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# **Power-duration relationship: physiology, fatigue and the limits of human performance**

Mark Burnley<sup>1</sup> and Andrew M. Jones<sup>2</sup>

<sup>1</sup>Endurance Research Group, School of Sport and Exercise Sciences, University of Kent, Chatham, Kent, UK; <sup>2</sup>Sport and Health Sciences, College of Life and Environmental Sciences, St. Luke's Campus, University of Exeter, Exeter, UK.

Address for correspondence:

Dr Mark Burnley

School of Sport and Exercise Sciences

University of Kent

The Medway Building

Chatham Maritime

Kent

ME4 4AG

UK

[m.burnley@kent.ac.uk](mailto:m.burnley@kent.ac.uk)

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## **Abstract**

The duration that exercise can be maintained decreases as the power requirements increase. In this review we describe the power-duration (PD) relationship across the full range of attainable power outputs in humans. We show that a remarkably small range of power outputs are sustainable (power outputs below the critical power, CP). We also show that the origin of neuromuscular fatigue differs considerably depending on the exercise intensity domain in which exercise is performed. In the moderate domain (below the lactate threshold, LT), fatigue develops slowly and is predominantly of central origin (residing in the central nervous system). In the heavy domain (above LT but below CP), both central and peripheral (muscle) fatigue are observed. In this domain, fatigue is frequently correlated with the depletion of muscle glycogen. Severe-intensity exercise (above the CP) is associated with progressive derangements of muscle metabolic homeostasis and consequent peripheral fatigue. To counter these effects, muscle activity increases progressively, as does pulmonary oxygen uptake ( $\dot{V}O_2$ ), with task failure being associated with the attainment of  $\dot{V}O_2$  max. Although the loss of homeostasis and thus fatigue develop more rapidly the higher the power output is above CP, the metabolic disturbance and the degree of peripheral fatigue reach similar values at task failure. We provide evidence that the failure to continue severe-intensity exercise is a physiological phenomenon involving multiple interacting mechanisms which indicate a mismatch between neuromuscular power demand and instantaneous power supply. Valid integrative models of fatigue must account for the PD relationship and its physiological basis.

**Keywords:** Endurance; fatigue; physiology; performance.

## **Introduction**

The ability of humans and other species to endure physical exercise has been a source of fascination since antiquity. This interest extends from simply describing the relationship between power output or locomotory speed and endurance time to the study of the purported physiological, mechanical and psychological bases of endurance. The relationship between power output and exercise duration (the power-duration (PD) relationship) has been studied since the turn of the 20<sup>th</sup> century and applies to constant-power output exercise (for reviews see Burnley & Jones, 2007; Jones, Vanhatalo, Burnley, Morton & Poole, 2010), all-out exercise (Vanhatalo, Doust and Burnley, 2007) and self-paced exercise (Chidnok et al., 2013a). Four ‘exercise intensity domains’ can be identified spanning the PD relationship, and the intensity domain in which the exercise task is performed dictates the type (and degree) of fatigue experienced. The purpose of this review is to detail the character of this PD relationship, the fatigue mechanisms which underpin it, and the events that lead to task failure across the exercise intensity spectrum. We will also briefly compare the predictions derived from the PD relationship with models of exercise performance outlined in other reviews. Our view is that any valid integrated model of fatigue must incorporate the physiological and performance characteristics enshrined within the PD relationship.

The limit of human endurance during constant-power exercise, i.e., the point at which a participant is unwilling or unable to continue a physical task, has been referred to as the point of ‘exhaustion’, ‘the limit of tolerance’, or the point of ‘fatigue’. We prefer the term ‘task failure’ to describe this event, as the task itself, and the criteria for failing to maintain it, can be

rigorously defined under experimental conditions. Regardless of the underlying mechanisms, the characteristics of the relationship between power output (or speed) and time to task failure are intuitively obvious: first, maximal neuromuscular power can only be maintained for at most a few seconds; second, humans have a high capacity to sustain exercise if the power (or speed) requirements are relatively low; and third, between these two extremes the sustainable power output declines in a characteristic curvilinear pattern. As shown in Figure 1, healthy young male participants can produce about 1000 W during maximal efforts (although values in excess of 2000 W may be observed in elite sprint cyclists; Gardner, Martin, Martin, Barras & Jenkins et al., 2007), whilst the maximum sustainable power (estimated by the critical power [CP], see below) is usually no more than 25-35% of the maximal power (Vanhatalo et al., 2007; Conley, Kemper & Crowther, 2001), equivalent to ~70% of the power output associated with maximal oxygen uptake ( $\dot{V}O_{2\max}$ ). Thus, almost 70% of the power-generating capacity of the neuromuscular system is unsustainable and will result in task failure within minutes of beginning an exercise task (Bundle & Weyand, 2012) whereas tasks performed at lower power outputs can be continued for many hours (e.g., Davies and Thompson, 1986; Martin et al., 2010). The ‘bandwidth’ of sustainable power is, therefore, surprisingly small. Above this sustainable power, the tolerable duration of exercise can be accurately predicted using very simple mathematical equations that describe the PD relationship.

Several formulations of the relationship between power output and endurance time (time to task failure) exist in the literature, including power law models (Kennelly, 1906; Garcia-Manso Martín-González, Vaamonde & Da Silva-Gigoletto, 2012), exponential decay functions (Wilkie, 1960; Weyand, Lin & Bundle., 2006), and hyperbolic models (Monod and Scherrer, 1965;

Moritani, Nagata, deVries & Muro, 1981; Morton, 2006). There is no clear answer to the question of which mathematical model best fits the PD relationship, and it is beyond the scope of the present review to provide such an answer. However, it is our view that hyperbolic formulations of the PD relationship come closest to achieving both a ‘good fit’ to the underlying data and a reasonable approximation of the underlying physiology (Jones et al., 2010; Poole et al., 2016). Power law functions predict no asymptotic behaviour indicative of distinct exercise intensity domains, even though the existence of such is well accepted (Whipp, 1994; Gaesser & Poole, 1996; see below). Exponential functions usually characterise continuous temporal processes in which the value of a datum is dependent on the value of its predecessor. Power-duration curves are usually not of this form, since each datum represents a discrete exercise test. We will, therefore, focus our attention on the hyperbolic form of the PD relationship (Figure 1B):

$$T_{\text{lim}} = W'/P - CP \quad [1]$$

Where  $T_{\text{lim}}$  is time to task failure,  $W'$  is the curvature constant parameter and  $CP$  is the critical power (see Morton, 2006, for the detailed mathematical basis of the PD relationship). The  $W'$  represents a finite amount of work that can be done when exercise is performed to task failure within the severe domain (Jones et al., 2010).

