THE EFFECT OF EXERCISE PRIMING ON $\dot{V}O_2$ KINETICS, MUSCLE TORQUE COMPLEXITY AND EXERCISE TOLERANCE DURING INTERMITTENT ISOMETRIC CONTRACTIONS.

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Abstract

Exercise priming can alter $\dot{V}O_2$ kinetics and improve the performance of subsequent exhaustive heavy exercise. During fatiguing isometric exercise there is a reduction in the complexity of muscle torque output, which correlates with metabolic changes observed in the same exercise domain. This study aims to investigate the effect of exercise priming on $\dot{V}O_2$ kinetics, muscle torque complexity and exercise tolerance during intermittent isometric exercise.

Five males and five females (25 ± 6 years, 171.4 ± 9.3 cm, 69.2 ± 12.0 kg) completed three experimental trials in a randomised order. The trials consisted of a six-minute priming exercise bout or rest period, followed by 20 minutes of rest, before completing a second exhaustive exercise bout. Participants performed intermittent isometric contractions of the knee extensors at 40% maximal voluntary contraction (MVC) with a duty cycle of 0.6. Participants' rate of perceived exertion (RPE) and muscle oxygen consumption were measured at regular intervals throughout the exercise.

There was no difference in the time to task failure between primed and non-primed exercise. There was a higher EMG amplitude at the start of the primed exhaustive bout compared to the non-primed exercise bout. The $\dot{V}O_2$ response to exhaustive exercise was not different between the primed and non-primed conditions. Peripheral fatigue was present at the onset of exercise following priming and a significant loss of muscle torque complexity with priming.

There was no improvement in performance of subsequent intermittent isometric contractions with prior exercise, nor was there change in the $\dot{V}O_2$ response. Loss of complexity could be attributed to the increase in arEMG at the onset of the exhaustive exercise, more specifically an increase in motor unit recruitment with the development of fatigue. These results suggest that there is some effect of high-intensity prior exercise on exhaustive isometric contractions of the knee extensors.

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Abbreviations

Ag/AgCl	Silver Chloride electrode
ANOVA	Analysis of variance
ApEn	Approximate Entropy
arEMG	Average rectified electromyography
ATP	Adenosine Triphosphate
CI	Confidence Interval
cm	Centimetre
CP	Critical power
CT	Critical torque
CV	Coefficient of variance
DFA (-α)	Detrended Fluctuation Analysis (exponent)
ECG	Electrocardiogram
EEG	Electroencephalogram
EMG	Electromyography
H^+	Hydrogen ion
Hb	Haemoglobin
HHb	Deoxygenated haemoglobin
Hz	Hertz
iEMG	Integrated electromyography
kg	Kilogram
LT	Lactate Threshold
M-wave	Compound muscle action potential
mA	Milliamp
min	Minute
mL/kg/min	Millilitres per kilogram per minute
mL/min	Millilitres per minute
mm	Millimetre
mmHg	Millimetre of mercury

MPF	Mean power frequency
MRT	Mean response time
ms	Millisecond
mV	Millivolt
MVC	Maximal voluntary contraction
$m\dot{V}O_2$	Mean oxygen uptake
N	Newton
NIRS	Near-infrared spectrometry
Nm	Newton metre
O_2	Oxygen
P	Significance level
PA	Primary amplitude
PCr	Phosphocreatine
pH	Logarithmic scale used to express acidity and alkalinity of solutions
$p\dot{V}O_2$	Pulmonary oxygen uptake
R-R intervals	Electrocardiographic cardiac interval
RPE	Rate of perceived exertion
s	Second
SampEn	Sample Entropy
SD	Standard deviation
sEMG	Surface electromyography
SR	Stochastic resonance
V	Volts
VA	Voluntary Activation
VCO_2	Carbon dioxide removal
$\dot{V}O_2$	Oxygen uptake
$\dot{V}O_{2max}$	Maximal oxygen uptake
$\dot{V}O_{2peak}$	Peak oxygen uptake
W	Watts
µm	Micrometre

σ	Standard Deviation

Chapter 1 – Introduction

1.1: Warm-up

A warm-up is now a widely recognised component of sport and exercise/activity and is used by coaches and individuals during recreational activity, training and sporting competition. A general warm-up is carried out prior to a main exercise event and is performed with the intention of preparing the body and muscles for the upcoming exercise. Warm-ups are now a common practice implemented to prevent injuries (Woods et al., 2007) and improve performance. However, there is not one warm-up protocol set out to be followed preceding a main exercise event (Bishop, 2003). Much research has gone into warm-up procedures, investigating the optimal type, duration and intensity of exercise to elicit the desired effects on human physiology and subsequent effects on performance.

A warm-up protocol can include an active component. Studies investigating the effects of warm-up on performance and coaches implementing a warm-up protocol have a vast range of options regarding the modality of the exercise. This is often specific to the sport or type of exercise being performed in the main event (Bishop, 2003). Research has focussed mostly on activities such running (Buchheit et al., 2009; Grodjinovsky and Magel, 1970), cycling and swimming (de Vries, 1959; Neiva et al., 2013), as well as team sports such as football (Zois et al., 2011) and have shown it to enhance exercise performance (Grodjinovsky and Magel, 1970; Thompson, 1958).

The exercise performed as part of an active warm up can be adapted to the demands of the individual or team and may depend on the sporting environment. The nature of the exercise can range from intermittent exercise performed with short rest periods between bouts, to continuous exercise with which there is no rest throughout. The rest periods during warm-up exercise and the recovery duration following the protocol can also be altered to suit the nature of the main exercise period or the abilities of the individual/group (Bishop, 2003). As well as the nature and modality of warm-up exercise, the intensity at which the athletes work must also be considered and can differ depending on the aforementioned factors and also the view of the coaches themselves. An inverse relationship has been observed between warm-up intensity and performance during subsequent high-intensity exercise (Sargeant and Dolan, 1987). Warm-ups at low intensities have also shown to have no benefit to performance (de Vries, 1959) and so it appears that a general active warm-up of a moderate intensity may be optimal for performance (Bishop et al, 2003b). The duration of a warm-up would depend

upon its nature, intensity and the subsequent recovery duration as it is important to increase muscle temperature during this period but also cause minimal fatigue (Bishop, 2003b)

Alongside an active exercise component, a warm-up can also include dynamic and static stretching, with static-stretching exercises being the more traditional component. More recent evidence suggests that dynamic stretching alone as a warm-up leads to a relative enhancement in performance, whereas static stretching has no greater effect on performance than no stretching at all (McMillian et al., 2006), may not prevent injury (Herbert, 2002; Pope et al., 2000) and can even degrade performance (Behm et al., 2004).

Not all warm-up protocols involve an active or exercise component. A warm-up can also be passive, focusing on raising core and muscle temperature through external means, such as hot showers/baths, saunas and heating pads (Bishop, 2003). This type of warm-up has been shown to be more beneficial than no warm-up at all on physical performance if there is enough increase in body temperature (Asmussen and Boje, 1945; Carlile, 1956). Passive warm-ups, as they do not involve prior activity, are particularly useful when investigating whether specific effects on sporting performance thought to be caused by warming-up are due to an increase in core and muscle temperature alone, or whether the benefits to performance are due to other elements of a warm-up only delivered through exercising the muscles. A passive warm-up does not require any physical work; therefore, it may reduce the risk of depleting energy substrates before the subsequent main activity, and so reduce the likelihood that this next exercise bout would be impaired in any way (Shellock and Prentice, 1985). For this reason, it is also less likely that the warm-up itself will cause any injury to the athletes.

The mechanistic basis of warm-up exercise/exercise priming

Exercise priming refers to a bout of exercise performed before the main exercise event, often more generally referred to as ‘warm-up’ exercise. Scientific studies have provided support for the use of warm-ups by coaches and athletes, demonstrating their ability to enhance muscle temperature and stimulate muscular contractions (Shellock and Prentice, 1985). Typical active warm-up exercises such as cycling, jogging and skipping (Shellock, 1983) can raise muscle and core temperature (Shellock and Prentice, 1985). Unlike passive warm-ups, active warm-ups are likely to induce metabolic and cardiovascular changes as-well as raising body temperature (O’Brien et al, 1997), priming the body for subsequent exercise. Specifically, the

exercise-induced increase in muscle temperature can aid subsequent movement dynamics by causing a decrease in the stiffness of muscles and joints and increasing joint range of motion (Wright and Johns, 1961) and can also increase muscle energetics through increased rates of glycolysis and high-energy phosphate degradation (Edwards et al., 1972; Febbraio et al., 1996), enabling greater energy availability during the subsequent main exercise event and better performance. Active warm-ups increase the delivery of oxygen to the working muscles (McCutcheon et al., 1999). The vasodilatation of the blood vessels and increase in heart rate as a result of the warm-up activity allow greater blood flow around the body and to the working muscles, enhancing the supply of oxygen that can be used for subsequent exercise (Bishop, 2003).

1.2: $\dot{V}O_2$ Kinetics

The Chambers English Dictionary describes kinetics as the science of the action of force in producing or changing motion, highlighting the relationship between work input and output. The definition of kinetics in the case of the present study is borrowed from the relationship to enzyme kinetics as opposed to free body physics. With the transient (during exercise) oxygen uptake known as $\dot{V}O_2$, the term $\dot{V}O_2$ kinetics refers to the physical mechanisms responsible for the dynamic $\dot{V}O_2$ response to exercise and subsequent recovery. Resting $\dot{V}O_2$ is typically around 400 mL/min in a human standing up, depending on body mass. However, during exhaustive exercise ($\dot{V}O_2$max), $\dot{V}O_2$ of male extreme endurance athletes such as crosscountry skiers can have an upper limit of close to 90 mL/kg/min (Jones and Poole, 2005).

$\dot{V}O_2$ kinetics during exercise

Principal determinants of the oxygen uptake response to exercise are internal work (as represented by resting metabolic rate), external work and efficiency. Primarily, the $\dot{V}O_2$ response is determined by tissue metabolic rate and the adjustments of the cardiovascular system with exercise, making this system's role an important one. During exercise of a moderate intensity, there is a clear pattern in the $\dot{V}O_2$ kinetics apparent from the onset of activity. Moderate intensity refers to exercise performed below the lactate threshold (LT), which is the point at which blood lactate starts to accumulate. During exercise at this

intensity there is not a significant increase in blood lactate (Poole et al., 1988). The initial observation of the $\dot{V}O_2$ response to moderate-intensity exercise of a constant load was described as a linear increase in $\dot{V}O_2$ as work rate increases. This was apparent from the onset of exercise. This rise in $\dot{V}O_2$ continues until a steady state is reached, demonstrated by a plateau in the response where $\dot{V}O_2$ values no longer increase (Hill and Lupton, 1923; Whipp and
Wasserman, 1972). Since these first observations were made, it has become apparent that the $\dot{V}O_2$ response to moderate-intensity, constant-load exercise is made up of three phases. The response begins with an initial sharp increase in pulmonary $\dot{V}O_2$ (Whipp et al., 1982), known as phase 1, which is not reflective of muscle oxygen uptake (Grassi et al., 1996). There then appears to be a short delay in the response to exercise, which is followed a rapid increase in $\dot{V}O_2$. The second phase of the response is described as a mono-exponential increase in $\dot{V}O_2$, as observed at first (Hill and Lupton, 1923). This rise in $\dot{V}O_2$ continues until a steady state is reached, and this steady state is considered the third phase of the response to constant-load exercise.

Heavy exercise is determined as that which is performed above the LT. During this exercise of a higher intensity, the initial response to exercise is like that of moderate exercise. The phase 1 response and subsequent delay is apparent in this exercise domain, and the exponential rise in $\dot{V}O_2$ with work rate known as phase 2 is also observed (Paterson and Whipp, 1991). However, unlike at lower intensities, the $\dot{V}O_2$ steady state is delayed or even may not be attained (Whipp, 1994). There is an additional component to the response to heavy exercise compared to moderate and low intensities which follows the rapid increase in $\dot{V}O_2$ described as the phase 2 response. This additional component is known as the slow component and can be described as a further rise in $\dot{V}O_2$ at a much slower rate until $\dot{V}O_2$ max/exhaustion is reached (Whipp and Mahler, 1980). Several possible mechanisms have been proposed as a result of much research into this additional slow component seen during high intensity exercise. Examples of potential mechanisms include the response of blood lactate to the exercise, body temperature, and muscle fibre activity (Jones and Poole, 2005) which will be discussed in detail in the review of literature.

An enhanced $\dot{V}O_2$ response is beneficial to performance, as faster and thus greater delivery of oxygen to the working muscles allows the transfer of energy necessary to continue to exercise for longer. Exercise priming performed at a high intensity can enhance $\dot{V}O_2$ kinetics

during subsequent high-intensity exercise, however moderate priming exercise does not seem to elicit these changes (Gerbino et al., 1996). Mostly studied on cycling exercise, prior exercise has enhancing effects on the amplitude of both the fast component and slow component of $\dot{V}O_2$, more specifically increasing the former and reducing the latter (MacDonald et al., 1997; Burnley et al., 2002b). As a result of these effects on $\dot{V}O_2$ improvements in overall exercise performance can be seen following prior high intensity exercise, which is typically measured by the time to exhaustion in a subsequent exercise bout to task failure. This has been demonstrated in various exercise modalities but primarily running (Ingham et al., 2013) and cycling (Bailey et al., 2009; Burnley et al., 2005).

As exercise progresses and the demands on the body continue to rise alongside the changes in $\dot{V}O_2$ and limitations in oxygen transport, the onset of fatigue is apparent within the working muscles.

1.3: Neuromuscular fatigue

Neuromuscular fatigue can be defined as a reduction in the maximal capacity for a muscle to generate force/velocity (Gandevia, 2001). The process of neuromuscular fatigue develops throughout exercise and is associated with a progressive deterioration in muscle and whole-body performance, but which can be recovered with a period of rest following exercise (Allen et al., 2008; Gandevia, 2001). Neuromuscular fatigue can be of a central or peripheral basis, with both thought to contribute to a decrease in performance (Kent-Braun., 1999; Burnley et al., 2012) albeit to different extents depending on multiple aspects of the exercise task (Enoka and Stuart, 1992). Both types of fatigue can be assessed using electrical stimulation (Behm et al., 1996) during and following a maximal voluntary contraction (MVC). Separated at the neuromuscular junction, central fatigue refers to mechanisms which occur within the central nervous system and can be identified through electrical stimulation by a reduction in voluntary activation (VA). Peripheral fatigue develops within the muscle and can be shown as a reduction in torque in response to electrical stimulation at rest after an MVC (BiglandRitchie et al., 1986a).

Neuromuscular fatigue is a complex process and there are several potential factors which may contribute to its development (Enoka and Duchateau, 2008) and are much dependent on

the type of exercise, the duration and the intensity (Allen et al., 1995a; Fitts, 1994; Taylor and Gandevia, 2008). Neuromuscular fatigue has been most apparent during sustained isometric contractions (Merton et al., 1954) and observed to a lesser degree during intermittent contractions of both maximal and submaximal intensity. The rate of fatigue is higher during contractions of a greater intensity (Dolmage and Cafarelli, 1991).

1.4: Variability and Complexity

What is noise?

In 1905 Albert Einstein observed the movement of atoms and discovered the Brownian molecular movement and thus accidentally also discovered noise (Cohen, 2005). Noise is traditionally thought of as an undesirable component to a system which interferes with or disturbs the system output. Many signal processes aim to reduce or eliminate noise to reduce the degrading effects it is thought to have on system performance. However, noise has also been shown to have opposing effects on system performance through signal processes including stochastic resonance (SR) is mentioned by Sejdíc and Lipsitz (2013), which describes the positive impact of noise when at an optimal input level. Sejdíc and Lipsitz (2013) define noise as a stochastic process and consider there to be three common types. White noise is a type of stochastic process characterised as equal energy over all frequencies, representing complete unpredictability (Goldberger et al., 2002). Pink noise (also known as fractal noise) is characterised by equal energy per octave and arises from multiple physiologic and biologic control systems interacting over different time or space scales, for example functional networks such as heart rate control (Sejdíc and Lipsitz, 2013). Brownian noise can be described as the integral of white noise, providing a much smoother landscape (Goldberger et al., 2002).

Noise and Variability in sports performance

Variation in physiological systems is shown as constant fluctuations in system output. Standard deviation (SD) and the coefficient of variation (CV) are measures used to quantify these fluctuations referred to as variability in output. In the context of sports performance, coaches and athletes look to try and reduce variability in order to enhance performance (Slifkin and Newell, 1998) and much like the traditional view of noise, variability in sports performance is often thought to be detrimental to performance. However, success in sport,

more specifically the ability to reach a target/goal, is often based on variability of performance. In sports such as archery and darts the consistency of performance determines the outcome and success in competition, with the ability to hit a target consecutively resulting in higher scores and match wins and conversely inconsistent performance leading to potential losses (Slifkin and Newell, 1998). It is now recognised that the fluctuations seen in physiological outputs reflect an ability to adapt to external perturbations and may be functional as opposed to detrimental to sports performance (Davids et al., 2004). With highly skilled athletes displaying greater functional ability they are able to adapt well to task constraints.

Complexity

More recent findings provide us with understanding that fluctuations in the output of more complex physiological systems contain meaningful structural information as opposed to noise, and this is known as complexity. An example of this is muscle force output, where the force produced by the muscle is not smooth (Contessa et al., 2009), but exhibits variability in the form of fluctuations, and these fluctuations have a distinct structure. Physiologic complexity relates to the presence of long-range (known as fractal) correlations and distinct classes of non-linear interactions and identifies the temporal structures within a time series (Goldberger et al., 2002). Complexity is used to describe the pattern of the fluctuations in output, as opposed to the magnitude of the fluctuations about a mean or target (variation). Lipsitz and Goldberger (1992) describe the complex interaction of multiple control mechanisms as a healthy physiological function, enabling the individual to adapt to changes in everyday life. Complexity can be measured using approximate entropy (ApEn) and sample entropy (SampEn), which quantify the apparent randomness and regularity of fluctuations and the rate of information production. Detrended fluctuation analysis (DFA) estimates the temporal fractal scaling of a system (Peng *et al*., 1994).

A complex system output reflects a heathy, controlled and adaptable system (Lipsitz, 2004). Any changes observed in the output of a system away from the typical levels of complexity may be regarded as a reduction in these characteristics and the functionality of the system (Lipsitz et al., 2004; Peng et al., 2009). The processes of ageing and disease have been associated with this described loss of system output complexity, with a loss of complexity first proposed with the ageing process by Lipsitz and Goldberger (1992). A reduction in

complexity is observed throughout many physiological systems, reducing their functionality and making them less able to adapt to external perturbations (Lipsitz and Goldberger, 1992; Seely and Macklem, 2012), for example in heart rate dynamics and muscle torque output with ageing (Goldberger et al., 2002; Manor and Lipsitz, 2013).

Neuromuscular fatigue is also a prominent factor influencing the complexity of human movement. Human movement exhibits great variability in its output (de C. Hamilton et al., 2004). Force output is measured through muscular contractions, and these contractions are of an unsmooth nature (de C. Hamilton et al., 2004), exhibiting complex fluctuations and fractal scaling. Neuromuscular fatigue is associated with a loss in the complexity of muscle torque output, with the complexity of the output fluctuations falling during isometric contractions as fatigue progresses (Pethick et al., 2015; 2016) and the fractal scaling of the torque signal changes (Pethick et al., 2016). The purpose of the present thesis is to add to existing literature regarding $\dot{V}O_2$ kinetics and exercise tolerance with exercise priming, and to extend research on exercise priming to investigate these parameters and also neuromuscular fatigue and muscle torque output complexity in the novel context of primed intermittent isometric knee extensor contractions.

Chapter 2 – Literature Review

This chapter will review the literature surrounding the basis of the present study. The review will discuss the early and more recent investigations into the $\dot{V}O_2$ response to exercise and the speculated explanations for this response. The literature on warm-up/priming exercise and the effects of this on $\dot{V}O_2$ kinetics and performance will then be reviewed. This will include a review of the potential mechanisms for the response to prior exercise and the influence of fatigue on subsequent activity. The next section in this chapter will review the literature surrounding variability and complexity in system output and the various measures of complexity. The complexity of physiological system outputs and the effects of ageing and disease will be discussed, leading into the complexity of human movement and muscle torque output in the context of isometric contractions and the presence of fatigue.

2.1: $\dot{V}O_2$ kinetics during exercise

Pioneering findings for the $\dot{V}O_2$ response to exercise were presented by Krogh and Lindhard (1913) who conducted investigations into respiration and circulation regulation during the initial stages of muscular work performed on a cycle ergometer. An increase in ventilation was observed immediately following the onset of exercise. A similar response was apparent when studying the absorption of oxygen, with an initial rise from the resting value at the beginning of the exercise. Following this first increase there was a further rise in absorption, until there was a plateau in the response, demonstrating a steady state. This was the first report of an exponential increase in the gas exchange response during constant-load exercise. In this study, Krogh and Lindhard (1913) proposed that the circulation rate response to muscular work must be almost proportional to that of oxygen absorption. They stated that given the venous blood reaching the lungs in the first 6-10 seconds of exercise is nearly equal to that during rest, a similar increase in circulation rate must be responsible for the increase in oxygen absorption. These findings presented two separate components of the ventilatory and gas exchange response. This oldest, traditional view of exercise energetics describes a monoexponential process right from the onset of exercise (Cerretelli and DiPrampero, 1987). This model does not display any delay in the response, and the changes in muscle metabolism are seen at the lungs immediately. Hill and Lupton (1923) found further evidence to support the mono-exponential increase in oxygen intake during moderate intensity exercise, followed by attainment of a steady state. In this study they measured oxygen intake during walking and

running exercise, finding that there was a predictable increase in ventilation and in oxygen intake with an increase in speed until steady state was reached and there is a plateau in the response. It is now known that this plateau signifies that the rate of O_2 consumption is a reflection that virtually all adenosine triphosphate (ATP) is being supplied via oxidative phosphorylation.

