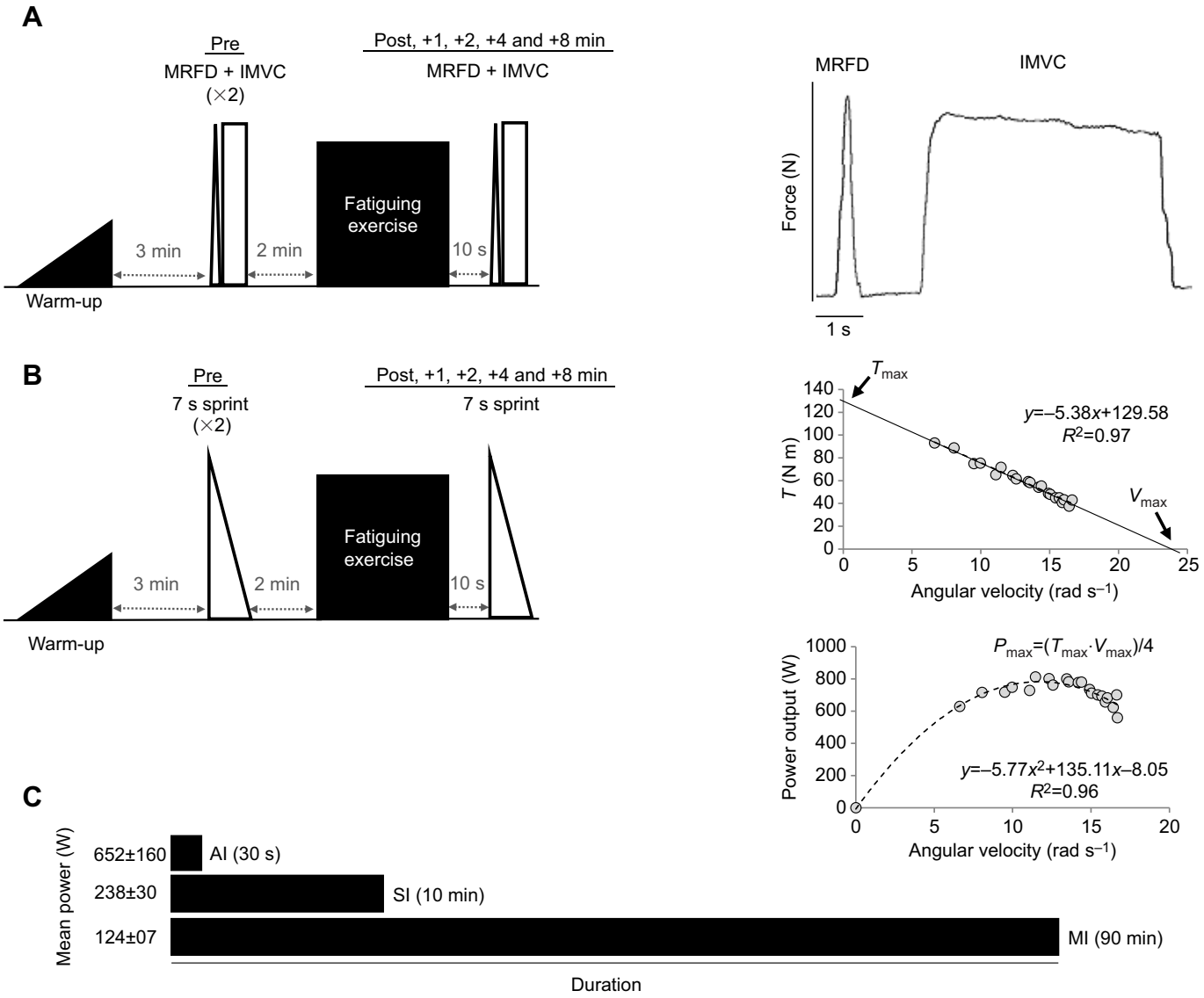

Fig. 1. The different tests and fatiguing exercises. (A) Neuromuscular (NM) function test. Subjects performed an explosive contraction to enable assessment of the maximal rate of force development (MRFD) followed by an isometric maximal voluntary contraction (IMVC) at baseline (Pre) and 10 s after the end of the fatiguing exercise (Post), and during recovery (+1, +2, +4 and +8 min). (B) Torque–velocity (*T*–*V*) sprint test. Subjects performed a 7 s sprint before (Pre) and 10 s following the fatiguing exercise (Post), and during recovery (+1, +2, +4 and +8 min). Maximal torque (T_{max}) and maximal velocity (V_{max}) represented the intercepts of the *T*–*V* relationships with the force and velocity axis, respectively. Maximal power (P_{max}) was determined as the product of T_{max} and V_{max} divided by 4. (C) Fatiguing exercise intensity and duration. AI: 30 s at all-out intensity; SI: 10 min at severe intensity; MI: 90 min at moderate intensity.

compromised the dynamic properties assessment. Consequently, V_{max} was highly extrapolated from the *T*–*V* relationship curve, which increased the inaccuracy of not only V_{max} but also P_{max} computation. Because of that, this subject was excluded from this analysis.

Data analysis

The highest IMVC and MRFD were recorded before the cycling task (Pre). MRFD was measured as the maximal slope of the force–time curve (Aagaard et al., 2002) (Fig. 1A). Instantaneous resultant torque, angular velocity and power output recorded at 240 Hz during cycling were averaged from each pedal downstroke of the acceleration phase (Samozino et al., 2007). Individual *T*–*V* relationships were determined from pedal downstroke averaged values using least-square linear regression (Samozino et al., 2007). Therefore, each point in the *T*–*V* and *P*–*V* relationship curves represents a pedal downstroke (Fig. 1B). *T*–*V* relationships were extrapolated to obtain T_{max} (the theoretical maximal torque that the lower limbs could produce) and V_{max} (the theoretical maximal velocity at which the lower limbs could still produce torque) as the intercepts of the *T*–*V* relationships with the force and velocity axis, respectively. P_{max} was determined as the product of T_{max} and V_{max} divided by 4 (Vandewalle et al., 1987). The dataset is given in Tables S1–S5.