## **Intensity dependence of fatigue processes**

The characteristic bioenergetic response to exercise varies as a function of the intensity domain in which the exercise in question is performed (for reviews see Burnley & Jones, 2007; Gaesser & Poole, 1996; Poole & Jones 2012; Whipp, 1994). Four intensity domains have so far been identified, namely moderate (power outputs below the lactate threshold, LT), heavy (power outputs between LT and CP), severe (power outputs above CP that can be sustained until  $\dot{V}O_2$  max is attained) and extreme (power output resulting in task failure before  $\dot{V}O_2$  max is attained). In each domain, the time course of the  $\dot{V}O_2$  response (i.e., the kinetics) differs, with moderate-intensity exercise being the only domain in which a steady state is attained within 2-3 minutes of exercise onset. In the heavy domain, the steady state is delayed by the emergence of a  $\dot{V}O_2$  slow component, which increases the  $O_2$  cost of exercise and results in 10-20 minutes being required for a steady state to be established. In severe-intensity exercise, no steady state is possible, and  $\dot{V}O_2$  rises to the  $\dot{V}O_2$  max. Extreme-intensity exercise represents those work rates for which task failure occurs before  $\dot{V}O_2$  reaches  $\dot{V}O_2$  max. The stark differences in the  $\dot{V}O_2$  responses in each domain are mirrored in the muscle metabolic and blood acid-base responses (Jones, Wilkerson, DiMenna, Fulford & Poole, 2008; Poole, Ward, Gardner & Whipp, 1988; Vanhatalo et al., 2016), which suggests distinct fatigue mechanisms may also characterise each intensity domain. There is a paucity of fatigue-related mechanistic studies performed in the moderate and extreme intensity domains and we will therefore focus most of our attention on fatigue and exercise tolerance in the heavy and severe domains (immediately below and above the CP, respectively).

## **Fatigue during exercise below the critical power**

Although the physiological responses to moderate and heavy intensity exercise are easy to distinguish, the fatigue processes and mechanisms of exercise limitation are more difficult to separate. This is largely due to the lack of exhaustive exercise data in the moderate intensity domain, because, at these work rates ( $<LT$ ), exercise can be continued for more than 3 hours, and consequently these tasks are almost always terminated before task failure occurs. Nevertheless, the growing popularity of ultra-endurance competitions has led to a small number of studies investigating physiological responses and fatigue processes during prolonged moderate intensity exercise (e.g., Davies & Thompson, 1986; Lepers, Maffiuletti, Rochette, Brugniaux & Millet 2002; Martin et al., 2010). In contrast, there are numerous studies that have been conducted in the heavy intensity domain, including many of the classic studies of exercise metabolism and thermoregulation (e.g., Bergström Hermansen, Hultman & Saltin, 1967; Costill, Bowers, Branam & Sparkes, 1971).

The physiological and fatigue responses to very prolonged moderate exercise have been assessed during both running (Davies & Thompson, 1986) and cycling (Lepers et al., 2002). Davies & Thompson (1986) studied ten ultramarathon runners who were tasked with running on a treadmill at the highest pace they could sustain for 4 hours. This was estimated to be 65-70%  $\dot{V}O_{2\max}$ , or the upper limit of the moderate domain in these trained runners. These participants exercised with blood [lactate] and RER remaining at resting levels throughout the task, confirming that the exercise was moderate. Nevertheless, the pulmonary  $\dot{V}O_2$  response gradually rose during exercise, and this increase amounted to  $\sim 390 \text{ mL}\cdot\text{min}^{-1}$  in the last 3 hours



of running. This increased O<sub>2</sub> cost of exercise developed much more slowly than the  $\dot{V}O_2$  slow component associated with heavy exercise, despite being similar in amplitude (the rate of increase was  $\sim 2 \text{ mL} \cdot \text{min}^{-2}$ , at least an order of magnitude lower than the typical trajectory of slow components in the heavy or severe domains; Burnley, Davison & Baker, 2011; Gaesser & Poole, 1996). The increase in energy expenditure does, however, imply that as exercise progressed muscle bioenergetic and/or motor unit recruitment alterations were required to sustain the task (Gollnick, Piehl & Saltin et al., 1974). For example,  $\dot{V}O_2$  will increase during prolonged exercise in part due to a shift towards fatty acid utilisation, which has a lower P:O ratio than carbohydrate. However, in the case of Davies & Thompson (1986), the change in RER was relatively small (from  $\sim 0.84$  to  $\sim 0.79$ ), suggesting that only  $\sim 50 \text{ mL} \cdot \text{min}^{-1}$  of the above increase could be accounted for by changes in substrate utilisation. Much of the increase in  $\dot{V}O_2$  thus appears to be a response to neuromuscular fatigue.

Fatigue has been assessed during moderate intensity exercise by measurement of the loss of maximal voluntary contraction (MVC) force, the reduction in force in response to peripheral muscle or nerve stimulation (to measure peripheral fatigue), or the increased force in response to the superimposition of electrical stimuli on MVCs (to quantify the reduction in voluntary activation percentage and thus central fatigue; for review see Gandevia, 2001). At the conclusion of 4 hours of treadmill running, Davies & Thompson (1986) observed a 25% reduction in MVC force, but no change in tetanic force output in response to peripheral stimulation. They therefore concluded that the loss of MVC force had a central origin. Other work supports the predominance of central fatigue during prolonged, moderate intensity running (Martin et al., 2010) and cycling (Leperes et al., 2002). Whether this limits performance is not

clear, since these studies were all continued for a fixed distance or duration rather than to task failure.

