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ORIGINAL ARTICLE

Power–duration relationship: Physiology, fatigue, and the limits of human performance

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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 is 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 twentieth 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, & Burnley, 2007), and self-paced exercise (Chidnok, DiMenna, Bailey et al., 2013). 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, that is, the point at which a participant is unwilling or unable to continue a physical task, has been referred to as the point of 'exhaustion',

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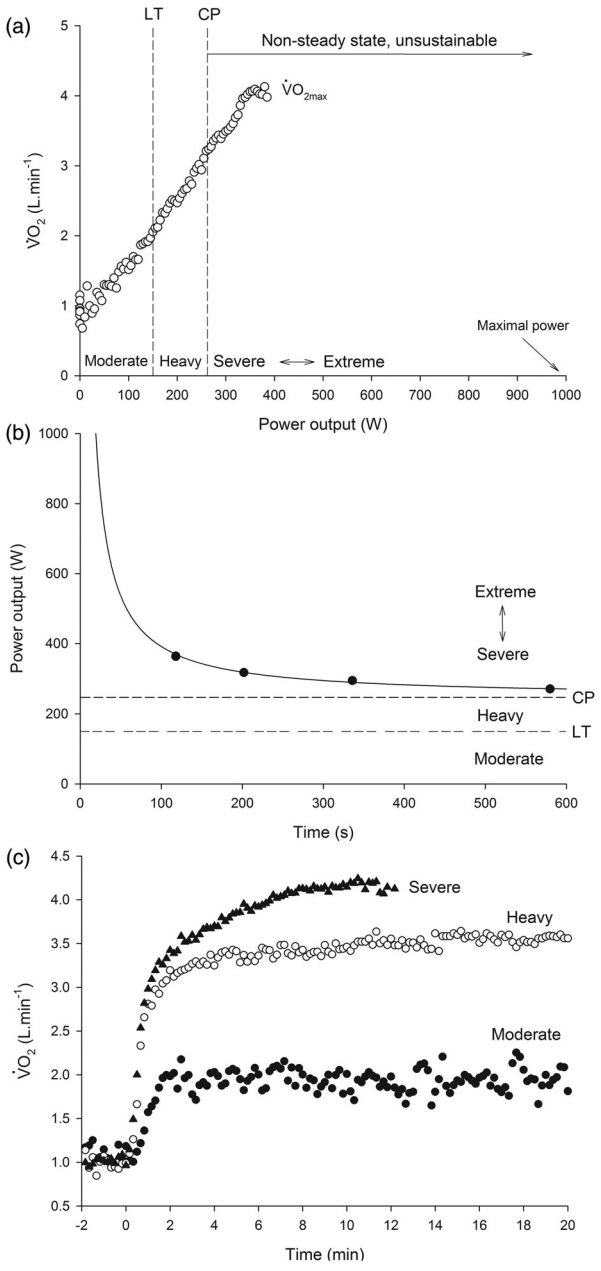

Figure 1. The oxygen uptake response to ramp exercise (a), the PD relationship (b), and the $\dot{V}O_2$ response to constant load exercise in the moderate, heavy, and severe-intensity domains (c). The *x*-axis in (a) provides the entire range of attainable power output in a typical fit young (but not 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 (b), the PD relationship of the same participant is plotted from four constant-power trials performed to task failure. The intensity domains are also annotated for comparison. In (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.

'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; Gardener, Martin, Matin, Barras, & Jenkins, 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 (Conley, Kemper, & Crowther, 2001; Vanhatalo et al., 2007), equivalent to ~70% of the power output associated with maximal oxygen uptake ($\dot{V}O_{2max}$). 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 & 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 (Garcia-Manso, Martín-González, Vaamonde, & Da Silva-Gigoletto, 2012; Kennelly, 1906), exponential decay functions (Weyand, Lin, & Bundle, 2006; Wilkie, 1960), and hyperbolic models (Monod & 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, Burnley, Vanhatalo, Rossiter, & Jones, 2016). Power law functions predict no asymptotic behaviour

indicative of distinct exercise intensity domains, even though the existence of such is well accepted (Gaesser & Poole, 1996; Whipp, 1994; see below). Exponential functions usually characterise continuous temporal processes in which the value of a datum is dependent on the value of its predecessor. PD 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 1 (b)):

$$T_{\text{lim}} = W'/(P - \text{CP}), \quad (1)$$

where T_{lim} is the 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). 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 min 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 min 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 that 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 CP

