REGULATION OF POWER OUTPUT DURING SELF-PACED CYCLING EXERCISE

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REGULATION OF POWER OUTPUT DURING SELF-PACED CYCLING EXERCISE

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by

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ABSTRACT

Fatigue is a universal phenomenon with functional and perceptual consequences. The study of fatigue in the exercise sciences has historically focussed on factors that limit performance during exercise. More recent proposals have shifted the focus of this understanding to examine how intensity is regulated during exercise through the study of the pacing strategy, which has both physiological and practical consequences. The aim of this thesis was to investigate the biological basis of self-pacing and the optimum pacing strategy for endurance time-trial events. Study 1 assessed the reproducibility of the pacing strategy and the consistency of the performance, perceptual and physiological response during self-paced time-trial exercise in well-trained cyclists. This study demonstrated the existence of a global pacing strategy that was reproducible on repeat 20 km cycling time-trials (TTs), and consistent between 4, 20 and 40 km TTs. The performance, perceptual and physiological response was also reproducible, confirming the feasibility of studying manipulations of the self-pacing strategy and the subsequent impact on these variables. Studies 2 and 3 adopted a model whereby participant's best self-paced TT performance was used to set time- and work-matched exercise bouts to study the effect of even- and variable-pacing. These studies revealed that a variable-pacing strategy that contains frequent periods of high-intensity exercise resulted in an augmented physiological response and higher perception of exertion compared to time- and work-matched even- and self-paced exercise. Conversely, even-pacing resulted in attenuation in the metabolic and perceptual cost of the bout, but only when the self-selected pacing strategy was sub-optimal. When self-pacing was optimal, time- and work-matched even-pacing resulted in cumulative metabolic stress that caused early exercise termination. In study 4 the biological basis to fatigue during 4, 20 and 40 km TTs was assessed. This study demonstrated that the contribution of central and peripheral mechanisms of fatigue during self-paced exercise is task-dependent. Specifically, the shorter, higher intensity 4 km time-trials were characterised by a greater degree of peripheral fatigue and less central fatigue compared to longer, lower intensity 20 and 40 km time-trials where less peripheral and more central fatigue was observed. The supraspinal contribution to fatigue was also greater during longer TT exercise. These studies have provided novel insight in to the biological factors that underpin the regulation of self-paced exercise, and the optimum pacing strategy for endurance TT events.

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LIST OF SYMBOLS AND ABBREVIATIONS

AP	Action potential
ATP	Adenosine triphosphate
BCAA	Branched Chain Amino Acids
Ca^{2+}	Calcium
CI	Confidence interval
CGM	Central Governor Model
CMEP	Cervicomedullary motor evoked potential
CNS	Central nervous system
CSP	Cortical silent period
CT	Contraction time
CV	Coefficient of variation
EMG	Electromyography
EMG_{RMS}	Root mean square of the electromyographic signal
ERT	Estimated resting twitch
H^+	Hydrogen ion
HR	Heart rate
H-reflex	Hoffman reflex
F_IO_2	Fraction of inspired oxygen
iEMG	Integrated electromyographic signal
K^+	Potassium
La^-	Blood lactate
MEP	Motor evoked potential
M_{max}	Maximal M-wave
MRFD	Maximum rate of force development
MRR	Maximum relaxation rate
MVC	Maximal voluntary contraction
M-wave	Compound muscle action potential
Na^+	Sodium
O_2	Oxygen
P_B	Barometric pressure
P_i	Inorganic phosphate
Q_{tw}	Quadriceps twitch force
$Q_{tw.pot}$	Potentiated quadriceps twitch force
RER	Respiratory exchange ratio
RPE	Rating of perceived exertion
rpm	Revolutions per minute
RMT	Resting motor threshold
RT=	One half relaxation time
SD	Standard deviation
SEM	Standard error of the mean
SIT	Superimposed twitch
SR	Sarcoplasmic reticulum
TMS	Transcranial magnetic stimulation
TE	Typical error
TEA	Task effort awareness
TT	Time-trial
VA	Voluntary activation
$\dot{V}CO_2$	Carbon dioxide output
$\dot{V}_E$	Minute ventilation
VL	Vastus lateralis
$\dot{V}O_2$	Oxygen uptake

PUBLICATIONS ARISING FROM THE THESIS

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Thomas, K. Stone, M. Thompson, K. St Clair Gibson A. & Ansley, L. (2013). The effect of an even-pacing strategy on exercise tolerance in well-trained cyclists. *European Journal of Applied Physiology*, doi: 10.1007/s00421-013-2734-4.

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DECLARATION

I declare that the work contained in this thesis has not been submitted for any other award and that it is all my own work. I also confirm that this work fully acknowledges opinions, ideas and contributions from the work of others.

Any ethical clearance for the research presented in this thesis has been approved. Approval has been sought and granted by the Faculty of Health and Life Sciences Ethics committee for each study.

Name: Kevin Thomas

Signature:

Date: 15th November 2013

CHAPTER 1 INTRODUCTION

1-1 Introduction

Fatigue is a universal and daily phenomena underpinned by a myriad of complex mechanisms. In the exercise sciences, fatigue is typically defined as an exercise-induced impairment in the ability to produce force (Gandevia, 2001) in the presence of an increased perception of effort (Enoka & Stuart, 1992). Whilst fatigue has both functional and perceptual consequences, the available research has been criticized for not considering both in the study of this phenomena (Barry & Enoka, 2007). Moreover, research into fatigue spans several disciplines, each of which typically defines fatigue in order to best suit the discipline under study (Abbiss & Laursen, 2005). This reductionist approach has led to a number of linear cause and effect models that describe fatigue as the point at which the "limit" of a particular physiological system has been reached (Callow *et al.*, 1986; Bangsbo *et al.*, 1996; Gonzalez-Alonso *et al.*, 1999; Gonzalez-Alonso & Calbet, 2003). It has been argued that this fragmented approach to the study of fatigue has provided an incomplete assessment of a complex phenomenon (Lambert *et al.*, 2005).

More recent proposals have attempted to explain the development of fatigue by considering how multiple physiological systems interact during exercise to regulate, rather than limit, exercise intensity (St Clair Gibson & Noakes, 2004; Lambert *et al.*, 2005). The complex systems, or central governor model proposes the central nervous system, through feed-forward control modifiable by metabolically triggered afferent feedback, regulates exercise intensity in an anticipatory manner to prevent against "catastrophic" threats to homeostasis (St Clair Gibson & Noakes, 2004; Lambert *et al.*, 2005). In this model fatigue is considered as a process rather than an absolute occurrence, the conscious manifestation of which is the sensation or emotion of fatigue experienced by the exerciser (St Clair Gibson *et al.*, 2003). A number of lines of evidence have emerged to support the key features of this model; namely that exercise intensity is regulated in an anticipatory manner (Ulmer, 1996; Ansley *et al.*, 2004a; Ansley *et al.*, 2004b; Tucker, 2009), afferent feedback modifies the degree of motor unit recruitment (Amann & Dempsey, 2008; Amann *et al.*, 2009; Amann *et al.*, 2011) and that the central nervous system plays a key role in this process (Amann *et al.*, 2009; Swart *et al.*, 2009b; Mauger *et al.*, 2010; Amann *et al.*, 2011).

Central to this model is the concept of "regulation" of exercise intensity. The subsequent protocols adopted to study this regulation usually allow athletes to self-pace their exercise intensity in trials with a known endpoint. Measurement of the resulting distribution of work, or pacing strategy, provides a marker of the underlying physiological regulation (Tucker & Noakes, 2009). Understanding the biological basis of self-pacing would help further our understanding of how the exerciser regulates intensity to manage the symptoms of fatigue and optimise performance. Whilst the neuromuscular mechanisms underpinning the exercise-induced decrease in the force producing capacity of muscle have been well-studied (e.g. Bigland-Ritchie *et al.*, 1978; Bigland-Ritchie, 1981; Bigland-Ritchie *et al.*, 1986a; Bigland-Ritchie *et al.*, 1986b; Kent-Braun, 1999; Schillings *et al.*, 2003), few have applied these methods to study the fatigue observed during self-paced locomotor exercise (Amann *et al.*, 2006a; Amann & Dempsey, 2008; Amann *et al.*, 2009; Ross *et al.*, 2010a). An appreciation of the functional consequences of fatigue during self-paced exercise, alongside an assessment of the pacing strategy and associated perceptual responses could address the disconnect in current research between the physical and emotional definitions of fatigue (Barry & Enoka, 2007).

The pacing strategy adopted by the athlete also has practical implications, as it significantly impacts race performance (Atkinson *et al.*, 2007c). For very short duration events (< 30-60 s) an all-out strategy to minimise the time spent accelerating is optimal (de Koning *et al.*, 1999; Corbett, 2009). For middle distance events (~1 to 4 min) a positive pacing strategy that speeds oxygen kinetics and the attainment of maximum oxygen uptake is recommended; this affords a greater sparing of the finite anaerobic energy reserve early in the bout allowing exercise to be prolonged through a greater total yield of ATP before exhaustion (Jones *et al.*, 2008b; Bailey *et al.*, 2011). For events of longer duration (> 4 min) a common assumption is that an even distribution of pace is optimal (Foster *et al.*, 1993; Thompson *et al.*, 2003; Gordon, 2005; Atkinson *et al.*, 2007c; Abbiss & Laursen, 2008). The theoretical basis to this assumption is based on the well-established hyperbolic relationship between exercise intensity and duration that dictate a duration-specific maximum sustainable intensity exists above which the development of fatigue is accelerated (Poole *et al.*, 1988; Fukuba & Whipp, 1999; Vanhatalo *et al.*, 2011). Attainment of an even pace would theoretically optimise performance by maximising the sustainable speed for the majority of the exercise bout

whilst also minimising kinetic energy losses (Atkinson *et al.*, 2007b). Despite this assumption, observations of elite athletes reveal a parabolic pacing strategy is common across modes and events (Tucker *et al.*, 2006b; Corbett, 2009; Muehlbauer & Melges, 2011; Mauger *et al.*, 2012) and the limited experimental data suggests even-pacing might not be an optimal strategy for prolonged endurance events (Billat *et al.*, 2006; Lander *et al.*, 2009). Further research is warranted to assess the utility of even-pacing in endurance time-trial events.

The main aim of this thesis was to investigate the biological basis of the pacing strategy during self-paced time-trial exercise in well-trained cyclists to better understand how the athlete regulates exercise intensity to achieve a best performance whilst managing the symptoms of fatigue. The consistency of pacing strategy across repeated 20 km trials and between 4, 20 and 40 km trials was assessed in Chapter 4. In Chapters 5 and 6 the utility of even- and variable- pacing was assessed by manipulating the athlete's self-selected pacing strategy in order to gain an insight in to the optimal pacing strategy for endurance events. Finally in Chapter 7 the neuromuscular basis to fatigue during self-paced 4, 20 and 40 km time-trial exercise was assessed to understand the biological factors underpinning exercise regulation in a range of self-paced exercise tasks.

CHAPTER 2 LITERATURE REVIEW

2-1 Introduction

The study of fatigue in the physiology of exercise stretches back centuries, but a thorough explanation of the aetiology of this condition still eludes scientists (Marino *et al.*, 2011). As far back as the 18th century, Mosso in his book *La fatica* identified the two phenomena that are still widely considered to characterise fatigue:

"The first is the diminution of the muscular force. The second is fatigue as a sensation. That is to say, we have a physical fact which can be measured and compared, and a psychic fact that eludes measurement" (Mosso, 1904, p.154, cited in Marino *et al.*, 2011)

The broad usage of the term' fatigue' in the scientific literature poses a challenge as fatigue can encompass several different phenomena that are the consequence of different physiological and perceptual processes (Enoka & Duchateau, 2008). In the exercise sciences, the functional consequence of fatigue has been defined as "failure to maintain the required or expected force" (Edwards, 1981), an "exercise-induced reduction in the ability of muscle to produce power or force, irrespective of task completion" (Bigland-Ritchie & Woods, 1984) and "an exercise-induced decrease in maximal voluntary force produced by a muscle" (Gandevia *et al.*, 1996). Whilst all definitions consider the reduction in muscular force as a measure of fatigue, some do not consider muscle fatigue as a point at which task failure occurs (Bigland-Ritchie & Woods, 1984) and others require a reduction in the *maximum* voluntary force output (Gandevia *et al.*, 1996). More recently the exercise sciences have considered the perceptual component of fatigue, defined as "the conscious perception of changes in subconscious homeostatic control systems" (St Clair Gibson *et al.*, 2003), with fatigue defined as an emotion experienced by the exerciser that is critical to the regulation of exercise intensity (St Clair Gibson *et al.*, 2003; Tucker, 2009). A consideration of both the functional and perceptual consequences of fatigue is necessary to understand the phenomena of fatigue during exercise (Barry & Enoka, 2007).

The following review will consider the nature of fatigue in the context of exercise, providing a synopsis of the literature pertaining to the mechanisms of exercise-induced fatigue in healthy adults, current perspectives on the physiology and psychology

underpinning these mechanisms, and how these mechanisms manifest during performance of exercise tasks of known distance/duration.

2-2 Exercise as a threat to homeostasis

The term exercise is precisely defined by Winter & Fowler (2009) as "a potential disruption to homeostasis by muscle activity that is either exclusively or in combination concentric, isometric or eccentric" (p. 451). The term homeostasis was first introduced by Walter Cannon (1932) to describe the regulation of the physiological internal environment that results in the dynamic equilibrium of a number of physiological variables within defined limits by specific control systems. Control systems work by way of negative feedback and consist of a receptor, integrating centre and an effector. Disturbances are sensed by a specific receptor, feedback is relayed and interpreted by the integrating centre, which evaluates the strength of the stimulus and sends an appropriate efferent output to the effector in order to correct the disturbance and return the internal environment towards its' desired set-point. Failure of any component in the system results in an imbalance which could result in disease or death. Exercise results in several threats to homeostasis; disrupting energy balance, acid-base balance, thermoregulation, cardiovascular function and hydration amongst others. Failure to control these disruptions results in premature fatigue at best, and in the worst case scenario, death.

The threat to homeostasis from exercise is largely as a result of the metabolic demands placed on the system by increased skeletal muscle activity, with not insignificant demand from cardiac and smooth muscle (Winter & Fowler, 2009). A consideration of how skeletal muscles function to produce force is therefore necessary. Attempts to explain how muscle functions date back to at least the ancient Greeks (Needham, 1971). It is commonplace in exercise physiology textbooks to refer to muscle action as "contraction" (Astrand & Rodahl, 1986; McArdle *et al.*, 2007). The term contraction implies a reduction in volume, however it has been demonstrated as early as 1663 by the Dutch anatomist Jan Swammerdam that muscle does not contract (Needham, 1971). Winter & Fowler (2009) suggest the use of the term muscle action in preference to muscle contraction, stating the function of muscle is "to produce force and it does so by attempting to shorten" (p.451). The use of the term contraction to describe muscle action, whilst technically incorrect, is understandable given its widespread historical use

by both the lay and scientific communities; thus this term will be used interchangeably with muscle "action" throughout this thesis.

2-3 Exercise; from brain to muscle

Voluntary force production from skeletal muscle follows a complex chain of command, originating in the brain (Figure 2-1). Activity in parieto-dependent, pre-motor areas of the motor cortex generate potential motor actions that are realised by prefronto-dependent motor areas (Rizzolatti & Luppino, 2001). The role of this subconscious pre-motor activity remains a topic of debate. The presence of "readiness potentials" – a period of negative potential measured with EEG that reliably precedes self-initiated movements – is well established (Libet *et al.*, 1983; Schlegel *et al.*, 2013). The precise role of the readiness potential is not, but there is general acceptance of the idea that movement-related neural activity precedes the awareness of willing to move (Desmurget & Sirigu, 2009; Desmurget, 2013; Schlegel *et al.*, 2013). The resulting descending drive from motor areas activates spinal motoneurons that propagate the signal to the motor end plate. This signal synapses at the neuromuscular junction and causes the release of the neurotransmitter acetylcholine (ACh). The release of ACh alters the permeability of the sarcolemma, triggering an action potential (AP) that causes depolarisation of the sarcolemma through the movement of sodium and potassium ions (Na^+ and K^+) into and out of the cell, propagating the AP across the sarcolemma. This signal stimulates the release of calcium (Ca^{2+}) from the sarcoplasmic reticulum (SR) into the sarcomere, a process that increases the concentration of Ca^{2+} in the sarcomere to 100 times resting levels within a millisecond. The link between the generation of an AP in the sarcolemma and the initiation of contraction is called excitation-contraction (EC) coupling. Calcium release drives the interaction of the skeletal muscle proteins actin and myosin to liberate chemical energy (adenosine triphosphate, ATP) to mechanical energy (and thus produce force) via the cross-bridge cycle (see section 2-4). Muscle relaxation occurs through the active reuptake of Ca^{2+} into the SR. If muscle action is repetitive or sustained, the processes that contribute to fatigue could theoretically arise at any step from the motor cortex in the brain to actomyosin binding (Debold, 2012). Key to understanding these processes is knowledge of how muscle produces force, and how aerobic and anaerobic processes provide the chemical energy that underpins force production.

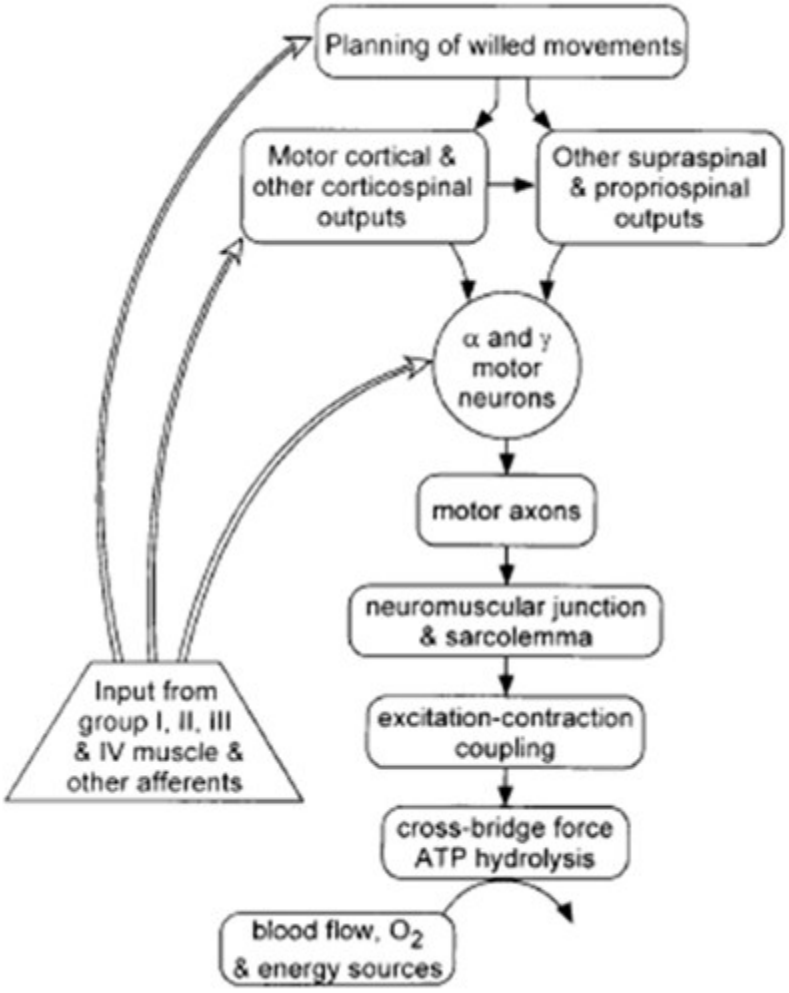


Figure 2-1. The chain of command involved in voluntary force production. Fatigue could potentially impair any step in the brain to muscle pathway (from Gandevia, 2001).

2-4 Muscle structure and mechanics

Skeletal muscle is composed of two principal proteins, actin and myosin, that constitute 80% of the total muscle protein mass (Jones *et al*., 2004). The cyclical interaction of these two proteins with ATP results in the conversion of chemical energy to mechanical work. The highly organised structure of skeletal muscle (Figure 2-2) permits the controlled generation of force.

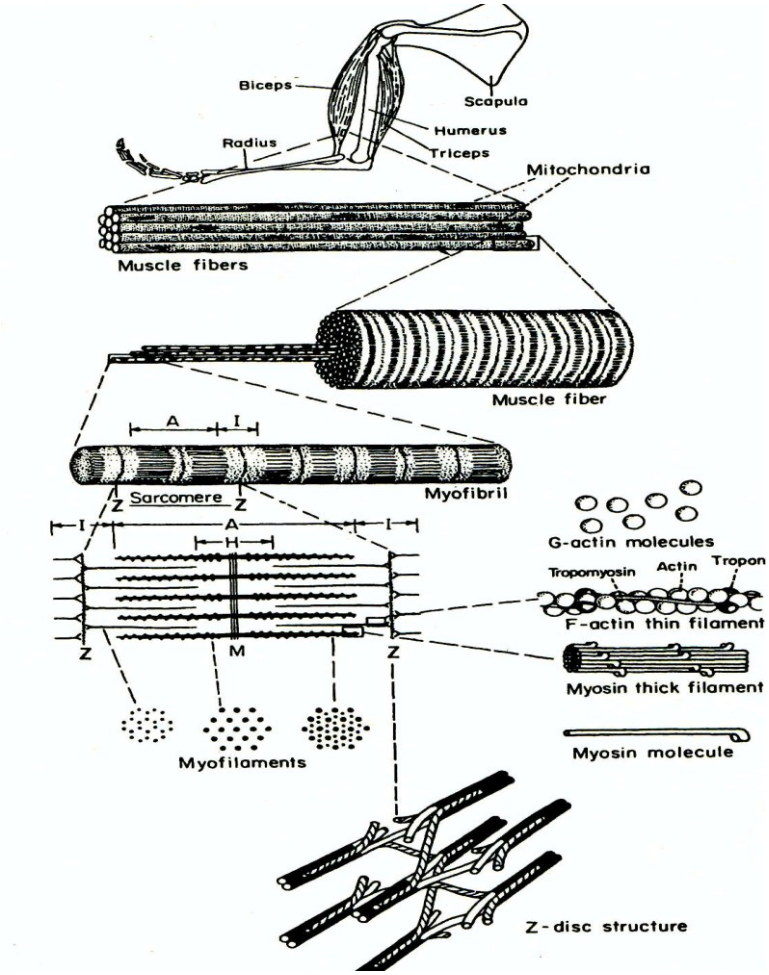


Figure 2-2. Organisation of skeletal muscle.

The functional unit of the muscle fibre is the sarcomere. Each sarcomere contains partially overlapping thin actin and thick myosin filaments, a pattern that gives muscle its' characteristic striated appearance when viewed under a light microscope. Force generation is the result of the interaction of actin and myosin filaments in a process known as the cross-bridge cycle.

The cross-bridge theory of muscle action was first proposed over 40 years ago. In his landmark paper, Huxley (1957) proposed that the head of the myosin molecule binds to the actin filament and then undergoes a change of state which results in the rotation of the myosin head and a subsequent pulling of the actin filament past the myosin filament. Experimental evidence for this theory came from a subsequent study by Huxley & Simmons (1971), and a wealth of structural, physiological and biochemical data now exists in support of this theory (Lymm & Taylor, 1971; Toyoshima *et al.*, 1987; Finer *et*

al., 1994), although direct visualisation of cross-bridge movement has proved difficult (Holmes & Geeves, 2000).

Although there are subtle details of the cross-bridge process that remain controversial, a simple model exists (illustrated in Figure 2-3) that incorporates the fundamental aspects (Holmes & Geeves, 2000) consistent with the scheme first proposed by Lymm & Taylor (1971). After hydrolysis of ATP, with ADP and P_i still in the active state, myosin exists in a rapid equilibrium between being weakly-bound and strongly-bound to actin (Sleep *et al.*, 2005). In the absence of nucleotide, myosin stereospecifically interacts with actin to form the strongly-bound state, or actomyosin complex. Myosin then releases P_i from the active state, an event that drives the rotation of the lever arm (Figure 2-3, *d*) and therefore force generation (Holmes & Geeves, 2000). Whilst in the strongly-bound state (Figure 2-3, duration t_{on}) P_i release is followed by two kinetic steps. First, the actomyosin complex releases ADP (Figure 2-3, t_{ADP}) placing actomyosin in a temporary rigour state (Figure 2-3, t_{rigor}). Myosin waits in this state for a new ATP molecule to bind and cause dissociation from actin. Whilst myosin is weakly-bound from actin, hydrolysis of ATP occurs, resetting the lever arm and preparing myosin for the next interaction with actin.

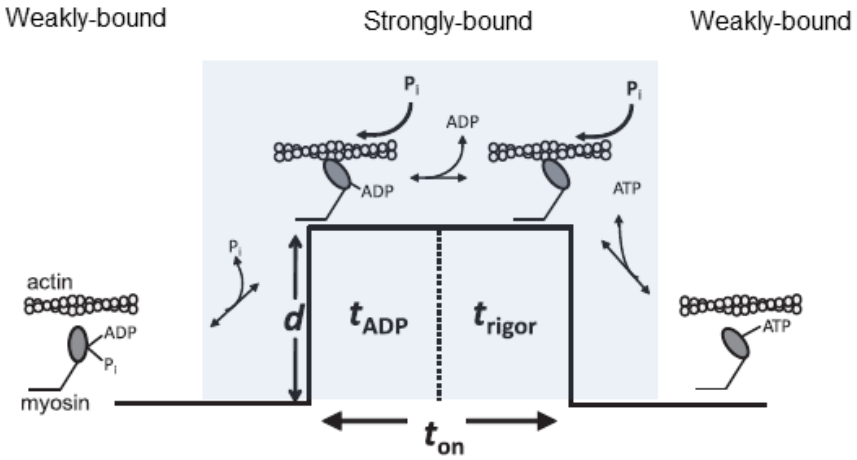


Figure 2-3. Model of the cross-bridge cycle linking the biochemical and mechanical events. (modified from Debold, 2012).

Recent technological advances in the field of biophysics have enabled researchers to examine the molecular basis of the cross-bridge cycle, right down to the level of a single myosin molecule (Debold, 2012). These experiments have provided further insights in

to the potential aetiology of fatigue that will be discussed in section 2.6. Before this it is necessary to consider how the aerobic and anaerobic processes in the cell interact to liberate ATP to provide energy for muscular work during exercise.

2-5 Energy provision during exercise

Humans are heliodependent; that is we derive our energy from the sun. The law of conservation of energy states that energy can be converted from one form to another, but not created or destroyed. During exercise, the simple soluble substances derived from the foods we eat (substrates) are acted upon by enzymes. The interaction between enzyme and substrates liberates chemical energy to potential kinetic energy for muscle to exert force as it attempts to shorten, and to heat energy and a consequent thermogenesis (Winter & Fowler, 2009). The currency of energy in human cells is adenosine triphosphate (ATP). Energy for muscular activity is thus obtained from the hydrolysis of ATP, catalysed by the enzyme ATPase:

$$ATP \leftrightarrows ADP + P_i + H^+ \text{ energy} \quad (1)$$

Where ADP is adenosine 5'-diphosphate, H^+ is a hydrogen ion and P_i is inorganic phosphate. Within muscle the human body typically stores 20-25 $mMol \cdot kg^{-1}$ dry muscle (dm) of ATP. With peak ATP turnover rates of 15 $mMol \cdot kg^{-1}$ $dm \cdot sec^{-1}$ this is enough to fuel 1-2 seconds of maximal exercise (Gaitanos *et al.*, 1993). Because ATP is only stored in small amounts, the ATP:ADP ratio changes rapidly with an increase in energy metabolism. As the store of ATP becomes depleted, ATP for continued muscular exercise is resynthesised by the integration of anaerobic and aerobic metabolic processes.

Anaerobic energy metabolism

At the onset of exercise there is a delay in oxygen uptake by the exercising muscle. If the duration is very short oxygen (O_2) dissolved in muscle, bound to myoglobin in the muscle and bound to haemoglobin in the blood, can buffer the initial demand of exercise. This initial aerobic contribution is not sufficient to provide all of the energy required at the onset of high-intensity exercise and anaerobic energy systems are rapidly activated to ensure muscular force development continues. There are two main

anaerobic energy-producing pathways that interact to maintain the supply of ATP: ATP-PCr and glycolysis.

The resynthesis of ATP via the ATP-PCr pathway is achieved by combining ADP with phosphocreatine (PCr) – a high energy compound – catalysed by the enzyme creatine kinase (CK) in the cytoplasm of the cell:

$$PCr^{2} + ADP^{3-} + H^{+} \rightarrow ATP^{4-} + Cr \quad (2)$$

The ATP-PCr pathway provides immediate energy for muscular contraction at the onset of exercise and during short-term high-intensity exercise, acting as an energy buffer to reduce the degradation of ATP stores within the muscle by driving the phosphorylation of ADP. However there is only enough PCr stored in the muscle to aid ATP resynthesis for approximately 10 s (Conley *et al.*, 2001). Glycolysis is activated at the onset of exercise and involves the resynthesis of ATP via degradation of carbohydrate (glucose or glycogen) to pyruvate in the cytoplasm of the cell (Gastin, 2001). At high intensities, where glycolytic flux exceeds mitochondrial activity and oxygen availability is insufficient, pyruvate is subsequently converted to lactate:

$$\text{Glucose} + 2\ ADP + 2\ P_i \rightarrow 2\ \text{lactate} + 2\ H^{+} + 2\ ATP \quad (3)$$

The rate of glycolysis is determined by the two rate limiting enzymes glycogen phosphorylase and phosphofructokinase. The activities of both are adversely affected by acidosis, thus the rate of glycolysis is reduced by its own products (i.e. P_i, H^+), and the faster the rate of glycolysis, the shorter the time to impaired ATP production.

Aerobic energy metabolism

The fate of pyruvate is dependent on the amount of oxygen available during exercise. At low sub-maximal intensities, where the oxygen supply is sufficient, pyruvate is transported to the mitochondria where it is oxidised to provide further ATP resynthesis. Pyruvate is transported to the mitochondria via a complex enzyme system (pyruvate dehydrogenase). This system catalyses an irreversible link reaction termed oxidative decarboxylation. The pyruvate molecule is attached to coenzyme A to form acetyl-coenzyme A. Acetyl-coenzyme A is also the product of initial fatty acid beta-oxidation.

Acetyl-coenzyme A combines with oxaloacetate to form citrate and enters the tricarboxylic acid cycle (TCA). The TCA breaks down the acetyl units and generates the reduced coenzymes nicotinamide adenine dinucleotide ($NADH_2$) and flavin adenine dinucleotide ($FADH_2$). These enter the electron transport chain (ETC). The flow of two electrons through the ETC will release energy for the phosphorylation of ADP to ATP, with water the by-product. Oxidative phosphorylation is represented by Figure 2-4:

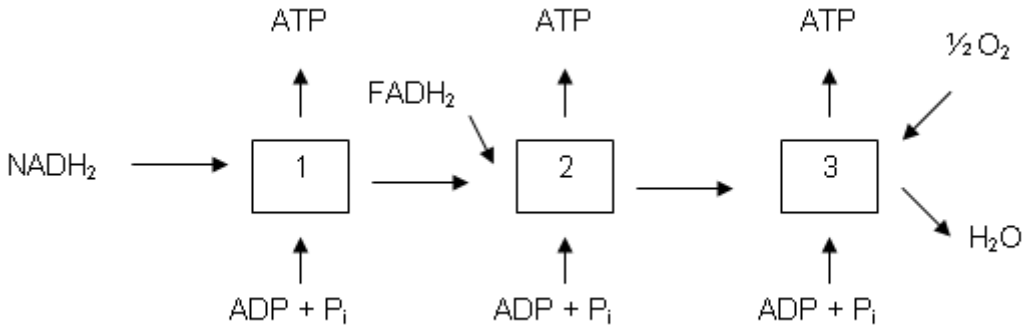


Figure 2-4. Oxidative phosphorylation in the electron transport chain (Åstrand and Rodahl, 1986)

These metabolic processes are limited by the maximum rate of ATP regeneration (power of the process) and the absolute amount of ATP that can be regenerated (capacity of the process) (Sahlin *et al.*, 1998). The energy pathways differ on a spectrum from the high power, low capacity of PCr hydrolysis, to the low power, very high capacity of oxidative processes. Figure 2-5 illustrates the differences in power and capacity of the three pathways.

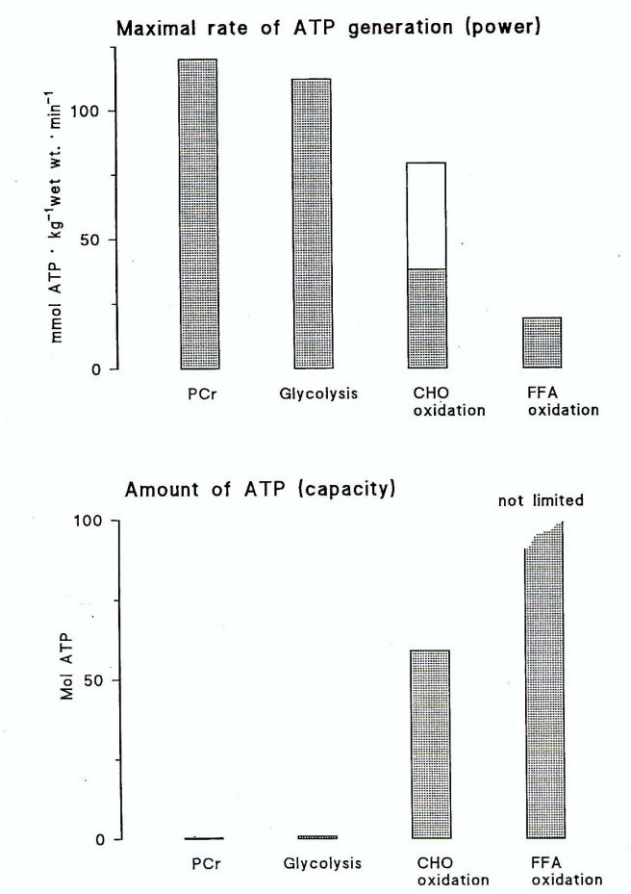


Figure 2-5. Maximum rates and capacities of metabolic processes for ATP regeneration (Sahlin *et al*, 1998).

The respective power and capacity of each system imposes limitations on the exercise performance capabilities of skeletal muscle. Figure 2-6 shows a typical power-duration curve, whereby the highest power outputs (and thus highest rates of ATP regeneration) can only be sustained for very short periods, and the sustainable power output decreases as a function of exercise duration. Wilkie (1985) demonstrated that the highest sustainable power output, the asymptote of the power-duration curve, was approximately one third of the maximum power output.

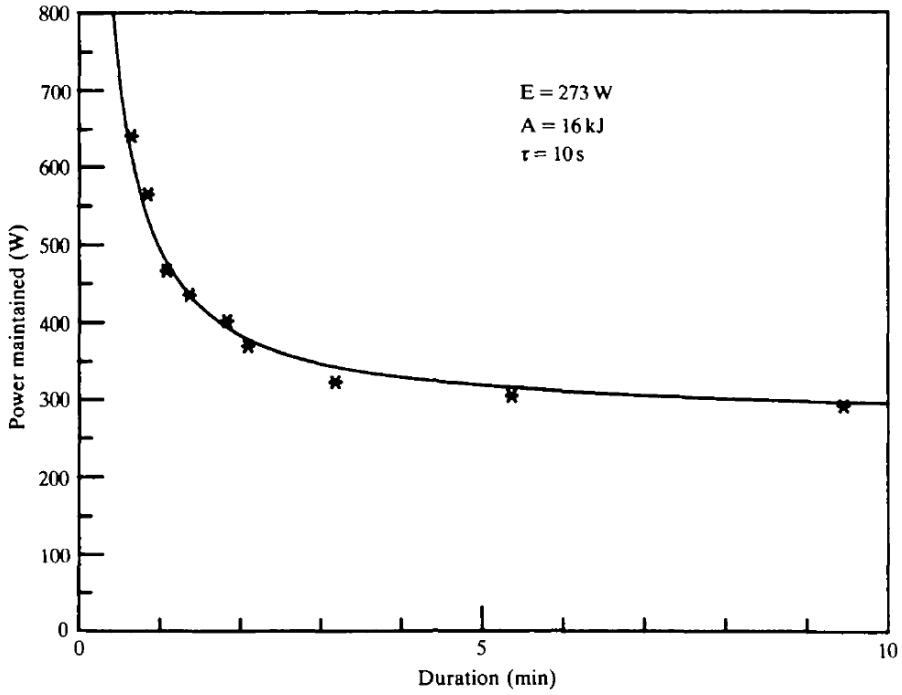


Figure 2-6. Typical power-duration curve, from Wilkie (1985).

Exercise performance is thus limited by the capacity and power of the respective energy systems to liberate chemical energy for mechanical work. The demands placed on these energy pathways through exercise results in the development of fatigue in the systems under stress. The mechanisms of fatigue that underpin this are task-dependent and can be broadly split in to those of central and peripheral origin. Muscle action is the result of a complex chain of events (Figure 2-1) and at each step in the chain there is potential for fatigue to impair force production. The following sections will outline the proposed mechanisms of central and peripheral fatigue, the methods for assessing these and the current knowledge pertaining to these mechanisms in different types of exercise.

2-6 Peripheral fatigue

Peripheral fatigue refers to processes that impair force production occurring at, or distal to, the neuromuscular junction (Gandevia, 2001). Exercise-induced alterations in the cross-bridge cycle due to fatigue can inhibit the production of muscular force or excitation-contraction (EC) coupling (Fitts, 2008). Given the complexity of muscle action and the long chain of events that precede cross-bridge formation, localising the cause of peripheral fatigue is difficult. Further difficulty arises when comparing the results of different models for studying peripheral fatigue. Evidence has been obtained from models studying whole muscle, single muscle fibres, skinned single muscle fibres

(Allen *et al.*, 2008b) and more recently single myosin molecules (Debold, 2012). It should thus be noted that the evidence for the underpinning mechanisms of peripheral fatigue is derived largely from the study of *in vitro* models. The following sections will briefly outline the primary mechanisms that are thought to contribute to peripheral fatigue.

Sodium (Na^+) & Potassium (K^+) activity

Muscle action is initiated by repeated short bursts of action potentials (Allen *et al.*, 2008b). Intrinsic to these action potentials is the action of the sodium (Na^+) potassium (K^+) pump. Specifically, the depolarisation required to generate an action potential is caused by an influx of Na^+ in to the muscle cell, followed by an efflux of K^+. At rest the chemical gradients of these ions are kept in a narrow range through active transport across the cell membrane (Nielsen & de Paoli, 2007). However during muscular contraction the passive movements of Na^+ and K^+ increase, resulting in increased intracellular concentrations of Na^+, and an increased extracellular concentration of K^+ (Clausen *et al.*, 2004). The shift of K^+ from intra- to extracellular compartments has been implicated as a cause of peripheral fatigue through inhibition of the action potential due to ion disturbances over the sarcolemma and possible effects on t-tubular membrane depolarisation (Sjogaard, 1991; McKenna, 1992), resulting in a reduction in the force generating capacity of muscle (Nielsen & de Paoli, 2007).

Calcium (Ca^{2+}) handling & inorganic phosphate (P_i)

The movement of calcium into and out of the cytoplasm functions as a signal for numerous cellular processes, including those required for the production of muscular force. The propagation of the action potential along the surface membrane of the muscle cell stimulates the release of Ca^{2+} from the sarcoplasmic reticulum (SR) which drives the cross-bridge cycle (Allen *et al.*, 2008b). The subsequent relaxation of muscle is caused by the reuptake of Ca^{2+} into the SR via the SR Ca^{2+} pump (Allen *et al.*, 2008b). Thus, alterations in the release and/or reuptake of calcium have been proposed as potential explanations for muscle fatigue (Allen *et al.*, 2008a; MacIntosh *et al.*, 2011). Eberstein & Sandow (1963; cited in Allen *et al.*, 2008b) were the first to demonstrate failure of EC coupling contributed to muscle fatigue by showing a regain in muscle function as a result of caffeine infusion, which facilitates Ca^{2+} release from the SR. It is

generally accepted that impaired Ca^{2+} release from the sarcoplasmic reticulum contributes to the decline in force observed in isolated skeletal muscle fibres (Allen *et al.*, 2008a). However, multiple mechanisms have been proposed that might mediate this impaired release, including a reduction in the amplitude of the action potential (possibly due to an increased extracellular K^+), a fall in intracellular ATP causing reduced effectiveness of SR Ca^{2+} channel opening, and the actions of inorganic phosphate (P_i) (Allen *et al.*, 2008b). The increase in P_i during muscular activity has been implicated as a potential inhibitor of Ca^{2+} release from the SR possibly through direct inhibition of ryanodine receptor-Ca^{2+} release channels, or increased Ca^{2+}-P_i precipitation that reduces the available free Ca^{2+} (Allen *et al.*, 2008a). Alterations in calcium handling thus likely plays a role in the development of peripheral fatigue, but multiple mechanisms might explain its effects.

Acidosis

The idea that lactic acid and the associated acidosis of the cell could cause fatigue arose from seminal studies in the early 1900's that observed increases in lactic acid concentration in skeletal muscle during fatigue, and that reversing this concentration could restore muscle function (Fletcher, 1907; Hill *et al.*, 1924c, a, b; Hill & Kupalov, 1930). During intense muscular activity, the accumulation of intramuscular lactic acid and hydrogen ions (H^+) causes a reduction in the pH of the cell, and this reduction is associated with reduced muscle function (Westerblad *et al.*, 2002). Postulated explanations for this decline in function include the inhibition of glycolysis (Bangsbo *et al.*, 1996), decreased myosin ATPase activity slowing ADP release and impairing cross bridge cycling (Allen *et al.*, 1995a; Westerblad *et al.*, 1998) and inhibition of EC coupling due to impaired calcium handling (Allen *et al.*, 1995a; Favero *et al.*, 1995). Early researchers attributed acidosis to the increased H^+ generated as a result of glycolysis when lactic acid dissociates into H^+ and the acid salt sodium lactate (Sahlin *et al.*, 1976; Spriet *et al.*, 1987a). More recently it has been shown that H^+ is formed during the glycolytic reactions associated with the hydrolysis of ATP (Robergs *et al.*, 2004). In the presence of oxygen these protons are used in the mitochondria for oxidative phosphorylation. At higher exercise intensities, where ATP must be hydrolysed through anaerobic processes, H^+ accumulates and causes acidosis. Lactate production increases under these conditions in order to prevent pyruvate accumulation,

thus lactate production attenuates (not causes) acidosis, but its' presence is indicative of acidosis and thus it remains a useful indirect marker (Robergs *et al.*, 2004).

A range of experiments on isolated muscle has provided evidence suggesting acidosis has a minimal effect on force production, and could even have an ergogenic effect (Cairns, 2006). Reductions in pH have little effect on contractile function under physiological temperatures (Pate *et al.*, 1995; Bruton *et al.*, 1998) and when pH is reduced through exposure to CO_2, muscle function declines markedly less than that observed during fatigue (Adams *et al.*, 1991). The lack of association between pH and reduced muscle function is reinforced by the observation that the recovery of muscle force or power is comparatively rapid compared to the recovery of pH (Sahlin & Ren, 1989). Conversely more recent work suggests acidosis slows the unloaded shortening velocity of muscle fibres, independent of temperature, via a slowing of the rate of ADP release, suggesting the potential negative effect of acidosis might not be related to the production of force (Knuth *et al.*, 2006; Debold *et al.*, 2008). In contrast to experiments on isolated muscle, during whole body exercise induced acidosis can exacerbate fatigue (Kowalchuk *et al.*, 1984) and induced alkalosis can improve exercise performance (Nielsen *et al.*, 2002). Thus whilst the effects of acidosis on the cell might not be detrimental, and could even be ergogenic, in whole body exercise severe acidosis might act as an afferent signaller to the CNS that is implicated in the development of fatigue (Amann *et al.*, 2011). These disparate conclusions highlight the caution that must be exercised when extrapolating the results of studies on *in vitro* preparations to *in vivo* scenarios.

2-7 Central fatigue

Central fatigue is a progressive decline in voluntary activation of muscle during exercise (Gandevia, 2001). The mechanisms underpinning this decline are less well understood than those for peripheral fatigue. "Central" fatigue could arise because of a number of potential impairments along the pathway from brain to muscle (Figure 2-1), including impairments in the motor cortex (Gandevia *et al.*, 1996; Sidhu *et al.*, 2009b; Sidhu *et al.*, 2013b), reflex responses at the spinal cord (Garland & McComas, 1990; Klass *et al.*, 2008) and intrinsic properties of motoneurons (McNeil *et al.*, 2011a; McNeil *et al.*, 2011b). The relatively recent introduction of transcranial magnetic stimulation (TMS) to the study of fatigue of the central nervous system has generated new insight into the

mechanisms underpinning a failure of central activation during exercise (Taylor *et al.*, 2006; Smith *et al.*, 2007; Goodall *et al.*, 2009; Sidhu *et al.*, 2009b; Goodall *et al.*, 2012a). These studies are considered in more detail in section 2-9. Furthermore, models of fatigue that attempt to explain the interaction of central and peripheral fatigue during exercise are considered in section 2-10.

2-8 Quantifying fatigue

An exercise-induced reduction in voluntary force production indicates the presence of fatigue, but localising the site responsible for this reduction is difficult given the complex chain of events involved in force production (Figure 2-1). The use of electrical and magnetic stimulation techniques in addition to measures of muscle force can provide information on the contributions of central and peripheral mechanisms of fatigue.

Evoked twitch force & EMG

Supramaximal stimulation of a motor nerve produces an evoked twitch, the characteristics of which can be studied to assess muscle contractile function and excitability. Reductions in the amplitude of the resting, potentiated twitch indicate peripheral fatigue (Kufel *et al.*, 2002). Measurement of the associated muscle compound action potential (M-wave) with electromyography (EMG) provides a measure of membrane excitability (Lepers *et al.*, 2002). In addition characteristics of the twitch can be studied to assess changes in muscle shortening velocity (maximum rate of force development and contraction time) and muscular relaxation (maximum rate of relaxation and one-half relaxation time). A reduced rate of force development indicates a decrease in the rate of cross-bridge formation (Stein & Parmiggiani, 1981). A prolonged contraction time is thought to reflect changes in Ca^{2+} release from the SR (Klitgaard *et al.*, 1989). A slower rate of relaxation and prolonged one half relaxation time reflect decreases in the maximum rate of weak to strong cross-bridge binding and rates of cross-bridge detachment (Westerblad *et al.*, 1997; Jones *et al.*, 2009).

Voluntary activation

In a landmark study, Merton (1954) demonstrated that during a voluntary effort, additional force could be evoked through stimulation of the motor nerve, and the

increment in force was inversely related to the level of initial force. Comparison of the amplitude of the superimposed twitch evoked during a maximum voluntary contraction (MVC) with that evoked at rest provides a measure of voluntary activation of muscle, a technique termed twitch interpolation. In a fatigued state, a decrease in voluntary activation indicates the presence of central fatigue. The twitch interpolation method is widely used in the literature as a measure of central fatigue, although it is not without limitation (Place *et al.*, 2008; Taylor, 2009). Place *et al*. (2008) used twitch interpolation to paradoxically demonstrate the presence of central fatigue in single mouse muscle fibres *in vitro*. The authors suggested an intracellular mechanism related to calcium handling could explain the additional force evoked by an interpolated twitch during fatigue and suggested the interpolated twitch technique might overestimate the extent of central fatigue (Place *et al.*, 2008). In a recent point/counterpoint debate, Taylor (2009) explained that motor nerve estimates of voluntary activation provide a measure of how much of the muscle's possible force is produced by voluntary contraction, but it does not measure descending drive or consider the non-linear input-output relationship of the motoneuron pool. These limitations notwithstanding, the use of the interpolated twitch technique is sufficient to reveal fatigue induced changes in voluntary activation in a range of muscle groups and exercise paradigms (Herbert & Gandevia, 1999; Todd *et al.*, 2003b; Goodall *et al.*, 2009; Taylor, 2009).

Cortical voluntary activation

A further limitation of the twitch interpolation method is that the exact site of failure cannot be identified. Recently, transcranial magnetic stimulation (TMS) has been used to measure the degree of central fatigue attributable to supraspinal mechanisms. A modified version of the twitch interpolation technique has been successfully validated and used to measure cortical voluntary activation in a range of muscle groups and exercise modes (Todd *et al.*, 2003b; Goodall *et al.*, 2009; Sidhu *et al.*, 2009a). A decrease in cortical voluntary activation implies that motor cortical output is sub-optimal and insufficient to activate all motor units to produce maximal force and is thought to indicate the presence of supraspinal fatigue, a sub-component of central fatigue (Taylor & Gandevia, 2008). Used in concert, peripheral and cortical methods of stimulation have the potential to reveal new insights into the aetiology of fatigue.

Motor evoked potentials (MEPs)

In addition to measures of cortical voluntary activation, EMG recording of the motor evoked potential (MEP) in response to stimulation of the motor cortex can be monitored at rest and during contraction to reveal changes in corticospinal excitability (Taylor & Gandevia, 2001). During voluntary contraction, both motor cortical neurons and motoneurons become more excitable and thus the same cortical stimulus will evoke a much larger MEP than that elicited at rest (Rothwell *et al.*, 1991). The MEP evoked during contraction is followed by a period of EMG silence, the length of which can be monitored to infer changes in spinal and/or intracortical inhibition (Inghilleri *et al.*, 1993; Taylor *et al.*, 1996; Taylor & Gandevia, 2001). Reductions in MEP size indicate a decrement in the responsiveness of the brain to muscle pathway (Brasil-Neto *et al.*, 1993; Brasil-Neto *et al.*, 1994). The exact site of this impairment can be further localised to the spinal cord through magnetic or electrical stimulation of the cervicomedullary tract. The resulting cervicomedullary evoked potential (CMEP) reflects the excitability of spinal motoneurons (Taylor, 2006). Stimulation at the cervicomedullary junction can be prohibitively painful however, and recording a valid CMEP is difficult in some motoneuron pools and participants (McNeil *et al.*, 2013). The assessment of CMEP size in the muscle groups responsible for locomotor/ambulatory exercise is currently limited because of these considerations (Sidhu *et al.*, 2012b).

Voluntary EMG

During exercise the EMG from voluntary muscle action can be recorded throughout as a surrogate of central motor drive (St Clair Gibson *et al.*, 2001b; Amann *et al.*, 2009) or to assess changes in peripheral function (Moritani *et al.*, 1992). During brief maximal contractions as fatigue manifests and voluntary force declines the amplitude of EMG also decreases, probably due to reduced firing rates (Gandevia, 2001) and a concomitant reduction in motor unit recruitment and/or fibre-type recruitment (Sogaard *et al.*, 2006). Peripheral changes might also explain the observed fatigue, as sarcolemmal excitability is altered with fatigue (Lepers *et al.*, 2002). During submaximal contractions, fatigue is characterised by an increase in the amplitude of voluntary EMG which has been suggested to reflect a compensatory increase in motor unit recruitment and/or motor unit firing rate to activate fatiguing motor units or recruit higher threshold ones (Enoka & Stuart, 1992; Dimitrova & Dimitrov, 2003; Taylor & Gandevia, 2008). Caution should be exercised however when interpreting changes in voluntary EMG during

exercise due to a number of technological limitations including surface EMG amplitude cancellation, decreases in firing rates independent of changes in recruitment and reflex effects at the spinal cord, amongst others (Farina *et al.*, 2002a; Farina *et al.*, 2002b; Weir *et al.*, 2006).