The progression of the V O_2 response to exercise differs depending on the intensity domain in which the exercise is performed, assigned on the basis of gas exchange and metabolic response profiles. Gaesser and Poole (1996) suggested three domains of exercise intensity, the first being moderate exercise.

Moderate intensity exercise

The progression of the $\dot{V}O_2$ response to exercise differs depending on the intensity domain in which the exercise is performed, assigned based on gas exchange and metabolic response profiles. Gaesser and Poole (1996) suggested three domains of exercise intensity, the first being moderate exercise. Moderate intensity refers to exercise at a work rate which does not induce a significant increase in blood lactate. The individual lactate threshold or anaerobic threshold is considered the upper limit of this exercise domain (Whipp et al., 1999). The $\dot{V}O_2$ at which the lactate threshold occurs can be determined using the $\dot{V}O_2$ response to incremental exercise. Here, the metabolic rate at the point where blood lactate rises above baseline value is used to estimate the threshold point, it can also be estimated non-invasively by using the gas exchange threshold (Jones and Poole, 2005).

Whipp et al. (1982) supported this first phase of the $\dot{V}O_2$ response, demonstrating an initial abrupt increase from rest, within the first complete respiratory cycle of exercise. This immediate increase in the $\dot{V}O_2$ response to exercise was followed by a short delay, and then the prominent exponential increase in the response until attainment of a steady state. This study utilised superimposed and averaged breath-by-breath measurements of the pulmonary $\dot{V}O_2$ response at exercise onset. The early phase of rapid increase seemed readily distinguishable from the subsequent response pattern to the constant-load cycling exercise and was subsequently referred to as the phase 1 response. The initial change in pulmonary blood flow largely dictates the gas exchange in this early period with ventilation and gasexchange responses to exercise found to be directly proportional to the pulmonary blood flow. The blood that is returning to the lungs had left the muscle before there was an increase

in muscle oxygen extraction and so the abrupt increase in $\dot{V}O_2$ was caused by increased venous return and increased pulmonary blood flow (Burnley and Jones, 2007). The pulmonary $\dot{V}O_2$ during this period at the onset of exercise therefore does not reflect muscle oxygen uptake (Grassi et al., 1996). There was a correlation between the $\dot{V}O_2$ and $\dot{V}\ CO_2$ responses and the magnitude of the heart rate response following linear correlation and regression analysis, supporting the term 'cardiodynamic' used to describe the phase 1 response. Whipp et al. (1982) also found that there was short 20-second delay in the response to the exercise following the initial abrupt increase in $\dot{V}O_2$ from the resting state. This delay, supported by the findings of Whipp (1987), seems to account for the transit time of oxygen from the exercising muscles extracted from the blood to the lungs (Burnley, 2000).

Following the short delay of the 'cardiodynamic' phase or phase 1, $\dot{V}O_2$ rises in an exponential manner, where $\dot{V}O_2$ increases in a linear function of work rate toward a steady state (Whipp and Wasserman, 1972). This dominant stage, known as the phase 2 response, now reflects the muscle metabolic changes on $\dot{V}O_2$ which are measured at the mouth. The $\dot{V}O_2$ kinetics advancement by Whipp et al. (1982) suggested that this non-steady state phase response seemed to represent the rise in pulmonary $\dot{V}O_2$ due to the superimposed rising muscle $\dot{V}O_2$. This phase reflects the effect of the O_2 extraction in the blood perfusing the exercising muscles on the mixed venous blood. Barstow and Mole (1991) provided support for Whipp and co-workers' findings and suggested that over a range of circulatory factors the response of pulmonary and muscle $\dot{V}O_2$ kinetics were very similar during phase 2. This phase can also be known as the 'primary' or 'fast' component due to its nature. The faster the phase 2 response, and so the faster the attainment of $\dot{V}O_2$ steady state, means that the O_2 deficit is lower as there is a smaller lag. This slope or gain in $\dot{V}O_2$ has both a time constant and an amplitude (Hill et al., 1994). Barstow and Mole (1991) demonstrated that the phase 2 response amplitude increased almost linearly with exercise. The time constant of this exponential process is approximately 25-35 seconds (Whipp, 1987) and tends to vary very little for work rates of moderate intensity (Whipp and Wasserman, 1972). Results by Henry and De Moor (1956) demonstrated that as the work rate increased, so did the time taken for the $\dot{V}O_2$ to reach a steady state. However, conflicting findings from Margaria et al. (1965) showed that the pattern of the $\dot{V}O_2$ rise to steady state did not vary at different work intensities. It was demonstrated here that different work rates had the same rate constants and that the increase in $\dot{V}O_2$ was a single exponential process.

$\dot{V}O_2$ rises in the described exponential manner until a steady state is attained. This is normally reached after approximately three minutes of exercise (Whipp and Wasserman, 1972) in young healthy adults however sooner in those with higher aerobic fitness and later in older adults and those suffering with cardio-pulmonary dysfunction. This steady state occurs when both the muscle and pulmonary time courses are complete (Jones and Poole, 2007). The steady state attained is termed phase 3. At mild or moderate intensity exercise, the $\dot{V}O_2$ rises linearly with work rate during this third phase.

High intensity or 'heavy' exercise

The $\dot{V}O_2$ response to heavy exercise, which is described as exercise performed above the LT where the rate of blood lactate appearance exceeds the rate of removal (Gaesser and Poole, 1996), is much more complex than the response to moderate intensity exercise. In the heavy exercise domain, blood lactate and $\dot{V}O_2$ profiles are tightly correlated. The $\dot{V}O_2$ in phase 2 still increases exponentially; however, unlike moderate exercise, the $\dot{V}O_2$ steady state is delayed or even unattained for work rates above the LT (Whipp, 1994). During heavy intensity exercise, a slower increase in $\dot{V}O_2$ emerges approximately 100-120 seconds following the primary/phase 2 response (Whipp and Wasserman, 1972; Linnarsson, 1974). This delayed onset of 'excess' $\dot{V}O_2$ occurring minutes into exercise is a result of what is known as the slow component of $\dot{V}O_2$ kinetics, which refers to a further, slower rise in $\dot{V}O_2$ above the steady state towards $\dot{V}O_{2max}$ (Whipp and Mahler, 1980) and exhaustion (Barstow et al., 1996). A review by Xu and Rhodes (1999) highlighted an association between the onset of the slow component and the point of lactate accumulation, and compiled evidence showing that with increased blood lactate the magnitude of the slow component was greater.

The discovery of this additional component of $\dot{V}O_2$ challenged the previous ideas of muscle energetics. Paterson and Whipp (1991) demonstrated that during exercise of heavy intensity, the primary component of the $\dot{V}O_2$ response is exponential and rises to a steady state with a similar gain to that during exercise in the moderate intensity domain. The fast component time constant was also not significantly different to exercise performed at work rates below the lactate threshold. This excess $\dot{V}O_2$ has therefore been considered to supplement the fundamental (fast) component of the $\dot{V}O_2$ response (Rossiter et al., 1999). The rise in $\dot{V}O_2$ caused by the delayed onset of the slow component goes above that which would be

predicted by extrapolation of the relationship between work rate and $\dot{V}O_2$ during subthreshold exercise (Roston et al., 1987). It was also demonstrated here that at supra-threshold 'heavy' work rates just above the threshold, steady state may be attained eventually. At higher 'very heavy' or 'severe' work rates, steady state is unattainable and the $\dot{V}O_2$ will continue to rise until $\dot{V}O_{2max}$ is reached. At heavy work rates, the slow phase of the response brings the subject to $\dot{V}O_{2max.}$ (Jones and Poole, 2005). The highest work rate at which a sustainable (steady state $\dot{V}O_2$) % $\dot{V}O_{2\,max}$ also coincides with the asymptote of the subject's power-duration curve (Poole et al., 1988). For work rates above this 'critical power' (CP) or 'fatigue/lactate threshold', the faster the slow component projects towards $\dot{V}O_{2max}$ the shorter the tolerable duration of the work rate (Jones and Poole, 2005).

2.2: Potential mechanisms of the $\dot{V}O_2$ slow component

The contracting muscles have been shown to contribute to the $\dot{V}O_2$ slow component, however it is unknown what the underlying mechanism is for this slow progressive rise in $\dot{V}O_2$. The $\dot{V}O_2$ slow component represents a reduction in muscle work efficiency, although the mechanisms behind this are unclear.

Core and body temperature

A progressive increase in muscle body temperature was suggested as a potential mechanism for the $\dot{V}O_2$ slow component. Xu and Rhodes (1999) outline that there is an increase in the metabolic activity within the working muscles during an exercising period which consequently increases the temperature of the working muscles. These authors go on to explain how a rise in body temperature may increase oxygen consumption due to the effect of temperature on the rates of reactions. However, studies have demonstrated that muscle temperature does not seem to significantly influence the muscle $\dot{V}O_2$ slow component (Koppo et al., 2002). Krustrup et al. (2004) conducted a study which saw the performance of cycle exercise for 20 minutes at a moderate intensity compared with the same exercise protocol at a heavy intensity. This study observed a $\dot{V}O_2$ slow component only in the higher intensity work bout, however there was no difference in the change in muscle temperature between the moderate and heavy exercise domains indicating that there was no influence on

the $\dot{V}O_2$ slow component. Koga et al. (1997) showed that a rise in muscle temperature prior to exercise, with no rise in core temperature, did not have any effect on the $\dot{V}O_2$ slow component during heavy exercise. Thus, it is apparent that there may be other mechanisms responsible for the slow rise in $\dot{V}O_2$ during heavy exercise aside from an increase in muscle temperature.

Blood lactate

Much research has been conducted regarding blood lactate as a factor for the emergence of the slow component. Krustrup and co-workers found, during the study described above (2004), that muscle pH was lower in the intense exercise compared to the moderate exercise, demonstrating an increase in muscle blood lactate which coincided with the appearance of the $\dot{V}O_2$ slow component. This seemed to suggest that muscle acidosis may be a cause of the reduction in efficiency. Several studies support these findings including Barstow et al. (1996) who found that both the relative and absolute amplitudes of $\dot{V}O_2$ slow component and the net increase in blood lactate were also significantly correlated. Many other studies have also demonstrated a correlation between the magnitude of the $\dot{V}O_2$ slow component and the rise in blood lactate during exercise, in most cases this is for cycle ergometry (Whipp and Wasserman, 1986; Roston et al., 1987; Poole et al., 1988). Infusion of sodium L-(+)-lactate during exercise in a study by Ryan et al. (1979) found that both blood lactate concentration and $\dot{V}O_2$ increased. However, there are other studies which indicate that this relationship may not be a causal. Steed et al. (1994) showed similar findings, having detected the emergence of a $\dot{V}O_2$ slow component during submaximal treadmill running without a rise in blood lactate that remained close to resting levels. Poole et al. (1988) demonstrated that absolute and relative amplitudes of the slow component were significantly correlated to the net increase in blood lactate but were not related to the fast component gain or time constant. These observations seem to imply that blood lactate and $\dot{V}O_2$ slow component are correlated, however there is not a causal effect.

Adrenaline

Adrenaline has been considered a possible $\dot{V}O_2$ slow component mediator, with several studies demonstrating that infusion of epinephrine increases metabolic rate (Fellows et al., 1985). Gaesser et al. (1994) conducted a study in which subjects performed constant-load heavy intensity cycle exercise for 20 minutes, they compared an exercise only condition to one with continuous intravenous infusion of epinephrine during the latter 10 minutes of the exercise. There was a significant increase in $\dot{V}O_2$ throughout the exercise from minute 10 to minute 20 in both trials however there was no significant difference between the two conditions. This study demonstrated that the infusion of epinephrine did not influence $\dot{V}O_2$.

Motor unit behaviour

There is a growing body of evidence that seems to suggest a relationship between the $\dot{V}O_2$ slow component and the motor unit recruitment patterns (Gaesser and Poole, 1996). In 1992, Shinohara and Moritani found that $\dot{V}O_2$ slow component was positively correlated with the iEMG of the working muscles between minutes four and seven of high-intensity exercise. With EMG measuring the activity of the specific muscles, an increase in this measure indicates changes in motor unit recruitment or firing frequency, however, cannot distinguish between fibre type recruitment patterns. Other studies have demonstrated that the emergence of the slow component occurs before the time point at which the increase in iEMG was observed. A study by Barstow and Mole (1991) found that the range of time constants for the processes in type 2 muscle fibres were of the same order of magnitude as those for the slow rise phase of the $\dot{V}O_2$ response. Vollestad et al. (1984) also previously demonstrated that during prolonged heavy exercise more oxidative fibres were preferred and as exercise progress more type 2 fast twitch fibres were recruited. The explanation behind this observation was that the original fibres recruited from the early stages of the exercise became depleted of glycogen as the exercise progressed and thus needed replacing further into the work bout. This shift in fibre-type would explain the decrease in efficiency as type 2 fibres are thought to be less efficient than type 1 (He et al., 2000). It was also suggested by Poole et al. (1988) that a progressive increase in the recruitment of type 2 muscle fibres as exercise progresses could lead to increased muscle O_2 consumption and may therefore generate the slow component in the response. The type 1 muscle fibres were also not significantly related to the change in blood lactate.

Barstow et al. (1996) conducted a study investigating the influence of muscle fibre type and pedal frequency on $\dot{V}O_2$ kinetics during heavy exercise. They specifically looked at the $\dot{V}O_2$ slow component and the relationship with type 2 muscle fibres. Different pedal frequencies were used in order to activate the specific types of fibres, following previous evidence that type 2 units are preferably recruited at lower pedal frequencies and at high pedal rates. Subjects performed four exercise bouts at different pedal frequencies. These bouts included eight minutes cycling at a specified work rate, and eight minutes cycling at a baseline work rate condition for that specific pedal frequency. Results showed that there was no significant correlation between the amplitude of the slow component and the percentage of type 1 fibres at any pedal frequency however, the $\dot{V}O_2$ slow component was inversely related to the %type 1 fibres with regards to the relative contribution to the overall increase in $\dot{V}O_2$. The influence of the muscle fibre type on $\dot{V}O_2$ kinetics was not different over different pedal frequencies however, the percentage of type 2 muscle fibres recruited was related to the relative contribution of the $\dot{V}O_2$ slow component. Barstow and co-workers discussed the influence of individual fitness levels and endurance training on contracting muscle fibre types, with previous findings (Costill et al., 1976) suggesting a positive association between type 1 muscle fibres and oxidative capacity in adults. However, they do highlight that relative fitness and muscle fibre type distribution can be either co-dependent or independent features of the $\dot{V}O_2$ response to heavy exercise. Positive associations between work efficiency and type 1 muscle fibres found in previous studies (Coyle et al., 1992) seem to conflict with the findings of this study as fibre type was not significantly correlated with the total gain for $\dot{V}O_2$. However, Barstow and authors highlighted a difference and potential limitation of their study in that they measured $\dot{V}O_2$ after eight minutes of exercise in comparison to either 3x5 minute stages of progressive or continuous exercise or one hour of maximally sustained work, which Coyle et al. (1992) used. This shorter length of exercise may not have been enough to represent the full $\dot{V}O_2$ response to an exercising period.

An association between the $\dot{V}O_2$ slow component and muscle fibre recruitment pattern was observed by Krustrup et al. (2004). In the first experimental visit of this study subjects performed two bouts of 20-minute exercise, one at moderate intensity (50% $\dot{V}O_{2\,max}$) and one at high intensity (80% $\dot{V}O_{2\,max}$), with a 60-minute rest in the supine position separating the two bouts. On a separate occasion subjects performed 20 minutes of moderate exercise followed by three and six minutes of intense exercise. There was also a 60-minute supine rest between these exercise bouts. Single muscle fibre phosphocreatine (PCr) content was

analysed, and it was found that additional type 1 and type 2 muscle fibres were recruited from three to six minutes of the intense exercise and this was associated with an observed $\dot{V}O_2$ slow component. The increase in fibre recruitment and so changes in recruitment pattern therefore seemed associated with a pronounced slow component. The study also examined glycogen depletion patterns and showed that during moderate intensity exercise only type 1 muscle fibres were recruited, as glycogen content decreased in only this type. However, during the intense exercise bout the glycogen content in both type 1 and type 2 fibres declined, which also showed the emergence of a $\dot{V}O_2$ slow component. During the high intensity exercise bout, creatine phosphate breakdown was observed in both type 1 and 2 fibres after three minutes, and then a further decrease in content from three to six minutes.

The initial breakdown of both fibres demonstrated that type 2 fibres are recruited in the early stages of intense exercise. Krustrup and co-workers concluded that this study supported the idea that additional type 1 and type 2 fibres are recruited during heavy sub-maximal exercise and showed an association between this recruitment and the appearance of the $\dot{V}O_2$ slow component. There was a large increase in the overall number of fibres recruited during the slow component phase of the $\dot{V}O_2$ response. Krustrup and co-workers also found a shift from type 1 to type 2-fibre recruitment in association with the $\dot{V}O_2$ slow component, supporting previous studies' findings. Krustrup et al. (2004) speculated that the shift in recruitment towards type 2 fibres could also have contributed to the continued slower elevation in $\dot{V}O_2$ at the higher exercise intensity.

2.3: Exercise priming

2.3.1: Warm-up exercise

For many years prior exercise has been recognised as an important component for physical activity in eliciting great effects on the metabolic, acid-base and cardiovascular responses to any subsequent exercise (Jones and Poole, 2005). Both competitive athletes and recreational activity participants typically perform some kind of warm-up procedure before commencing any strenuous exercise. Shellock and Prentice (1985) reviewed the use of warm-ups, the various components and techniques commonly used, and the benefits gained through warming-up. The act of warming up is used to enhance physical performance and to prevent

potential injuries. These authors outlined the three typical warm-up regimes as passive warmup, general warm-up and specific warm-up. Passive warm-up involves externally increasing body temperature. Asmussen and Boje (1945) demonstrate that warming of the muscles led to faster completion of a given amount of work. Passive warming of the muscles, as opposed to an active warm-up, also increased the capacity for work. Harder preliminary work which rose temperature higher elicited even better performance in short duration work. Although this method reduces the risk of impairing the physical work completed during the main activity as it does not deplete any energy stores, it is not practical for most athletes (Shellock and Prentice, 1985). In this review these authors described a general warm-up as the most widely used technique, raising body temperature through active movements. Whereas, a specific warm-up was that which focused on the neuromuscular components to be used in the main event/activity. A general warm-up can involve movements such as jogging or cycling, which are not specific to the activity/event. In 2003, Bishop reviewed a large range of studies investigating warm-up exercise, he used passive and active warming up as two broad categories. In this review, Bishop (2003) looked into the potential mechanisms of an active warm-up such as temperature effects, metabolic effects and baseline oxygen consumption. Temperature-related mechanisms such as reduced stiffness and increased nerve conduction rate, and potential effects on $\dot{V}O_2$ kinetics such as an elevated baseline $\dot{V}O_2$, which allows an initial sparing of anaerobic capacity, could contribute to an improved time to exhaustion and task performance following an active warm-up. Ingjer and Stromme (1979) compared the performance of active, passive or no warm-up on subsequent heavy treadmill exercise. The active warm-up led to a significant increase in oxygen uptake and blood pH, and a reduction in lactate concentration during the standard work bout when compared to passive warm-up and no warm-up at all.

2.3.2: Exercise priming on $\dot{V}O_2$ kinetics

Early studies have looked into the effects of prior exercise on the $\dot{V}O_2$ kinetics of a subsequent exercise bout. Weltman et al. (1979) investigated the effect of a maximal effort exercise bout on a subsequent exercise bout. The subjects performed a five-minute maximal effort performance test on a bicycle ergometer, followed by 20 minutes of recovery and then a second five-minute maximal performance test. This study observed that that $\dot{V}O_2$ was

higher in the first two minutes of the second exercise bout compared to the first bout. Buono and Roby (1982) conducted a study which involved subjects performing a bout of prior cycling exercise for five minutes, before 25-minute recovery exercise and then a second fiveminute exercise bout. The authors observed that the cumulative $\dot{V}O_2$ was significantly larger in the second of the two exercise bouts, and the immediate post-exercise lactic acid level were significantly lower in the second compared to the first bout. The findings led to the conclusion that a prior high-intensity exercise bout can alter the acid-base and metabolic responses of a subsequent exercise bout. Both these studies demonstrate a clear 'priming' effect of prior exercise, specifically in terms of the physiological response to a second exercise bout as there appears to be a rise in the aerobic contribution to this subsequent exercise. Inbar and Bar-Or (1975) investigated the effect of a 15-minute intermittent warm-up on subsequent exercise bouts. After four minutes of recovery, subjects performed either an aerobic or anaerobic exercise task on a bicycle. $\dot{V}O_2$ was shown to be higher at all time points during the subsequent aerobic exercise task, and the warm-up also increased the $\dot{V}O_2$ peak achieved in the subsequent bout. The performance in the criterion task, measured by total pedal revolutions performed throughout, was improved. However, as outlined by Jones and Poole (2005), these studies lack the temporal resolution that is needed in order to describe the specific time course of the $\dot{V}O_2$ response.