Although 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 h, 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, & Sparks, 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 and Thompson (1986) studied 10 ultramarathon runners who were tasked with running on a treadmill at the highest pace they could sustain for 4 h. This was estimated to be 65–70% $\dot{V}O_{2max}$, or the upper limit of the moderate domain in these trained runners. These participants exercised with blood [lactate] and respiratory exchange ratio (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 ~390 mL min^{-1} in the last 3 h of running. This increased O_2 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 ~2 mL 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, 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 and Thompson (1986), the change in RER was relatively small (from ~0.84 to ~0.79), suggesting that only ~50 mL 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 a review, see Gandevia, 2001). At the conclusion of 4 h of treadmill running, Davies and 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 (Lepers 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 h (Coyle, Coggan, Hemmert, & Ivy, 1986). These heavy-intensity power outputs typically range from 60% to 85% $\dot{V}O_{2max}$. 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 results in excitation–contraction coupling failure at the fibre level (for a 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; Coyle et al., 1986; Gollnick et al., 1974). In addition, fatigue-related metabolites (such as ADP, P_i, and H^+) 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 a single fibre (phosphorylcreatine (PCr)) during exhaustive (Sahlin, Söderlund, Tonkonogi & Hirakoba, 1997) 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 has come to light (for a review, see Ørtenblad, Westerblad & Nielsen, 2013). 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 & 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, & Heilmeyer, 1992). The intra-myofibrillar 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 & 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 (Gandevia, 2001; Meeusen, Watson, Hasegawa, Roelands, & Piacentini, 2006; Nybo & Secher, 2004). 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 h; 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, & Thatcher, 2011). As a result of repeated activity, a reduction in motoneurone 'gain' could occur (i.e. the level of excitation required to maintain motoneurone discharge rate increases; Johnson, Edwards, Van Tongeren, & Bawa, 2004; McNeil, Giesebrecht, Gandevia, & Taylor, 2011), 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 a non-steady state:$\dot{V}O_2$, muscle metabolic, and blood acid–base responses all fail to stabilise above the CP (Jones et al., 2008; Poole et al., 1988). 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 $\dot{V}O_{2max}$ close to the point of task failure (Burnley & Jones, 2007; Murgatroyd, Ferguson, Ward, Whipp & Rossiter, 2011; Poole et al., 1988; Whipp, 1994), even though the power output producing this behaviour can be considerably below that associated with the attainment of $\dot{V}O_{2max}$ 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 $\dot{V}O_{2max}$, *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_i] accelerate as contractile intensity is increased above the CP, but – crucially – all reach consistent values at task failure (Vanhatalo, Fulford, DiMenna, & Jones, 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 (Burnley et al., 2012; Jones et al., 2008; Vanhatalo et al., 2016). The reduction in muscle pH and the increase in [P_i] have each been repeatedly implicated in reduced muscle fibre force, shortening velocity, Ca^{2+} handling (P_i), and thus muscle power (for a review, see Allen et al., 2008). Recently, it has been suggested that P_i and H^+ accumulation may act synergistically to reduce muscle force (Nelson & Fitt, 2014). This is precisely the metabolic profile observed during severe-intensity exercise, with PCr and pH reaching their nadir and P_i 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, Sharpe, Williams, &