Perception of exertion and effort

Fatigue refers not only to a physical or physiological state but also has a cognitive element. This cognitive element is thought to have two components; the sense of effort required to maintain or increase exercise intensity (an efferent component), and the perception of exertion based on the physical symptoms induced by exercise (an afferent component) (Smirmaul, 2012; Swart *et al.*, 2012). The rating of perceived exertion (RPE) introduced by Borg (Borg & Dahlstrom, 1962; Borg, 1982b) acknowledged this distinction, with RPE described as "being an individual's total physical and psychic reaction to exertion" (Swart *et al.*, 2012). Controversy exists over the exact contribution of each to the sensations of fatigue elicited during exercise, and attempts have been recently made to develop a scale that could delineate the two (Swart *et al.*, 2012). Distinct neurological mechanisms have also been proposed to explain these components. The sense of effort has been shown to be strongly influenced by centrally generated corticofugal motor commands giving rise to corollary discharges that project directly onto the somatosensory cortex (Enoka & Stuart, 1992; Williamson *et al.*, 2006). A homeostatic afferent pathway that generates an interoceptive sense of self has been identified from functional imaging studies in the dorsal posterior insula that might explain the perception of exertion (Craig, 2002, 2003). This pathway is sensitive to a number of inputs including pain, temperature, touch and muscle sensations, giving the individual a conscious awareness of underlying subconscious homeostatic processes (Craig, 2003). The role of perception in contributing to the decline of force seen in a range of exercise tasks is relatively under studied in comparison to the role of physical factors (Barry & Enoka, 2007).

Summary

Fatigue has both a physical and perceptual component. The physical manifestation of fatigue is a reduction in the voluntary force produced by a muscle that can be attributed to central and peripheral mechanisms. Peripheral mechanisms of fatigue operate at, or distal to, the neuromuscular junction. Central fatigue is defined as a progressive

reduction in voluntary activation of a muscle. A sub-component of central fatigue is supraspinal fatigue, which reflects a suboptimal output from the motor cortex. The perceptual component of fatigue has both efferent and afferent components, and remains an under-studied area in comparison to the physical component. These mechanisms of fatigue can be studied using voluntary and evoked contractions, changes in EMG parameters and perceptual scales of effort and exertion. A number of techniques are thus available to scientists to study the aetiology of fatigue during exercise; the results of such study will be discussed in the following section which will critically discuss the task-dependent nature of exercise-induced fatigue.

2-9 Mechanisms of exercise-induced fatigue

The prevailing mechanism limiting exercise performance varies depending on a number of factors including the type of muscle action involved (isometric, isokinetic, locomotor), whether exercise is sustained or intermittent, the muscle groups employed (e.g. biceps femoris vs. vastus lateralis, running vs. skiing vs. cycling), the duration and intensity of exercise and the age and/or sex of the participants under study. In short, fatigue is largely task-dependent, and this task-dependency has been identified as the central issue in the study of fatigue (Enoka & Stuart, 1992; Barry & Enoka, 2007). As discussed previously (sections 2-6 to 2-7) the prevailing cause of fatigue can arise from a range of both central and peripheral mechanisms, and the dominant contributor will depend on the exercise task.

Sustained maximum muscle actions

Even in short-duration maximum voluntary efforts, the application of electrical and magnetic stimulation can elicit a superimposed twitch, indicating that either motor unit recruitment or firing frequency is sub-optimal (Gandevia, 2001). As the duration of the maximum voluntary effort is maintained, force will decline as fatigue develops. During the early part of the bout this decline can be attributed almost exclusively to peripheral factors (Bigland-Ritchie *et al.*, 1978; Schillings *et al.*, 2003). Peripheral fatigue during sustained MVC is manifested as a reduction in twitch force and slowed twitch dynamics, with no change in M-wave parameters, suggesting that the contractile machinery, and not impulse propagation, is impaired (Bigland-Ritchie *et al.*, 1978). Evidence of central fatigue, where voluntary force declines more rapidly than the force

that can be elicited through stimulation, is manifest as the contraction is prolonged (Thomas *et al.*, 1989; Schillings *et al.*, 2003). Schillings *et al*. (2003) reported the decline in voluntary force during the first minute of a 2 min maximal contraction of the biceps is almost exclusively attributable to peripheral factors. After 60 s, peripheral fatigue levels off and the remaining drop in force can be explained by central mechanisms of fatigue (Schillings *et al.*, 2003). Interestingly, the early dominance of peripheral fatigue in maximum voluntary exercise tasks can also be extended to locomotor exercise (see subsequent sections).

It is also worth noting that peripheral fatigue is the dominant contributor to the observed decline in force in this type of short-duration "all-out" task. Kent-Braun (1999) assessed voluntary force and twitch responses pre- and post- a 4 minute maximum contraction of the ankle dorsi-flexors and reported an estimated 80% contribution of peripheral mechanisms to the observed decrement in force. Integrated EMG, pH and force all declined in parallel, providing evidence of a feedback loop between intramuscular metabolism and central motor drive that has since been extended to locomotor exercise (Amann *et al.*, 2009; Amann, 2011).

During sustained maximal contractions the use of TMS has revealed part of the observed central fatigue can be explained by corticospinal changes. The development of fatigue during an MVC is accompanied by an increase in the superimposed twitch evoked by motor cortex stimulation, indicating the presence of supraspinal fatigue (Todd *et al.*, 2005). Todd *et al*. (2005) estimated a 25% contribution of supraspinal processes to the force loss observed during a 2 min maximum contraction of the elbow flexors. In addition to changes in superimposed twitch, MEP size increases during sustained MVC. This increase was previously thought to indicate enhancements in the excitability of motoneurons in the motor cortex and/or spine (Taylor *et al.*, 1996). Further work from the same research group used both motor cortical and cervicomedullary stimulation methods during the silent period following TMS to assess the contribution of cortical and spinal mechanisms to the observed fatigue in the absence of voluntary drive (McNeil *et al.*, 2009; McNeil *et al.*, 2011b). These studies revealed rapid reductions in motoneuron excitability during MVC that are compensated for by sufficient on-going voluntary drive. Reductions in motoneuron excitability were attributed to changes in intrinsic motoneuron properties caused by repetitive discharge

(McNeil *et al.*, 2011b). This conclusion was based on the observation that increased muscle spindle discharge had no impact on the observed fatigue (McNeil *et al.*, 2011b), and there was no difference in the evoked potentials elicited by motor cortex and cervicomedullary stimulation (McNeil *et al.*, 2009), thereby indicating neither a decreased muscle spindle afferent input nor a change in motor cortical excitability could explain the observed fatigue.

Submaximal contractions

During submaximal contractions (sustained or intermittent) the extent of fatigue is dependent on the strength of the contraction. At low fractions of MVC (< 30%) the contribution of central fatigue is substantially higher than that observed at higher-intensity submaximal contractions (> 30% MVC) where peripheral fatigue predominates and central fatigue is modest or absent (Bigland-Ritchie *et al.*, 1986a; Eichelberger & Bilodeau, 2007; Yoon *et al.*, 2007). Burnley *et al*. (2012) investigated the neuromuscular fatigue associated with submaximal, intermittent contractions around critical torque. These authors showed that the critical torque represented a distinct point above which the rate of peripheral fatigue development accelerates. Central fatigue, measured as a reduction in voluntary activation, progressively increased as the exercise intensity above critical torque decreased, and thus duration increased. To illustrate, at exercise intensities just above critical torque, exercise duration was 18 min on average and accompanied by a 24% drop in VA. At the highest exercise intensity, where exercise duration was 3 min, the drop in VA was only 6%. In contrast, the drop in potentiated twitch (i.e. degree of peripheral fatigue) was not different between trials, providing evidence for the existence of a threshold for peripheral fatigue during exercise to exhaustion above critical torque (Burnley *et al.*, 2012).

Unlike maximal activity, submaximal muscle activity does not induce maximal motor unit recruitment, and thus changes in descending drive occur to counteract the reduction in force due to fatigue (St Clair Gibson *et al.*, 2001a). This is manifested as a rise in EMG, reflecting an increase in motor unit recruitment and/or motor unit firing rate (Dimitrova & Dimitrov, 2003). The size of the cervicomedullary evoked potential (CMEP) also rises during a sustained submaximal effort (Levenez *et al.*, 2008; Hoffman *et al.*, 2009), but this is likely a result of the increased excitatory drive to motoneurons as a result of the progressive increase in voluntary EMG rather than an increase in

motoneuron excitability *per se* (Levenez *et al.*, 2008). To assess this, McNeil *et al*. (2011a) studied the behaviour of the motoneuron pool when voluntary EMG (rather than torque) was held constant at 25% of that observed during a "fresh" MVC. Similar to their work on sustained MVCs, these authors assessed the MEP and CMEP response during the silent period following TMS, allowing the assessment of cortical and spinal contributions to fatigue in the absence of voluntary drive. McNeil *et al*. (2011a) showed that reductions in motoneuron excitability were responsible for the observed reduction in MEP and CMEP, a finding later attributed to changes in intrinsic motoneuron properties (McNeil *et al.*, 2011b). Interestingly, when the TMS stimulus was high, and therefore capable of activating higher threshold motor units, the reduction in MEP and CMEP was much less, suggesting the presence of task-dependent fatigue that is specific to the low-threshold motor units dominant in the exercise bout (McNeil *et al.*, 2011a).

Motor cortex stimulation has been successfully used to demonstrate the presence of supraspinal fatigue during prolonged weak contractions of the elbow flexors (Sogaard *et al.*, 2006; Smith *et al.*, 2007). Both studies demonstrated an increase in the superimposed twitch evoked by TMS that progressively increased as the exercise bout was prolonged. These results demonstrate that high levels of motor output or recruitment of a high proportion of the motoneuron pool are not required for the development of supraspinal fatigue (Taylor & Gandevia, 2008). A lengthened silent period, indicating increased cortical inhibition, and an increase in MEP size also occurs in response to submaximal contractions (Taylor *et al.*, 1996). The increase in MEP size suggests increases in corticospinal excitability, however as previously discussed this increase should be considered with respect to the presence of volitional drive, as when this is absent MEP and CMEP size are reduced and thus excitability is impaired (McNeil *et al.*, 2011a).

Fatigue during locomotor exercise

The aetiology of fatigue during locomotor exercise is influenced by the type and duration of exercise (Enoka & Stuart, 1992; Barry & Enoka, 2007). A number of studies have attempted to characterise fatigue development during locomotor exercise, with the available literature suggesting a time- and intensity-dependent contribution of peripheral and central mechanisms. Generally, short duration high-intensity exercise is primarily

limited by mechanisms of peripheral fatigue, whilst central fatigue becomes exacerbated as the exercise bout is prolonged.

Lepers *et al*. (2002) and Place *et al*. (2004) investigated fatigue development during prolonged (5 h) bouts of constant intensity cycling and running respectively. Using electrical stimulation methods after each hour of exercise, peripheral fatigue (reduced evoked twitch and contraction time) was manifested after the first hour of exercise (Lepers *et al.*, 2002) whereas failure of activation was only evident after 4 h of running and 5 h of cycling (Lepers *et al.*, 2002; Place *et al.*, 2004). These central impairments were accompanied by reductions in M-wave amplitude, indicating membrane excitability was impaired. Similar findings with regards impaired membrane excitability and voluntary activation have also been reported after 2 h of cycling exercise (Lepers *et al.*, 2000) and during a simulated Tour de France (Ross *et al.*, 2010b).

The observed mechanisms of fatigue during less prolonged (< 2 h) endurance exercise are similar, with reductions in voluntary activation and peripheral twitch responses widely reported (Millet *et al.*, 2003; Sidhu *et al.*, 2009b; Ross *et al.*, 2010a; Decorte *et al.*, 2012). There is less clear evidence of the contribution of transmission failure (i.e. M-wave reductions) to the observed fatigue, with some authors reporting reductions (Millet *et al.*, 2003) and others observing no change (Ross *et al.*, 2010a). The kinetics of fatigue follow a similar pattern to longer duration exercise, with evidence of peripheral impairments occurring early in the exercise bout and central fatigue becoming exacerbated later (Ross *et al.*, 2010a; Decorte *et al.*, 2012). Ross *et al*. (2010a) reported that reductions in VA were only evident in the final 5 km of a self-paced 20 km treadmill run. Decorte *et al*. (2012) measured fatigue during intermittent exercise consisting of repeated 6 min bouts at 80% of aerobic power until task failure, showing most of the peripheral fatigue occurred by 50% of the exercise bout, with reductions in VA manifest only after 80% of the exercise duration, and no change in the M-wave characteristics. Collectively these studies suggest that peripheral fatigue develops early during fatiguing locomotor endurance exercise, central fatigue manifests later, and alterations in membrane excitability are likely when the exercise bout is > 2 hours.

A limited number of studies have adopted TMS protocols to investigate the mechanisms of central fatigue during locomotor exercise. Those studies that have adopted these

techniques have successfully demonstrated the presence of supraspinal fatigue in a range of locomotor exercise paradigms (Ross *et al.*, 2007; Sidhu *et al.*, 2009b; Goodall *et al.*, 2012a; Sidhu *et al.*, 2012a; Sidhu *et al.*, 2013b). In addition it has been demonstrated that the degree of supraspinal fatigue is exacerbated during exercise in hypoxia (Goodall *et al.*, 2012a) and could be modulated by pharmacologically manipulating brain neurotransmitters, specifically noradrenaline (Klass *et al.*, 2012). More recent research using a novel experimental set up has demonstrated the potential use of TMS to measure corticospinal responses during locomotor exercise (Sidhu *et al.*, 2012a; Sidhu *et al.*, 2013b). These studies suggest a supraspinal inhibition (decreased MEPs, increased intracortical inhibition) that is compensated for by increased motoneuron excitability (increased CMEPs) during exhaustive cycling exercise. Collectively, these studies demonstrate the potential for this technique to reveal a more comprehensive understanding of the aetiology of fatigue.

Summary

The measurement of neuromuscular fatigue during exercise has received much attention. Studies assessing the relative contribution of central and peripheral mechanisms to fatigue demonstrate that fatigue is largely task-dependent. Due to the difficulty of standardising conditions, and the awareness that fatigue dissipates rapidly on exercise cessation (Power *et al.*, 2010; Froyd *et al.*, 2013), most of these experimental protocols have sacrificed ecological validity in favour of more robust experimental control. Consequently the data on fatigue during self-paced exercise is limited and the field of research has been criticised for the apparent negligence of the role of perceived effort in contributing to the decline of force (Barry & Enoka, 2007). Recent efforts have been made to better understand the biological basis of fatigue with the proposal of a new model that could explain the aetiology of fatigue regardless of the exercise task. The evidence for this model will be considered in the following section with particular emphasis on the development of fatigue during self-paced exercise.

2-10 Fatigue during self-paced exercise; Limitations vs. Regulation

Previous research has largely implicated fatigue through a number of linear cause and effect models. For example, it has been suggested that fatigue might be caused by attainment of high core temperature (Gonzalez-Alonso *et al.*, 1999; Walters *et al.*,

2000), depletion of muscle glycogen (Callow *et al.*, 1986), or metabolite accumulation (Bangsbo *et al.*, 1996). Within these models, exercise intensity is dictated by the inability of an organism to maintain homeostasis of an individual physiological system (Abbiss & Laursen, 2005). As the study of fatigue spans several disciplines, the explanation and definition of this concept is often defined to best suit the discipline. For example neuroscientists and biomechanists define fatigue as impairment in force output, psychologists view fatigue as a sensation of tiredness, and physiologists have viewed fatigue as the failure of a specific physiological function (Abbiss & Laursen, 2005). It has been argued that this type of fragmented, reductionist approach to fatigue, where one factor is implicated as the "cause" of fatigue or a "limit" beyond which exercise can't continue, provides an incomplete assessment of a complex phenomenon (Lambert *et al.*, 2005).

A group of influential scientists from South Africa have attempted to advance the study of the aetiology of fatigue by proposing a new model that could explain the development of fatigue in all exercise conditions (Noakes, 1988, 1997; St Clair Gibson *et al.*, 2003; Noakes *et al.*, 2004; St Clair Gibson & Noakes, 2004; Lambert *et al.*, 2005; Noakes *et al.*, 2005; St Clair Gibson *et al.*, 2006). These authors proposed current understanding attributed fatigue during exercise to a peripherally based, metabolite induced failure of contractile function, due principally to the failure of the cardiovascular system to supply oxygen to the active muscle(s). Noakes (1997) termed this the cardiovascular, anaerobic or catastrophe model of fatigue, and traced its' origins to pioneering work by Fletcher and Hopkins (Fletcher, 1907) and Archibald Vivian Hill in the 1920's. Fletcher (1907) showed that lactic acid was spontaneously produced under anaerobic conditions in excised amphibian skeletal muscle. These concentrations fell in the presence of oxygen and increased when the muscle was stimulated to contract. When Hill and colleagues (Hill *et al.*, 1924c, a, b; Hill & Kupalov, 1930) observed a rise in lactic acid in skeletal muscle as a result of exercise, they interpreted it as evidence that the exercising muscle was working in an anaerobic environment; indicating that the oxygen supply was inadequate for the metabolic demands. Further experiments by the same group seemingly demonstrated the existence of a maximum oxygen uptake ($\dot{V}O_2$) during running exercise where "however much the speed be increased … no further increase in oxygen intake can occur. At higher speeds the requirement of the body for oxygen … cannot be satisfied … lactic acid accumulates, a

continuously increasing oxygen debt being incurred, fatigue and exhaustion setting in" (Hill *et al.*, 1924c). Thus arose the concept that an inadequate oxygen supply limits high intensity exercise performance.

Hill hypothesised the inadequacy in oxygen supply was the result of a cardiac output limitation. Hill theorised the existence of a "governor" in the heart or brain that functioned to prevent the development of myocardial ischemia during maximal exercise, although subsequent models based on Hill's theory seemed to ignore this collary (Noakes & St Clair Gibson, 2004). Noakes & St Clair Gibson (2004) termed these the cardiovascular/anaerobic/catastrophe models of exercise physiology. Perhaps the most pivotal example was the study by Taylor *et al*. (1955) that reported an absolute "ceiling" in oxygen uptake in 94% of participants during repeated laboratory testing; although paradoxically they also observed an increase in the "maximum" oxygen uptake with the addition of a greater amount of exercising muscle mass.

Noakes & St Clair Gibson (2004) argued the cardiovascular/anaerobic/catastrophe model ignored the role of sensory feedback and the central nervous system in the regulation of exercise intensity and that the study of fatigue had been restricted by the prevailing study of "limitations" to exercise performance. The subsequent implementation of exercise protocols to study fatigue involved the researcher dictating exercise intensity (e.g. incremental or constant load tests); protocols that did not represent real-life exercise and encouraged the view of fatigue as an absolute occurrence or event. In a landmark series of papers an alternative complex systems model of fatigue was proposed; termed the "central governor model" (Noakes *et al.*, 2004; Lambert *et al.*, 2005; Noakes *et al.*, 2005). This model (Figure 2-7) proposed that the central nervous system, through a system of feed-forward control modifiable by afferent sensory feedback, regulates skeletal muscle recruitment and subsequent exercise intensity in an anticipatory manner to protect against severe, or "catastrophic", threats to homeostasis (Noakes & St Clair Gibson, 2004). Central to this model is the concept of "regulation" of exercise intensity. Rather than an absolute event, fatigue in this model is considered as a process, the conscious manifestation of which is the sensation of fatigue experienced by the exerciser (St Clair Gibson *et al.*, 2003).

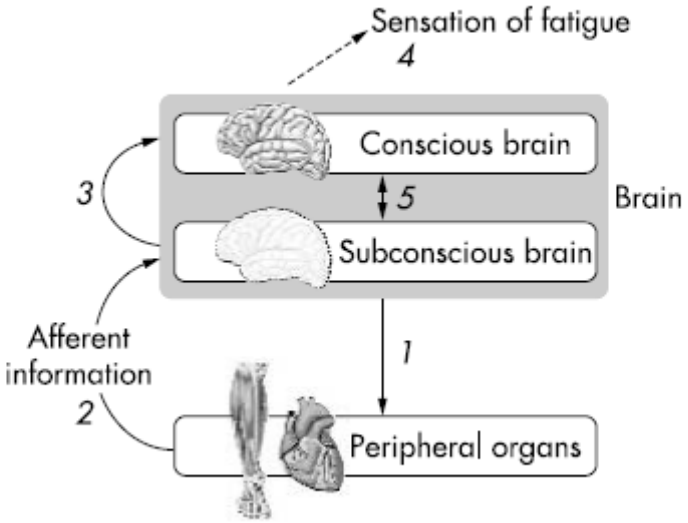


Figure 2-7. The original central governor model of exercise regulation, as presented in 2004 by Noakes & St Clair Gibson.

The central governor model is an extension of the teleoanticipation model originally proposed by Ulmer in 1996. Ulmer (1996) suggested the presence of a central "programmer", most likely operating at a subconscious level, which predicts the metabolic demand of an activity and pre-emptively sets the exercise intensity to complete the task whilst protecting homeostasis. A key feature of teleoanticipation is that knowledge of the endpoint of exercise acts as a controlling variable so that the central nervous system can select and continuously modify exercise intensity in an anticipatory manner (Noakes *et al.*, 2004; Lambert *et al.*, 2005). Ulmer (1996) also described a feedback control loop between efferent neural command to skeletal muscle, and the associated subsequent afferent input from mechano- and chemo-receptors which would feedback to the central programmer and influence or modify intensity accordingly. This afferent feedback might arise from both muscle and peripheral organs and could be influenced by endogenous reference signals, prior experience and training, all of which might alter interpretation of this afferent input (Ulmer, 1996). The complex systems model elaborated on these concepts, explaining how different physiological systems are regulated during exercise in a complex, dynamic, non-linear manner to protect against "catastrophic" disruptions to homeostasis in response to the exercise bout (Lambert *et al*., 2005).

A key distinction of the central governor model is the redefining of fatigue from a term that describes an exercise-induced decline in the force producing capability of muscle, to one of sensation or emotion (St Clair Gibson *et al.*, 2003). The sensation of fatigue is proposed to reflect the conscious perception of subconscious control processes that acts as a restrainer or modulator of exercise intensity (Lambert *et al.*, 2005). This interpretation is supported by data from a number of studies reviewed by Craig (2003), which collectively identify a homeostatic afferent pathway that represents the physiological condition of all tissues of the body. Using functional imaging techniques, a primary interoceptive representation has been identified in the dorsal posterior insula that is sensitive to pain, temperature, itch, touch, muscle and visceral sensations, and which generates a subsequent sensation or motivation. This concept of a conscious awareness, formed from sensations that represent the underlying homeostatic condition of the individual, is consistent with previous ideas (Damasio, 1993) and imaging studies that correlate homeostatic processing with emotional awareness (Damasio *et al.*, 2000; Critchley *et al.*, 2002). With this distinguishing feature, the complex systems model of fatigue has gone some way to address the previous omission of the role of perception in the reduction in force generating capacity (Barry & Enoka, 2007).

The redefinition of fatigue as a sensation has placed extra emphasis on the role of the rating of perceived exertion (RPE) during exercise. The RPE provides a measure of the conscious sensations associated with the integration of afferent sensory information from peripheral physiological systems (Borg, 1982b). The RPE also reflects the perception of effort, which describes the sensations associated with the requirement for efferent output during exercise. These efferent and afferent components can be differentiated (Swart *et al.*, 2012) although most research tends to ascribe the afferent component to RPE. Tucker (2009) has recently proposed the conscious perception of exertion is not only the result of an integration of afferent feedback, but also plays a role in the anticipatory regulation of exercise intensity. Specifically, Tucker (2009) proposed the existence of a subconscious "template" RPE set in advance of the exercise bout. The template is generated as a result of previous experience and knowledge of the exercise duration and/or distance, and is used as an anchor throughout an exercise bout to ensure a desired rate of increase of RPE and attainment of a maximum tolerable RPE only at the end of the exercise bout (Tucker, 2009; Tucker & Noakes, 2009). This proposition

was subsequently incorporated in to updated versions of the central governor model (Noakes, 2011b, 2012).

Does the CGM exist?

A number of research groups have provided critiques of the central governor model of fatigue at various stages of its development (Bassett & Howley, 1997; Bergh *et al.*, 2000; Weir *et al.*, 2006; Brink-Elfegoun *et al.*, 2007b; Marcora, 2008b; Shephard, 2009; MacIntosh & Shahi, 2011). Many of these have focussed on the posited plateau in oxygen uptake at high aerobic intensities and the factors that limit $\dot{V}O_2$max. The CGM predicts that during maximal exercise to exhaustion, the brain regulates skeletal muscle recruitment, and therefore peripheral blood flow, in order to limit the work of the heart and prevent the development of myocardial ischemia (Noakes, 2011a). Opponents of the CGM argue that the peak $\dot{V}O_2$ is limited by the physiological factors underpinning the Fick equation and oxygen delivery to the muscle, not by the amount of muscle that the brain is "willing" to recruit (Bassett & Howley, 1997; Brink-Elfegoun *et al.*, 2007b; Marcora, 2008b; Shephard, 2009). Proponents of the CGM have pointed to the low incidence of a plateau in oxygen uptake during incremental tests (St Clair Gibson & Noakes, 2004), even in elite endurance athletes (Doherty *et al.*, 2003), as indirect evidence for central regulation. Furthermore others have demonstrated achievement of higher maximum $\dot{V}O_2$ values using non-traditional self-paced (Mauger & Sculthorpe, 2012) and decremental (rather than incremental) (Beltrami *et al.*, 2012) protocols. However, opponents of the CGM argue that a maximum $\dot{V}O_2$ is routinely demonstrated in healthy adults with appropriate methodology (Shephard, 2009), and is consistent in shorter duration bouts where the extent of skeletal muscle recruitment is larger but the measured peak $\dot{V}O_2$ is unchanged (Brink-Elfegoun *et al.*, 2007a). Moreover, there is evidence that the heart maintains a reserve at $\dot{V}O_2$max but this has been interpreted to both support (Elliott *et al.*, 2013) and oppose (Brink-Elfegoun *et al.*, 2007b) a central nervous system governor.

The focus on the limiting factors to maximum oxygen uptake is perhaps an unfortunate consequence of some of the early iterations of the CGM, which heavily criticised the proposed "traditional model" of exercise physiology interpreted from A.V. Hill's early work. There is however potential for both models to co-exist, and the presence or absence of a plateau in this context provides neither support nor refutation for a central

governor model of exercise performance. Cheung (2009) elegantly conceptualised this, describing the CGM as a behavioural mechanism that regulates exercise intensity in most circumstances, with the traditional model acting as a safety measure only when this regulation is insufficient. The behavioural or perceptual limit imposed by a proposed central governor is either effort (Marcora, 2008b) and/or exertion (St Clair Gibson *et al.*, 2003) moderated, and only in extreme cases (i.e. death, collapse) are both mechanisms over-ridden by the conscious will of the exerciser (St Clair Gibson *et al.*, 2013). Thus it would seem unreasonable to suggest an ultimate physiological limit does not exist given that these limits are exceeded on rare occasions in extreme circumstances (St Clair Gibson *et al.*, 2013). Equally the role of the brain in the regulation of exercise performance is clearly important, but whether the central governor model is actually needed to describe this is open to debate (Marcora, 2008b).

Other critiques of the CGM have identified further limitations of the model and the evidence used to support it. The use of EMG as an indicator of motor unit recruitment has been questioned (Weir *et al.*, 2006), as has the applicability of the model to all fatiguing tasks, particularly those of a very short duration (e.g. sustained MVCs) where decrements in force are evident within seconds of exercise commencing (Gandevia, 2001) and are difficult to explain with the CGM (Weir *et al*., 2006). The CGM also omits any contribution of fatigue at the spinal level, which has been demonstrated in a number of exercise paradigms (Garland & McComas, 1990; Walton *et al.*, 2002; Levenez *et al.*, 2008). Proponents of the CGM have also been criticised for a lack of experimental data to support their model (Shephard, 2009). This is particularly true when examining the neuromuscular basis of fatigue during self-paced exercise, where the available evidence is limited (Amann & Dempsey, 2008; Amann *et al.*, 2009; Ross *et al.*, 2010a; Froyd *et al.*, 2013). Collectively, these studies have led some to suggest a general model that considers the task-dependent nature of fatigue is a more accurate description of a complex phenomenon (Weir *et al.*, 2006).

Despite these criticisms, there are a number of observations and original studies that have provided support for the key corollaries of the CGM; namely the concept of anticipatory regulation, the importance of afferent feedback as a modifier of exercise intensity, and the role of the brain and central nervous system in determining exercise intensity. These observations cannot be explained by any other model of exercise

physiology (Noakes, 2011a), and in this respect the CGM currently represents the best explanation of how exercise performance is regulated, particularly during self-paced exercise. Figure 2-8 summarises the most recent iteration of the CGM and the studies providing evidence to support it (Noakes, 2012). These studies are discussed in the proceeding sections.

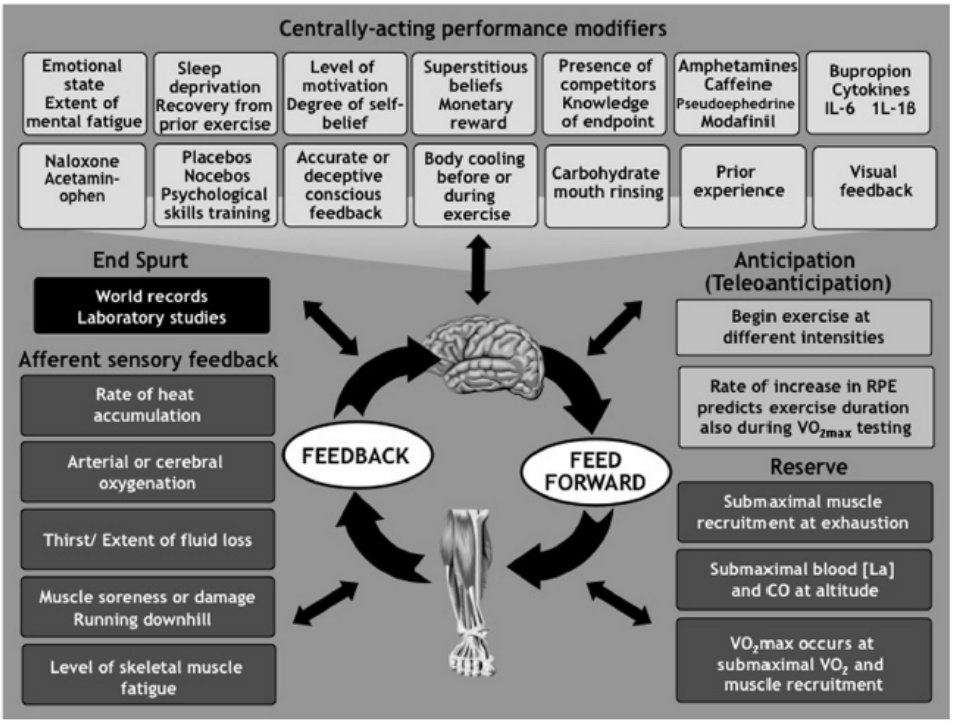


Figure 2-8. The most recent iteration of the central governor model of exercise regulation and the evidence to support the key components of this model. From Noakes (2012).

Evidence for anticipatory regulation of exercise performance

Evidence for anticipatory regulation of exercise performance can be found in the simple observation that starting speed in a race is dependent on the expected duration of that race, and that even when participants are told to run maximally, over longer durations speed is always submaximal (Ulmer, 1996). A number of lines of evidence exist that demonstrate the presence of anticipatory regulation during exercise (Ansley *et al.*, 2004a; Ansley *et al.*, 2004b; Marino, 2004; Castle *et al.*, 2006) and the role of RPE in this process (Tucker, 2009; Tucker & Noakes, 2009). These include the observation that RPE increases linearly over time during constant load exercise (Nethery, 2002; Baldwin *et al.*, 2003; Joseph *et al.*, 2008), that this increase can be used to accurately predict time to exhaustion (Crewe *et al.*, 2008) and has a scalar quality as the increase in RPE is

proportional to the duration of the exercise (Noakes, 2004). The rate of increase in RPE during constant load exercise is augmented in conditions of high temperature (Nybo & Nielsen, 2001b; Crewe *et al.*, 2008), low muscle glycogen (Rauch *et al.*, 2005) and reduced oxygen availability (Noakes, 2004). During self-paced exercise, RPE also increases linearly and in proportion to the relative duration/distance of exercise (Joseph *et al.*, 2008). In response to environmental manipulations, exercise intensity is modified in an anticipatory manner to ensure the rate of increase in RPE stays the same; e.g. exercise intensity is reduced in hot (Tucker *et al.*, 2006c) and hypoxic (Joseph *et al.*, 2008) conditions, and is increased in hyperoxia (Tucker *et al.*, 2007).

A distinguishing observation of the central governor model is that the CNS modifies skeletal muscle motor unit recruitment in an anticipatory manner in order to maintain a motor unit or metabolic reserve (Swart *et al.*, 2009a). The most obvious evidence for such a reserve is the "end spurt" phenomena; where athletes increase their speed at the end of endurance events, theoretically when they are most fatigued (Noakes, 2012). Support for the role of the CNS in maintaining a metabolic reserve has also been demonstrated by studies employing repeated sprints during long duration cycling exercise (Kay *et al.*, 2001; St Clair Gibson *et al.*, 2001b). These studies showed that the decline in sprint performance over the course of exercise was paralleled by reductions in iEMG activity, indicating a regulation of motor unit recruitment by the CNS. In addition, all participants increased power output, in conjunction with increased iEMG, on the final sprint, suggesting the presence of a subconsciously controlled motor unit reserve (Kay *et al.*, 2001; St Clair Gibson *et al.*, 2001b). Further support for the concept of a "neural reserve" comes from observations that artificially stimulated muscles can produce greater maximum force output than can be achieved voluntarily *in vivo* (Enoka, 1995), and classic studies from Ikai & Steinhaus (1961) that showed an increase in "maximum" force after a number of psychological interventions including hypnosis, shouting and unexpected gun-shots. Finally, the observation of the "lactate paradox" at high altitude, where recruitment of motor units is reduced in conditions of severe hypoxia and restored with supplemental oxygen in conjunction with an increase in motor unit recruitment (Kayser *et al.*, 1994) cannot be explained by peripherally based models of fatigue and suggests a controlling role of the CNS.

Evidence for the importance of afferent feedback as a modifier of exercise intensity

A series of elegant studies by Amann and colleagues (2006a; 2006b; 2008; 2009; 2011; 2011) have provided the strongest available evidence on the role of afferent feedback and its interaction with the CNS in the regulation of intensity during self-paced locomotor exercise. These authors hypothesised that exercise-induced alterations of the metabolic milieu, and associated peripheral muscle fatigue, provides inhibitory feedback to the CNS that influences the magnitude of central motor drive to the muscle (Figure 2-9). During exercise, the metabolic state of the muscle is communicated via projection of metabosensitive group III and IV thin fibre muscle afferents that relate information to the CNS on the current (and changing) metabolic milieu in the muscle (Amann, 2011). The CNS then modifies skeletal muscle recruitment accordingly. Thus afferent feedback as a consequence of locomotor muscle fatigue is proposed to have a direct inhibitory effect on central motor drive.

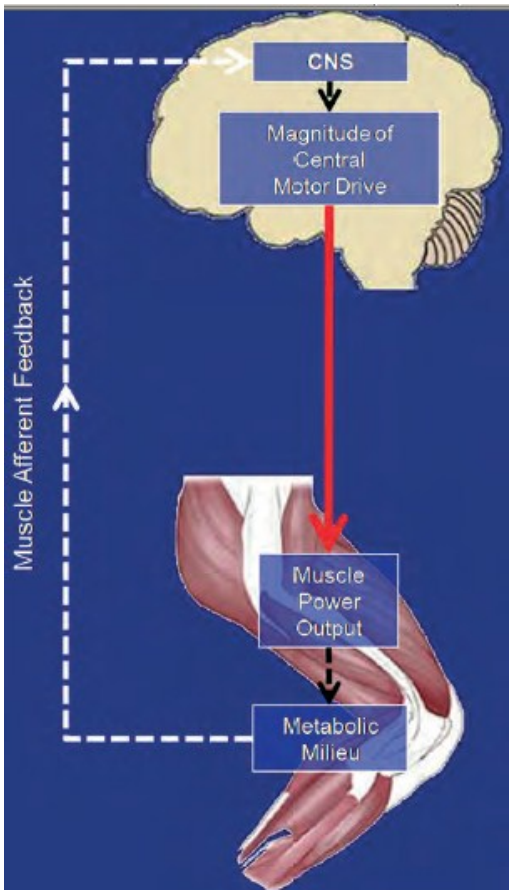


Figure 2-9. Proposed interaction between the central nervous system and afferent feedback from the muscle during exercise. The solid line indicates the central motor drive to the locomotor muscle; the dashed line indicates neural feedback from thin-fibre muscle afferents. From Amann (2011).

Amann *et al*. (2006a) first tested this hypothesis by altering arterial oxygen content through manipulation of the fraction of inspired oxygen (F_IO_2) during self-paced 5 km time-trials and constant load trials to exhaustion. As expected, performance in these trials worsened in hypoxia, and improved in hyperoxia. A novel and interesting finding of this study was the existence of a remarkably similar end-trial peripheral fatigue; that is, potentiated quadriceps twitch force measured in response to supra-maximal magnetic femoral nerve stimulation dropped by a similar amount (~35%) in each trial. The authors suggested the existence of an individual critical threshold for peripheral fatigue and associated sensory tolerance limit that could not be voluntarily exceeded (Amann *et al.*, 2006a). Amann & Dempsey (2008) followed up this work with an exercise intervention that modified the level of locomotor muscle fatigue prior to a self-paced 5 km time-trial, such that participants began each trial with different levels of pre-existing fatigue. This study again provided support for a critical threshold of peripheral fatigue. Participants moderated their 5 km time-trial performance through alterations in central motor drive such that when pre-fatigue was greatest, overall performance was worse and vice versa. Despite differences in the pre-trial level of locomotor muscle fatigue, the decrement in potentiated twitch force was again remarkably similar between trials. These studies provided support for the working hypothesis that locomotor muscle fatigue has an inhibitory effect on central motor drive during exercise.

To provide further evidence for the role of group III/IV afferents in the modification of central motor drive, three further studies were conducted that involved attempts at blocking the projection of these afferents (Amann & Dempsey, 2008; Amann *et al.*, 2009; Amann *et al.*, 2011). These studies would thus circumvent the potential confounding effects of the previous interventions (pre-fatigue and hypoxia/hyperoxia) on central fatigue, and address the criticism by Marcora (2008a) that the consistency in end-trial peripheral fatigue was simply a function of the task and required motor unit contribution.

In the first of these studies, Amann *et al*. (2008b) had trained cyclists perform two 5 km time-trials with and without lumbar epidural anaesthesia via administration of lidocaine. Administration of the anaesthetic blocked afferent feedback but also negatively impacted peripheral motor nerves such that efferent output was compromised. This was evidenced by lower pre-trial MVC and quadriceps VA, and worse time-trial

performance in the lidocaine trial, despite higher drive throughout. These limitations notwithstanding, the observation of a higher central drive in the absence of afferent feedback supported the suggestion of an inhibitory influence of somatosensory feedback from fatiguing locomotor muscles. However, the confounding effects of the anaesthetic on efferent output did not allow for adequate testing of the role of afferent feedback on exercise performance and the development of exercise-induced fatigue.

To circumvent the negative impact of lidocaine on efferent output, these authors subsequently used fentanyl, an opioid analgesic, to selectively block activity of afferent sensory pathways (Amann *et al.*, 2009; Amann *et al.*, 2011). In the first of these studies, trained competitive cyclists completed three self-paced 5 km time-trials: control, placebo (interspinous ligament injection of saline) and fentanyl (intrathecal injection). The impairment of afferent feedback from locomotor muscles resulted in a higher central motor drive and power output for the first 2.5 km of the trial (Figure 2-10). The final 2.5 km was completed with a similar level of central motor drive compared to placebo and control conditions, but interestingly power output was lower, suggesting dissociation between central drive and the response of the contractile machinery (Figure 2-10). The change in quadriceps twitch force post-exercise was greater post-exercise in the fentanyl trial (−46%) compared to the placebo trial (−33%), an important finding that indicated the "uninformed" or "naïve" CNS allowed the development of peripheral fatigue beyond the aforementioned sensory tolerance limit that is not normally voluntarily exceeded. In a subsequent study, Amann *et al*. (2011) employed a similar experimental method but with constant-load exercise to the limit of tolerance to better assess the impact of blocking ascending sensory feedback on endurance performance. Supporting their previous work, participants demonstrated enhanced central motor drive throughout constant-load exercise when sensory feedback was blocked, and peripheral fatigue was again exacerbated compared to placebo (Figure 2-11, −44% vs −34%; Amann *et al.*, 2011). Interestingly, despite a higher central drive throughout, time to the limit of tolerance was lower when afferent feedback was blocked (Figure 2-12). In both these studies, efferent motor output was unimpaired as indicated by no differences in the pre-trial MVC and peripheral twitch characteristics.

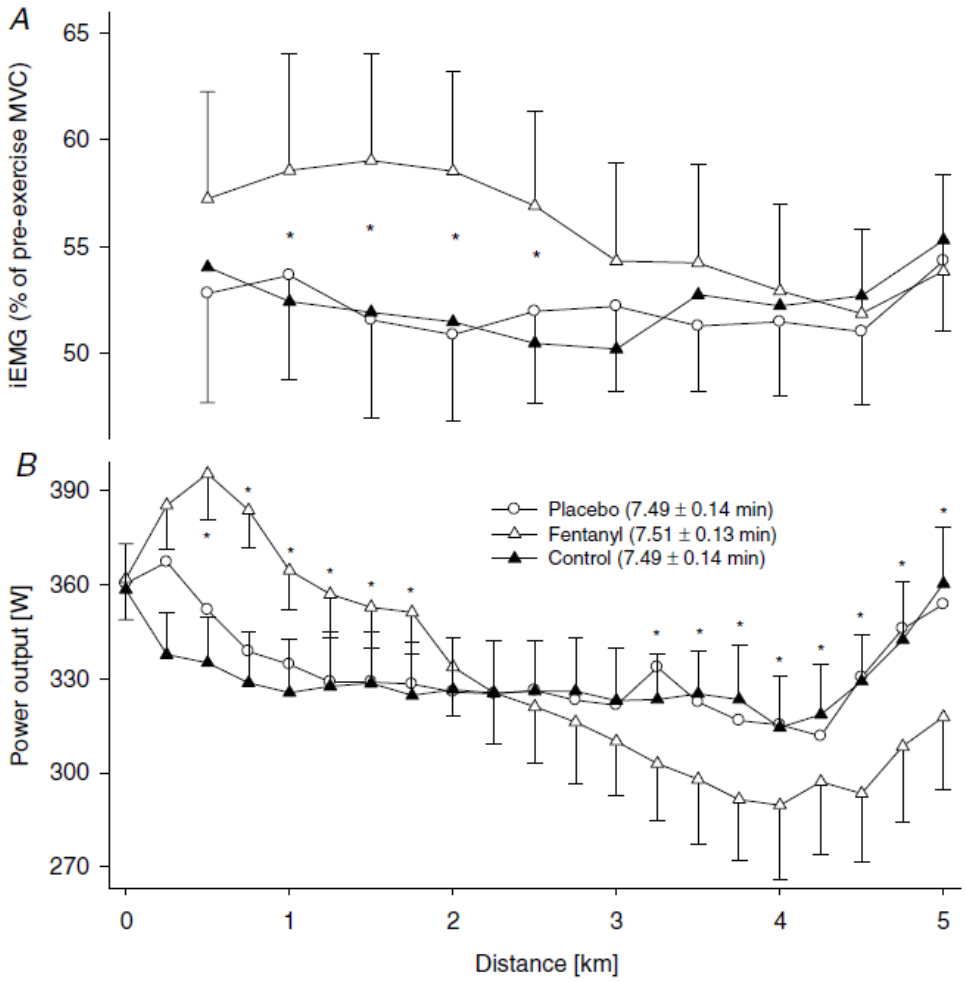


Figure 2-10. Integrated EMG of vastus lateralis (A) and power output (B) during self-paced 5 km time-trials under conditions of an intact CNS (Placebo, Control) and when sensory feedback is selectively blocked by administration of an opioid analgesic (Fentanyl). When somatosensory feedback is absent, participants had higher central motor drive and power output in the first 2.5 km of the trial. In the second 2.5 km central motor drive was similar to placebo and control, but power output was lower. From Amann *et al*. (2009).

These studies were the first to selectively block the central projection of opioid muscle afferents during locomotor exercise in humans without affecting pre-exercise muscle function. As a result of this blockade, a centrally mediated "brake" on motor drive to muscle during high-intensity endurance exercise was released, and the naïve CNS "allowed" or "tolerated" the development of locomotor muscle peripheral fatigue beyond an individual critical threshold and associated sensory tolerance limit (Amann *et al.*, 2009; Amann, 2011; Amann *et al.*, 2011). These findings confirmed the role of metabosensitive afferent feedback as a potential modifier of skeletal muscle recruitment during high-intensity aerobic exercise. The worse performance during constant load-exercise also highlights the important role these afferents play in optimising endurance

performance. When group III & IV afferents were selectively blocked, the missing feedback attenuated the cardiorespiratory response to exercise. This was the likely reason behind the accelerated development of peripheral fatigue, and the worse endurance performance despite the higher degree of motor drive and greater absolute level of peripheral fatigue (Amann *et al.*, 2011).

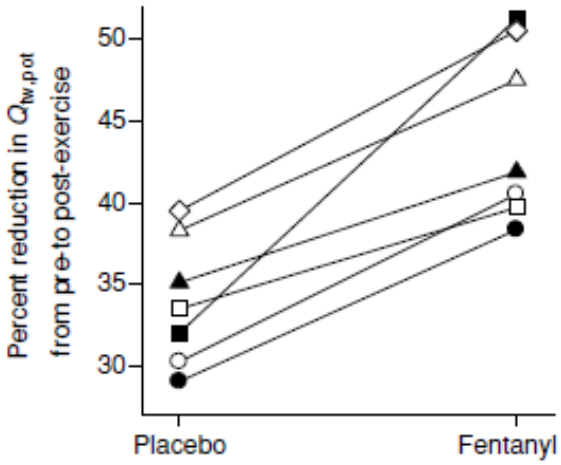


Figure 2-11. Relative reduction in potentiated quadriceps twitch force after constant load exercise in Placebo, and fentanyl trials where somatosensory feedback is blocked. When afferent feedback is blocked, participants exceed a sensory tolerance limit that is not voluntarily exceeded in normal exercise. From Amann *et al*. (2011).

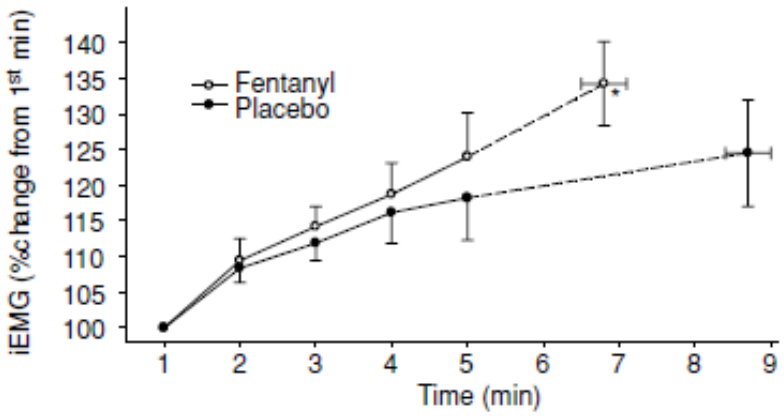


Figure 2-12. Integrated EMG of vastus lateralis during constant load exercise under conditions of an intact CNS (Placebo) and when sensory feedback is selectively blocked by administration of an opioid analgesic (Fentanyl). When sensory feedback is blocked central motor drive is higher, but endurance performance is worse. From Amann *et al*. (2011).

Is there a peripheral governor?

As well as providing support for the importance of afferent feedback in the regulation of exercise intensity through central mechanisms, the data presented by Amann *et al*. (2009; 2011) might also indicate the presence of a "peripheral" governor. In both constant load and self-paced exercise, the peripheral fatigue experienced was in excess of that which is normally tolerated by an intact CNS. As a result of the fentanyl intervention, the degree of central motor drive was elevated, but this augmented drive "could not be "translated" into sustained power output and better endurance performance" (Amann *et al.*, 2011, p. 5307). The question thus arises, if the drive to recruit skeletal muscle was present, and if it is the CNS that determines exercise intensity (Noakes & St Clair Gibson, 2004; Noakes *et al.*, 2004; Noakes, 2012), why did the contractile machinery not respond to this drive?

The obvious answer is the level of peripheral fatigue was so high that the muscle simply could not respond, but what mediates this is not clear. If the muscle and associated motor units are simply the slave to the CNS, the logical end point of such unrestrained drive would be muscle rigor, or some other catastrophic event. That the contractile machinery simply stopped responding to the motor input might support the idea of a peripheral mechanism proposed by MacIntosh & Shahi (2011). These authors postulated the existence of a regulatory process at the cellular level that modulates the rate of ATP use when the rate of hydrolysis threatens to exceed the rate of replenishment. The peripheral governor would thus attenuate cellular activation to avert this, potentially via decreases in membrane excitability (Cairns *et al.*, 1997) and disturbances in calcium handling (Favero *et al.*, 1995). Evidence for a peripheral governor can be found in the observation that single muscle fibres electrically stimulated *in vitro* show marked changes in PCr, P_i and decreases in force generating capability with little change in ATP concentration, despite the absence of any CNS involvement (Russ *et al.*, 2002).

If a peripheral governor exists, it might predominantly function during short duration tasks where peripheral fatigue is the dominant contributor to the decline in force (Burnley *et al.*, 2012). With regards locomotor exercise, Ulmer (1996) postulated the characteristic slowing down at the end of a 400 m maximal run could be due to a "delay" in the afferent feedback reaching the CNS. St Clair Gibson *et al*. (2003)

proposed the existence of a "lag phase" in the communication of sensory afferent information to the CNS which results in periods of "uncertainty" during the exercise bout where the brain is not fully aware of the extent of the metabolic disruption in the muscle. In this situation of "uncertainty" a peripheral over-ride would be ostensibly useful. The original proposed complex systems model of fatigue also alluded to regulatory systems in the periphery that contribute to a hierarchical control system with redundant properties (Noakes & St Clair Gibson, 2004), though this component seems to have been disregarded in subsequent iterations (Noakes, 2011b, 2012). Nonetheless, during short duration trials, a peripheral governor might function to prevent catastrophic fatigue caused by an over-eager and uninformed CNS attempting to drive motor units beyond their normal tolerance. Limited data exists on fatigue in such short duration events, and comparisons of peripheral fatigue measurements between studies should be made with caution, due to differences in protocol. However no study on any exercise mode in the presence of intact afferent feedback has observed the magnitude of peripheral fatigue that Amann *et al*. (2009; 2011) have observed when afferent feedback is blocked and the sensory tolerance limit is exceeded (Millet & Lepers, 2004; Goodall *et al.*, 2009; Sidhu *et al.*, 2009b; Goodall *et al.*, 2010; Decorte *et al.*, 2012; Goodall *et al.*, 2012a; Froyd *et al.*, 2013). Thus if a peripheral governor exists, the degree of locomotor muscle fatigue and the additional observations by Amann *et al*. (2009; 2011) of severe ambulatory problems and muscle soreness that existed after the trials in which afferent feedback was compromised suggest that this governor might only operate in extreme circumstances, and is secondary to regulation by an "informed" CNS.