Following some exploratory work by Gausche et al. (1989), the same group conducted a study investigating the effect of moderate and heavy prior exercise on the $\dot{V}O_2$ kinetics of subsequent high-intensity exercise (Gerbino et al., 1996). The study consisted of a series of four exercise protocols on a cycle ergometer. In all trials, subjects cycled continuously for 24 minutes. Within this time subjects performed two six-minute constant-load exercise bouts which were each followed by six minutes of unloaded cycling. The initial exercise period was at sub-LT (moderate) intensity for two of the protocols, followed by a second exercise bout of either sub- LT or supra-LT (heavy) intensity. The other two protocols consisted of a supra-LT first work bout, followed by either a sub-LT or supra-LT second bout. This study's results supported those of Gausche et al. (1989) demonstrating that prior supra-threshold exercise speeds the $\dot{V}O_2$ kinetics in a subsequent supra-threshold work bout. However, it was also shown that prior moderate exercise had no influence on the subsequent heavy $\dot{V}O_2$ kinetics and neither prior moderate or heavy exercise had any effect on subsequent moderate exercise. This protocol was also compared to bouts of moderate and heavy exercise without any prior warm-up exercise. $\dot{V}O_2$ kinetics in the heavy exercise bout were not different with a

moderate intensity warm-up compared with no warm-up at all. However, kinetics were speeded with a heavy warm-up in comparison to no warm-up. Gerbino et al. (1996) speculated various explanations for their findings. The speeded $\dot{V}O_2$ kinetics in the high-intensity exercise bout following supra-LT warm-up resulted in a significant decrease in the partial oxygen deficit, a greater decrease than with sub-LT warm-up or no warm-up. The speeding of $\dot{V}O_2$ kinetics in the high-intensity exercise was associated with a smaller increase in blood lactate and a smaller decline in arterial ph. This supports the suggestion that there is a lower requirement of blood lactate production during this type of exercise when kinetics is fast, and raises the possibility that lactate clearance may be faster. Gerbino et al. (1996) stated that their results (the metabolic changes elicited by high-intensity exercise having an effect on subsequent exercise above but not below the LT) implied that two mechanisms may be involved in the control of $\dot{V}O_2$; vasodilation and increased muscle blood flow at the start of the second exercise bout, and improved O_2 diffusion gradient between the capillary blood and mitochondria of the muscles caused by the acidemia-induced Bohr shift. The concluding suggestion made by Gerbino and co-workers was that the speeded $\dot{V}O_2$ kinetics by suprathreshold warm-up exercise was due to residual metabolic acidemia which led to improved muscle perfusion during the subsequent high-intensity exercise.

MacDonald et al. (1997) conducted a two-part study further investigating the effects of heavy submaximal exercise on $\dot{V}O_2$ kinetics. Part one of the study consisted of cycle exercise with step changes in work rate both below and above the subject's ventilation threshold. This was performed in normoxia and in hyperoxia. The second part of the study involved a heavy exercise bout with an increase from a baseline work rate for ten minutes followed by a transition back to baseline for six minutes, before a subsequent exercise bout with identical transition in work rate. These experiments were performed with normoxia and hyperoxia; four conditions, with the first exercise bout either normoxia or hyperoxia and the subsequent exercise bout in either the same or the different gas-breathing condition. For work rates above the ventilation threshold there was a speeding/acceleration of $\dot{V}O_2$ kinetics following prior exercise and as a result of hyperoxia. This was demonstrated through a faster mean response time (MRT) and also a reduced $\dot{V}O_2$ slow component. There was greater speeding of the kinetics when the combination of prior exercise and hyperoxia was used, which MacDonald and co-workers thought indicated that the two stimuli independently had an increasing effect of O_2 transport at the onset of exercise. Prior exercise above the ventilation rate resulted in a smaller MRT in both normoxia and hyperoxia conditions, demonstrating a speeding of $\dot{V}O_2$

kinetics and supporting the findings of Gerbino et al. (1996). The results of MacDonald et al. (1997) support the possible explanation that O_2 transport is a limiting factor to $\dot{V}O_2$ kinetics in high-intensity exercise (Cochrane and Hughson, 1992) however, if the conditions fully alleviate the O_2 transport deficit, these results may also show there may be other contributing factors as the high-step kinetics were not as fast as the low-step in any of the conditions. Jones and Poole (2005) evaluated this study, stating that the finding of an overall speeding of $\dot{V}O_2$ kinetics in heavy exercise with hyperoxia should be interpreted with caution. The study data showed that there was no difference in the time constant of the primary component between normoxia and hyperoxia but also displayed data indicating a significantly longer time constant in the hyperoxia conditions. There was no significant effect of prior heavy exercise on the primary time constant of the second exercise bout in both normoxia and hyperoxia, which together with the previous statement could demonstrate that the speeding of the overall $\dot{V}O_2$ kinetics were actually largely due to a reduction in the amplitude of the slow component.

Burnley et al. (2000) further investigated the effects of prior heavy exercise on the phase 2 $\dot{V}O_2$ kinetics of a subsequent heavy exercise bout. Phase 2 kinetics were not used in the interpretation of data in MacDonald et al. (1997) study, and Gerbino et al. (1996) did not measure the $\dot{V}O_2$ kinetics. Therefore, purpose of this study was to determine whether the reduction in MRT or $\dot{V}O_2$ time constant observed in the previous studies by Gerbino et al. (1996) and MacDonald et al. (1997) was due to the speeding of $\dot{V}O_2$ kinetics in phase 2 or actually due to a reduction in the $\dot{V}O_2$ slow component. The methods of Burnley et al. (2000) replicated those of Gerbino et al. (1996) with a six-minute cycle exercise bout of either moderate or heavy intensity followed by six minutes of baseline cycling and then a subsequent six-minute moderate or high-intensity exercise bout. In order to analyse the different parts of the $\dot{V}O_2$ response separately, Burnley and co-workers (2000) used a triple exponential model for the $\dot{V}O_2$ response in contrast to the mono-exponential curve used by Gerbino et al. (1996). This triple exponential model incorporates the single curve describing the phase 2 kinetics followed by the slow component response (phase 3). Results from this study showed that prior exercise of both moderate and high intensity did not alter the $\dot{V}O_2$ kinetics or amplitude of the subsequent moderate exercise. Prior moderate exercise had no effect on the response to subsequent heavy exercise alike the findings of Gerbino et al. (1996). Prior heavy exercise did not affect the phase 2 $\dot{V}O_2$ kinetics of a second heavy exercise bout, however, did support the findings of both Gerbino et al. (1996) and

MacDonald et al. (1997) in that the effective time constant and MRT were significantly reduced. Use of the triple exponential model thus demonstrated that the speeding of $\dot{V}O_2$ kinetics found by Gerbino et al. (1996) was not a representation of the phase 2 kinetics as these did not change as a result of prior heavy exercise, but in fact reflected a decrease in the $\dot{V}O_2$ slow component amplitude. Other studies using the triple exponential model to separate the components of the response have also found that prior heavy exercise does not speed primary $\dot{V}O_2$ kinetics (Koppo and Bouckaert, 2001; Scheuermann et al., 2001). Burnley and co-workers (2000) therefore suggested that the $\dot{V}O_2$ time constant and MRT should not be used to understand the phase 2 response kinetics during high intensity exercise. They also speculated, using the findings of Whipp (1994) and Barstow et al. (1996) regarding muscle fibre recruitment as an explanation for the $\dot{V}O_2$ slow component, that the reduced amplitude of the slow component as a result of prior exercise could be due to a lower recruitment of type 2 muscle fibres in the second of the two exercise bouts.

Koppo and Bouckaert (2000) deemed that the effect of prior exercise on the $\dot{V}O_2$ fast and slow component response needed further investigation. This study consisted of a six-minute high-intensity cycling exercise bout at a work rate corresponding to 90% of $\dot{V}O_{2\ peak.}$ Subjects were then given six minutes of recovery (3-minute rest, 3-minute unloaded cycling). Following the recovery period, a second constant-load exercise bout was performed, of the same intensity and duration as the prior exercise bout. The $\dot{V}O_2$ kinetic response in the second heavy exercise bout was compared to a control bout, which was not preceded by prior heavy intensity exercise. Analysis using a biexponential model enabled the authors to observe the changes in the fast component and slow component of the $\dot{V}O_2$ response separately. There was no change in the time constant or amplitude of the fast component with the performance of prior heavy exercise, suggesting to the authors that muscle O_2 utilisation was not greatly affected by prior high-intensity exercise and thus a greater O_2 availability from metabolic acidosis is not necessarily the underlying mechanism for the observed $\dot{V}O_2$ response in a second exercise bout. The time constant and amplitude of the slow component were reduced significantly following prior high-intensity exercise, similar to Macdonald et al. (1997) findings. Findings from previous studies, such as the aforementioned study by Barstow and Mole (1991) and Poole et al. (1994), provide evidence that fibre recruitment pattern could be a mediator of the $\dot{V}O_2$ slow component response, as they showed a relationship between the $\dot{V}O_2$ slow component and the recruitment of fast twitch fibres which

have a higher O_2 cost of contraction for a given tension development and longer time constant compared to slow twitch. This led to speculation by Koppo and Bouckaert (2000) that the decrease in slow component observed in the second of two high-intensity exercise bouts in this study could be due to a change in muscle fibre recruitment pattern, more specifically a change in the efficiency or number of fast twitch muscle fibres in the second exercise bout.

An investigation into the correlation between muscle activity, through electromyography (EMG), and the $\dot{V}O_2$ slow component during repeated heavy exercise bouts was conducted by Scheuermann et al. (2001). Specifically, these authors tested whether the slow component during heavy exercise and the reduction following prior heavy exercise is correlated with changes in neuromuscular activity and muscle fibre recruitment. The protocol for this study involved a step increase in work rate from a baseline of unloaded cycling. The exercise was of moderate intensity for six minutes followed by a six-minute recovery, or heavy exercise for eight minutes with an eight-minute recovery. Subjects performed three transitions to the moderate work rate and two transitions to the heavy work rate, on two occasions. Prior heavy exercise led to a speeding of the MRT, consistent with previous findings (Gerbino et al., 1996; MacDonald et al., 1997). The triple exponential model separating the three phases of the $\dot{V}O_2$ response was used in this study which enabled identification and analysis of all three phases of the response. Scheuermann et al. (2001) reported an apparent speeding of the $\dot{V}O_2$ kinetics with the repeated heavy intensity exercise bouts. There was a significant reduction in the amplitude of the $\dot{V}O_2$ slow component in the second of the two heavy exercise bouts however, there was no change in mean power frequency (MPF) or power. There was no association between the $\dot{V}O_2$ slow component and the MPF and iEMG during the second heavy exercise bout, contradicting the proposal that the $\dot{V}O_2$ slow component is due to increased recruitment of motor units or a change in the distribution of different fibre types.

Burnley et al. (2001) investigated further following the results found in their previous study. This study (Burnley et al. 2001) was designed to test whether the elevation in the absolute $\dot{V}O_2$ amplitude at the end of phase 2 would still be apparent in the second heavy exercise bout if the baseline $\dot{V}O_2$ at the start of this bout was restored as opposed to elevated as it appeared to be in the previous study. Previous studies (Gerbino et al., 1996; Burnley et al., 2000) have demonstrated that prior heavy exercise aided the response to a subsequent heavy exercise bout, but moderate-intensity prior exercise did not elicit the same response. Neither intensity

of prior exercise effected the response to subsequent moderate exercise. Following these results, Burnley et al. (2001) also examined whether a prior bout of moderate-intensity exercise, which involved the same amount of work as a six-minute heavy bout, would elicit the same responses in a second heavy bout (increased absolute $\dot{V}O_2$ amplitude at the end of phase 2 and a reduction in the slow component amplitude). The first part of this study consisted of two six-minute heavy exercise bouts with either six or 12 minutes of recovery in between them. This was in order to test whether a restored baseline $\dot{V}O_2$ at the onset of the second exercise bout (after 12-minute recovery) would elicit the same response as an elevated baseline after six minutes of recovery. The results from this study replicated those of Burnley et al. (2000) for the six-minute recovery protocol, with an increase in baseline $\dot{V}O_2$ at the onset of the second bout and no significant change in the amplitude or kinetics of the phase 1 or phase 2 response. The absolute $\dot{V}O_2$ response was increased and the $\dot{V}O_2$ slow component was reduced in the second heavy exercise bout. The 12-minute recovery restored $\dot{V}O_2$ to its baseline levels before the second bout. In this protocol the $\dot{V}O_2$ amplitude of phase 2 was increased with no change in the $\dot{V}O_2$ time constant. There was also a reduction in the $\dot{V}O_2$ slow component amplitude like that found after six minutes of recovery. This demonstrates that these effects on the stated $\dot{V}O_2$ components persist for at least 12 minutes following heavy intensity exercise. These findings by Burnley et al. (2001) suggest that the increase in $\dot{V}O_2$ amplitude at the end of phase 2 as shown by Burnley et al. (2000) was caused not only by an elevation in baseline $\dot{V}O_2$ but also an increase in the net amplitude of the phase 2 response, suggesting that prior heavy exercise increases the amplitude of the $\dot{V}O_2$ phase 2 amplitude whether the baseline $\dot{V}O_2$ is altered or not.

In the second part of the study (Burnley et al., 2001), subjects performed a prior bout of exercise at a moderate intensity, followed by six minutes of recovery and then a second exercise bout of heavy intensity lasting six minutes. The moderate exercise bout was of a duration which ensured the subject performed the same amount of work as they did during the six-minute heavy exercise bouts. This moderate exercise had no effect on $\dot{V}O_2$ or blood lactate in the heavy exercise bout, demonstrating that the effects of prior exercise are only apparent following exercise at an intensity which elicits a residual increase in blood lactate, in line with the authors previous findings (Burnley et al., 2000).

Following the speculation by Burnley et al. (2000) that increased motor unit recruitment at the onset of the second heavy exercise bout could explain an increased primary $\dot{V}O_2$

amplitude during that second bout, Burnley et al. (2002b) conducted a study with the aim of testing whether the higher primary $\dot{V}O_2$ amplitude in the second exercise is accompanied by an increase in iEMG during the first two minutes. This protocol consisted of two six-minute heavy cycling bout with 12 minutes of recovery separating them, the same as that used by Burnley et al. (2001). Muscle activity and oxygen status of the gluteus maximus, vastus lateralis, and vastus medialis were measured. However, the iEMG values from the three muscles were averaged, which meant that the contribution of each individual muscle was not known. The primary $\dot{V}O_2$ time constant was not affected by prior heavy exercise, but there was a significant increase in the absolute primary $\dot{V}O_2$ response. Prior heavy exercise led to a significantly higher iEMG in the first two minutes of exercise in the second bout and was correlated to the primary $\dot{V}O_2$ amplitude and there was no change in the MPF. These results indicate an increase in motor unit recruitment following prior heavy exercise as opposed to an increased firing frequency or recruitment of higher threshold motor units. An explanation for this interpretation by Burnley et al. (2001) was aided by Hughson et al. (2000) who suggested that recruitment of more fibres was needed to maintain power output and the increase in the O_2 cost of exercise. This contradicted the findings of Scheuermann et al. (2001) as described previously, however the exercise intensity was higher in this study and the data were normalised to different times of exercise. There was also a reduction in the steepness of the iEMG increase in the final three minutes of exercise which corresponded to a significant reduction in the amplitude of the $\dot{V}O_2$ slow component, demonstrating a very similar profile for iEMG and $\dot{V}O_2$. This provides only qualitative support that the slow component is attributed in part to an increase in motor unit recruitment. Burnley and authors highlighted that due to inter-subject variability in the later stages of the exercise bouts during this study, the change in EMG responses and the reduction in the $\dot{V}O_2$ slow component were not significantly correlated.

Tordi et al. (2003) reported findings which contradict the muscle fibre recruitment explanation for the priming effect. This study, which aimed to find explanations for the effect of prior exercise, involved two six-minute bouts of constant-load cycling for at a high intensity which were separated by ten minutes of rest, three all-out 30-seond sprint cycle tests (Wingate test), and then a further ten minutes of recovery. The performance of sprint exercise between the two constant-load bouts was in order to induce metabolic acidosis, as they hypothesised that an increased level of metabolic acidosis during leg cycling would cause a further detectable speeding of $\dot{V}O_2$ kinetics in the second bout of constant-load cycling

exercise. It was also hypothesised that the slow component would occur earlier and have a larger magnitude in the second exercise bout as a result of the fatiguing exercise. These authors found that the MRT in the second exercise bout was significantly faster than before the sprint exercise. The $\dot{V}O_2$ at the end of the exercise was not different between the two bouts. The primary amplitude time constant was significantly higher in the second heavy exercise bout, which supported the idea that induced metabolic acidosis altered the $\dot{V}O_2$ kinetics.

This was in contrast to Burnley et al. (2000; 2001; 2002b) who, as previously discussed, found that elevated $\dot{V}O_2$ in a second heavy exercise bout was not associated with a faster primary component time constant. However, these studies had different exercise models, with Burnley and co-workers using rest as recovery as opposed to sprint exercise between the two constant-load exercise bouts. Tordi et al. (2003) found that the onset of the slow component was earlier in the second bout of heavy exercise than the first, however there was no change in the EMG signal (assessing muscle fibre recruitment) which indicated no significant difference in the muscle activation between the primed and un-primed bouts. Thus, the surface EMG (sEMG) did not detect any changes in muscle fibre recruitment which could have coincided with the $\dot{V}O_2$ slow component onset, supporting the findings of Scheuermann et al. (2001). Tordi and co-workers (2003) suggested that the acidosis contributed to the increased vasodilation so enhanced muscle blood flow and O_2 delivery were accompanied by higher heart rate and cardiac output in the early stages of exercise (first few minutes). They found a more rapid adaptation of oxidative metabolism in the second bout of heavy exercise and put this down to improved O_2 delivery. However, a limitation presented by this study is that the researchers did not measure blood lactate concentration or muscle vasodilation and so they could not fully support their claim.

Wilkerson et al. (2004) followed this study by investigating whether the metabolic acidosis caused by sprint exercise would speed $\dot{V}O_2$ kinetics in a subsequent exercise bout performed at 105% of $\dot{V}O_{2\,peak.}$ In this study blood lactate concentration was measured to assess metabolic acidosis and Near Infrared Spectrometry (NIRS) was used to assess muscle blood volume and oxygenation. Subjects performed peri-maximal-intensity cycle exercise followed by a 60-minute rest. After this rest subjects then performed a multiple-sprint exercise protocol

(used as 'priming' exercise) followed by 15 minutes of rest and then a second peri-maximalintensity exercise bout. The time constant of the primary component of the second perimaximal-intensity exercise bout was not affected by the prior multiple-sprint exercise, suggesting that it was not limited by O_2 availability. The gain of the primary component increased following the sprint exercise and $\dot{V}O_2$ projected toward a higher amplitude with the same time constant.

2.3.3: Effects of exercise priming on performance

A growing body of research has observed the effects of priming exercise on sporting performance, looking specifically its effect on exercise tolerance as an indicator of performance. Prior warm-up exercise of a moderate intensity has been found to have no enhancing effect on the performance of subsequent high-intensity exercise (Bishop et al., 2001; Koppo and Bouckaert, 2001). A study by Jones and co-workers (2003) demonstrated that moderate-intensity exercise in which the same amount of work was performed as a highintensity exercise bout had very small effects on the time to exhaustion of peri-maximal exercise.

Burnley et al. (2005) conducted a study into the performance of severe intensity cycling following prior warm-up exercise compared with no prior exercise. The warm-up exercise was either moderate, heavy or sprint exercise and the subsequent exercise bout was a sevenminute severe exercise bout. These bouts were separated by ten minutes of recovery. This study found that both moderate and heavy prior exercise improved the performance of severe cycling exercise by 2-3%. Bailey et al. (2009) investigated the effect of prior high-intensity exercise on the performance of a second high-intensity exercise bout. This study manipulated the intensity of the prior exercise and the recovery duration between the two exercise bouts, and results demonstrated that high-intensity prior exercise improved exercise tolerance.

Ingham et al. (2013) more recently investigated the effect of a high-intensity warm-up consisting of running and mobility drills on the performance of an 800-metre run. Ingham and co-workers observed a significantly faster 800-metre time, indicating an improvement in running performance, when preceded by a high-intensity warm-up compared to no prior warm-up. Another study by Jones et al. (2003) found a significant increase in time to

exhaustion of peri-maximal exercise, which was preceded by a bout of high-intensity exercise, when compared to a control condition with no priming exercise. The authors speculated that an increase in blood lactate at exercise onset could be a contributing factor, which was supported by Burnley et al. (2005) who found an increase in blood lactate at the onset of the second exercise bout following prior heavy and sprint exercise. However, conflicting results by Bishop et al. (2001) showed that continuous heavy priming exercise increased blood lactate but did not have an enhancing effect on the performance of subsequent high-intensity kayak exercise test. Jones et al. (2003) also considered other possible mechanisms for the improvement in performance including the accumulation of other fatiguing metabolites and $\dot{V}O_2$ kinetics.

2.3.4: Recovery duration

Studies investigating the effects of prior exercise on a second bout of exercise have used recovery durations of 3-15 minutes. Burnley (2001; 2002b) used both six and 12 and only 12minute recoveries respectively, and Wilkerson et al. (2004) used durations of 15 minutes. Burnley et al. (2006) were the first to manipulate the duration of the recovery period between prior heavy exercise and the subsequent heavy exercise bout. They stated that the mechanism underpinning the effect of prior exercise must account for the effect and have a similar recovery duration to that of the decay in the effect of the prior exercise. This study measured the time required to restore the normal $\dot{V}O_2$ kinetic response to heavy exercise following a prior heavy bout, with the aim to clarify the mechanisms behind the observed effects. The experimental tests involved two bouts of six-minute heavy cycling exercise separated by various durations of recovery. The durations of recovery tested were 10, 20, 30, 45 and 60 minutes, where subjects would remain in a seated position. Prior heavy exercise induced a significant increase in the primary $\dot{V}O_2$ amplitude after all recovery durations up to 45 minutes however this effect was not apparent after 60 minutes recovery, with the amplitude returning to the control value. The increase in absolute primary amplitude also shown after the first bout of exercise was not evident after 45 minutes of recovery. A reduction in the slow component was observed after all recovery periods up to 45 minutes, where it was similar to the response in the control bout. These findings were temporally associated with a fall in blood lactate, which was also highly correlated to with the increase in primary $\dot{V}O_2$ amplitude which both had recovery time constants of around 14-15 minutes, and the $\dot{V}O_2$

response to prior exercise was only observed when there was also a rise in baseline blood lactate. Although this study demonstrates a correlation between the $\dot{V}O_2$ response and blood lactate, Burnley et al. (2006) state that this may be a 'proxy variable' for another process as there is no mechanistic basis for the association between blood lactate and the changes in the $\dot{V}O_2$ response.