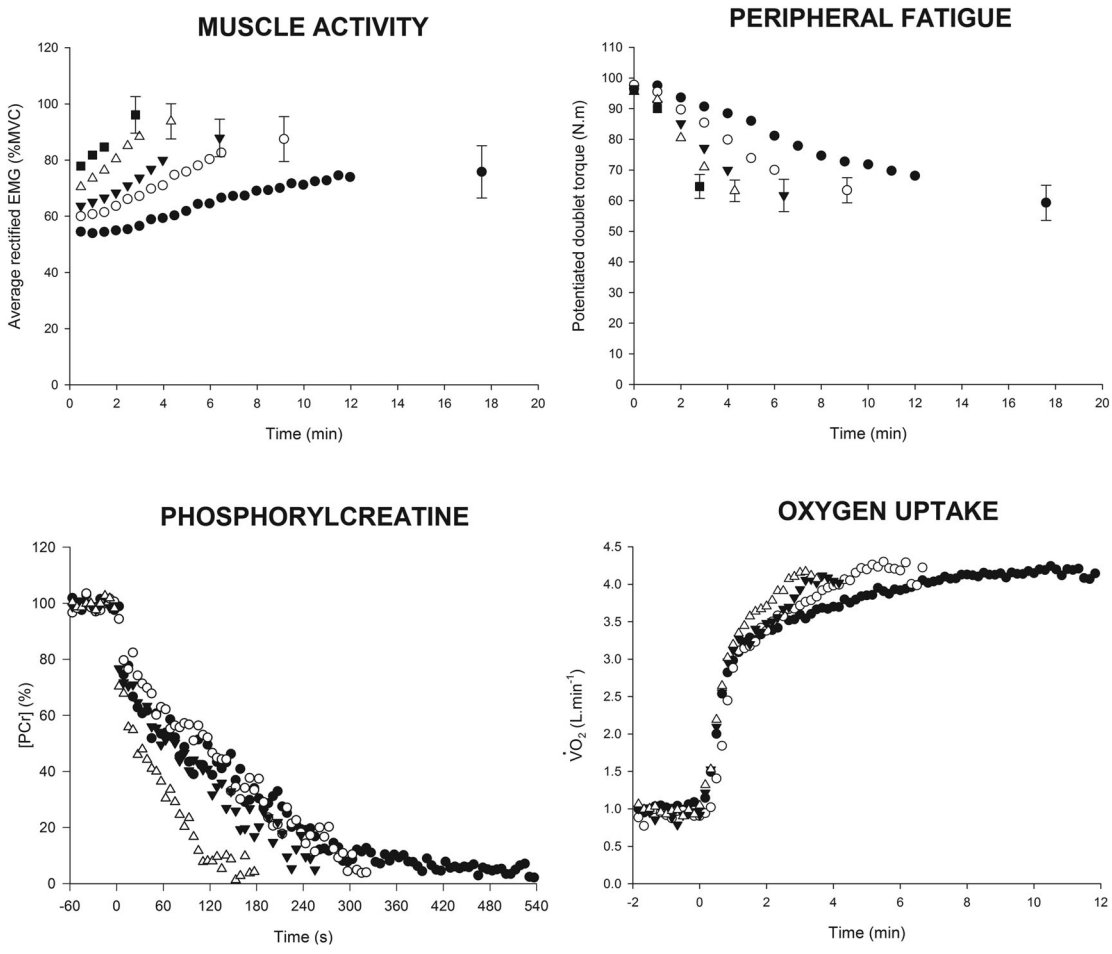

Figure 2. Muscle activity, peripheral fatigue, muscle phosphorylcreatine (PCr), and pulmonary $\dot{V}O_2$ responses to severe-intensity exercise. The lowest exercise intensity (power output or muscle torque) is represented by black circles, followed by white circles, black triangles, white triangles, 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.

Hannah, 2015; Thomas, Elmeua, Howatson, & Goodall, 2016). Notwithstanding the difficulty in measuring metabolite-induced peripheral fatigue in whole-body exercise (which introduces 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 $\dot{V}O_{2max}$ makes task failure inevitable because, by definition, oxidative phosphorylation cannot contribute to further increases in energy demand. Once $\dot{V}O_{2max}$ 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 $\dot{V}O_{2max}$ 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^+, and K^+) 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, & Venturelli, 2015). Recently, a role for these afferents in limiting central motor drive has been proposed, as reviewed in this issue and elsewhere (Amann, 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 central nervous system (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 $\dot{V}O_{2max}$ 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_2 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 & 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 & St Clair Gibson, 2004); or (3) an effort-based decision to disengage from the task (Marcora & 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 a 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 & 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, Romer, Subudhi, Pegelow, & Dempsey, 2007; Bundle, Ernst, Bellizzi, Wright, & Weyand, 2006), task failure can occur *before* participants voluntarily terminate exercise. This is illustrated in Figure 3, wherein torque declines during isometric contractions, but the electromyogram (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 integrated EMG occurred at task failure during cycle ergometry (Bundle et al., 2006; Chidnok, DiMenna, Bailey et al., 2013) or dynamic knee-extension exercise (Sundberg & Bundle, 2015), which is not consistent with a sudden withdrawal of effort and thus motor drive. That 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 (Chidnok, Fulford, Bailey et al., 2013; Coats et al., 2003). 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 min (Chidnok, Fulford, Bailey et al., 2013; Coats et al., 2003). 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, Fulford, Bailey et al., 2013). 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.

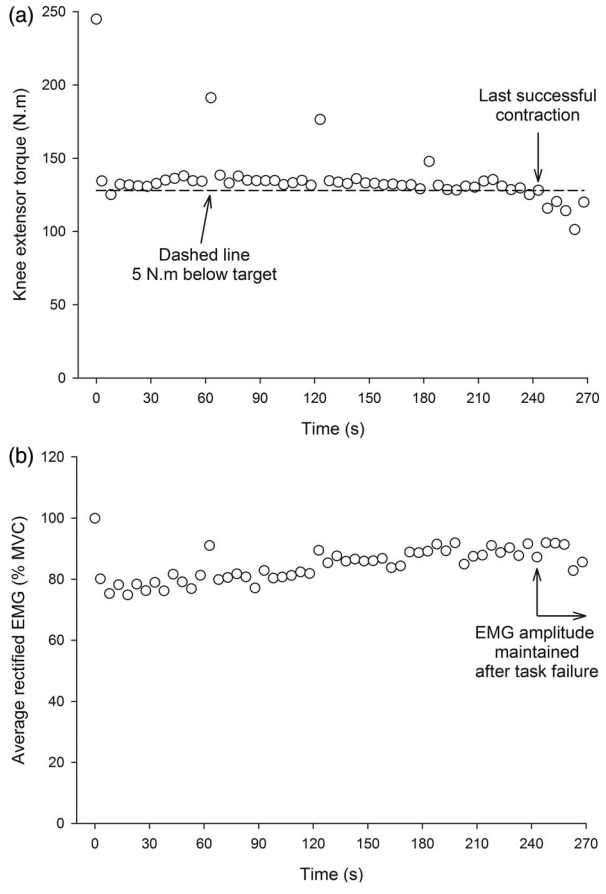

Figure 3. Knee extensor torque (a) and vastus lateralis EMG (b) during severe-intensity intermittent contractions (3 s contraction, 2 s rest) performed to task failure (Burnley et al., 2012).In (a), task failure was defined as the failure to achieve a knee extensor torque within 5 N m of the target for three 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 (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 (i.e. task disengagement did not occur).