When the LT is exceeded, exercise tolerance is limited to between ~40 min and ~3 hours (Coyle, Coggan, Hemmert & Ivy, 1986). These heavy-intensity power outputs typically range from 60-85%  $\dot{V}O_{2\text{ max}}$ . The crucial features of the physiological response to heavy exercise are the development of the  $\dot{V}O_2$  slow component and an increase in blood [lactate], both of which eventually stabilise. Fatigue of both global and peripheral origin undoubtedly occurs during heavy intensity exercise: at task failure following heavy cycle ergometry, the isometric MVC declines to ~75% of its initial value (Sahlin & Seger, 1995), and during one hour of non-exhaustive intermittent isometric contractions, the MVC is reduced to 65-70% of baseline (Burnley, Vanhatalo & Jones, 2012). In the latter study, we demonstrated that peripheral fatigue developed progressively, albeit more slowly in comparison to that observed during severe-intensity exercise (see below). A variety of processes may underpin the development of peripheral fatigue during heavy exercise, including the production of reactive oxygen species,  $K^+$  accumulation and glycogen depletion which, alone or in combination, ultimately result in excitation-contraction coupling failure at the fibre level (for review see Allen, Lamb & Westerblad, 2008).

The depletion of muscle glycogen may be central to the fatigue processes of heavy-intensity exercise. The higher  $O_2$  cost of exercise that results from the development of the  $\dot{V}O_2$  slow component implies that the body's finite energy reserves (chiefly muscle glycogen) will be utilised at a greater rate, and task failure in this domain is often associated with low muscle

[glycogen] (Bergström et al., 1967; Gollnick et al., 1974; Coyle et al., 1986). In addition, fatigue-related metabolites (such as ADP, P<sub>i</sub>, H<sup>+</sup>) do not accumulate as exercise progresses (Jones et al., 2008), in spite of the fact that peripheral fatigue gradually develops (Burnley et al., 2012; Sahlin & Seger, 1995). During heavy exercise, muscle glycogen is utilised by both type I and type II fibres (Gollnick et al., 1974). The recruitment of both type I and type II motor units during heavy exercise has also been inferred from measurements of single fibre [PCr] during exhaustive (Sahlin, Söderlund, Tonkonogi & Hirakoba, 1992) and non-exhaustive cycling (Krustrup, Söderlund, Mohr & Bangsbo, 2004). These studies demonstrate that both fibre types are activated early in heavy intensity exercise but that muscle high-energy phosphate concentrations do not systematically fall as exercise progresses. Nevertheless, a small population of fibres experience considerable metabolic stress as exercise progresses (be it through PCr or glycogen depletion), with the fall in their power output necessitating the recruitment of additional, predominantly type II muscle fibres in order to sustain exercise (Krustrup et al., 2004).

It is only relatively recently that the mechanistic basis of the fatiguing effects of glycogen depletion have come to light (for review, see Ørtenblad, Westerblad & Nielsen, 2011). It is sometimes assumed that glycogen depletion is not limiting exercise performance because glycogen does not fall to zero and is not associated with significant diminutions in cellular [ATP] (e.g., Noakes and St Clair Gibson, 2004). However, myocyte ATP stores are compartmentalised, with [ATP] in the triadic junction being dependent on membrane-bound glycolytic enzymes (Han, Thieleczek, Varsányi and Heilmeyer, 1992). The intramyofibrillar store, often the first to be depleted during exercise, serves the triad junction (Nielsen, Holmberg, Schrøder, Saltin &

Ørtenblad, 2011). Thus, depletion of this particular store likely results in triadic ATP depletion without significantly impacting overall myocyte [ATP] (Han, et al., 1992). The net effect of this would be excitation-contraction coupling failure in the absence of global cellular energy depletion. The observation of a close coupling between glycogen concentration and  $Ca^{2+}$  transients supports the idea that excitation-contraction coupling during prolonged exercise is a glycogen-dependent process (Chin and Allen, 1997). Therefore, glycogen depletion may be a major contributor to fatigue processes during heavy-intensity exercise, and by extension to task failure.

Central fatigue also develops during heavy-intensity muscular contractions (Burnley et al., 2012). Again we refer readers to other reviews in this series and elsewhere which cover central fatigue processes specifically (Nybo and Secher, 2004, Gandevia, 2001; Meeusen, Watson, Hasegawa, Roelands & Piacentini, 2006). A number of mechanisms could plausibly contribute to the reduction in the ability to voluntarily activate the muscle. Changes in serotonin and/or dopamine have been suggested to play a role in central fatigue during exercise (Meeusen et al., 2006), but they are unlikely to play a major role in the progressive loss of voluntary activation during heavy-intensity exercise. The elevation in brain serotonin consequent to increased plasma free fatty acid concentration and its competition with tryptophan for albumin binding takes considerable time (>2 hours; Nybo & Secher, 2004), and does not, therefore, seem likely to contribute to exercise limitation in the upper reaches of the heavy-intensity domain. Similarly, interventions intended to alter dopamine concentrations in the brain only seem to be effective, if at all, during exercise in the heat (Tumilty, Davison Beckman and Thatcher, 2011). As a result of repeated activity, a reduction in motoneurone 'gain' (the level of excitation required to

maintain motoneurone discharge rate; Johnson, Edwards, Van Tongeren and Bawa, 2004; McNeil, Giesebrecht, Gandevia & Taylor, 2011) could occur, which would also contribute to central fatigue in this intensity domain. Under these conditions, continued constant-power exercise would necessitate increased central motor drive. Each of these mechanisms, in combination with those peripheral processes noted above, would require greater effort to sustain the task. Task failure is likely to occur when the sum of these processes render the participant unwilling or unable to continue. Importantly, the above discussion makes it clear that no single mechanism, central or peripheral, is likely to explain neuromuscular fatigue and exercise intolerance during moderate or heavy exercise.

### **Severe intensity exercise**

The principal feature of severe-intensity exercise is that it is non-steady state:  $\dot{V}O_2$ , muscle metabolic, and blood acid-base responses all fail to stabilise above the CP (Poole et al., 1988; Jones et al., 2008). Exercise above CP is tolerable for less than ~40 min, but the precise duration of exercise depends upon the curvature of the PD relationship discussed above. In the severe-intensity domain, the  $\dot{V}O_2$  slow component rises to achieve  $\dot{V}O_{2\max}$  close to the point of task failure (Poole et al., 1988; Whipp, 1994; Burnley & Jones, 2007; Murgatroyd, Ferguson, Ward, Whipp & Rossiter, 2011), even though the power output producing this behaviour can be considerably below that associated with the attainment of  $\dot{V}O_{2\max}$  during incremental exercise. Importantly, the rapidity with which the  $\dot{V}O_2$  slow component develops increases as the power demand is increased above CP, even though its amplitude, constrained by the prevailing  $\dot{V}O_{2\max}$ , decreases (e.g., Burnley et al., 2011). Consequently, it is the kinetics (trajectory) of the

$\dot{V}O_2$  slow component, not its amplitude, which best represents fatigue development in the severe-intensity domain. Similarly, the fall in muscle [PCr], pH, and the increase in [P<sub>i</sub>] accelerate as contractile intensity is increased above the CP, but – crucially – all reach consistent values at task failure (Vanhatalo et al., 2010; Figure 2).