Statistical analyses

All data were analyzed using the Statistical Package for Social Sciences (SPSS) version 24 (SPSS Inc., Chicago, IL, USA). Descriptive statistics (mean±s.d.) were used to describe the data. Levene's test was used to test the homogeneity of variance. Mauchly's sphericity test was used to assess the sphericity assumption. If sphericity was not confirmed, the

Journal of Experimental Biology (2019) 222, jeb197483. doi:10.1242/jeb.197483

Table 2. Reliability of neuromuscular function and torque–velocity sprint tests at baseline

	AI	SI	MI	ANOVA	*P*	CV (%) (95% CI)	ICC (95% CI)	TEM
IMVC (N)	362±66	361±50	356±51	$F_{2,29}$=0.032	0.969	4.5 (2.7–6.4)	0.950 (0.853–0.986)	17
T_{max} (N)	156±40	163±34	159±33*	$F_{2,28}$=0.088	0.916	8.5 (6.3–10.7)	0.942 (0.831–0.984)	15
P_{max} (W)	920±218	1026±198	951±201*	$F_{2,28}$=0.689	0.511	9.0 (6.1–17.1)	0.918 (0.834–0.960)	89
V_{max} (rad s^{-1})	24±3	26±5	24±2*	$F_{2,28}$=0.757	0.479	7.5 (4.6–10.4)	0.850 (0.620–0.965)	2
MRFD (N s^{-1})	3909±1668	3774±832	3558±802	$F_{2,29}$=0.228	0.797	24.3 (13.1–35.4)	0.250 (−1.197–0.797)	1019

AI, 30 s all-out intensity; SI, 10 min at severe intensity; MI, 90 min at moderate intensity; CV, coefficient of variation; ICC, intraclass correlation; TEM, typical error of measurement; IMVC, isometric maximal voluntary contraction; T_{max}, maximal torque; P_{max}, maximal power; V_{max}, maximal velocity; MRFD, maximal rate of force development. Data are means±s.d. (n=10; *n=9).

Greenhouse–Geisser correction factor was applied. A one-way analysis of variance (ANOVA) was used to test reproducibility of the NM function and *T–V* sprint tests at baseline across the three testing sessions. Relative reliability was assessed through coefficient of variation (CV) and intraclass correlation coefficients (ICC) and the absolute reliability was tested through the calculation of typical error of measurement (TEM) (Hopkins, 2000).

Values obtained after exercise (Post) and during recovery were normalized to the highest baseline measures collected at the beginning of each session (Pre). To compare the changes of dynamic measures versus isometric force production properties after fatigue and during recovery (IMVC versus P_{max}, IMVC versus T_{max}, and V_{max} versus MRFD), two-way repeated measures ANOVA performed on the relative decrease (Post, and +1, +2, +4 and +8 min) were used for each type of fatiguing exercise. Spearman (correlations with IMVC) and Pearson (all other correlations) correlation coefficients were calculated to explore the associations between dynamic measures versus isometric force production properties (i.e. IMVC versus P_{max}, IMVC versus T_{max} and V_{max} versus MRFD). A one-way ANOVA followed by Bonferroni *post hoc* test was used to compare the relative changes for each dependent variable (IMVC, MRFD, P_{max}, V_{max} and T_{max}) at the end of the exercise (Post) between three types of fatiguing exercise. Then, a two-way repeated measures ANOVA was conducted to compare the influence of the three cycling exercises on each dependent variable (IMVC, MRFD, P_{max}, V_{max} and T_{max}) during the recovery (Post,