The recent observation of a substantial reserve in muscle power (Marcora & 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 are 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, DiMenna, Bailey et al., 2013; Figures 2 and 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 only 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, DiMenna, Bailey et al., 2013; 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 Equation (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, DiMenna, Bailey et al., 2013). 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). Whilst 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, DiMenna, Bailey et al., 2013; Chidnok, DiMenna, Fulford et al., 2013; Chidnok, Fulford, Bailey et al., 2013; Vanhatalo et al., 2010); the pacing strategy selected may alter the *pattern* of W' utilisation (Chidnok, DiMenna, Bailey et al., 2013), but it does not alter the underpinning determinants of task failure (Figure 4).

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., 2012; Skiba et al., 2012) and is again associated with the consistent attainment of critical indices of metabolic and cardiorespiratory strain (Chidnok et al., 2012; Chidnok, DiMenna, Fulford et al., 2013). 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 athletes exceeding their CP, experiencing the pace to have become unsustainable (presumably linked to altered neural or humoral stimuli) and them 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 on 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_2 cost of exercise (the $\dot{V}O_2$ slow

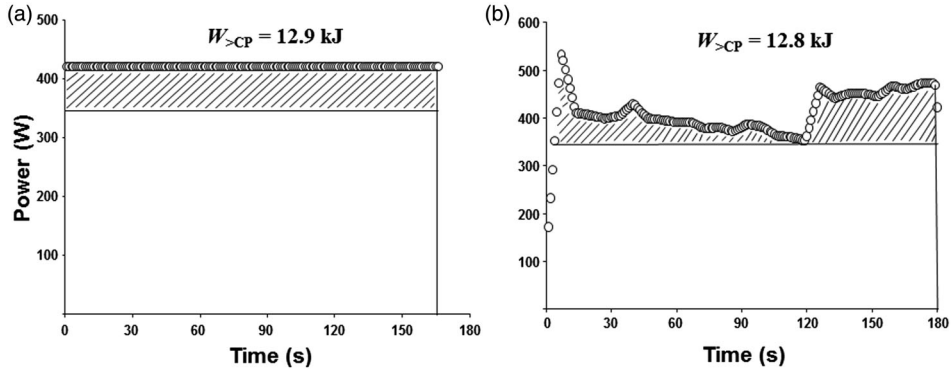

Figure 4. Examples of utilisation of W' during constant-power output and self-paced severe-intensity exercise (~3-min duration). Note that the total work done above CP is not different, irrespective of the pacing strategy.

component). Indirectly, the accumulation of metabolites results in inhibitory feedback and increases respiratory drive. The former makes it harder to translate the descending drive into excitatory synaptic input (to which the motoneurones 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 such as health, age, and familiarity with hard exercise. In our view and experience, 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 PD relationship. Consequently, no sensible integrative model of fatigue can ignore the PD relationship or its physiological basis.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References

Allen, D. G., Lamb, G. D., & Westerblad, H. (2008). Skeletal muscle fatigue: Cellular mechanisms. *Physiological Reviews*, *88*, 287–332. doi:10.1252/physrev.00015.2007

Amann, M. (2011). Central and peripheral fatigue: Interaction during cycling exercise in humans. *Medicine and science in Sports and Exercise*, *43*, 2039–2045. doi:10.1249/MSS.0b013e31821f59ab

Amann, M., Romer, L. M., Subudhi, A. W., Pegelow, D. F., & Dempsey, J. A. (2007). Severity of arterial hypoxaemia affects the relative contributions of peripheral muscle fatigue to exercise performance in healthy humans. *Journal of Physiology*, *581*, 389–403. doi:10.1113/jphysiol.2007.129700

Amann, M., Sidhu, S. K., Weavil, J. C., Mangumb, T. S., & Venturelli, M. (2015). Autonomic responses to exercise: Group III/IV muscle afferents and fatigue. *Autonomic Neuroscience*, *188*, 19–23. doi:10.1016/j.autneu.2014.10.018

Bergström, J., Hermansen, L., Hultman, E., & Saltin, B. (1967). Diet, muscle glycogen and physical performance. *Acta Physiologica Scandinavica*, *71*, 140–150.