Peripheral fatigue, measured using supramaximal muscle stimuli at rest, also develops inexorably above the critical torque (CT), at a rate proportional to the torque requirement above the CT (Burnley et al., 2012). At task failure, the degree of peripheral fatigue is similar irrespective of the torque requirements or the duration of the exercise (Burnley et al., 2012). The behavioural similarities between peripheral fatigue development, pulmonary and muscle  $\dot{V}O_2$  kinetics and muscle substrate and metabolite alterations in the severe-intensity domain should not be surprising, since these variables are likely to be mechanistically linked (Poole et al., 2016; Figure 2). They are all also likely to underpin, directly or indirectly, the hyperbolic character of the PD relationship itself. This is because metabolite-mediated peripheral fatigue only develops progressively above the CP (Jones et al., 2008; Burnley et al., 2012; Vanhatalo et al. 2016). The reduction in muscle pH and the increase in [P<sub>i</sub>] have each been repeatedly implicated in reduced muscle fibre force, shortening velocity, Ca<sup>2+</sup> handling (P<sub>i</sub>), and thus muscle power (for review see Allen et al., 2008). Recently, it has been suggested that P<sub>i</sub> and H<sup>+</sup> accumulation may act synergistically to reduce muscle force (Nelson & Fitts, 2014). This is precisely the metabolic profile observed during severe-intensity exercise, with PCr and pH reaching their nadir and P<sub>i</sub> reaching its maximum at the point of task failure (Jones et al., 2008; Vanhatalo et al., 2010; Vanhatalo et al., 2016). That said, recent studies of whole-body exercise suggest that task failure is not necessarily associated with consistent levels of peripheral fatigue (Johnson et al., 2015;

Thomas et al., 2016). Notwithstanding the difficulty in measuring metabolite-induced peripheral fatigue in whole-body exercise (which introduce significant delays between exercise cessation and neuromuscular measurement), these results invite the intriguing possibility that the degree of peripheral fatigue reached during severe-intensity exercise may depend somewhat on both exercise intensity and duration.

The loss of contractile function above CP requires the progressive recruitment of additional motor units to maintain the power demand and thus sustain further exercise (Burnley et al., 2012). These adjustments are most likely to contribute, at least in part, to the  $\dot{V}O_2$  slow component, and would explain why the slow component develops more rapidly above the CP (Burnley & Jones, 2007). But these adjustments cannot continue indefinitely: the attainment of  $\dot{V}O_{2\max}$  makes task failure inevitable because, by definition, oxidative phosphorylation cannot contribute to further increases in energy demand. Once  $\dot{V}O_{2\max}$  is attained, additional motor unit recruitment will compromise muscle function by either being reliant on substrate-level phosphorylation (exacerbating peripheral fatigue), or by drawing on the now finite  $O_2$  supply (further compromising the function of the fibres under significant metabolic stress). The tolerable duration of severe-intensity exercise upon the attainment of  $\dot{V}O_{2\max}$  is seldom more than a few minutes and is often considerably less (Hill, Poole & Smith, 2002; Figure 2). Against this background, it is tempting to ascribe the mechanism(s) producing task failure during exercise above the CP to metabolic factors alone: muscle PCr and pH reach low, possibly limiting values (Hogan, Richardson, Haseler, 1999; Jones et al., 2008; Vanhatalo et al., 2010), and  $P_i$  rises to levels that have been shown to compromise contractile function and  $Ca^{2+}$  kinetics

(Allen et al., 2008). However, this provides an incomplete picture of the circumstances that attend task failure in severe-intensity exercise.

The accumulation of metabolites (such as Pi, lactate, H<sup>+</sup>, and K<sup>+</sup>) in the muscle and interstitium during severe-intensity exercise may not simply compromise contractile and ionic function. The appearance of metabolites in the interstitial space exposes them to the receptive fields of free nerve endings of thinly myelinated or unmyelinated afferents (group III and group IV afferents, respectively), which are sensitive to both mechanical and metabolic stimuli (Amann, Sidhu, Weavil, Mangumb and Venturelli, 2015). Recently, a role for these afferents in limiting central motor drive has been proposed, as reviewed in this issue and elsewhere (Amann et al., 2011). Additionally, if motoneurone gain is reduced during severe-intensity exercise (McNeil et al., 2011), simply maintaining a given level of muscle activation requires a greater degree of excitatory synaptic input. In the latter stages of severe intensity exercise, therefore, the recruited motor units are both fatiguing and becoming intrinsically harder to drive, and the CNS is receiving increasing levels of inhibitory feedback. Under these circumstances, task failure would occur if the increased excitatory input (motor drive) does not adequately compensate for the loss of power and excitability (Dideriksen, Enoka & Farina, 2011).

A further important facet of the physiological response to ‘whole-body’ severe-intensity exercise is the extent to which it places acute stress on other organ systems, particularly the respiratory and cardiovascular systems. That  $\dot{V}O_{2\max}$  is attained in the latter stages of severe exercise is evidence enough of the stress placed on the cardiovascular system, but in the last 10-15 years an important role of the respiratory system for severe-intensity exercise tolerance has become



apparent (Romer & Polkey, 2008). Specifically, the inability to prevent the fall in arterial pH means that minute ventilation increases dramatically during severe exercise, due primarily to an increase in breathing frequency (Poole et al., 1988). This increases the O<sub>2</sub> cost of breathing, and may eventually result in respiratory muscle fatigue (Johnson, Babcock, Suman & Dempsey, 1993; Taylor & Romer, 2008). The former adds to the amplitude of the  $\dot{V}O_2$  slow component (Cross, Sabapathy, Schneider & Haseler, 2010) and the latter compromises limb blood flow either by stealing cardiac output from the muscle, or by metaboreflex-induced vasoconstriction (Romer & Polkey, 2008). Both effects would most likely exacerbate the metabolic stress within the muscle, directly or indirectly compromising exercise tolerance.