The role of the brain; centrally acting performance modifiers

A number of studies have assessed the role of the brain in the regulation of exercise intensity by attempting to manipulate the concentrations of brain neurotransmitters. Newsholme *et al*. (1987) first proposed that alterations in serotonin and their interaction with blood-borne tryptophan and branched chain amino acids (BCAA) could contribute to an increased feeling of fatigue and reduced performance during prolonged exercise. The experimental test of this hypothesis via BCAA supplementation during exercise has yielded equivocal results (van Hall *et al.*, 1995; Blomstrand, 2006), with some limited evidence that inhibiting serotonin reuptake could have negative effects on self-paced exercise performance, specifically by blunting the magnitude of the end spurt (Roelands *et al.*, 2009). However, neuronal function relies on an array of neurotransmitters and a

number of studies have employed centrally acting drugs or chemicals to successfully impact self-paced performance, including amphetamines (Swart *et al.*, 2009b), naloxone (Sgherza *et al.*, 2002) and acetaminophen (Mauger *et al.*, 2010). Manipulations of dopamine through administration of buspirone (Bridge *et al.*, 2003) methylphenidate (Roelands *et al.*, 2008) and bupropion (Watson *et al.*, 2005; Roelands *et al.*, 2012) result in better exercise performance in the heat compared to placebo. A range of other studies have also demonstrated that self-paced performance can be impacted by non-pharmacological interventions that are hypothesised to be centrally acting. These include music (Lim *et al.*, 2009), self-belief (Micklewright *et al.*, 2010), prior experience (Ansley *et al.*, 2004b; Mauger *et al.*, 2011) and provision of inaccurate time (Morton, 2009), distance (Paterson & Marino, 2004) and surreptitious performance feedback (Stone *et al.*, 2012). Collectively these studies suggest athletes operate with a "reserve capacity" that can be potentially accessed through a range of centrally acting interventions.

Summary

> *"Discovering the biological basis of pacing, not of fatigue, is the most important challenge for those studying exercise performance."* (Noakes, 2011, p.30)

Fatigue during exercise is multi-factorial and multiple mechanisms interact in a task dependent manner to explain the development of fatigue during exercise. Proponents of the central governor model argue that the body functions as a complex system during exercise using elements of feed-forward and feedback control in a paradigm that places emphasis on the factors that regulate rather than limit exercise performance. Detractors of this model argue that fatigue is task-specific and that one model cannot explain the multiple mechanisms of fatigue that have been proposed in the literature. Despite this, a large degree of evidence exists supporting the key features of the CGM, namely that exercise is regulated in an anticipatory manner, afferent feedback from physiological systems modifies the degree of motor unit recruitment, and that the central nervous system is the key controller of this process. In addition, the introduction of the central governor model has successfully encouraged new research to better understand the role of perception in the regulation of exercise (Enoka & Stuart, 1992; Barry & Enoka, 2007; Enoka & Duchateau, 2008). Thus whilst the central governor model might not be a complete explanation of fatigue, its introduction has addressed the disconnect in

current research between the physical and emotional definitions of fatigue and inspired a number of researchers to better understand the basis of fatigue during self-paced exercise by studying the biological basis of the pacing strategy. The results of this renewed endeavour will be discussed in the final section of this review, which will discuss the literature pertaining to pacing strategy and exercise performance.

2-11 Pacing strategy and performance

Pacing is the distribution of energy expenditure during an exercise task (Foster *et al.*, 1994). With regards athletic performance, the pacing strategy adopted by an athlete can have a significant impact on race performance. The recording of variations in pace through a race can be thought to reflect a behavioural response to the models of exercise regulation presented in section 2-10, or a marker of the underlying physiological regulation (Tucker & Noakes, 2009). How the athlete paces themselves will be informed by a number of potential factors including knowledge of the endpoint, previous experience, environmental factors, the perception or sensation of fatigue, their motivation for the exercise task and, in the case of some events, other competitors.

Types of pacing strategy

The scientific literature has identified a number of types of pacing strategy that can be broadly split in to positive, negative, even and variable/parabolic strategies (Figure 2-13) (Abbiss & Laursen, 2008). A positive pacing strategy requires the early attainment of a high exercise intensity or speed that declines over the course of the event (Figure 2-13, panel a). A negative pacing strategy is one where the second half of the race is completed at a higher intensity than the first (Figure 2-13, panel b). An evenly-paced strategy is one where the distribution of work is uniform over the course of the exercise bout (Figure 2-13, panel c). A variable or parabolic pacing strategy is one where there is some variation in the distribution of work over the trial (Figure 2-13, panel d).

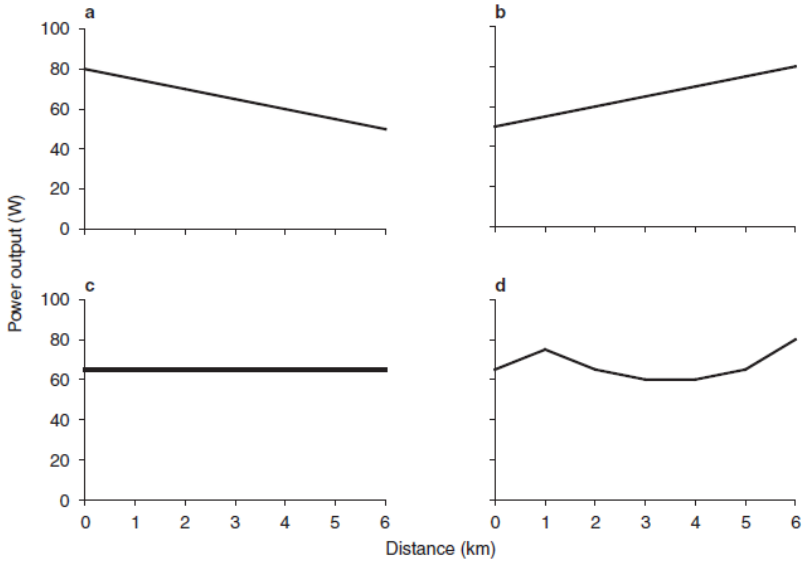


Figure 2-13. Types of pacing strategies adopted by athletes; a = positive pacing, b = negative pacing, c = even pacing, d = variable/parabolic pacing. From Abbiss & Laursen (2008).

Even in very short duration exercise, the decrease in exercise intensity due to fatigue without deliberate pacing is large, with power output declining to 50% of peak values after 40 s of all-out cycling (Foster *et al.*, 1994). Thus some form of pacing is a necessity in any event lasting more than a few seconds (Foster *et al.*, 1994). The optimal pacing strategy is largely dependent on the mode and duration of the event, and some general guidelines are evident in the scientific literature. The available evidence suggests very short duration events (< 30-60 s) might benefit from an "all-out" strategy (Corbett, 2009), whereas when duration is prolonged (> 4 min) a more even distribution of pace might be more optimal (Abbiss & Laursen, 2008). During middle distance (1.5-4 min) and ultra-endurance (> 4 hours) races a positive pacing strategy is commonly observed, and in the case of middle distance events recent evidence has supported the use of this strategy over previous recommendations of a more even pace (Jones *et al.*, 2008b). Knowledge pertaining to effective pacing has been garnered from studies that use simulated models, observations of elite athletes and experimental manipulations of pacing strategy. The following sections will review these studies with specific reference to event duration, which is the primary factor dictating the type of pacing strategy employed.

Simulated models of pacing strategy

A number of studies have attempted to mathematically model performance for a range of exercise modes including cycling, speed skating, running, rowing and swimming

(Keller, 1974; di Prampero *et al.*, 1979; van Ingen Schenau & Cavanagh, 1990; van Ingen Schenau *et al.*, 1990; de Koning *et al.*, 1992; van Ingen Schenau *et al.*, 1992; Olds *et al.*, 1993; van Ingen Schenau *et al.*, 1994; Olds *et al.*, 1995; Maronski, 1996; Swain, 1997; Martin *et al.*, 1998; de Koning *et al.*, 1999; Fukuba & Whipp, 1999; de Koning *et al.*, 2005; Gordon, 2005; Atkinson *et al.*, 2007b). A number of these studies have also provided insight in to the optimal pacing strategy for a range of events through race simulation. For short duration events, an all-out strategy is recommended (Keller, 1974; van Ingen Schenau *et al.*, 1990; de Koning *et al.*, 1992; van Ingen Schenau *et al.*, 1992; de Koning *et al.*, 1999). de Koning *et al*. (1999) predicted that optimal pacing for 1 km track cycling (~60 s) consisted of an all-out strategy whereby peak velocity is attained early and a slowdown occurs before the end of the race. Keller (1974) predicted an upper limit of 291 m for the effectiveness of this type of strategy in running exercise, with longer distances benefiting from a more constant pace. Van Ingen Scheneau *et al* (1994) suggested events lasting < 90 s would benefit from an "all-out" strategy whilst longer events (< 260 s) needed a fast start prior to a more constant pace. de Koning *et al*. (1999) supported this assertion regarding longer events and concluded the optimal pacing strategy for 4 km track cycling consisted of an initial fast start followed by a uniform distribution of work.

Collectively, modelling studies have thus shown an all-out strategy is optimal for short duration events (~30-90 s). As the duration of the event is short, the starting strategy contributes relatively more to overall performance, thus the athlete must minimise the time spent accelerating. As the cost of accelerating is inevitable, it is recommended that this energy is distributed early so the athlete can spend longer at close to peak velocities (Abbiss & Laursen, 2008). This is particularly the case for cycling and rowing events, where the acceleration phase is longer due to greater impact of air and fluid resistance respectively compared to running races. This fast starting strategy inevitably results in a slow down towards the end of the race, but it is better for the athlete to be slowing down as they cross the line, as any velocity that exists as they pass the finish line is essentially wasted kinetic energy (de Koning *et al.*, 1999).

For longer events, modelling studies conclude a short powerful start followed by a more uniform distribution of work is optimal (Keller, 1974; van Ingen Schenau *et al.*, 1992; de Koning *et al.*, 1999). The theoretical support for the utility of this type of strategy is

based on physiological and biophysical principles that state speed is dictated by the maximum sustainable force an athlete can exert balanced against the resistive forces experienced (Abbiss & Laursen, 2008). Fukuba & Whipp (1999) modelled the effect of pacing for endurance events based on models of critical power that have demonstrated the existence of an individual maximum sustainable exercise intensity above which the rate of fatigue development disproportionately increases (Vanhatalo *et al.*, 2011; Burnley *et al.*, 2012). These authors demonstrated that performance is compromised if an athlete's power output drops below this fatigue threshold at any point during an event, even if an athlete attempts to make up for lost time with an end spurt towards the end of the event (Fukuba & Whipp, 1999). Moreover, as the event duration lengthens, the influence of starting strategy decreases as the relative contribution of the acceleration phase to the overall duration decreases, rendering an overly aggressive start as a potential waste of energy. During the race, when the athlete attains high velocities, a greater proportion of power is required to overcome resistance (air or drag) rather than producing forward motion. Thus minimising accelerations and decelerations within a race could optimise performance by minimising "wasted" energy spent changing speed (Atkinson *et al.*, 2007c).

A limitation of these mathematical models is that a number of physiological constants pertaining to acceleration, velocity and endurance are assumed, whereas the various unique physiological and technical attributes of the individual athlete will dictate the utility or otherwise of such strategies in real-life competition (Abbiss & Laursen, 2008). A further criticism is they assume the possibility of a zero contribution of anaerobic energetic output (van Ingen Schenau *et al.*, 1994; de Koning *et al.*, 1999), which does not occur during actual time-trial exercise where athletes spontaneously vary intensity and retain an anaerobic contribution until the termination of the trial (Foster *et al.*, 2003; de Koning *et al.*, 2005). Indeed for short trials it has been proposed the distribution of this anaerobic energy is an important component of optimal pacing (Jones *et al.*, 2008b).

Observations of elite athletes

Observations of elite athletes during short duration races suggest the type of all-out strategy recommended by modelling studies is the actual strategy adopted during competition in 1 km track cycling (Wilberg & Pratt, 1988; de Koning *et al.*, 1999;

Corbett, 2009) (Figure 2-14) and 500 m and 1 km speed skating (van Ingen Schenau *et al.*, 1990). This type of strategy is particularly suited to cycling and speed skating, where resistive drag forces are lower than those found in water or overland ambulation, and thus the slowdown with a reduction in power output is not as pronounced (Foster *et al.*, 1993; Foster *et al.*, 1994). Nonetheless, elite 400 m runners have also been shown to adopt this type of "all-out" or positive pacing strategy, reaching peak velocity by 100 m before experiencing a gradual slowdown over the remainder of the race (Hanon & Thomas, 2011). This positive pacing pattern is also evident during 800 m running races, though the relatively low peak velocities attained would indicate these were not "all-out" strategies and observations are limited by a low frequency of sampling (Tucker *et al.*, 2006b; Hanon & Thomas, 2011).

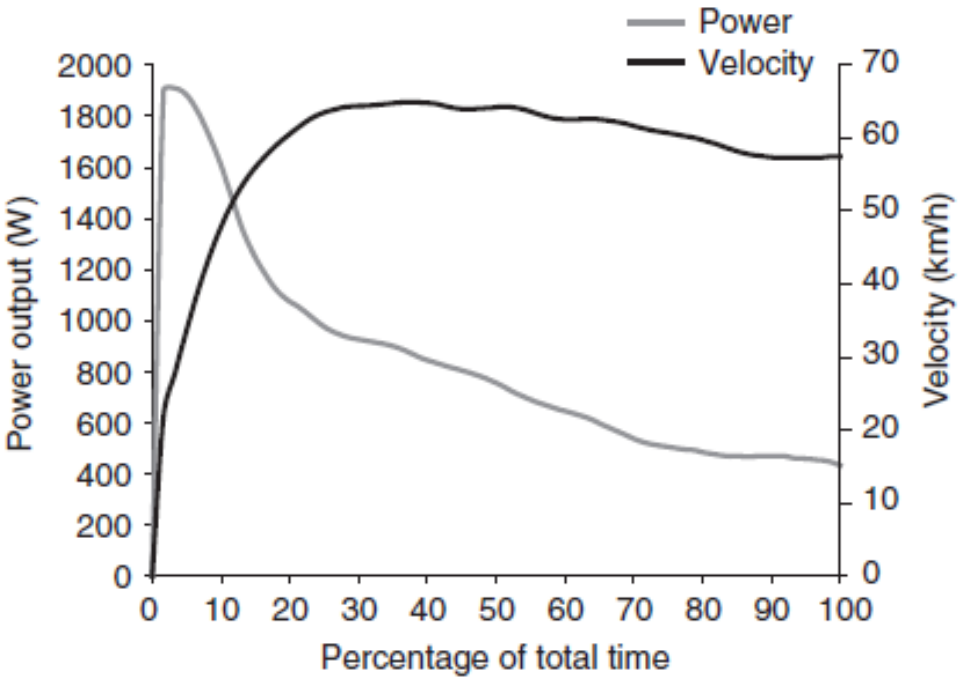


Figure 2-14. Power output and velocity profiles during a 1 km track cycling event demonstrating the use of an all-out pacing strategy. From Abbiss & Laursen (2008).

For longer duration races (> 2 min) modelling studies would suggest a short powerful start followed by an even distribution of pace would be optimal, but observations of elite athletes suggest deviations from this. In running for example, as the distance is extended to 1500 m, athletes maintain energy for a terminal end spurt and velocity is highest in the last 300 m (Tucker *et al.*, 2006b; Hanon & Thomas, 2011). Indeed for all distances from 1500 m to 10 km, world record pacing performances consist of a fast

start, progressively declining pace in the middle section, and a fast finish (Figure 2-15, Tucker *et al.*, 2006b). This parabolic type of pacing strategy, broadly fitting J-shaped, reverse J-shaped or U-shaped curves (Figure 2-16) is common across exercise modes in well-trained and elite athletes. In 2000 m rowing (6-8 min duration) the typical pacing strategy is characterised by an aggressive start (perhaps for tactical reasons) and an increase in speed at the end of the race (Garland, 2005; Muehlbauer & Melges, 2011). Mauger *et al*. (2012) analysed 264 elite 400 m freestyle swims (~4 min duration) and revealed that athletes most commonly selected a parabolic strategy, or a fast start followed by an even pace. Corbett *et al*. (2009) showed that elite track cyclists adopted a parabolic pacing strategy in the 3 km (~3.68 min duration) and 4 km (~4.46 min duration) pursuit events. These observations suggest this type of pacing strategy is common across modes for events > 3.5 min duration.

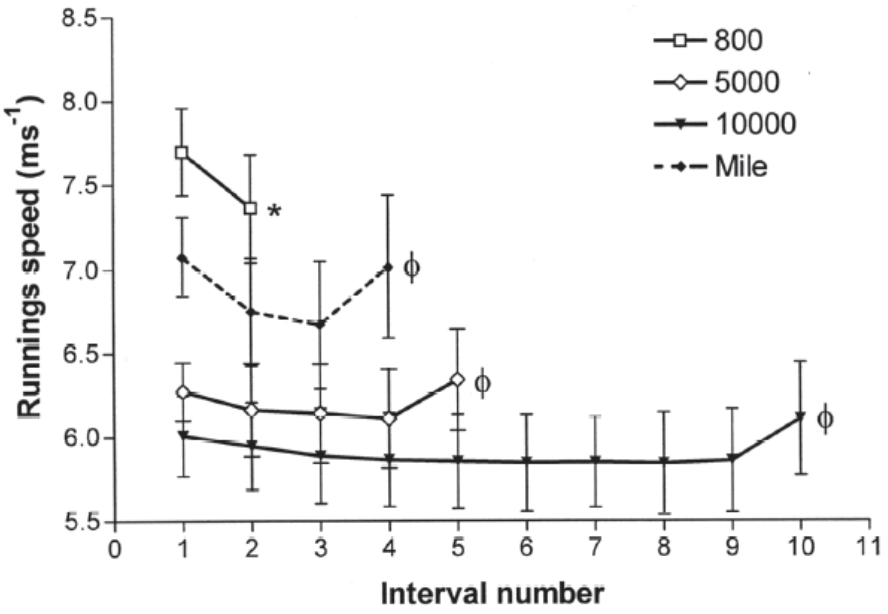


Figure 2-15. Pacing profiles from world record performances in running events from 800 m to 10 km. Note the parabolic pacing strategy and presence of an end spurt in all events > 800 m. From Tucker *et al*. (2006b).

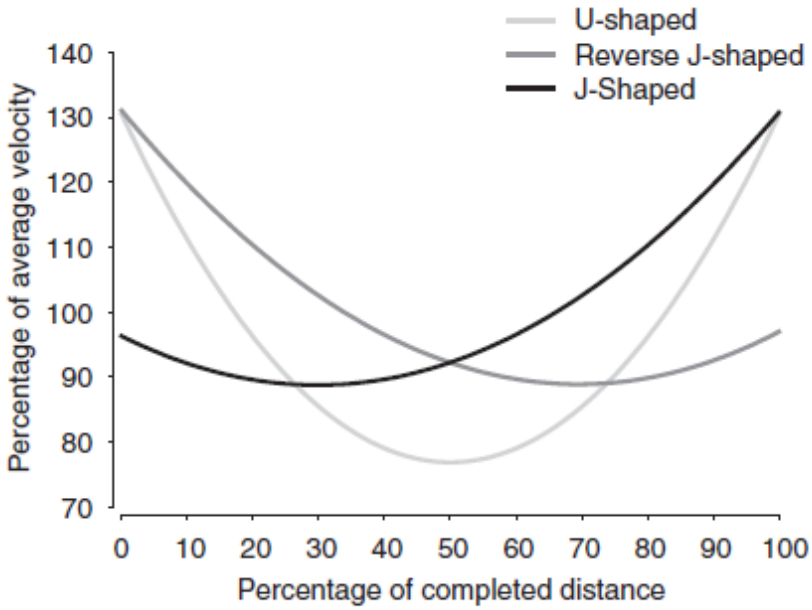


Figure 2-16. Schematic illustration of the type of parabolic pacing strategy typically employed by athletes during prolonged endurance events. From Abbiss & Laursen (2008).

The observation that athletes attain high speeds at the finish line is congruent with the previously discussed models of exercise regulation. However, any kinetic energy spent after the athlete crosses the finished line is essentially wasted and this type of strategy is contrary to the predicted evenly-paced "optimum". Would a more even distribution of the available energetic resource result in better performance? Support for an even-pacing strategy can be found in the successful 1 h cycling record attempt of Miguel Indurain (Figure 2-17, Padilla *et al.*, 2000a), and the observation by Palmer *et al*. (1994) that Chris Boardman won an elite 80 km TT whilst measurements of heart rate deviated by only 5 b·min^{-1} from the 178 b·min^{-1} average during the race. Thus, even-pacing might be more suitable for prolonged endurance races. Despite these observations, the prevalence of even-pacing profiles in elite competition is scarce.

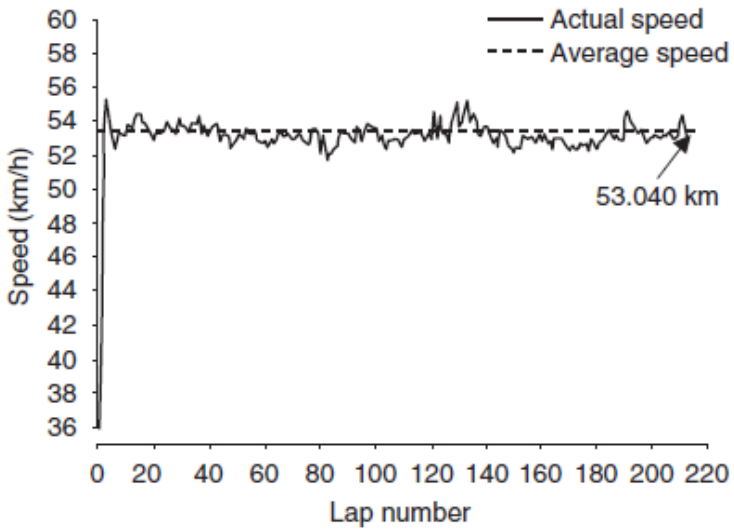


Figure 2-17. Average speed of Miguel Indurian during a successful attempt at the 1 h track cycling world record. Note the speed deviates little from the trial mean resulting in the adoption of an even pacing strategy. From Padilla *et al*. (2000).

Experimental manipulations of pacing strategy

Whilst observations of elite athletes would support an all-out type pacing strategy to optimise performance in very short duration events, there is limited experimental data to support this posit. Hettinga *et al*. (2011) showed no performance benefit of this type of pacing strategy when it was imposed during an actual 1500 m speed skating trial (~2 min). Although their findings might be explained by the negative effects on speed skating technique rather than the effect of the pacing strategy *per se*, and that the athlete's preferred pacing strategy already included a fast start. A trade off clearly exists in short events between the effective mechanical power generated by higher energy expenditures at the start of a race, and the inevitable faster rate of fatigue that causes a slowdown towards the end of the race (Abbiss & Laursen, 2008).

For event durations longer than 2 min, a common assumption since the results of an early study by Robinson *et al*. (1958) is that an even distribution of work is optimal. It is somewhat surprising then, that recently few studies had experimentally investigated the distribution of work in athletic performance, despite the observation in elite athletes that different races are characterised by distinct pacing profiles (Foster *et al.*, 1993; Foster *et al.*, 1994). In one of the first well-designed experimental studies, Foster *et al*. (1993) predetermined the first 1 km of a 2 km cycling TT (very slow, even paced, fast or very fast), with the second half of the race completed "as fast as possible". The best

performance time (2.77 ± 0.18 min) was found when the pacing strategy was even (first 1 km at 50.9% of total time). Small variations above and below this strategy elicited negative performance consequences, but no difference in the metabolic response (oxygen deficit, blood lactate accumulation, percentage of work attributable to oxidative metabolism) (Foster *et al.*, 1993). This study thus provided support for the adoption of even-pacing in middle distance events, though it should be noted that speed, and not power output, was measured and thus the distribution of work can't be accurately quantified. Nonetheless this early seminal study is often cited as support for even-pacing strategies, even for time-trial events of longer duration (Atkinson *et al.*, 2007c; Abbiss & Laursen, 2008). However, more recent evidence has challenged the utility of even-pacing in both middle distance and longer duration endurance events.

For middle distance events (2 to 4 min) recent studies from researchers at the University of Exeter have demonstrated a positive pacing strategy might be optimal (Jones *et al.*, 2008b; Bailey *et al.*, 2011; Chidnok *et al.*, 2013). Jones *et al*. (2008b) observed a fast-start strategy resulted in a longer time to exhaustion during a short duration (2 to 3 min) constant load trial to exhaustion compared to slow- and even-start strategies. The authors suggested a fast-start strategy increases the oxidative contribution to energy turnover early in the exercise by speeding oxygen uptake kinetics and the attainment of $\dot{V}O_2max$, thus the rate of expenditure of the finite anaerobic energy reserve (*W'*) is attenuated allowing exercise to be prolonged through a greater total yield of ATP before exhaustion (Jones *et al.*, 2008b). Further support for the utility of fast-start pacing was provided by Bailey *et al*. (2011), who controlled the first 2 min of a 3 min high-intensity exercise bout to elicit fast-, slow- and even-paced starting strategies. A fast starting strategy enabled the athlete to perform more work in the same amount of time in comparison to even- and slow starts (Bailey *et al.*, 2011). Interestingly, these authors also showed that this fast-start strategy did not result in performance enhancements during a 6 min bout of exercise, indicating that short-term exercise in the "extreme" exercise domain might be improved by fast-start pacing, but longer term exercise in the "severe" domain was unaffected, despite observing the same speeding of $\dot{V}O_2$ kinetics. This observation is supported by (Aisbett *et al.*, 2003) who showed no performance improvement when employing a fast start strategy compared to slow and even paced starts during a 6 min cycle test, despite differences in oxygen deficit. Additional support for fast-start pacing can be found in a study on 2 min kayak ergometer performance

(Bishop *et al.*, 2002). These authors showed that an all-out start resulted in a higher mean power output then an even-paced start (349 ± 48 W vs. 336 ± 45 W). These results suggest that performance in events of 2 – 4 min duration might be enhanced by the use of a fast starting strategy. Whilst it should be noted none of these studies actually assessed race performance, it is likely that the differences observed would translate to performance improvements in a time-trial scenario.

For longer duration endurance events (> 4 min) the utility of even-pacing is also unclear. As previously discussed, even-pacing is proposed as optimal based on mathematical laws of motion, and critical power models of known physiological thresholds (Fukuba & Whipp, 1999). A fast start in this type of event might result in the early accumulation of fatigue and thus compromise performance later in the event (Thompson *et al.*, 2002, 2003), whilst a slow start in an attempt to preserve metabolic reserves would theoretically compromise performance as the athlete will not be able to recover the time lost early in the race (Fukuba & Whipp, 1999). Performance in prolonged endurance events, where the contribution of oxidative metabolism to energy provision is high, is primarily limited by the athlete's maximum sustainable speed. As the event duration lengthens the contribution of the start phase and the potential contribution of the finite anaerobic reserve would be progressively less important (Foster *et al.*, 1994; Foster *et al.*, 2004). Race performance in longer duration events would thus largely depend on maintaining an exercise intensity as close as possible to the individual maximum sustainable intensity, and an even-pacing strategy would ostensibly be an optimal strategy to achieve this.

Ham & Knez (2009) presented indirect evidence to support the utility of an even-pacing strategy for prolonged endurance events when they showed that cyclists who completed the first 5 km of a 30 km self-paced time-trial at a relative speed of between 100-104% of the overall mean speed had a shorter time to exhaustion in a subsequent trial where power output was fixed at the mean power output of the self-paced trial. These cyclists also exhibited low variability in speed during the self-paced trial. A shorter time to exhaustion at the same mean power output and lower variability in speed was interpreted as evidence that the pacing strategy adopted during the self-paced trial was more optimal than faster starting strategies and more variable changes in pace. However, the failure of these cyclists to complete a similar amount of work during an

even-paced trial based on a best self-paced performance would refute the utility of a strict even-pacing strategy (Ham & Knez, 2009).

Other studies that have directly compared self- and even-pacing suggest that self-pacing reduces the metabolic and perceptual stress of a given performance. Lander *et al*. (2009) studied nine novices who completed a self-paced 5 km rowing exercise pegged to a fixed RPE ("Hard") and subsequently compared it to an even-paced bout where the intensity was set at the same mean intensity of the self-paced bout. These authors observed higher core temperature, post-test blood lactate, perception of exertion and integrated EMG activity in response to the matched even-paced bout, and concluded that self-paced exercise is less challenging than even-paced exercise since the intensity of exercise can be regulated and adapted to minimise physiological strain and the perception of exertion (Lander *et al*., 2009). Similarly Billat *et al*. (2006) examined self- and even-paced 10 km running trials in three well-trained runners and showed even-pacing resulted in a higher metabolic stress. Billat *et al*. (2006) reported a coefficient of variation for 10 m running speed of 8.7 ± 2.7% over the course of the self-paced 10 km, and interpreted these pace variations as an intentional strategy to minimise the physiological strain during severe exercise. This "microvariation" in pacing is an increasingly measureable phenomena as technology improves and the resolution at which data is collected is increased (Tucker *et al.*, 2006a; Thiel *et al.*, 2012). Thiel *et al*. (2012) reported a mean variation in running speed of 1.6-2.7% on successive 100 m splits in data from track events at the 2008 Beijing Olympics. Tucker *et al*. (2006a) applied fractal analysis techniques to data collected during 20 km simulated time-trials, and argued the observed oscillations in power output common to these trials were not random but rather exhibited distinct characteristics that indicated the presence of system control mechanisms.

If the variation observed in self-paced exercise is important, the adoption of an even-paced race strategy is questionable. Rather than reject the potential of even-pacing, it might be more accurate to consider how a *more* even pace might impact performance compared to a *less* even pace. For example, whilst cyclists seem to select a supraoptimal power output at the start of endurance time-trials, there is some limited evidence that blunting this can lead to better performance (Firth, 1998 cited in Atkinson *et al.*, 2007c). Other studies investigating the effect of starting strategy on performance have shown

that aggressive starting strategies (+5-15% of the trial average) result in premature fatigue and poorer race performance (Mattern *et al.*, 2001; Ham & Knez, 2009). Thompson *et al*. (2003) also showed that even-pacing attenuated the metabolic and perceptual cost of a 175 m breaststroke swim compared to positive and negative pacing strategies. More experienced athletes are also better able to achieve and maintain an even pace during running exercise compared to novice athletes (Green *et al.*, 2010) and training results in a progressively more even distribution of work during 2 km rowing trials (Kennedy & Bell, 2003). When examining elite athletes, Wilberg & Pratt (1988) showed that the best Canadian track cyclists adopted a more even pace during 3 km and 4 km time-trials compared to less successful cyclists. Finally, as previously described, the 1 h world cycling record was broken using a pacing strategy best described as even (Padilla *et al.*, 2000a). Further research is warranted to elucidate the utility of even-pacing for prolonged endurance events, particularly in comparison to the strategies adopted during best self-paced efforts.

Variable pacing in competition

Whilst studies have provided insight in to the optimal race strategies for events of different durations, in real life competition pacing is complicated by the prevailing environmental conditions and the presence of other competitors. During track racing and road cycling against other competitors the potential for drafting leads to varied, stochastic changes in pace (Palmer *et al.*, 1994; Thiel *et al.*, 2012). Race tactics also significantly alter pacing strategy. Thiel *et al*. (2012) showed that only 2 of 8 track finals in the Beijing Olympics were run with a pacing strategy approximating the world record performance. In contrast, most races were characterised by stochastic changes in pace, and all races ended with an end-spurt which decided the medal places (Thiel *et al.*, 2012).

Even in longer duration time-trials "against the clock" that remove the effect of other athletes, pacing is complicated by variations in gradient and environmental conditions. A number of simulated models investigating cycling performance in varying conditions of wind and gradient have provided support for the concept of a uniform speed, demonstrating that variations in power to maintain a more constant speed can result in significant time savings on hilly and windy courses (di Prampero *et al.*, 1979; Swain, 1997; Martin *et al.*, 1998; Gordon, 2005; Atkinson *et al.*, 2007b). Though speed is

constant in these models, the variation in power and thus distribution of work describes a variable, or stochastic pacing strategy. These models predict that greater variations in exercise intensity would result in greater time savings (Swain, 1997), but the added metabolic cost of such a strategy cannot be predicted, and thus a number of experimental studies have been undertaken to assess the physiological acceptability of variable paced strategies.

To study the potential application of variable pacing, studies have assessed time- and work-matched bouts of even- and variable-paced exercise based on self-paced performance. The available data suggests athletes might be able to tolerate deviations of up to ± 5% of that which they can maintain as a constant load for exercise durations of up to 1 h (Liedl *et al.*, 1999; Atkinson & Brunskill, 2000; Atkinson *et al.*, 2007a), though there is also evidence that this might not be tolerable for all athletes (Atkinson *et al.*, 2007a). There is less data available on pacing strategies incorporating deviations above this threshold, with none of these latter studies using a previous best self-paced performance as the standard. One study demonstrated a greater metabolic cost and higher neuromuscular fatigue during variable- (from 50% to short periods at 100%, 150% and 200% maximum aerobic power) compared to constant-paced cycling (70% maximum aerobic power) (Theurel & Lepers, 2008). Another study from the same group demonstrated no difference in the metabolic response to constant power exercise at 75% of maximum aerobic power, and variable intensity exercise incorporating periods at ± 5, 10 and 15% of 75% maximum aerobic power (Lepers *et al.*, 2008). Given the non-linearity of the physiological response at higher exercise intensities (Jones *et al.*, 2008a), it might be assumed that exercise intensity excursions in to the severe and extreme exercise domains would potentially incur a greater metabolic cost in comparison to more evenly-paced exercise. Whilst the available data is limited and complicated by differences in protocol, the research available would support this posit, and more research specific to self-paced performance is warranted.

Summary

The regulation of exercise intensity during self-paced exercise is anticipatory and designed to optimise performance whilst limiting homeostatic disturbance within an acceptable range (de Koning *et al.*, 2011). The extent of acceptable disturbance is influenced by other competitors and a range of other centrally acting performance

modifiers (Noakes, 2012). The "optimal" pacing strategy is dependent on both exercise duration and exercise mode. It is well-established that an "all-out" or positive pacing strategy is optimal for short duration and middle distance events. For prolonged endurance events the ideal pacing strategy is unclear. An even-pacing strategy has been recommended, but observations of athletes suggest a parabolic pacing strategy is more common. It is unclear whether a more even-paced strategy might result in performance improvements and/or attenuate the physiological or perceptual cost of the exercise bout. Understanding the biological basis of the pacing strategy and how the athlete regulates exercise intensity to achieve optimum performance whilst simultaneously managing the symptoms of fatigue is the focus of this series of studies, the aims of which are outlined below:

2-12 Study aims and hypotheses

Study 1: Reproducibility of pacing and performance within- and between- 4, 20 and 40 km simulated cycling time-trials in well-trained cyclists

Aims: To quantify the reproducibility of the pacing strategy and performance during repeated time-trials in well-trained cyclists and to investigate whether a global pacing strategy exists independent of time-trial distance

Study 2: The effect of self, even and variable pacing strategies on the physiological and perceptual response to cycling

Aims: To test the posit that an even-pacing strategy is optimal for endurance events > 5 min, this study assessed the effect of time- and work-matched self-, even- and variable-pacing strategies on physiological and perceptual responses to a bout of cycling exercise based on 20 km TT performance

Study 3: The effect of an even-pacing strategy on exercise tolerance in well-trained cyclists

Aims: The aim of this study was to investigate the efficacy of even-pacing for endurance time-trials by comparing best self-paced performance with the performance of a matched even-paced time to exhaustion task.

Study 4: Central and peripheral contributions to fatigue after 4, 20 and 40 km cycling time-trials

Aims: To better understand the regulation of exercise intensity during self-paced cycling time-trials of different duration, this study assessed the contribution of central and peripheral mechanisms to the fatigue observed during 4, 20 and 40 km cycling time-trials

CHAPTER 3 GENERAL METHODS

3-1 Introduction

The general methods employed within this series of studies are outlined in this chapter. Specifics relating to their application are contained within the respective chapters.

3-2 Pre-test procedures

3-2.1 Ethical approval

Institutional ethics approval was obtained from the Northumbria University School of Life Sciences or Faculty of Health & Life Sciences ethics committee. All participants were provided with information sheets that described the purpose of the study, and gave written informed consent to participate (appendix 1). All studies were conducted following national (Hull *et al.*, 2008) and international (WMA, 2008) guidelines.

3-2.2 Participants

Experienced male cyclists were recruited for all studies. All participants were classed as "well-trained" as per the criteria of Jeukendrup *et al*. (2000). All participants were training regularly and partaking in competition at local and national level (2^{nd} and 3^{rd} category cyclists).

3-2.3 Experimental design

All studies were conducted in the exercise physiology laboratories at Northumbria University which are accredited by the British Association of Sport & Exercise Sciences. A repeated measures experimental design was employed for all studies. This type of design is advantageous in that less participants are needed to achieve the required statistical power compared to an independent groups design due to less unsystematic variation between groups (Field, 2005). There is however greater potential for learning, fatigue and order effects, and any potential confounding variables must be strictly controlled. To achieve this, the order of experimental trials in all studies was randomised and counterbalanced and practice trials were included where appropriate. Repeat trials were conducted at the same time of day, separated by a minimum of 2 and a maximum of 7 days, and all were conducted within an allotted time frame for each study. Prior to each visit, participants were required to refrain from caffeine (for at least 12 h), strenuous exercise (for at least 24 h) and to arrive in a fully rested, hydrated state. Before the first visit in each study participants completed a 48 h food and activity diary

and were instructed to replicate their exercise and nutrition as closely as possible for each subsequent trial.

3-3 Apparatus and procedures

3-3.1 Anthropometry

Stature was measured to the nearest mm using a wall mounted stadiometer (Seca, Bonn, Germany) using the stretch stature method (Marfell-Jones *et al.*, 2006). Briefly, this required participants to stand with heels, buttocks and the upper part of the back in contact with the stadiometer. The participants head was then aligned in the Frankfort plane. The participant was instructed to inhale and hold a deep breath whilst the experimenter applied gentle upward lift through the mastoid processes and adjusted the headboard to make firm contact with the vertex (Marfell-Jones *et al.*, 2006). Body mass was assessed to the nearest 0.5 kg using a precision balance scale (Seca 200, Vogel and Halke, Germany) with participants wearing lightweight exercise clothing and no footwear.

3-3.2 Cycling time-trials

A majority of studies assessing the biological basis of self-pacing have used laboratory based simulated cycling time-trials. This paradigm allows for the high frequency capture of data whilst the athlete competes "against the clock" in an exercise task that is more ecologically valid than an externally controlled protocol such as an incremental or constant load task (Marino, 2010). Cycling exercise also allows for conscious and subconscious oscillations in power output through variations in cadence, the force exerted by the individual and changing the gearing ratio. The controlled environment of the laboratory increases the reproducibility of such trials, although does not mimic the effects of wind, gradient and other ambient conditions experienced during outdoor time-trialling (Swain, 1997).

Endurance cycling time-trials range in distance from 1 to 4 km in track cycling, and from 3 to 100 km in road cycling (Jeukendrup *et al.*, 2000). In road cycling distances of 16.1 km and 40 km are common, and in triathlon sprint and Olympic distance events have 20 and 40 km time-trials respectively. Consequently most researchers have employed cycling time-trials of between 4 and 40 km to study self-pacing as well-

trained athletes are well-practiced in trials over this range (e.g. Atkinson & Brunskill, 2000; Smith *et al.*, 2001; Laursen *et al.*, 2003; Ansley *et al.*, 2004b; Tucker *et al.*, 2006a; Sporer & McKenzie, 2007; Tucker *et al.*, 2007; Zavorsky *et al.*, 2007; Ham & Knez, 2009).

Several cycle ergometers are now commercially available that allow for the high frequency capture of power output and cadence data in both laboratory and field settings. The cycle ergometer used in this series of studies was the Velotron Pro cycle ergometer (Racermate Inc, Seattle, USA). The Velotron Pro is an electromagnetically braked cycle ergometer that uses an eddy current braking system around a large diameter copper flywheel to control resistance. An adjustable electronic gearing system is available to the cyclist and operated through computer controlled software (Velotron Coaching Software 2008, Racermate Inc.). The ergometer is calibrated using an "Accuwatt" run down procedure. This requires deceleration of the flywheel from a speed of 36.8 $km \cdot h^{-1}$. The rate of decline of angular velocity of the flywheel is used to confirm calibration within the range of the factory settings. The manufacturer claims the accuracy of this system in measuring power output is ± 1.5%. Abbiss *et al*. (2009) assessed these claims during constant load, incremental load and repeated sprint protocols using a calibration rig. During constant load and incremental trials the ergometer was accurate to < 2%, and measurement error was similarly very low (< 1%) over a range of intensities between 200-600 W, with more error at intensities above and below this range. During trials with repeated rapid accelerations to power outputs up to 1700 W, the ergometer under-reported the initial surge in power by up to 55%, probably as a consequence of having to accelerate a heavy flywheel (Abbiss *et al.*, 2009). The Velotron Pro ergometer thus provides accurate measurements of power during trials where the fluctuations in power are relatively minor, but does not provide an accurate measurement of peak power.

3-3.3 Cardiorespiratory measurements

Ventilatory and pulmonary gas exchange indices were obtained via an online breath by breath metabolic cart (Cortex Metalyser 3b, Leipzig, Germany) interfaced with accompanying software (Metasoft III, Cortex, Leipzig, Germany). Ventilatory volumes were inferred from measurements of gas flow using a digital turbine transducer. The turbine houses a lightweight low resistance vane that is rotated when air is passed

through in a spiral motion via helical conveyors. Each rotation is detected by a photocell device and is summed to provide a gas volume. Prior to all testing sessions the digital turbine was calibrated for flow and volume using a 3 L syringe (Hans Rudolph Inc. Kansas City, USA).

Expired air was sampled continuously at the mouth for estimation of whole body rates of $\dot{V}O_2$ and $\dot{V}CO_2$ and associated pulmonary variables. Air was sampled using a Nafion® tube sampling line, which is a semipermeable capillary tube that removes excess moisture from the gas without affecting its composition. Concentrations of CO_2 were analysed from the sampled air using a non-dispersive infrared cell (range 0-13%). Oxygen concentrations were measured using a Zirconia electro-chemical galvanic cell (range 0-100%) that acts as a semipermeable membrane that is selective for oxygen ions (Macfarlane, 2001). Prior to all experimental trials the O_2 and CO_2 analysers were calibrated using certified gas mixtures (15% O_2, 5% CO_2 and N_2 balance). Heart rate was recorded using short range telemetry (Polar Electro Oy, Kempele, Finland) interfaced with the metabolic cart. The reliability and validity of this method has been previously established for both physically and mentally stressful conditions (Achten & Jeukendrup, 2003).

The reproducibility and validity of this model of metabolic cart has not been reported in the literature. Data from our laboratory shows good agreement between this system and the Douglas Bag method at a range of exercise intensities (bias ± 95% confidence intervals, -0.24 ± 0.32 $L \cdot min^{-1}$). The reproducibility of this system is assessed in Chapter 4. Data from the metabolic cart were interpolated to 1 s averages using the manufacturers software in order to time align this data with the power output data. Where this data has been averaged (e.g. for determination of $\dot{V}O_2max$), recommendations from (Robergs *et al.*, 2010) of a 30 s time average or 15 breath running average have been employed.

3-3.4 Blood [lactate] measurements

Capillary blood lactate concentration [La^-] is one of the most widely measured variables during exercise testing in both sport and clinical settings. The lactate shuttle hypothesis described by Brooks (2000) explains the metabolism of lactate in humans. Briefly, the lactate shuttle posits that La^- formation and its subsequent movement throughout

various tissues in the body plays a key role in the distribution of carbohydrate potential energy (Brooks, 2000; Gladden, 2008). Indeed, during moderate intensity exercise blood La^- flux might exceed glucose flux, underlining the importance of La^- as a carbohydrate fuel source (Stanley *et al.*, 1988). Skeletal muscle is the both the major consumer and producer of La^- at rest and during exercise (Gladden, 2008). During exercise La^- exchange is a dynamic process. At low to moderate exercise intensities net La^- production is matched or exceeded by net La^- uptake by active and inactive skeletal muscle, cardiac muscle and the liver. At higher exercise intensities where glycolytic flux is high, La^- production exceeds removal, and this coincides with reductions in pH and cellular acidosis. Thus whilst lactate does not cause acidosis, its measurement in the blood is indicative of acidosis and it remains a useful and simple indirect marker (Robergs *et al.*, 2004).

Capillary blood was sampled from the fingertip using a disposable automated lancet device (AccuCheck Safe-T-Pro, Indianapolis, USA). Samples of 20 µl blood were collected in end-to-end capillary tubes and immediately put into a 10 mL vial containing 2.0 mL of a heparinised phosphate buffered solution (pH 7.2) and analysed for [La^-] using an automated analyser (Biosen C_Line, EKF diagnostic, Barleben, Germany). The analyser was calibrated prior to use and at 60 minute intervals during testing with a 12 $mMol \cdot L^{-1}$ standard. No independent studies exist that have assessed the reproducibility and validity of the Biosen C_Line. In our laboratory, we have observed good agreement between this system and the YSI 2300 (Yellow Springs Instruments, Ohio, USA) lactate analyser (bias ± 95% limits of agreement, -0.4 ± 1.6 $mMol \cdot L^{-1}$). The YSI 3200 analyser was used in Chapter 5, and has been previously validated (Clark *et al.*, 1984). The manufacturer of the Biosen C_Line claim a high degree of reproducibility (CV = 1.5% at ~ 12 $mMol \cdot L^{-1}$). Our in-house instrument reproducibility procedures assess repeated measurements of samples of low (0.5 to 2 $mMol \cdot L^{-1}$) and moderate (4 to 8 $mMol \cdot L^{-1}$) blood [La^-] on a biannually basis. The reproducibility of these is high, with observed CV's averaging 0.82% (range from 0.26 to 1.9%). The reproducibility of La^- measurements during time-trial exercise is considered in Chapter 4.

3-3.5 Perceptual measurements: Rating of Perceived Exertion and Affect

Subjective ratings of perceived exertion (RPE) and affect were measured during and post time-trial exercise using Borg's 6-20 RPE scale (Borg, 1982b; appendix 2) and Hardy & Rejeski's 11-point feeling scale (Hardy & Rejeski, 1989; appendix 3). The RPE is a subjective measure of the total physical strain experienced during exercise and contains both physical and psychic components. This measure has been previously discussed in detail (Chapter 2, sections 2-8 to 2-10). The affect scale measures an individual's subjective feelings, characterised by moods or sensations of pleasure or displeasure (Hardy & Rejeski, 1989). Verbal and written instructions (Table 3-1) were provided to participants prior to each trial. Both perceptual scales have been previously validated (Borg, 1982a; Borg *et al.*, 1987; Hardy & Rejeski, 1989) and the reproducibility of these during time-trial exercise is assessed in Chapter 4.

Table 3-1. Verbal instructions provided to participants prior to the measurement of RPE and affect. Adapted from Borg (1998) and Hardy & Rejeski (1989)

Measure	Explanation to participants
Rating of perceived exertion	While participating in exercise it is common to have a sense for how hard you are working. We would like you to consider the total amount of exertion you feel, taking into account all sensations of physical stress, effort and fatigue in your whole body. When asked, please rate this exertion as honestly as possible on this scale, where 6 is very light activity like slow walking, and 20 is the strongest perception of fatigue you have ever experienced.
Affective response	When exercising it is common to experience changes in mood. Some individuals find exercise pleasurable, whereas others find it to be unpleasurable. Additionally, feeling might fluctuate across time, so you might feel good and bad at different points during exercise. When asked, please rate your feelings in response to the exercise as honestly as possible.

3-3.6 Neuromuscular fatigue

In Chapter 7 measures of neuromuscular function for the assessment of central and peripheral fatigue were evaluated using transcranial magnetic stimulation (TMS) of the motor cortex and electrical stimulation of the femoral nerve, with evoked responses recorded with surface electromyography (EMG). Additional detail on these procedures is provided below.

Force & EMG recordings

Knee-extensor force (N) during voluntary and evoked contractions was measured using a calibrated load cell (MuscleLab force sensor 300, Ergotest technology, Norway) fixed to a custom built chair and connected to a noncompliant strap attached round the participant's right leg superior to the ankle malleoli. The height of the load cell was individually adjusted to ensure a direct line with the applied force. During all measurements participants sat upright with the hips and knees at 90 degrees flexion. The load cell was calibrated across the physiological range by suspending known masses (kg), with regression analysis used to convert raw analogue signals (mV) to force (N).

Voluntary and artificially evoked muscle activity results in an electrical response termed a compound muscle action potential (M-wave) that can be measured on the surface of the skin using EMG. Electromyography of the knee extensors and flexors was recorded from the vastus lateralis and lateral head of the biceps femoris, respectively. The vastus lateralis has been suggested as the most appropriate muscle to monitor when studying fatigue of the knee extensors and consequently this method is widely used (Millet *et al.*, 2002; Amann *et al.*, 2006a; Hettinga *et al.*, 2006; Place *et al.*, 2007). Activity of the biceps femoris muscle was measured to ensure low antagonist co-activation, as high levels can affect the measurement of voluntary activation (Allen *et al.*, 1995b). To lower electrical impedance, the skin was shaved, abraded and cleaned with an alcohol swab before being left to dry (Basmajian & DeLuca, 1985). Surface electrodes (Kendall H87PG/F, Covidien, Mansfield, MA, USA) were placed transcutaneously 2 cm apart over the belly of each muscle, in a bipolar configuration. A reference electrode was placed on the patella. The positions of the electrodes were marked with indelible ink to ensure a consistent placement on repeat trials.

Femoral nerve stimulation

Galvanic currents, or continuous direct currents, are widely used in therapeutic settings and for stimulation of peripheral nerves in experimental research (Low & Reed, 1994). In Chapter 7, single electrical stimuli (200 μs duration) were delivered to the right femoral nerve via surface electrodes (CF3200, Nidd Valley Medical Ltd, Harrogate, UK) using a constant-current stimulator (DS7AH, Digitimer Ltd, Welwyn Garden City,

UK) to assess knee extensor contractility during voluntary action and at rest. The cathode was placed over the nerve high in the femoral triangle; the anode was positioned midway between the greater trochanter and the iliac crest (Goodall *et al*., 2010). The exact positioning was determined by the response that elicited the maximum quadriceps twitch amplitude (Q_{tw}) and M-wave (M_{max}) at rest. To determine the stimulation intensity, single stimuli were delivered in 20 mA step-wise increments from 100 mA until a plateau in Q_{tw} and M-wave were observed. This final intensity was increased by 30% to account for activity dependent changes in axonal excitability that occur in fatigue (Burke, 2002). Further detail on these evoked responses is provided below.