Black, M. I., Jones, A. M., Bailey, S. J., & Vanhatalo, A. (2015). Self-pacing increases critical power and improves performance during severe-intensity exercise. *Applied Physiology Nutrition and Metabolism*, *40*, 662–670.

Bundle, M. W., Ernst, C. L., Bellizzi, M. J., Wright, S., & Weyand, P. G. (2006). A metabolic basis for impaired muscle force production and neuromuscular compensation during sprint cycling. *American Journal of Physiology Regulatory Integrative and Comparative Physiology*, *291*, R1457–R1464. doi:10.1152/ajpregu.00108.2006

Bundle, M. W., & Weyand, P. G. (2012). Sprint exercise performance: Does metabolic power matter? *Exercise and Sport Sciences Reviews*, *40*, 174–182.

Burnley, M., Davison, G., & Baker, J. R. (2011). Effects of priming exercise on $\dot{V}O_2$ kinetics and the power-duration relationship. *Medicine and Science in Sports and Exercise*, *43*, 2171–2179. doi:10.1249/MSS.0b013e31821ff26d

Burnley, M., & Jones, A. M. (2007). Oxygen uptake kinetics as a determinant of sports performance. *European Journal of Sport Science*, *7*, 63–79. doi:10.1080/17461390701456148

Burnley, M., Vanhatalo, A., & Jones, A. M. (2012). Distinct profiles of neuromuscular fatigue during muscle contractions below and above the critical torque in humans. *Journal of Applied Physiology*, *113*, 215–223. doi:10.1152/japplphysiol.00022.2012

Chidnok, W., DiMenna, F. J., Bailey, S. J., Vanhatalo, A., Morton, R. H., Wilkerson, D. P., & Jones, A. M. (2012). Exercise tolerance in intermittent cycling: Application of the critical power concept. *Medicine and Science in Sports and Exercise*, *44*, 966–976.

Chidnok, W., DiMenna, F. J., Bailey, S. J., Wilkerson, D. P., Vanhatalo, A., & Jones, A. M. (2013). Effects of pacing strategy on work done above critical power during high-intensity exercise. *Medicine and Science in Sports and Exercise*, *45*, 1377–1385. doi:10.1249/MSS.0b013e3182860325

Chidnok, W., DiMenna, F. J., Fulford, J., Bailey, S. J., Skiba, P. F., Vanhatalo, A., & Jones, A. M. (2013). Muscle metabolic responses during high-intensity intermittent exercise measured by 31P-MRS: Relationship to the critical power concept. *American Journal of Physiology Regulatory Integrative Comparative Physiology*, *305*, R1085–R1092.

Chidnok, W., Fulford, J., Bailey, S. J., DiMenna, F. J., Skiba, P. F., Vanhatalo, A., & Jones, A. M. (2013). Muscle metabolic determinants of exercise tolerance following exhaustion: Relationship to the 'critical power'. *Journal of Applied Physiology*, *115*, 243–250. doi:10.1152/japplphysiol.00334.2013

Chin, E. R., & Allen, D. G. (1997). Effects of reduced muscle glycogen concentration on force, Ca2+ release and contractile protein function in intact mouse skeletal muscle. *Journal of Physiology*, *498*, 17–29.

Coats, E. M., Rossiter, H. B., Day, J. R., Miura, A., Fukuba, Y., & Whipp, B. J. (2003). Intensity-dependent tolerance to exercise after attaining $\dot{V}O_2$ max in humans. *Journal of Applied Physiology*, *95*, 483–490. doi:10.1152/japplphysiol.01142.2002

Conley, K. E., Kemper, W. F., & Crowther, G. J. (2001). Limits to sustainable muscle performance: Interaction between glycolysis and oxidative phosphorylation. *Journal of Experimental Biology*, *204*, 3189–3194.

Costill, D. L., Bowers, R., Branam, G., & Sparks, K. (1971). Muscle glycogen utilization during prolonged exercise on successive days. *Journal of Applied Physiology*, *31*, 834–838.

Coyle, E. F., Coggan, A. R., Hemmert, M. K., & Ivy, J. L. (1986). Muscle glycogen utilization during prolonged strenuous exercise when fed carbohydrate. *Journal of Applied Physiology*, *61*, 165–172.

Cross, T. J., Sabapathy, S., Schneider, D. A., & Haseler, L. J. (2010). Breathing He-O2 attenuates the slow component of O2 uptake kinetics during exercise performed above the respiratory compensation threshold. *Experimental Physiology*, *95*, 172–183. doi:10.1113/expphysiol.2009.048975

Davies, C. T. M., & Thompson, M. W. (1986). Physiological responses to prolonged exercise in ultramarathon athletes. *Journal of Applied Physiology*, *61*, 611–617.