In 2009, Bailey and co-workers manipulated both exercise intensity and recovery duration in order to understand the optimal interaction to influence $\dot{V}O_2$ kinetics and exercise tolerance. Six different combinations of either heavy, severe or no priming (control) exercise followed by three, nine or 20 minutes of recovery were performed, before a subsequent high-intensity exercise bout. The severe intensity priming exercise followed by 20 minutes of recovery was the only condition which increased the amplitude of the fast component response above the control. Exercise tolerance was improved above the control in the higher intensity exercise priming conditions with nine- and 20-minutes recovery, but was impaired with only three minutes recovery, and the time to exhaustion was significantly longer with a 20-minute recovery compared to nine minutes. The influential recovery durations were those which allowed baseline $\dot{V}O_2$ and blood lactate to return toward the control values. Bailey et al. (2009) concluded that prior exercise of an intensity which leads to a speeding of $\dot{V}O2$ kinetics alongside a recovery period of nine minutes or more can enhance the exercise tolerance of subsequent high-intensity exercise.

2.3.5: Exercise priming modalities

A large amount of research into exercise priming and the $\dot{V}O_2$ response has been conducted on cycle ergometers, these are effective apparatus for data acquisition and enable imposition of specific work rates. Jones and Burnley (2005) reviewed research on exercise priming to compare results of running and cycling exercise. It has been reported that running exercise seemed to elicit faster $\dot{V}O_2$ kinetics than cycling exercise in a control (un-primed) condition (Billat et al., 1998). The time constant of the fast component has been shown to be shorter in running compared to cycling, and the relative amplitude of the $\dot{V}O_2$ slow component seems to be smaller. Jones and Burnley (2005) highlight several possible factors contributing to this difference in exercise modalities including the amount of active muscle mass, contraction regimes, fatigue resistance and fibre recruitment. They also noted that there is a difference in the % $\dot{V}O_{2\,max}$ at which the lactate threshold occurs in cycling and running exercise. It has

been suggested that the difference in the relative amplitude of the slow component may be attributed to the greater amount of eccentric muscle contractions performed during running exercise (Pringle et al., 2002).

Burnley et al. (2002a) studied the effect of prior exercise on the $\dot{V}O_2$ kinetics during a second six-minute heavy exercise bout of isokinetic cycle sprinting. The type of exercise performed in the priming bout was manipulated throughout the study. Subjects performed either six minutes of heavy exercise (as performed in previous studies e.g. Burnley et al. (2000) and Gerbino et al. (1996)), a bout of sprint exercise consisting of a 30-second period of all-out sprint cycling, or passive warming of the lower limbs in a hot bath for a duration of 40 minutes. The sprint exercise was designed to elevate blood lactate and elicit a slight increase in muscle temperature. The passive warming was to increase muscle temperature but cause no residual increase in blood lactate. Each exercise 'priming' bout was followed by a sixminute recovery period before commencement of the heavy exercise bout. The prior heavy exercise protocol caused an increase in the absolute amplitude of the primary $\dot{V}O_2$ response and a reduction in the amplitude of the slow component. The change in blood lactate was also reduced following the prior heavy exercise bout, but the end-exercise blood lactate and $\dot{V}O_2$ responses were not different from the initial heavy exercise bout. Following the prior sprint exercise, baseline $\dot{V}O_2$ at the start of the heavy exercise was slightly higher, and blood lactate significantly higher, than those following the performance of a prior heavy exercise bout. Prior sprint exercise also increased the absolute amplitude of the primary $\dot{V}O_2$ response and reduced the $\dot{V}O_2$ slow component, similar effects to those induced by prior heavy exercise. The end-exercise blood lactate after sprint exercise was much higher than that following both the heavy exercise and passive warming protocols, and the end-exercise $\dot{V}O_2$ response to heavy exercise was significantly higher following sprint exercise compared to prior heavy exercise. Passive warming of the lower limbs had no effect on the $\dot{V}O_2$ and blood lactate responses to subsequent heavy exercise. There was no change in the amplitude of the primary component or the slow component. The blood lactate response was similar to the first heavy exercise bout in the prior heavy exercise protocol. The results from the passive warming protocol suggest that muscle temperature does not influence the $\dot{V}O_2$ responses to heavy exercise. The $\dot{V}O_2$ response to prior exercise therefore seems to be related to the performance of heavy exercise which elicits a residual blood lactic acidosis, as both the prior heavy exercise and prior sprint exercise had this in common. The $\dot{V}O_2$ response was similar despite

the significant difference in baseline blood lactate between these two conditions, suggesting that lactate accumulation may not play a 'direct role in the treatment effect' (Burnley et al. 2002a).

Rossiter et al. (2001) conducted a study investigating the effect of priming on knee extension exercise. Subjects performed two bouts of continuous high-intensity knee extension exercise each lasting six minutes, separated by a six-minute rest period. This study found a faster overall $\dot{V}O_2$ kinetic response in the second exercise bout in comparison to the first. The amplitude of the slow component was reduced in the second exercise bout, as was the phase 2 time constant. This speeding of kinetics was in contrast to previous studies such as Burnley et al. (2000) and Koppo and Bouckaert (2000) and it was speculated that this could be because of differences in the muscle mass utilised, the exercise intensity where Burnley et al. (2000) reached close to 80% $\dot{V}O_{2max}$ compared to approximately 70% $\dot{V}O_{2max}$ in this study, or the exercise modality where Rossiter et al. (2001) was the only of these three studies to involve knee extension exercise as opposed to ergometer cycling. Furthermore, Rossiter et al. (2001) was the first to show that the slow component is temporally associated with a reduction in PCr and the change in $\dot{V}O_2$ kinetics during heavy exercise following a prior high-intensity exercise bout is alongside a reduction in the PCr-derived O_2 deficit. This supports the control models for muscle respiration proposed by Mahler (1980) who suggested a relation to the PCr profiles during both the fast component and the slow component of the $\dot{V}O_2$ response to a second bout of square-wave exercise.

Koga et al. (2005) compared the pulmonary $\dot{V}O_2$ ($p\dot{V}O_2$) kinetics during upright two-leg knee extension exercise and upright cycle ergometer exercise. Subjects performed constant workrate exercise for six minutes. This exercise was of either moderate or heavy intensity and was either knee extension exercise or cycling. The two exercise modalities were performed such that the subjects were exercising at the same absolute work rate in both conditions. The gain in the $p\dot{V}O_2$ fast component was greater in knee extension exercise than cycling exercise, as was the contribution of the slow component to the overall response. The fast component time constants were not different between the conditions. This supports the statement by Rossiter et al. (2001) that they have observed no difference in the time constant of the primary/fast component between prone knee extension (Rossiter et al., 2001) and upright cycle ergometry (Rossiter et al., 1999), although it must be noted that exercise in the prone position could have been a limitation. The relative amplitude of the $\dot{V}O_2$ slow

component was higher in the knee extension exercise than the cycling. Previous evidence suggests that with the onset of a smaller muscle mass O_2 delivery is facilitated, which in turn should result in a smaller slow component in the knee extension exercise. Thus, Koga and co-workers (2005) speculated that a compromised O_2 delivery meant that less efficient, more fatigable muscle fibres were recruited which masked any perfusion improvements that may have been due to the smaller muscle mass used.

Jones et al. (2008) investigated the effect of priming exercise on the $\dot{V}O_2$ kinetics during treadmill running. Subjects performed a square-wave protocol consisting of a transition from six minutes of walking to a six-minute high-intensity running bout, followed by another six minutes of walking and then a second high-intensity six-minute running bout. This study found that there was no significant difference in $\dot{V}O_2$ kinetics between the first and second bouts of exercise, apart from a difference in baseline $\dot{V}O_2$ that was higher at the start of the second exercise bout compared to the first. This demonstrated that a prior heavy bout of treadmill running did not alter the $\dot{V}O_2$ response in a subsequent identical exercise bout. The amplitude of the phase 2 response and of the slow component were not different between bouts. This presented a different finding to previous studies conducted on cycling (Gerbino et al., 1996; Burnley et al., 2000), arm crank (Koppo and Bouckaert, 2005) and leg extension exercise (Rossiter et al., 2001). Buchheit et al. (2009) conducted a study also looking at the effect of exercise priming on running exercise. The study investigated moderate intensity field running in men, who performed two moderate-intensity exercise bouts separated by repeated-sprint exercise and then five minutes of passive recovery. These authors reported that prior sprint exercise quickened $\dot{V}O_2$ kinetics during the subsequent running bout but only in subjects who had moderately fast $\dot{V}O_2$ kinetics without warm up. The lag in local O_2 delivery in un-primed moderate intensity running seemed to affect the magnitude of the speeding of kinetics with those who had a longer lag initially showing a greater shortening of $\dot{V}O_2$ time constant.

The majority of research investigating exercise priming has used protocols which involve use of the same muscles in the prior exercise bout and the subsequent main exercise. Fukaba et al. (2002) compared the $\dot{V}O_2$ response to high intensity leg exercise (cycling) after prior heavy exercise of the same muscles with the same leg exercise after prior heavy exercise of a different muscle group (arm cranking). The authors followed a similar protocol to previous studies (Gerbino et al., 1996) with each exercise bout lasting six minutes and a recovery

baseline cycle separating the two bouts. It was demonstrated here that warm-up arm cranking exercise had no effect on the $\dot{V}O_2$ kinetics of the following exercise bout. The response in the second exercise bout in this condition was very similar to the prior leg exercise performed in the other condition. The hyperemia observed in the leg muscles at the onset of the second exercise bout was greater when prior exercise had been using the same muscle group. These findings seem to support the idea that it is not solely lactic acidosis that is accountable for the changes in $\dot{V}O_2$ kinetics and that it must be induced hyperemia at the working site which induces the response (Fukaba et al.,2002).

2.4: Influence of fatigue

Fatigue, $\dot{V}O_2$ kinetics and the power-duration relationship

Occurrence of fatigue as a result of exercise is often represented by a decrease in the efficiency of the body and is reflected in an intolerance to exercise and/or a reduction in performance. Fatigue can often be associated with a reduction in the force produced by contracting muscles (Woledge, 1998). In biological terms, a system aims to maintain the conditions of a metabolic state in order to prevent/minimise the occurrence of fatigue (Jones et al., 2011) and the $\dot{V}O_2$ slow component seems to represent a deviation from this steady metabolic state during high intensity exercise. Salvadego et al. (2010) demonstrated that the greater the amplitude of the slow component, the shorter the time to exhaustion which indicates a greater/faster development of fatigue.

Poole et al. (2016) define fatigue as "an ongoing dynamic process during highintensity exercise involving central and peripheral mechanisms that temporarily limit the power-producing capabilities of the integrated neuromuscular system." The powerduration relationship involves the plotting of constant power outputs against exercise tolerance (time). This relationship is curvilinear, and the ability to maintain exercise is increasingly difficult as the power output increases. The concept consists of an asymptote of power which separates exercise intensities where a steady state can and cannot be reached, this is known as the critical power (CP), representing the highest power output that can be sustained and also the greatest metabolic rate at which energy provision is solely oxidative. This CP threshold is situated in between the lactate threshold and the gas exchange threshold. The curvature

constant is the second component of this constant which refers to the amount of work that can be performed above the CP (Fukuba, 2003). Poole et al. (1988) compared cycling exercise performed below (heavy intensity) and above (severe intensity) CP, giving subjects a target of 24 minutes of exercise to complete. They observed that subjects could reach and maintained a steady state in gas exchange, ventilation and blood lactate when exercising below the CP and were able to complete the 24-minute cycle. On the other hand, $\dot{V}O_{2\,max}$ was reached and blood lactate continued to increase during the exercise above CP, and this led to exercise being stopped before 24 minutes. The $\dot{V}O_2$ slow component demonstrates a continued increase in $\dot{V}O_2$ as a function of time at a given work rate, deviating from a % $\dot{V}O_{2max}$ work rate (Poole et al., 2016).

A review by Burnley and Jones (2007) looked to explain the role of $\dot{V}O_2$ kinetics in establishing the power-duration relationship and their role in determining sports performance. The emergence of the $\dot{V}O_2$ slow component during heavy and severe exercise correlates with the development of fatigue, with this phase of the response adding a further cost of oxygen. The more pronounced the slow component, the greater the influence on fatigue. These authors go on to describe the role of the LT, which represents the maximum power output before the emergence of the $\dot{V}O_2$ slow component. The greater the difference between the CP (maximum lactate steady state) and the power output by the muscles during exercise performed above the lactate threshold, the steeper the slow component trajectory and thus the shorter the exercise tolerance, with exhaustion occurring soon after $\dot{V}O_{2\,max}$ is reached (Poole et al., 1988). The power-duration relationship may be determined by the interaction between the $\dot{V}O_2$ kinetics and the $\dot{V}O_{2\,max.}$ Extending the time before $\dot{V}O_{2\,max}$ is reached and thus time to exhaustion would require the rate of development of the slow component to be decreased (Burnley et al., 2007).

Exercise priming of a heavy intensity and with sufficient recovery has been shown to elicit changes in the $\dot{V}O_2$ kinetics, increase exercise tolerance and increase power output. The increase in exercise tolerance has also been associated with an increase in critical power (Miura et al., 2009) and the curve of the power-duration (Jones et al., 2003). Burnley et al. (2011) further studied the effect of heavy and severe priming exercise on $\dot{V}O_2$ kinetics and the power-duration relationship. Subjects performed a square-wave exercise test at a severe intensity to exhaustion preceded by either no exercise, prior heavy exercise or prior severe exercise. The exercise priming bouts lasted six minutes, and the recovery duration of ten

minutes. The heavy exercise was performed at an intensity above the gas exchange threshold but below CP, and the severe exercise was performed above the CP. These authors found that the prior heavy and severe exercise increased the amplitude of the $\dot{V}O_2$ primary component and reduced the $\dot{V}O_2$ slow component trajectory. Prior heavy exercise extended time to exhaustion due to an increased curvature constant of the power-duration relationship. The CP was not affected by either exercise intensity in comparison to the control condition, making this the first study to demonstrate that prior heavy exercise can increase the curvature constant without increasing the CP. An explanation speculated by Burnley and co-workers (2011) is that the performance of prior heavy exercise primed $\dot{V}O_2$ kinetics (increased aerobic contribution to early exercise, reduced amplitude and trajectory of the $\dot{V}O_2$ slow component and increased $\dot{V}O_{2\ peak}$) which reduced the rate of substrate-level phosphorylation and extended the time to $\dot{V}O_{2\ peak,}$ subsequently extending time to exhaustion and the curvature constant of the power-duration relationship. These authors concluded that the priming of $\dot{V}O_2$ kinetics without the development of muscle fatigue can increase the amount of work that can be performed above the CP.

Fatigue and critical torque during isometric contractions

For isometric muscular contractions, CP is known as critical torque (CT) and constitutes the torque-duration relationship. The development of fatigue in relation to the CT was investigated by Burnley et al. (2012). On five separate occasions, subjects performed an intermittent contraction regime (3s on, 2s off) similar to that of Bigland-Ritchie et al. (1986a) at a specific target torque, with a maximal voluntary contraction (MVC) at the end of each minute. This was to determine CT and curvature constant. Two further trials were performed with a target torque of 10% and 20% below CT. For all tests, subjects performed this contraction regime for 60 minutes or until task failure (could not maintain target torque). Results demonstrated that during contractions below the CT, MVC torque decreased and at task-end this torque was higher than that of the target, EMG increased modestly and there was a reserve of muscle activity at task failure. This shows little evidence of fatigue. Whereas during contractions performed above the CT torque decreased and EMG unavoidably increased until task failure where target torque was only reached through a maximal contraction and muscle activity during the MVC was no different to that at task-end. Peripheral fatigue was shown to increase slowly below the CT, and at a much faster rate

above it. Burnley and co-workers (2012) therefore concluded that they had found for the first time that although central and peripheral fatigue do occur below the CT, there is a threshold for the development of fatigue and the rate of development increases suddenly when CT is exceeded. However, this study used cycle ergometer exercise and these measures are difficult to make during this type of exercise. In the present study we adopted an isometric model which allows these measures to be made more easily and accurately.

As shown by Burnley et al. (2012), there is a more pronounced increase in the development of fatigue above CT. Exercise at an intensity above this threshold can lead to a loss of motor function, which has been shown by a reduction in muscle torque/power-generating capacity (Bigland-Ritchie et al., 1986a; Burnley, 2009). There are constant fluctuations in the force output of a muscle (Matthews and Muir, 1980). These fluctuations exhibit greater variation with increasing demand on the system, thus a loss of motor function as a result of exercise above CT and neuromuscular fatigue will in turn cause an increase in variation and loss of complexity in torque output. The next part of this review will go on to discuss the literature surrounding the variability and complexity of muscle torque output fluctuations, with further reference to CT and the development of fatigue.

2.5: Complexity

Variability and complexity

Any physiological system displays constant fluctuations in its output. The fluctuations in muscle force allow for efficient adaptation to the constant changes and stresses of the environment and thus is an important feature of a healthy physiological system. The variation in the force output of a muscle is commonly measured and refers to the magnitude of these fluctuations around a mean or target. This has been quantified using standard deviation (SD) and the coefficient of variation (CV) (Tracy and Enoka, 2002). However, these measures can give conflicting results when data is not normally distributed or random. There is an underlying pattern in muscle force output, where the fluctuations in force contain more meaningful structural information than the measures of variability can capture.

There is no single statistical measure that can assess the complexity of physiological systems (Goldberger et al., 2002), but rather a developing series of measures that assess different

features of a system. Fractal structures and processes which display complex variability cannot be measured with the classic geometric measurements such as length, area and volume. This is because these complex structures show structure over multiple scales of length and so they have non-integer dimensions. Complex, chaotic behaviour cannot be measured with mean and variance. The dynamics of one process can be very different from that of another, yet the mean and variance are almost identical, as complexity refers to the structure of the fluctuations within a process (Lipsitz and Goldberger, 1992).

2.5.1: Measures of complexity

Approximate Entropy (ApEn)

Entropy is a measure of the disorder or randomness of a system output (Seely and Macklem, 2004), and the amount of information needed to predict the future state of the system (Lipsitz and Goldberger, 1992). The calculation of formal entropy assumes that data is noiseless and infinite in length, however biological time series are the opposite. Approximate entropy (ApEn) was developed based on the constraints in data length in data sets such as heart rate and electroencephalograms (EEG), and thus has the ability to quantify the regularity and complexity of a wide variety of systems including those with data outputs of a relatively short (few data points) and noisy time-series (Pincus, 1991). ApEn provides a measure of system complexity, evaluating the degree of regularity and predictability of data points (Pincus, 1991; Goldberger et al., 2002). In order to calculate ApEn, the data is matched to a template of itself (self-matching) and is evaluated based on the recurrence of the pattern of the template in the data-series (Pincus, 1991; Richman and Moorman, 2000). The more regular a system output is, the lower the ApEn value and the less complex the output. A more irregular system output indicates greater complexity and has a higher ApEn value. The more complex the dynamics of an output, the less predictable the system (Lipsitz and Goldberger, 1992).

Sample Entropy (SampEn)

ApEn can become a biased measure of regularity as it counts sequences similar to that of the template, including the template itself, and can therefore be sensitive to the size of the data set and can produce lower and inconsistent values (Richman and Moorman, 2000). Sample

entropy (SampEn) was developed and characterised by Richman and Moorman (2000), a measure which does not include self-matches in its analysis.

Detrended Fluctuation Analysis (DFA)

Detrended Fluctuation Analysis (DFA) which was introduced by Peng et al. (1994) evaluates trends which exhibit fractal properties. Fractals display irregularity however, this irregularity has an underlying pattern and reveals a specific structure (Lipsitz and Goldberger, 1992). Self-similarity is a key feature of irregularity, and processes which display this feature are composed of multiple units and sub-units which make up the whole object. The term fractal applies to processes that generate fluctuations over multiple time scales as opposed to a single time scale (Goldberger et al., 2002). A fractal scaling index provides information about the range of timescales over which the fluctuations are repeated, and DFA is used to calculate the scaling parameter.

When calculating DFA, the total length of the time-series is integrated and then split into several boxes of equal length. The trend in each box is represented by a least-squares line fit to the data. The integrated time-series is then detrended and the root-mean-square fluctuation of the time-series calculated. Each time scale (number of data points) is represented by a different sized box, and this process is repeated for each in order to see the relationship between the box size (number of data points in a box) and the average fluctuations as a function of box size (Peng et al., 1994). White noise is represented as $\alpha=0.5$ and reflects a time series which is completely random and unpredictable, with each value being completely independent of any previous values (Peng et al., 1994). Brown noise, the integration of white noise and represented as $1/f$, is indicated by $\alpha=1.5$ (Peng et al., 1994). Brown noise is predictable in that each value can be predicted by the previous values. $\alpha = 1$ indicates the midpoint between the completely random white noise and the completely predictable brown noise (pink noise).

2.5.2: Complexity and ageing

Lipsitz and Goldberger (1992) proposed that human ageing is associated with and may be characterised by a progressive loss of complexity due to the impairment of and interaction between the functional components of a physiological system. Loss of system complexity is

shown by increased randomness or periodicity; a system whose characteristics change from 1/*f* or pink noise towards more white or Brownian noise (Vaillancourt and Newell, 2002; Lipsitz, 2004). Lipsitz (2004) evaluates the complexity of healthy physiological systems with regards to ageing and the resulting frailty in older adults, which is reflected in the reduction in an ability to adapt to internal and external stimuli. A healthy biological system has a rich network of biological inputs which lead to complex outputs with high functionality (Lipsitz, 2004). With ageing comes a reduction in the connections of these inputs resulting in a less complex output and a reduction in functionality, thus reducing the capacity and ability of the system to adapt to and cope with stress. With a decline in complexity over time, the human system becomes less functional and increasingly frail. This can lead to a greater likelihood of falling, injuries and a higher susceptibility to environmental and emotional stress (Lipsitz, 2004).