### **What causes task failure during severe-intensity exercise?**

The consistent observation of hyperbolic PD relationships across exercise modalities strongly suggests that common processes underpin task failure (Burnley and Jones, 2007; Jones et al., 2010; Poole et al., 2016). That said, the PD relationship is ultimately an empirical and integrated model of performance; it does not predict or describe physiological processes during exercise, nor does it provide a physiological mechanism to explain task failure during severe-intensity exercise. Indeed, the proximal cause(s) of task failure during exercise remains a topic of intense debate. The most recent proposals for the cause of task failure include: 1) the attainment of a sensory tolerance limit related to the highest tolerable level of peripheral fatigue (Amann, 2011); 2) central regulation by a brain-centred governor to prevent metabolic catastrophe (Noakes and St Clair Gibson, 2004); or 3) an effort-based decision to disengage from the task (Marcora and Staiano, 2010). The physiological and peripheral fatigue responses to severe-intensity exercise

may support the existence of a sensory tolerance limit, since consistent levels of metabolic stress and peripheral fatigue are observed at task failure above the CP in healthy young participants (Burnley et al., 2012; Vanhatalo et al., 2010, Figure 2). The neural anatomy exists to produce such a reflex spinally or supraspinally (Haouzi, Chenuel & Huszczuk, 2004), but whether this mechanism has a direct influence on exercise performance is debated (see Froyd, Beltrami, Millet, & Noakes, 2016; Thomas et al., 2016). Similarly, the idea that a central governor regulates skeletal muscle recruitment on the attainment of maximal cardiac output (thus preventing catastrophic muscular metabolic perturbations) is plausible, but the evidence collected to date does not support it (see Ekblom [2009] for review). On the other hand, that task failure is typically associated with near-maximal perception of effort (Marcora, Bosio & de Morree, 2008; Marcora, Staiano & Manning, 2009), and perhaps a significant muscle power reserve (Marcora and Staiano, 2010; but see discussion below), might also support the notion that task failure is a form of voluntary task disengagement.

It is our view that task failure during severe-intensity exercise is not caused by task disengagement (cf. Marcora et al., 2008), at least in healthy individuals accustomed to high-intensity exercise. This is because in isometric contractions (Burnley et al., 2012) and cycle ergometry (Amann et al., 2007; Bundle, Ernst, Bellizi, Wright and Weyand, 2006) task failure can occur before participants voluntarily terminate exercise. This is illustrated in Figure 3, wherein torque declines during isometric contractions but EMG amplitude remains high after task failure has occurred (Burnley et al., 2012). Exercise was only terminated when the participants were told to stop. In addition, no decrease in iEMG occurred at task failure during cycle ergometry (Bundle et al., 2006; Chidnok et al., 2013a) or dynamic knee-extension exercise

(Sundberg and Bundle, 2015), which is not consistent with a sudden withdrawal of effort and thus motor drive. That the task failure in cycling occurs before participants stop pedalling (see Amann et al., 2007) clearly demonstrates that no decision to voluntarily terminate the exercise had occurred. Lastly, studies in which participants attempted to sustain exercise after task failure had occurred in the severe-intensity domain reveal that this was only possible if the power output was reduced (Coats et al., 2003; Chidnok et al., 2013c). When the power requirement was reduced but the intensity remained severe, exercise could only be tolerated for a few seconds, whereas exercise in the heavy- or moderate-intensity domains could usually be tolerated for more than 10 minutes (Coats et al., 2003; Chidnok et al., 2013c). Continuation of exercise in the heavy domain was associated with a recovery of muscle metabolic homeostasis, whereas in the severe domain this was not possible (Chidnok et al., 2013c). Thus, motivated participants could continue to exercise at a lower power output after task failure if the experimental protocol allowed them to; they do not disengage.

The recent observation of a substantial reserve in muscle power (Marcora and Staiano, 2010; Morales-Alamo et al., 2015) has been interpreted as evidence that central and peripheral fatigue do not limit exercise tolerance. However, the size and functional significance of this reserve is disputed (Ferguson, Wylde, Benson, Cannon & Rossiter, 2016). We would add that such an experimental design commits the post hoc ergo propter hoc fallacy: measuring maximal neuromuscular output after task failure has occurred does not allow one to infer the cause of task failure during submaximal exercise. That task failure can occur in the absence of task disengagement, and at ostensibly submaximal EMG amplitudes (Bundle et al., 2006; Chidnok et al., 2013a; Figure 2, Figure 3), suggests that task failure is a failure of motor control, not motor

capacity. It is, therefore, the power-generating capacity of the recruited motor units which determines whether a given task can be sustained or not, not the power-generating capacity of the entire motor unit pool. As a result, the functional significance of a 'neuromuscular reserve' measured after task failure has occurred is questionable.

It is important to recognise that the PD relationship exists not just for constant-power laboratory-based exercise but also for variable-paced, self-paced, and intermittent or stochastic exercise, which more closely reflects 'real-world' athletic performance (Black, Jones, Bailey & Vanhatalo, 2015; Chidnok et al., 2012; Chidnok et al., 2013a; Skiba, Chidnok, Vanhatalo & Jones, 2012). For example, if a subject chooses a pacing strategy involving an initial and/or final power output that is greater than the mean during a severe-intensity exercise bout, the total work done and the time to task failure are still accurately predicted with Eqn. 1. Indeed, assuming that CP remains constant, the total work done above CP (i.e.  $W'$ ) is not different during severe-intensity exercise, and is associated with the attainment of  $\dot{V}O_2$  peak at task failure, irrespective of the manner in which the exercise is performed (all-out, self-paced, constant-power, or incremental; Chidnok et al., 2013a). The existence of a so-called 'end spurt' during some forms of severe-intensity exercise, therefore, is not incompatible with task failure during such exercise being bound to the PD relationship (cf. Noakes, 2011). While the selection of a pacing strategy of this type, based on prior experience, is not contrary to the notion of 'teleoanticipation' (Ulmer, 1996), it does indicate that the pacing strategy template is based upon intimate 'knowledge' of the  $W'$  remaining which may be linked to the metabolic perturbation and associated afferent traffic related to  $W'$  utilisation. Ultimately, however, task failure in this domain is associated with the complete utilisation of  $W'$  and the attainment of a consistent 'intolerable' muscle metabolic

milieu (Chidnok et al., 2013a; Chidnok et al., 2013b; Chidnok et al., 2013c; Vanhatalo et al., 2010); the pacing strategy selected may alter the pattern of  $W'$  utilisation (Chidnok et al., 2013a) but it does not alter the underpinning determinants of task failure.