Transcranial magnetic stimulation

Magnetic stimulators rely on principles of electromagnetism first elucidated by Michael Faraday in the 19th century. A changing magnetic field is capable of inducing currents in electrically conductive regions, such as the human brain (Barker *et al.*, 1985). If the induced current is of sufficient amplitude and duration it will excite underlying neuronal tissue in the same manner as electrical stimulation, but with less discomfort. Through appropriate choice and placement of a stimulating coil on the motor cortex (Rothwell *et al.*, 1991), TMS can be used to cause activity in specific parts of the brain that activate discrete collections of neurons associated with specific muscles (Goodall *et al.*, 2012b). The evoked force and electrical responses can be studied to assess the degree of supraspinal fatigue, intracortical inhibition and responsiveness of the brain to muscle pathway (discussed below).

Voluntary activation

The twitch interpolation technique first described by Merton (1954) was used to quantify voluntary activation of the knee extensors as a measure of central fatigue. Voluntary activation is the recruitment of motor units in a muscle through increasing descending drive (Taylor, 2009). The twitch interpolation technique measures the drive by the motoneurons to the muscle, and how this translates to force. The measured voluntary activation is the proportion of the maximum possible force generated during voluntary contraction (Taylor, 2009).

Voluntary activation was assessed by comparing the amplitude of the potentiated twitch ($Q_{tw.pot}$) elicited at rest through electrical stimulation of the femoral nerve with that evoked during an MVC (superimposed twitch (SIT)) using the following equation:

$$\text{Voluntary activation (\%)} = (1 - \text{SIT}/Q_{tw.pot}) \times 100$$

During MVC the root mean square of the EMG (EMG_{RMS}) was also recorded. The EMG_{RMS} reflects the mean power of the signal and thus provides an estimate of the neural drive to the muscle during voluntary contraction (De Luca, 1997). Maintenance of EMG_{RMS} post-exercise would indicate voluntary drive to the muscle was similar pre- and post-trial and thus alterations in force producing capability would not simply be due to a change in voluntary effort by the participant.

Cortical Voluntary Activation

The assessment of voluntary activation through magnetic stimulation of the motor cortex can be used to further localise the site of central fatigue (Todd *et al.*, 2003b). The presence of a superimposed twitch during an MVC indicates the presence of supraspinal fatigue, whereby the impairment in neural drive can be attributed to processes at or above the level of the motor cortex (Taylor & Gandevia, 2001; Goodall *et al.*, 2012b). The traditional twitch interpolation technique requires some modification in order to measure cortical voluntary activation. The resting twitch is estimated from linear extrapolation of the SIT amplitude elicited through TMS during contractions at 50%, 75% and 100% MVC (Figure 3-1). Estimation is necessary as motor cortical and motoneuronal excitability increase with voluntary activity (Rothwell *et al.*, 1991), such that at rest the absence of background excitability induced by voluntary drive means the same cortical stimulus activates fewer motoneurons (Lee *et al.*, 2008). The resting twitch is a measure of the resting motor cortical output that would be evoked by TMS if background excitability were maintained during rest (Todd *et al.*, 2003b). The estimated resting twitch (ERT) is subsequently used in the twitch interpolation formula to calculate voluntary activation as per the equation below:

$$\text{Cortical Voluntary Activation (\%)} = (1 - \text{SIT}/\text{ERT}) \times 100$$

In addition to these requirements, co-activation of antagonist muscles should be carefully considered. The muscle of interest should be stronger and more easily excited by TMS than its antagonist (Todd *et al.*, 2003a). Because of these requirements, the measurement of cortical voluntary activation has been measured in a small number of muscles, including the elbow flexors (Todd *et al.*, 2003a), wrist extensors (Lee *et al.*, 2008) and back extensors (Lagan *et al.*, 2008). The method of measuring cortical voluntary activation employed in Chapter 7 has been previously validated to demonstrate supraspinal fatigue of the knee extensors (Goodall *et al.*, 2009; Sidhu *et al.*, 2009a).

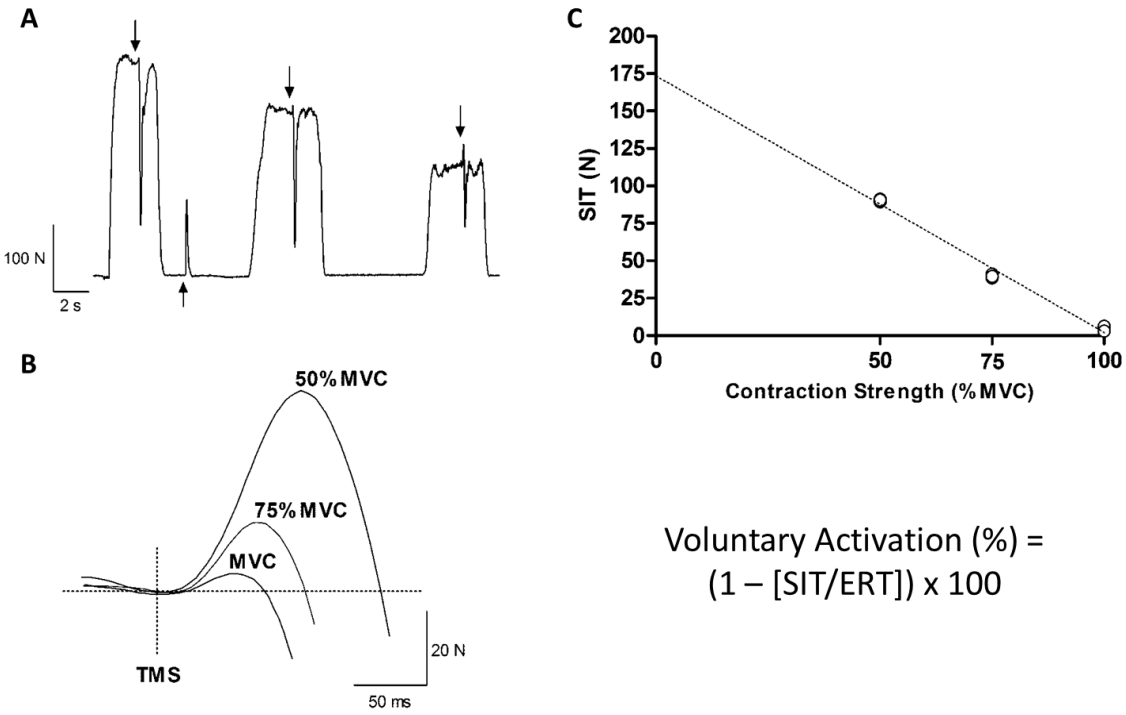


Figure 3-1. Measurement and calculation of cortical voluntary activation. A, force trace illustrating the measurement of superimposed twitch (SIT) elicited by single pulse transcranial magnetic stimulation (TMS, downward arrows) of the motor cortex during voluntary contraction at 100%, 75% and 50% MVC. B, raw force traces illustrating the magnitude of the SIT elicited at 100%, 75% and 50% MVC, used to calculate the estimated resting twitch (ERT) force via linear extrapolation and, subsequently, cortical voluntary activation (C). From Goodall *et al*. (2012).

Muscle function

The characteristics of the evoked potentiated twitch elicited through electrical stimulation of the femoral nerve were studied to quantify the degree of exercise-induced peripheral fatigue. It is well established that a prior strong muscle action facilitates the

resting twitch response through post-activation potentiation (Hodgson *et al.*, 2005). The purported mechanism for this potentiation is the phosphorylation of myosin regulatory chains that increases the sensitivity of the actomyosin complex to Ca^{2+} (Hodgson *et al.*, 2005). Increased Ca^{2+} sensitivity increases the rate by which myosin cross-bridges move from a weak to strong binding state (Allen *et al.*, 2008a), thus increasing the potential for force generation and subsequent amplitude of the resting twitch. The sensitivity of the potentiated twitch to exercise induced fatigue is higher than the unpotentiated twitch (Kufel *et al.*, 2002). Any exercise intervention could also serve to both potentiate and cause fatigue of the resting twitch. For these reasons, the potentiated twitch was evaluated for the assessment of peripheral fatigue.

The following mechanical measures of muscle contractility were derived from the potentiated twitch response: twitch amplitude, maximum rate of force development (MRFD), maximum relaxation rate (MRR), contraction time (CT) and one-half relaxation time ($RT_{0.5}$). The methods for determining $Q_{tw.pot}$, CT and $RT_{0.5}$ are illustrated in Figure 3-2 for a representative resting twitch. Specially, CT was defined as the time between stimulus delivery (including mechanical delay) and peak force, and $RT_{0.5}$ was calculated as the time taken for twitch force to decrease to half of the peak twitch amplitude. The highest slopes of the tangent drawn to the steepest part of the upward and downward curves were assessed for measurement of MRFD and MRR respectively. Since both MRFD and MRR are force dependent they were normalised relative to the twitch amplitude so twitches of varying intensity could be compared.

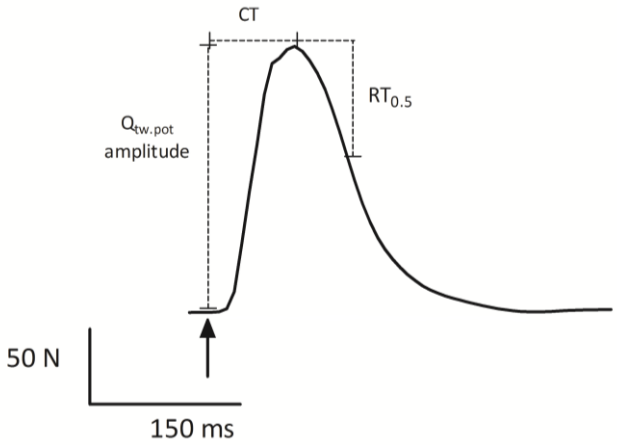


Figure 3-2. Potentiated quadriceps twitch from a representative participant showing twitch amplitude, contraction time (CT) and half relaxation time (RT0.5). The arrow indicates when the electrical stimulus was delivered.

Evoked potential responses to magnetic and electrical stimulation

The characteristics of the electrical potentials elicited by the electrical and magnetic stimulation techniques employed were recorded using EMG and analysed post-test (Signal 5.04 and Spike2, Cambridge Electronic Design, Cambridge, UK). When responses were evoked by electrical stimulation of the femoral nerve, the M-wave was used to assess changes in membrane excitability. For motor cortical stimulation, the motor evoked potential (MEP) response was used to assess changes in corticospinal excitability during contraction and at rest. For both evoked potentials, the peak-to-peak amplitude and area were measured (Figure 3-3). The peak-to-peak amplitude is measured as the absolute difference between the maximum and minimum points of the biphasic M-wave or MEP. The area was calculated as the integral of the reflected value of the entire M-wave or MEP. After an MEP is evoked by TMS there is a period of silence in the on-going EMG known as the cortical silent period (CSP). Lengthening of the CSP indicates increases in intracortical inhibition (Taylor & Gandevia, 2001). The CSP was quantified during the MVC as the duration between the point of cortical stimulation until the post-stimulus EMG exceeded ± 2 SD of the pre-stimulus EMG for > 100 ms (Goodall *et al.*, 2010).

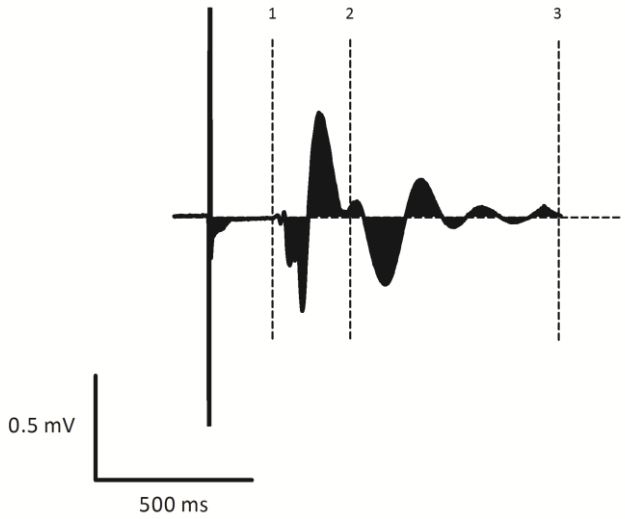


Figure 3-3. Representative motor evoked potential (MEP) showing calculation of peak-to-peak amplitude (between dashed vertical lines 1&2) and area (shaded area between dashed lines 1 and 3).

CHAPTER 4 REPRODUCIBILITY OF PACING AND PERFORMANCE WITHIN- AND BETWEEN- 4, 20 AND 40 KM SIMULATED CYCLING TIME-TRIALS IN WELL-TRAINED CYCLISTS

4-1 Introduction

The estimation of the error in a measurement tool is a key consideration for determination of sample sizes in research and for making pragmatic assumptions on the effectiveness of an intervention (Hopkins, 2000; Hopkins *et al.*, 2001). Research that assesses the efficacy of an intervention using cycling performance as the outcome measure has traditionally adopted one of two methodological paradigms. The first is an open-loop paradigm in which exercise intensity is externally imposed and participants exercise as long as possible; the most well-known of these is probably the maximal incremental test. The second is a closed-loop paradigm where the participants complete a given distance or amount of work as quickly as possible; exercise intensity is variable and determined by the participant. This format is usually referred to as a time-trial (Hopkins *et al.*, 2001). Compared to open-loop trials, the closed-loop, self-paced trial offers greater external validity (Sporer & McKenzie, 2007), but the potential for variations in pacing strategy adds noise to self-paced performance tests compared to trials where exercise intensity is fixed (Hopkins *et al.*, 2001). Therefore the inherent variability within self-paced trials needs to be established before results can be meaningfully interpreted.

Although the reproducibility of mean power and time to completion for self-paced laboratory cycling time-trials is well established, with reported coefficients of variation of 1.9 -3.6% (Smith *et al.*, 2001; Laursen *et al.*, 2003; Sporer & McKenzie, 2007; Zavorsky *et al.*, 2007), few studies have looked at the reproducibility of the actual pacing strategy during repeated time-trials (Ansley *et al.*, 2004b; Corbett *et al.*, 2009). St Clair Gibson *et al*. (2006) theorised that pacing strategy is dependent on a pre-established template defining the pattern of power output in an event. This template of motor unit sequencing is programmed into the motor cortex as a result of prior athletic performance, potentially from early childhood (St Clair Gibson *et al.*, 2001a). Well-trained athletes would theoretically have a robust pacing strategy, given their long experience in developing such a template. Hettinga *et al*. (2006) suggested the stability of this template would apply across trials of different durations or distances, but this assertion has yet to be studied experimentally. Indirect support for the assumption of a robust pacing template has been demonstrated by Hulleman *et al*. (2007) who showed cyclists were unable to improve their 1500 m cycling time-trial performance by > 1 s

despite the incentive of monetary reward; the authors suggested that it would take a long time or an unusually high motivation to modify the pacing strategy.

Nevertheless, changes in pacing strategy do seem to occur on repeat trials, even in experienced athletes. Data from Ansley *et al*. (2004b) showed that well-trained cyclists adjusted their pacing strategy during successive 4 km cycling time-trials separated by short (17 min) rest periods, and Schabort *et al*. (1999) showed elite rowers adopted a more even pacing strategy on repeat 2 km rowing trials. Neither of these studies analysed these changes statistically. One study has systematically studied changes in pacing strategy, demonstrating a blunted start and larger end spurt across repeated 2 km cycling time-trials, in novice cyclists (Corbett *et al.*, 2009). Foster *et al*. (2009) also studied novice participants and showed a progressively more aggressive pacing strategy over repeat cycling and rowing trials. No study has yet systematically assessed the consistency of pacing strategy across repeat trials, or between trials of different duration, in well-trained athletes. Based on the aforementioned studies, it is likely that the pacing strategy adopted during repeat time-trials is subject to some degree of variability independent of any intervention. Quantifying this variability would enable future studies to better assess causality when studying closed-loop trials. This is particularly important given that previous studies have demonstrated the same performance outcome can be achieved through the adoption of a variety of different pacing strategies (Ansley *et al.*, 2004b; Hettinga *et al.*, 2006; Corbett *et al.*, 2009; Micklewright *et al.*, 2010) and that even small changes in pacing strategy can elicit different physiological responses (Thompson *et al*., 2003). Using time to completion or mean power as the only performance indicator might mask the effect of an intervention on pacing strategy and related physiological variables. Accordingly, the aim of the present study was to assess the reproducibility of performance and pacing strategy, and the consistency of the physiological and perceptual response, in repeat 20 km cycling time-trials in well-trained cyclists (part A). A second related study was conducted to quantify the consistency of pacing strategy between 4, 20 and 40 km time-trials, to establish whether a global pacing template exists in well-trained athletes independent of trial distance (part B).

4-2 Methods

4-2.1 Participants

A total of twenty nine well-trained male cyclists in regular cycling time-trial training and competition volunteered to participate in the study (Table 4-1). Written informed consent was obtained from all the participants prior to the start of the study, which was approved by the local research ethics committee. The study adhered to national (Hull *et al.*, 2008) and international (WMA, 2008) guidelines.

Table 4-1. Participant characteristics (n = 29). Peak incremental test power is the final completed 15 s stage in the incremental test. Values are mean ± SD

Age (years)	33 ± 7
Stature (m)	1.80 ± 0.07
Mass (kg)	74.8 ± 9.8
Maximum oxygen uptake ($L \cdot min^{-1}$)	4.62 ± 0.50
Peak incremental test power (P_{max}, W)	386 ± 26

4-2.2 Procedures

In part A of the study participants (n = 17) completed a preliminary visit followed by three 20 km time-trials (TT). Successive TT's were separated by 2-7 days and all three were completed within a maximum duration of 14 days. In part B of the study participants (n = 21) completed 4, 20 and 40 km, each preceded by a practice trial, in a randomised, counterbalanced order. Each trial was separated by 2-7 days and completed within a 21 day period. A subset of these participants completed a third time-trial for each distance to allow assessment of the reproducibility of performance during 4 (n = 15) and 40 km (n = 12) repeat time-trials. Prior to each visit participants were asked to refrain from strenuous exercise (> 24 h and caffeine (> 12 h) and to arrive in a fully rested, hydrated state. Before the first TT, participants completed a 48 hour food and activity diary and were instructed to replicate their exercise and nutrition as closely as possible before each subsequent trial. Trials were conducted at the same time of day (± 1 h) to minimise diurnal variation. Mean ± SD ambient laboratory temperature and relative humidity were 21 ± 2°C and 51 ± 8% respectively.

All exercise was completed on an electromagnetically braked cycle ergometer (Velotron Pro, RacerMate Inc., USA), which recorded power output and cadence at a frequency of

20 Hz. Participants adjusted the ergometer to their preferred racing position (which was recorded and replicated for each trial) and wore their own cycling shoes and cleats. Expired breath-by-breath respiratory gas exchange was analysed continuously by an automated metabolic cart (Cortex Metalyser 3b, Leipzig, Germany), and heart rate was recorded telemetrically (Polar Electro Oy, Kempele, Finland). All equipment was calibrated prior to each trial according to the manufacturer's instructions. Blood lactate concentration was determined from 20 μl samples of fingertip capillary blood immediately analysed for lactate concentration using an automated analyser (Biosen C_Line, EKF diagnostic, Barleben, Germany), which was calibrated prior to use with a 12 $mMol \cdot L^{-1}$ standard. An electrical fan was positioned 0.5 m in front of the ergometer for cooling during each trial.

4-2.3 Preliminary visit

Maximum oxygen uptake was determined with an incremental test to exhaustion which started at 200 W and incremented by 5 W every 15 s. Maximum oxygen uptake was calculated as the highest 30 s mean $\dot{V}O_2$.

4-2.4 Time-trials

A standardised 10 min warm-up was employed before each trial that consisted of 5 min at 150 W and 5 min at 70% P_{max}. Participants were given instructions to complete the distance in as fast a time as possible. The same range of electronic gear ratios was used for each trial, and participants started each trial in the same gear ratio, but were permitted to adjust this throughout the trial to reflect their preferred cadence. Feedback was limited to distance updates every 10% of trial distance covered, at which point participants were asked to rate their perceived exertion (RPE) using the Borg 6-20 (Borg, 1982b) scale and their affective perceptions of the exercise intensity using an 11 point bipolar scale (+5 (very good) to −5 (very bad)) with verbal anchors at two point intervals (Rejeski, 1985). Finger-prick blood samples were obtained at intervals equating to 20% of the distance covered.

4-2.5 Data analysis

Descriptive statistics are presented as means (±SD). To display the serial pattern of responses, data from the cycle ergometer and metabolic cart were interpolated and

averaged over 1 s intervals. For between trial comparisons (4 vs. 20 vs. 40 km) data were normalised relative to the distance covered in 1% means. Mean whole trial values for time (min) power output (W), cadence (rpm), oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), minute ventilation ($\dot{V}_E$), respiratory exchange ratio (RER), heart rate (HR), blood lactate ($mMol \cdot L^{-1}$) and RPE were computed. Differences between trials for these scores were assessed using one way repeated measures ANOVA, and reproducibility was quantified using typical error (90% confidence intervals) between successive trials as raw scores and as percentages derived from log transformed data. To investigate differences in pacing strategy across repeat 20 km trials, the mean power output for each 1 km epoch was normalised relative to the mean power for that trial, and typical error and change in the mean (90% confidence intervals) between trials 1-2 and 2-3 were calculated for each 1 km epoch of the trials from these raw percentage scores. Pearson correlation coefficients were calculated to assess associations between starting and finishing strategy. To investigate the variability in pacing strategy between 4, 20 and 40 km time-trials mean power output for epochs equating to 5% of the distance covered were normalised relative to the trial mean power and analysed with the same method. Data were analysed using a published spreadsheet (Hopkins, 2009) in Microsoft Excel (Microsoft Excel 2007).

4-3 Results

4-3.1 Part A: Reproducibility of 20 km time-trials

Mean ± SD power was not different ($p = 0.65$) between trials (276 ± 24 W, 276 ± 26 W and 277 ± 25 W for trials 1, 2 and 3 respectively), nor was mean performance time (31.99 ± 0.99 min, 31.98 ± 1.05 min, 31.90 ± 1.02 min, $p = 0.59$). The typical error for mean power was 1.6% (1.2 to 2.3%) between trials 1-2, and 2.2% (1.6 to 2.6%) between trials 2-3. The serial pattern of power output (Figure 4-1) and cardiorespiratory (Figure 4-2), RPE, affect and blood lactate responses (Figure 4-3) were similar for all three trials. There were no differences ($p = 0.28$ to 0.98) between trials for any of the physiological or perceptual variables recorded (Table 4-2). Typical error for the trial mean of all variables (except for blood lactate) was low (range = 1.0 to 4.0%, Table 4-2).

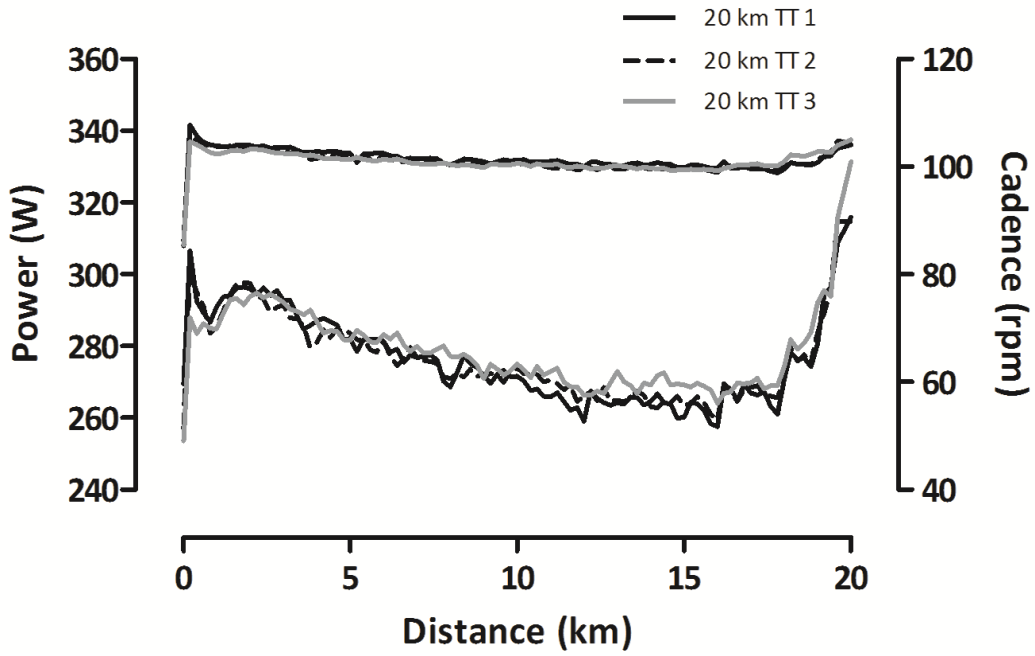


Figure 4-1 Serial pattern of power output (lower traces, primary y axis) and cadence (upper traces, secondary y axis) during repeat 20 km time-trials in well-trained cyclist.

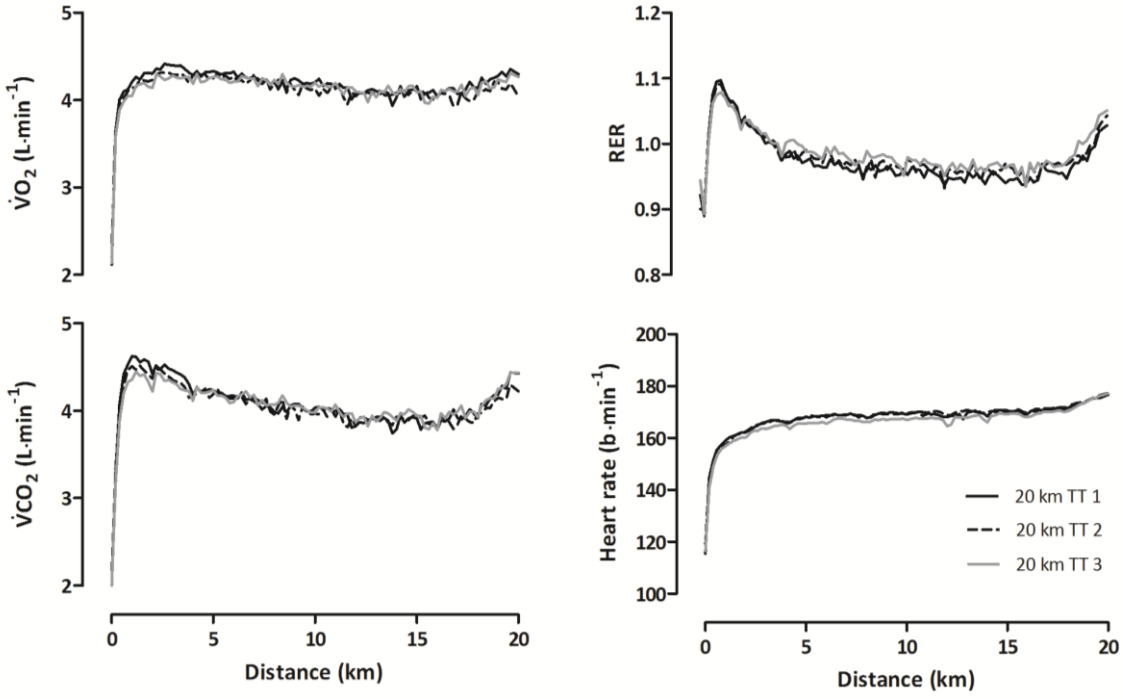


Figure 4-2. Serial pattern of cardiorespiratory responses (oxygen uptake, carbon dioxide production, respiratory exchange ratio and heart rate) to repeat 20 km time-trials in well-trained cyclists.

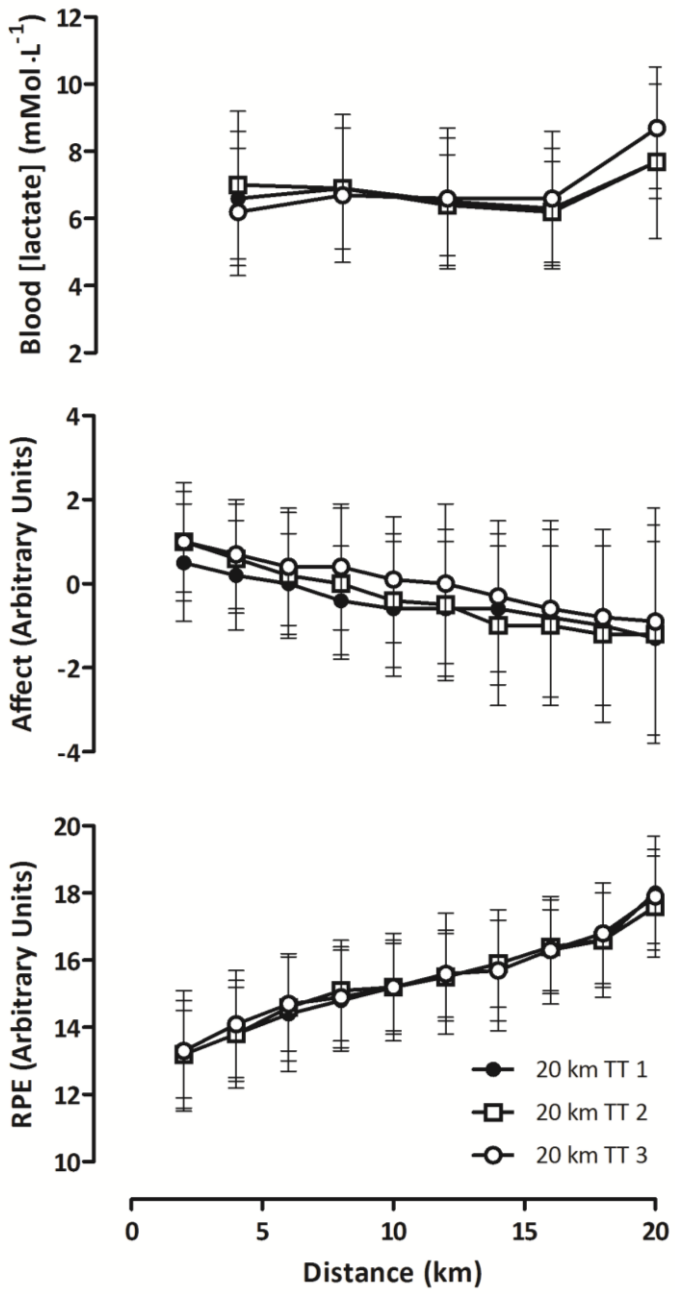


Figure 4-3. Serial pattern of RPE and affective response, and blood lactate concentration during repeat 20 km time-trials in well-trained cyclists.

With regards pacing strategy, participants adopted a fast start with the first 6 km of the trial completed above the mean power, the remaining distance below the mean power and an end spurt in the final 2 km (Figure 4-1). The typical error in the pacing strategy - variability between trials in power output relative to the mean - was highest for the first 1 km epoch (TE = 6.6% (5.5 to 8.8%)) and last 1 km epoch (TE = 6.8% (5.6 to 9.1%)), and lower for the intervening 18 km (TE range = 1.8 – 3.4%), indicating a greater variability in pacing strategy at the start and end of repeat trials (Figure 4-4). There was a trend for a progressively blunted start in successive time-trials; the power

output relative to the mean for the first 1 km epoch decreased by 1.2% (−4.5 to 2.1%) between trial 1 and 2, then further decreased by 3.3% (−8 to 1%) between trial 2 and 3. There was no association between the variability in starting strategy (TE for 1st km epoch) and finishing strategy (TE for last 1 km epoch; $r = -0.21$, $p = 0.43$), and no association between starting power output and finishing power output in each 20 km ($r = -0.30$ to -0.45, $p > 0.05$).

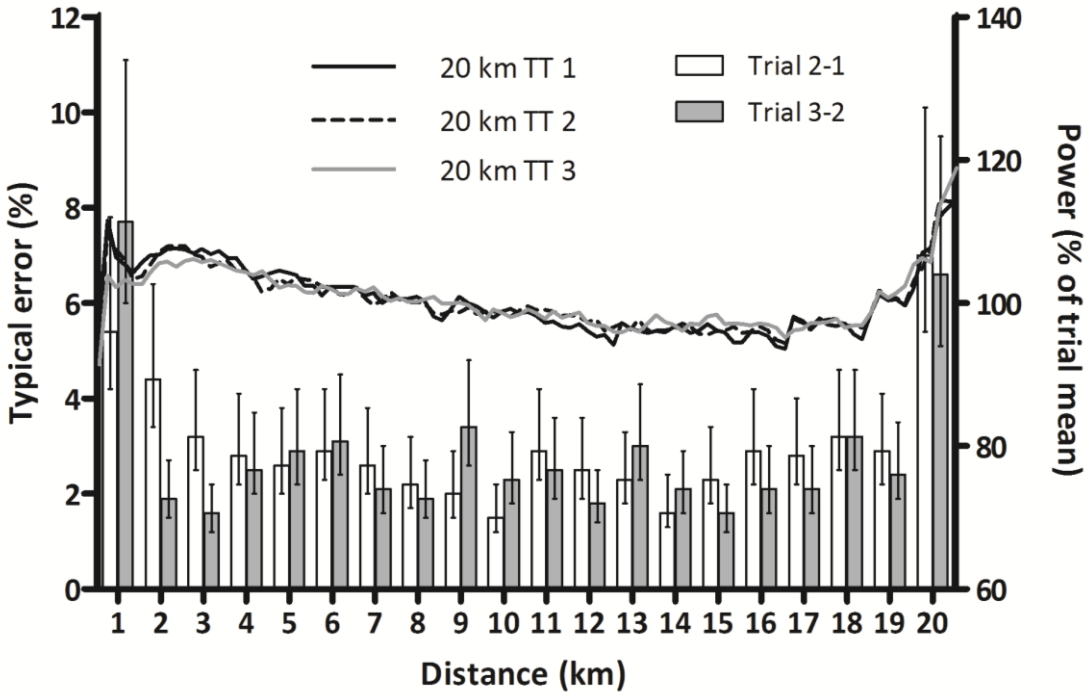


Figure 4-4. Typical error (90% confidence intervals) in the pacing strategy for 20 km time-trials 1-2 and 2-3 for each 1 km epoch. Error is calculated from the power output data relative to the mean (displayed on secondary y axis). Typical error was highest in the first and last km of the trial, and lower for the intervening 18 km.

4-3.2 Part B: Reproducibility within and between 4, 20 and 40 km time-trials

For 4 km, mean power output was not different between successive trials (335 ± 26 W, 336 ± 33 W, 335 ± 31 W for trials 1, 2 and 3 respectively, $p > 0.05$) nor was time to completion (6.02 ± 0.17 min, 6.02 ± 0.22 min, 6.02 ± 0.20 min, $p > 0.05$). Typical error was 2.3% (1.7 – 3.3%) between trials 1-2 and 1.9% (1.5 – 2.8%) between trials 2-3. For 40 km mean power and time to completion were not different between successive trials (248 ± 33 W, 241 ± 35 W, 246 ± 32 W, 66.58 ± 2.78 min, 67.25 ± 3.19 min, 66.92 ± 3.33 min for trials 1, 2 and 3 respectively, $p > 0.05$). Typical error was 3.5% (2.6 to 5.7%) between trials 1-2 and 3.8% (2.8 to 6.2%) between trials 2-3.

Between 4, 20 and 40 km trials participants adopted a similar pacing strategy independent of the distance to be covered (Figure 4-5). The variability in the pacing strategy between trials of different distance was similar to that observed across repeated trials of the same distance, with more variability when comparing the first 10% (TE range = 8 – 12% and last 10% of the distance covered between trials (TE range = 5 – 6%) compared to the intervening 80% (mean TE = 3.8%, range = 2.1 – 6.9%). Subjectively, there was a trend for a more aggressive start in the 4 km trial, and more variability when comparing the 4 km to the 20 and 40 km than when comparing the 20 to the 40 km (Figure 4-5).

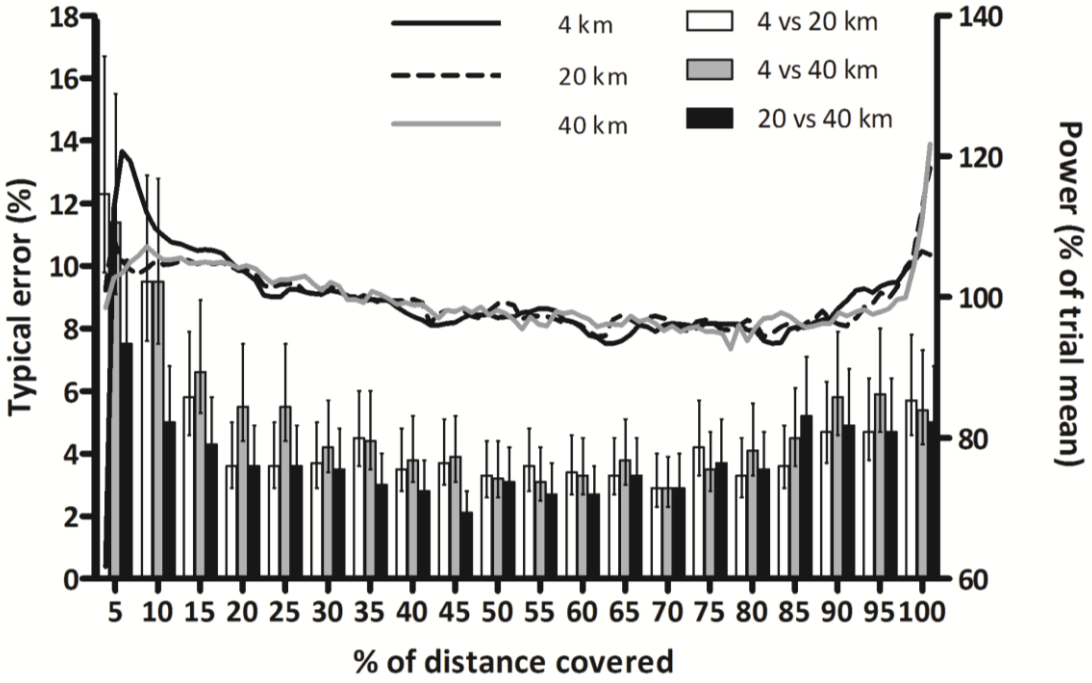


Figure 4-5. Typical error (90% confidence intervals) in the pacing strategy between 4, 20 and 40 km time-trials relative to distance covered for each trial. Error is calculated from the power output data relative to the mean (displayed on secondary y axis). Typical error in the pacing strategy was highest when comparing the first and last 10% of each trial, and lower for the intervening 80%.

Table 4-2. Mean ± SD for whole trial performance, physiological and perceptual measures during repeat 20 km time-trials and the associated typical error (TE) (±90% confidence intervals) for trials 1-2, 2-3 and as a mean across all 3 trials. Percentage TE based on log-transformed data and TE for the raw scores are provided.

	20 km TT1	20 km TT2	20 km TT3	TE (90% CIs)	CV (90% CIs)
Time (min)	31.99 ± 0.99	31.98 ± 1.05	31.90 ± 1.02	0.24 (0.29-0.32)	0.7 (0.6-1.0)
Power (W)	276 ± 24	276 ± 26	277 ± 25	5 (4-7)	1.9 (1.6-2.6)
Cadence (rpm)	101 ± 9	101 ± 10	101 ± 8	2 (2-3)	2.2 (1.8-3.0)
$\dot{V}O_2$ ($L \cdot min^{-1}$)	4.18 ± 0.34	4.12 ± 0.33	4.14 ± 0.30	0.11 (0.09-0.16)	2.7 (2.2-3.8)
$\dot{V}CO_2$ ($L \cdot min^{-1}$)	4.07 ± 0.34	4.04 ± 0.29	4.06 ± 0.26	0.15 (0.12-0.20)	3.7 (3.1-5.2)
$\dot{V}_E$ ($L \cdot min^{-1}$)	131 ± 15	129 ± 15	131 ± 18	4 (4-6)	3.5 (2.8-4.9)
$\dot{V}_E / \dot{V}O_2$	31.3 ± 2.6	31.4 ± 2.2	31.4 ± 3.1	1.1 (0.9-1.5)	3.5 (2.8-5.0)
$\dot{V}_E / \dot{V}CO_2$	32.1 ± 2.7	32.0 ± 2.3	32.2 ± 3.3	1.4 (1.2-2.0)	4.5 (3.6-6.4)
RER	0.97 ± 0.03	0.98 ± 0.03	0.99 ± 0.04	0.02 (0.02-0.03)	2.0 (1.6-2.8)
HR ($b \cdot min^{-1}$)	168 ± 9	168 ± 10	166 ± 9	2 (2-3)	1.2 (1.0-1.6)
$[La^-]$ ($mMol \cdot L^{-1}$)	6.96 ± 1.87	6.93 ± 1.35	7.01 ± 1.62	1.2 (1.0-1.6)	17.7 (13.7-25.7)
RPE	15 ± 1	15 ± 1	15 ± 1	1 (0-1)	2.8 (2.2-4.3)

TE; typical error in raw units, CV; typical error as a coefficient of variation, $\dot{V}O_2$; oxygen uptake, $\dot{V}CO_2$, carbon dioxide output; $\dot{V}_E$, minute ventilation; $\dot{V}_E/\dot{V}O_2$, ventilatory equivalent for oxygen; $\dot{V}_E / \dot{V}CO_2$, ventilatory equivalent for carbon dioxide; RER; respiratory exchange ratio, HT; heart rate, $[La^-]$; blood lactate concentration, RPE; rating of perceived exertion.

4-4 Discussion

The novel findings of this study indicate the existence of a global pacing strategy that operates independent of the race distance to be covered and is consistent across repeated trials of the same distance. Though the pacing strategy adopted was broadly similar across repeat 20 km trials, and between 4, 20 and 40 km trials, there was a higher degree of variability when comparing the start and end of the trial both within and between different distances (Figures 4-4 and 4-5), and a trend for a progressively blunted start on repeat trials of the same distance (Figure 4-4).

Ulmer (1996) first introduced the notion of teleoanticipation, by which the pre-programmed template for the power output during an exercise bout is modified or "fine-tuned" by metabolically triggered feedback during the exercise. By its' very nature this results in the interpretation of afferent physiological signals being subject to an uncertainty that is resolved as the bout progresses (Lambert *et al.*, 2005; St Clair Gibson *et al.*, 2006; Tucker, 2009). This concept explains the higher levels of variability in power output that we observed during the first 10% between our self-paced time-trials compared to the low degree of variability in power output for most of the remainder of the distance between trials, until the final 10% where participants increased power output. This end spurt phenomenon, as the endpoint approaches and the chance of premature fatigue reduces, reflects the considered reserve the athlete maintains for the majority of the race in order to reduce the hazard of catastrophic collapse (de Koning *et al.*, 2011). Theoretically, as an athlete becomes more experienced with the exercise task the amplitude of the end spurt would fall. There was no evidence of this in the group of well-trained athletes studied despite the consistency of overall performance, which suggests that the maintenance of a reserve is a feature of self-paced exercise performance in experienced athletes; an assertion supported by the presence of an end spurt in elite athletes' world record performances (Tucker *et al.*, 2006b). Moreover, the lack of association between starting and finishing power output indicates that the starting strategy doesn't appear to influence the magnitude of the finishing sprint. Studying the characteristics of the end spurt across repeated trials in novice and well-trained exercisers could be a worthwhile area of future research. When interpreting the effect of interventions on pacing strategy, researchers should be aware that variability at the start and end of repeat self-paced cycle time-trials is likely, independent of any intervention employed.

The consistency of pacing strategy between time-trials of different distance support the hypothesised existence of a stable, global pacing template in well-trained athletes (St Clair Gibson *et al.*, 2001a; Hettinga *et al.*, 2006; Baron *et al.*, 2011). This is contrary to previous work with novice participants, where it has been suggested it takes more than six exposures to the same exercise challenge before a stable performance template is learned (Foster *et al.*, 2009). In contrast, in the present study pacing strategy was similar between different distances and across repeated trials, indicating well-trained athletes employ a consistent pacing strategy during endurance events. The typical strategy adopted in all trials broadly consisted of an initial period above the mean power, a progressively declining and relatively even pace for the majority of the trial thereafter until a terminal end spurt at the finish (Figures 4-4 & 4-5). This type of parabolic pacing strategy is commonly observed in endurance events across different modes in well-trained and elite athletes (Tucker *et al.*, 2006b; Corbett, 2009; Muehlbauer & Melges, 2011; Mauger *et al.*, 2012).

Subjectively, there was a trend for a faster start in the 4 km trial compared to the 20 and 40 km trials and the variability in pacing strategy between the 4 km and the longer trials was greater than that observed between the 20 and 40 km (Figure 4-5). The faster start in the 4 km might reflect a conscious decision by the athlete to minimise the time spent accelerating, as the starting strategy would contribute relatively more to the overall performance in comparison to the longer duration trials (Abbiss & Laursen, 2008). The greater variability in pacing strategy between the 4 km and the relatively longer duration trials might indicate differences in the factors regulating performance during these trials. The contribution of central and peripheral mechanisms to fatigue during exercise is task specific; generally peripheral mechanisms dominate during short duration, high intensity tasks and central fatigue manifests more during longer duration, lower intensity tasks (Schillings *et al.*, 2003; Ross *et al.*, 2010a). Limited data exists on self-paced exercise, and no studies have directly compared time-trials of varying durations, but it is plausible to suggest the shorter duration 4 km trial might be influenced by different mechanisms of fatigue compared to the longer, lower intensity trials. An alternative explanation for the observed differences in variability might simply be a function of the resolution of data. All trials were expressed relative to the distance covered. For the 4 km, 5% of the distance covered equated to 200 m, compared to 1000

m and 2000 m for the 20 and 40 km respectively. The lower resolution of averaging in the shorter trials would likely result in more variability in the calculated mean response and could explain the higher variability observed when compared to the longer trials.

The trend for a progressively slower start across repeat 20 km trials has previously been demonstrated in physically active males completing repeat 2 km cycling time-trials on separate days (Corbett *et al.*, 2009), and in well-trained cyclists performing successive 4 km cycling time-trials on the same day (Ansley *et al.*, 2004b). This effect has also previously been demonstrated (although not statistically analysed) in well-trained athletes performing repeat trials despite familiarity with the exercise task employed (Schabort *et al.*, 1999; Foster *et al.*, 2003). These findings are consistent with the concept of an intelligent, complex regulatory system (Ulmer, 1996; St Clair Gibson *et al.*, 2001a; St Clair Gibson & Noakes, 2004; St Clair Gibson *et al.*, 2006) and suggest that information gained from the first time-trial is utilised to make minor modifications to the exercise template, either consciously or subconsciously, on subsequent bouts (Corbett *et al.*, 2009). The blunted start could theoretically serve to minimise the disruption to the peripheral physiological milieu relative to the previous trial template (Micklewright *et al.*, 2010). This pattern has previously been demonstrated in both trained and untrained participants (Ansley *et al.*, 2004b; Corbett *et al.*, 2009; Micklewright *et al.*, 2010) and could reflect a learning associated feed-forward control mechanism that is influenced by prior experience. However, after this initial 'uncertain' start, the majority of the trial thereafter was accomplished with little variability in the pacing strategy and overall performance between trials. This, coupled with the similarity in the physiological response between trials, suggests that pacing strategy for the majority of the exercise bout after the initial uncertain start is tightly regulated by afferent feedback, and the resulting performance is largely determined by these feedback mechanisms.

The typical error for mean power across repeat 20 km time-trials (1.9% (1.6 to 2.6%)) was similar to that reported in previous studies utilising 20 km and 40 km indoor time-trials (Palmer *et al.*, 1996; Smith *et al.*, 2001; Laursen *et al.*, 2003; Sporer & McKenzie, 2007; Zavorsky *et al.*, 2007). Sporer & McKenzie (2007) and Zavorsky *et al*. (2007) both assessed 20 km time-trial reproducibility using the Velotron Pro ergometer. Zavorsky *et al*. (2007) reported slightly higher variation for 18 trained cyclists than the present study (3.6%) although the range of mean power outputs for 20 km was large

(158-353 W) and, when considering the top 8 performers only, the variation was much reduced (1.2%). Sporer & McKenzie (2007) reported similar variation to the present study (1.9%, 95% CI's 1.4 to 2.8%) using a homogenous group of highly-trained cyclists (mean 20 km power = 322 ± 34 W). Taken together, these findings indicate that the variation in performance of a flat 20 km time-trial in both well-trained and highly-trained cyclists on the Velotron Pro ergometer is comparable to that expected during competition time-trials (Paton & Hopkins, 2006).

The hypothetical minimum meaningful change in performance is an important consideration in research, both to estimate the required sample size to detect such an effect and to determine whether any observed performance change has practical significance (Atkinson & Nevill, 2001). Whilst the Neyman-Pearson hypothesis testing approach is ubiquitous in sport and exercise research, more progressive statistical approaches have been proposed which promote *a priori* estimates of practically/clinically worthwhile effect magnitudes as a must for meaningful interpretation of data analysis (Hopkins *et al.*, 2009). Careful consideration of the smallest-worthwhile effect is also a requirement of Neyman-Pearson inference in order to control the type II error rate by estimating appropriate sample sizes. Determination of such an effect is challenging. For data that has a 1:1 relationship with competitive performance (e.g. power output, time), a minimal important change can be estimated from the within-subject standard deviation of actual race performance and the likelihood that an athlete would improve their finishing position (Hopkins *et al*. 1999). When the primary change of interest is centred around the average person in the population group sampled, Cohen (1988) suggested estimating the smallest effect as a proportion of the between-subject standard deviation, using standardised thresholds (Hopkins, 2000). Adopting this approach on the data presented here for 20 km time-trials, the estimated smallest-worthwhile change in power output was 5 W, or 1.8%, which is similar to the observed typical error (1.9%). Using methods described by Hopkins (2000) an estimated sample of nine participants would be required to detect 80% power in a crossover or simple test-retest design, or 27 participants in a randomised control trial.

A further finding in the present study and that of Sporer & McKenzie (2007) was the lack of performance improvement or reduction in variability over repeat time-trials. Repeat assessments usually enhance reproducibility by ensuring participants are well-

practiced (Hopkins *et al.*, 2001). However, where participants are experienced in producing a performance for a specific distance, a practice trial might not be necessary (Sporer & McKenzie, 2007). This finding is not consistent with all previous research (Laursen *et al.*, 2003; Zavorsky *et al.*, 2007; Stone *et al.*, 2011) and inclusion of a practice trial in a research design, even with experienced participants, would be prudent.

The physiological response to repeat 20 km time-trials, with the exception of blood lactate, exhibited low typical error. To our knowledge, only one previous study has measured cardiorespiratory and blood lactate variables during repeat 40 km laboratory time-trials (Smith *et al.*, 2001). These authors reported a narrow CV range for oxygen uptake (3.0 & 2.9%) and heart rate (3.2 & 1.7%) but a broader range for blood lactate (16.4 & 5.7%). The low variability in the whole trial cardiorespiratory response reflects the ability of well-trained athletes to consistently produce a best effort performance during a trial with a known endpoint, and the importance of afferent feedback in the control of the pacing strategy, as previously discussed. That blood lactate exhibited higher variability reflects the sensitivity of lactate to the power output preceding the measurement. Monitoring the lactate response in higher resolution during self-paced trials would be desirable; however the invasive nature of blood sampling renders this problematic.