Healthy heart rate is an example of a physiological non-stationary time-series within the cardiovascular system which exhibits irregular, multifractal fluctuations in its output, making one of the more complex of physiological processes (Ivanov et al., 1999). The changes in structure and function of this system over time lead to a decline in the variability and complexity of heart rate, resulting in a reduced capacity to adapt to ever-growing stresses such as hypertension as the system ages (Lipsitz and Goldberger, 1992). Kaplan et al. (1991) was the first to investigate the changes in complexity of heart rate dynamics in relation to ageing. These authors studied the function of the cardiovascular control system and the process of ageing by analysing the complexity of heart rate (using EEG) and blood pressure (arterial tonometry) in a group of young adults (21-35 years) compared to an elderly group (62-90 years). This study revealed fractal scaling in the fluctuations of both cardiovascular dynamics observed. These authors used ApEn to measure complexity and found that the ApEn values for heart rate and blood pressure were lower in the elderly than in the young. This showed that older subjects had less complexity in their electrocardiographic (R-R) interval and blood pressure than the young group. Pikkujamsa et al. (1999) also used ApEn to measure the complexity of R-R intervals across and range of ages, finding a decrease from a young to middle age and from middle age to old age.

Research suggests that neuroendocrine function output is of a complex nature and this complexity is affected by the ageing process (Lipsitz and Goldberger, 1992). EEG measures have shown that healthy brain function exhibit chaotic fluctuations. The EEG responses to

various stimuli seem to decline with age, with changes in the anatomic structure and internal connections (Frolkis and Bezrukov, 1979) along with branching patterns of cells in the brain and spinal cord reflecting a reduction in complexity (Scheibel, 1985). The secretion of hormones also exhibits complex-like outputs reflected in the pulsation patterns. Anterior pituitary hormone, growth hormone and thyrotropin are amongst those whose secretion regulation has been shown to decline with age (Lipzitz and Goldberger, 1992). These hormones are secreted through a pattern of pulses, which with age seem to grow more dispersed and less complex, demonstrating a reduction in regulatory control. Using ApEn to measure irregularities, it has been shown that there was a decrease in the secretion of growth hormone into adulthood through puberty (Veldhuis et al., 1997) and the mean interval between thyrotropin pulses is smaller in elderly subjects in comparison to younger subjects (Greenspan et al., 1991). Fractal correlations with complex, non-stationary characteristics have also been observed in human respiratory dynamics (Peng et al., 2002), more specifically in the breathing cycle time series. The effect of ageing on the complexity of respiratory breath-by-breath dynamics was investigated by Peng et al. (2002), comparing young and elderly men and women. The use of DFA to measure fractal correlations demonstrated that the complexity of respiratory dynamics seemed to degrade with age, with the fractal correlations being less complex in elderly men compared to younger men. The mechanism behind this observation has been speculated to lie with the interaction of multiple time scales of different control and feedback systems (Hausdorff and Peng, 1996).

2.5.3: Complexity and disease

The measurement of complexity provides insight into the physiological changes related to disease and pathology (Pincus and Goldberger, 1994). It has been established that a change in the heart rate dynamics with ageing display a loss of complexity, and this is also apparent with several cardiac diseases and disorders such as heart failure (Ho et al., 1997), using measures of complexity ApEn and DFA to analyse electrocardiogram (ECG) readings and measure heart rate variability. Ho et al. (2011) studied patients with systolic heart failure and demonstrated that long-term complexity was a significant predictor of both heart transplantation and mortality. Lower complexity has also been associated with people with traumatic brain injury (Beharelle et al., 2012), with higher variability in brain signals being linked to an improvement in behaviour particularly in those with brain injury.

Disease can cause a loss of multiple structural components within a system and this can contribute to the reduction in the complexity of a physiological system output (Vaillancourt and Newell, 2002). Vaillancourt and Newell (2000) studied the dynamics (time and frequency structure) of tremor in patients with Parkinson's disease. Parkinson's patients were compared with matched controls and the complexity of the tremors in postural and resting condition was measured using ApEn. There was an increase in the regularity of the Parkinson's tremor, as shown by a decrease in ApEn. There was also a decrease in ApEn from the least affected to the most affected limb of the diseased subjects. These reductions in ApEn and thus increases in the regularity of the tremor show a loss of complexity within this patient population in comparison to the control and an association between the severity of the Parkinson's disease and the tremor regularity. ApEn enables differentiation between physiological tremor in healthy patients and tremor in those with Parkinson's disease where other measures such as frequency and amplitude cannot (Vaillancourt and Newell, 2000). Parkinson's disease patients lose approximately 80% of their dopaminergic cells before they get any behavioural symptoms (Weiner and Lang, 1989), a reduction in these cells reduces the outflow from the basal ganglia which is associated with a loss of complexity (Vaillancourt et al., 2001). A decrease in the dimensional complexity of the EEG structure is apparent in the brains of those with Alzheimer's dementia which is possibly due to non-linear EEG dynamics (Jelles et al., 1999) and lower numbers of electrophysiologically active elements such as neurones and synapses (Besthorn et al., 1995).

2.5.4: Complexity and muscle force production

Noise and variability in human movement is a common and pronounced feature. Contracting muscles do not produce a smooth and steady force (de C. Hamilton et al., 2004), but rather exhibit slight physiological tremor (Matthews and Muir, 1980). Force output fluctuations during muscular contractions have a complex, fractal structure (Newell et al., 2003). Slifkin and Newell (1999) were the first to study the structure of the variability and complexity of force output. These authors measured flexion of the index finger at a wide range of contraction intensities using ApEn. The results demonstrate that with an increase in isometric force output came an increase in the complexity. This was apparent up until a certain point (40%MVC), after which complexity started to decrease as force continued to rise. This developed an inverted-U shaped relationship between force and complexity (Slifkin and

Newell, 2000; Svendsen and Madeleine, 2010). These results demonstrated to the authors that the force output region of peak complexity represented a region where information transfer related to target force production was optimal, and greatest noise in the structure of the output was observed. For generation of force up to approximately 40%MVC, an increasing number of active motor units increases the force until all units are recruited. For forces beyond this point, the frequency of discharge can adjust the force (Kamen et al., 1995). In the optimal region of force production observed (40%MVC), both of these control strategies can be implemented, leading to maximal information transfer and structural complexity through provision of greater adaptability in scaling force production to a target (Slifkin and Newell, 2000).

An inverted-U shaped relationship between force output and complexity was found by Slifkin and Newell again in 2000. Here they found that there was an increase in complexity as demonstrated by an increase in ApEn up to 24%MVC. Complexity values then levelled at around 48%MVC, and subsequently decreased from approximately 60%MVC and continued to do so until values were similar to that found at low forces (approximately 10%MVC). Svendsen and Madeleine (2010) investigated complexity in the force output of the elbow flexors. An inverted-U shaped relationship was also apparent here with peak complexity, measured by SampEn, apparent at contraction intensities of 55-85%MVC, before subsequently declining with increasing force.

A study by Newell et al. (2003) found an increase in ApEn and thus complexity in force production in isometric index finger abduction up to 40%MVC but did not observe an inverted-U shaped relationship. This study was not testing the effect of force variation on complexity and so forces above 40%MVC were not tested. Forrest et al. (2014) was the first study to really challenge the inverted-U shaped relationship between complexity and force output. These authors investigated the effect of the pattern of ApEn and of the different signalling choices used on the complexity-contraction intensity relationship. From their results they recommended specific sampling frequencies and appropriate signal setting for measuring ApEn of muscle torque. These recommendations were different from those used by Slifkin and Newell (1999; 2000) and so the relationship between contraction intensity and complexity may be different with these changes.

Cashaback et al. (2013) investigated the effect of contraction intensity on the temporal complexity of surface electromyography (sEMG) during contractions of the biceps-brachii.

Following evidence from entropy measures that EMG signals from contracting muscles are non-linear and produce complex fractal-like characteristics (Potvin and Brown, 2004; Kaufman et al., 2007), these authors measured the complexity of the biceps-brachii muscle during three fatiguing isometric contractions of different intensities (40%, 70% and 100% of maximal elbow joint movement). This protocol resulted in a reduction in the complexity of the sEMG from 40% to 70% of elbow joint movement as shown by a decrease in multiscale entropy. The complexity of these two conditions were not different from the 100% movement condition which can be explained by previous evidence suggesting that the majority of motor unit recruitment of the biceps brachii occurs up to 70% of maximal force production, and at higher force outputs discharge rates are the greatest augmenters (Kukulka and Clamann, 1981).

2.5.5: Complexity and neuromuscular fatigue

Neuromuscular fatigue can be defined as an exercise-induced decline in maximal forcegenerating capacity (Taylor and Gandevia, 2008). Neuromuscular fatigue has effects on both maximal and submaximal exercise tasks. There are both central and peripheral components of fatigue. Central fatigue refers to that which resides in the central nervous system and peripheral fatigue exists in the muscle. Both components can be measured through supramaximal motor stimulation during and after an MVC (Gandevia, 2001). Both central and peripheral fatigue develops progressively during submaximal contractions performed to fatigue, where the neuromuscular system loses peripheral output and so increases central motor drive. This leads to a loss in force-generating capacity (Bigland-Ritchie et al., 1986a; Burnley et al., 2012).

Fluctuations observed in force output have been shown to increase during submaximal fatiguing contractions (Furness et al., 1977). It has been recognised since the early 20th century and supported by more recent literature that during sustained isometric contractions there is an increase in the variability of force output as fatigue develops and subjects exercise to exhaustion (Bousfield, 1932; Hunter and Enoka, 2001). Further investigation into variability and fatigue in isometric exercise was conducted by Contessa et al. (2009). These authors observed increased variability, measured by SD and CV, in muscle force output during isometric intermittent contractions in addition to sustained contractions as found

previously. This contraction protocol involved repeated ramp contractions which were then held for 50 seconds, with a 60 second rest between each. The force fluctuations during these intermittent contractions were found to change at a slower rate than during sustained contractions and took longer to become significant.

Fluctuations in motor unit firing rates have been associated with the fluctuations in muscle force output of the muscle (De Luca et al. 1982). Moritz et al. (2005) suggested that increased firing rate variability was a major determinant of the fluctuation in isometric force. However, Contessa et al. (2009) investigated the association between various motor unit parameters and increased force fluctuations and found that the variation in the firing rate was not significantly related to the force fluctuations. Instead, the increase in the variability in force output with fatigue could reflect changes in motor unit recruitment also discharge rate/timing as the subject gets close to task failure (Contessa et al., 2009; Hunter and Enoka, 2003). As new motor units are recruited throughout the successive contractions, the firing rate decreases, and the number of individual twitches increases as they become unfused. This would therefore increase the variability in force output.

In contrast to the increase in variability, it has more recently been observed that with the development of neuromuscular fatigue comes a gradual reduction in muscle torque output complexity and a breakdown in fractal scaling (Pethick et al., 2015; Pethick et al., 2016). Pethick et al. (2015) was the first to investigate the effect of fatigue on the complexity of the fluctuations in knee extensor force output as opposed to the amplitude of the fluctuations (variability). Subjects performed a maximal exercise test of five minutes of intermittent MVCs and a submaximal test of intermittent contractions at 40%MVC to task failure. These contractions had a 60-second duty cycle consisting of a six-second contraction and foursecond rest. Central and peripheral fatigue were measured by supramaximal femoral nerve stimulation during and after MVCs every minute. The complexity in motor unit, measured by ApEn and SampEn, declined with fatigue during both the maximal and submaximal repeated isometric contractions. The fluctuations in output also became increasingly Brownian in character, as measured by DFA, demonstrating that the reduced complexity was associated with a change in the fractal scaling as fatigue developed. The decline in complexity indicates a loss of system adaptability to external perturbations, as demonstrated here by the reduction in torque-generating capacity of the knee extensors during intermittent isometric contractions (Pethick et al., 2015). The neuromuscular system

becomes less able to rapidly adapt its motor unit output to match a required target, as the relative demand of a submaximal task increases. With the presence of fatigue came a reduction in the torque of MVCs, increasing the demand of the submaximal task. It was suggested that the loss of muscle torque complexity is due to fatigue-induced changes in the behaviour of the motor unit pool, specifically motor unit recruitment and firing rates (Pethick et al*.,* 2015). As fatigue develops, the neuromuscular system increases the number of activated motor units and their firing frequency (Adam & De Luca, 2003; 2005). Castronovo et al. (2015) reported that along with neuromuscular fatigue came an increase in common synaptic input to the motor pool and motor unit synchronisation, supporting the idea that changes in motor unit behaviour could lead to loss of muscle torque complexity.

It has recently been discovered that there is a critical threshold for the development of neuromuscular fatigue (Burnley et al., 2012). This study examined the process of fatigue development with respect to critical torque (CT). Participants performed submaximal intermittent isometric contractions of the quadriceps to task failure or 60 minutes, each contraction lasting three seconds with a two-second rest in-between. MVCs were performed every minute, with motor nerve stimulation during and after the contraction to measure central and peripheral fatigue. The submaximal contractions were performed at a range of intensities both above and below CT and it was observed that fatigue does develop below the CT however the rate of fatigue development suddenly and substantially accelerates when CT is exceeded, demonstrating a critical threshold. Burnley and co-workers (2012) propose a relationship with torque production and metabolic rate. Below CT, little increase in motor unit recruitment is needed to maintain target torque and the torque generating capacity of the muscle is high. CP has been shown to represent the point above which a progressive depletion of muscle high-energy phosphates and an accumulation of metabolites such as H^+ occurs. These processes are associated with the fatiguing process (Jones et al., 2008). Above the threshold, higher threshold and thus more fatigable motor units are recruited, meaning that additional units are needed to maintain the torque demand (Adam and Luca, 2003; Bigland-Ritchie et al., 1986b), and muscle oxygen uptake increases gradually until task failure (Vollestad et al., 1990).

Pethick et al. (2016) extended this research, investigating the effect of fatigue on the complexity of knee extensor torque with reference to CT. Subjects performed intermittent isometric contractions lasting six seconds with four seconds of rest between each for 30

minutes or task failure at a range of intensities both below and above CT (approximately 1560%MVC), an extension of their previous protocol including intensities up to 40%MVC (Pethick et al., 2015). This study demonstrated the development of fatigue for intensities both above and below CT, albeit to a greater extent above CT, as there was a reduction in MVC torque in both conditions. This supports the findings of Burnley et al. (2012). A decrease in muscle efficiency above the critical threshold results from the metabolic and neuromuscular responses which increase muscle and pulmonary $\dot{V}O_2$ (Poole et al., 1988). With metabolicinduced peripheral fatigue becoming evident above CT (Burnley, 2009; Burnley et al., 2012) and increases as a result of the additive effect of metabolites (Jones et al., 2008), it is thought this is a dominant mechanism of fatigue above CT. Pethick et al. (2018) studied the effect of priming-induced peripheral fatigue and central fatigue in the contralateral limb on muscle torque complexity and exercise tolerance of repeated submaximal isometric knee extensor contractions. Results are consistent with previous findings (Burnley et al., 2012; Pethick et al., 2015) that peripheral fatigue is the main contributor to fatigue-induced loss of torque complexity. Pre-existing peripheral fatigue reduced torque complexity at the start of the second exercise bout, whereas central fatigue caused by prior exercise of the contralateral limb did not significantly affect torque complexity during the subsequent bout using the opposite leg.

Results from Pethick et al. (2016) showed a loss of complexity and increasingly Brownian fluctuations in torque output observed through ApEn and DFA measures, exclusively at contraction intensities above CT. This reduction in complexity as a function of time above CT supports previous speculations that there is an inversely proportional relationship between metabolic rate and system output complexity (Seely and Macklem, 2012) as there is an unavoidable rise in muscle $\dot{V}O_2$ as a function of time, only above the CT/CP. More recent results are consistent with this hypothesis, where a progressive decline in muscle torque complexity during high-intensity intermittent isometric knee contractions correlated with an increase in metabolic rate (Pethick et al., in press).

2.6: The present study

The existing literature surrounding the present study demonstrates that the $\dot{V}O_2$ response to exercise can be altered following a bout of prior exercise (Gerbino et al., 1996). Priming exercise performed at a high intensity (above critical torque/power) and the presence of

neuromuscular fatigue have been shown to elicit changes in the $\dot{V}O_2$ response to subsequent heavy exercise. The effects of exercise priming have mostly been examined during cycle exercise and have demonstrated an increase in the $\dot{V}O_2$ fast component amplitude and a reduction in the amplitude of the $\dot{V}O_2$ slow component (Burnley et al., 2002b). Prior exercise can also lead to an improvement in performance during subsequent exercise, measured by an increase in exercise tolerance/time to exhaustion. Several mechanisms responsible for the changes in the $\dot{V}O_2$ response to prior exercise have been speculated. However, recent evidence suggests that the response can be attributed to changes in motor unit behaviour, more specifically an increase in motor unit recruitment (Burnley et al., 2000; Koppo and Bouckaert, 2000). Muscle force output exhibits fluctuations of a complex nature which reflect a healthy, adaptable system. With the presence of neuromuscular fatigue comes a reduction in the complexity of muscle torque output during isometric contractions. This loss of complexity occurs during contractions performed above CT (Pethick et al. 2016), where there are also changes in motor unit recruitment (Adam and Luca, 2003). More recent studies which have observed this have suggested a potential link between metabolic rate and muscle torque output complexity during exercise (Pethick et al., in press; Seely and Macklem, 2012).

The purpose of this present study is to investigate the effects of prior exercise on oxygen uptake kinetics, muscle torque output complexity and exercise tolerance during intermittent submaximal isometric contractions. It looks to further investigate the relationship between system output complexity and metabolic rate with the development of fatigue at contraction intensities above critical torque. The majority of studies have used cycle exercise to explore both $\dot{V}O_2$ kinetics and priming, this study is the first to examine the effect of exercise priming during intermittent isometric exercise. Isometric exercise is suited to measuring neuromuscular mechanisms of fatigue *in vivo* and allows the measurement of torque output complexity alongside metabolic rate. The experimental hypotheses to be tested are: 1) priming exercise will increase exercise tolerance, demonstrated by increased time to task failure; 2) priming exercise will increase the amplitude of the primary $\dot{V}O_2$ response, and reduce the amplitude of $\dot{V}O_2$ slow component; 3) priming exercise will result in a reduction in muscle torque output complexity at the start of the subsequent exercise bout as $\dot{V}O_2$ and muscle activity increase, however as priming has been shown to enhance exercise tolerance (Jones et al., 2003), it may blunt the rate of decline in muscle torque complexity.

Chapter 3 – Methods

3.1: Participants

This research study and methodology was ethically approved by the University of Kent School of Sport and Exercise Sciences Research Ethics Committee (Prop 20_2018_19). Prior to commencement of the study the laboratory itself and all equipment was health and safety checked, approved and checked at the beginning of each experimental visit to ensure that all tests were conducted in a clean, safe environment.

Ten participants (5 male and 5 female) recruited from the staff and student cohorts at the University of Kent volunteered to take part in this study. The participants were all healthy,

active adults with various training statuses with (mean ± SD) an age of 25 ± 6 years, a height of 171.4 ± 9.3 cm and a weight of 69.2 ± 12.0 kg. A minimum of ten participants was the target for this study, with this being an appropriate number to conduct statistical analyses. A sample of ten participants was appropriate for this study based on previous studies investigating priming exercise and $\dot{V}O_2$ kinetics (Burnley et al., 2002b), although this study used different methods to those used in previous studies. However, recent investigations of fatigue and muscle torque complexity which used the same methods as the present study used participant samples of 9 and 11 (Pethick et al., 2015; 2016; 2018). No prior calculations were made to determine appropriate participant numbers as none have been done previously regarding the complexity of isometric torque output with neuromuscular fatigue, this sample was a convenience sample.

Participants were given verbal and written information about the procedures, benefits, risks and commitment required for the study. Participants were free from lower limb muscular and neurological injury in the past three months. They were also asked to fill out a general health and physical activity questionnaire (Version 7) to ensure they fulfilled the necessary health requirements to participate, and each gave written informed consent prior to starting the study. Participants were advised that they could withdraw from the study at any time and were not obliged to give a reason. The participants were made aware that their data gathered from the study would be kept anonymous and any information given would be treated with strict confidence.

3.2: Testing procedure

Visits

Participants were required to visit the sport and exercise science laboratory at Medway Park on four separate occasions over a two-three-week period, and were instructed to arrive to each visit fully rested and hydrated, having refrained from strenuous exercise and the consumption of alcohol for 24 hours. Participants abstained from food or caffeine intake for the two hours prior to each visit, verbally verifying that they had done so prior to commencing each test. Each visit was separated by a minimum of 48 hours and visits were conducted at approximately the same time of day. The first of these visits was a familiarisation session, and the subsequent three visits were experimental trials (referred to as

'priming', 'non-priming' as the control condition, and 'extra MVC' throughout this text). All experimental trials followed the same preparation techniques and baseline measures, and all consisted of an exercise bout performed to task failure following an identical contraction regime (see Fig 3.1). The 'priming' and 'extra MVC' trials also included a priming exercise bout which followed the same contraction regime and preceded the exhaustive exercise. During the 'nonpriming' control trial, participants would instead rest during this time. The 'extra MVC' experimental trial consisted of an additional MVC performed one minute before the second exercise bout to task failure. This was performed in order to test for any residual effects of the priming exercise bout, before commencing the subsequent exhaustive exercise bout. A repeated measures randomised design was used to assess the effects of priming exercise on $\dot{V}O_2$ kinetics, muscle torque complexity and time to exhaustion in the three conditions.