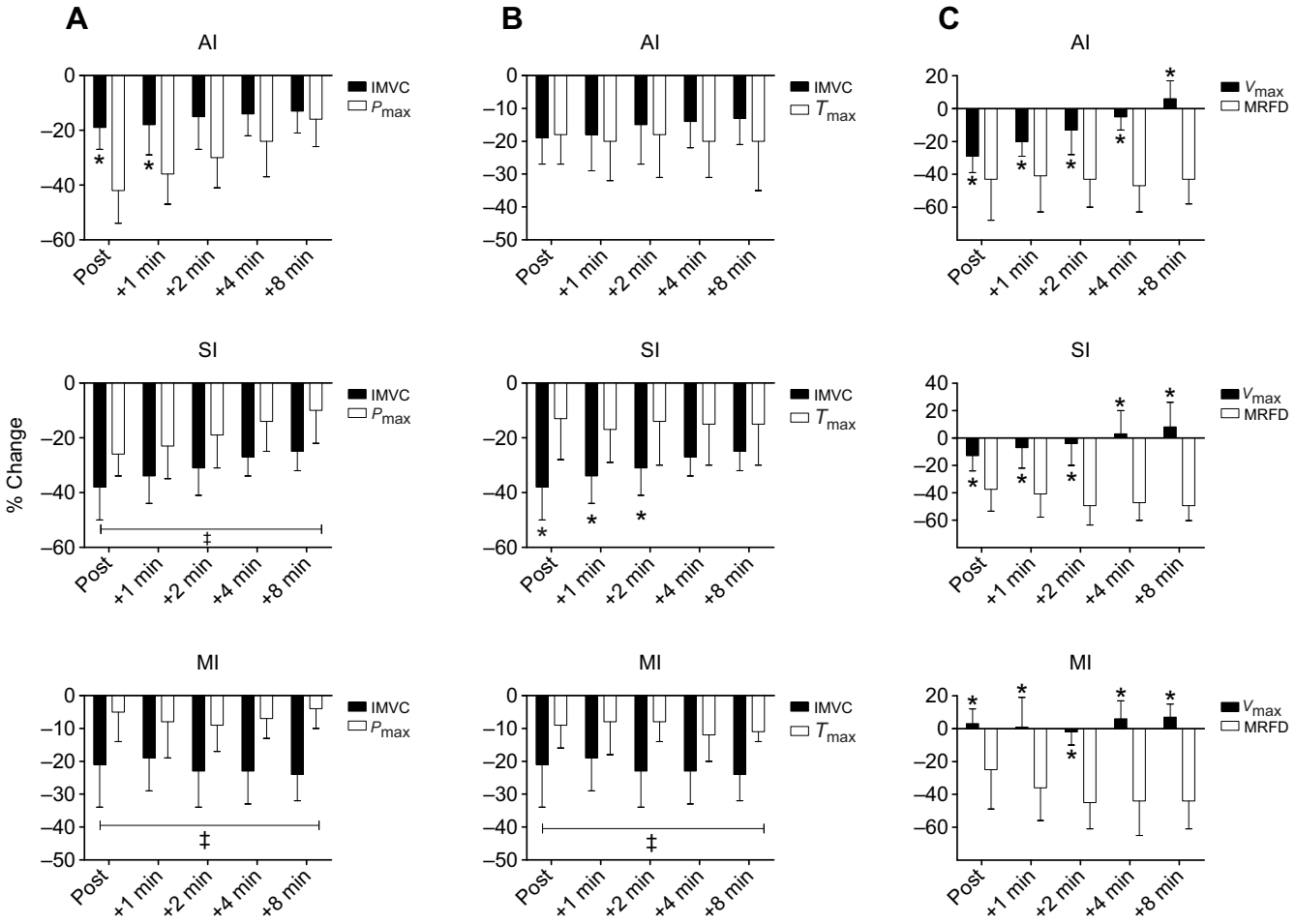

Fig. 2. Comparison of decreases in dependent variables following the three fatiguing exercises. (A) IMVC and P_{max}; (B) IMVC and T_{max}; and (C) MRFD and V_{max}. AI: 30 s at all-out intensity; SI: 10 min at severe intensity; MI: 90 min at moderate intensity. Data are means±s.d. (n=10; P_{max}, T_{max} and V_{max} in MI condition: n=9). Significant differences between dependent variables are indicated (*two-way ANOVA followed by multiple paired *t*-tests adjusted for multiple comparison, P<0.05; ‡two-way ANOVA followed by Bonferroni *post hoc* test, P<0.05).

Journal of Experimental Biology (2019) 222, jeb197483. doi:10.1242/jeb.197483

+1 min, +2 min, +4 min, and +8 min). For the two-way ANOVA, when a main effect of time or fatiguing task was observed, Bonferroni *post hoc* tests were applied. If there was an interaction, multiple paired *t*-tests were performed followed by Holm–Bonferroni correction for multiple comparisons. Effect sizes for the ANOVA were reported as partial eta-squared (partial η^2). For hypothesis testing, the 95% confidence level was predetermined as the minimum criterion to denote a statistical difference ($P \leq 0.05$).

RESULTS

Reliability of NM function and *T*–*V* tests at baseline (Pre) is presented in Table 2. There was no difference at baseline between the three exercise conditions for any variable. Mean power outputs for the three fatiguing exercises are presented in Fig. 1C.

Comparisons between the main indices

IMVC versus P_{max}

There was a time×variable interaction after the AI exercise ($F_{4,36}$=13.035, P<0.001, partial η^2=0.592; Fig. 2A), showing that P_{max} decreased more than IMVC after exercise (Post) (P=0.005) and at +1 min of recovery (P=0.048), but the difference was no longer significant from +2 min. Conversely, IMVC was more reduced than P_{max} at the 'Post' time point and during recovery from the SI exercise (variable, $F_{1,9}$=15.700, P=0.003, partial η^2=0.636; Fig. 2A) and the MI exercise (variable, $F_{1,8}$=77.809, P<0.001, partial η^2=0.907; Fig. 2A) without any time×variable interaction. There was no correlation between the decrease in IMVC and the decrease in P_{max} (r=0.079, P=0.683; Fig. 3A).

IMVC and T_{max}

There was no difference between the decrease in IMVC and the decrease in T_{max} after the AI exercise (Fig. 2B). After the SI exercise, there was a time×variable (IMVC and T_{max}) interaction ($F_{4,36}$=3.738, P=0.012, partial η^2=0.293; Fig. 2B). IMVC was significantly more reduced than T_{max} after exercise (Post) and at +1 min and +2 min of recovery (P<0.042), i.e. the differences between the two variables tended to shrink during recovery. IMVC was also more reduced than T_{max} after exercise (Post) and during recovery after the MI task (variable, $F_{1,8}$=36.138, P<0.001, partial η^2=0.819; Fig. 2B) without any time×variable interaction. There was no correlation between the decrease in IMVC and the decrease in T_{max} (r=−0.070, P=0.720; Fig. 3B).

MRFD and V_{max}

There was a time×variable interaction for the AI task ($F_{4,36}$=9.748, P<0.001, partial η^2=0.520; Fig. 2C), SI task ($F_{4,36}$=7.953, P<0.001, partial η^2=0.469; Fig. 2C) and MI task ($F_{4,36}$=2.859, P=0.039, partial η^2=0.263; Fig. 2C). MRFD demonstrated a much greater depression than V_{max} after exercise (Post) and during recovery for all the fatiguing exercises (all P<0.05). There was a moderate but significant correlation between the reduction in V_{max} and the reduction in MRFD (r=0.426, P=0.021; Fig. 3C).

Fatigue and recovery responses after each type of fatiguing exercise

There was a significant difference in the relative change in the measured variables (Pre to Post) between the exercise conditions for IMVC ($F_{2,29}$=8.810, P=0.001; Fig. 4A), P_{max} ($F_{2,28}$=32.546, P<0.001; Fig. 4B) and V_{max} ($F_{2,28}$=24.572, P<0.01; Fig. 4C) but not for T_{max} and MRFD (Fig. 4D,E). IMVC was lower after the SI trial (62±12% of baseline) than after both the AI (81±8% of baseline) and MI trials (79±13% of baseline) (P<0.006). The reduction of P_{max} was greater after the AI trial (to 58±12% of baseline), followed by the SI trial (to 74±8% of baseline) and then by the MI trial (to 94±10% of baseline) (all P<0.01). V_{max} decreased more after the AI trial (to 71±10% of baseline), followed by the SI trial (to 87±11% of baseline) and was not affected by the MI trial (to 103±9% of baseline) (P<0.005).