In conclusion, the pacing strategy adopted by well-trained cyclists during repeat laboratory time-trial exercise is subject to variability, particularly at the start and end of the trial, independent of any intervention employed. The overall aim of this thesis is to understand the biological basis of pacing, and the optimum pacing strategy for endurance time-trial events. The consistency of pacing strategy between 4, 20 and 40 km time-trials observed in this chapter indicates the existence of a global pacing template in well-trained athletes that operates independent of the race distance. This finding, and the observation of a reproducible performance, perceptual and physiological response to self-paced exercise, provides a framework for further study. Specifically knowledge of the variability inherent in self-paced exercise allows a more informed assessment of the effect of any subsequent intervention or manipulation of the pacing strategy, and the data presented here can be used to calculate appropriate sample sizes and estimate magnitudes of effects for the variables studied during this mode of exercise. This chapter thus forms the basis for the investigations conducted in the

following two chapters which manipulate the athlete's self-selected pacing strategy and study the subsequent impact on performance and the perceptual and physiological response to exercise.

CHAPTER 5 THE EFFECT OF SELF, EVEN AND VARIABLE PACING STRATEGIES ON THE PHYSIOLOGICAL AND PERCEPTUAL RESPONSE TO CYCLING

5-1 Introduction

The pacing strategy adopted by an athlete during a race will influence the relative contribution and temporal distribution of energy derived from oxidative and non-oxidative pathways (Jones *et al.*, 2008b), the perception of exertion (St Clair Gibson *et al.*, 2006) and ultimately the race performance (Atkinson *et al.*, 2007c). Perception of exertion has been described as the conscious awareness of changes in subconscious homeostatic control systems (St Clair Gibson *et al.*, 2003) and has been identified as a potential mediator of voluntary exercise output (Tucker, 2009). The ideal pacing strategy would maximise performance for the same rating of perceived exertion. Numerous researchers have suggested that, for events lasting longer than 2 min, an even distribution of work is optimal (Foster *et al.*, 1993; Thompson *et al.*, 2003; Gordon, 2005; Atkinson *et al.*, 2007c). Despite this recommendation, self-paced exercise is rarely sustained at a constant intensity (Ansley *et al.*, 2004b; Tucker *et al.*, 2006a), and in events where athletes compete directly against each other, racing is characterised by variable, stochastic changes in pace (Palmer *et al.*, 1994).

The physiological responses to time- and work-matched even-paced (EP) and variable-paced (VP) exercise bouts have been previously examined using a range of exercise protocols. When the variation in power output is small (± 10% or less), the physiological responses to VP exercise (respiratory exchange, muscle metabolism, blood metabolites and neuromuscular fatigue) are similar to that observed during EP exercise (Liedl *et al.*, 1999; Atkinson *et al.*, 2007b; Lepers *et al.*, 2008). When the variation in power output incorporates high intensity periods in the extreme exercise domain, where the physiological response is non-linear, neuromuscular fatigue is greater in VP compared to EP (Theurel & Lepers, 2008); although when the recovery period between high intensity efforts is long (2 min) there is no additional physiological stress (Brickley *et al.*, 2007). Whilst the physiological responses to matched EP and VP bouts are well-described, most studies have imposed relative intensities based on measured physiological thresholds such as critical power, or maximal aerobic power, and have seldom been compared with those characterised by self-paced exercise (SP) (Billat *et al.*, 2006; Lander *et al.*, 2009) even though it has been demonstrated that athletes can achieve mean intensities in excess of such thresholds during SP exercise (Kenefick *et al.*, 2002).

Limited data is available comparing EP and VP strategies to time- and work-matched SP bouts (Billat *et al.*, 2006; Atkinson *et al.*, 2007a; Ham & Knez, 2009; Lander *et al.*, 2009). It has been hypothesised that an even distribution of work might be physiologically optimal (Foster *et al.*, 1993); however when EP exercise bouts based on a previous SP performance have been examined, studies have reported EP exercise to be more challenging, with evidence of augmented physiological responses and an inability to complete the required work in EP compared to SP (Billat *et al.*, 2006; Atkinson *et al.*, 2007a; Lander *et al.*, 2009). When comparing time- and work-matched SP and VP bouts, the same exercise intolerance has been reported in some participants during VP bouts with small variations (± 5%) in power output (Atkinson *et al.*, 2007a), but no studies exist that assess the impact of larger variations incorporating exercise intensities in the extreme exercise domain. Lander *et al*. (2009) proposed SP exercise is less challenging since the intensity can be regulated and adapted to minimise physiological strain and perception of exertion as part of a complex, central regulatory process. The perception of exertion is proposed to be the conscious awareness of subconscious homeostatic control processes, and alterations in pacing strategy are a behavioural response to these sensations to prevent unreasonably large disturbances to homeostasis during the exercise bout (St Clair Gibson *et al.*, 2003; de Koning *et al.*, 2011). It is somewhat surprising therefore that no studies have examined how adoption of these different types of pacing strategy affects the perceived exertion of completing a task.

The aim of the present study was to assess the effect of time- and work-matched self-, even- and variable-pacing strategies on physiological and perceptual responses to a bout of cycling exercise. It was hypothesised that an even-paced strategy would result in the lowest perturbation to the physiological systems and therefore be associated with the lowest perception of exertion. It was also hypothesised that variable-paced cycling which incorporates large variations in exercise intensity would result in the greatest perturbations and highest perception of exertion.

5-2 Methods

5-2.1 Participants

Ten well-trained male cyclists who regularly perform cycling training and time-trial competitions volunteered to participate in the study. Participant characteristics are

presented in Table 5-1. Sample size was estimated using typical error and standard deviation scores derived from the reproducibility study reported in Chapter 4 (Thomas *et al.*, 2012b), and methods described by Hopkins (2000). Small, moderate and large effects were determined as 0.2, 0.5 and 0.8 of the between-subject standard deviation for each outcome measure (Cohen, 1988; Hopkins *et al*., 1999). An estimated sample size of nine was required to detect small or moderate effects with 80% statistical power in the outcome measures studied. Written informed consent was obtained from all the participants prior to the start of the study, which was approved by the local research ethics committee. The study was performed in accordance with national and international guidelines (Hull *et al.*, 2008; WMA, 2008).

Table 5-1. Participant characteristics (N = 10), values are mean ± SD

Age (years)	33	±	7
Stature (m)	1.77	±	0.06
Mass (kg)	76.7	±	7.2
Maximum oxygen uptake ($L \cdot min^{-1}$)	4.89	±	0.32
Power output at $\dot{V}O_2max$ (P_{max}, W)	353	±	30

5-2.2 Procedures

Each participant completed an incremental cycling test, one practice 20 km time-trial (TT) and three experimental 20 km TTs. The design of the study was crossover with the order of the experimental TTs partially randomised. Participants followed pre-test preparations as previously described. Trials were conducted at the same time of day (± 1 hour) to minimise diurnal variation. Each visit was separated by at least 3 and no more than 7 days. All exercise was conducted on an electromagnetically braked cycle ergometer (Velotron Pro, RacerMate Inc., USA) as previously described. Expired air and heart rate were recorded using procedures described previously. Blood [lactate] was determined from 25 µl samples of fingertip capillary blood collected in heparinised capillary tubes. The blood samples were immediately analysed for lactate concentration using an Analox P-GM7 Micro-stat (Analox instruments Ltd. London, UK) automated analyser, which was calibrated prior to use with an 8 $mMol \cdot L^{-1}$ standard. An electrical fan was positioned in front of the ergometer at a distance of 0.5 m for cooling during each trial.

Incremental exercise test

After a self-determined warm-up, participants completed an incremental test to volitional exhaustion to determine $\dot{V}O_2max$, starting at 110 W with 30 W increments every 150 s. Maximum oxygen uptake was calculated as the highest 30 s mean value. Power at maximum oxygen uptake (P_{max}) was calculated from:

$$P_{max} = \left(\frac{P_{final^{-1}}}{150} \times 150 - t_{final} \right) + \left(\frac{P_{final}}{150} \times t_{final} \right)$$

Where:

P_{final} = final power output

P_{final}^{-1} = penultimate stage power output

t_{final} = time completed at final stage power output.

20 km time-trials

Participants completed a standardised 10 min warm-up before each trial. Following a practice self-paced 20 km TT, participants completed three experimental 20 km TTs: a self-paced trial (SP), an even-paced trial (EP) and a variable-paced trial (VP). The SP trial was always performed first and participants were instructed to 'complete the distance as fast as possible'. The order of the subsequent EP and VP trials was randomised and evenly counterbalanced. The constant workload during EP was fixed at the mean power maintained during SP. The workload during VP varied between 72% and 142% of the mean power maintained during SP in a 1:1.5 ratio (approximately 40 s:60 s depending on SP performance). The VP protocol was purposefully designed to examine the effect of variable pacing when the imposed variations in intensity incorporated frequent, sustained periods of exercise in the extreme exercise domain, where the physiological response is non-linear (Jones & Doust, 2001), whilst maintaining an exercise intensity in the moderate domain during the low power segments that could still be representative of race performance (Palmer *et al.*, 1994). All three trials were equal in terms of total work done (kJ) and time (s), but the distribution of work varied.

During SP, participants were informed of distance at 2 km intervals, and 500 m intervals in the final 1 km. During EP and VP, participants were informed of progress at

intervals equating to 10% of total work done. At the start of each interval, participants rated their perceived exertion (RPE) and affect as previously described. Blood lactate was sampled every second interval; in the VP trial this occurred halfway into a low-intensity period of exercise. On completion of each time-trial and after a standardised 5 minute cool down, participants were asked for a whole trial 'gestalt' RPE that best represented the effort over the entire session.

5-2.5 Data analysis

Descriptive statistics are presented as means (±SD). For estimates of an average rate (i.e. power output, a rate of work) it has been suggested the harmonic, rather than arithmetic, mean might be a more appropriate summary of the data in order to mitigate the influence of large outliers and increase the influence of small values. The harmonic mean was thus calculated and is reported for all trials where power output could vary to ensure the appropriateness of the arithmetic mean as a summary statistic. Data from the cycle ergometer and metabolic cart were converted to percentages of work done (kJ) for each trial to display the pattern of responses, and further delimited into 10% 'bins' for subsequent analysis. Normality was assessed via visual inspection of normal probability plots and Shapiro-Wilks hypothesis tests (Newell *et al.*, 2010). Assuming a normal distribution, the effect of pacing strategy on cadence (rpm), oxygen uptake ($\dot{V}O_2$, $L \cdot min^{-1}$) carbon dioxide production ($\dot{V}CO_2$, $L \cdot min^{-1}$), minute ventilation ($\dot{V}E$, $L \cdot min^{-1}$), ventilatory equivalents, respiratory exchange ratio (RER), heart rate (HR, $b \cdot min^{-1}$) and blood lactate ($mMol \cdot L^{-1}$) was assessed for statistical significance using factorial (trial x distance) repeated measures ANOVA. Where a significant main effect between trials was indicated, Tukey's least significant difference and 95% confidence intervals were used for pairwise comparisons. Differences between trials for RPE and affect were assessed using Friedman's ANOVA, with post-hoc Wilcoxon signed-rank tests employed where a significant main effect was indicated. Effect sizes were calculated using Cohen's *D*. Statistical significance was assumed at p values < 0.05. Statistical analysis was performed using PASW 17.0 and Microsoft Excel 2007.

5-3 Results

5-3.1 Performance variables

During SP participants adopted a fast start strategy with the first 6 km of the trial completed 4-10% above the mean power, the next 12 km 1-7% below the mean power and an end spurt 6% above the mean power in the final 2 km (Figure 5-1). Performance in SP was not different to the practice trial (mean difference, 95% CI's = 5 W, −2 to 11 W, $p = 0.22$) and within the expected typical error of measurement for 20 km time-trials in this population (Thomas *et al.*, 2012b) (Figure 5-1). Time taken to complete the SP trial was 32.53 ± 1.54 min and the mean power output was 265 ± 29 W (75 ± 6 % of calculated P_{max}). Based on performance in SP, EP was set at 265 ± 29 W and the VP trial alternated between 374 ± 44 W and 189 ± 23 W in a 1:1.5 high:low power ratio (37-43 s of high intensity and 56-64 s of low intensity). The harmonic mean for self-paced and variable trials was similar to the arithmetic mean (harmonic mean ± SD SP, 265 ± 31 W, VP, 264 ± 31 W). Figure 5-2 depicts an example of the power profiles for a representative participant.

All participants successfully completed all trials. There were differences between trials for cadence ($p = 0.02$). Participants adopted a higher cadence during SP (98 ± 8 rpm) compared to VP (90 ± 11 rpm, mean difference, 95% CI's = 9, 2 to 15 rpm, $p = 0.02$, $D = 1.05$) and EP (93 ± 8, mean difference, 95% CI's = 6, 1 to 12 rpm, $D = 0.70$) although the latter did not reach statistical significance ($p = 0.07$).

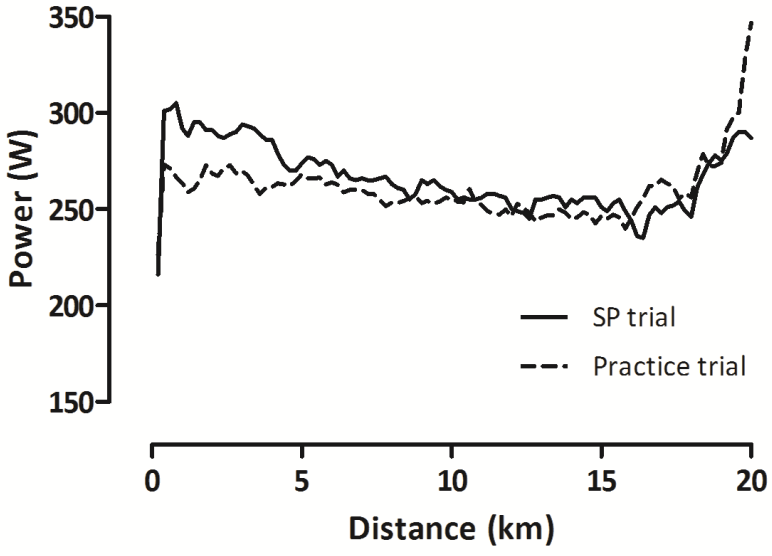


Figure 5-1. Power output profiles for self-paced (SP) and practice self-paced 20-km time-trials. Performance was not different between trials ($p = 0.22$).

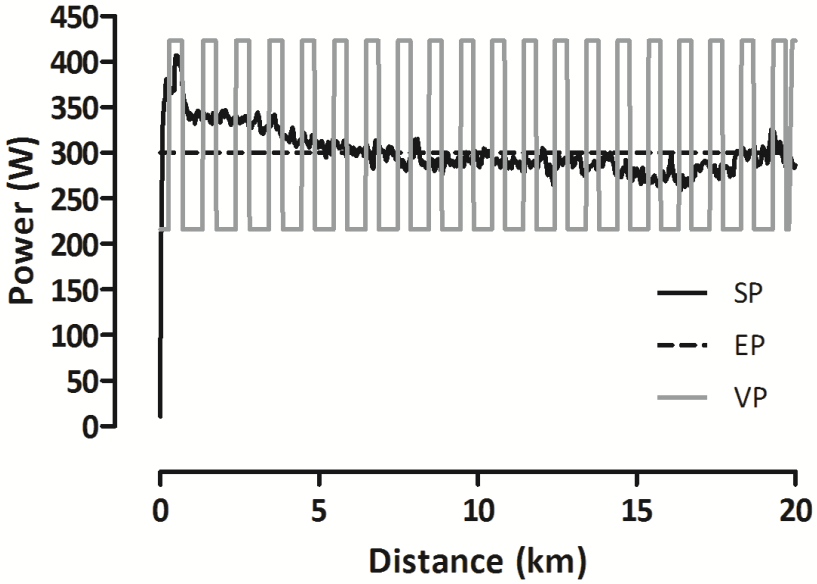


Figure 5-2. Example power output profiles for self-paced (SP), even-paced (EP) and variable-paced (VP) trials from a representative participant. The average power and time to completion from the self-paced trial (black line) was used to set time- and work-matched even-paced (dashed black line) and variable paced (grey line) trials.

5-3.2 Physiological variables

Oxygen consumption was 87 ± 4 %, 86 ± 5% and 85 ± 5% $\dot{V}O_2$max for SP, EP and VP respectively. The pattern of response in all of the measured physiological variables was different (Figure 5-3), indicated by significant interaction effects ($p < 0.05$), but there were no whole trial differences for $\dot{V}O_2$ ($p = 0.44$), $\dot{V}CO_2$ ($p = 0.29$) or RER ($p = 0.09$), although the slightly elevated RER in VP compared to EP represented a moderate effect (mean difference, 95% CI's = 0.02, 0.00 to 0.03, $D = 0.44$). For ventilatory indices, $\dot{V}_E$ was lower in EP ($p < 0.05$) compared to both SP (mean difference, 95% CI's = −7.2, −12.9 to −1.6 L·min^{-1}) and VP (mean difference, 95% CI's = −10.0, −15.7 to −4.3 L·min^{-1}). Variable paced exercise also resulted in a reduced ventilatory efficiency compared to EP exercise, with higher variables for the ventilatory equivalent for oxygen (mean difference, 95% CI's = −2.8, −4.6 to −1.0) and carbon dioxide (mean difference, 95% CI's = −2.4, −3.9 to −1.0, Figure 5-4). Heart rate was lower in EP compared to both SP (mean difference, 95% CI's = −5, −7 to −3 b·min^{-1}, $p = 0.001$) and VP (mean difference, 95% CI's = −6, −9 to −3 b·min^{-1}, $p = 0.002$). Blood lactate concentrations (Figure 5-5) were different between trials ($p < 0.05$). Blood lactate in VP was higher than in EP (mean difference, 95% CI's = 1.8, 1.0 to 2.5 mMol·L^{-1}, $p = 0.001$, $D = 1.02$) and SP (mean difference, 95% CI's = 0.8, 0.3 to 1.4 mMol·L^{-1}, $p = 0.008$, $D = 0.45$) and

lower in EP compared to SP (mean difference, 90% CI's = −1.0, −1.3 to −0.6 mMol·L^{-1}, p = 0.001, D = 0.56).

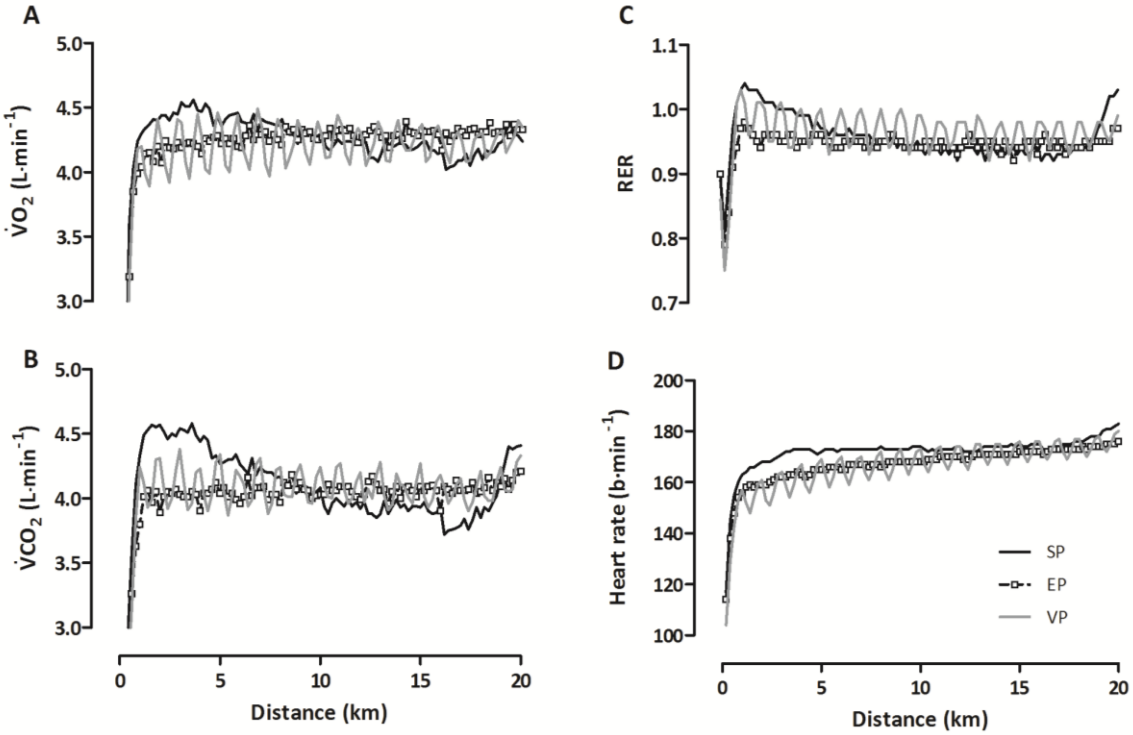


Figure 5-3. Respiratory (Panels A, B & C) and heart rate responses (Panel D) to time- and work-matched self-paced (SP), even-paced (EP) and variable-paced (VP) trials.

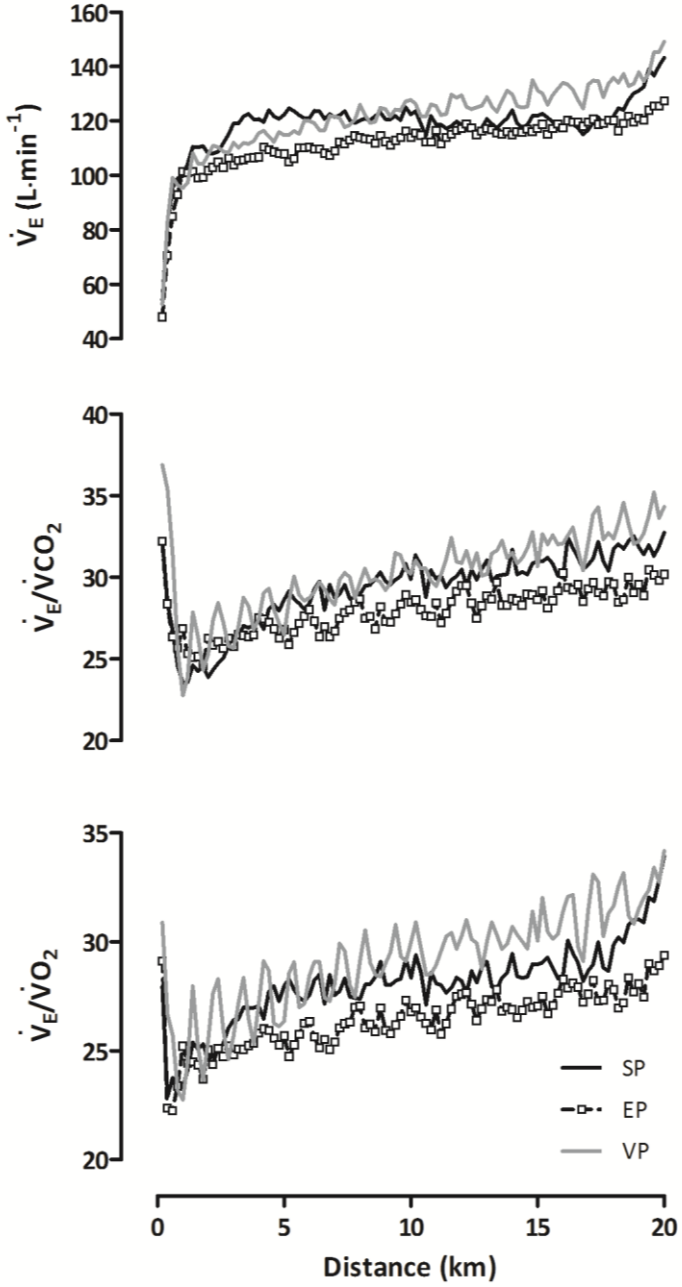


Figure 5.4. Ventilatory responses ($\dot{V}_E$, minute ventilation; $\dot{V}_E/\dot{V}CO_2$, ventilatory equivalent for carbon dioxide; $\dot{V}_E/\dot{V}O_2$, ventilatory equivalent for oxygen) to time- and work-matched self-, even- and variable-paced trials. Even-pacing resulted in a reduced $\dot{V}_E$ and higher ventilatory efficiency in compared to self- and variable-paced trials ($p < 0.05$).

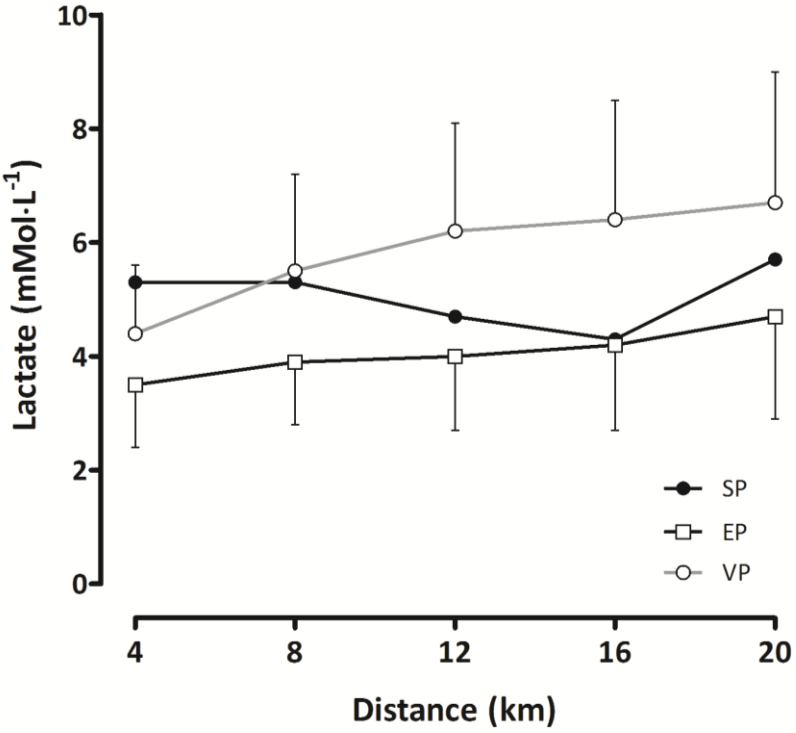


Figure 5-5. Blood [lactate] response to time- and work-matched self-paced (SP), even-paced (EP) and variable-paced (VP) trials. Blood [lactate] was lower in EP compared to VP and SP, and lower in SP compared to VP ($p < 0.05$).

5-3.3 Perceptual responses

Both RPE and affect (Figure 5-6) were different between trials ($p < 0.01$). RPE was lower in EP (14 ± 1) compared to both SP (15 ± 1, $p < 0.001$, $D = 1.53$) and VP (15 ± 1, $p = 0.006$, $D = 1.31$). Affect was more positive in EP (1 ± 2) compared to both SP (0 ± 2, $p = 0.02$, $D = 0.47$) and VP (0 ± 2, $p = 0.02$, $D = 0.50$). Post-trial the participants also reported lower 'gestalt' RPE in EP (14 ± 2) compared to SP (16 ± 2, mean difference, 95% CI's = −1, −2 to −1, $p = 0.01$, $D = 0.94$) and VP (16 ± 2, mean difference, 95% CI's = −2, −1 to −3, $p = 0.02$, $D = 1.37$).

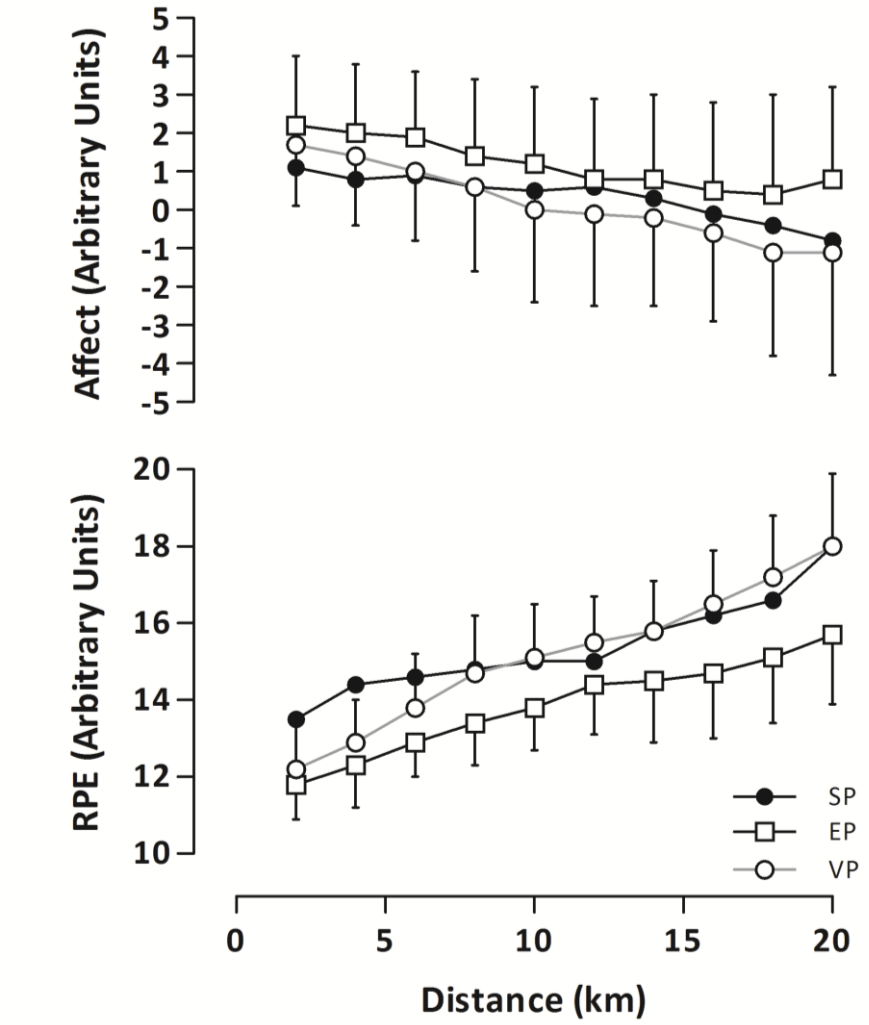


Figure 5-6. Affective response (top panel) and rating of perceived exertion (bottom panel) during time- and work-matched self-paced (SP), even-paced (EP) and variable-paced (VP) trials. Affect was more positive, and RPE lower in EP compared to both SP and VP ($p < 0.05$).

5-4 Discussion

The principal finding of this study was that an even-pacing strategy dampened the perturbations in the physiological response and minimised perception of exertion in comparison to time- and work-matched self-paced and variable-paced cycling. In contrast, variable-pacing resulted in an augmented physiological response and elevated perception of exertion in order to complete the same amount of work.

The finding that an EP strategy resulted in lower perception of exertion, more positive affect rating and a dampened physiological response supports previous research that has suggested an even pacing strategy is optimal for endurance events lasting > 2 min (Foster *et al.*, 1993; Gordon, 2005; Atkinson *et al.*, 2007b). A more even distribution of the proposed finite anaerobic capacity allows the athlete to maintain an anaerobic reserve for a greater proportion of the trial (Jones *et al.*, 2008b) which directly impacts on the perception of exertion (de Koning *et al.*, 2011). de Koning *et al*. (2011) theorised that the RPE at any given time point in a closed loop trial is dependent on the magnitude and rate of homeostatic disturbance, and the fraction of the duration or distance remaining. Accordingly, a faster start would result in higher reported RPE values for the entire race as a result of an increased 'hazard of catastrophic collapse' (de Koning *et al.*, 2011). Our data support this conceptualisation, since the perception of exertion (Figure 5-6) remained elevated for the entire trial during the SP and VP conditions as a result of the augmented perturbations in the initial physiological responses - higher heart rate, blood lactate and oxygen uptake - due to the higher power output at the start of the trials; despite there being little difference in the overall mean physiological response between trials.

Whilst our data support the implementation of an even-pacing strategy, not all previous research is in agreement. Lander *et al*. (2009) reported higher RPE in 7 of 9 novice rowers during a time- and work-matched EP 5000 m rowing trial based on the mean power achieved during a SP trial at a fixed RPE, and Billat *et al*. (2006) anecdotally reported a higher perception of exertion during an even-paced 10 km run based on a previous self-paced effort in 3 well-trained runners. Both of these studies also reported differences in the physiological response to time- and work-matched SP and EP exercise bouts. Billat *et al*. (2006) reported higher oxygen uptake, heart rate and post-exercise blood lactate during the even-paced trial while Lander *et al*. (2009) reported no

difference in oxygen uptake and heart rate, but a small (1 $mMol \cdot L^{-1}$) difference in post-exercise blood lactate after EP compared to SP.

Resolving the conflicting results between these studies and the present study is difficult given differences in the mode of exercise (running and rowing vs. cycling), level of athlete (novice rowers vs. well-trained runners and cyclists) and the small sample sizes involved (n = 3, 9 and 10). A potential explanation could reside in the nature of the even-paced task. In previous studies (Billat *et al.*, 2006; Lander *et al.*, 2009) the EP task required participants to consciously maintain a pre-specified target constant intensity, but the actual intensity was free to vary. In contrast, in our study the power output during EP was fixed independent of cadence, akin to a constant-load task. This allowed the participants to alter the mechanical and metabolic stress within the parameter of the imposed work by increasing or decreasing pedalling cadence, respectively (Ansley & Cangley, 2009). In the present study, cadence was lower in EP compared to SP, and closer to the theoretical energetically optimum cadence (Ansley & Cangley, 2009). Although this had no significant impact on the metabolic cost of the bout, it might have reduced the perception of exertion required to complete the task (Ansley & Cangley, 2009).

An alternative explanation could be that pacing in the initial SP trial was sub-optimal. Although the mean oxygen uptake for the SP trial was 87 ± 6 % of maximum and RPE reported at the finish were consistent with a best effort (18 ± 2), participants adopted a relatively fast starting strategy in SP with the first 4 km conducted at a power output 8 ± 4% above the mean power for the entire trial. Previous studies have suggested that a fast start (> 6% of the race mean) might be detrimental to race performance (Mattern *et al.*, 2001; Gosztyla *et al.*, 2006), although this assertion has been refuted for short duration (~2-4 min) trials (Bishop *et al.*, 2002; Jones *et al.*, 2008b) and is not well-established for longer duration time-trials. Comparison of the blood lactate responses between the SP trial and the EP trial, which was conducted at the mean power achieved in SP, offers an insight to the relative intensity of the self-paced effort. Blood lactate increased progressively in EP by 1.2 ± 0.9 $mMol \cdot L^{-1}$ between the first sampling point (at approximately 6-7 min) and the last sampling point (at approximately 32.5 min), which suggests that the EP trial (and by extension, the mean intensity of the SP trial) was performed close to the maximum lactate steady state (MLSS; Tegtbur *et al.*, 1993).

Previous data in well-trained cyclists have shown that the speed at MLSS corresponds closely with the average speed during a 40 km time-trial (Harnish *et al.*, 2001). Whilst our trials were shorter it would be reasonable to assume that the power output at MLSS would be a strong predictor of performance in exercise of this duration, given that both 20 km and 40 km time-trials would be completed at an intensity close to the asymptote of the well-established hyperbolic relationship between exercise intensity and duration (Vanhatalo *et al.*, 2011) . Whether participants could have actually achieved a higher mean exercise intensity is not known. Theoretically, optimal 20 km time-trial performance would require maintenance of a maximum sustainable speed throughout the trial accompanied by an exhaustion of the anaerobic energy reserve; yet the characteristic pattern of falling blood lactate (Figure 5-5) during the majority of the SP trial in this and other similar studies (Kenefick *et al.*, 2002; Thomas *et al.*, 2012b) suggests cyclists pace their efforts for the majority of the bout at an intensity where lactate clearance exceeds lactate production. Previous studies have demonstrated that competition (Corbett *et al.*, 2012) and provision of deceptive feedback (Stone *et al.*, 2012), can motivate cyclists to beat a previous 'best' self-paced effort through a more complete use of the proposed finite anaerobic reserve. However, the trials adopted in these other studies were much shorter than the present study (2 km and 4 km, respectively) and therefore the relative contribution of energy provision from anaerobic sources would have been higher. Regardless of whether performance in SP was optimal, the subsequent matched EP bout was perceived as easier, and the VP bout perceived as harder, both of which have implications for exercise.

A further observation with regards RPE highlighted by the current study concerns the proposed linearity of the RPE response during closed loop exercise. Previous work examining RPE during best effort SP trials and EP exercise trials to exhaustion have suggested RPE has a scalar, linear relationship with time (Noakes, 2004; Eston *et al.*, 2007; Crewe *et al.*, 2008). Noakes (2004) further suggested that in constant-load trials, the maximum tolerable RPE is set in advance of the exercise bout, and that the brain increases the RPE as a proportion of the exercise time or distance completed. Based on the pattern of RPE response during the SP and EP trials in this study and other studies (Baden *et al.*, 2004; Swart *et al.*, 2009a; Micklewright *et al.*, 2010) we would offer an alternative interpretation. The rise in RPE during exercise is non-linear (Figure 5-6) with periods of flat RPE interjected with sharp increases in RPE, even in the EP trial

where the exercise intensity was constant. Furthermore, in 40% of the SP trials a reduction in RPE in conjunction with a reduction in power output was observed. These observations are consistent with the information processing model proposed by St Clair Gibson *et al*. (2006), where power output and the associated RPE in self-paced exercise are generated in a 'quantal' unit manner based on feed-forward control and afferent feedback information. The RPE is the conscious manifestation of the on-going change in the metabolic profile as the exercise bout progresses, and is subject to periods of cyclical certainty and uncertainty as the brain algorithm responsible for the pacing strategy continuously interprets the afferent information from the periphery (St Clair Gibson *et al.*, 2006). The majority of the exercise bout is controlled subconsciously, and it is only when a change in the perceptual state occurs that the exerciser becomes aware of it (Damasio *et al.*, 2000; Parvizi & Damasio, 2001; St Clair Gibson *et al.*, 2003). The RPE does not increase linearly, but in relation to the certainty of the metabolic demand of the exercise bout and the participant's confidence in meeting this demand (Swart *et al.*, 2009a). The non-monotonic changes in RPE reflect these underlying control processes.

In contrast to EP, the VP trial resulted in an augmented physiological response and increased perception of exertion. The elevated RER in VP compared to EP approached statistical significance ($p = 0.053$) and this, in conjunction with the higher blood lactate, suggests a greater reliance on non-oxidative energy provision. This was likely due to cumulative lags in the $\dot{V}O_2$ on-kinetics at the start of each high-intensity period (20-25 s in trained individuals: Zoladz *et al.*, 2006) and an increased recruitment of higher threshold, more fatigable muscle fibres to meet the power output demand of the high-intensity periods (Christmass *et al.*, 1999). These findings support previous research that has demonstrated lower fat oxidation and a greater contribution from glycolysis during intermittent exercise compared to time and work-matched continuous exercise (Christmass *et al.*, 1999; Ferrauti *et al.*, 2001). Based on the progressively increasing blood [lactate] (Figure 5-5), the augmented ventilatory response and reduced ventilatory efficiency (Figure 5-4) and perception of exertion (Figure 5-6) it is likely that the duty cycle employed in this study (1:1.5 ratio with 37-43 s work intervals at ~106% P_{max} and a recovery interval at ~53% P_{max}) was close to a tolerable maximum. This assertion is supported by the findings of Turner *et al*. (2006), who showed participants could adhere to a 30 min intermittent cycling bout comprising of 30 s supramaximal exercise and 60 s

recovery, but maintaining the same work:recovery ratio and increasing the duration of the supramaximal interval to 60 s led to premature exercise termination, an augmented $\dot{V}O_2$ response and a progressive accumulation in blood lactate.

Although performance wasn't directly measured, with the assumption of a flat course with no wind, the pacing strategy adopted in EP would have resulted in a faster 20 km completion time than VP (Swain, 1997; Atkinson *et al.*, 2007b). The ecological validity of the present study could be questioned as competition TT's have variations in gradient and wind to account for. Numerous authors (Swain, 1997; Gordon, 2005; Atkinson *et al.*, 2007b) have suggested that varying the power output in parallel to changes in wind / gradient will result in better TT performance. Swain (1997) suggested variations of up to 15% might be acceptable, although Atkinson *et al*. (2007a) reported that some cyclists cannot fully adhere to a pacing strategy involving variations in mean power of ± 5%. A further limitation of the VP protocol is the relative proportion of time spent in high (~40 s) and low (~60 s) power segments; for real-world time-trialling on a hilly course if the net gradient was 0% cyclists would spend a greater proportion of time going uphill compared to downhill. Further work on ecologically valid TT models is warranted. These limitations notwithstanding, stochastic efforts are common during road cycling races when establishing a breakaway, where repeated short duration (5-15 s) high intensity (9.5-14 $W \cdot kg^{-1}$) surges have been observed in the activity immediately preceding a successful break, followed by sustained high power outputs (~450-500 W) for up to 5 min depending on the response of the chasing group (Abbiss *et al.*, 2013a). The robustness of the physiological response demonstrated in the present study suggests significant variations in power for short periods of time might be acceptable, but are likely to incur an additional perceptual and physical cost.

In conclusion, the results of this study show that, for a time and work matched 20 km TT, an even-paced strategy results in attenuated perturbations in the physiological response and lower perception of exertion in comparison to self- and variable-paced strategies. The overall aim of this thesis is to understand the physiology of self-pacing and the optimum pacing strategy for endurance time-trial events. The results of this chapter support previous work that suggests an even-paced strategy might be optimal in endurance time-trial events (Atkinson *et al.*, 2007c). A limitation of this conclusion is that it is assumed the attenuation in the perceptual and physiological response would

translate to an improved time-trial performance. In addition, it is not possible from this data to assess how efficacious the self-selected pacing strategy was, and the constant-load nature of the even-pace task might lack ecological validity. The subsequent chapter will address these limitations and further investigate the proposed efficacy of even-pacing for endurance time-trials.

CHAPTER 6 THE EFFECT OF AN EVEN-PACING STRATEGY ON EXERCISE TOLERANCE IN WELL-TRAINED CYCLISTS

6-1 Introduction

The distribution of energy, or pacing strategy, during a race can significantly impact on the overall race performance (Atkinson *et al.*, 2007c). Numerous authors have suggested that, for events lasting longer than four minutes and in conditions of unvarying wind and gradient, an even distribution of energy is both physiologically and biophysically optimal (Foster *et al.*, 1993; Atkinson *et al.*, 2003; Thompson *et al.*, 2003; Gordon, 2005; Tucker *et al.*, 2006b). However, evidence from the few studies that have examined optimal pacing during prolonged endurance events does not always support this posit (Billat *et al.*, 2006; Lander *et al.*, 2009; Thomas *et al.*, 2012a), and observations of elite athletes suggest a parabolic pacing strategy is common across exercise modes in elite athletes (Tucker *et al.*, 2006b; Corbett, 2009; Muehlbauer & Melges, 2011; Mauger *et al.*, 2012).

In Chapter 5 of this thesis it was reported that adopting an even-pacing strategy during 20 km cycling time-trials dampens perturbations in the physiological response and reduces perception of exertion compared to time- and work-matched self-paced and variable-paced trials (Thomas *et al.*, 2012a). In contrast, some evidence suggests that self-pacing reduces the metabolic and perceptual stress of a given performance. Lander *et al*. (2009) used an RPE clamp model to compare a self-paced 5 km rowing exercise at a fixed RPE ("Hard") to a subsequent matched even-paced bout. They concluded that self-paced exercise is less challenging than even-paced exercise since the intensity of exercise can be regulated and adapted to minimise physiological strain and the perception of exertion. Similarly when Billat *et al*. (2006) examined self- and even-paced 10 km running trials in three well-trained runners they interpreted pace variations as an intentional strategy to minimise the physiological strain during severe exercise.

Ham & Knez (2009) used a novel method to investigate the effect of pacing strategy on 30 km TT performance. These authors used a similar paradigm to that implemented in Chapter 5; participants cycled an even-paced trial at a fixed intensity equivalent to their best self-paced performance, however this trial was continued to exhaustion. The authors hypothesised that sub-optimal self-pacing would result in longer time to exhaustion on a matched even-paced trial, and optimal self-pacing strategies would result in shorter time to exhaustion. Interestingly, four of the seven cyclists studied terminated the even-paced exercise before completing the same amount of work as they

achieved in their self-paced time-trial. Ham & Knez (2009) speculated that starting strategy and variability in the pacing profile might explain the observed exercise intolerance; cyclists who began the self-paced trial at a relative speed of 100-104% of the trial mean and exhibited low variability in speed throughout terminated the even-paced task earlier than those cyclists who adopted faster starting strategies (> 105% of trial mean) and exhibited more variability. A shorter time to exhaustion at the same mean power output and lower variability in speed was interpreted as evidence that the pacing strategy adopted during the self-paced trial was more optimal than faster starting strategies and more variable changes in pace (Ham & Knez, 2009).

The efficacy of the self-selected pacing strategy might therefore explain the contradictions observed in the literature. In Chapter 5 of this thesis we speculated that the self-paced strategy adopted by the cyclists studied could have been sub-optimal, based on the observation of a fast starting strategy (8 ± 4% above the mean power for the trial during the first 4 km). A subsequent time- and work-matched even-paced bout resulted in attenuation of the metabolic and perceptual cost of the exercise. Thus an even-pace moved these cyclists closer to an optimal strategy, but whether this strategy was the best cannot be determined. Previous research would suggest that aggressive starting strategies result in sub-optimal self-paced performance (Gosztyla *et al*., 2006; Ham & Knez, 2009). Ham & Knez (2009) are the first to elucidate the impact of the pacing strategy on performance of a subsequent matched even-pace trial, though their conclusions were limited by a small sample size (n = 7). Lander *et al*. (2009) and Billat *et al*. (2006) both observed negative consequences of even-pacing, but neither provided any information on how the self-paced trial was completed. Whether an even-pace is optimal or not for endurance exercise is therefore unclear, but could be related to the efficacy of the self-paced strategy.

The aim of the present study was to investigate the efficacy of even-pacing for endurance time-trials by comparing best self-paced performance with the performance of an even-paced time to exhaustion task (Ham & Knez, 2009). The physiological, performance and perceptual responses to self- and even-pacing were also compared. Addressing this aim will provide stronger evidence regarding the utility of even-pacing for endurance time-trials and resolve the contradictions that exist in the current available

literature (Billat *et al*., 2006; Lander *et al*., 2009; Ham & Knez, 2009; Thomas *et al*., 2012a).

6-2 Methods

6-2.1 Participants

After institutional ethical approval, fifteen well-trained male competitive time-trial cyclists (mean ± SD age, 30 ± 10 years, mass, 71.5 ± 7.1 kg, $\dot{V}O_2max$, 4.80 ± 0.38 $L \cdot min^{-1}$) gave written, informed consent to participate. Sample size was estimated as previously described (Chapter 5). A sample size of nine was required to detect small or moderate effects with 80% statistical power in the outcome measures studied. The study was performed in accordance with national and international guidelines (Hull *et al.*, 2008; WMA, 2008).

6-2.2 Design

Each participant completed three best effort self-paced 20 km time-trials (TT) and two even-paced TTs based on best self-paced trial performance. The design of the study was crossover; self-paced trials were always performed first with the subsequent order of the even-paced TTs randomised. Two even-paced trials were performed in order to verify any observed effect of even-pacing on exercise tolerance, and to ensure the nature of the even-paced task did not explain the observed effects (described in detail below). Participants followed the same pre-test preparations as previously described. All exercise was conducted on an electromagnetically braked cycle ergometer (Velotron Pro, RacerMate Inc., USA) as previously described. Expired air, heart rate and blood lactate were recorded using procedures described previously (Chapter 3 & 4).

6-2.3 Procedures

Participants first visited the lab for a practice trial where they completed an incremental exercise test to assess blood lactate transition thresholds, which consisted of 4-minute stages with 20 W increments until lactate turnpoint (defined as a sudden inflection of the blood lactate curve in the 2-4 $mMol \cdot L^{-1}$ range) (Jones, 2007). Following a ten min rest, participants completed an incremental test to exhaustion to measure $\dot{V}O_2max$ as previously described (Chapter 4).

6-2.4 Experimental trials

A standardised ten minute warm-up was employed before each trial. Participants completed three self-paced (SP) 20 km time-trials, and two even-paced trials. In all SP trials participants were instructed to 'complete the distance as fast as possible'. Multiple SP trials were completed to ensure a maximal self-paced performance. Participants' best self-paced performance (highest mean power output) was subsequently used to define the power output for an even-paced trial that was continued to exhaustion (EP_{tlim}). In this trial the power output was imposed, or fixed independent of cadence (EP_{tlim}), akin to a constant load task using computer controlled software (Velotron CS 2008, Racermate Inc., Seattle, USA). Participants could vary their cadence, but the required power output would remain at the level required. Participants were instructed to complete as much distance as possible, and were given updates at 2 km intervals to relate the work done to their self-paced trial. This protocol allows assessment of the effectiveness of the self-selected pacing strategy; an optimal pacing strategy in the self-paced trial would lead to the shortest time to exhaustion, and sub-optimal self-pacing strategies would result in a longer time to exhaustion (Ham & Knez, 2009).

To verify any effects observed in the EP_{tlim} trial, a second even-paced trial was conducted. In this even-paced trial (EP-maintained) participants were instructed to maintain a target power output (i.e. the mean power achieved during best SP), but the actual power was free to vary depending on the effort (force) and cadence of the cyclist. This trial was deemed complete when the participant had completed 20 km, with the target to achieve the same mean power (and thus a similar performance time) as best SP performance. This type of trial is more ecologically valid in that it better replicates what would be required of an athlete adopting an even-pacing strategy in competition. It is also the type of trial adopted by previous work that has demonstrated even-pacing is physically and perceptually more challenging than self-pacing exercise (Billat *et al*., 2006; Lander *et al*., 2009). Including this trial would thus allow verification of any effects observed in the EP_{tlim} trial, and also determine whether the nature of the even-paced task was an explanatory factor for the observed effects. The order of the even-paced trials was counterbalanced to avoid any order effects. Figure 6-1 illustrates these trials for a representative participant.

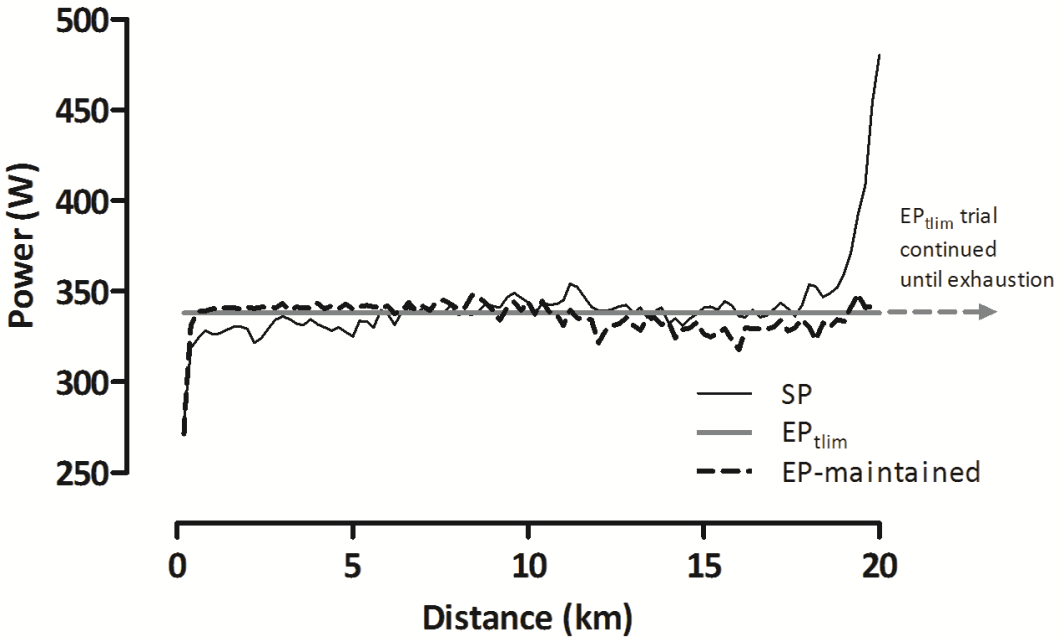


Figure 6-1. Power output profiles from a representative participant to illustrate experimental protocol. The average power output from participant's best self-paced performance (SP; black line) was used to set two even-paced trials. In EP_{tlim} (grey line) power output was fixed at the average power output achieved in SP and participants were instructed to cycle to exhaustion. In EP-maintained (dashed black line) participants were instructed to maintain the same average power output but the actual power output could vary.