Descriptive data

On first arrival to the laboratory, anthropometric measures including age (years), height to the nearest 0.1 cm using a Harpenden Stadiometer (Holtain Ltd., Crymych, UK) and body mass to the nearest 0.1 kg using laboratory scales (Seca GmbH & Co., Hamburg, Germany) were recorded, along with descriptive data about general activity levels. Participants wore the same active wear as that worn during the exercise trials and were unshod.

Familiarisation

The familiarisation session was designed to ensure the participants were comfortable with testing equipment and protocols that would be used during the experimental trials, in order to minimise the learning effects of the protocol. It was also in place to try to minimise, where possible, any discomfort throughout the protocol. All necessary individual settings for equipment were recorded for use in the subsequent experimental trials. This visit included all set-up procedures and baseline measures conducted during the experimental trials (described in detail below). Participants then performed an exercise bout using an identical protocol of equal duration as the priming exercise bout in the trials. This was to ensure the participants could adequately perform and maintain the contraction regime at the desired intensity for the

duration of the priming exercise bout. If the participant failed to do so, they would not be able to continue in the study.

3.3: Experimental Trials

Preparation

Prior to the placement of any equipment on the surface of the skin (NIRS optode, electrodes), the specific area was adequately prepared. Skin was shaved and abraded with a standard razor and subsequently cleaned with an alcohol-soaked cotton pad in order to reduce any impedance.

Dynamometer

During all visits in the study, participants were seated on a Cybex isokinetic dynamometer (HUMAC Norm; CSMi, Massachusetts, USA) on arrival to the laboratory for the experimental tasks. The seating position for the chair was set up using measures established and recorded during the familiarisation session. The participant's right leg was strapped to a lever arm in a seated position, with the lateral epicondyle of the femur in line with the axis of rotation of the lever arm. Hip and knee angles were set at 85 and 90 degrees respectively, using a computer set up opposite the dynamometer, with full extension at 0 degrees. A padded Velcro strap secured the right leg just above the malleoli, to the lever arm. To prevent use of the hip extensors, and any extraneous movement during the isometric contractions, straps were fastened across both shoulders and a belt secured round the waist. A screen displaying the participant's instantaneous force (a green line and diamond cursor), along with any target forces throughout the trial (horizontal purple line), was set up approximately one metre opposite the chair so that the participants had a visual representation of their performance.

Near Infrared Spectrometry (NIRS)

A rapid-inflating blood pressure cuff was wrapped securely round the top of the right leg, proximal to the belly of the vastus lateralis and was attached to a Hokanson AG101 inflation

device (D.E. Hokanson Inc., Washington, USA). A NIRS optode (Oxymon Mk III, Artinis Medical Systems, Netherlands) was placed on the surface of the skin distal to the blood pressure cuff across the largest circumference of the vastus lateralis. The NIRS optode was secured to the skin with bio adhesive tape (Hypafix) and then connected via a wire to a computer system. A piece of black cloth was placed and secured with tape over the NIRS optode in order to block out any light from the surroundings.

Surface Electromyogram (EMG)

Two Ag/AgCl electrodes (32 x 32 mm; Nessler Medizintechnik, Innsbruck, Austria) were placed on the belly of the vastus lateralis muscle on the right leg, to measure the EMG of the muscle. To ensure correct location of the electrodes, a single contraction of the vastus lateralis muscle was performed by the participant to indicate the muscle's length and belly. The electrodes were placed on the belly of the muscle, parallel to the alignment of the muscle fibres. A reference electrode was placed medial to the tibial tuberosity. The raw EMG signals were sampled at 1000 Hz, amplified (gain 1000) and band-pass filtered (10-500 Hz, Biopac MP150, Biopac Systems Inc., California, USA).

Warm-up

Once all necessary preparation and set-up procedures were complete, participants were instructed to warm-up their knee extensor muscles. This was important to ensure muscles were accustomed to the isometric exercise, and to minimise any muscle soreness. Participants were instructed to perform a series of isometric contractions, done so by performing extensions of the right knee. The researcher advised the participants to practice contractions of various intensities ranging from little effort to close to maximal effort, and of varying durations lasting a few seconds at most. This was advised for the participants to get used to the movement required, and to prepare the vastus lateralis for the range of movements that will be performed throughout the trial.

Electrical Stimulation

Prior to being seated on the dynamometer, an anode (100 x 50 mm; Phoenix Healthcare Products Ltd., Nottingham, UK) was placed on the surface of the skin, lateral to the ischial tuberosity, on the posterior aspect of the leg. This anode was a carbon rubber electrode with adhesive gel. Once the participant had verbally communicated that they had completed a sufficient warm-up, the cathode (32 x 32 mm; Nessler Medizintechnik, Innsbruck, Austria), an Ag/AgCl electrode coated in adhesive gel, was placed in the femoral triangle of the right leg over the femoral nerve. To determine the exact location of the cathode, a motor point pen (Compex, DJO Global, Guildford, UK) was placed on the area, and a single stimulation at 100 milli-Amps (mA) was given. This was repeated in several different locations, adjusting the motor point pen slightly each time. The established location was that which produced the largest twitch and greatest peak-to-peak amplitude of the compound muscle action potential (M-wave). Single (200-µm pulses) and double stimuli (200-µm pulses at 10 ms intervals) were delivered by a constant-current, variable voltage stimulator (Digitimer DS7AH, Welwyn Garden City, UK) at 400 V.

Once the location of the cathode had been established, a series of single stimulations were delivered. These stimulations started at a current of 100 mA and increased in 20 mA increments until the measured twitch torque and M-wave showed no further increase. Immediately following the plateau in torque and M-wave, the participant then performed a brief maximal voluntary contraction (MVC) lasting three seconds. Participants were instructed to extend their right leg, producing maximum force, and to hold the contraction at the peak for the three seconds. A three-second countdown followed by a verbal command of 'push' was used by the researcher to signal to the participant when to begin the contraction. A verbal command of 'stop' was used to terminate the contraction. Immediately following this MVC, participants performed two contractions at 50% of the peak torque reached during the MVC, with a few seconds in between each effort. The participant's target force was displayed as a purple line on the screen in front of them, along with a marker to indicate their force production. Participants were required to maintain the contraction at 50% MVC until the researcher delivered a stimulation at the current previously found to produce the plateau in M-wave and twitch torque. This stimulation was given in order to test whether there was any further increase in the M-wave, to verify the point of plateau during the incremental single stimulations. If there was a change in the M-wave during these stimulations at 50% MVC,

the current was increased again until the M-wave plateaued. Once this plateau was established, the current on the stimulator was increased by 30% (to 130% of the maximal stimulus) for the remainder of the experimental trial so that the stimuli delivered throughout was to be supramaximal.

Maximum Torque

To establish maximum torque, participants were instructed to perform three isometric MVCs. Each contraction again lasted three seconds and there was a minimum of 60 seconds rest inbetween them. As in the previous MVCs, a verbal countdown followed by a 'push' instruction by the researcher was given leading up to each contraction, and verbal encouragement throughout to maximise and maintain peak torque for the full three seconds. Participants were again verbally instructed to relax after three seconds using the command 'stop'. The first MVC was used to establish a maximal fresh EMG signal, which was later used to normalise all subsequent signals (see data acquisition). The second and third MVCs were accompanied by two doublet stimulations to the femoral nerve. Each doublet stimulation was performed at 100 Hz with an inter-stimulus interval of 10 ms. The first of these doublets was delivered during the maximal contraction to coincide with peak torque plateau. This doublet superimposed onto the contraction assessed the maximality of the contraction and allowed calculations of fresh voluntary activation. A second doublet stimulation was delivered at complete rest two seconds after the maximal contraction to provide a resting potentiated torque.

Resting metabolic rate

Once maximum torque had been established and the three MVCs performed, participants rested for ten minutes. A continuous-wave NIRS device (Oxymon MK III, Artinis Medical Systems, Netherlands), was then used to measure the resting metabolic rate of the knee extensors, using the methods highlighted in Ryan et al. (2012) and Ryan et al. (2013). NIRS is a non-invasive method for determining relative or absolute tissue oxygenation. Resting muscle oxygen consumption was assessed using four resting arterial occlusions. This involved rapid inflation of the blood pressure cuff to 300 millimetres of mercury (mmHg) for

ten seconds. The pressure was limited to ensure minimal pain/discomfort, and this amount of pressure has been suggested to work in previous research (Grassi et al., 2003). Each occlusion was separated by 60 seconds. Resting oxygen consumption was then calculated from the increase in deoxygenated Hb (HHb) during the occlusion, using linear regression with the first eight seconds of each occlusion.

Contraction Regime

The participants rested for another ten minutes following the assessment of resting muscle oxygen consumption, before beginning the exercise protocol. In the 'priming' and 'extra MVC' experimental trials, participants performed the priming exercise bout at the end of this rest period. The following exercise regime was performed for six minutes as the priming exercise.

The contraction regime (Bigland-Ritchie, 1986a) consisted of intermittent isometric contractions lasting six seconds at a target torque of 40% of MVC. This target was calculated based on the highest pre-test MVC during the first trial. Four seconds rest separated each contraction. The torque produced by the participant on the dynamometer and the target torque were displayed on a screen 1m in front of the seat, and the participants were instructed to match their torque to the target line on the screen. Participants were required to match this target torque for the entire duration of the six second contraction if possible. The intensity of 40% MVC ensured contractions were intended to be above critical torque in order to elicit changes in metabolic rate and torque complexity, this has been demonstrated in previous studies (Burnley et al., 2012; Pethick et al., 2016). To start the exercise bout, a verbal countdown was given followed by an instruction to 'push'. The verbal command of 'push' was used to indicate to the participant the start of each subsequent contraction, and verbal encouragement was provided throughout the six second contraction to ensure the target torque was matched for as much of the duration as possible. A command of 'stop' was used to terminate each contraction. Each minute cycle consisted of five contractions. Every sixth contraction (i.e. at the end of each minute) there was a five-second arterial occlusion involving inflation of the blood pressure cuff, to measure metabolic rate. For this, the blood pressure cuff was inflated to 300 mmHg. Five seconds rest then followed this occlusion. During the occlusion and rest period, participants were asked to rate their perceived exertion

using the Borg Scale (Borg, 1970). A printed and enlarged copy of the scale (6-20) was displayed on the wall opposite the participant and they were advised to refer to this when asked to rate their exertion. It was made clear to the participants that this rating referred to the effort during the previous five contractions, as opposed to the current state during the occlusion/rest and based only on the ability to drive the limb (Pageaux et al., 2015). Upon completion of the six-minute exercise period, participants were instructed to perform another MVC lasting three seconds, accompanied by a doublet stimulation of the femoral nerve, both during the contraction at a plateau in force and at rest two seconds following the contraction completion. In the 'non-priming' trial, participants rested for the six minutes instead of performing the priming exercise. In all trials, participants were then required to rest for 20 minutes.

All three experimental trials then involved an exercise bout during which participants were required to perform the 6:4 on: off exercise regime but this time until task failure. The inability to match the target torque (40% MVC) for the majority of the six-second contraction was considered a 'missed' contraction and this was verbally communicated to the participant as a 'miss'. Task failure was regarded as three consecutive 'misses', and when this point occurred the exercise was terminated. Immediately after the third missed contraction, there was a five-second arterial occlusion to measure metabolic rate at task failure. An identical MVC to those at the end of the priming bout was performed following the occlusion. The participant was then given five minutes rest, before an occlusion lasting three-five minutes was performed in order to normalise the NIRS signal.

3.4: Data acquisition and participant interface

Data was acquired from all peripheral devices through BNC cables connected to a Biopac MP150 (Biopac Systems Inc., California, USA) and CED Micro 1401-3 (Cambridge Electronic Design, Cambridge, UK) interfaced with a personal computer. All signals were sampled at 1000 Hz. The data was collected in Spike2 (Version 7; Cambridge Electronic Design, Cambridge, UK). A chart containing the instantaneous torque was projected onto a screen placed in front of the participant. A scale consisting of a 1 mm thick purple line was

superimposed on the torque chart and acted as a target, so that participants were able to match their instantaneous torque output (1 mm thick green line) to the target torque during the tests.

3.5: Calculations and Quantification

Determination of task failure

As mentioned previously, task failure was considered as the point where the participant could not reach or maintain the target torque (40% MVC) for the majority of the contraction on three consecutive occasions. To determine the exact point of task failure post-hoc, the mean torque for the first five contractions was used as the mean torque of all successful contractions. This would work out lower than the target torque due to the rise and fall at the beginning and end of each contraction. Therefore, the first of the three contractions with a mean torque of 5 N below that of the mean torque of the first five contractions was recorded as the point of task failure. Exercise tolerance was measured as the time taken to reach task failure during the exhaustive exercise bout.

Central and peripheral fatigue

Central fatigue was calculated based on the femoral nerve stimulations delivered during the MVCs throughout the trial. Peripheral fatigue was calculated based on the stimulations delivered immediately following the MVCs. The measure of peripheral fatigue was the decrease in potentiated doublet torque, which was the peak torque attained following the doublet stimuli at rest. Central fatigue was measured using the superimposed doublet torque calculated as the increase in peak torque immediately following the doublet stimuli delivered during the contraction. Voluntary activation was determined using the twitch interpolation technique (Belanger and McComas, 1981) and calculated using this equation:

$$Voluntary\ activation\ (\%) = 1 - \left(\frac{superimposed\ doublet}{potentiated\ doublet}\right) \times 100$$

where the superimposed doublet refers to that measured during the contraction, and the potentiated doublet is that measured at rest upon completion of the contraction.

Torque and EMG

Mean and peak torques were measured for each contraction during each test, with the mean torque determined using the steadiest (least variation) five seconds of the contraction. The EMG output for the vastus lateralis during each contraction was filtered (10-500 Hz) and full wave rectified with a gain of 1000. The average rectified EMG (arEMG) was calculated also over the steadiest five seconds of the contraction, and then normalised by being expressed as a fraction of the arEMG obtained during the MVC performed before the tests commenced.

Muscle metabolic rate

The methods of Ryan et al. (2012) and Ryan et al. (2013) were used to calculate muscle metabolic rate. To ensure an equal change in oxygenated and deoxygenated haemoglobin during arterial occlusion, the data was corrected for blood volume changes. Muscle oxygen consumption was calculated as the slope of the change in oxygenated haemoglobin and deoxygenated haemoglobin during the first three seconds of the arterial occlusion at the end of each minute of exercise, using simple linear regression.

Five minutes after completion of the fatiguing test, an arterial occlusion lasting 3-5 minutes was performed. This occlusion fully deoxygenated the tissue under the NIRS optode, and then caused a peak hyperaemic response upon release of the cuff. The maximum value during the occlusion represents fully deoxygenated haemoglobin (HHb), and the minimum value is the lowest value measured (fully re-saturated haemoglobin (Hb)). An occlusion of this duration was used to normalise the NIRS signal. The method of continuous-wave spectrometry provides relative changes in signal intensity and so the NIRS data was normalised to a physiological scale (physiological calibration) in order to provide additional quantification (Barstow, 2019). There are various methods available to measure muscle oxygenation and deoxygenation, and several types of near-infrared methods. The continuous wave method that was used in this current study has been shown to remove any influence of adipose tissue thickness (Lucero et al., 2017), which can affect the signal strength.

Variability

For each contraction, the variability in muscle torque was measured using the steadiest five seconds of each contraction. This was done by calculating standard deviation (SD) which provides a measure of the absolute variability of a time series, and coefficient of variation (CV) providing a measure of SD of a time-series normalised to the mean of this time-series. The formula was used to calculate the CV:

$$C_v = \frac{(\sigma)}{\mu} 100$$

where σ is the standard deviation and μ is the mean.

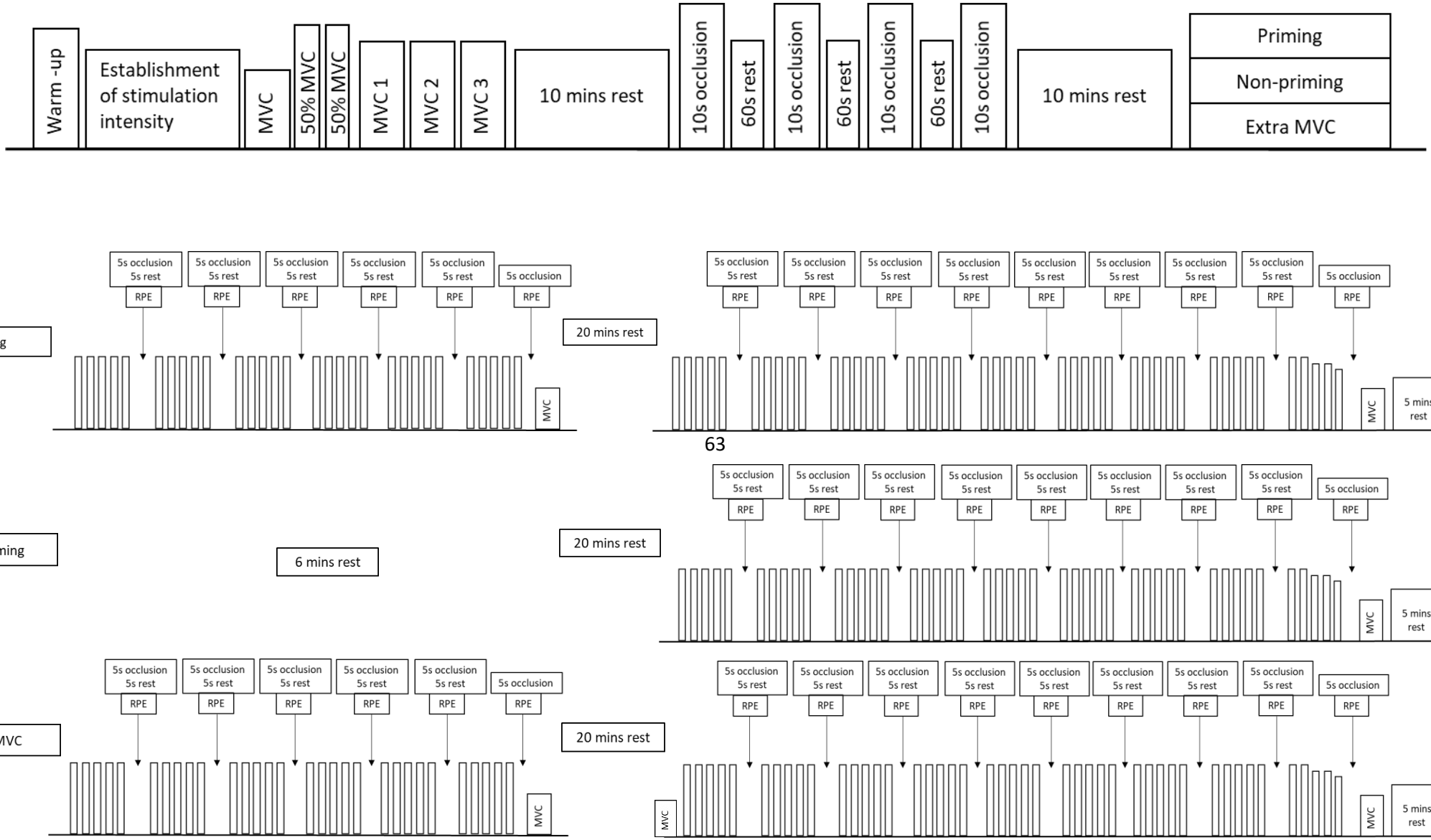
Complexity and fractal scaling

The complexity of torque output was estimated using approximate entropy (ApEn) and sample entropy (SampEn), which both assess the randomness and regularity of system output (Pincus, 1991). Detrended fluctuation analysis (DFA) was used to estimate noise colour and temporal fractal scaling (Peng et al., 1994). SampEn was recorded as raw data however was not analysed post-hoc as it has been shown that this does not add any extra information or relevance to the results (Pethick et al., 2015). ApEn and DFA were calculated post-hoc for each six-second contraction using the methods of Pethick *et al*. (2015). ApEn was calculated with a template length (m) of 2 and the tolerance (r) set at 10% of the standard deviation of torque output. ApEn provided a measure of the regularity of the system with values close to zero representing regular signals and higher values representing more irregular and thus more complex signals. DFA, calculated across time scales, provides an estimation of temporal fractal scaling of torque and allows differentiation between regularity and complexity.

3.6: Statistical analyses

Date was extracted from raw files using code custom written in MATLAB (The MathWorks, Massachusetts, USA) and statistical tests were performed in IBM SPSS Statistics V25 software (SPSS, IBM, New York, USA). Two-way repeated measures ANOVA were used to analyse muscle metabolic rate, torque complexity and torque variability measures obtained in the priming exercise bout and the subsequent exhaustive exercise bout. When main effects were observed, Bonferroni-adjusted 95% paired-samples confidence intervals were used to identify specific differences. This was based on the three comparisons subsequently made. 95% paired samples t-tests were used to compare these measures obtained in the primed and non-primed exhaustive exercise bouts. One-way repeated measures ANOVA tests were used to analyse the fatigue measures (MVC torque, potentiated doublet torque and voluntary activation) obtained from the 'MVC' trial. When main effects were observed, Bonferroniadjusted 95% paired-samples confidence intervals were used to identify specific differences. Rates of change were calculated for all measures (MVC torque, muscle metabolic rate, potentiated doublet torque, voluntary activation, torque complexity, torque variability, rate of perceived exertion) and paired samples t-tests were used to analyse all measures. If paired comparisons were not normally distributed (determined using the Shapiro-Wilk test) the Wilcoxon signed-rank test was used. Only perceived exertion at task failure failed this normality test. A p value of 0.05 was used to assess significance.

Fig. 3.1. The method of collecting baseline measures during all experimental visits, and the protocol and exercise regime for each trial.