Similarly, during intermittent exercise in which severe-intensity exercise bouts might be interspersed with recovery intervals performed below CP, the time to task failure can be accurately predicted using equations which account for the extent and rate of  $W'$  utilisation during the periods of time spent above and below CP (i.e., the  $W'$  balance; Chidnok et al., 2012a; Skiba et al., 2012) and is again associated with the consistent attainment of critical indices of metabolic and cardiorespiratory strain (Chidnok et al., 2012a; Chidnok et al., 2013b). During longer endurance events, such as the marathon or some cycle stage races, pacing is rarely constant and it is likely that athletes select their speed or power based on intuitive knowledge of their proximity to CP (or critical speed) along with information on the distance or time remaining. A surge in pace by an opponent or the encountering of an uphill section might result in an athlete exceeding their CP, experiencing the pace to have become unsustainable (presumably linked to altered neural or humoral stimuli) and then adjusting their pace downward in compensation. Decisions made by athletes on pacing during competition have been reported to be well matched to the calculated  $W'$  remaining (Skiba, Clarke, Vanhatalo & Jones, 2014).

The above discussion of the fatigue processes attending severe-intensity exercise indicates that multiple mechanisms compromise neuromuscular output, and that they likely do so in a collective fashion. These processes can be summarised thus: severe-intensity power demands

result in the inexorable loss of muscle metabolic homeostasis, which directly compromises muscle power output, necessitating additional motor unit recruitment and increasing the O<sub>2</sub> cost of exercise (the  $\dot{V}O_2$  slow component). Indirectly, the accumulation of metabolites results in inhibitory feedback and increases respiratory drive. The former makes it harder to translate descending drive into excitatory synaptic input (to which the motoneurons are becoming intrinsically less responsive [Johnson et al., 2004; McNeil et al., 2011]), and the latter fatigues the respiratory muscles, which might compromise limb blood flow during whole-body exercise of sufficient duration (Romer & Polkey, 2008). The attainment of  $\dot{V}O_2$  max means that further motor unit recruitment, which at that point would be drawn from increasingly fatigue-sensitive fibres, can only be supported by substrate-level phosphorylation, amplifying all of the above processes. Unfortunately, it is not possible to measure all of these processes simultaneously in exercising humans. Nevertheless, we contend that task failure in the severe-intensity domain is likely the result of a mismatch between the power demand of the task and its instantaneous supply by the neuromuscular system. This mismatch involves multiple interacting mechanisms, mechanisms which will differ from those at lower intensities: as the intensity decreases, the relative importance of central (and perhaps psychological) factors seems to increase.

## **Conclusions**

In this review we have highlighted how mechanisms of neuromuscular fatigue are intensity-domain specific and how these mechanisms combine to influence exercise performance, either through reducing the drive to exercise during extremely prolonged exercise (in the moderate intensity domain), by drawing heavily on muscular fuel reserves (during heavy intensity

exercise), or by the accumulation of fatigue-inducing metabolites (severe-intensity exercise). These processes each have knock-on effects that may conspire to limit the synaptic input to the motoneurone pool and/or disrupt the processes of excitation-contraction coupling in the muscle. Task failure will occur if a participant decides to terminate exercise, or if the compensatory adjustments made by the CNS fail to match the power demands of the task even though the participant wishes to continue it. Individuals will have a certain pain tolerance/motivation to exercise and whether there is any 'reserve' may depend on this, along with factors like health, age, and familiarity with hard exercise. Our view and experience is that, at least in young healthy motivated people, no amount of additional (internal or external) motivation or coercion can increase exercise tolerance at task failure during severe exercise – this particular task failure is purely 'physical' and can be understood through bioenergetic, muscle metabolite/substrate, and neuromuscular considerations. These physiological phenomena, in turn, define the hyperbolic power-duration relationship. Consequently, no sensible integrative model of fatigue can ignore the PD relationship or its physiological basis.

## Figure legends

### Figure 1

**The oxygen uptake response to ramp exercise (Panel A), the power-duration relationship (Panel B), and the  $\dot{V}O_2$  response to constant load exercise in the moderate, heavy and severe intensity domains (Panel C).** The x-axis in Panel A provides the entire range of attainable power output in a typical fit young (but not specifically trained) participant. The exercise intensity domains, and their physiological boundary points are annotated, as is the  $\dot{V}O_2$  max value of the participant. Note the large range of power outputs that are non-steady state and thus unsustainable (all power outputs above CP). In Panel B, the PD relationship of the same participant is plotted from 4 constant power trials performed to task failure. The intensity domains are also annotated for comparison. In Panel C, the  $\dot{V}O_2$  responses to moderate, heavy, and severe intensity exercise are plotted, with steady states being attained for moderate and heavy exercise (the latter delayed by the  $\dot{V}O_2$  slow component), whereas no steady state is evident in the severe intensity domain. Instead, the continued increase in  $\dot{V}O_2$  is constrained by the attainment of  $\dot{V}O_2$  max.

### Figure 2

**Muscle activity, peripheral fatigue, muscle phosphorylcreatine (PCr) and pulmonary  $\dot{V}O_2$  responses to severe intensity exercise.** The lowest exercise intensity (power output or muscle torque) is represented by black circles, followed by white circles, black triangles, white triangles and black squares as the intensity is increased. The muscle activity and peripheral fatigue



responses to intermittent isometric knee extension exercise are redrawn from Burnley et al. (2012), the PCr responses to dynamic knee extension exercise are drawn from the data of Vanhatalo et al. (2010), and the  $\dot{V}O_2$  responses are data collected during cycle ergometry. Each plot represents the performance of four different severe-intensity trials to task failure at a constant torque or power demand. Note that at task failure peripheral fatigue reaches consistent values, PCr declines to effectively zero, and pulmonary  $\dot{V}O_2$  reaches  $\dot{V}O_2$  max. Only muscle activity (surface EMG recordings of the vastus lateralis) shows different values at task failure, suggesting that despite differing degrees of neuromuscular activation the respiratory, metabolic and fatigue processes collectively reach limiting values at task failure.