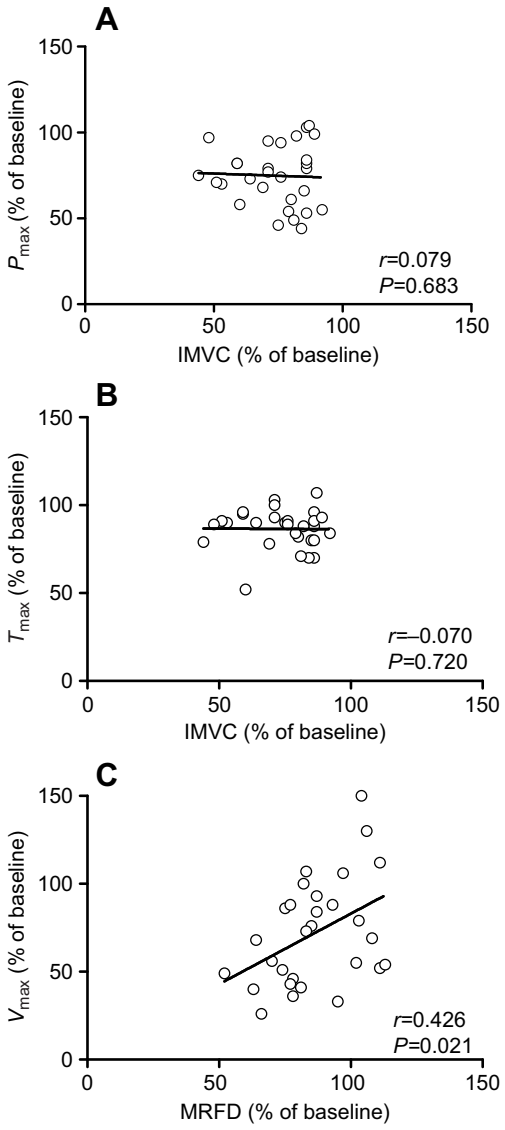

Fig. 3. Correlation between decreases in dependent variables following the three fatiguing exercises. (A) IMVC and P_{max}. (B) IMVC and T_{max}. (C) MRFD and V_{max}. Spearman (correlations with IMVC) and Pearson (all other correlations) correlation coefficients (r) are shown. Data are means±s.d. (n=29).

During recovery, there was a time×fatiguing exercise interaction for IMVC ($F_{8,72}$=2.973, P=0.006, partial η^2=0.248; Fig. 4A), P_{max} ($F_{8,64}$=10.631, P<0.001, partial η^2=0.571; Fig. 4B) and V_{max} ($F_{8,64}$=3.899, P<0.001, partial η^2=0.328; Fig. 4C) but there was neither an interaction nor an effect of time or fatiguing exercise for T_{max} and MRFD (Fig. 4D,E).

Rating of perceived exertion

There was a time×condition interaction for RPE ($F_{2,59}$=9.726; P<0.001). Although at the end of the exercises RPE was slightly increased, it was significantly greater after the AI (18±3) and the SI

Journal of Experimental Biology (2019) 222, jeb197483. doi:10.1242/jeb.197483

(19±1) tasks than following the MI exercise (15±4) (P=0.009 and P<0.001, respectively).

DISCUSSION

This is the first investigation to compare the magnitude of NM fatigue quantified by dynamic and isometric assessment immediately after dynamic fatiguing exercise of different intensity and duration as well as during recovery for a large muscle mass. The main findings of this study are that dynamic properties and isometric force present divergent responses to fatigue induced by cycling, suggesting distinct mechanisms for decline in maximal velocity, power, force and rate of force development. Interestingly, the relative comparisons between the different indices vary between exercise durations. Therefore, and despite the advantage that isometric measurements allow the use of evoked stimulation to understand fatigue etiology, the assessment of isometric force only after fatiguing exercise may result in an underestimation of the functional impairment after fatigue, particularly after very severe-intensity exercises (e.g. AI), in which P_{max} is much more reduced than IMVC. The different patterns of decline and recovery of the dynamic and isometric variables following distinct types of exercise further suggest that these measures of fatigue do not entirely share the same physiological mechanisms. Thus, dynamic and isometric assessments are not interchangeable but instead complement each other to better understand the consequences of fatiguing exercise on NM properties.

IMVC versus P_{max}

IMVC decreased the most after the SI exercise and showed some recovery in the following 8 min but appeared to recover only modestly after the AI and not at all after MI exercise (Fig. 2A). This is a complex pattern of change that can only be explained by different