Dideriksen, J. L., Enoka, R. M., & Farina, D. (2011). Neuromuscular adjustments that constrain submaximal EMG amplitude at task failure of sustained isometric contractions. *Journal of Applied Physiology*, *111*, 485–494. doi:10.1152/japplphysiol.00186.2011

Ekblom, B. (2009). Counterpoint: Maximal oxygen uptake is not limited by a central nervous system governor. *Journal of Applied Physiology*, *106*, 339–341. doi:10.1152/japplphysiol.90844.2008a

Ferguson, C., Wylde, L. A., Benson, A. P., Cannon, D. T., & Rossiter, H. B. (2016). No reserve in isokinetic cycling power at intolerance during ramp incremental exercise in endurance-trained men. *Journal of Physiology*, *120*, 70–77. doi:10.1152/japplphysiol.00662.2015

Froyd, C., Beltrami, F. G., Millet, G. Y., & Noakes, T. D. (2016). Central regulation and neuromuscular fatigue during exercise of different durations. *Medicine and Science in Sports and Exercise*, *48*, 1024–1032. doi:10.1249/MSS0000000000000867

Gaesser, G. A., & Poole, D. C. (1996). The slow component of oxygen uptake kinetics in humans. *Exercise and Sport Sciences Reviews*, *24*, 35–71.

Gandevia, S. C. (2001). Spinal and supraspinal factors in human muscle fatigue. *Physiological Reviews*, *81*, 1725–1789.

Garcia-Manso, J. M., Martín-González, J. M., Vaamonde, D., & Da Silva-Gigoletto, M. E. (2012). The limitations of scaling laws in the prediction of performance in endurance events. *Journal of Theoretical Biology*, *300*, 324–329. doi:10.1016/j.jtbi.2012.01.028

Gardener, A. S., Martin, J. C., Matin, D. T., Barras, M., & Jenkins, D. G. (2007). Maximal torque- and power-pedaling rate relationships for elite sprint cyclists in laboratory and field tests. *European Journal of Applied Physiology*, *101*, 287–292. doi:10.1007/s00421-007-0498-4

Gollnick, P. D., Piehl, K., & Saltin, B. (1974). Selective glycogen depletion pattern in human muscle fibres after exercise of varying intensity and varying pedalling rates. *Journal of Physiology*, *241*, 45–57.

Han, J. W., Thieleczek, R., Varsányi, M., & Heilmeyer, L. M. G. (1992). Compartmentalized ATP synthesis in skeletal-muscle triads. *Biochemistry*, *31*, 377–384.

Haouzi, P., Chenuel, B., & Huszczuk, A. (2004). Sensing vascular distension in skeletal muscle by slow conducting afferent fibers: Neurophysiological basis and implication for respiratory control. *Journal of Applied Physiology*, *96*, 407–418. doi:10.1152/japplphysiol.00597.2003

Hill, D. W., Poole, D. C., & Smith, J. C. (2002). The relationship between power and the time to achieve $\dot{V}O_2$ max. *Medicine and Science in Sports and Exercise*, *34*, 709–714.

Hogan, M. C., Richardson, R. S., & Haseler, L. J. (1999). Human muscle performance and PCr hydrolysis with varied inspired oxygen fractions: A 31P-MRS study. *Journal of Applied Physiology*, *86*, 1367–1373.

Johnson, B. D., Babcock, M. A., Suman, O. E., & Dempsey, J. A. (1993). Exercise-induced diaphragmatic fatigue in healthy humans. *Journal of Physiology*, *460*, 385–405.

Johnson, K. V. B., Edwards, S. C., Van Tongeren, C., & Bawa, P. (2004). Properties of human motor units after prolonged activity at a constant firing rate. *Experimental Brain Research*, *154*, 479–487. doi:0.1007/s00221-003-1678-z

Johnson, M. A., Sharpe, G. R., Williams, N. C., & Hannah, R. (2015). Locomotor muscle fatigue is not critically regulated after prior upper body exercise. *Journal of Applied Physiology*, *119*, 840–850. doi:10.1152/japplphysiol.00072.2015

Jones, A. M., Vanhatalo, A., Burnley, M., Morton, R. H., & Poole, D. C. (2010). Critical power: Implications for the determination of $\dot{V}O_2$ max and exercise tolerance. *Medicine and Science in Sports and Exercise*, *42*, 1876–1890. doi:10.1249/MSS.0b013e3181d9cf7f

Jones, A. M., Wilkerson, D. P., DiMenna, F., Fulford, J., & Poole, D. C. (2008). Muscle metabolic responses to exercise above and below the 'critical power' assessed using 31P-MRS. *American Journal of Physiology Regulatory Integrative and Comparative Physiology*, *294*, R585–R593. doi:10.1152/ajpregu.00731.2007

Kennelly, A. E. (1906). An approximate law of fatigue in the speeds of racing animals. *Proceedings of the American Academy of Arts and Sciences*, *42*, 275–331.