During all trials participants were provided continuous feedback for power output, cadence and distance covered. At 2 km intervals participants were asked to rate their perceived exertion (RPE) and affect as previously described (Chapters 3 to 5). Finger prick blood lactate samples were taken at 4 km intervals. On completion of each time-trial and after a standardised 5 minute cool down, participants were asked for a 'gestalt' RPE and affect score that best represented the effort over the entire session.

6-2.5 Data analysis

Descriptive statistics were calculated as means (±SD). The harmonic mean was also calculated for all trials where power output was free to vary to ensure the appropriateness of the arithmetic mean as a summary statistic. Data from the cycle ergometer and metabolic cart were averaged over 1 s intervals and converted to percentages of work done (kJ) for each trial to display the serial pattern of responses. For each trial, mean and/or peak values for power output (W), time (s), cadence (rpm), oxygen uptake ($\dot{V}O_2$, $L \cdot min^{-1}$) carbon dioxide production ($\dot{V}CO_2$, $L \cdot min^{-1}$), minute ventilation ($\dot{V}_E$, $L \cdot min^{-1}$), respiratory exchange ratio (RER), heart rate (HR, $b \cdot min^{-1}$),

blood lactate ($mMol \cdot L^{-1}$), RPE and affect were assessed. For parametric data, the underlying assumptions for each statistical procedure were assessed and verified using methods described by Newell *et al*. (2010). Differences for three group comparisons were assessed with one-way repeated measures ANOVA, with Bonferroni adjusted 95% confidence intervals (95% CI) calculated for pairwise comparisons. For two group comparisons paired-samples and independent t-tests were used as appropriate. For non-parametric data (RPE and affect) differences between trials were assessed using Friedman's ANOVA, with Wilcoxon signed-rank tests employed for two group comparisons. Pearson's product moment correlations (where data were linear) and polynomial regression (where data were non-linear) were used to assess relationships between self-paced 20 km time-trial pacing strategy and performance and performance of the EP_{tlim} task. This analysis has previously been used to demonstrate associations between starting strategy and even-paced exercise performance and allows an assessment of the efficacy of the self-selected pacing strategy (Ham & Knez, 2009). Statistical significance was assumed at $p < 0.05$. Statistical analysis was performed using SPSS 17.0 (SPSS Inc., Chicago, IL.) and Microsoft Excel 2007.

6-3 Results

Nine out of fifteen cyclists failed to complete the EP_{tlim} trial; that is, they reached exhaustion before completing the same amount of work as their best SP trial upon which the even-paced trial was based. Data were subsequently split into finisher (FIN: cyclists who successfully completed the EP_{tlim} trial, n= 6) and non-finisher (DNF: cyclists who failed to complete the EPt_{lim} trial, DNF, n = 9) groups where appropriate for analysis.

6-3.1 The utility of even-pacing during endurance TTs; self- vs. even-pacing

In the group of cyclists who successfully completed the EP_{tlim} trial, SP mean power output was 277 ± 37 W, with a time-trial time of 1925 ± 82 s. In the group of cyclists for whom even-pacing resulted in exercise intolerance, SP mean power output was 288 ± 21 W with a time to completion of 1888 ± 54 s. The harmonic mean was similar (276 ± 38 W and 287 ± 22 W for FIN and DNF respectively.

Even-paced trial performance & self-pacing strategy

For cyclists who successfully completed the EP_{tlim} trial (FIN group), work done ranged from 100% to 137% of self-paced 20 km TT performance (distance covered of 20 to 27.4 km). For those cyclists who failed the EP_{tlim} trial (DNF group), work done ranged from 51% to 83% (10.3 to 15.3 km) of the target work determined from the mean PO of their SP trial. The self-pacing strategies adopted by these two groups were different (Figure 6-2). In the DNF group self-paced performance was characterised by a faster starting strategy (first 6 km 1-2% above the mean power output for the trial, Figure 6-2) compared to the FIN group who adopted a relatively cautious approach (first 6 km 1-4% below the mean power, Figure 6-2). Thereafter participants in the FIN group adopted a pace that remained close to the trial average, whereas participants in the DNF group had a relatively even but progressively declining power output, until the final 2 km when both groups increased speed (Figure 6-2). The effect of pacing strategy during SP on EP task performance was investigated by correlating relative power output during 2 km segments in SP with the time to exhaustion during the EP_{tlim} trial. There was a moderate, negative correlation between relative power output in the first 6 km of SP and distance covered during the EP_{tlim} trial ($r = -0.47$ to -0.52 for 0-2, 2-4 and 4-6 km, summarised in Figure 6-3 for 0-6 km combined), with no relationships from 6 km onwards (r values ranging from -0.31 to 0.35 for successive 2 km increments, $p > 0.05$), thus indicating that faster starting strategies in SP were associated with earlier even-paced exercise termination.

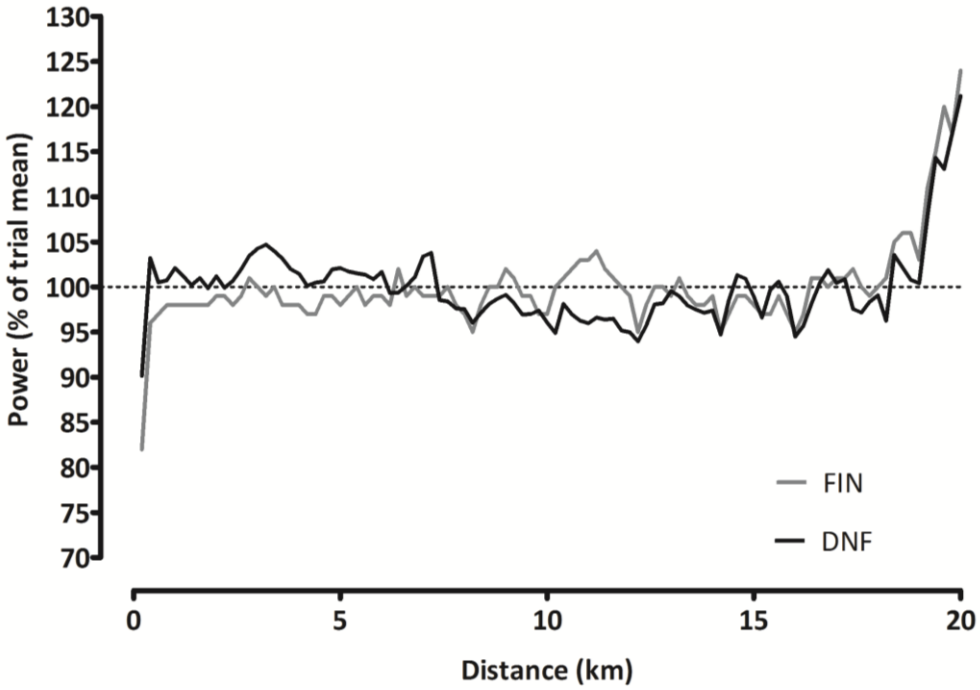


Figure 6-2. Pacing strategy (power output expressed relative to the trial mean power output) for cyclists during self-paced (SP) 20 km time-trials. The black line is the self-pacing strategies of cyclists who subsequently failed a matched even-paced task (DNF group, n = 9). The grey line is the self-pacing strategies for cyclists who successfully completed a subsequent matched even-paced task (FIN group, n = 6).

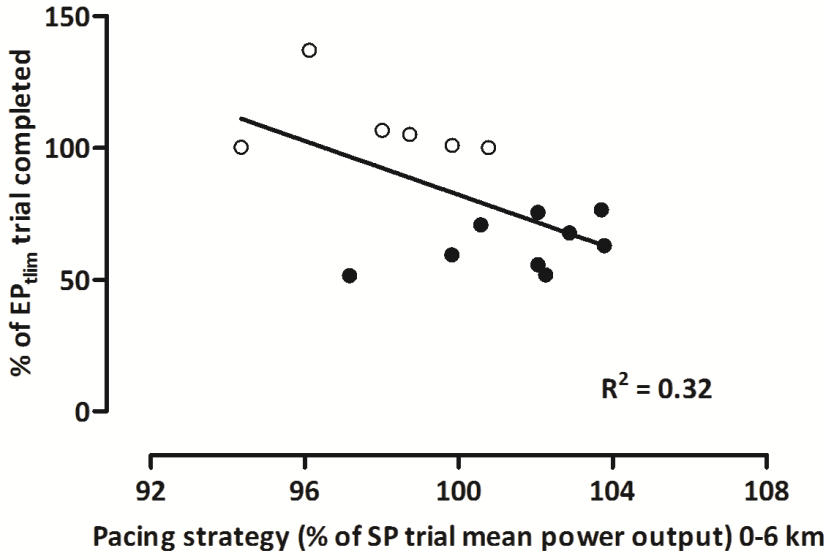


Figure 6-3. Relationship between self-paced 20 km starting strategy expressed as a % of the mean power output for the trial and distance completed in a matched even-paced trial (EP_{tlim}) to exhaustion (n = 15). ○ = cyclists who successfully completed the EP_{tlim} trial (FIN group), ● = cyclists who failed the EP_{tlim} trial (DNF group). Faster starting strategies were associated with earlier exercise termination.

Physiological and perceptual responses to even-paced vs. self-paced exercise

There were no discernible differences in the average cardiorespiratory response to self- and even-paced trials for either FIN or DNF groups (Table 6-1). In the FIN group there was also no difference in the perceptual response to even-pacing exercise (Table 6-1). In the DNF group however, even-pacing was associated with negative perceptions characterised by lower mean- and post-trial affect scores, a similar end trial peak RPE and a higher post-trial session RPE despite a shorter trial duration in the EP_{tlim} trial (Table 6-1).

For blood [lactate] whilst there were no differences in the mean blood lactate response between self-paced and EP_{tlim} trials for both groups ($p > 0.05$, Table 6-1), there was a pattern for a faster rise in lactate during the EP_{tlim} trial in the DNF group until task failure compared to a slower rise in the FIN group (Figure 6-4, panel B). The magnitude of this rise between sampling points was higher in the DNF group compared to the FIN group (1.99 ± 0.61 $mMol \cdot L^{-1}$ vs. 0.61 ± 0.49 $mMol \cdot L^{-1}$, $p < 0.001$). This was reflected in an augmented ventilatory response in EP_{tlim} for the DNF group compared to self-paced exercise (Figure 6-5). Peak blood lactate was lower in EP_{tlim} compared to SP for the FIN group ($p = 0.03$, Figure 6-4), but not for the DNF group where participants terminated the trial at a similar peak blood lactate as SP ($p = 0.36$, Figure 6-4). In relation to this, the DNF group had a mean power output in their SP trial corresponding to 112 ± 6% of their lactate turnpoint, which was higher than those in the FIN group (105 ± 2% of lactate turnpoint, $p = 0.01$). Polynomial analysis revealed 56% of the variability observed in EP_{tlim} time to exhaustion could be explained by the relative intensity achieved during the SP trial ($p = 0.03$, Figure 6-6).

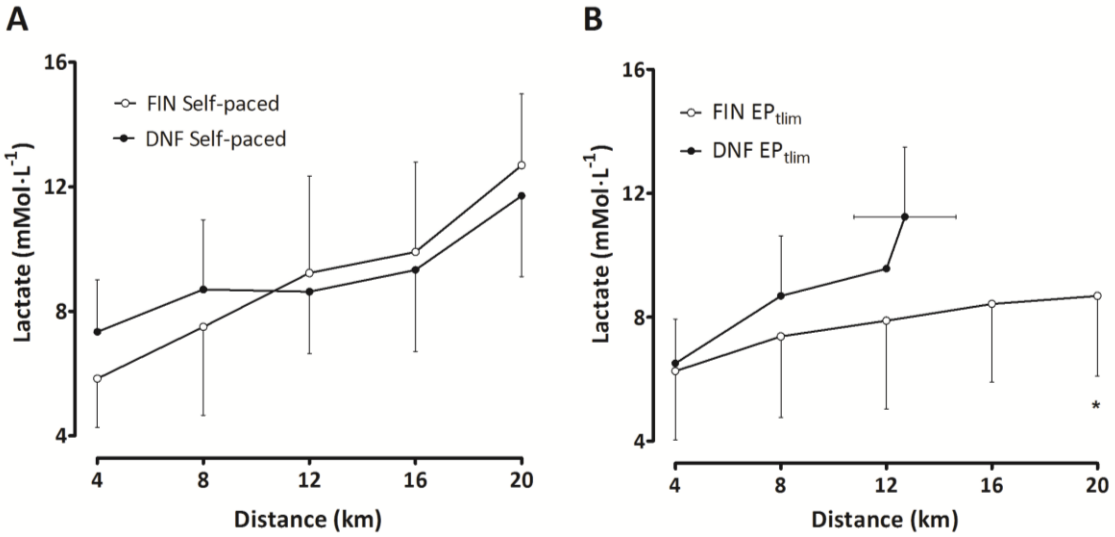


Figure 6-4. Blood [lactate] response to a self-paced 20 km TT (SP, panel A) and an even-paced trial to exhaustion at a matched power output (EP_{tlim}, panel B). Closed circles (●) are for cyclists for whom matched even-paced exercise resulted in exercise intolerance (DNF group); the horizontal SD error bars on the final point in panel B indicate the variability in EP_{tlim} performance. Open circles (○) are for cyclists who successfully completed the even-paced task. (* = peak blood lactate lower in EP_{tlim} compared to SP, $p < 0.05$).

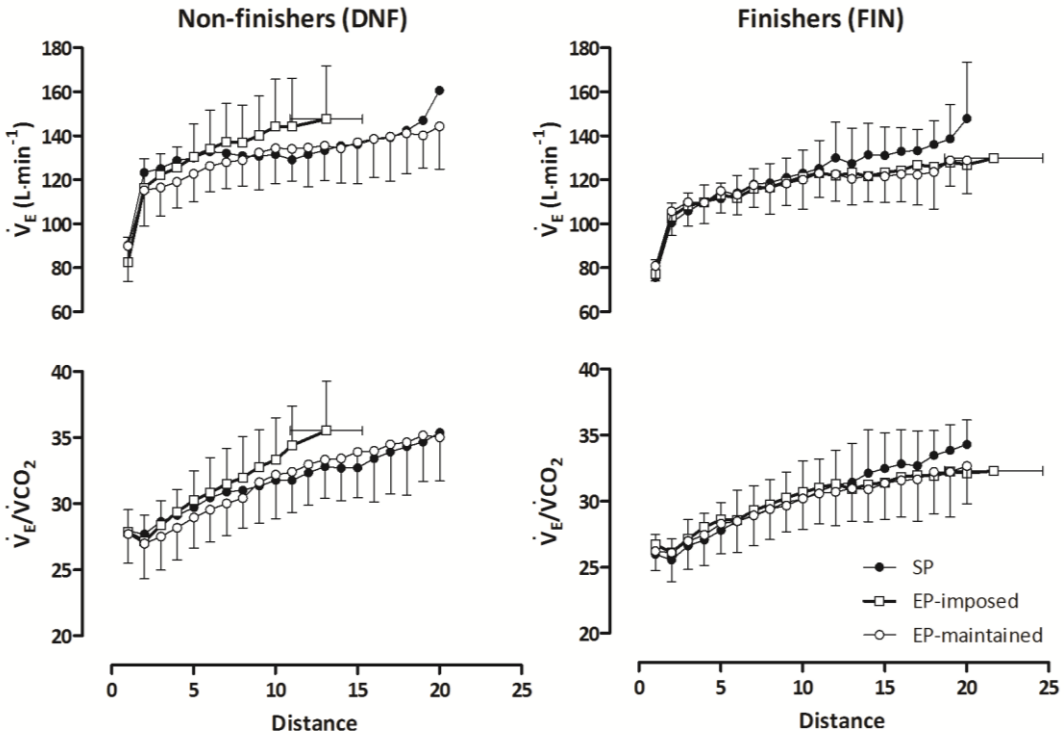


Figure 6-5. Ventilatory responses to self- and even-paced exercise in non-finishers (DNF group, left panels) and finishers (FIN group, right panels). Even-pacing in the DNF group resulted in a relative hyperventilation and reduced ventilatory efficiency compared to self-paced exercise. Horizontal SD error bars on the final point indicate the variability in EP_{tlim} performance.

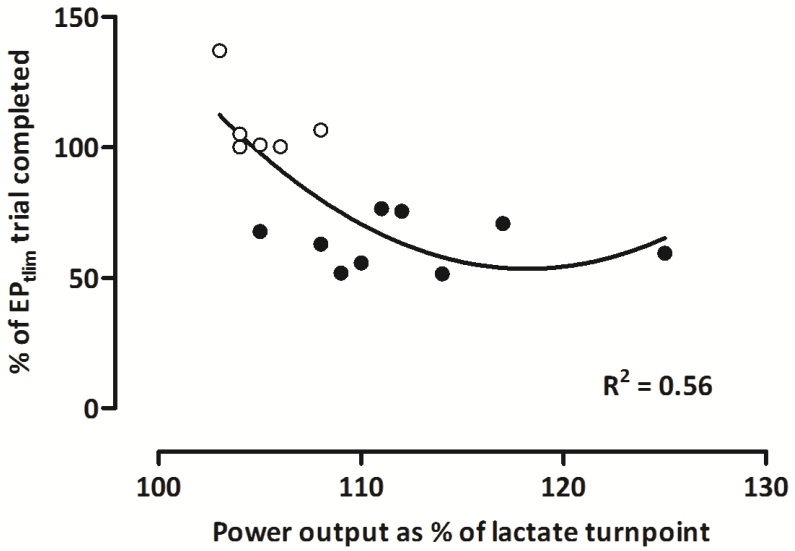


Figure 6-6. Relationship between relative intensity of SP trial expressed as a % of individual lactate turnpoint and distance completed in a matched even-paced trial to exhaustion (n = 15). ○ = cyclists who successfully completed the EP_{tlim} task (FIN group), ● = cyclists who failed the EP_{tlim} trial (DNF group).

6-3.2 The nature of the even-pacing task; EP_{tlim} vs. EP-maintained

Those cyclists who successfully completed the EP_{tlim} trial also successfully completed the EP-maintained trial (where power output could vary) at a similar average power output as SP (278 ± 37 W vs. 275 ± 36 W for SP and EP-maintained respectively, 95% CI for difference = 0 to 5 W, $p = 0.06$, Figure 6-6) and for the same performance time (1925 ± 82 s vs. 1924 ± 86 s for SP and EP-maintained respectively, $p = 0.64$), with no difference in cadence ($p = 0.86$, Table 6-1). Those cyclists who failed the EP_{tlim} trial also failed the EP-maintained trial. Despite the target of an equivalent power output to SP, power output was lower in EP-maintained with a mean difference of −8 W (95% CI −1 to −15 W, $p = 0.03$, Figure 6-7). For both groups the harmonic mean for power output was similar to the arithmetic mean (harmonic mean ± SD = 279 ± 24 W and 275 ± 36 W for DNF and FIN respectively). For the finishers group who successfully completed both time- and work-matched even-paced bouts, there were no discernible differences in the physiological or perceptual response regardless of the nature of the even-paced task ($p > 0.05$, Table 6-1). Compared to self-paced exercise, there was also no difference in the cardiorespiratory response ($p > 0.05$, Table 6-1), although peak blood lactate was lower in both even-paced trials compared to SP ($p < 0.05$, Table 6-1).

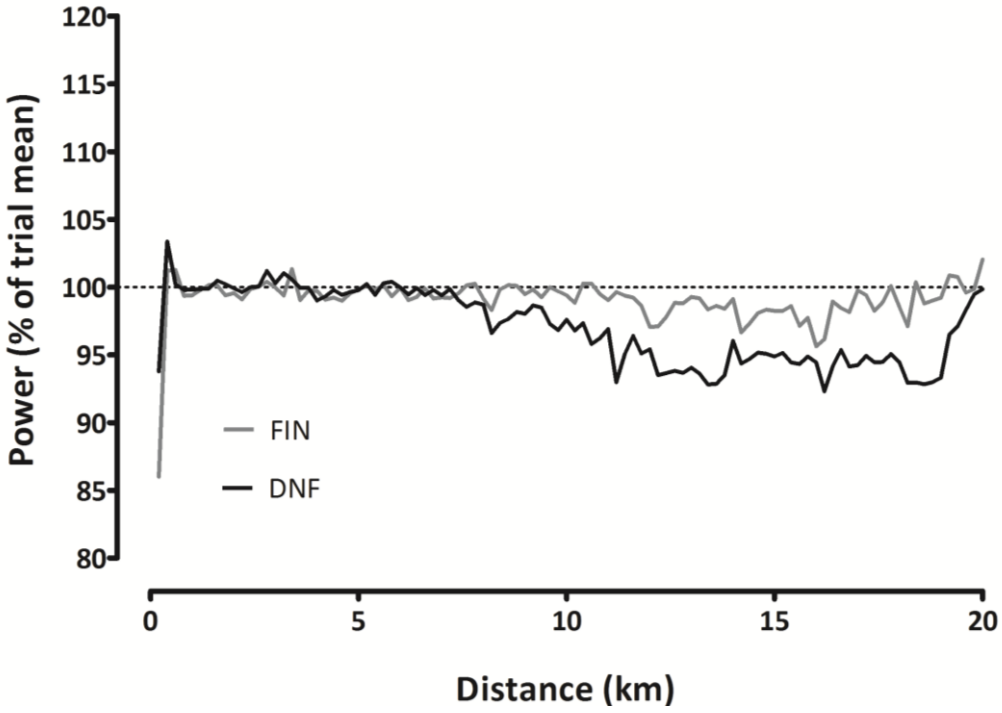


Figure 6.7. Power output profiles for an even-paced task where participants were required to maintain a power output equivalent to their best self-paced performance for 20 km, but the actual power output was free to vary. The dashed line represents the target power output. The grey line is for cyclists who successfully completed the even-paced trials (n = 6), the black line is for cyclists who failed the even-paced trials (n = 9).

Table 6-1. Whole trial physiological and perceptual responses to self-paced, fixed even-paced (EP_{tlim}) and maintained even-paced (EP-maintained) trials. Data are split in to non-finisher (DNF; n = 9) and finisher (FIN; n = 6) groups.

	Non-finishers (DNF)			Finishers (FIN)		
	Self-paced	**EP_{tlim}**	**EP-maintained**	**Self-paced**	**EP_{tlim}**	**EP-maintained**
Cadence (rpm)	97 ± 10	95 ± 11	96 ± 9	96 ± 4	96 ± 6	96 ± 5
$\dot{V}O_2$ ($L \cdot min^{-1}$)	4.24 ± 0.28	4.18 ± 0.32	4.15 ± 0.34	3.98 ± 0.30	4.00 ± 0.35	4.05 ± 0.30
$\dot{V}CO_2$ ($L \cdot min^{-1}$)	4.19 ± 0.26	4.19 ± 0.34	4.11 ± 0.35	3.91 ± 0.24	3.81 ± 0.34	3.90 ± 0.34
RER	0.99 ± 0.03	1.00 ± 0.05	0.99 ± 0.02	0.98 ± 0.03	0.95 ± 0.04	0.96 ± 0.03
$\dot{V}_E$ ($L \cdot min^{-1}$)	132.5 ± 13.6	129.8 ± 16.0	129.7 ± 13.8	119.9 ± 9.5	115.8 ± 13.0	117.6 ± 11.1
$\dot{V}_E/\dot{V}CO_2$	31.6 ± 3.1	31.2 ± 2.6	31.6 ± 2.7	30.7 ± 2.0	30.7 ± 4.4	30.2 ± 2.5
HR ($b \cdot min^{-1}$)	171 ± 7	168 ± 6	171 ± 7	177 ± 9	175 ± 8	173 ± 8
Mean [lactate] ($mMol \cdot L^{-1}$)	9.2 ± 2.1	8.9 ± 1.7	7.7 ± 1.5	9.3 ± 2.5	8.1 ± 2.4	7.5 ± 2.3
Peak [lactate] ($mMol \cdot L^{-1}$)	11.7 ± 2.6	11.1 ± 2.1	9.3 ± 1.9	12.9 ± 2.3	8.9 ± 2.5*	9.1 ± 2.6*
Mean RPE	16 ± 2	16 ± 1	16 ± 2	15 ± 2	15 ± 1	15 ± 1
Peak RPE	18 ± 2	19 ± 1	18 ± 2	19 ± 1	18 ± 2	17 ± 1
Mean Affect	0 ± 2	−1 ± 2*	0 ± 2	2 ± 1	1 ± 1	1 ± 2
Session RPE	17 ± 2	18 ± 1*	17 ± 2	16 ± 2	16 ± 1	16 ± 1
Session Affect	1 ± 2	−2 ± 1*	0 ± 2*†	2 ± 1	2 ± 2	1 ± 2

$\dot{V}O_2$, oxygen uptake; $\dot{V}CO_2$, carbon dioxide production; RER, respiratory exchange ratio; $\dot{V}_E$, minute ventilation; $\dot{V}_E/\dot{V}CO_2$, ventilatory equivalent for carbon dioxide; HR, heart rate; RPE, rating of perceived exertion. * = different from SP, † = different from EP_{tlim} ($p < 0.05$)

6-4 Discussion

Previous research has suggested that an even-pacing strategy might be biophysically and physiologically optimal for endurance events lasting > 4 min (Foster *et al.*, 1993; Atkinson *et al.*, 2003; Thompson *et al.*, 2003; Gordon, 2005; Tucker *et al.*, 2006b). The results of this study challenge this posit for endurance time-trial events lasting ~30 min; nine out of 15 of the trained cyclists studied failed to complete an even-paced exercise bout based on a previous best self-paced performance. This failure was independent of the nature of the even-paced task - i.e. imposed or self-maintained – but related to the mean power of the SP trials relative to power at lactate turnpoint. These findings are in agreement with previous literature, in other modes of exercise that found self-paced exercise to be less physically challenging than even-paced exercise (Billat *et al.*, 2006; Lander *et al.*, 2009).

The theoretical basis to the utility of a uniform distribution of work is based on models of critical power and the hyperbolic relationship between exercise intensity (for cycling exercise, power) and duration (Fukuba & Whipp, 1999; Vanhatalo *et al.*, 2011). The power-duration relationship is defined by two constants; the asymptote of the curve which represents the maximum sustainable exercise intensity, termed critical power, and a curvature constant (*W'*) which represents a finite capacity for work above the critical power. Optimal performance in longer duration events requires the complex management of energy reserves to maximise the sustainable exercise intensity whilst simultaneously exhausting *W'*. Considering the physiological responses to exercise above critical power are increasingly non-linear at higher intensities (Burnley *et al.*, 2012), that performance in events of the duration employed in the current study (~30 min), are limited primarily by intramuscular substrate/metabolite changes (Foster *et al.*, 1994; Jones *et al.*, 2008a), and that minor accelerations and decelerations can incur an additional energy cost compared to constant speed motion (Atkinson *et al.*, 2007b) it would ostensibly appear an even distribution of the finite anaerobic reserve would provide the optimal pacing strategy.

However, the cyclists in this study who optimised their race performance adopted a pacing strategy consisting of a cautious fast start, a relatively even but declining middle period and an end spurt in the final 10% of the trial. This type of pacing strategy has been commonly reported in both elite (Wilberg & Pratt, 1988; Tucker *et al.*, 2006b;

Mauger *et al.*, 2012) and well-trained athletes (Atkinson & Brunskill, 2000; Nikolopoulos *et al.*, 2001; Albertus *et al.*, 2005). We speculate from these observations that this type of pacing strategy offers the best performance by optimising the trade-off between maximising intensity and minimising metabolite accumulation to a tolerable level, whilst enabling a more complete utilisation of the finite amount of work that can be completed above the critical power. In the present study, cyclists who failed the even-paced task were cycling at a higher intensity relative to their individual lactate turnpoint in SP than cyclists who successfully completed the even-paced task, and performance on the even-paced task was negatively correlated with the relative intensity achieved during SP. Considering the mean rise in lactate between sampling points (1.99 ± 0.61 mMol·L^{-1} vs. 0.61 ± 0.49 mMol·L^{-1} for DNF and FIN groups, respectively), it is clear that some cyclists were able to achieve an average intensity in SP that was in excess of their critical power, probably by intelligently distributing work to maximise the utilisation of the finite *W'*. Maintenance of this intensity during a matched even-paced bout was not possible and could be attributed to an intolerable accumulation of fatigue-inducing metabolites (e.g. P_i, H^+, $H_2PO^-_4$). There were no other discernible differences in the physiological response to the trials.

The obvious question raised by this data is what enabled these cyclists to achieve a relative intensity during SP that could not be maintained in a matched even-paced bout? Analysis of the pacing strategies adopted during the SP trial offers some tentative insight; there was a moderate relationship between starting strategy (first 6 km) in the SP trial and time to exhaustion in the EP_{tlim} trial. Specifically, cyclists in the non-finisher group for whom even-pacing was catastrophic generally started the SP trial faster over this initial distance (102 ± 2% of mean power output) than the finishers group (98 ± 2% of mean power output). The distribution of work during a self-paced bout of exercise is an important determinant of performance. If the starting strategy is too slow in an attempt to preserve metabolic reserves, the power output required later in the race might be too high to sustain (Fukuba & Whipp, 1999), whereas starting strategies that are too aggressive (> 5% of the mean power for the trial) result in premature fatigue (Mattern *et al.*, 2001). Significantly, a more cautious fast start (< 5% above the mean speed) produces the best 5 km (~20 min) run performance (Gosztyla *et al.*, 2006) and best 30 km cycling TT performance (Ham & Knez, 2009) and this appears to be the strategy adopted by experienced cyclists during self-paced endurance

time-trials (Atkinson & Brunskill, 2000; Nikolopoulos *et al.*, 2001; Albertus *et al.*, 2005). In the present study a moderate fast start was associated with better self-paced performance, whereas a slower start was associated with sub-optimal performance. Whilst the available data for longer duration endurance events is limited, the available data suggest a moderate fast start strategy might be an important component of optimal pacing for this type of event. Further research is warranted to test this posit.

The results of the current study contrast somewhat with the data presented in Chapter 5 that demonstrated even-pacing exercise resulted in attenuation of the metabolic and perceptual cost of a time- and work-matched exercise bout based on a previous self-paced performance (Thomas *et al.*, 2012a). It was hypothesised in this previous study that the performance during the SP trial might not have been optimal based on the aggressive starting strategy (power output in the first 6 km was 107 ± 3% of mean power for the trial) and the slow rise in lactate during the time- and work-matched EP bout: a rise between sampling points of 0.30 ± 0.22 $mMol \cdot L^{-1}$, compared to the 0.61 ± 0.49 $mMol \cdot L^{-1}$ and 1.99 ± 0.61 $mMol \cdot L^{-1}$ for cyclists in the current study in the FIN and DNF groups, respectively. This comparison provides further evidence for the potential benefit of a cautious fast starting strategy, with overly aggressive or too slow starting strategies resulting in sub-optimal self-paced performance (Mattern *et al.*, 2001; Gosztyla *et al.*, 2006; Ham & Knez, 2009; Thomas *et al.*, 2012a).

An interesting feature of the current data is the drop off in intensity during the EP-maintained trials that occurred in the DNF and, to a lesser extent, the FIN group during the middle portion of the race (Figure 6-7). It would seem from this data that the slowdown in the middle of a race is likely, even when the early exercise pace is moderated. de Koning *et al*. (2011) theorised that changes in pace are informed by the product of the magnitude and rate of homeostatic disturbance and the amount of distance remaining. They conceptualised a 'hazard of catastrophic collapse' model that can be described by an inverted U shape: the risk is low at the start of the race when homeostatic disturbance is low, peaking during the middle portion of the race where both homeostatic disturbance and the distance remaining are high, and progressively decreasing towards the end of the race as the distance remaining progressively decreases (de Koning *et al.*, 2011). The increased hazard during the middle portion of a race compels a reduction in exercise intensity to ensure homeostatic disturbances remain

within acceptable limits (de Koning *et al.*, 2011). Whilst a faster start would result in a higher risk of hazard by increasing homeostatic disturbance (Mattern *et al.*, 2001), it would seem from our data that a moderate fast start might take advantage of the lower hazard scores (and consequent lower RPE) at the start of the race where homeostatic disturbance is low. Interestingly, studies assessing the kinetics of peripheral (i.e. distal to the neuromuscular junction) and central (brain and nervous system) fatigue development have shown that the majority of peripheral fatigue is manifest in the first half of an exercise bout, with an increasing contribution of central mechanisms later in the exercise (Decorte *et al.*, 2012; Froyd *et al.*, 2013). This observed pattern of fatigue development concurs with the model proposed by de Koning *et al*. (2011) and might explain the mid-race slowdown observed.

Current opinion and the results of the present study suggest that the ability to vary intensity is an important component of optimal self-paced exercise performance (Billat *et al.*, 2006; Tucker *et al.*, 2006a; Lander *et al.*, 2009). The utility of an even-pacing strategy could thus be questioned. Rather than rejecting the potential utility of even-pacing, it might be more accurate to consider how a *more* even-pace might impact performance compared to a *less* even-pace. For example, whilst cyclists seem to select a supra-optimal power output at the start of endurance time-trials, there is some limited evidence showing blunting this can lead to better performance (Firth, 1998 cited in Atkinson *et al.*, 2007c) and as previously discussed, aggressive starting strategies (+5 to +15% of the trial average) result in premature fatigue and poorer race performance (Mattern *et al.*, 2001; Gosztyla *et al.*, 2006; Ham & Knez, 2009). More experienced athletes are also better able to achieve and maintain an even-pace during running exercise compared to novice athletes (Green *et al.*, 2010), and training results in a progressively more even distribution of work during 2 km rowing trials (Kennedy & Bell, 2003). Observations of elite athletes also provide support for even-pacing. Elite cycling time-trialists race at remarkably constant heart rates (varying less than 5%, Palmer *et al.*, 1994; Padilla *et al.*, 2000b), better cyclists adopt a more even-pace during track time-trials compared to less successful cyclists (Wilberg & Pratt, 1988), the 1 h cycling world record was broken using an even-paced strategy (Padilla *et al.*, 2000a) and better performance in elite cross-country mountain biking is associated with attainment of a more even-pace (Abbiss *et al.*, 2013b). Thus whilst the data of the present study and others would suggest strict adherence to an even-paced strategy is not

desirable (Billat *et al*., 2006; Lander *et al*., 2009; Ham & Knez, 2009), better performance seems to be associated with minor deviations from an even-pace within a broadly parabolic strategy.

Although time-trial performance was not directly measured, the extended time to exhaustion as a result of even-pacing in the FIN group, and the premature fatigue of those in the DNF group indicates a likely impact of pacing strategy on exercise performance. Whether this impact was meaningful or not is difficult to discern from the current data. In this Chapter and in Chapter 5 of this thesis a time- and work-matched model was used that allowed us to isolate the effect of the predictor variable of interest (i.e. the pacing strategy) on the physiological and perceptual response to exercise. A limitation of this approach is a direct assessment of time-trial performance has not been possible. In Chapter 4 we estimated a meaningful change in performance of a 20 km time-trial in the population under study to be 1.8%, with variability in performance from trial-to-trial of 1.9%. Performance on a time-to-exhaustion trial is inherently more variable (CV ≈10-30%) however when considered alongside the change in performance (i.e. the signal to noise ratio) it has been demonstrated that time-to-exhaustion and time-trial estimates of changes in endurance performance exhibit similar sensitivity in trained cyclists (Amann *et al.*, 2008a). A direct relationship between changes in time-trial performance and changes in time-to-exhaustion can't be inferred from the current data however, and whether the observed change in time-to-exhaustion during EP-imposed for the DNF (−35% on average) and FIN (+8% on average) groups could be classified as meaningful is open to interpretation. Further research of a more applied nature studying time-trial performance would help address this limitation.

The nature of the even-pace task was not a factor in the development of fatigue. Previous research that has observed even-pacing to be more physically and perceptually challenging than self-pacing have adopted an even-paced task where participants were required to maintain a target exercise intensity but the actual intensity could vary depending on the effort exerted (Billat *et al*., 2006; Lander *et al*., 2009). In the present study those cyclists who terminated the even-paced trial to exhaustion early, where power output was fixed, could also not achieve the required intensity during an even-paced trial where power output was free to vary. Similarly those cyclists who successfully completed the even-paced trial to exhaustion also achieved the same

performance during this alternative even-paced trial. The implication of this finding is twofold. Firstly, it verifies the observations of exercise intolerance were due to an inability to maintain an even-pace and not simply because of variability in the cyclists day-to-day condition. Secondly, it confirms that the nature of the even-pacing task could not explain the exercise intolerance, as failure occurred independent of the type of even-pacing employed. For those cyclists who successfully completed both even-paced tasks, there were also no differences in the physiological and perceptual responses (Table 6-1). Future research could therefore employ either protocol to investigate even-pacing during exercise, with the caveat that the type of task employed during the EP-maintained trial would have a greater ecological validity.

Based on the results of this study, we conclude that even-pacing based on a best self-paced performance is sub-optimal and results in cumulative metabolic stress that cannot be managed by *ex tempore* changes in power output. The aim of this thesis is to understand the biological basis of self-pacing and the impact of pacing strategy on endurance time-trial performance. Taken together, the results of the previous chapters have demonstrated that the typical parabolic pacing strategy self-selected by well-trained and elite athletes is close to optimal (Chapter 6). There exists a delicate balance however, as even-pacing can improve on self-pacing strategies that are sub-optimal (Chapter 5). These results have provided novel insight in to the utility of even-pacing and the optimal pacing strategy for endurance time-trials. Thus far we have demonstrated that well-trained cyclists consistently reproduce a similar self-pacing strategy on repeat occasions and across events of different duration (Chapter 4), and that these self-selected strategies are close to optimal (Chapter 6). The final chapter of this thesis will provide further understanding of the biological basis of this self-pacing strategy by assessing the neuromuscular basis of fatigue during time-trial exercise of different durations.

CHAPTER 7 CENTRAL AND PERIPHERAL CONTRIBUTIONS TO FATIGUE AFTER 4, 20 AND 40 KM CYCLING TIME-TRIALS

7-1 Introduction

Muscle fatigue is defined as an exercise-induced decrease in the maximum voluntary force produced by a muscle, or an inability to sustain exercise at a required force (Gandevia, 2001). Fatigue can be attributed to various processes along the motor pathway that are broadly split in to central and peripheral origins. Peripheral fatigue attributes the decline in force to processes at, or distal to, the neuromuscular junction (Gandevia, 2001; Allen *et al.*, 2008b) and is typically assessed through electrical stimulation of the motor nerve of the muscle of interest at rest. Central fatigue attributes the decline in force to processes residing within the central nervous system, commonly assessed by supramaximally stimulating the peripheral motor nerve during an isometric maximum voluntary contraction (MVC; Merton, 1954). An increase in the magnitude of the superimposed twitch response post-exercise implies a reduction in voluntary activation and the presence of central fatigue. A limitation of this method is the accuracy with which the exact site of central fatigue can be determined (Taylor, 2009). Transcranial magnetic stimulation (TMS) has been used to localise the evaluated site of central fatigue, allowing the assessment of cortical voluntary activation and the relative contribution of supraspinal processes to the observed fatigue (Todd *et al.*, 2003a; Todd *et al.*, 2003b). This technique has been successfully used to demonstrate the presence of supraspinal fatigue across a range of exercise paradigms (Ross *et al.*, 2007; Goodall *et al.*, 2009; Sidhu *et al.*, 2009a, b; Goodall *et al.*, 2010; Goodall *et al.*, 2012a). Used in concert, these techniques can reveal a deeper understanding of the mechanisms underpinning fatigue.

The extent to which peripheral and central mechanisms contribute to fatigue is dependent on the nature of the exercise task (Enoka & Duchateau, 2008) and hence task-dependency remains the central theme in the study of fatigue (Barry & Enoka, 2007). During sustained isometric maximal contractions of a single muscle group, peripheral mechanisms are dominant, particularly during the early (>60 s) portion of the exercise bout, with central mechanisms increasing in influence as the exercise bout extends (Bigland-Ritchie *et al.*, 1978; Bigland-Ritchie *et al.*, 1982; Kent-Braun, 1999; Schillings *et al.*, 2003; Schillings *et al.*, 2005). During submaximal contractions (sustained or intermittent) at low intensities (< 30% MVC) the contribution of central fatigue is substantially higher than that observed during higher-intensity submaximal contractions (> 30% MVC), where the extent of peripheral fatigue is substantial and

central fatigue is modest or absent (Bigland-Ritchie *et al.*, 1986a; Sogaard *et al.*, 2006; Eichelberger & Bilodeau, 2007; Yoon *et al.*, 2007). Though less data are available, these patterns of central and peripheral fatigue can also be extended to locomotor exercise. Peripheral fatigue develops early during fatiguing locomotor exercise (Decorte *et al.*, 2012) and reductions in voluntary activation are evident only when the exercise bout is prolonged (Lepers *et al.*, 2002; Place *et al.*, 2004; Ross *et al.*, 2010a; Decorte *et al.*, 2012). In general, the higher the intensity of the exercise and the shorter the duration, the more peripheral fatigue appears to be predominate, whereas failure of the central nervous system to adequately activate working muscles becomes more dominant at lower intensity, but longer exercise durations.

In an attempt to ensure a high degree of experimental control, previous studies investigating fatigue during whole body locomotor exercise have largely employed constant-load exercise protocols. Few studies have employed locomotor exercise paradigms that allow self-selected pacing strategies in response to sensations of fatigue, such as those that would be found in real life training and competition (Amann *et al.*, 2006b; Ross *et al.*, 2007; Amann & Dempsey, 2008; Amann *et al.*, 2009). A series of recent studies by Amann and colleagues (2006b; 2008; 2009) have demonstrated the potential for studying fatigue using self-paced, whole body locomotor exercise modes. These authors demonstrated that, during self-paced 5 km cycling time-trial exercise, the magnitude of exercise-induced peripheral fatigue is regulated to an 'individual critical threshold', as evidenced by a remarkably similar end-exercise peripheral fatigue following self-paced exercise in different experimental conditions (Amann *et al.*, 2006a; Amann & Dempsey, 2008; Amann *et al.*, 2009). This centrally mediated restriction is proposed to be regulated by inhibitory afferent feedback from the periphery in order to prevent excessive homeostatic disruption (Amann, 2011), supporting the concept of the human body as an intelligent, regulatory system, where sensory afferent feedback is assimilated and acted upon by an overall 'controller' of exercise intensity that functions to optimise performance whilst preventing catastrophic failure in any single homeostatic system (St Clair Gibson & Noakes, 2004; Lambert *et al.*, 2005). Thus far, these studies are limited to time-trials of 5 km, and less is known about self-paced exercise of longer duration. In Chapter 4, we observed greater variability in the pacing strategy during shorter (4 km) compared to longer (20 km and 40 km) time-trials, and theorised this might reflect differences in the mechanisms regulating performance. Given the task

dependent nature of fatigue, and the relative contribution of central and peripheral mechanisms to exercise tasks of different durations (Lepers *et al.*, 2002; Place *et al.*, 2004; Ross *et al.*, 2010a; Decorte *et al.*, 2012) the existence of a critical peripheral threshold during self-paced exercise warrants further investigation. In addition, the relative role of supraspinal fatigue in limiting self-paced exercise performance in exercise tasks of different duration has yet to be established.

Accordingly, the aim of the present study was to examine the aetiology of fatigue during self-paced cycling exercise of different durations. Based on previous research we hypothesised the existence of a consistent critical threshold of peripheral fatigue between time-trials of different durations, while an increased degree of central fatigue would manifest as the length of the exercise bout is extended.

7-2 Method

7-2.1 Participants

Following institutional ethical approval, thirteen well-trained male cyclists (mean ± SD age, 31 ± 8 years; stature, 1.80 ± 0.07 m; body mass, 72.9 ± 9.1 kg; maximum oxygen uptake ($\dot{V}O_2max$), 4.26 ± 0.38 $L \cdot min^{-1}$) gave written informed consent to take part in the study. Sample size was estimated using typical error and standard deviation scores derived from the reproducibility study reported in Chapter 4 (Thomas *et al.*, 2012b), and additional measures of reproducibility for outcome measures where reproducibility has not previously been quantified (see section 7-2.10, Data analysis). Small, moderate and large effects were determined as 0.2, 0.5 and 0.8 of the between-subject standard deviation for each outcome measure (Cohen, 1988; Hopkins *et al*., 1999). For the primary outcome measures of interest an estimated sample size of thirteen was required to detect at least a moderate effect with 80% statistical power. All participants were regularly competing in cycling time-trial events similar in duration to those employed in the study.

7-2.2 Design

Using a repeated measures design, each participant visited the lab on 4 separate occasions to complete a practice time-trial, and three experimental time-trials of 4 km, 20 km and 40 km in length. Trials were separated by a minimum of two and a

maximum of seven days, and were conducted at the same time of day (± 1 h). The order of experimental trials was randomised and counterbalanced. Prior to each visit, participants followed the same pre-test preparations as previously outlined (Chapters 4 to 6). Cardiorespiratory, blood lactate and perceptual responses were recorded during each time-trial, and measures of central and peripheral fatigue were assessed pre-trial and within 2.5 min post-trial (described below).

7-2.3 Procedures

Participants first completed a practice trial to habituate to the measurement tools of the study, in particular electrical stimulation of the femoral nerve and magnetic stimulation of the motor cortex. A 4 km time-trial was chosen as the distance for the practice trial as the participant group were regularly competing in trials of distances approximating 20 km and 40 km, but were less practiced in shorter duration time-trials. In addition, previous data from our lab has shown evidence of a learning effect in well-trained cyclists for 4 km (Stone *et al.*, 2011) but not 20 km (Chapter 4, Thomas *et al.*, 2012b) simulated time-trials. As reported in Chapter 4, the typical error for mean power for these trials is low (1.6-3.5%, Stone *et al.*, 2011; Thomas *et al.*, 2012b). The procedures adopted during the practice trial replicated that of the experimental trials (described below).

7-2.4 Experimental trials

Participants completed 4 km, 20 km and 40 km time-trials on separate occasions with instructions to "complete the distance as fast as possible". Self-paced trials were conducted using apparatus previously described (Chapters 4 to 6).

Neuromuscular function

Measures of neuromuscular function for the assessment of central and peripheral fatigue were evaluated pre-trial, and immediately after (< 2.5 min post) each time-trial using transcranial magnetic stimulation (TMS) of the motor cortex and electrical stimulation of the femoral nerve, with evoked responses recorded with surface electromyography (EMG). After three practice attempts to ensure adequate potentiation, participants completed three isometric maximum voluntary contractions with femoral nerve stimulation delivered during and 2 s post MVC to assess voluntary activation and

potentiated quadriceps twitch force ($Q_{tw.pot}$), respectively. Subsequently, TMS was delivered during brief (~3-5 s) contractions at 100%, 75% and 50% MVC, separated by ~5 s of rest, for determination of cortical voluntary activation. This procedure was repeated 3 times with 15 s rest between each set. Resting MEPs (eight stimuli) were recorded prior to these baseline measures of fatigue, and immediately after the final TMS set post-trial to assess the excitability of the corticospinal pathway. Further detail on these procedures follows.

Force & EMG recordings

Knee-extensor force (N) during voluntary and evoked contractions was measured using a calibrated load cell (MuscleLab force sensor 300, Ergotest technology, Norway) fixed to a custom built chair and connected to a noncompliant strap attached round the participant's right leg superior to the ankle malleoli. The height of the load cell was individually adjusted to ensure a direct line with the applied force. During all measurements participants sat upright with the hips and knees at 90 degrees flexion. Electromyography of the knee extensors and flexors was recorded from the vastus lateralis and lateral head of the biceps femoris, respectively. After the skin was shaved and cleaned, surface electrodes (Ag/AgCl; Kendall H87PG/F, Covidien, Mansfield, MA, USA) were placed 2 cm apart over the belly of each muscle. A reference electrode was placed on the patella. The positions of the electrodes were marked with indelible ink to ensure a consistent placement on repeat trials. The electrodes were used to record the root-mean-square amplitude for maximal voluntary contractions (MVC_{RMS}), the compound muscle action potential (M-wave) from the electrical stimulation of the femoral nerve, and the motor evoked potential (MEP) elicited by TMS. Surface electrode signals were amplified (× 1,000; 1902, Cambridge Electronic Design, Cambridge), band-pass filtered (EMG only; 20-2,000 Hz), digitised (4 kHz, micro 1401, Cambridge Electronic Design) and acquired for off-line analysis (Spike 2 version 7.01, Cambridge Electronic Design).

Femoral nerve stimulation

Single electrical stimuli (200 μs duration) were delivered to the right femoral nerve via surface electrodes (CF3200, Nidd Valley Medical Ltd, Harrogate, UK) using a constant-current stimulator (DS7AH, Digitimer Ltd, Welwyn Garden City, UK). The cathode was placed over the nerve high in the femoral triangle; the anode was positioned

midway between the greater trochanter and the iliac crest (Goodall *et al*., 2010). The exact positioning was determined by the response that elicited the maximum quadriceps twitch amplitude (Q_{tw}) and M-wave (M_{max}) at rest. To determine the stimulation intensity, single stimuli were delivered in 20 mA step-wise increments from 100 mA until a plateau in Q_{tw} and M-wave were observed. To ensure a supramaximal stimulus the final intensity was increased by 30% (mean ± SD current = 194 ± 101 mA). The peak-to-peak amplitude and area of the electrically evoked M_{max} was used as a measure of membrane excitability (Fowles *et al.*, 2002). Measures of muscle contractility were derived for each resting twitch; twitch amplitude, maximum rate of force development (MRFD), maximum relaxation rate (MRR), contraction time (CT) and one-half relaxation time ($RT_{0.5}$).

Transcranial magnetic stimulation

Using a concave double cone coil (110 mm diameter; maximum output 1.4 T), single pulse magnetic stimuli of 1 ms duration were delivered to the left motor cortex, powered by a monopulse magnetic stimulator (Magstim 200, The Magstim Company Ltd., Whitland, UK). The coil was held and tilted lateral to the vertex (1.5 ± 0.6 cm) to stimulate the left hemisphere (postero-anterior intracranial current flow) over the area relating to Brodmann Area 4, the primary motor cortex. The coil position was such, that it elicited a large MEP in the vastus lateralis and a concurrent small MEP in the antagonist muscle. Coil position was marked on the scalp using indelible ink to ensure consistent placement on repeat trials. Resting motor threshold (rMT) was determined prior to each experimental trial. Starting at sub-threshold intensity (35% of stimulator output), single pulse TMS were delivered over the optimal site of stimulation in 5% increments until the peak-to-peak amplitude of the evoked MEP consistently exceeded 50 μV. Subsequently, the stimulus intensity was reduced in 1% decrements until the MEP response was below 50 μV in more than half of 10 stimuli (Rossini *et al.*, 1994; Groppa *et al.*, 2012). Resting motor threshold (rMT) for the knee extensors occurred at 49 ± 12% of maximum stimulator output, and subsequently during experimental trials TMS was delivered at 130% of rMT (64 ± 15%; Taylor & Gandevia, 2001). This intensity elicited a large MEP in the vastus lateralis (area > 60% of M_{max} during knee extensor contractions) and a small MEP in the biceps femoris (area < 15% of M_{max} during knee extensor contractions).