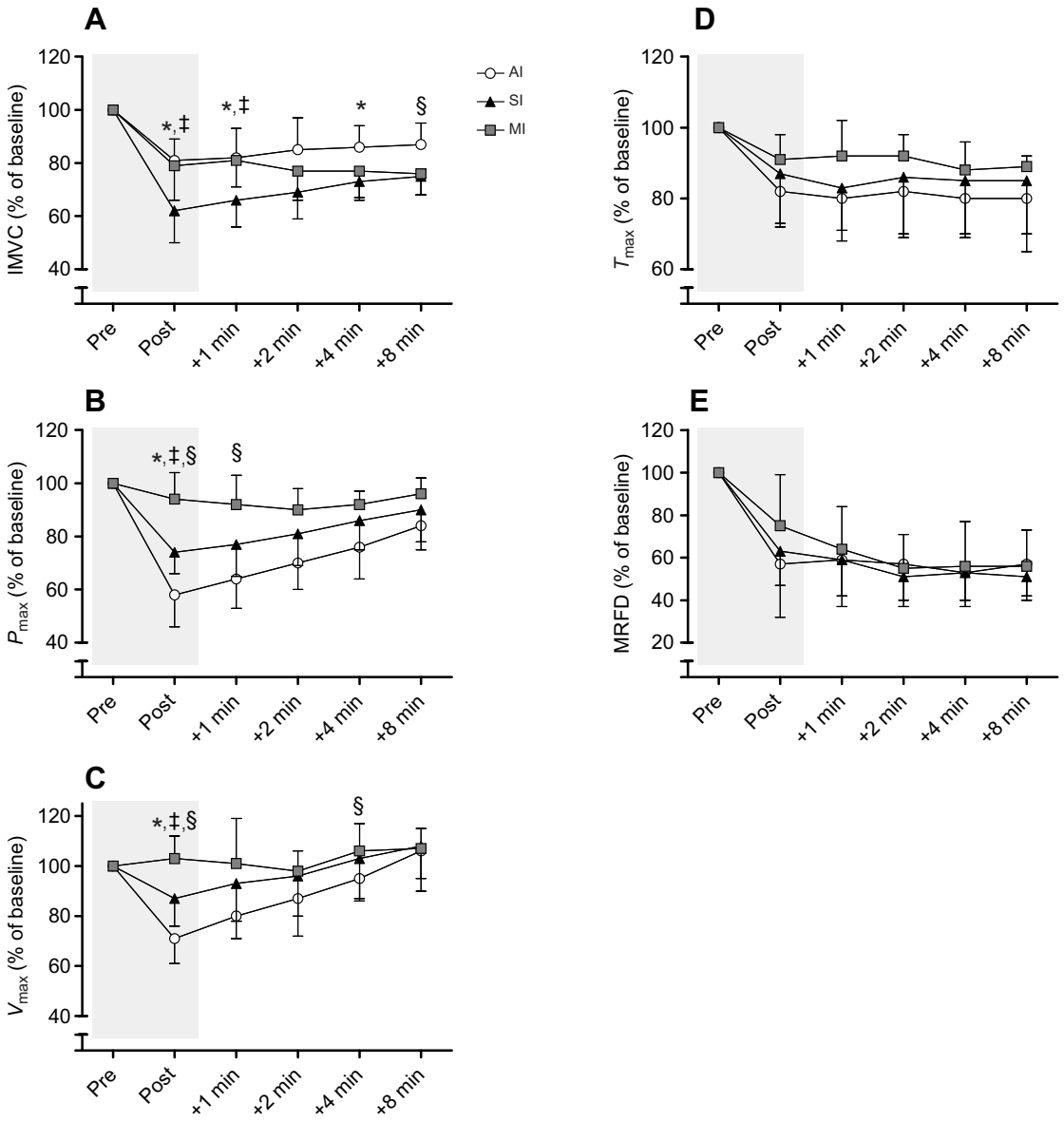

Fig. 4. NM function and *T–V* sprint test responses following the three fatiguing exercises. (A) IMVC; (B) P_{max}; (C) V_{max}; (D) T_{max}; and (E) MRFD. AI: 30 s all-out intensity; SI: 10 min at severe intensity; MI: 90 min at moderate intensity. A one-way ANOVA followed by Bonferroni *post hoc* test was used to test differences at the end of exercise (Post). A two-way ANOVA followed by multiple paired *t*-tests (adjusted for multiple comparisons) was used to test differences during recovery. Data are means±s.d. (n=10). *AI versus SI task (P<0.05); §AI versus MI task (P<0.05); ‡SI versus MI task (P<0.05).

physiological mechanisms of fatigue being associated with the different exercises. In contrast, P_{max} decreased the most after the AI test and least after the MI trial. Peak power output is the product of torque and velocity at the optimal torque and corresponding optimal velocity. For this reason, changes in maximal torque and maximal velocity will influence the decline in peak power. Considering that the relationship between torque and angular velocity for cycling is linear (MacIntosh et al., 2004), P_{max} occurs at 0.5 of apparent maximum torque and 0.5 of apparent maximum velocity. For this reason, the decrease in P_{max} should be proportional to the product of the relative values for T_{max} and V_{max}. In confirmation, this was the case with our data, e.g. the impact of the AI test on V_{max} (decreased 27% to 0.73 of original), T_{max} (decreased 18% to 0.82 of original) and P_{max} (was 58% of original; compare with 0.73×0.82=0.599 or 60%) after exercise (Post) (Fig. 4). For this exercise, recovery of P_{max} (−18% after 8 min) relies on recovery of V_{max} (to +4%) while T_{max} (−21%) does not appear to change much during the recovery period. Therefore, the greater decrease in P_{max} after the AI exercise is mainly explained by the fact that T_{max} decreased similarly across the exercises whereas V_{max} decreased more after the AI exercise (Fig. 4). This may be related to the greater fatigue in fast-twitch motor units which would be expected to be most pronounced during the AI trial (Gregor et al., 1979; Mannion et al., 1995), because this trial required the greatest power output and most likely included recruitment of fast-twitch motor units, right from the beginning of the trial. P_{max} recovery after the AI trial was faster than IMVC (and T_{max}) recovery because of the fast recovery of V_{max} (Fig. 2C), as cross-bridge kinetics recovers quickly as it may be related to ATP concentration (see below), which recovers quickly post-exercise.

Alternatively, the greater decrease in IMVC after the severe-intensity but longer-duration exercise (SI) may be associated with an increase in concentration of metabolites [e.g. inorganic phosphate (Pi), protons (H^+), and plasma potassium (K^+)] for a prolonged period (Black et al., 2017). Higher concentrations of Pi can reduce free Ca^{2+} availability by binding Ca^{2+} inside the sarcoplasmic reticulum (Fryer et al., 1995). Nevertheless, it is worth considering that decreased myoplasmic [Ca^{2+}] can result from a variety of possible mechanisms, e.g. decreased Ca^{2+} release due to metabolic inhibition of ryanodine receptors (MacIntosh et al., 2012), and decreased availability of Ca^{2+} due to redistribution of Ca^{2+} to mitochondria and across the sarcolemma as well as sequestration in the sarcoplasmic reticulum (Allen et al., 1995). Although changes within the muscle (i.e. peripheral fatigue) are possibly the main factors affecting IMVC after fatigue in this study, it is important to note that fatigue can also be related to a failure in the central nervous system to maximally drive motoneurons voluntarily, i.e. central fatigue (Gandevia, 2001). In other words, a decrease in [Ca^{2+}] can also be the result of a decreased frequency of action potentials (Glass et al., 2018), particularly high threshold motor units (Gandevia, 2001).

We conclude from these observations that (i) the decrease in IMVC probably relates to decreased myoplasmic [Ca^{2+}] and/or Ca^{2+} sensitivity, (ii) compromised P_{max} results from a combination of decreases in both maximal velocity and force and (iii) metabolic disturbance affecting V_{max} recovers quickly, allowing partial recovery of P_{max} in the absence of T_{max} recovery. For these reasons, the assessment of P_{max} and IMVC, both of which are used in the common definition of fatigue, are not similarly affected after a given exercise and, therefore, they are not interchangeable.

IMVC versus T_{max}

The difference between trials for T_{max} was small and recovery was not apparent (Fig. 4D). One could expect the mechanisms responsible for depression and recovery of IMVC and T_{max} to be the same, as both represent the maximal force produced by a muscle. Force depression in response to fatigue is closely related to lower myoplasmic concentrations of Ca^{2+} and/or decreased Ca^{2+} sensitivity due to fatigue (MacIntosh et al., 2012), which should similarly affect these two indices. We found low-frequency fatigue (assessed by the low-frequency doublet to high-frequency doublet ratio Db10:100) after the AI and SI exercise (Krüger et al., 2019). In addition, lower levels of ATP and high concentrations of Pi during fatigue can affect force production by reducing the energy charge, decreasing the specific force per cross-bridge and the rate of cross-bridge dissociation (Edwards et al., 1975; Jones et al., 2009), which should also affect both IMVC and T_{max}.