### **Figure 3**

**Knee extensor torque (Panel A) and vastus lateralis EMG (Panel B) during severe-intensity intermittent contractions (3 s contraction, 2 s rest) performed to task failure (Burnley et al., 2012).** In Panel A, task failure was defined as the failure to achieve a knee extensor torque within 5 N.m of the target for 3 consecutive contractions, with the first of these being the point of task failure. Each minute, an MVC is performed, and the MVC achieved declines as the contractions progress (i.e., fatigue systematically developed). Note that the participant continues muscular contractions for ~25 s after task failure. During this period, EMG amplitude (Panel B) remains as high as, or higher than, those values before task failure occurred, indicating that task failure was not caused by a sudden withdrawal of voluntary effort (that is, task disengagement did not occur).

#### **Figure 4**

**Examples of utilisation of  $W'$  during constant-power-output and self-paced severe-intensity exercise (~ 3 min duration).** Note that the total work done above CP is not different irrespective of pacing strategy.

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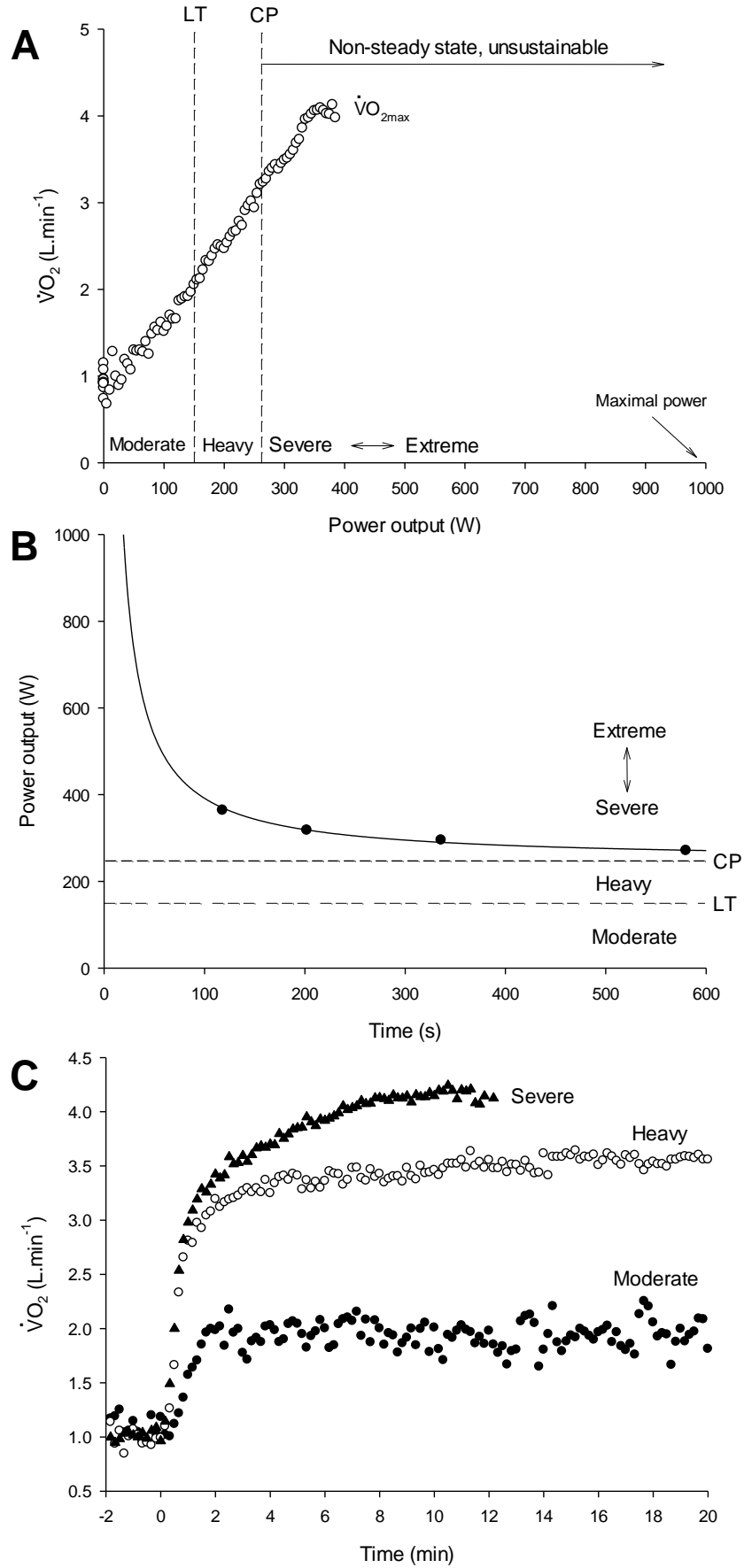
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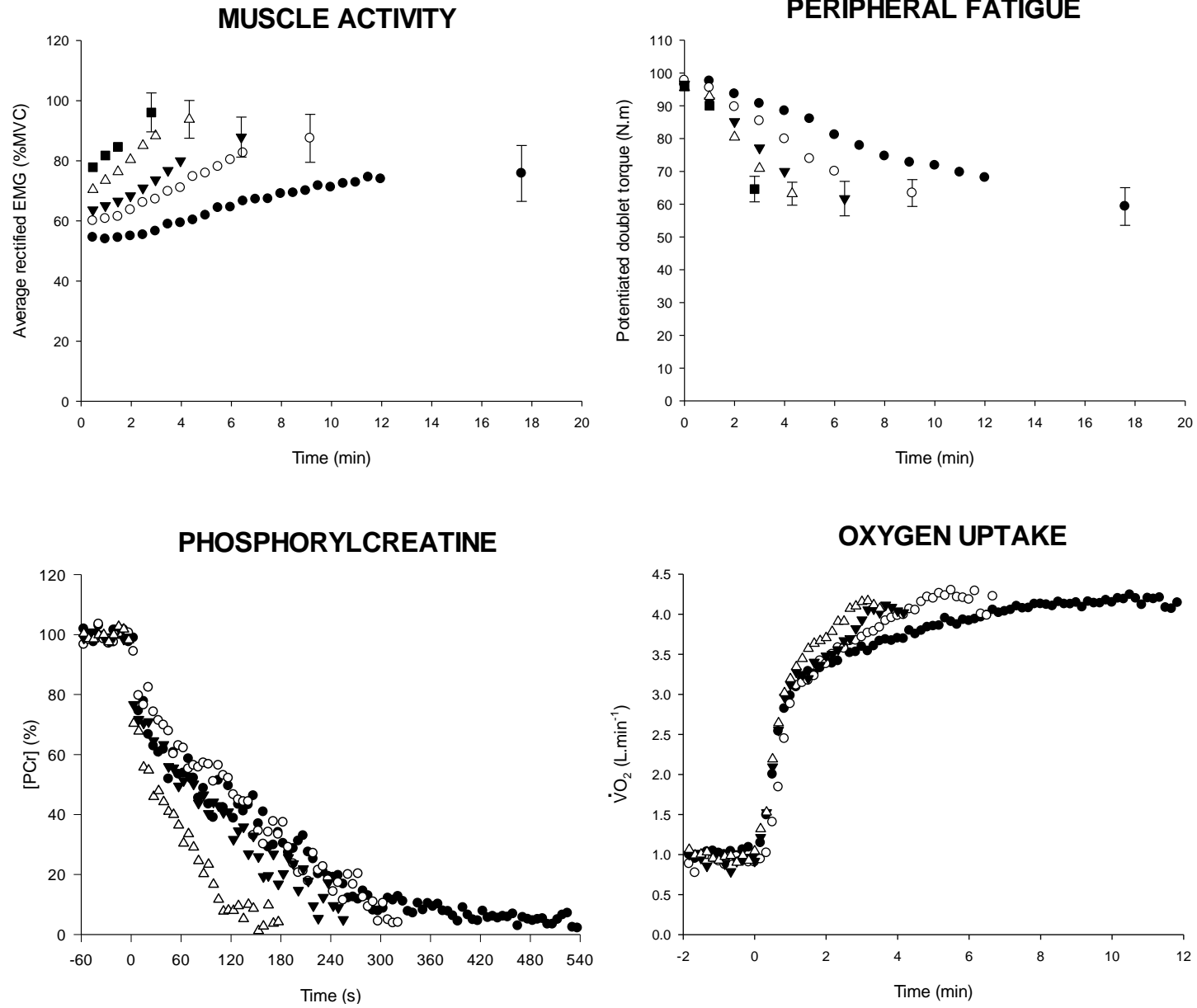
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**Figure 1**