Cardiorespiratory, Blood [Lactate] & Perceptual measures

During each trial expired air, heart rate and blood lactate were measured using procedures previously described (Chapter 4 & 6). Blood sampling was aligned between trials such that samples occurred at the same distance covered in each, based on sampling blood at 20% of the distance covered in each trial. Ratings of perceived exertion (RPE) were obtained every 10% of trial distance covered, and post-trial after a 5 minute standardised cool down participants were asked for a whole trial RPE score that best represented the effort over the entire time-trial.

7-2.10 Data analysis

Typical error (TE) and intra-class correlation coefficients (ICC) between the pre-trial scores were calculated to quantify reproducibility of the outcome measures of interest. Reproducibility was high for MVC (ICC = 0.98, TE = 4.0%), $Q_{tw.pot}$ (ICC = 0.98, TE = 6.6%), VA (ICC = 0.96, TE = 3.0%), cortical VA (ICC = 0.98, TE = 1.7%) and moderate for ERT (ICC = 0.91, TE = 10.8%), CSP (ICC = 0.95, TE = 12.8%), M_{max} (ICC = 0.86, TE = 29.1%) and MEP/M_{max} ratio (ICC range = 0.71 to 0.74, TE range = 12.6 to 18.2%).

Peripheral voluntary activation was quantified using the twitch interpolation method (Merton, 1954). Briefly, the amplitude of the superimposed twitch force (SIT) measured through electrical stimulation during the MVC was compared with the amplitude of the potentiated twitch force assessed ~ 2 s post-MVC at rest: Voluntary activation (%) = [1 – (SIT/$Q_{tw.pot}$)] × 100. Cortical voluntary activation was assessed by measurement of the force responses to cortical stimulation at 100%, 75% and 50% MVC. Corticospinal excitability increases during voluntary contraction, therefore it is necessary to estimate, rather than directly measure, the amplitude of the resting twitch in response to motor cortex stimulation (Rothwell *et al.*, 1991). The amplitude of the resting twitch was calculated as the *y*-intercept of the linear regression between the mean amplitude of the superimposed twitches evoked by TMS at 100%, 75% and 50% MVC and voluntary force (ERT: Todd *et al.*, 2003a; Todd *et al.*, 2003b; Goodall *et al.*, 2009). Cortical voluntary activation was subsequently calculated as [1 – (SIT/ERT)]) × 100. The reproducibility and validity of this procedure for the knee extensors has been previously established (Goodall *et al.*, 2009; Sidhu *et al.*, 2009a). The peak-to-peak amplitude and area of the evoked M_{max} and MEP responses were quantified offline. The area of vastus

lateralis MEP was normalised to the M_{max} measured during the MVC at the beginning of each trial to ensure the magnetic stimulus was activating a high proportion of the knee-extensor motor units (Taylor *et al.*, 1999). The cortical silent period (CSP), was quantified during the MVC as the duration between the point of cortical stimulation until the post-stimulus EMG exceeded ±2 SD of the pre-stimulus EMG for > 100 ms (Goodall *et al.*, 2010).

Statistical procedures were planned *a priori*. For all neuromuscular measures, one way repeated measures ANOVA on the pre-trial scores were conducted to ensure no differences between variables at baseline. Paired samples t-tests were used to assess the expected impact of each time-trial on measures of fatigue. The effect of time-trial length was assessed using one-way repeated measures ANOVA on the pre- to post-change scores, with pairwise 95% confidence intervals for the difference (95% CI_{diff}) calculated using the Least Significant Differences method in the event of a significant main effect. Mean scores for time-trial performance (power output, W) cardiorespiratory, blood lactate and perceptual measures were assessed using repeated measures ANOVA, and Friedman's ANOVA with *post-hoc* Wilcoxon signed-ranks test in the case of non-parametric data. Previous data have demonstrated association between the degree of peripheral fatigue and capillary blood lactate accumulation (Sidhu *et al.*, 2009b), thus Pearson's product moment correlations were used to determine relationships between these variables. The assumptions underpinning these statistical procedures were verified as per the guidelines outlined by Newell *et al*. (2010). Descriptive data are presented as means ± SD in text, tables and figures. Statistical analysis was conducted using SPSS (IBM SPSS, version 19.0, Chicago, IL.). Statistical significance was assumed at $p < 0.05$.

7-3 Results

7-3.1 Exercise Responses

Mean power output was significantly higher in the 4 km (340 ± 30 W) compared to the 20 km (279 ± 22 W; 95% CI_{diff} = 49 to 75 W, $p < 0.001$), and the 20 km compared to the 40 km (255 ± 21 W; 95% CI_{diff} = 14 to 34 W, $p < 0.001$) (Figure 7-1). Oxygen uptake, $\dot{V}_E$, $\dot{V}_E/\dot{V}O_2$ and RER were higher in the 4 km compared to both the 20 km and 40 km ($p < 0.01$), and higher in the 20 km compared to the 40 km ($p < 0.05$, Table 7-1).

Heart rate was higher in both the 4 km and 20 km in comparison to 40 km ($p < 0.05$, Table 7-1). Both mean and peak blood lactate were higher in the 4 km (mean = 9.6 ± 1.9 mMol·L^{-1}, peak = 14.5 ± 2.8 mMol·L^{-1}) compared to both 20 km and 40 km ($p < 0.05$), and higher in the 20 km (mean = 7.8 ± 0.9 mMol·L^{-1}, peak = 11.5 ± 1.8 mMol·L^{-1}) compared to the 40 km (mean = 5.1 ± 1.3 mMol·L^{-1}, peak = 8.1 ± 2.2 mMol·L^{-1} ; $p <$ 0.05, Figure 7-2). Participants perceived the 4 km to be harder than both the 20 km and 40 km, with differences between the average RPE, peak RPE and the session RPE ($p <$ 0.01, Table 7-1).

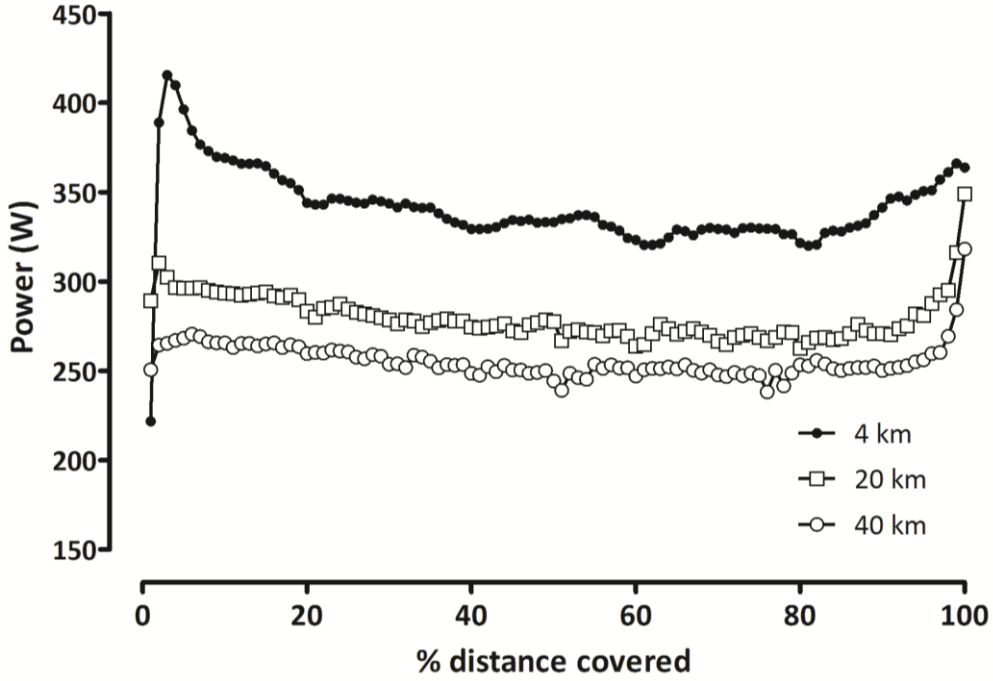


Figure 7-1. Pattern of power output (W) during 4, 20 and 40 km cycling time-trials. Values are 1% means of the total distance covered.

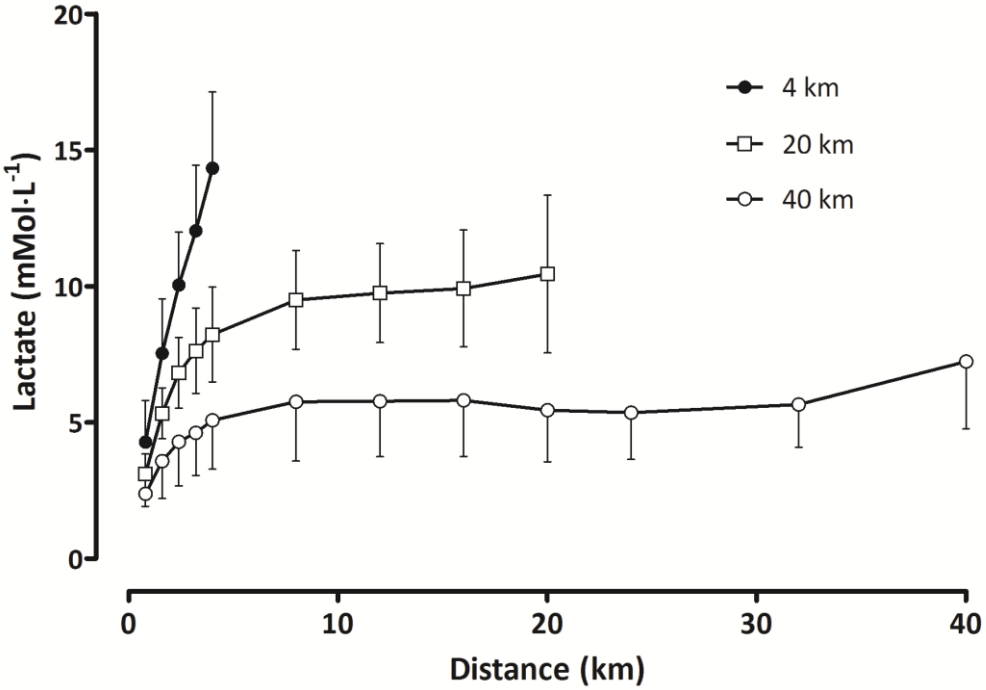


Figure 7-2. Pattern of blood [lactate] (mMol·L^{-1}) response to 4, 20 and 40 km cycling time-trials (values are mean ± SD). Capillary blood sampling was aligned between trials such that samples occurred at the same distance covered in each, based on sampling blood at 20% of the distance covered in each trial.

Table 7-1. Performance, cardiorespiratory, ventilatory and perceptual responses to 4, 20 and 40 km cycling time-trials.

	4 km	20 km	40 km
Exercise time (min)	5.96 ± 0.20*†	31.84 ± 1.04†	65.76 ± 2.18
Mean power (W)	340 ± 30*†	279 ± 22†	255 ± 21
Cadence (rpm)	100 ± 7†	97 ± 3†	92 ± 5
$\dot{V}O_2$ (L·min^{-1})	4.10 ± 0.36*†	3.92 ± 0.38†	3.70 ± 0.31
$\dot{V}CO_2$ (L·min^{-1})	4.45 ± 0.54*†	3.79 ± 0.36†	3.41 ± 0.29
$\dot{V}_E$ (L·min^{-1})	152 ± 25*†	130 ± 16†	111 ± 16
$\dot{V}_E/\dot{V}O_2$	36.8 ± 4.1*†	33.2 ± 2.6†	30.0 ± 2.9
$\dot{V}_E/\dot{V}CO_2$	34.1 ± 3.6	34.4 ± 2.6	32.4 ± 2.7
RER	1.08 ± 0.06*†	0.96 ± 0.03†	0.92 ± 0.03
f_R	55 ± 7†	52 ± 7	48 ± 9
Heart rate (b·min^{-1})	178 ± 14†	177 ± 13†	172 ± 14
RPE (mean)	17 ± 1*†	15 ± 1	15 ± 1
RPE (peak)	19 ± 1*†	18 ± 2	18 ± 1
RPE (post)	17 ± 2*†	16 ± 1	16 ± 1

$\dot{V}O_2$; oxygen uptake, $\dot{V}CO_2$, carbon dioxide output; $\dot{V}_E$, minute ventilation; $\dot{V}_E/\dot{V}O_2$, ventilatory equivalent for oxygen; $\dot{V}_E$ /$\dot{V}CO_2$, ventilatory equivalent for carbon dioxide; RER; respiratory exchange ratio, f_R; respiratory frequency, RPE; rating of perceived exertion. *$p < 0.05$ different from 20 km, †$p < 0.05$ different from 40 km.

7-3.2 Peripheral responses

Details on the effect of exercise trial on neuromuscular function are shown in Table 7-2. At baseline there was no difference between any of the measured variables. Exercise

resulted in significant peripheral fatigue in all time-trials ($\Delta Q_{tw.pot}$) along with alterations in muscle contractility (Table 7-2). Conversely, there were no differences in MVC_{RMS}, or measures of membrane excitability pre- to post-trial (M_{max} amplitude and area). The reduction in MVC was not different between trials (102 ± 85 N, 84 ± 62 N and 84 ± 41 N drop for 4 km, 20 km and 40 km, respectively; $p = 0.56$, Figure 7-3, Panel A). The drop in $Q_{tw.pot}$ was different between trials ($p = 0.03$). There was evidence of a greater reduction in the 4 km trial (–61 ± 37 N) compared to both the 20 km trial (–46 ± 28 N, 95% CI_{diff} = –28 to –2 N, $p = 0.03$) and the 40 km trial (–44 ± 28 N, 95% CI_{diff} = –34 to –1 N, $p < 0.05$) with no difference between 20 km and 40 km (95% CI_{diff} = –14 to 9 N, $p = 0.67$; Figure 7-3, Panel B). Greater decrements in MRFD of the potentiated twitch were observed after the 4 km compared to both 20 and 40 km ($p < 0.05$), whilst MRR, CT and $RT_{0.5}$ changed similarly independent of TT length (Table 7-2). Lactate concentration post-exercise was correlated with the reduction in potentiated twitch force for the 4 km trial ($r = –0.76$, $p = 0.004$) but not for 20 km ($r = –0.37$, $p = 0.22$) or 40 km ($r = 0.17$, $p = 0.66$).

7-3.3 Central responses

Voluntary activation at baseline was similar for both motor nerve stimulation and TMS methods (92% vs. 95% respectively). Exercise resulted in significant reductions in both cortical and peripheral voluntary activation (Table 7-2). The change in peripheral VA was different between trials ($p = 0.003$). Specifically the drop in peripheral VA was less in the 4 km (Δ6%) compared to both the 20 km (Δ10%, 95% CI_{diff} = –1 to –7%, $p < 0.05$, $p = 0.03$) and the 40 km (Δ11%, CI_{diff} = –1 to –9%, $p = 0.02$, Figure 7-3, panel C). The reduction in cortical voluntary activation was also different between trials ($p = 0.015$) and mirrored the pattern observed for peripheral VA. The decline in cortical voluntary activation was less in the 4 km (Δ4%) compared to both 20 km (Δ11%, 95% CI_{diff} = –1 to –10%, $p = 0.02$) and the 40 km (Δ10%, 95% CI_{diff} = –1 to –9%, $p = 0.04$, Figure 7-3, panel D). The responsiveness of the corticomotor pathway (MEP amplitude and area) measured at rest was reduced in the 20 km and 40 km post-trial compared to baseline, but not in the 4 km time-trial (Table 7-2). Analysis of the percentage drop in MEP characteristics between trials revealed greater decrements in the 20 km compared to 4 km ($p = 0.005$) and 40 km compared to 4 km ($p = 0.003$, Figure 7-4). The cortical silent period was unchanged in all trials ($p > 0.05$, Table 7-2).

Table 7-2. Neuromuscular function pre- and post- 4, 20 and 40 km cycling time-trials.

		4 km	20 km	40 km
Global fatigue				
MVC (N)	Pre	548 ± 144	536 ± 143	535 ± 137
	Post	445 ± 137*	452 ± 121*	451 ± 120*
Peripheral fatigue				
$Q_{tw.pot}$ (N)	Pre	147 ± 34	143 ± 33	145 ± 37
	Post	85 ± 25*	97 ± 25*	101 ± 28*
ERT (N)	Pre	146 ± 47	130 ± 44	133 ± 49
	Post	84 ± 43*	87 ± 39*	89 ± 47*
MRFD ($N \cdot ms^{-1}$)	Pre	4.40 ± 3.32	4.62 ± 3.07	4.72 ± 1.82
	Post	2.22 ± 1.27*	3.06 ± 1.71*	3.67 ± 1.52*
CT (ms)	Pre	86 ± 13	89 ± 15	84 ± 12
	Post	81 ± 11	78 ± 13*	76 ± 13*
MRR ($N \cdot ms^{-1}$)	Pre	−1.47 ± 0.85	−1.96 ± 1.13	−1.67 ± 0.72
	Post	−1.15 ± 0.49	−1.60 ± 0.98	−1.59 ± 0.57
$RT_{0.5}$ (ms)	Pre	87 ± 26	75 ± 25	82 ± 25
	Post	65 ± 22*	61 ± 26*	60 ± 16*
Central fatigue				
Cortical VA (%)	Pre	95 ± 6	94 ± 7	94 ± 6
	Post	91 ± 7*	84 ± 11*	85 ± 11*
Peripheral VA (%)	Pre	92 ± 8	92 ± 8	92 ± 6
	Post	85 ± 13*	81 ± 15*	82 ± 15*
Surface EMG				
Resting responses				
M_{max} amplitude (mV)	Pre	4.53 ± 2.63	5.21 ± 1.99	5.67 ± 2.98
	Post	4.86 ± 2.36	4.89 ± 1.82	5.17 ± 3.21
MEP amplitude (mV)	Pre	0.31 ± 0.20	0.25 ± 0.19	0.34 ± 0.30
	Post	0.24 ± 0.16	0.10 ± 0.09*	0.08 ± 0.05*
During contraction				
MVC_{RMS} (mV)	Pre	0.29 ± 0.13	0.28 ± 0.11	0.34 ± 0.17
	Post	0.27 ± 0.15	0.26 ± 0.14	0.32 ± 0.17
M_{max} amplitude (mV)	Pre	3.96 ± 2.28	4.56 ± 2.10	4.94 ± 2.01
	Post	3.79 ± 2.16	4.24 ± 1.64	4.84 ± 2.37
MEP amplitude 100% (mV)	Pre	1.68 ± 0.90	1.60 ± 0.47	2.38 ± 1.24
	Post	1.77 ± 0.89	1.76 ± 0.59	2.52 ± 1.56
MEP amplitude 75% (mV)	Pre	1.71 ± 0.81	1.76 ± 0.83	2.48 ± 1.18
	Post	1.91 ± 0.94	1.63 ± 0.67	2.10 ± 1.16
MEP amplitude 50% (mV)	Pre	1.68 ± 0.66	1.46 ± 0.60	2.29 ± 1.25
	Post	1.88 ± 0.87	1.54 ± 0.56	1.90 ± 0.98
MEP/M_{max} (%) 100% MVC	Pre	53 ± 13	45 ± 14	47 ± 15
	Post	56 ± 22	46 ± 25	46 ± 14
MEP/M_{max} (%) 75% MVC	Pre	48 ± 18	43 ± 23	50 ± 15
	Post	55 ± 20	42 ± 23	43 ± 18
MEP/M_{max} (%) 50% MVC	Pre	48 ± 21	39 ± 16	46 ± 17
	Post	54 ± 20	42 ± 23	39 ± 19
CSP (ms)	Pre	191 ± 81	194 ± 89	185 ± 77
	Post	199 ± 68	181 ± 94	180 ± 67

MVC; maximum voluntary contraction, $Q_{tw.pot}$; potentiated twitch, ERT; estimated resting twitch, CT; contraction time, MRR; maximum rate of relaxation; $RT_{0.5}$; half relaxation time, VA; voluntary activation; M_{max}; maximum M-wave , MEP; motor evoked potential, CSP; cortical silent period. All MEP/M_{max} ratio expressed relative to M_{max} determined during MVC. *$p < 0.05$ different from pre-trial.

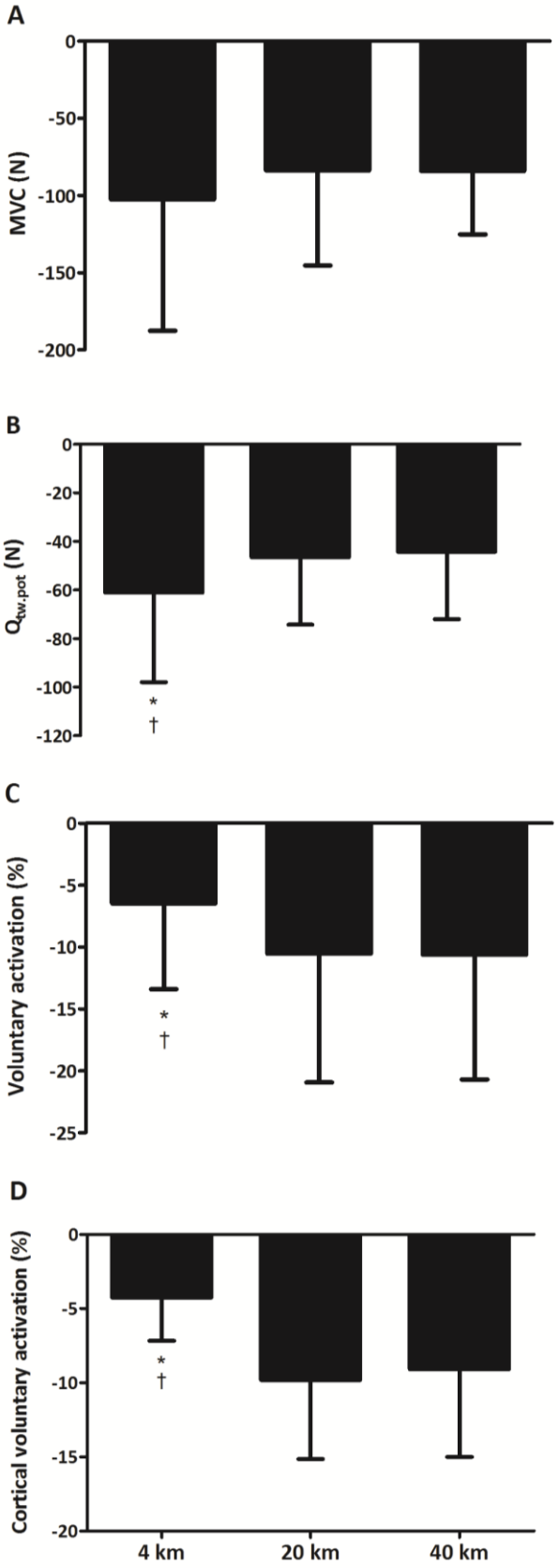


Figure 7-3. Pre- to post-trial change in maximum voluntary contraction (A), potentiated twitch (B), voluntary activation (C) and cortical voluntary activation (D) in 4, 20 and 40 km cycling time-trials. Values are mean + SD. *$p < 0.05$ different from 20 km, †$p < 0.05$ different from 40 km.

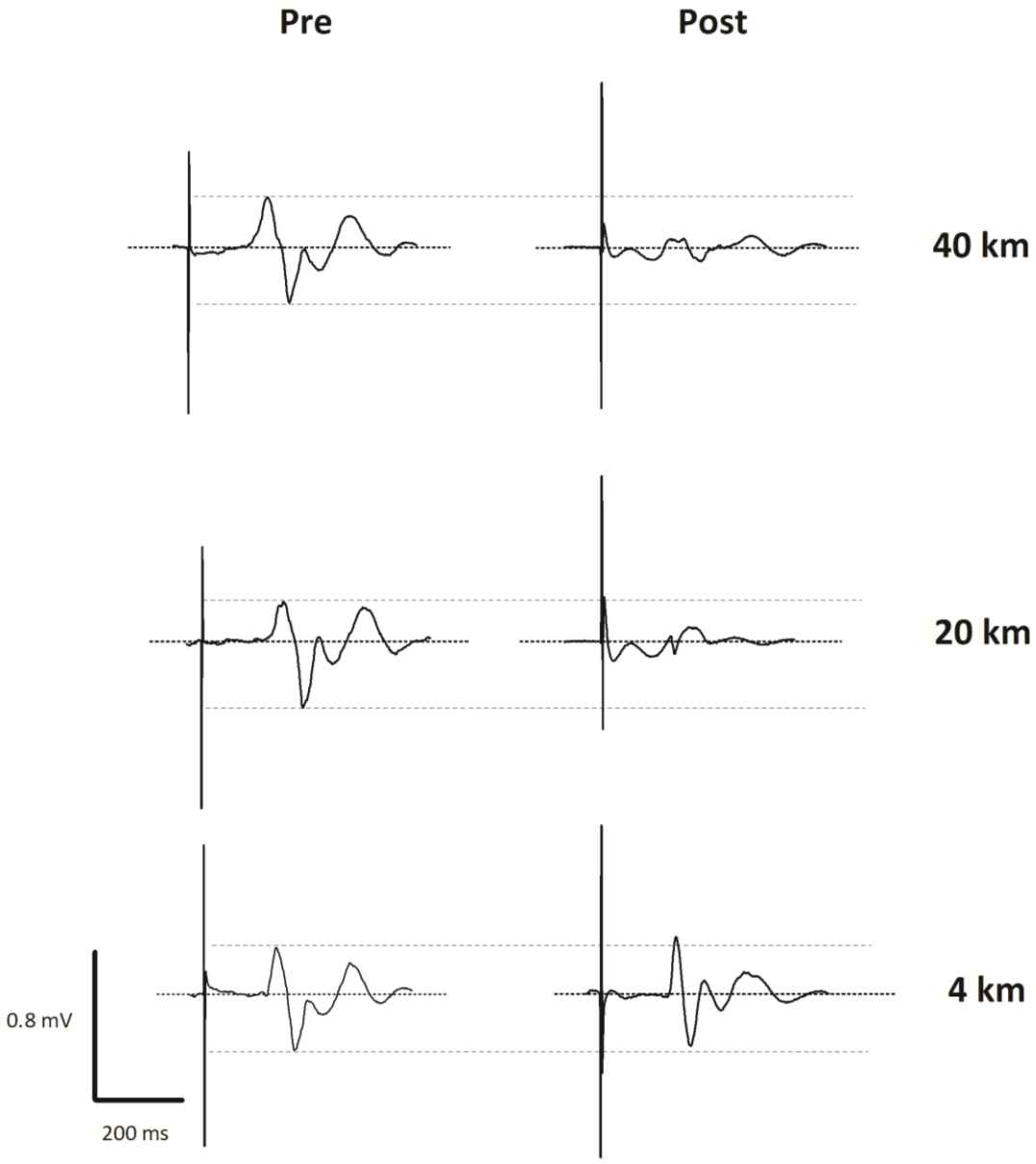


Figure 7-4. Resting motor evoked potentials (MEP) pre- and post- 4, 20 and 40 km time-trials from a representative participant. Note the depression in MEP after the 20 and 40 km time-trials, and no change in the 4 km.

7-4 Discussion

This study assessed the neuromuscular basis of fatigue after self-paced locomotor exercise of different durations. The main findings indicate that, in self-paced exercise, the degree of peripheral and central fatigue is task-dependent. Specifically in high intensity, short duration time-trial exercise (~6 min) the degree of peripheral fatigue is greater than lower intensity, longer exercise bouts (≥ 30 min), where central, and supraspinal, fatigue is greater. These findings provide new insight in to the regulation of exercise intensity during self-paced locomotor exercise.

Previous research has demonstrated the existence of an individual critical level of peripheral fatigue and associated sensory tolerance that is never voluntarily exceeded during high-intensity endurance cycling (Amann *et al.*, 2006a; 2008; 2009). These authors were careful, however, to emphasise this critical threshold might be task-dependent (Amann & Secher, 2010), and have recently demonstrated differences in the sensory tolerance limit between exercise requiring small vs. large muscle mass (Rossman *et al.*, 2012). Some support for the concept of an exercise mode-dependent critical threshold has however been provided during isolated muscle exercise by Burnley *et al*. (2012). Based on this work, we hypothesized that such a limit would exist across self-paced cycling time-trials of different demand. However, contrary to our hypothesis, we observed a greater degree of peripheral fatigue after the 4 km (40% reduction in $Q_{tw.pot}$), compared to both the 20 km and 40 km time-trials (31 and 29% reduction, respectively). Furthermore, fatigue after the longer time-trials was characterized by a greater contribution of central fatigue.

From these observations it would seem peripheral fatigue after self-paced cycling exercise is task-dependent; in particular we propose the intensity domain in which the exercise bout is completed determines the degree of peripheral fatigue. The 4 km was completed at an exercise intensity that was in excess of the athlete's maximum sustainable power output, or critical power, evidenced by the high and rising blood lactate response to this trial (Figure 7-2). Fatigue during exercise in the severe intensity domain (i.e. above critical power, or torque) is well-studied in single-limb (Yoon *et al.*, 2007; Jones *et al.*, 2008a; Goodall *et al.*, 2010; Burnley *et al.*, 2012; Froyd *et al.*, 2013) and locomotor paradigms (Amann & Dempsey, 2008; Amann *et al.*, 2009; Amann *et al.*, 2011; Goodall *et al.*, 2012a). During exercise in the severe domain, the rate of

peripheral fatigue development is disproportionately increased, and is reflected in a progressive recruitment of higher-threshold, less fatigue-resistant motor units (Burnley *et al.*, 2012). This results in a gradual accumulation of inorganic phosphate, a progressive reduction in pH, a depletion of the high-energy phosphagen pool and an exhaustion of the finite capacity for anaerobic work until task failure (Jones *et al.*, 2008a). Whether these changes in the intramuscular metabolic state of the muscle cause peripheral fatigue *per se* is debatable, but their association is supported by the relationship between the degree of peripheral fatigue and metabolite accumulation observed in the present, and other investigations (Spriet *et al.*, 1987b, a; Sidhu *et al.*, 2009b). In addition, the role of metabosensitive group III/IV afferents in limiting high-intensity cycling performance has been elegantly demonstrated (Amann *et al.*, 2009; Amann *et al.*, 2011), and fatigue during single-limb knee extensor exercise at different intensities above critical torque is associated with a similar level of peripheral fatigue (Burnley *et al.*, 2012). These observations and our current data suggest that exercise in the severe domain is characterised by attainment of a critical level of peripheral fatigue, likely caused by the progressive recruitment and failure of a greater portion of the motoneuron pool, and a concomitant large disruption to intramuscular homeostasis.

In contrast to the 4 km, the 20 and 40 km time-trials were characterised by a smaller (albeit significant) degree of peripheral fatigue. Based on the elevated but stable blood [lactate] response (Figure 7-2), the exercise intensity in these trials was below critical power for the majority of the bout. The limiting factors to exercise performance below critical power, in the heavy and moderate domains of exercise, are less well-characterised than for exercise in the severe domain. During single-limb exercise below critical power, muscle metabolites and motor unit recruitment are stabilised early in the exercise bout, and exercise terminates with a substantial motor unit reserve (Jones *et al.*, 2008a; Burnley *et al.*, 2012). Significant peripheral fatigue still occurs, though it is unlikely that this is due primarily to the accumulation of fatigue-induced metabolites or depletion of high-energy phosphates; a suggestion supported by the lack of association between decrements in $Q_{tw.pot}$ and [lactate] accumulation in the longer time-trials in this study. Recent evidence has implicated intramyofibrillar glycogen depletion after prolonged exercise as a potential cause of peripheral fatigue through localised effects on Ca^{2+} release (Gejl *et al.*, 2013; Ortenblad *et al.*, 2013). We observed decrements in Ca^{2+} handling post-exercise, but no effect of time-trial length on these changes (Table 7-2).

In addition there was no reduction in muscle membrane excitability post-exercise, though recently Sidhu *et al*. (2012a) showed reduced excitability *during* a 30 min bout of locomotor cycling exercise. Specifically, M_{max} amplitude was reduced after 20 min of exercise at 75% of P_{max} (Sidhu *et al.*, 2012a), suggesting reductions in membrane excitability might manifest during the latter stages of prolonged endurance exercise, but recover quickly on exercise cessation. The exact cause of impairment in contractile function as a result of exercise below critical power cannot be clearly identified from this data, and studying the limit to performance during this type of exercise is an area warranting further research.

Whilst the degree of peripheral fatigue was lower after longer time-trials, central fatigue was exacerbated. This pattern supports previous research in both single limb and locomotor exercise models that has demonstrated a duration-dependent contribution of central fatigue (Lepers *et al.*, 2002; Place *et al.*, 2004; Burnley *et al.*, 2012; Decorte *et al.*, 2012). The cause of this is likely repetitive activation of the motoneurons responsible for the exercise task, altering their intrinsic properties and rendering them less responsive to input (McNeil *et al.*, 2009; McNeil *et al.*, 2011b). The reflex activity of fatigue sensitive small-diameter muscle afferents have also been proposed to act at cortical levels to impair maximal voluntary drive and thus cause central fatigue (Gandevia *et al.*, 1996; Taylor *et al.*, 2006). During the longer duration time-trials however the magnitude of peripheral disturbance (i.e. peripheral fatigue, blood [lactate] accumulation) was less than in the shorter duration trials, whilst central fatigue was higher. Thus whilst the reflex activity of chemically sensitive intramuscular afferents are important in the regulation of central motor drive (Amann *et al.*, 2009; Amann *et al.*, 2011), their role (if any) in determining reductions in voluntary activation (and thus central fatigue) must be related to their prolonged firing. Alternatively, it is more likely that the repetitive activation of the motoneurons responsible for the task is the predominant explanatory factor for the greater reduction in voluntary activation after longer duration exercise.

The exercise intensity domain in which the time-trials were performed probably explains the observed difference in the contributions of central and peripheral fatigue. Whilst this is the first experiment to explicitly compare different durations of self-paced, locomotor exercise, this conclusion is perhaps not surprising based on previous

similar observations during single-limb exercise (Bigland-Ritchie *et al.*, 1986a; Burnley *et al.*, 2012). However, given the self-paced nature of the exercise bout, we hypothesised a similar degree of peripheral fatigue would manifest across time-trials of different lengths. In self-paced time-trials, participants would theoretically be able to increase power output in the final portion of the trial to exhaust the available motor unit reserve and finite anaerobic work capacity, and maximise time-trial performance. Contrary to this, participants finished the longer time-trials with a lower degree of peripheral fatigue, indicating some locomotor muscle reserve. Why the CNS did not tolerate or "allow" access to this reserve in order to maximise time-trial performance is an interesting question arising from our data. Whilst we cannot specifically answer this question with certainty from the current dataset, we offer some potential explanations below.

Firstly, the similar degree of global fatigue (decreased MVC, Figure 7-3, panel A) after 4, 20 and 40 km time-trials raises the intriguing possibility of a combined central + peripheral limit of fatigue. The higher degree of central fatigue experienced at the end of the longer time-trials, coupled with the significant degree of peripheral fatigue, could act (either consciously or subconsciously) to prevent the central nervous system from accessing the available motor unit reserve. Such a limit would conceivably not be present in the 4 km, where a higher rate and magnitude of peripheral fatigue accumulation might be tolerated when central fatigue is modest. A combined peripheral + central limit of fatigue is not supported however by data presented by Burnley *et al*. (2012), at least for single limb exercise. These authors showed that both central and peripheral fatigue reached peak values at exercise just above critical torque (duration ~18 min). As exercise intensity increased (and thus duration decreased), peripheral fatigue remained consistent but central fatigue declined. In contrast, after lower intensity, longer duration exercise below the critical torque, central fatigue was substantial but peripheral fatigue was less. These data do not support the existence of a combined central + peripheral limit of fatigue, but further support the suggestion that the degree of fatigue is primarily determined by the intensity and subsequent duration of the exercise bout. Specifically, during exercise in the severe domain (i.e. 4 km), the rate of peripheral fatigue development is accelerated, and the magnitude of this is regulated to an individual sensory tolerance limit that is probably related to the intramuscular metabolic milieu (Jones *et al.*, 2008a) and fatigue of a greater portion of the motoneuron

pool (Burnley *et al.*, 2012). During exercise in the heavy (i.e. 20 km) or moderate (i.e. 40 km) domains the intramuscular and metabolic disturbance is quickly stabilised (Jones *et al.*, 2008a), central fatigue is exacerbated but the degree of peripheral fatigue is lower and probably specific to the lower threshold motor units responsible for the exercise task (McNeil *et al.*, 2011a).

An alternative explanatory factor for the observed difference in peripheral fatigue is that the sum of the ensemble afferent feedback during longer trials was quantitatively similar to that of shorter trials, but the proportional contribution of locomotor muscle fatigue was less. Rossman *et al*. (2012) demonstrated a greater degree of peripheral fatigue after single-limb compared to double-limb high-intensity cycling exercise, and hypothesised this was associated with a similar ensemble afferent feedback. Specifically, during exercise of a small muscle mass the greater degree of peripheral fatigue generated a strong local afferent signal that was similar in magnitude to the sum of more numerous, diffuse afferent signals from exercise of a greater muscle mass (Rossman *et al.*, 2012). During longer duration exercise, the sum of signals from other mechanical and chemically sensitive afferents might restrict the development of locomotor muscle fatigue by increasing the ensemble afferent feedback to the CNS. For example, longer duration exercise places greater demands on temperature regulation, substrate utilisation, and additional central fatigue; factors that might limit endurance exercise below critical power (Nybo & Nielsen, 2001a; Jones *et al.*, 2008a). It is possible that some, or all, of these signals might have increased the ensemble afferent feedback to the CNS during the longer time trials and limited the further development of locomotor muscle fatigue.

Finally, our data might simply reflect the conscious desire of the well-trained cyclists studied to over-ride the feeling of muscular fatigue in order to optimise short duration performance. Afferent feedback is an important limiting factor to self-paced exercise performance (Amann, 2011), but the conscious perception of the fatigue experienced by the athlete will be balanced against the desire to perform, knowledge of the endpoint and previous experience of similar exertion (Marcora, 2010). The shorter duration of the 4 km trial, where the endpoint of exercise is within reach for much of the bout, might permit a higher sensory tolerance limit than could be reached during longer duration trials. In contrast, the substantial degree of both central and peripheral fatigue in the

latter stages of the longer time-trials might act collectively to negatively impact motivation, and the perceived effort required to sustain a higher power output might have been perceived as unattainable. This suggestion is supported by the finding that perceived exertion was higher in the 4 km compared to the 20 km and 40 km, indicating that participants were consciously aware of the greater degree of peripheral fatigue in response to the 4 km trial, but were willing to tolerate this in order to achieve the best performance.

A novel aspect of the current study is the use of motor cortical and motor nerve stimulation methods in combination, which allows a more thorough assessment of the site of fatigue and the contribution of suprapsinal mechanisms (Taylor, 2009; Goodall *et al.*, 2012b). The reduction in cortical voluntary activation, measured using TMS, followed a similar pattern to that measured using peripheral stimulation of the motor nerve, with greater reductions after the 20 km and 40 km compared to the 4 km, indicating a duration-dependent contribution of supraspinal processes to the observed central fatigue. The resting responsiveness of the corticospinal pathway was also significantly depressed after the 20 and 40 km, with no apparent depression after the 4 km (Figure 7-4). The functional consequence of this depression in the relaxed muscle is unclear (Gruet *et al.*, 2013) particularly considering corticospinal excitability was unchanged when measured during contraction (Table 7-2), a finding that has previously been reported after prolonged constant-load locomotor exercise (Sidhu *et al.*, 2009b). Decreases in resting corticospinal (Gandevia *et al.*, 1996; Taylor *et al.*, 2000) and motoneuron (Butler *et al.*, 2003) responsiveness have also been previously dissociated from activation failure in the elbow flexors, though extensor muscles behave differently (Martin *et al.*, 2006) and the pattern of changes in corticospinal responsiveness differs between single-joint and locomotor exercise (Sidhu *et al.*, 2013a). Whether reductions in resting corticospinal excitability could thus contribute to the observed central fatigue and/or decline in force is not clear, and is an area warranting further research.

In conclusion, the aetiology of fatigue in self-paced time-trial cycling exercise is task-dependent, with a greater degree of peripheral fatigue evident during short, high intensity (< 6 min) time-trials, and an increased contribution of central fatigue in longer, lower intensity time-trials (≥ 30 min). The increased central fatigue in longer time-trials is partly explained by an increased contribution from supraspinal mechanisms; that is,

fatigue caused by sub-optimal output from the motor cortex. These findings provide novel insight in to the regulation of exercise intensity during self-paced locomotor exercise and the neuromuscular underpinning to the observed fatigue during self-paced exercise.

CHAPTER 8 GENERAL DISCUSSION AND CONCLUSIONS

8-1 Introduction

The overall aim of this thesis was to investigate the biological basis of the pacing strategy during self-paced exercise to better understand how the athlete regulates exercise intensity to achieve a best performance whilst managing the symptoms of fatigue. Chapter 4 assessed the reproducibility of the pacing strategy both on repeat trials and between trials of different durations. Chapters 5 and 6 investigated the utility of even- and variable-pacing strategies in comparison to the self-selected strategy in order to provide insight in to the optimum pacing strategy for endurance events. Chapter 7 assessed the neuromuscular basis of fatigue during self-paced exercise in order to better understand the underpinning limitations to performance across a range of endurance events. This chapter will discuss the main findings of this thesis in the context of existing literature, with specific focus on the regulation of intensity and aetiology of fatigue during self-paced exercise, and the optimal pacing strategy for endurance time-trial events.

8-2 Main findings

8-2.1 Regulation of intensity during self-paced exercise

A novel observation of this thesis was the existence of a global pacing strategy that was consistent on repeated trials (Chapter 4) and between trials of different distances (Chapter 4 & 7). It has been previously theorised that the pacing strategy is dependent on a pre-established template that is modified by prior experience (St Clair Gibson *et al.*, 2001a). Hettinga *et al*. (2006) postulated that this template would be stable across different durations or distances, and that well-trained athletes would theoretically have a robust template to inform their pacing strategy given their extensive experience and practice. Observations of elite athletes support this assumption, as typically a parabolic pacing strategy is employed across a range of events and modes of endurance exercise (Tucker *et al.*, 2006b; Corbett, 2009; Hanon & Thomas, 2011; Muehlbauer & Melges, 2011). Whilst it has been previously demonstrated that novice athletes can take more than six exposures to develop a stable pacing template (Foster *et al.*, 2009), the consistency of this in experienced athletes has not been previously assessed.

In Chapter 4 we observed a consistent pacing strategy was adopted on repeat 20 km time-trials that conformed to the typical parabolic strategy observed in elite athletes.

Broadly, this consisted of a fast start with the first quarter of the race completed above the mean power, a relatively even but progressively declining pace for the majority of the trial thereafter until a terminal end spurt at the finish. Power output in the middle portion of the race was very consistent on repeat trials, with more variability observed at the start and the end of the race. We interpreted the high variability at the start and end of the time-trials to reflect the presence of anticipatory, feed-forward regulation of exercise intensity that is subject to a degree of uncertainty even in experienced athletes. The initial power output set by the athlete is influenced by prior experience and a number of other potential modifying factors including the physical and emotional state of the athlete, the level of motivation and the degree of self-belief (Ulmer, 1996; Lambert *et al.*, 2005). As the trial progresses this initial power output is modified by metabolically triggered feedback during the exercise. Thus at the start of an exercise bout the initial power output is subject to an uncertainty that is resolved as the bout progresses (Lambert *et al.*, 2005; St Clair Gibson *et al.*, 2006; Tucker, 2009). At the end of the race, the pacing strategy is subject to more variability depending on the magnitude of the end spurt. The end spurt reflects the considered reserve the athlete maintains for the majority of the race in order to reduce the hazard of catastrophic collapse (de Koning *et al.*, 2011). As the finish line approaches, the certainty of successfully completing the exercise task increases, and the athlete is able to expend this reserve. The resulting variability observed in the final portion of the trial reflects the magnitude of this considered reserve, which might be subject to a degree of miscalculation by the athlete.

During repeat trials of the same distance the consistency of pacing strategy during the middle portion of the race, and of the overall performance and physiological responses, suggests that pacing strategy is tightly regulated by afferent feedback for the majority of the exercise bout. The low variability in exercise intensity throughout the race reflects the athletes endeavour to maximise their sustainable speed whilst managing the symptoms of fatigue. The role of afferent feedback from group III/IV muscle afferents as a modifier of central motor drive has been previously well established (Amann *et al.*, 2009; Amann *et al.*, 2011). These data indicate that the resulting performance of endurance time-trials is predominantly determined by these feedback mechanisms, as power output during the trials is regulated within narrow limits for a large portion of the distance covered (Chapter 4). The prolonged attainment of maximum sustainable

exercise intensity is therefore an important component of optimal pacing; this will be discussed in further detail in section 8-2.2.

The consistency of pacing strategies observed between 4, 20 and 40 km time-trials (Chapter 4 & 7) is a novel finding that supports the existence of a stable, global pacing template in well-trained athletes that operates independent of the distance/duration of the race (St Clair Gibson *et al.*, 2001a; Hettinga *et al.*, 2006; Baron *et al.*, 2011). This is contrary to previous work with novice participants, where it has been suggested it takes more than six exposures to the same exercise challenge before a stable performance template is learned (Foster *et al.*, 2009). In Chapter 4 there was a trend for larger variations from the mean power output in shorter (4 km) compared to longer (20 and 40 km) time-trials. We speculated that this might reflect differences in the mechanisms of fatigue underpinning shorter and longer time-trials. We subsequently investigated these mechanisms in Chapter 7 and demonstrated a duration and intensity specific contribution of central and peripheral mechanisms of fatigue during self-paced exercise. These findings are discussed in detail in section 8-2.3 below.

The perceptual responses to exercise in this thesis provide some support for the role of RPE in the anticipatory regulation of exercise (Tucker, 2009). Tucker (2009) proposed the existence of a subconscious "template" RPE set in advance of the exercise bout that is used as an anchor throughout exercise to ensure a desired rate of increase of RPE and attainment of a maximum tolerable RPE only at the end of the exercise bout (Tucker, 2009; Tucker & Noakes, 2009). Support for this concept is provided by observations that RPE increases linearly over time during self-paced (Joseph *et al.*, 2008) and constant load exercise (Nethery, 2002; Baldwin *et al.*, 2003; Joseph *et al.*, 2008) and has a scalar quality as the increase in RPE is proportional to the duration of the exercise (Noakes, 2004). During constant load exercise the rate of increase in RPE can also be used to accurately predict time to exhaustion (Crewe *et al.*, 2008). The RPE response to exercise in this thesis was consistent on repeat trials (Chapter 4, Figure 8-1, panel A) and was similar between trials of different distances when expressed relative to distance covered (Chapter 7, Figure 8-1, panel B). During even-pacing exercise, where intensity was fixed akin to a constant load task, RPE also showed scalar qualities. In Chapter 6, when even-pacing was associated with exercise intolerance and shorter exercise time compared to self-paced exercise, the RPE response scaled with time. That is, RPE rose

faster and attained a similar peak RPE during even-paced exercise compared to self-paced exercise (Figure 8-1, panel C). When self-paced performance was sub-optimal, even-pacing exercise was perceptually less challenging, as evidenced by attainment of lower mean and peak RPE's during constant load exercise, and a slower rate of rise (Chapters 5 & 6, Figure 8-1, panel D). Collectively these data provide support for the existence of an RPE template that acts to regulate exercise intensity, as proposed by Tucker (2009).

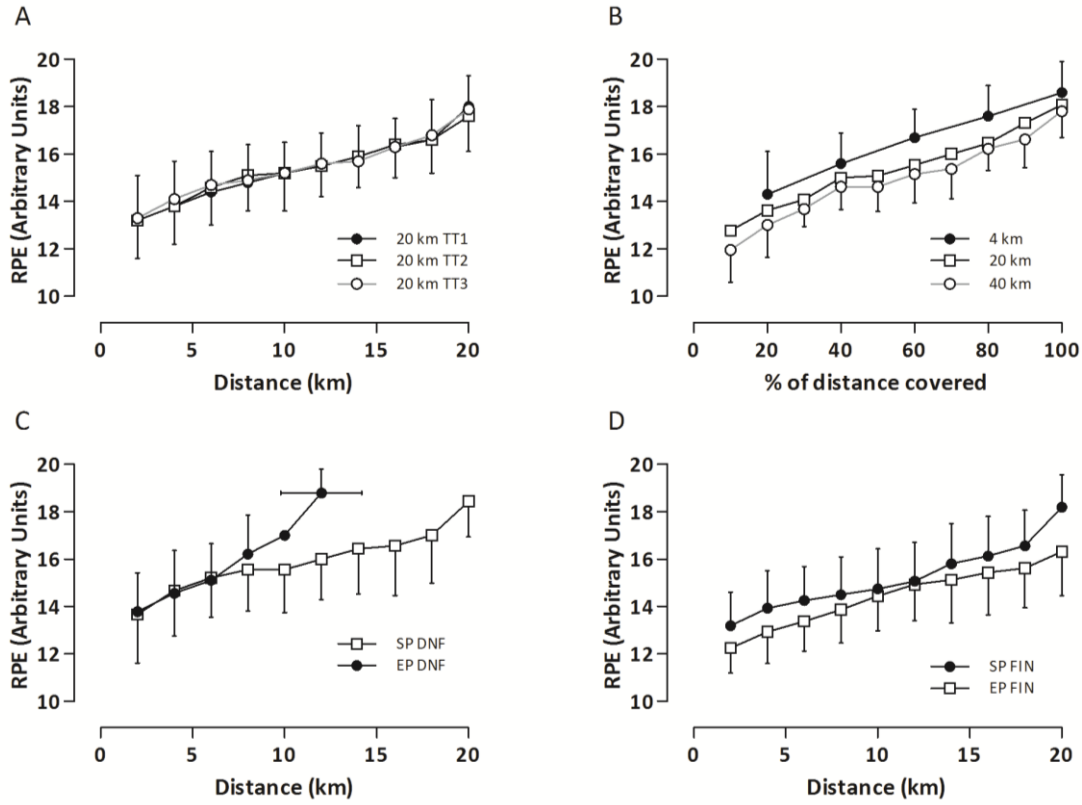


Figure 8-1. The RPE response to exercise illustrates the concept of anticipatory regulation. A, the RPE response is consistent on repeat trials of the same distance. B, the RPE response shows scalar qualities depending on the distance to be covered. C, RPE scales with time during constant load exercise to exhaustion, reaching a similar peak RPE to self-paced exercise. D, when self-paced performance is sub-optimal, even-pacing results in lower RPE, including a lower peak RPE, in a work- and time-matched bout.