Nevertheless, our results show that T_{max} and IMVC are affected differently by the physiological mechanisms of fatigue, as although T_{max} and IMVC were similarly affected after the AI trial, IMVC was decreased much more than T_{max} after the SI and MI trials (Fig. 2B). There are a few methodological aspects that need to be considered. First, T_{max} was extrapolated from averaged values from one pedal downstroke, which includes non-maximal force levels applied to the pedal at the beginning and at the end of the downstroke. In contrast, IMVC represents the peak voluntary force. Thus, while T_{max} is measured from an effort that lasts only a fraction of a second, IMVC represents the maximal force sustained for ∼5 s. Second, different muscles contribute distinctly to the development of force during cycling sprints and IMVC. Indeed, T_{max} was extrapolated from dynamic measurements during cycling sprints. Studies have shown that there is a substantial contribution in the hip transfer power across the pelvis to the leg during maximal cycling (Driss and Vandewalle, 2013; Elmer et al., 2011). In other words, the co-activation of knee extensors and hip extensor–knee flexor muscles increases the energy transfer between hip and knee joints to maximize cycling efficiency and total power production during maximal cycling (Driss and Vandewalle, 2013; Elmer et al., 2011). This is different from what happens during an IMVC, in which the quadriceps muscles are predominantly recruited during the contractions while the knee flexors play a very small role in force production (Bampouras et al., 2017). Accordingly, the contribution of the knee flexors during the cycling sprint may reduce the total force and/or power applied by the knee extensors to the pedal by the quadriceps muscles (Bobbert et al., 2016). Thus, it is possible that the contrast between the different contraction modes and muscle groups involved in the assessments may explain the discrepancy between the fatigue-induced reduction in T_{max} and IMVC. Still, it is interesting to note that this is not the case for the AI exercise.

V_{max} versus MRFD

V_{max} decreased much more after the AI test than after the other trials (Fig. 4C). In fact, our study shows that V_{max} does not always decrease after dynamic fatiguing tasks, as it was decreased by only 13% after the SI exercise and not reduced after the MI trial. The characteristic feature of changes in V_{max} after the AI and SI exercise was that recovery appears to occur within the very first minutes after the end of the exercise. This implies that V_{max} is decreased by a factor(s) associated with high metabolic rate that recovers quickly. Intriguingly, changes in MRFD after the three trials were very similar and there was no apparent recovery during the 8 min following these trials (Fig. 4E). For this reason, changes in MRFD cannot be associated with any factor that recovers during this time, such as metabolic disturbance. Thus, we believe the physiological mechanism of fatigue detected by V_{max}, but not by MRFD, is related to a quickly recovering property of muscle metabolism such as

increased [ADP]. Increased [ADP] and/or decreased [ATP] would reduce the energy charge, resulting in less force per cross-bridge as discussed above, and possibly a decreased rate of cross-bridge dissociation. It is known that increased [ADP] slows the maximal velocity of isolated single muscle fibers (Westerblad et al., 1998; Westerblad and Lannergren, 1995), which is dependent on the rate of dissociation of cross-bridges. These metabolic disturbances should resolve within a few minutes of stopping the exercise, allowing recovery of processes that are affected by these mechanisms. It is not clear whether or not a decrease in maximal velocity results from decreased Ca^{2+} release as dantrolene, a drug that inhibits Ca^{2+} release, has been reported to impair V_{max} estimated from the fit of the Hill equation to measured force and velocity of shortening in whole muscle (Kristensen et al., 2018), while maximal rate of unloaded shortening is not affected by dantrolene in single fibers (Allen et al., 1995). Thus, it is probable that the high energy demand during the AI exercise contributed to increased ADP levels after exercise (Post), which compromised the ability of the muscle to produce V_{max} and, as a consequence, P_{max} (Bogdanis et al., 1995). Alternatively, the decrease in V_{max} after the AI exercise may also be associated with the greater fatigue in fast-twitch motor units, which would be expected to be most active during the 30 s sprint all-out trial (Gregor et al., 1979; Mannion et al., 1995), as previously discussed.

Previous studies have proposed that the decrease in both MRFD and V_{max} is correlated with a reduction in the maximal motor unit firing rate in fatigue (Harwood and Rice, 2012; Morel et al., 2015; Thorlund et al., 2008). One of the main reasons for this positive association could be that the capacity to produce both a rapid rise in force (MRFD) and force at a high velocity (V_{max}) relies on a high discharge rate at the onset of the contraction (i.e. motor unit firing rate) (Maffiuletti et al., 2016). However, the pattern of fatigue and recovery in MRFD and V_{max} was quite different across the exercise trials, so the same physiological changes associated with a given exercise must affect these measures differently. It is important to recognize that lack of recovery of MRFD, but not V_{max}, is consistent with persistent low-frequency fatigue during recovery (data not shown). Low-frequency fatigue is known to be a consequence of decreased peak [Ca^{2+}].

Limitations

It should be noted that the SI and MI exercises were not performed to exhaustion. Nevertheless, there was clear evidence of NM fatigue following all the exercise trials and the RPE was significantly increased from baseline (Pre) at the end of the exercises (AI: from 8±2 to 18±3; SI: from 9±2 to 19±1; and MI: from 7±1 to 15±4). Moreover, the workload was exactly the same for dynamic and isometric measurements so the comparison of variables is still valid.

Conclusion

This study showed that isometric versus dynamic measurements identify distinct fatigue responses following different durations of dynamic exercise with large muscle mass. Most of the differences in the responses between isometric force and dynamic properties are explained by different physiological mechanisms contributing to the given measure of fatigue. Our findings indicate that isometric and dynamic assessment of fatigue are not interchangeable following dynamic exercise with a large muscle mass and that the results from isometric function cannot be extrapolated to dynamic function and vice versa. The assessment of dynamic properties and isometric force together can bring greater insight into the overall magnitude and etiology of fatigue. Therefore, future researches should consider the task specificities (e.g. exercise contraction mode, intensity and duration) when using different fatigue measures (dynamic versus isometric) to assess NM fatigue. Whether the differences between isometric and dynamic indices of fatigue for a given exercise depend on age, training status, disease or sex remains to be investigated to better understand the effects of these parameters on fatigability.

Competing interests

The authors declare no competing or financial interests.

Author contributions

Conceptualization: R.L.K., S.J.A., P.S., G.Y.M.; Methodology: R.L.K., S.J.A., P.S., G.Y.M.; Software: R.L.K., L.M.J., P.S.; Validation: R.L.K., S.J.A., L.M.J., B.R.M., P.S., G.Y.M.; Formal analysis: R.L.K., S.J.A., L.M.J.; Investigation: R.L.K., S.J.A., L.M.J., B.R.M., P.S., G.Y.M.; Resources: R.L.K., P.S., G.Y.M.; Data curation: R.L.K., L.M.J., B.R.M.; Writing - original draft: R.L.K., B.R.M.; Writing - review & editing: R.L.K., S.J.A., L.M.J., B.R.M., P.S., G.Y.M.; Visualization: R.L.K., B.R.M., P.S., G.Y.M.; Supervision: R.L.K., S.J.A., B.R.M., P.S., G.Y.M.; Project administration: R.L.K., P.S., G.Y.M.; Funding acquisition: R.L.K.