**Figure 2**



**Figure 3**

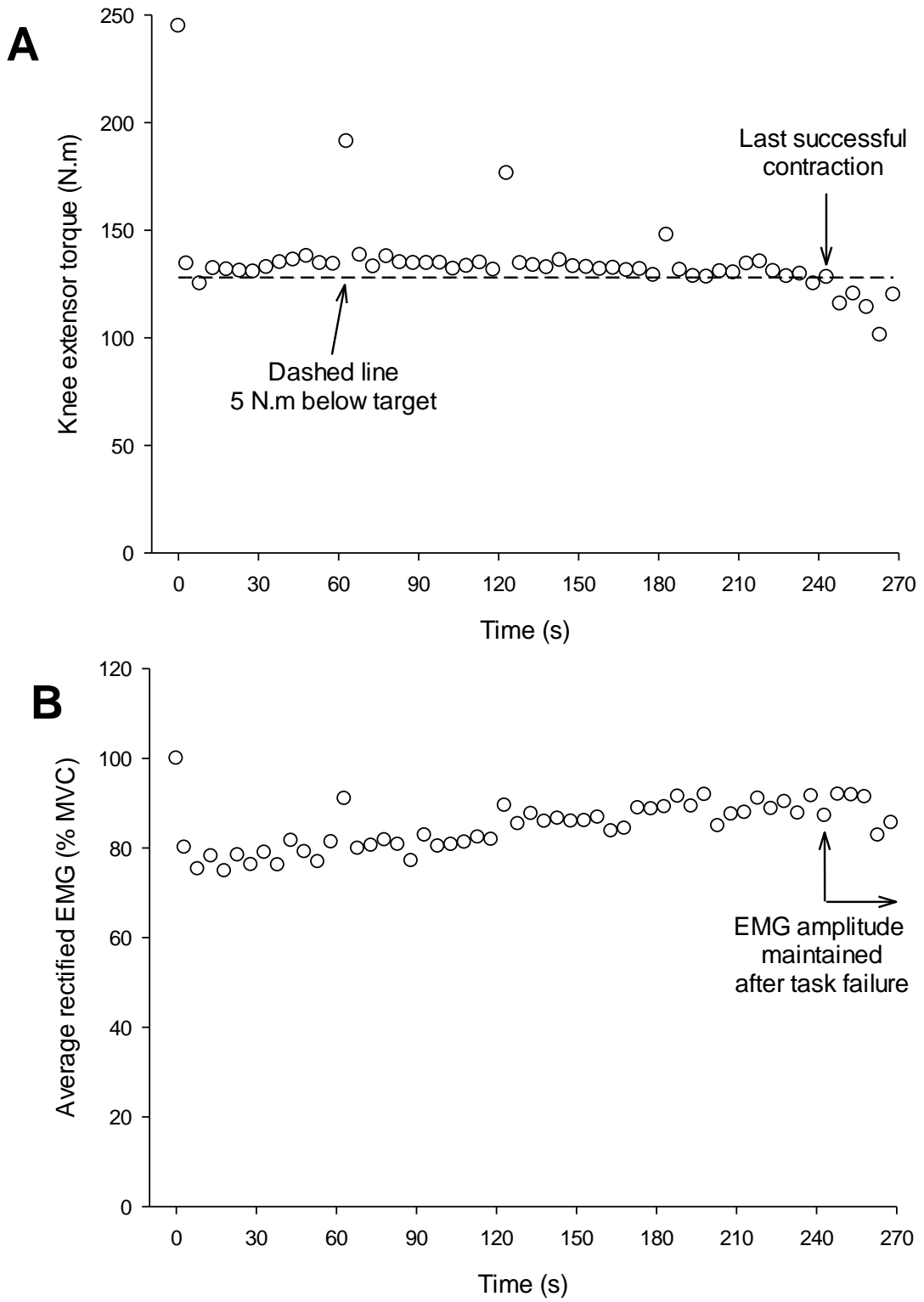


Figure 4