Chapter 4 – Results

4.1: Time to task failure, torque and EMG

There was no significant difference in time to task failure between the primed (10.1 ± 3.5 min) and non-primed (11.8 ± 4.4 min) exhaustive exercise bouts (Table 4.1), suggesting that priming exercise did not alter time to exhaustion. There was a significant main effect of time ($F=50.056$, $p<0.001$) and condition ($F=52.463$, $p<0.001$) on MVC peak torque. There was a significant decrease in MVC peak torque from pre-priming to post priming (65.2 ± 14.7 Nm). There was a significant decrease in MVC peak torque from preexhaustive bout to task failure (82.3 ± 20.6 Nm). There was also a significant difference in MVC peak torque between pre-priming and pre-exhaustive bout (33.5 ± 7.4 Nm), showing that participants did not fully recover during the 20-minute rest period following the priming exercise. There was no significant difference in the rate of change in MVC peak torque between the priming bout and the exhaustive bout (2.2 ± 0.4 Nm).

There was a significant main effect of time ($F=38.510$, $P<0.001$) and condition ($F=21.371$, $p=0.001$) on EMG. There was a significant increase in EMG from the PA of the priming bout to the end of priming (9.2 ± 3.1 %MVC). There was a significant difference in EMG between the PA of the priming bout and the PA of the exhaustive bout (9.2 ± 5.8 %MVC), demonstrating that muscle activity did not make a full recovery following the priming exercise. There was no statistical difference in EMG from the PA of the primed exhaustive bout to task failure (9.2 ± 7.4 %MVC). However, there was a significant increase in EMG in the non-primed exercise bout from PA to task failure (17 ± 5.5 %MVC). There was a significantly higher rate of increase in EMG in the priming bout compared with the subsequent exhaustive exercise bout (1.4 ± -0.5 %MVC). There was also a significantly higher rate of increase in EMG in the non-primed exhaustive exercise bout compared to the primed exhaustive bout (1.1 ± -0.5).

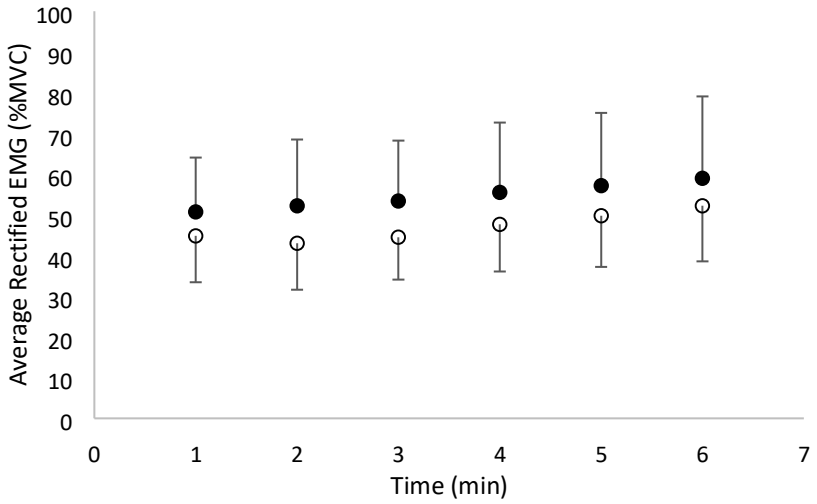


Fig. 4.1. Muscle activity during the submaximal contractions performed in the priming bout and subsequent exhaustive exercise bouts

Average rectified EMG (arEMG) amplitude during the priming (open circles) exercise bout and the subsequent exhaustive (closed circles) exercise bout. The final data point represents the last common contraction. Values are mean ± SD.

4.2: Peripheral and central fatigue

There was a significant effect of time (F=28.127, P=0.001) on doublet values. There was no significant change in doublet value from pre to post priming (-10.4 ± 4.7 Nm). There was also no change in doublet value from pre-exhaustive exercise to task failure (-6.8 ± 7.1 Nm). There was a significant difference in doublet value between pre-priming exercise and preexhaustive exercise (-14.6 ± 7.4 Nm) indicating the presence of peripheral fatigue and demonstrating that there was not a full recovery following priming after the rest period. There was no difference in the rate of change in doublet values during the priming exercise bout and the exhaustive exercise bout (-1 ± 0.3 Nm).

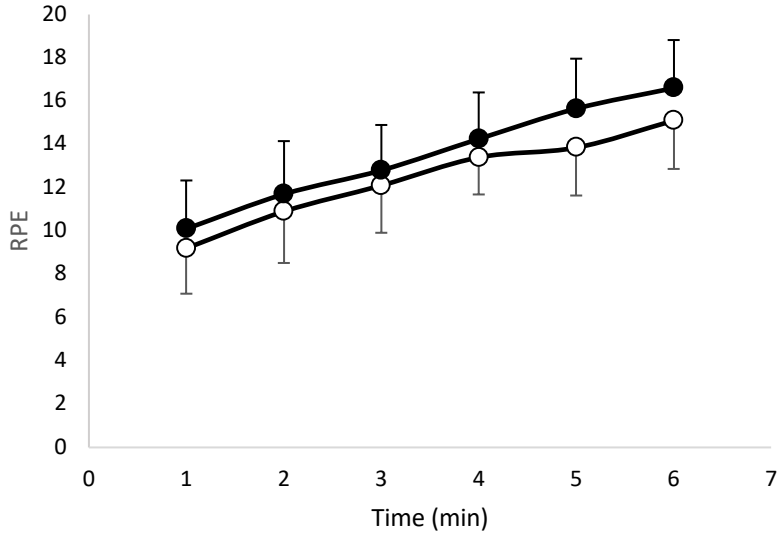
There was a significant main effect of time (F=23.159, P=0.001) and condition (F=29.247, P=0.001) on VA. There was no statistical difference in VA between pre-priming and post priming (-9.3 ± 6.7 %). There was also no difference in VA between pre-priming and preexhaustive exercise (-9.4 ± 7.6 %), indicating that the priming exercise did not elicit the development of central fatigue. There was a significant decrease in VA from pre-exhaustive exercise to task failure (15.8 ± 1.8 %), demonstrating a presence of central fatigue throughout

this exercise bout. There was no difference in the rates of change in VA between the priming and exhaustive exercise bout (-0.4 ± 0.4 %) indicating that priming exercise did not have any effect on the rate of development of central fatigue.

4.3: Perceived exertion

There was a no difference in the ratings of perceived exertion (RPE) between the PA of the priming bout and the PA of the subsequent exhaustive bout (0.8 ± 0.3). There was also no difference in RPE between the primed and non-primed exhaustive exercise bouts at task failure (0.5 ± 1.3).

A



B

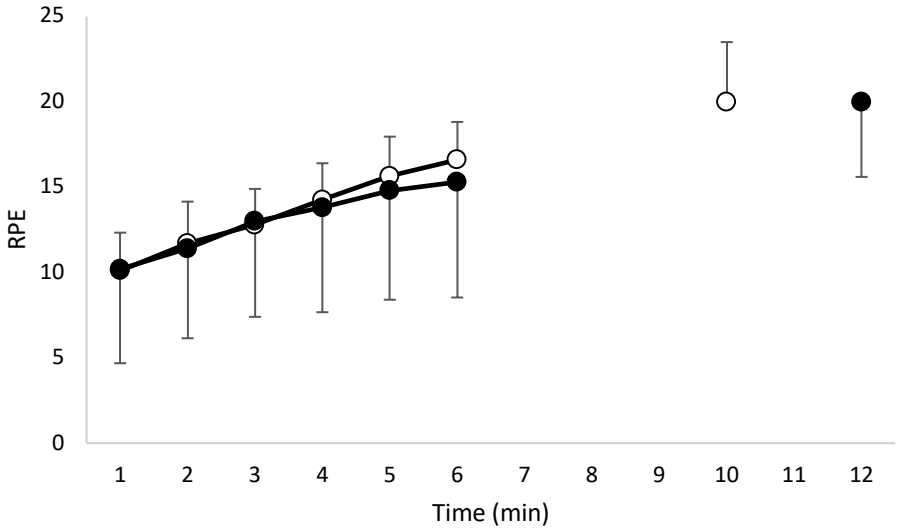


Fig 4.2. Mean RPE. Comparison between the priming bout and subsequent exhaustive bout, and between the primed and un-primed exhaustive bouts.

Mean RPE values during the priming (open circles) exercise bout and the subsequent exhaustive (closed circles) exercise bout (A), and mean RPE during the primed (open circles) and non-primed (closed circles) exhaustive exercise bouts (B). The final data point for the priming exercise bout (A) and penultimate data point for the exhaustive bouts on both graphs represent the last common contraction. The final data point for the exhaustive exercise bouts represents $\dot{V}O_2$ at task failure. Values are mean ± SD.

Table. 4.1. Voluntary torque, potentiated doublet torque, voluntary activation, EMG, and RPE responses during contractions in the priming, control and extra MVC trials.

Parameter	**Priming**	**Control**	**Extra MVC**
Time to task failure (min)	10.1 ± 3.5	11.8 ± 4.4	12.6 ± 6.8
Global fatigue			
Pre MVC, Nm	221.4 ± 59.3	219.5 ± 53.2	234.5 ± 65.3
Post priming MVC, Nm	161.6 ± 46.2*	-	169.3 ± 50.6
Pre-exhaustive bout MVC, Nm	-	-	201.0 ± 57.9*
Peak MVC at task failure, Nm	113.2 ± 37.4	118.4 ± 41.8	118.7 ± 37.3*
Mean MVC at task failure, Nm	92.3 ± 33.1	95.2 ± 33.4	99.8 ± 34.3
Peripheral fatigue			
Pre-doublet, Nm	84.4 ± 25.2	85.8 ± 27.0	90.8 ± 31.4
Post priming doublet, Nm	75.4 ± 23.9	-	80.4 ± 26.7
Pre-exhaustive bout doublet, Nm	-	-	76.2 ± 24.0*
Doublet at task failure, Nm	61.2 ± 26.7	66.0 ± 31.6	69.4 ± 31.1
Central fatigue			
Pre VA, %	88.9 ± 10.3	90.5 ± 6.0	88.6 ± 10.9
Post priming VA, %	82.6 ± 16.4	-	79.3 ± 17.6
Pre-exhaustive bout VA, %	-	-	79.2 ± 18.5
VA at task failure, %	73.5 ± 18.2	68.6 ± 19.5	63.4 ± 20.3*
Surface EMG			
arEMG at PA of priming, % MVC	43.0 ± 10.3	-	37.0 ± 13.9
arEMG at end of priming, % MVC	52.2 ± 13.4*	-	44.7 ± 19.8
arEMG at PA of exhaustive bout, % MVC	52.2 ± 16.1*	43.6 ± 10.9	37.0 ± 13.9
arEMG at task failure, % MVC	61.4 ± 23.5	60.6 ± 16.4*	51.2 ± 22.2
RPE			
RPE at PA of priming	10.9 ± 2.4	-	10.4 ± 2.3
RPE post priming	15.1 ± 2.2	-	15.1 ± 2.4
RPE at PA of exhaustive bout	11.7 ± 2.5	10.2 ± 2.2	11.5 ± 2.2
RPE at task failure	18.9 ± 2.6	19.4 ± 1.3	19.5 ± 1.1

Values are means ± SD. * indicates a significant change in values. PA = primary amplitude.

4.4: Variability and complexity

There was a significant main effect of time ($F=28.898$, $p<0.001$) and of condition ($F=13.979$, $p=0.005$) on standard deviation (SD) comparing the priming bout with the exhaustive bout in the same trial. There was no significant change in SD from the PA of the priming bout to the end of priming (0.08 ± 0.24 Nm) as indicated in Table 4.2. There was also no difference in SD between the PA of the priming bout and the PA of the exhaustive bout (0.11 ± 0.04 Nm). There was a significant increase in SD during the primed exhaustive exercise bout, from PA to task

failure (3.14 ± 1.94 Nm) and also in the non-primed exhaustive bout from PA to task failure (2.75 ± 1.33 Nm). There was a significantly higher rate of increase in SD during the exhaustive bout compared to the priming exercise bout (0.44 ± 0.02 Nm). There was no difference in the rates of change in SD between the primed and non-primed exhaustive exercise bouts (0.12 ± 0.26 Nm).

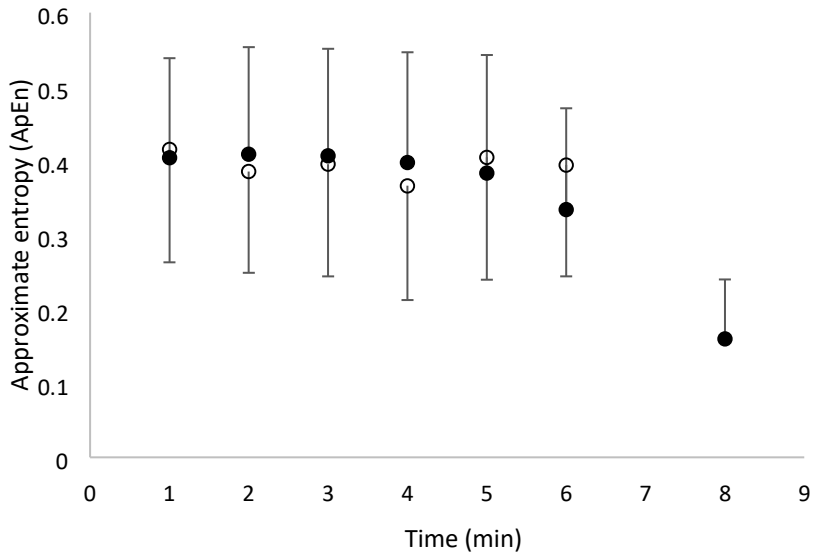
There was a significant main effect of time ($F=38.510$, $p<0.001$) and condition ($F=21.371$, $p=0.001$) on CV. There was no change in CV during the priming bout, from PA to end of priming (0.04 ± 0.12 %), indicating no change in the extent of variability in relation to the mean. There was also no significant difference in CV between the PA during priming and the PA during the exhaustive exercise bout (-0.06 ± 0.28 %). There was an increase in variability shown by a significant increase in CV during the exhaustive bout from the PA to task failure (4.18 ± 2.12 %). The rate of increase in CV in the exhaustive exercise bout was significantly higher than the priming bout (0.61 ± 0.00 %) but there was no difference in the rate of change in CV between the primed exhaustive exercise and the nonprimed exercise (0.11 ± 0.05 %).

There was a significant main effect of time on ApEn when comparing the priming bout with the exhaustive bout ($F=44.733$, $P<0.001$). There was also a significant main effect of condition on ApEn ($F=14.611$, $p<0.004$). There was no significant change in ApEn during the priming bout (0.01 ± 0.02) indicating no change in the complexity of muscle torque output, nor was there a difference between the PA of the priming bout and the PA of the exhaustive bout (0.03 ± 0.01). There was a significant decrease in ApEn during the primed exhaustive bout, from PA to task failure (-0.25 ± 0.03), demonstrating a decrease in complexity as fatigue developed. There was a significant decrease in ApEn, and thus decrease in complexity, in the non-primed exhaustive bout from PA to task failure (-0.23 ± 0.00). The rate of decrease in ApEn was significantly greater in the exhaustive exercise bout compared to the priming bout (0.04 ± 0.00) where fatigue was developing. There was no significant difference in the rate of change in ApEn between the primed exhaustive bout and the non-primed exhaustive bout (0.01 ± 0.00).

There was a significant main effect of condition on DFA-α ($F=18.872$, $p<0.002$), and a significant interaction effect of time and condition ($F=28.713$, $p<0.001$). There was no significant change in DFA-α during the priming bout (0.00 ± 0.02). There was no significant change in DFA-α from the PA of the priming bout to the PA of the exhaustive bout (0.05 ± 0.00). DFA-α significantly increased during the primed exhaustive exercise bout, becoming more Brownian in colour, from PA to task failure (0.17 ± 0.05) showing a reduction in

complexity as a result of priming. There was a significant increase in DFA-α in the nonpriming exercise bout from PA to task failure (0.15 ± 0.08) as fatigue developed. There was a significantly higher rate of increase in DFA-α during the exhaustive exercise bout than throughout the priming exercise bout (0.02 ± 0.01). There was no difference in the rate of change in DFA-α between the primed and non-primed exhaustive exercise bouts (0.00 ± 0.01).

A



B

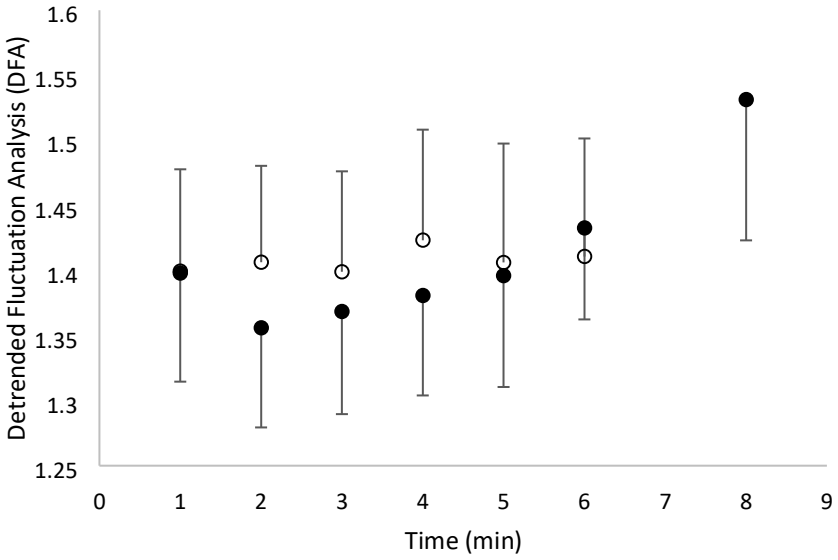


Fig. 4.3. Muscle torque complexity during submaximal contractions. Comparison between the priming bout and subsequent exhaustive bout, and between the primed and non-primed exhaustive bouts.

Approximate entropy (A) and Detrended Fluctuation Analysis (B) during the priming (open circles) and exhaustive (closed circles) exercise bouts. The penultimate data point represents the last common contraction. The final data point for the exhaustive exercise bout represents mean task failure. Data are mean ± SD.

Table. 4.2. Complexity, variability and coefficient of variance values obtained during intermittent isometric contractions in the priming and control trials.

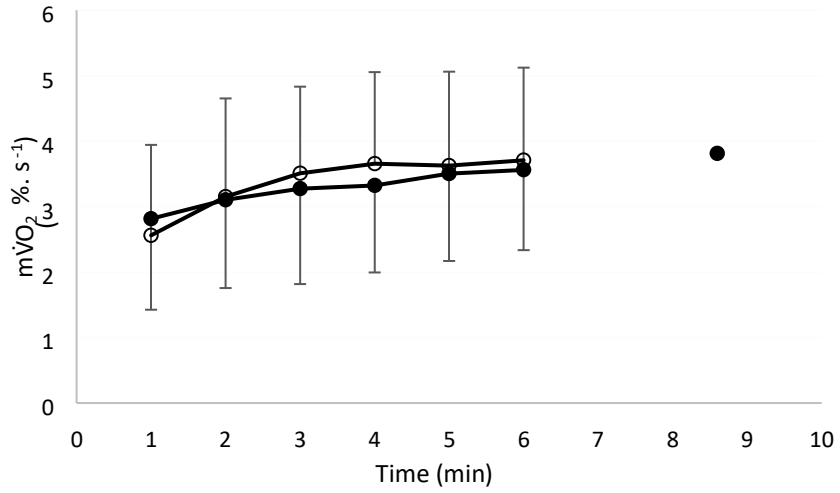
Parameter	Priming	Control
ApEn		
ApEn at PA of priming	0.38 ± 0.10	-
ApEn at end of priming	0.39 ± 0.12	-
ApEn at PA of exhaustive bout	0.41 ± 0.11	0.38 ± 0.10
ApEn at task failure	0.16 ± 0.08*	0.15 ± 0.10*
DFA-α		
DFA-α at PA of priming	1.41 ± 0.06	-
DFA-α at end of priming	1.41 ± 0.08	-
DFA-α at PA of exhaustive bout	1.36 ± 0.06	1.41 ± 0.06
DFA-α at task failure	1.53 ± 0.11*	1.56 ± 0.14*
SD		
SD at PA of priming, Nm	2.10 ± 0.55	-
SD at end of priming, Nm	2.18 ± 0.79	-
SD at PA of exhaustive bout, Nm	2.21 ± 0.59	2.35 ± 0.62
SD at task failure, Nm	5.35 ± 2.53*	5.10 ± 1.95*
CV		
CV at PA of priming, %	2.50 ± 0.77	-
CV at end of priming, %	2.54 ± 0.89	-
CV at PA of exhaustive bout, %	2.44 ± 0.49	2.53 ± 0.72
CV at task failure, %	6.79 ± 2.61*	6.62 ± 3.58

Values are means ± SD. * indicates a significant change in values. PA = primary amplitude.

4.5: Metabolic rate

The parameters of the mean $\dot{V}O_2$ response in the priming exercise bout and the subsequent exhaustive exercise bout are illustrated in Fig. 4.3. There was a significant main effect of condition ($F=11.553$, $p=0.009$) on $\dot{V}O_2$. There was a significant increase in $\dot{V}O_2$ throughout the priming bout, from PA to end of priming (0.50 ± 0.10 %. s^{-1}). There was no difference in $\dot{V}O_2$ between the PA of the exhaustive bout and task failure (0.60 ± 0.20 %. s^{-1}), nor was there a statistical difference in $\dot{V}O_2$ between the PA of the priming bout and the PA of the exhaustive bout (0.00 ± 0.10 %. s^{-1}) suggesting that priming exercise did not alter the $\dot{V}O_2$ response to exercise. There was a significant increase in $\dot{V}O_2$ from PA to task failure in the non-primed exercise trial (0.70 ± 0.20 %. s^{-1}). There was a significantly higher rate of increase in $\dot{V}O_2$ during the priming exercise bout compared to the exhaustive bout (0.10 ± 0.00 %. s^{-1}). There was no difference in the rate of change in $\dot{V}O_2$ between the primed and non-primed exhaustive exercise bouts from the PA to task failure (0.10 ± 0.1 %. s^{-1}).