Krustrup, P., Söderlund, K., Mohr, M., & Bangsbo, J. (2004). The slow component of oxygen uptake during intense, sub-maximal exercise in man is associated with additional fibre recruitment. *Pflugers Archive – European Journal of Physiology*, *447*, 855–866. doi:10.1007/s00424-003-1203-z

Lepers, R., Maffiuletti, N. A., Rochette, L., Brugniaux, J., & Millet, G. Y. (2002). Neuromuscular fatigue during a long-duration cycling exercise. *Journal of Applied Physiology*, *92*, 1487–1493. doi:10.1152/japplphysiol.00880.2001

Marcora, S. M., Bosio, A., & de Morree, H. M. (2008). Locomotor muscle fatigue increases cardiorespiratory responses and reduces performance during intense cycling exercise independently from metabolic stress. *American Journal of Physiology Regulatory Integrative and Comparative Physiology*, *294*, R874–R883. doi:10.1152/ajpregu.00678.2007

Marcora, S. M., & Staiano, W. (2010). The limit to exercise tolerance in humans: Mind over muscle?*European Journal of Applied Physiology*, *109*, 763–770. doi:10.1007/s00421-010-1418-6

Marcora, S. M., Staiano, W., & Manning, V. (2009). Mental fatigue impairs physical performance in humans. *Journal of Applied Physiology*, *106*, 857–864. doi:10.1152/japplphysiol.91324.2008

Martin, V., Kerhervé, H., Messonnier, L. A., Banfi, J.-C., Geyssant, A., Bonnefoy, R., … Millet, G. Y. (2010). Central and peripheral contributions to neuromuscular fatigue induced by a 24-h treadmill run. *Journal of Applied Physiology*, *108*, 1224–1233. doi:10.1152/japplphysiol.01202.2009

McNeil, C. J., Giesebrecht, S., Gandevia, S. C., & Taylor, J. L. (2011). Behaviour of the motoneurone pool in a fatiguing submaximal contraction. *Journal of Physiology*, *589*, 3533–3544. doi:10.1113/jphysiol.2011.207191

Meeusen, R., Watson, P., Hasegawa, H., Roelands, B., & Piacentini, M. F. (2006). Central fatigue: The serotonin hypothesis and beyond. *Sports Medicine*, *36*, 881–909.

Monod, H., & Scherrer, J. (1965). The work capacity of a synergic muscle group. *Ergonomics*, *8*, 329–338.

Morales-Alamo, D., Losa-Reyna, J., Torres-Peralta, R., Martin-Rincon, M., Perez-Valera, M., Curtelin, D., … Calbet, J. A. (2015). What limits performance during whole-body incremental exercise to exhaustion in humans? *Journal of Physiology*, *593*, 4631–4648. doi:10.1113/JP270487

Moritani, T., Nagata, A., deVries, H. A., & Muro, M. (1981). Critical power as a measure of physical work capacity and anaerobic threshold. *Ergonomics*, *24*, 339–350.

Morton, R. H. (2006). The critical power and related whole-body bioenergetic models. *European Journal of Applied Physiology*, *96*, 339–354. doi:10.1007/s00421-005-0088-2

Murgatroyd, S. R., Ferguson, C., Ward, S. A., Whipp, B. J., & Rossiter, H. B. (2011). Pulmonary O_2 uptake kinetics as a determinant of high-intensity exercise tolerance in humans. *Journal of Applied Physiology*, *110*, 1598–1606. doi:10.1152/japplphysiol.01092.2010

Nelson, C. R., & Fitt, R. H. (2014). Effects of low cell pH and elevated inorganic phosphate on the pCa-force relationship in single muscle fibers at near-physiological temperatures. *American Journal of Physiology Cell Physiology*, *306*, C670–678. doi:10.1152/ajpcell.00347.2013

Nielsen, J., Holmberg, H. C., Schrøder, H. D., Saltin, B., & Ørtenblad, N. (2011). Human skeletal muscle glycogen utilization in exhaustive exercise: Role of subcellular localization and fibre type. *Journal of Physiology*, *589*, 2871–2885. doi:10.1113/jphysiol.2010.204487

Noakes, T. D. (2011). Time to move beyond a brainless exercise physiology: The evidence for complex regulation of human exercise performance. *Applied Physiology Nutrition and Metabolism*, *36*, 23–35.