Funding

R.L.K. is currently being sponsored by the Brazilian National Research Council (Conselho Nacional de Desenvolvimento Científico e Tecnológico, CNPq, 201013/2015-0). S.J.A. is funded by an Eyes High Postdoctoral Fellowship from the University of Calgary. The remaining authors were not in receipt of any additional funding.

Supplementary information

Supplementary information available online at
http://jeb.biologists.org/lookup/doi/10.1242/jeb.197483.supplemental

References

Aagaard, P., Simonsen, E. B., Andersen, J. L., Magnusson, P. and Dyhre-Poulsen, P. (2002). Increased rate of force development and neural drive of human skeletal muscle following resistance training. *J. Appl. Physiol.* **93**, 1318-1326.

Allen, D. G., Lannergren, J. and Westerblad, H. (1995). Muscle cell function during prolonged activity: cellular mechanisms of fatigue. *Exp. Physiol.* **80**, 497-527.

Bampouras, T. M., Reeves, N. D., Baltzopoulos, V. and Maganaris, C. N. (2017). The role of agonist and antagonist muscles in explaining isometric knee extension torque variation with hip joint angle. *Eur. J. Appl. Physiol.* **117**, 2039-2045.

Behm, D. G. and St-Pierre, D. M. M. (1997). Effects of fatigue duration and muscle type on voluntary and evoked contractile properties. *J. Appl. Physiol.* **82**, 1654-1661.

Bigland-Ritchie, B. and Woods, J. J. (1984). Changes in muscle contractile properties and neural control during human muscular fatigue. *Muscle Nerve* **7**, 691-699.

Bigland-Ritchie, B., Furbush, F. and Woods, J. J. (1986). Fatigue of intermittent submaximal voluntary contractions: central and peripheral factors. *J. Appl. Physiol.* **61**, 421-429.

Black, M. I., Jones, A. M., Blackwell, J. R., Bailey, S. J., Wylie, L. J., McDonagh, S. T., Thompson, C., Kelly, J., Sumners, P., Mileva, K. N. et al. (2017). Muscle metabolic and neuromuscular determinants of fatigue during cycling in different exercise intensity domains. *J. Appl. Physiol.* **122**, 446-459.

Bobbert, M. F., Casius, L. J. and Van Soest, A. J. (2016). The relationship between pedal force and crank angular velocity in sprint cycling. *Med. Sci. Sports Exerc.* **48**, 869-878.

Bogdanis, G. C., Nevill, M. E., Boobis, L. H., Lakomy, H. K. and Nevill, A. M. (1995). Recovery of power output and muscle metabolites following 30 s of maximal sprint cycling in man. *J. Physiol.* **482**, 467-480.

Cheng, A. J. and Rice, C. L. (2005). Fatigue and recovery of power and isometric torque following isotonic knee extensions. *J. Appl. Physiol.* **99**, 1446-1452.

Cheng, A. J. and Rice, C. L. (2009). Isometric torque and shortening velocity following fatigue and recovery of different voluntary tasks in the dorsiflexors. *Appl. Physiol. Nutr. Metab.* **34**, 866-874.

Cunha, G., Lorenzi, T., Sapata, K., Lopes, A. L., Gaya, A. C. and Oliveira, A. (2011). Effect of biological maturation on maximal oxygen uptake and ventilatory thresholds in soccer players: an allometric approach. *J. Sports Sci.* **29**, 1029-1039.

Dalton, B. H., Power, G. A., Paturel, J. R. and Rice, C. L. (2015). Older men are more fatigable than young when matched for maximal power and knee extension angular velocity is unconstrained. *Age* **37**, 9790.