The concept of anticipatory, scalar regulation of exercise intensity by a pre-defined RPE template is an attractive and simple explanation; however it is not without critique. For example, whilst the rate of rise in RPE is similar during 4, 20 and 40 km time-trials, both the average and peak RPE were higher in the 4 km trials compared to both the 20 and 40 km (Figure 8-1, panel B). If an RPE template exists, it would seem it operates

differently depending on the duration of the self-paced task; perhaps because the higher exercise intensity required in the 4 km requires a greater efferent command and subsequent sense of effort, and/or a greater homeostatic disturbance and subsequent perception of exertion. Additionally, closer inspection of the RPE response in this thesis and previous studies (Baden *et al.*, 2004; Swart *et al.*, 2009a; Micklewright *et al.*, 2010) suggests the RPE response might be non-linear. Specifically, there are periods where RPE is constant, interjected with sharp increases, even in the even-pacing trials where intensity is constant (Figure 8-1, panels C & D). During self-paced exercise we also observed a reduction in RPE with a parallel reduction in power output in 40% of participants (Chapter 5). Proponents of the RPE model would argue that these adjustments and non-monotonic changes are a behavioural response to ensure the perception of exertion remains close to the pre-defined RPE template, and could be conceptualised as a miscalculation or "correction" in power output (Tucker, 2009; Swart *et al.*, 2012). Others would argue the non-linearity of the response reflects underlying control processes, and the RPE at any point is the conscious manifestation of the on-going change in the metabolic profile (St Clair Gibson *et al.*, 2003; Swart *et al.*, 2009a). Proponents of these concepts thus differ in the extent to which changes in RPE are attributed to feed-forward or feedback control of exercise intensity, but both would agree that there are elements of both in the regulation of exercise intensity.

8-2.2 Optimal pacing strategy for endurance time-trials

In Chapters 5 and 6 the manipulation of self-selected pacing strategy revealed insights in to the optimal pacing strategy for endurance events. Previous research has suggested that an even-pacing strategy is optimal for events longer than 4 min (Foster *et al.*, 1993; Atkinson *et al.*, 2003; Thompson *et al.*, 2003; Gordon, 2005). The theoretical basis to the utility of even-pacing is based on models of critical power (CP), or maximal lactate steady state (MLSS), and the hyperbolic relationship between exercise intensity and duration (Fukuba & Whipp, 1999; Vanhatalo *et al.*, 2011). This relationship is defined by two constants; the asymptote of the curve which represents the maximum sustainable exercise intensity, termed critical power, and a curvature constant (W') which represents a finite capacity for work above the critical power. The critical power and maximum lactate steady state are theoretically equivalent though these measured thresholds differ in practice (Pringle & Jones, 2002). As a concept, both MLSS and CP demarcate the boundary between the "heavy" and "severe" exercise domains, and therefore represent a

maximum sustainable exercise intensity. Exercise in the heavy domain is characterised by an elevated but stable blood [lactate] and a $\dot{V}O_2$ slow component. When exercise intensity traverses into the severe domain the physiological responses are increasingly non-linear (Burnley *et al.*, 2012); blood [lactate] rises continuously, and oxygen uptake attains maximum values unless volitional exhaustion ensues earlier (Poole *et al.*, 1988). Optimal pacing in longer duration events would therefore theoretically maximise the sustainable exercise intensity in the heavy exercise domain whilst simultaneously exhausting *W'*. Adopting an even-pace to attain this maximum sustainable intensity would seem to be an appropriate strategy.

Longer duration endurance events have not been well-studied experimentally, but the limited available evidence does not support the utility of even-pacing (Billat *et al.*, 2006; Ham & Knez, 2009; Lander *et al.*, 2009). Moreover, observations of elite athletes suggest a parabolic pacing strategy is common across exercise modes (Tucker *et al.*, 2006b; Corbett, 2009; Muehlbauer & Melges, 2011; Mauger *et al.*, 2012). We implemented a model whereby participant's best self-paced performance was used to set time- and work-matched exercise bouts. The subsequent redistribution of work allowed us to assess the utility of even- (Chapters 5 & 6) and variable- (Chapter 5) pacing strategies, and the efficacy of the athlete's self-selected pacing strategy. Based on the findings from Chapters 5 and 6 of this thesis, we concluded that an even-pacing strategy is not optimal for performance in prolonged (~30-35 min) endurance cycling time-trials (Chapter 6). However, if the athlete's self-selected strategy is sub-optimal, a subsequent time- and work-matched even-paced bout can result in an attenuation of the metabolic and perceptual cost of exercise (Chapter 5). These findings have important implications for performance in athletic populations and for the implementation of exercise protocols in populations where exercise adherence and minimising the perceptual cost of an exercise bout is important.

Even-pacing is not an optimal strategy for endurance time-trials

In Chapter 6 an even distribution of work based on a previous best self-paced performance resulted in exercise intolerance in 9 out of 15 of the well-trained cyclists studied. This intolerance was associated with attainment of a relative exercise intensity that was in excess of maximal lactate steady state, as evidenced by an elevated and rising blood [lactate], indicative of exercise in the severe intensity domain (Tegtbur *et*

al., 1993; Burnley & Jones, 2007). These data demonstrate that this group of athletes were able to push themselves during a self-paced time-trial to achieve an average intensity for the bout that was above their maximum sustainable intensity for that duration of exercise. The subsequent imposition of an even-pace was "catastrophic", pushing these cyclists in to the severe exercise domain and accelerating the development of fatigue. We thus hypothesised that the self-selected pacing strategy adopted by these athletes was close to an optimal distribution of work that maximised the sustainable exercise intensity whilst ensuring a more complete expenditure of the anaerobic energy reserve. The key features of this strategy are presented in Figure 8.2, and discussed below.

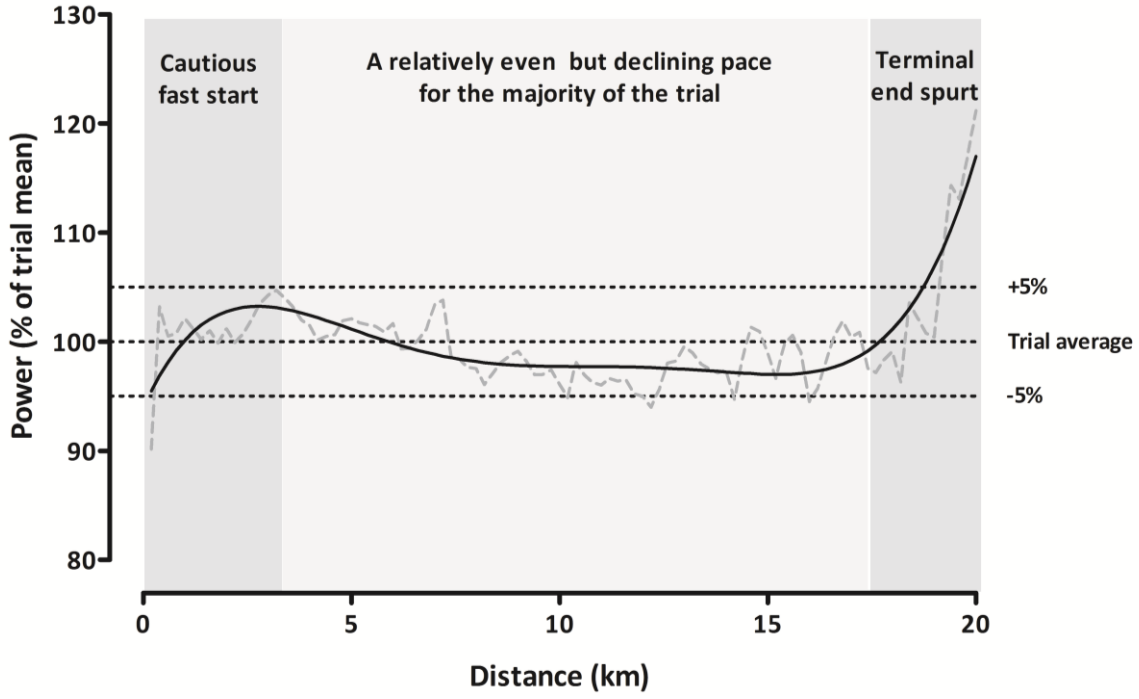


Figure 8-2. Self-selected pacing strategy of cyclists for whom matched even-pacing exercise resulted in "catastrophe" (dashed grey line, Chapter 6, n = 9) with a stylised overlay of the proposed optimum pacing strategy for endurance events (black line & text). A cautious fast start maximises the sustainable exercise intensity without inducing excessive homeostatic disturbance when the athlete is "fresh". The slow decay in pace in the middle of the race is inevitable as the fatiguing motor unit pool would require recruitment of higher threshold motor units to maintain the same intensity. The terminal end spurt accesses the protected motor unit reserve in order to fully utilise the available finite anaerobic energy as the endpoint of the race approaches.

A fast start and relatively even but declining pace

In Chapter 6, the cyclists studied adopted a moderate fast start, with the first 4 km completed at 102 ± 2% of mean PO (Figure 8-2). The optimum starting strategy is a

balancing act; too slow a start can result in a requirement for an unsustainable high power output later in the trial to make up time (Fukuba & Whipp, 1999) whilst overly fast starts produce large homeostatic disturbances and result in premature fatigue (Mattern *et al.*, 2001; Ham & Knez, 2009). Significantly in the context of the current data, a more cautious fast start (< 5% above the mean speed) produces the best 5 km run performance (Gosztyla *et al.*, 2006) and this type of start was observed in these cyclists. For the majority of the exercise bout thereafter there was a relatively even, but progressively declining power output (Figure 8-2). The average deviation from an even pace was ± 3%, and didn't exceed ± 5% until the terminal end spurt (Figure 8-2). The maintenance of PO within narrow limits is a common feature of pacing in elite athletes (Wilberg & Pratt, 1988; Palmer *et al.*, 1994; Padilla *et al.*, 2000a; Padilla *et al.*, 2000b), and more experienced athletes are better able to achieve and maintain an even-pace compared to novice athletes (Green *et al.*, 2010). Maintaining a close to even-pace would theoretically permit the athlete to optimise performance by maximising the sustainable speed within physiological limits (Burnley & Jones, 2007) and minimising potential energy losses through inefficient accelerations and decelerations (Atkinson *et al.*, 2007c). These data support the premise that a more even-pace might be beneficial compared to a less even-pace (Ham & Knez, 2009), but that the ability to vary pace within narrow limits is important.

The slow decay in power output during the middle portion of a time-trial is a common feature of self-pacing. Indeed in almost every trial in this thesis where power output was free to vary, we observed a progressively declining power output in the middle portion of the race, regardless of the starting strategy. This was observed even in those trials where participants were instructed to try and maintain as close to an even-pace as possible (Chapter 6, Figure 6-7). It would seem from these data that this progressive slow-down is unavoidable even when the early exercise pace is somewhat moderated. This characteristic of self-pacing might be explained by recent studies assessing the kinetics of peripheral and central fatigue. These studies show the majority of peripheral fatigue occurs in the first half of an exercise bout, with an increasing contribution of central mechanisms later in the exercise (Decorte *et al.*, 2012; Froyd *et al.*, 2013). The progressive reduction in exercise intensity during the middle portion of the bout could be attributed to a decrease in the responsiveness of the fatigued motor unit pool to an equivalent efferent central command, which in turn is subject to progressive central

fatigue. Previous research has demonstrated that when exercise is sustained at a constant intensity, central drive is forced to progressively increase to counteract this reduction in muscle contractility and force output that occurs with fatigue (Shinohara & Moritani, 1992; Saunders *et al.*, 2000; St Clair Gibson *et al.*, 2001a). During self-paced exercise however, central drive is relatively consistent (Duc *et al.*, 2004; Bini *et al.*, 2008; Amann *et al.*, 2009; Stone *et al.*, 2012). In order to counteract the mid-race decline in power output due to fatigue the athlete would have to increase central drive, which in turn would likely result in the recruitment of larger, higher threshold motor units, and thus would exacerbate the homeostatic disturbance and the likelihood of premature fatigue (de Koning *et al.*, 2011). Rather than risk this occurrence, athletes simply slow down to manage the symptoms of fatigue to a tolerable level and ensure exercise intensity remains below the threshold of the severe domain. Evidence for this can be observed in the blood [lactate] response to self-paced exercise in the group of cyclists for whom even-pacing was "catastrophic". During self-paced exercise these cyclists maintained an elevated and relatively stable blood [lactate] despite a declining power output for the majority of the exercise bout, until the terminal end spurt (Chapter 6, Figure 6-4). When forced to cycle at the same mean intensity but at an even-pace, blood [lactate] rose continuously until volitional exhaustion occurred before these athletes were able to achieve the even-pacing task.

Considering these data, it might be more appropriate to consider how an even distribution of effort might optimise performance, rather than an even distribution of work. The sense of effort required to maintain or increase exercise intensity is thought to be mediated by a centrally generated "copy" of the efferent command to the motor cortex (Enoka & Stuart, 1992; Bigland-Ritchie *et al.*, 1995). As described above, this increases with fatigue as a result of a concurrent requirement for an increased neural drive to compensate for contractile failure in the active motor units (Bigland-Ritchie *et al.*, 1995). An even distribution of effort would thus result in a varying distribution of work, as the fatiguing motor units become less responsive to the same command. This would result in the pacing strategy observed; a moderate, or cautious, fast start followed by a relatively even but declining power output. We hypothesise this is close to an optimal strategy that maximises performance whilst minimising the "hazard of catastrophic collapse" as per the model proposed by de Koning *et al*. (2011). This model proposes that changes in pace are informed by the magnitude of homeostatic

disturbance and amount of distance remaining, the product of which represents a "hazard of catastrophic collapse" or hazard score. We speculate that a cautious fast starting strategy might take advantage of the lower hazard scores (and consequent lower RPE) at the start of the trial when homeostatic disturbance to the peripheral physiological milieu is low. As previously discussed there exists a balancing act, as too fast a starting strategy can result in premature fatigue and sub-optimal performance (Mattern *et al.*, 2001). As the trial progresses, an even distribution of effort results in a slowly declining power output as exercise intensity is maintained close to what would be the maximum sustainable considering the fatiguing motor unit pool, and thus maintains homeostatic disturbance within acceptable levels (de Koning *et al.*, 2011). Alternatively, if athletes adopt an even distribution of work, the effort required would progressively increase during the trial as muscle contractility decreases. Considering the catastrophic responses to an imposed even-pace observed in Chapter 6, and the mid-race slowdown observed in all trials where power output was free to vary, we would suggest that this strategy would be sub-optimal.

A terminal end spurt

The end spurt is a common feature of self-paced exercise performance and was evident in all self-paced trials conducted in this thesis. The end spurt is thought to reflect the considered reserve the athlete maintains for the majority of the race. As the endpoint approaches and the risk of hazard or premature fatigue reduces the athlete is able to access this reserve to increase speed (de Koning *et al.*, 2011). It should be noted that maintenance of this reserve is a conscious decision, as recruitment of these higher threshold motor units during the middle portion of the trial would exacerbate the symptoms of fatigue and compel a disproportionate reduction in exercise intensity as a result. The magnitude of the end spurt might reflect the athletes attempt to maximise utilisation of the finite anaerobic energy reserve, or *W'*. A more complete utilisation of this might explain why the cyclists in Chapter 6 were able to attain an average exercise intensity that could not be sustained during constant-load exercise. However, as the magnitude of this end spurt was similar between these cyclists and those who could sustain time- and work-matched even-paced bouts (Chapters 5 & 6), it is likely that maintenance of a higher relative exercise intensity during the majority of the bout, and/or a better starting strategy were the main contributing factors to their better performance. Nonetheless, maximising use of the available anaerobic reserve can

improve self-paced exercise performance (Stone *et al.*, 2012) and the end spurt is the opportune time to optimise this as the negative consequences of increased homeostatic disturbance are of less importance (de Koning *et al.*, 2011). In most of the trials observed in this thesis, cyclists were travelling fastest as they crossed the line because of this terminal end spurt. A simple intervention that could potentially improve performance in trials of this nature would be to commence the end spurt earlier, in order to minimise what is essentially wasted kinetic energy as the athlete crosses the finish line (de Koning *et al.*, 1992).

Insights into sub-optimal pacing

In this thesis we also observed groups of cyclists for whom even-pacing resulted in either an attenuation of the metabolic and perceptual cost of exercise (Chapter 5) or no difference (Chapter 6) in comparison to self-paced exercise. Considering the metabolic and perceptual responses to these trials were consistent with a best effort, the pacing strategy adopted might explain their sub-optimal performance. Figure 8-3 displays these pacing strategies. In Chapter 5 the group of cyclists studied adopted an aggressive fast starting strategy (black line, 107 ± 3% of mean power output), and had greater variability in their pacing strategy (± 6% of mean PO). For these cyclists implementation of even-pacing resulted in a lower perceptual and metabolic cost. This suggests that imposing an even-pace on this group resulted in moving them closer to an optimal pacing strategy, and that by extension the observed fast starting strategy and greater variation in pace were components of a sub-optimal pacing strategy. For cyclists who started slowly (98 ± 2% of mean PO, grey line, Chapter 6) but had a relatively even-pace (± 3% of mean PO) for the majority of the trial imposing an even-pace had no impact on the metabolic or perceptual cost of the bout. These cyclists were however able to maintain a subsequent even-paced bout to exhaustion at the same average intensity for at least the same amount of time as their self-paced trial, which suggests their self-selected strategy was sub-optimal (Chapter 6). We speculate that these data provide further support for the proposed optimal pacing strategy, as too fast or too slow starts and greater variability characterise sub-optimal pacing. It should be reiterated however that the sub-optimal performance observed might not be due to pacing strategy *per se*, but rather could be due to a sub-optimal effort from the cyclists studied.

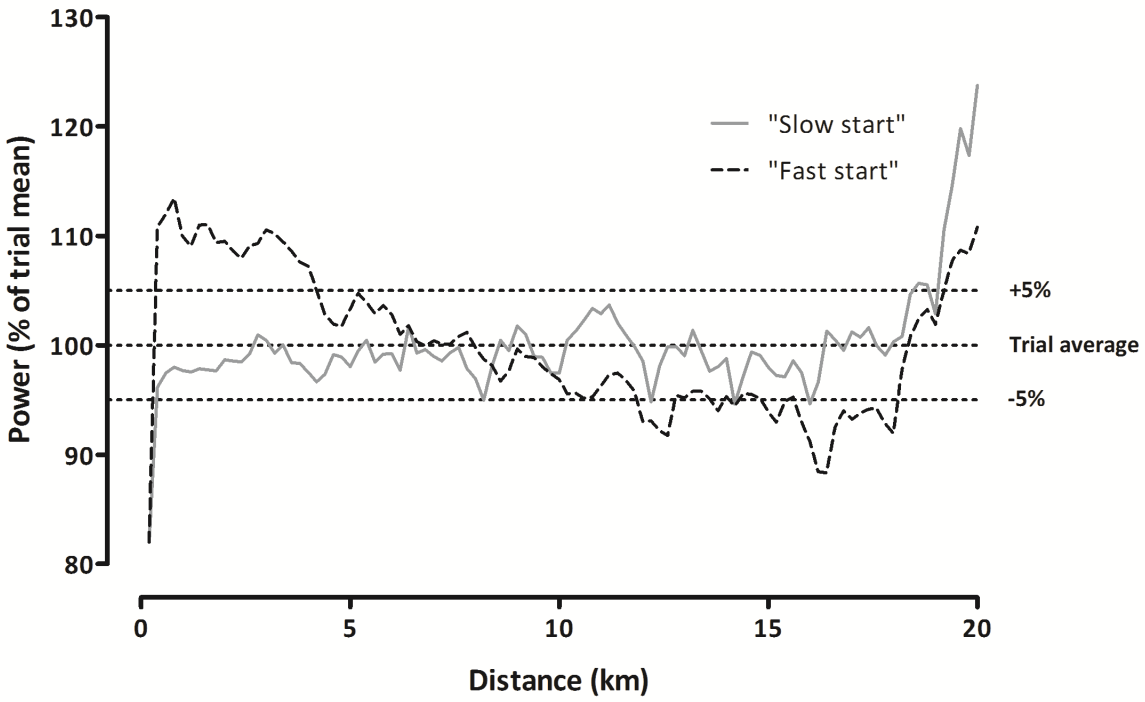


Figure 8-3. Self-selected pacing strategies for cyclists who successfully completed time- and work-matched even-paced bouts (dashed line, Chapter 5, n = 11. Grey line, Chapter 6, n = 6). We speculate that in these cyclists, self-selected pacing strategy was sub-optimal due to either too fast (dashed line) or two slow (grey line) starting strategies and too high a variability (dashed line).

8-2.3 Aetiology of fatigue during self-paced exercise

In Chapter 4 of this thesis we studied the pacing strategies adopted during 4, 20 and 40 km time-trials. There was evidence of a global pacing strategy that operated independent of the distance to be covered, but we also subjectively observed a trend for more variability between the shorter 4 km time-trial and the longer 20 and 40 km time-trials. Considering a 4 km time-trial is completed at an average exercise intensity in the severe or extreme exercise domain, and that 20 and 40 km time-trials are completed in the heavy domain, we speculated that there might be differences in the mechanisms of fatigue underpinning performance in these trials.

In Chapter 7 we tested this hypothesis and showed a duration and intensity dependent contribution of peripheral and central mechanisms to the observed fatigue in 4, 20 and 40 km time-trials. Specifically we observed a greater contribution of peripheral mechanisms of fatigue to a 4 km time-trial, and a greater contribution of central mechanisms of fatigue to 20 and 40 km time-trials. The greater contribution of central fatigue in longer time-trials was partly explained by an increased amount of supraspinal

fatigue, and a decrement in the responsiveness of the brain to muscle pathway at rest. This study is the first to elucidate the contribution of supraspinal mechanisms to fatigue during self-paced exercise. The magnitude of supraspinal fatigue observed was similar to that reported in previous studies adopting constant-load locomotor exercise (Sidhu *et al.*, 2009b; Goodall *et al.*, 2012a).

Task-dependency is a central theme in the study of neuromuscular fatigue (Barry & Enoka, 2007). Most previous research has sacrificed a degree of ecological validity for tighter experimental control, opting to study fatigue in single limb models. During whole body locomotor exercise, performance is constrained by systemic factors (e.g. cardiovascular and respiratory capacity, fluid, temperature and fuel regulation) that do not apply in single limb exercise (Taylor *et al.*, 2008). Despite these differences, the patterns of fatigue are broadly similar across single limb and whole body exercise studies. For example, during short-duration sustained maximum isometric contractions the predominant fatigue mechanism is peripheral, with central factors increasing as the exercise bout extends (< 60 s) (Bigland-Ritchie *et al.*, 1978; Bigland-Ritchie *et al.*, 1982; Kent-Braun, 1999; Schillings *et al.*, 2003; Schillings *et al.*, 2005). When contractions are submaximal (sustained or intermittent) the contribution of central mechanisms is substantially higher at lower intensities (< 30% MVC) and longer exercise durations compared to higher intensities (> 30% MVC) and shorter exercise durations where peripheral fatigue is substantial and central fatigue is modest or absent (Bigland-Ritchie *et al.*, 1986a; Sogaard *et al.*, 2006; Eichelberger & Bilodeau, 2007; Yoon *et al.*, 2007). These patterns of central and peripheral fatigue are also evident during locomotor exercise, where peripheral fatigue develops early (Decorte *et al.*, 2012) and reductions in voluntary activation manifest when the exercise bout is prolonged (Lepers *et al.*, 2002; Place *et al.*, 2004; Ross *et al.*, 2010a; Decorte *et al.*, 2012). Our data extend these findings to self-paced locomotor exercise as we observed a greater degree of peripheral fatigue in shorter (4 km) time-trials, and a greater degree of central fatigue in longer (20 and 40 km) time-trials. This similar pattern of fatigue development and universal applicability of the hyperbolic intensity-duration relationship across exercise tasks has been proposed to reflect a unitary process in the aetiology of neuromuscular fatigue (Bigland-Ritchie *et al.*, 1995).

The greater degree of peripheral fatigue observed in short (4 km) compared to long (20 and 40 km) self-paced time-trials is a novel finding. Previous research has demonstrated that peripheral fatigue during 5 km time-trials is regulated to an individual critical threshold and associated sensory tolerance limit that is never voluntarily exceeded (Amann *et al.*, 2006a; Amann *et al.*, 2006b; Amann *et al.*, 2007; Amann & Dempsey, 2008; Amann *et al.*, 2009; Amann *et al.*, 2010). These authors emphasised that this critical threshold might be specific to the exercise task being performed (Amann & Secher, 2010). Our data support this posit, as the degree of peripheral fatigue differs for shorter, higher intensity tasks compared to longer duration, lower intensity tasks. Based on these observations and other data (Burnley *et al.*, 2012) we suggest that the pattern of central and peripheral fatigue is dependent on the exercise domain in which the exercise is performed, and the duration of the exercise bout. These suggestions are discussed in detail below.

Burnley *et al*. (2012) studied the central and peripheral contributions to fatigue during intermittent submaximal isometric contractions at intensities above and below critical torque. In this investigation, the reduction in potentiated doublet torque was consistent across a range of intensities above critical power (exercise duration range 2.8 ± 0.3 to 17.6 ± 2.2 min, reduction in $Q_{tw.pot}$ range −32 ± 4 to −38 ± 6 N·m; data redrawn in Figure 8-4). The reduction in potentiated twitch at an exercise intensity 10% below critical power (exercise duration 57.1 ± 2.1 min) was less (−29 ± 4 N·m) than that observed at intensities above critical power, though this exercise was capped at 60 min and thus task failure only occurred in 1 of 9 participants (Burnley *et al.*, 2012). The contribution of central fatigue (reductions in peripheral voluntary activation) increased with exercise duration at intensities above critical power (−29 ± 6% vs. −6 ± 4% for exercise durations of ~18 and ~3 min respectively, Figure 8-4) and was substantial during ~60 min of exercise below critical power (−24 ± 10%).

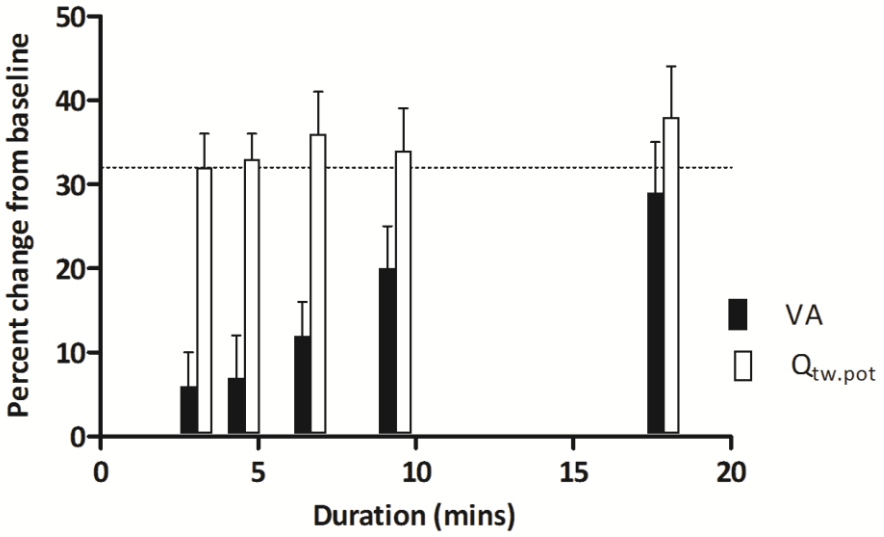


Figure 8-4. Reductions in voluntary activation and potentiated doublet twitch during intermittent isometric knee extensor exercise to exhaustion at various intensities above critical power. Peripheral fatigue was not different between exercise durations, but central fatigue increased with increasing duration. Data redrawn from Burnley *et al*. (2012).

Based on these data and our observations in Chapters 6 and 7, we hypothesise that the contribution of peripheral mechanisms is dependent on the exercise domain in which the exercise is completed. When exercise is completed at intensities above critical power, in the severe or extreme domain (e.g a 4 km time-trial), end-exercise peripheral fatigue is higher than that observed during trials conducted below critical power. We speculated that this might reflect the recruitment of higher threshold, more fatigable motor units to attain the higher power outputs observed, resulting in a more complete recruitment (and subsequent fatigue) of the available motor unit pool. At intensities below critical power, in the heavy domain (e.g. 20 and 40 km time-trials) the neuromuscular and metabolic responses are stabilised, but significant peripheral and central fatigue still occurs. The mechanisms underpinning the peripheral fatigue observed during exercise below critical power are likely to be different than those underpinning severe exercise. For example, significant peripheral fatigue occurs without the same level of disruption in muscle metabolites observed during severe intensity exercise, and could perhaps be due to substrate depletion and subsequent impacts on calcium handling (Chin & Allen, 1997; Helander *et al.*, 2002), though the exact mechanism is unknown (Burnley *et al.*, 2012).

With regards the degree of central fatigue, it would seem from our data and that of Burnley *et al*. (2012) that exercise duration is a determining factor. This conclusion is based on observations of substantial central fatigue at prolonged exercise durations above and below critical power that progressively decline as exercise duration shortens (Chapter 7 & Figure 8-4). The greater degree of central fatigue in longer duration exercise could be due to an increased potential for metabosensitive group III/IV afferents to provide inhibitory feedback to the CNS (Amann *et al.*, 2009) and/or because of repetitive activation of the motoneuron pathway. St Clair Gibson *et al*. (2006) postulated the existence of a time lag between the receipt and interpretation of afferent information by the CNS and the subsequent generation of efferent commands. In longer duration exercise there is greater potential for an "informed" CNS to regulate power output during exercise, as information from the periphery can be processed and acted upon. For shorter exercise durations, this time lag could create a situation where the CNS is naïve to the metabolic milieu of the motor units it is attempting to drive, and thus central fatigue would not be as pronounced. Whilst peripheral fatigue seems to be a closely regulated variable, this regulation might not always be centrally mediated (Burnley *et al.*, 2012). The original complex systems model of exercise regulation postulated the existence of regulatory systems existing in the periphery (Noakes *et al.*, 2004). We would suggest from these data that the regulation of exercise intensity is subject to both short-loop and long-loop feedback control. If the exercise duration is long, the potential for long-loop feedback and subsequent control of exercise is high, and thus central fatigue is more pronounced as inhibitory feedback from the periphery is more influential. If the exercise duration is short, the contribution of short-loop feedback, or perhaps a peripheral governor (MacIntosh & Shahi, 2011), limits exercise performance and central fatigue is thus lower. An alternative explanation for the observed central fatigue could simply reside in the repetitive activation of the motoneuron pathway. The longer the exercise duration, the more this pathway is subject to activation, and this repetitive discharge could reduce motoneuron excitability. The reduction in resting MEP observed after the longer time-trials in Chapter 7, the observations of increasing central drive during prolonged submaximal exercise (Shinohara & Moritani, 1992; Saunders *et al.*, 2000; St Clair Gibson *et al.*, 2001a) and the finding that changes to intrinsic motoneuron properties occur with reductions in MEP and CMEP (McNeil *et al.*, 2011b) provide some support for this proposed explanation.

8-3 Directions for future research

The data from this thesis has provided an insight into the optimal pacing strategy for endurance time-trial events. We propose the optimal pacing strategy requires an even distribution of effort that results in a parabolic distribution of work that maximises the sustainable intensity for a majority of the trial (Figure 8-2). The proposed components of this strategy include a moderate fast start, a relatively even pace throughout that varies within narrow limits but remains close to the maximum sustainable intensity, and a terminal end spurt that maximises expenditure of the finite anaerobic energy reserve. Each of these components warrants experimental study. Firstly, the influence of starting strategy during endurance time-trial events has been previously studied experimentally (Mattern *et al.*, 2001; Gosztyla *et al.*, 2006). Whilst the study of Mattern *et al*. (2001) used unrealistic slow and fast starting strategies that were ± 15% above mean power, the limited available evidence does suggest a cautious fast start strategy (< 5% above mean power) might be optimal (Gosztyla *et al.*, 2006) and this posit warrants further experimental investigation. Secondly, our data clearly show that an unvarying even-pace is not an optimal pacing strategy, but that maintaining a close to even-pace for the majority of the trial is important. Further study could assess the impact of this relative to a more accurate measurement of an athlete's maximum sustainable exercise intensity, and how this intensity might alter during the exercise bout due to fatigue of the active motoneuron pool. Finally a more complete expenditure of the available anaerobic energy reserve can result in improved performance during self-paced exercise (Stone *et al.*, 2012). A simple but as yet unstudied intervention could be to instruct an athlete to begin their end spurt earlier and thus minimise the kinetic energy wasted as the athlete crosses the finish line (de Koning *et al.*, 1992). Collectively or in isolation, experimental study of these proposals might result in improved time-trial exercise performance.

Distinguishing between the sense of effort required to complete a task and the perception of exertion experienced during exercise is an area that warrants research. The sense of effort is the conscious awareness of the central motor command to the active muscles (Morree *et al.*, 2012). The perception of exertion was originally conceived to represent both the sense of effort and the physical sensations experienced during exercise (Borg, 1982b), but more recently it has been suggested that this scale should be used to isolate and measure the afferent component of this definition (Smirmaul, 2012; Swart *et al.*, 2012). The relative contribution of efferent and afferent components to the

regulation of exercise intensity is the subject of debate (St Clair Gibson & Noakes, 2004; Marcora, 2009; Smirmaul *et al.*, 2010; Smirmaul, 2012; Swart *et al.*, 2012); delineating these concepts might help to improve understanding of this. A recent study by Swart *et al*. (2012) successfully used a novel "Task Effort Awareness" (TEA) scale to successfully distinguish between the physical sensations of exercise and the psychological/psychic effort required to maintain exercise intensity. In this study, the TEA score increased in parallel with RPE during prolonged constant load exercise, but reached maximal values during intermittent periods of all-out sprinting independent of the RPE score (Swart *et al.*, 2012). This novel scale has yet to be studied in relation to self-paced exercise. We hypothesised that during self-paced exercise an even distribution of effort might be an optimal perceptual strategy to optimise performance. If this hypothesis is correct we would expect to see a relatively consistent TEA score throughout self-paced exercise, a rising perception of exertion to reflect an increased homeostatic disturbance, and a slowly decaying power output reflecting fatigue of the locomotor muscles responsible for the task. Studying the interactive effects of the sense of effort and the perception of exertion in the regulation of exercise, and in the decision to terminate exercise or reduce intensity, could be a worthwhile area for future research (Smirmaul, 2012).

The use of motor cortical and peripheral nerve methods of stimulation in concert in Chapter 7 of this thesis allowed a more complete assessment of the contribution of central and peripheral mechanisms of fatigue. These methods are being increasingly employed to assess fatigue during locomotor exercise (Ross *et al.*, 2007; Sidhu *et al.*, 2009b; Goodall *et al.*, 2012a). These studies demonstrate the potential for these methods to provide a better understanding of fatigue during locomotor exercise, and Chapter 7 of this thesis extends this potential to the study of fatigue during self-paced exercise. Understanding the biological basis of self-pacing has been proposed as the most important challenge facing scientists who study exercise performance (Noakes, 2011b); the methods employed in this thesis could be used to further this understanding.

The study of fatigue with specific reference to the critical power concept might provide a unifying framework to better understand fatigue across a range of exercise tasks. Human endurance capacity changes similarly with the type or intensity of the exercise task. Bigland-Ritchie *et al*. (1995) were the first to theorise that this might reflect a

unitary process in the aetiology of neuromuscular fatigue. The available evidence supports this posit as the contribution of peripheral and central mechanisms of fatigue follows a similar pattern in sub-maximal and maximal single limb exercise (Bigland-Ritchie *et al.*, 1986a; Kent-Braun, 1999; Schillings *et al.*, 2003; Sogaard *et al.*, 2006; Eichelberger & Bilodeau, 2007; Yoon *et al.*, 2007; Froyd *et al.*, 2013) and whole body locomotor exercise (Sidhu *et al.*, 2009b; Ross *et al.*, 2010a; Decorte *et al.*, 2012). Burnley *et al*. (2012) demonstrated that the critical torque represents a distinct threshold for the rate of peripheral fatigue development. These authors also showed that central fatigue changes depending on the intensity and subsequent duration of the exercise task. At intensities close to critical power both central and peripheral fatigue are substantial. As the intensity of exercise increases above critical power, and consequently duration decreases, the contribution of peripheral fatigue is consistent but the contribution of central fatigue progressively decreases (Burnley *et al.*, 2012). It is likely that this pattern of fatigue development is consistent across exercise tasks if studied relative to the critical, or maximum sustainable, exercise intensity for that task. Further research is warranted to test this posit.

The extent of neuromuscular fatigue induced by exercise is typically quantified by comparing responses elicited from the muscle group of interest in the "fresh" state pre-exercise with those elicited in the "fatigued" state post-exercise (Chapter 7). Two recent studies have highlighted the potential to study the kinetics of fatigue development during exercise (Decorte *et al.*, 2012; Froyd *et al.*, 2013). Decorte *et al*. (2012) examined fatigue during the recovery periods of a constant-load intermittent cycling task consisting of repeated 6 min bouts until task failure. Froyd *et al*. (2013) assessed fatigue after every 20% of a self-paced isokinetic knee extension/flexion task. Despite differences in exercise task (cycling vs. single limb flexion/extension) and the duration of exercise (28 ± 8 min vs. 6 ± 2 min) both of these studies demonstrated that the majority of peripheral fatigue was manifest within the first 50% of the exercise bout. Decorte *et al*. (2012) also demonstrated that reductions in VA were not evident until late in the exercise bout. Recent studies have also successfully applied TMS techniques without interruption during locomotor exercise to demonstrate increases in intra-cortical inhibition (Sidhu *et al.*, 2013b), and no change in corticospinal excitability (Sidhu *et al.*, 2012a; Sidhu *et al.*, 2012b). Further research on the kinetics of fatigue development during exercise is warranted, including the study of different exercise modes and the use

of techniques in combination to better understand the contribution of central and supraspinal mechanisms.

It is important to note the TMS evoked measures used in Chapter 7 of this thesis do not allow the determination of spinal sites of fatigue. The changes observed in MEP size, for example, could be due to changes in the excitability of corticospinal cells, but also by the excitability of the spinal motonuerones onto which they project (Morita *et al.*, 2000). The use of stimulation methods at the cervicomedullary junction can exclude changes in cortical excitability. The resulting cervicomedullary motor evoked potential (CMEP) is largely conducted by the large diameter axons of the corticospinal tract (McNeil *et al.*, 2013), and provides a measure of motoneuron excitability independent of the excitability of corticospinal cells (Taylor, 2006). This technique is not without limitation. Stimulation at the cervicomedullary junction can be prohibitively painful, and recording a valid CMEP is difficult in some motoneuron pools (McNeil *et al.*, 2013). Most assessments of CMEP size have been evoked from the upper limb, where proximal muscles are more easily activated than distal muscles (Taylor, 2006). Lower limb muscles have been less studied. Consistent responses have been evoked in more excitable lower limb muscles (tibialis anterior and extensor digitorum brevis), but these require high levels of electrical stimulation (Ugawa *et al.*, 1995). Currently the use of this method to study the motoneuron excitability of the knee extensor muscles is limited to a single study (Sidhu *et al.*, 2012b) with a small sample (n = 5). Nonetheless this study reveals there is potential to use this method in concert with motor cortical stimulation to further localise the site of changes in motoneuron excitability.

APPENDICES

Appendix 1 – Examples of participant information & informed consent forms

PARTICIPANT INFORMATION.

TITLE OF PROJECT: The aetiology of fatigue during time-trial cycling exercise of varying durations

Participant ID Number:

Principal Investigator: Kevin Thomas T: 0191 227 4863 M: 07743 068791 Email: kevin2.thomas@northumbria.ac.uk
Research team: Dr Les Ansley (les.ansley@northumbria.ac.uk) Dr Stuart Goodall (stuart.goodall@northumbria.ac.uk)

INFORMATION TO POTENTIAL PARTICIPANTS

1. What is the purpose of the project?
The study of what causes fatigue has been at the forefront of research in sport science. With advanced experimental techniques we can determine whether fatigue is related to central factors – e.g. due to the brain or central nervous system limiting exercise output, or whether fatigue is caused by peripheral factors – e.g. the muscle not responding to signals from the brain to exercise. Relatively little is known about the cause of fatigue during self-paced cycling exercise of different durations. The purpose of this study is to find out whether the cause of fatigue is different during different length cycling time-trials.

2. Why have I been selected to take part?
You have been selected to take part as you are a well-trained male cyclist aged 20-45 in regular training and competition in cycling time-trials, and there are no medical reasons why you should not take part in the study.

3. What will I have to do?
You will have to attend five separate testing sessions at our sport science laboratories at Northumbria University. The testing sessions will be scheduled at your convenience but must be separated by a minimum of 2 & a maximum of 7 days. Each visit will last between 2-3 hours.

Visit 1 –Practice trial
On the first visit you will complete a practice time-trial where you will be required to complete a self-paced time-trial lasting approx. 30 mins in duration. The purpose of this visit is to allow you to practice completing an indoor time-trial and give you a chance to practice the experimental techniques to be used on the remaining visits (see 'Measurements' section for details).

Visits 2, 3, 4 & 5 – Experimental trials
During these visits you will complete an incremental assessment to measure maximum oxygen uptake and time-trials of either 4-km, or 20-km or 40-km in length on a stationary cycle ergometer. In the time-trials you will be required to complete the distance as fast as possible. During the incremental assessment to measure maximum oxygen uptake you will be required to cycle to exhaustion whilst the exercise intensity increases every 60 s. The order of these trials is decided randomly. The measurements taken during these trials are described below.

Measurements
During all trials you will wear a rubber face mask connected by thin tubing to a machine that will analyse your expired air, and capillary blood samples will be taken from the fingertip to measure blood lactate concentration. This procedure samples a very small amount of blood & causes mild discomfort. You will also wear a heart rate monitor to record heart rate, and will be asked to rate your perception of effort and affective response (very bad to very good) at regular intervals. During the trials we will also be measuring the electrical activity of your quadriceps, hamstrings and calf muscles, which will require the application of small adhesive electrodes to your skin. We will have to clean, shave and abrade the area of application to

remove any dead skin and sweat.

Before and after each bout of exercise we will measure the degree of central and peripheral fatigue using transcranial magnetic stimulation (TMS), and electrical stimulation of the femoral nerve. During these measures you will sit in a chair and your leg will be attached at the ankle to a non-compliant strap which will measure the force output of your quadriceps. Detail on each procedure is below:

TMS
To assess the brain to muscle pathway, a single pulse magnetic stimuli will be delivered through a coil placed on top of your head at rest, and whilst you perform quadriceps contractions of varying intensities up to your maximum. This will be assessed both pre- and post-exercise and will allow us to assess the degree of central fatigue in response to the exercise bout.

Electrical stimulation
To assess quadriceps muscle function, an electrical stimulus will be administered to your femoral nerve at rest and while you contract your quadriceps. Small adhesive pads will be placed over your femoral nerve in the upper groin area, and over the fleshy part of your hip. This will again be assessed both pre- and post-time-trial exercise and will allow us to assess the degree of peripheral fatigue in response to the exercise bout.

Each trial requires you to give a best effort, and leading up to the tests you will be asked to refrain from strenuous exercise for 48 hours, alcohol for 24 hours, caffeine for 12 hours and food for 2 hours. You will also be asked to record your nutrition in the 24 hours leading up to the first test, and you will have to replicate this before each visit. If you are uncomfortable during the testing with any of these procedures, please inform the researcher immediately.

4. What are the exclusion criteria (i.e. are there any reasons why I should not take part)?
You should not take part if you do not meet the inclusion criteria in box 2 or if you have any kind of injury or medical reason that precludes high intensity exercise. With regards the TMS assessment, you should not take part in the study if you have any intracranial plates, internal electrical regulators or neurological disorders including a history of epilepsy and seizures

5. Will my participation involve any physical discomfort?
Exercise tests
There are foreseeable discomforts during the exercise tests, including temporary fatigue and shortness of breath. These sensations should resolve within minutes after the test is done, and you should be familiar with these sensations as a result of your regular training and competition schedule.

Stimulation
There may be some discomfort during electrical stimulation of the femoral nerve, including muscle spasm and muscle tightening. Single pulse stimuli will be delivered, which are more tolerable than other electrical stimulation techniques (paired and repetitive stimulation). The first electrode will be positioned in the upper groin area and the second will be placed on the fleshy part of your hip.

There is an initial unusual sensation to TMS; however, the procedure does not cause pain. The probability of discomfort with TMS is very low. An infrequent, harmless, but uncomfortable effect is a mild headache, which is probably caused by the activation of scalp and neck muscles. The headache may persist after the end of the stimulation session. In some cases, you may experience feelings of elevated mood as a consequence of TMS. There is a slight risk of fainting, however the investigator will be vigilant when monitoring you during the test and will take appropriate action if you are showing signs or symptoms of fainting. You might experience temporary hearing changing from the noise generated by the TMS pulses. This will subside within a few hours of leaving the laboratory.

Blood sampling
Fingerprick blood sampling results in mild discomfort and a small amount of localised

bruising.

6. Will my participation involve any psychological discomfort or embarrassment?
No

7. Will I have to provide any bodily samples (i.e. blood, saliva)?
Yes, capillary blood via a fingerprick sample for the determination of blood lactate concentration

8. How will confidentiality be assured?
The research team has put into place a number of procedures to protect the confidentiality of participants. You will be allocated a participant code that will always be used to identify any data that you provide. Your name or other personal details will not be associated with your data, for example the consent form that you sign will be kept separate from your data. Only the research team will have access to any identifiable information; paper records will be stored in a locked filing cabinet and electronic information will be stored on a password-protected computer. This will be kept separate from any data and will be treated in accordance with the Data Protection Act.

9. Who will have access to the information that I provide?
Any information and data gathered during this research study will only be available to the research team identified in the information sheet. Should the research be presented or published in any form, then that information will be generalized (i.e. your personal information or data will not be identifiable).

10. How will my information be stored / used in the future?
All information and data gathered during this research will be stored in line with the Data Protection Act and will be destroyed 3 years following the conclusion of the study. During that time the data may be used by members of the research team only for purposes appropriate to the research question, but at no point will your personal information or data be revealed. Insurance companies and employers will not be given any individual's information, samples, or test results, and nor will we allow access to the police, security services, social services, relatives or lawyers, unless forced to do so by the courts.

11. Has this investigation received appropriate ethical clearance?
Yes, the study and its protocol has received full ethical approval from the School of Life Sciences Ethics Committee.

12. Will I receive any financial rewards / travel expenses for taking part?
No.

13. How can I withdraw from the project?
The research you will take part in will be most valuable if few people withdraw from it, so please discuss any concerns you might have with the investigators. During the study itself, if you do decide that you do not wish to take any further part then please inform one of the research team as soon as possible, and they will facilitate your withdrawal and discuss with you how you would like your data to be treated in the future. After you have completed the research you can still withdraw your data by contacting one of the research team (their contact details are provided above), give them your participant number or if you have lost this give, them your name.

INFORMED CONSENT FORM

Project Title: The aetiology of fatigue during time trial cycling exercise of varying durations

Principal Investigator: Kevin Thomas

Participant Number: _____

	please tick where applicable
I have read and understood the Participant Information Sheet.	☐
I have had an opportunity to ask questions and discuss this study and I have received satisfactory answers.	☐
I understand I am free to withdraw from the study at any time, without having to give a reason for withdrawing, and without prejudice.	☐
I agree to take part in this study.	☐
I would like to receive feedback on the overall results of the study at the email address given below. Email address……	☐

Signature of participant…… Date……

(NAME IN BLOCK LETTERS)……

Signature of Parent / Guardian in the case of a minor

……

Signature of researcher…… Date……

(NAME IN BLOCK LETTERS)……

FOR USE WHEN TISSUE IS BEING REMOVED BUT NOT STORED

Project Title: The aetiology of fatigue during time-trial cycling exercise of varying durations

Principal Investigator: Kevin Thomas

Participant Number: _____

I agree that the following tissue or other bodily material may be taken and used for the study:

Tissue/Bodily material	Purpose	Removal Method
Capillary blood	Measurement of blood lactate concentration	Fingertip puncture

I understand that if the material is required for use in any other way than that explained to me, then my consent to this will be specifically sought. I understand that I will not receive specific feedback from any assessment conducted on my samples, but should any kind of abnormality be discovered then the investigator will contact me.

Signature of participant..... Date.....……..

Signature of Parent / Guardian in the case of a minor

..... Date.....……..

Signature of researcher..... Date.....……..

Participant Screening

Telephone / Personal Interview / Eligibility Checklist

Name _____Phone number: _____Date_____

How old are you? (18 to 40) _____ Weight _____ Height _____

If you answer yes to any of the following questions you are not eligible to take part in the study.

Do you have pain in your arms and your hands?

Have you ever been diagnosed with a neurological disorder?

Have you ever been diagnosed with a brain disorder such as Parkinson's disease?

Have you ever had a stroke?

Do you have any metal objects in your head?

Are you taking any medications that you know would affect neuronal conduction?

Do you have a pacemaker?

Have you had any operations involving your heart?

Do you have a metal plate in the skull, metal objects in the eye or skull (for example after brain surgery or shrapnel wounds)?

Do you know of any reason you should not exercise?

Are you recovering from an illness, injury or operation?

When you perform physical activity, do you feel a pain in your chest?

When not performing physical activity, have you recently suffered chest pain?

Do you ever lose consciousness or lose your balance due to dizziness?

Do you have bone or joint problems that may be made worse with physical activity?

Have you had to suspend your training in the last 2 weeks due to injury or illness?

Do you suffer from any muscle or joint injury that could affect your ability to exercise?

Do you have any history of stroke, epilepsy, head trauma or migrane?

The information I have given is correct to the best of my knowledge at the time of completion.

Signature of Participant.....Date.....

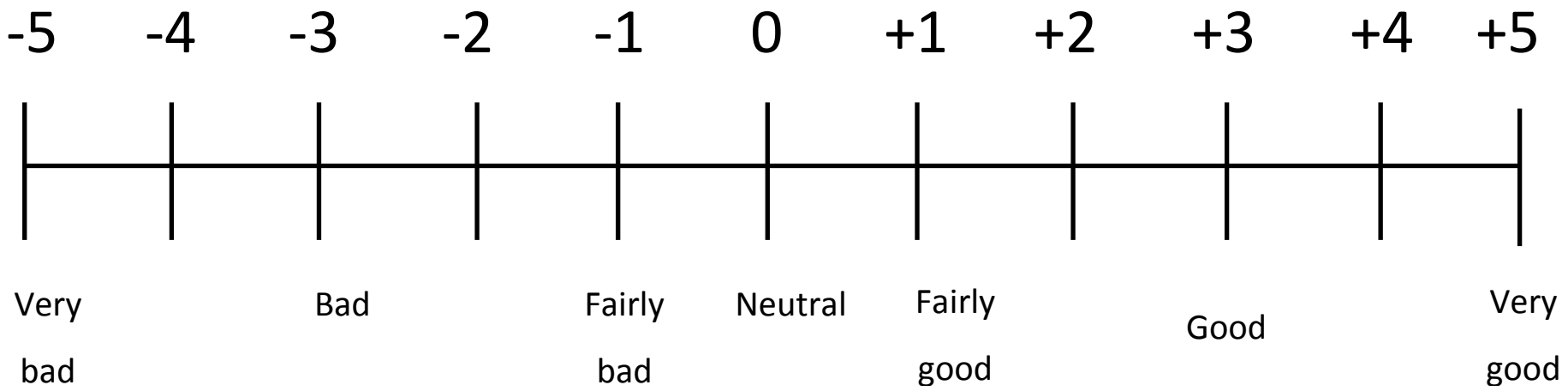
Appendix 2 – Rating of Perceived Exertion Scale

Rating of perceived exertion

6	
7	Very, very light
8	
9	Very light
10	
11	Fairly light
12	
13	Somewhat hard
14	
15	Hard
16	
17	Very hard
18	
19	Very very hard
20	Maximum

Appendix 3 – Affect scale

Affect scale



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