Noakes, T. D., & St Clair Gibson, A. (2004). Logical limitations to the 'catastrophe' models of fatigue during exercise in humans. *British Journal of Sports Medicine*, *38*, 648–649. doi:10.1136/bjsm.2004.009761

Nybo, L., & Secher, N. H. (2004). Cerebral perturbations provoked by prolonged exercise. *Progress in Neurobiology*, *72*, 223–261. doi:10.1016/j.pneurobio.2004.03.005

Ørtenblad, H., Westerblad, H., & Nielsen, J. (2013). Muscle glycogen stores and fatigue. *Journal of Physiology*, *591*, 4405–4413. doi:10.1113/jphysiol.2013.251629

Poole, D. C., Burnley, M., Vanhatalo, A., Rossiter, H. B., & Jones, A. M. (2016). Critical power: An important fatigue threshold in exercise physiology. *Medicine and Science in Sports and Exercise*, *48*, 2320–2334. doi:10.1249/MSS.0000000000000939

Poole, D. C., & Jones, A. M. (2012). Oxygen uptake kinetics. *Comprehensive Physiology*, *2*, 993–996. doi:10.1002/cphy.c100072

Poole, D. C., Ward, S. A., Gardner, G. W., & Whipp, B. J. (1988). Metabolic and respiratory profile of the upper limit for prolonged exercise in man. *Ergonomics*, *31*, 1265–1279.

Romer, L. M., & Polkey, M. I. (2008). Exercise-induced respiratory muscle fatigue: Implications for performance. *Journal of Applied Physiology*, *104*, 879–888. doi:10.1152/japplphysiol.01157.2007

Sahlin, K., & Seger, J. Y. (1995). Effects of prolonged exercise on the contractile properties of human quadriceps muscle. *European Journal of Applied Physiology*, *71*, 180–186.

Sahlin, K., Söderlund, K., Tonkonogi, M., & Hirakoba, K. (1997). Phosphocreatine content in single fibers of human muscle after sustained submaximal exercise. *American Journal of Physiology Cell Physiology*, *273*, C172–C178.

Skiba, P. F., Chidnok, W., Vanhatalo, A., & Jones, A. M. (2012). Modeling the expenditure and reconstitution of work capacity above critical power. *Medicine and Science in Sports and Exercise*, *44*, 1526–1532.

Skiba, P. F., Clarke, D., Vanhatalo, A., & Jones, A. M. (2014). Validation of a novel intermittent W′ model for cycling using field data. *International Journal of Sports Physiology and Performance*, *9*, 900–904.

Sundberg, C. W., & Bundle, M. W. (2015). Influence of duty cycle on the time course of muscle fatigue and the onset of neuromuscular compensation during exhaustive dynamic isolated limb exercise. *American Journal of Physiology Regulatory Integrative and Comparative Physiology*, *309*, R51–R61. doi:10.1152/ajpregu.00356.2014

Taylor, B. J., & Romer, L. M. (2008). Effect of expiratory muscle fatigue on exercise tolerance and locomotor muscle fatigue in healthy humans. *Journal of Applied Physiology*, *104*, 1442–1451. doi:10.1152/japplphysiol.00428.2007

Thomas, K., Elmeua, M., Howatson, G., & Goodall, S. (2016). Intensity-dependent contribution of neuromuscular fatigue after constant-load cycling. *Medicine and Science in Sports and Exercise*, *48*, 1751–1760. doi:10.1249/MSS.0000000000000950

Tumilty, L., Davison, G., Beckman, M., & Thatcher, R. (2011). Oral tyrosine supplementation improves exercise capacity in the heat. *European Journal of Applied Physiology*, *111*, 2941–2950. doi:10.1007/s00421-011-1921-4

Ulmer, H. V. (1996). Concept of an extracellular regulation of muscular metabolic rate during heavy exercise in humans by psychophysiological feedback. *Experientia*, *52*, 416–420.

Vanhatalo, A., Black, M. I., DiMenna, F. J., Blackwell, J. R., Schmidt, J. F., Thompson, C., … Jones, A. M. (2016). The mechanistic bases of the power–time relationship: Muscle metabolic responses and relationships to muscle fibre type. *Journal of Physiology*, *594*, 4407–4423. doi:10.1113/JP271879

Vanhatalo, A., Doust, J. H., & Burnley, M. (2007). Determination of critical power using a 3-min all-out cycling test. *Medicine and Science in Sports and Exercise*, *39*, 548–555. doi:10.1249/mss.0b013e31802dd3e6

Vanhatalo, A., Fulford, J., DiMenna, F., & Jones, A. M. (2010). Influence of hyperoxia on muscle metabolic responses and the power-duration relationship during severe-intensity exercise in humans: A 31P magnetic resonance spectroscopy study. *Experimental Physiology*, *95*, 528–540. doi:10.1113/expphysiol.2009.050500

Weyand, P. G., Lin, J. E., & Bundle, M. W. (2006). Sprint performance-duration relationships are set by the fractional duration of external force application. *American Journal of Physiology Regulatory Integrative and Comparative Physiology*, *290*, R758–R765. doi:10.1152/ajpregu.00562.2005

Whipp, B. J. (1994). The slow component of O_2 uptake kinetics during heavy exercise. *Medicine and Science in Sports and Exercise*, *26*, 1319–1326.

Wilkie, D. R. (1960). Man as a source of mechanical power. *Ergonomics*, *3*, 1–8.