de Haan, A., Jones, D. A. and Sargeant, A. J. (1989). Changes in velocity of shortening, power output and relaxation rate during fatigue of rat medial gastrocnemius muscle. *Pflugers Arch.* **413**, 422-428.
Doyle-Baker, D., Temesi, J., Medysky, M. E., Holash, R. J. and Millet, G. Y. (2018). An innovative ergometer to measure neuromuscular fatigue immediately after cycling. *Med. Sci. Sports Exerc.* **50**, 375-387.
Driss, T. and Vandewalle, H. (2013). The measurement of maximal (anaerobic) power output on a cycle ergometer: a critical review. *Biomed. Res. Int.* **2013**, 589361.
Edwards, R. H., Hill, D. K. and Jones, D. A. (1975). Heat production and chemical changes during isometric contractions of the human quadriceps muscle. *J. Physiol.* **251**, 303-315.
Elmer, S. J., Barratt, P. R., Korff, T. and Martin, J. C. (2011). Joint-specific power production during submaximal and maximal cycling. *Med. Sci. Sports Exerc.* **43**, 1940-1947.
Enoka, R. M. (2012). Muscle fatigue–from motor units to clinical symptoms. *J. Biomech.* **45**, 427-433.
Froyd, C., Beltrami, F. G., Millet, G. Y. and Noakes, T. D. (2016). Central regulation and neuromuscular fatigue during exercise of different durations. *Med. Sci. Sports Exerc.* **48**, 1024-1032.
Fryer, M. W., Owen, V. J., Lamb, G. D. and Stephenson, D. G. (1995). Effects of creatine phosphate and P(i) on Ca2+ movements and tension development in rat skinned skeletal muscle fibres. *J. Physiol.* **482**, 123-140.
Gandevia, S. C. (2001). Spinal and supraspinal factors in human muscle fatigue. *Physiol. Rev.* **81**, 1725-1789.
Gandevia, S. C., Allen, G. M., Butler, J. E. and Taylor, J. L. (1996). Supraspinal factors in human muscle fatigue: evidence for suboptimal output from the motor cortex. *J. Physiol.* **490**, 529-536.
Glass, L. D., Cheng, A. J. and MacIntosh, B. R. (2018). Role of Ca(2+) in changing active force during intermittent submaximal stimulation in intact, single mouse muscle fibers. *Pflugers Arch.* **470**, 1243-1254.
Gregor, R. J., Edgerton, V. R., Perrine, J. J., Campion, D. S. and DeBus, C. (1979). Torque-velocity relationships and muscle fiber composition in elite female athletes. *J. Appl. Physiol. Respir. Environ. Exerc. Physiol.* **47**, 388-392.
Harwood, B. and Rice, C. L. (2012). Changes in motor unit recruitment thresholds of the human anconeus muscle during torque development preceding shortening elbow extensions. *J. Neurophysiol.* **107**, 2876-2884.
Hopkins, W. G. (2000). Measures of reliability in sports medicine and science. *Sports Med.* **30**, 1-15.
Hureau, T. J., Olivier, N., Millet, G. Y., Meste, O. and Blain, G. M. (2014). Exercise performance is regulated during repeated sprints to limit the development of peripheral fatigue beyond a critical threshold. *Exp. Physiol.* **99**, 951-963.
Jones, D. A., Turner, D. L., McIntyre, D. B. and Newham, D. J. (2009). Energy turnover in relation to slowing of contractile properties during fatiguing contractions of the human anterior tibialis muscle. *J. Physiol.* **587**, 4329-4338.
Kennedy, D. S., McNeil, C. J., Gandevia, S. C. and Taylor, J. L. (2016). Effects of fatigue on corticospinal excitability of the human knee extensors. *Exp. Physiol.* **101**, 1552-1564.
Kristensen, A. M., Nielsen, O. B. and Overgaard, K. (2018). Effects of manipulating tetanic calcium on the curvature of the force-velocity relationship in isolated rat soleus muscles. *Acta Physiol.* **222**, e12977.
Kruger, R. L., Aboodarda, S. J., Samozino, P., Rice, C. L. and Millet, G. Y. (2018). Isometric versus Dynamic Measurements of Fatigue: does age matter? a meta-analysis. *Med. Sci. Sports Exerc.* **50**, 2132-2144.
Krüger, R. L., Aboodarda, S. J., Jaimes, L. M., Samozino, P. and Millet, G. Y. (2019). Cycling exercises performed at different intensities-durations in men: neuromuscular fatigue and recovery kinetics revisited. *Appl. Physiol. Nutr. Metab.* In press.
MacIntosh, B. R., Grange, R. W., Cory, C. R. and Houston, M. E. (1994). Contractile properties of rat gastrocnemius muscle during staircase, fatigue and recovery. *Exp. Physiol.* **79**, 59-70.
MacIntosh, B. R., Svedahl, K. and Kim, M. (2004). Fatigue and optimal conditions for short-term work capacity. *Eur. J. Appl. Physiol.* **92**, 369-375.
MacIntosh, B. R., Holash, R. J. and Renaud, J.-M. (2012). Skeletal muscle fatigue–regulation of excitation-contraction coupling to avoid metabolic catastrophe. *J. Cell Sci.* **125**, 2105-2114.
Maffiuletti, N. A., Aagaard, P., Blazevich, A. J., Folland, J., Tillin, N. and Duchateau, J. (2016). Rate of force development: physiological and methodological considerations. *Eur. J. Appl. Physiol.* **116**, 1091-1116.
Mannion, A. F., Jakeman, P. M. and Willan, P. L. (1995). Skeletal muscle buffer value, fibre type distribution and high intensity exercise performance in man. *Exp. Physiol.* **80**, 89-101.
Millet, G. Y., Martin, V., Martin, A. and Vergès, S. (2011). Electrical stimulation for testing neuromuscular function: from sport to pathology. *Eur. J. Appl. Physiol.* **111**, 2489-2500.
Morel, B., Rouffet, D. M., Saboul, D., Rota, S., Clemencon, M. and Hautier, C. A. (2015). Peak torque and rate of torque development influence on repeated maximal exercise performance: contractile and neural contributions. *PLoS ONE* **10**, e0119719.
Morris, M. G., Dawes, H., Howells, K., Scott, O. M., Cramp, M. and Izadi, H. (2012). Alterations in peripheral muscle contractile characteristics following high and low intensity bouts of exercise. *Eur. J. Appl. Physiol.* **112**, 337-343.
O'Bryan, S. J., Billaut, F., Taylor, J. L. and Rouffet, D. M. (2017). Knee extensor fatigue developed during high-intensity exercise limits lower-limb power production. *J. Sports Sci.* **36**, 1030-1037.
Samozino, P., Horvais, N. and Hintzy, F. (2007). Why does power output decrease at high pedaling rates during sprint cycling? *Med. Sci. Sports Exerc.* **39**, 680-687.
Temesi, J., Rupp, T., Martin, V., Arnal, P. J., Feasson, L., Verges, S. and Millet, G. Y. (2014). Central fatigue assessed by transcranial magnetic stimulation in ultratrail running. *Med. Sci. Sports Exerc.* **46**, 1166-1175.
Thomas, K., Goodall, S., Stone, M., Howatson, G., St Clair Gibson, A. and Ansley, L. (2015). Central and peripheral fatigue in male cyclists after 4-, 20-, and 40-km time trials. *Med. Sci. Sports Exerc.* **47**, 537-546.
Thomas, K., Elmeua, M., Howatson, G. and Goodall, S. (2016). Intensity-dependent contribution of neuromuscular fatigue after constant-load cycling. *Med. Sci. Sports Exerc.* **48**, 1751-1760.
Thorlund, J. B., Michalsik, L. B., Madsen, K. and Aagaard, P. (2008). Acute fatigue-induced changes in muscle mechanical properties and neuromuscular activity in elite handball players following a handball match. *Scand. J. Med. Sci. Sports* **18**, 462-472.
Vandewalle, H., Pérès, G. and Monod, H. (1987). Standard anaerobic exercise tests. *Sports Med.* **4**, 268-289.
Wallace, J. W., Power, G. A., Rice, C. L. and Dalton, B. H. (2016). Time-dependent neuromuscular parameters in the plantar flexors support greater fatigability of old compared with younger males. *Exp. Gerontol.* **74**, 13-20.
Westerblad, H. and Lannergren, J. (1995). Reduced maximum shortening velocity in the absence of phosphocreatine observed in intact fibres of Xenopus skeletal muscle. *J. Physiol.* **482**, 383-390.
Westerblad, H., Dahlstedt, A. J. and Lannergren, J. (1998). Mechanisms underlying reduced maximum shortening velocity during fatigue of intact, single fibres of mouse muscle. *J. Physiol.* **510**, 269-277.
Wüthrich, T. U., Eberle, E. C. and Spengler, C. M. (2014). Locomotor and diaphragm muscle fatigue in endurance athletes performing time-trials of different durations. *Eur. J. Appl. Physiol.* **114**, 1619-1633.