A



B

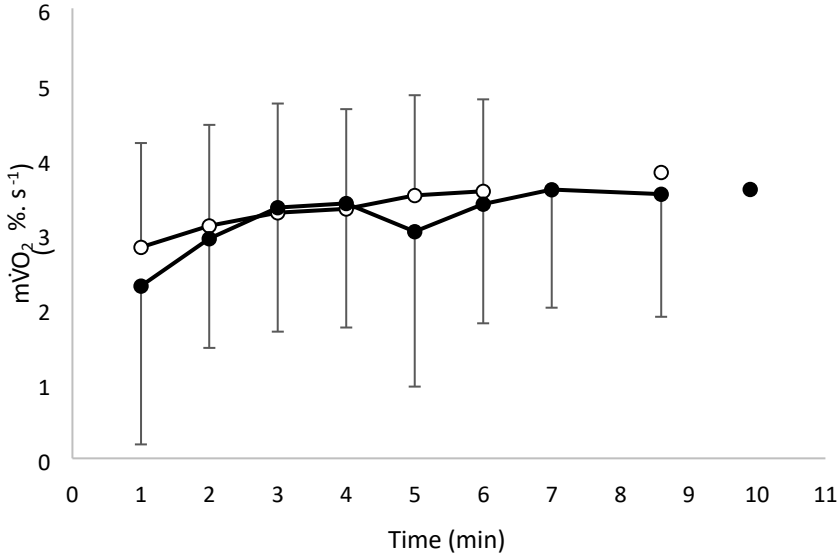


Fig. 4.4. Mean O_2 uptake ($\dot{V}O_2$) response. Comparison between the priming bout and subsequent exhaustive bout, and between the primed and un-primed exhaustive bouts.

Mean $\dot{V}O_2$ during the priming (open circles) exercise bout and the subsequent exhaustive (closed circles) exercise bout (A), and mean $\dot{V}O_2$ during the primed (open circles) and non-primed (closed circles) exhaustive exercise bouts (B). The final data point for the priming exercise bout (A) and penultimate data point for the exhaustive bouts on both graphs represent the last common contraction. The final data point for the exhaustive exercise bouts represents $\dot{V}O_2$ at task failure. Values are mean ± SD.

Chapter 5 – General Discussion

5.1: Main Findings

The purpose of this present study was to investigate the effects of prior exercise on oxygen uptake kinetics, muscle torque output complexity and exercise tolerance during intermittent submaximal isometric contractions. The hypotheses investigated in this present study were 1) exercise priming would increase exercise tolerance demonstrated by an increase in time to task failure in a subsequent exercise bout to exhaustion; 2) exercise priming would alter the $\dot{V}O_2$ response during a subsequent exercise bout by increasing the amplitude of the fast component and reducing that of the slow component; and 3) exercise priming would result in a reduction in the complexity of muscle torque output at the start of a subsequent exercise bout, but may blunt the rate of decline in complexity throughout the second exercise bout. There are several novel findings of this present study. The amplitude of the EMG response in this isometric contraction model was higher at the start of the primed exhaustive exercise bout compared to the start of the priming bout. Exercise priming in this modality also led to the presence of peripheral fatigue at the start of the subsequent exhaustive bout, which has also not been shown before. There was no difference in the rate of fatigue progression between the primed and un-primed exhaustive exercise bouts. Other main findings from the present study include no difference in the time to task failure between the primed and unprimed exhaustive exercise bouts. There was also no difference in the $\dot{V}O_2$ response to exercise between an exhaustive bout that was preceded by a prior exercise bout and an unprimed identical exhaustive exercise bout. There was no change in the $\dot{V}O_2$ response at the beginning of the exercise bout to fatigue compared to that at the beginning of the priming exercise bout. Complexity decreased throughout fatiguing exercise however, there was no difference in the rate of DFA-α and ApEn progression in the primed exhaustive bout when compared to the un-primed bout, indicating no difference in the change in complexity over time throughout exhaustive exercise between priming and non-priming.

5.2: Exercise priming and time to exhaustion/exercise tolerance

The vast majority of research investigating the effects of exercise priming have involved cycling exercise. This present study was the first to examine this concept in intermittent isometric

contractions. The influence of exercise priming on whole-body exercise is likely to produce different results to exercise of an individual limb or muscle, therefore direct comparisons of findings with recent literature regarding the effects of exercise priming are difficult to make. It has been shown that exercise modality can influence the effects of exercise priming on subsequent exercise, and this has specifically been examined between cycling and running exercise (Jones and Burnley, 2005). The effects of priming are broadly similar between cycling and running, but there is a clear difference in $\dot{V}O_2$ kinetics between these two exercise modalities (Carter et al., 2000). We can speculate that differences in findings when comparing the present study to previous literature could be partly attributed to the exercise modality used, as there is a difference between what we have found here and what has been found in cycling/running exercise.

This present study's findings are not consistent with those found in previous research studying exercise priming on performance. Previous studies have investigated the effects of prior cycling exercise on a subsequent high-intensity exercise bout and have observed that heavy prior exercise improves subsequent cycling performance as measured by exercise tolerance (Burnley et al., 2005; Burnley et al., 2011), and this can be by up to 15-30% (Bailey et al. 2009; Jones et al. 2003). In contrast, in the present study we found that prior high intensity exercise did not affect time to exhaustion of a subsequent heavy exercise bout. As well as the previously highlighted difference in exercise modalities used in the studies (cycling vs intermittent isometric contractions), the difference in results between the present study and Burnley et al. (2005) could be partly attributed to the fact that these authors used severe intensity exercise as the exhaustive bout, whereas exercise performed in the present study was of a severe intensity in both priming and exhaustive bouts. There is support for the results of the present study by previous research, which have demonstrated no improvement, in fact an impairment, in performance as measured by exercise tolerance of high-intensity exercise following high-intensity priming exercise (Ferguson et al., 2007). Albeit a difference exercise modality, Wilkerson et al. (2004) concluded that prior sprint exercise did not improve exercise tolerance to subsequent peri-maximal exercise, with time to exhaustion being reduced by around 19%.

The recovery duration is important for restoring baseline $\dot{V}O_2$ values before the subsequent exercise bout (Bailey et al. 2009; Burnley et al., 2006) and a significant difference in exercise tolerance has been observed with various recovery durations during cycle ergometer exercise.

Baseline $\dot{V}O_2$ can be restored to its control value after a recovery duration of 20 minutes (Burnley et al. 2001; Burnley et al., 2006), however it has been shown that there is a gradual decay in the effects of exercise priming throughout passive recovery and after 60 minutes of rest the control state is fully restored (Burnley et al., 2006). Bailey et al. (2009) manipulated the recovery duration between the two exercise bouts using durations of three, nine and 20 minutes, and results demonstrated that durations of nine minutes and 20 minutes were of sufficient length to increase exercise tolerance in the subsequent exercise bout. The results by Bailey et al. (2009) were consistent with previous studies (Burnley et al., 2001; Burnley et al., 2006) showing that a 20-minute recovery period elicited the greatest time to exhaustion and this correlated with a reduction in $\dot{V}O_2$ values back to baseline level at the start of the exhaustive exercise bout. The findings of Burnley et al. (2005) were also supported by Bailey et al. (2009) who used a recovery duration of ten minutes which improved exercise tolerance. The present study used a recovery duration of 20 minutes. This duration elicited results in line with those of previous work (Bailey et al., 2009; Burnley et al., 2006; Burnley et al., 2001) where we found that the 20-minute rest enabled the recovery of $\dot{V}O_2$ by the start of the second exercise bout. However, this recovery duration did not lead to an improvement in time to exhaustion. The aforementioned recent studies were conducted on cycling exercise. The isometric exercise performed in the present study may require a different recovery duration in order to improve time to exhaustion, even though the 20-minute rest period seemed to effectively restore baseline $\dot{V}O_2$ to control value. This also suggests that the restoration of baseline $\dot{V}O_2$ is not reliable as a marker of readiness to begin exercise again.

5.3: Metabolic rate

The metabolic results of the present study as shown by Fig. 4.3. display an overall trend similar to that described by Burnley et al. (2000) and Koppo and Bouckaert (2000). There is an initial rise in $\dot{V}O_2$ at the onset of exercise. Following this initial increase, $\dot{V}O_2$ continues to rise but at a slower rate, which represents the emergence of the slow component. This is in line with the known response to exercise performed above the lactate threshold (LT) (Whipp and Wasserman, 1972). We used NIRS in this present study as a measure of oxygen consumption of the individual muscle in question as opposed to breath-by-breath pulmonary gas exchange measured by mass spectrometry which was used by the aforementioned authors. NIRS is a more direct measure of muscle oxygenation, but only for a very small volume of

muscle. Measures of pulmonary gas exchange pick up much more information, which includes that from surrounding tissues as well as the individual muscle of interest. This makes it difficult to make direct comparisons of respiratory measures between these studies.

The oxygenation of the muscle as measured by NIRS in the present study was not significantly different between the first two minutes of the initial exercise bout and the second bout. The priming exercise did not influence the speed of the $\dot{V}O_2$ response. A speeding effect of the $\dot{V}O_2$ response as a result of exercise priming was originally observed in high-intensity cycle ergometer exercise (Gerbino et al., 1996; MacDonald et al., 1997; Bohnert et al., 1998). Further studies addressing the effect of prior cycling exercise on subsequent cycling $\dot{V}O_2$ kinetics, which apportioned the different kinetic components, observed different findings (Burnley et al., 2000; Koppo and Bouckaert, 2000). These studies which are two of first that used a triple exponential model to examine the separate components of the response found that there was no change in the amplitude or the time constant of the $\dot{V}O_2$ fast component response during a high-intensity exercise bout preceded by high-intensity priming exercise and thus speculated that muscle oxygen utilisation is not affected by priming exercise. Although, these studies measured breath-by-breath gas exchange as opposed to NIRS, the present study supports these more recent findings as there was no significant difference between the rate of change in the $\dot{V}O_2$ response between the primed and un-primed exhaustive exercise bouts. Exercise priming has been shown to have no significant effect on the $\dot{V}O_2$ time constant or the speed of the overall response as demonstrated in early literature (Gerbino et al., 1996; MacDonald et al., 1997, Bohnert et al., 1998). However, the measures of $\dot{V}O_2$ derived from NIRS in the present study cannot be used to infer the value of the time constant. It may actually be that this data may not be sensitive enough to detect a priming effect.

In contrast to the present study and the findings of Koppo and Bouckaert (2000), Burnley et al. (2002b) observed a greater $\dot{V}O_2$ response during the first two minutes of the second exercise bout compared to the initial priming bout, showing an increase in the primary amplitude of the response. These authors also observed that the $\dot{V}O_2$ response remained greater throughout the duration of the second heavy exercise bout than it did throughout the first, whereas there was no difference in the overall response between the two bouts in the present study. Wilkerson et al. (2004) showed no effect of priming on the $\dot{V}O_2$ time constant but an increase in the amplitude of the primary component, albeit following multiple sprint

priming exercise and a longer recovery duration. These previous studies (Burnley et al. 2002b; Wilkerson et al., 2004) were conducted on cycle exercise and although they did used NIRS, they measured the oxygenation status of the muscle but did not measure $\dot{V}O_2$.

Although exercise priming in intermittent isometric exercise has not been examined before as it has here, other investigators have studied the effects in the exercise modality but with different regimes (Rossiter et al., 2001). In contrast to the present study's findings, these authors demonstrated that prior high-intensity exercise sped the overall $\dot{V}O_2$ kinetics of a subsequent identical high-intensity exercise bout of knee extension exercise of the same duration. We observed in the present study that a prior exercise bout did not significantly alter the rate of change in the slow component phase of the $\dot{V}O_2$ response during a subsequent identical exercise bout when compared to an un-primed exercise bout. The exercise bouts used by Rossiter et al. (2001) were both six minutes in duration, as was the priming exercise bout in the current study. However, the exercise was constant rhythmic alternate-leg knee extensions which differed from the single-limb intermittent isometric contractions used presently, and the second bout of exercise in the present study was of an exhaustive nature. These differences in exercise regime could both therefore contribute to the differences in findings between this study and the present.

Further to the influences of the recovery duration on exercise tolerance previously mentioned, the effect on $\dot{V}O_2$ can be discussed more specifically. In this present study, we found that following a priming bout and 20 minutes of recovery there was no difference in the $\dot{V}O_2$ in the first two minutes of exercise between the exhaustive bout and the priming bout. This aligns with the findings of Bailey et al. (2009) who observed a return of $\dot{V}O_2$ back to baseline levels at the start of the second bout of cycle exercise following recovery duration of nine and 20 minutes. Rossiter and co-workers (2001) and Jones et al. (2008) observed a higher $\dot{V}O_2$ at the start of the second exercise bout compared to the first, indicating that $\dot{V}O_2$ did not recover fully to baseline level before the onset of the second bout. The recovery duration in both of these studies was six minutes, shorter than that used in the present study (20 minutes), which could explain why these findings differ from those found in the present study and by Bailey et al., (2009). The higher $\dot{V}O_2$ at the start of the second exercise bout than the start of the first indicates that $\dot{V}O_2$ has not recovered to baseline values throughout the recovery period. This could partly explain differences in the speed of $\dot{V}O_2$ kinetics in the second bout observed by Rossiter et al. (2001) which were not observed in this present study.

5.4: EMG response

EMG data has been analysed during exercise in order to investigate the mechanisms of the $\dot{V}O_2$ response to exercise, and it has become increasingly apparent that changes in the activity of the muscle may contribute, in particular to the emergence of the $\dot{V}O_2$ slow component response (Barstow et al., 1996; Krustrup et al., 2004; Shinohara and Moritani, 1992).

Progressive research into exercise priming and the mechanistic effects on subsequent exercise have grown to speculate around the influence of muscle activity and the changes elicited by prior exercise (Burnley et al., 2001; 2002b; Koppo and Bouckaert, 2000; Scheuermann et al., 2001; Tordi et al., 2003). The present study showed that the EMG response at the beginning of the exhaustive exercise bout was higher than that at the start of the priming bout, indicating greater muscle activity at the onset of the second exercise bout as a result of the priming. The two exercise bouts followed essentially the same pattern of increase thereafter. Burnley et al. (2002b) also found that there was a higher iEMG response at the start of a second heavy exercise bout which was preceded by prior heavy exercise, following previous speculation (Burnley et al., 2001). Specifically, a 19% increase in the averaged iEMG in the first two minutes was observed compared to the priming exercise bout by Burnley et al. (2002b). The priming exercise was the same length as in the present study and both studies used heavy exercise; however, this was cycle exercise. Scheuermann et al. (2001) and Tordi et al. (2003) did not find any change in iEMG during a second bout of heavy cycling exercise that correlated with $\dot{V}O_2$ kinetics. These authors investigated the link between the $\dot{V}O_2$ slow component and the iEMG response but found no correlation between the emergence of this kinetic phase and changes in muscle activity. These findings contested the speculation by Burnley and co-workers (2005) that motor unit recruitment could be a possible mechanism of the priming effect as they found that there was no difference in the EMG response between the first and second exercise bouts despite an earlier emergence of the slow component in the second bout (Tordi et al. 2003). Burnley et al. (2002b) considered the normalisation of the EMG signal as a possible explanation of the difference between their findings and the previous observations by Scheuermann et al. (2001), as they ran this method at the beginning of the exercise whereas Scheuermann et al. (2001) normalised their EMG data at the end of exercise trials. The results of the present study suggest that there were changes in the EMG response as a result of priming, in support of Burnley et al. (2002b), but the EMG was

normalised to the participants' MVC as opposed the start or end of exercise, which does not support the suggested explanation behind the different findings.

5.5: Peripheral and central fatigue

The present study demonstrated that exercise priming led to the presence of peripheral fatigue at the onset of the second exercise bout however did not show any significant enhancement of central fatigue at this point compared to the beginning of the priming bout. The progression of fatigue, as measured by the rate of change, was not altered by prior exercise. Burnley et al. (2012) investigated the development of fatigue at different exercise intensities and found that for exercise above CT fatigue was present and progressed at a faster rate than exercise below CT. Although this present study did not manipulate the exercise intensity, the contractions were performed at an intensity above CT and the development of peripheral fatigue observed is in line with the findings of Burnley et al. (2012) who using the same exercise modality of intermittent isometric contractions. The extent of this fatigue at task failure and the length (minutes) of the exhaustive trials supports the exercise bouts being performed in the severe exercise domain. Pethick et al. (2016) used the same type of exercise and the same contraction regime as the present study and demonstrated a development of fatigue at intensities above CT. As in this present study, both Burnley et al. (2012) and Pethick et al. (2016) also used peripheral stimulation alongside MVCs to examine the presence and development of fatigue. The present study strengthens these existing findings regarding the development of fatigue and presents additional information in that exercise priming at an intensity above CT appears to elicit development of peripheral fatigue which is still apparent at the onset of a subsequent exercise bout.

Although the presence of fatigue is apparent here, the present study observed no significant increase in peripheral fatigue throughout the primed exhaustive exercise bout, this was shown by no significant reduction in doublet torque. This contradicts the findings of Burnley et al. (2012) and Pethick et al. (2015; 2016; 2018) who found a reduction in potentiated doublet torque throughout submaximal trials above CT, indicating a progressive increase in peripheral fatigue to exhaustion. However, the fact that we did not observe a significant change in peripheral fatigue throughout the exercise could be because fatigue was already present at the start of the exercise bout. The present study did not observe an effect of

exercise priming on the presence of central fatigue as measured by a decline in voluntary activation (VA) at the start of the primed exhaustive bout compared with the start of the priming exercise, however VA significantly decreased during the primed exhaustive bout which demonstrated a progressive increase in central fatigue to exhaustion. This reduction in VA during exercise was also apparent in Pethick et al. (2016; 2018) for exercise trials performed above CT and Burnley et al. (2012) found a decrease in VA from start to end of three out of five exercise trials performed above CT. However, the present study used a slightly different contraction regime to Burnley et al. (2012) in which the duty cycle was much shorter. The contraction regime was identical to that in Pethick et al. (2016; 2018) using a duty cycle of 0.6 and so these findings may be more comparable.

5.6: Muscle torque output complexity

Early research highlighted a loss of complexity as a characteristic of the process of ageing and of several disease states (Lipsitz and Goldberger, 1992) and further investigation has been made into the complexity of muscle force output during exercise and the influence of contraction intensity (Slifkin and Newell, 1999; 2000). An exercise intensity of approximately 40% MVC has been shown to be the optimal intensity for maximum muscle force output complexity (Slifkin and Newell, 2000). More recently the study of muscle torque complexity during submaximal isometric exercise has been a focus with regards to CT and the development of fatigue (Pethick et al., 2015; 2016; 2018).

This is the first study to measure the effect of exercise priming on the complexity of muscle torque output in isometric knee extensor exercise however, previous research has investigated the course of change in complexity during this type of exercise and the effects that fatigue can have on the complexity of muscle torque output. Pethick et al. (2015; 2016; 2018) used measures of ApEn and DFA to measure the complexity of muscle toque output during intermittent isometric contractions of the knee extensors. These studies consisted of an identical contraction regime and duty cycle to the present study. Pethick et al. (2015) observed that with the development of fatigue came a reduction in the complexity of force output during the submaximal contractions performed at an intensity of 40% MVC. This was demonstrated by a decrease in ApEn and an increase in DFA-α, indicating a decline in the adaptability of the system. The same observations were made during the submaximal

contractions to exhaustion in the present study, with the additional finding of a greater rate of reduction in complexity in the exhaustive bout compared to the priming bout which coincided with the progression of fatigue throughout the exhaustive bout and not the priming bout.

Pethick et al. (2016) extended the range of contraction intensities studied and examined the role of CT and produced results in line with Burnley et al. (2012) in that for exercise performed above CT there was a greater development of fatigue. This study also demonstrated that a reduction in complexity was apparent only for intensities above CT. The present study is consistent with this, with contractions performed at 40% MVC which is above CT leading to a reduction in complexity throughout the intermittent isometric exercise. A further study by Pethick et al. (2018) involved two exercise bouts using the same contraction regime as the present study. Here it was observed that there was development of fatigue in the initial bout which led to a reduction in complexity. The present findings are in line with those by Pethick et al. (2018) as a reduction in complexity was observed alongside the presence of peripheral fatigue at the onset of the second exercise bout. The present study extends the literature to reflect the effect of exercise priming on intermittent, isometric single limb exercise.

5.7: Interpretation of processes to explain present findings

The present study has shown that heavy exercise priming of the knee extensors using intermittent, isometric contractions did not extend the time to exhaustion in a subsequent identical exercise bout to task failure. As mentioned, previous studies mostly involving cycle ergometer exercise have demonstrated an extended time to exhaustion as a result of heavy exercise priming. The findings of the present study could differ to this prior research based on the fact that the type of exercise was different here and has not been investigated before. The observation that there was no change in $\dot{V}O_2$ kinetics as a result of priming could contribute reasoning as to why there was no improvement in time to exhaustion during this study. However, there was a change in EMG with priming exercise. The presence of fatigue at the onset of the second exercise bout could be a factor involved in the effect of priming in the present study. Previous studies have shown that an increase in the primary amplitude and/or a reduction in the $\dot{V}O_2$ slow component (Burnley et al., 2002b; Koppo and Bouckaert, 2000; Wilkerson et al., 2004), which may contribute to time to exhaustion. The changes as a results of exercise priming have been attributed to an increase in muscle activity. This was shown in the

present study however did not result in any changes in the $\dot{V}O_2$ response or in exercise tolerance.

There have been several proposed explanations for the previously observed alterations in $\dot{V}O_2$ kinetics as a result of exercise priming. Changes in the motor unit behaviour of the exercised muscles as a mechanism for the priming effect has been speculated (Burnley et al. 2000) and subsequently supported (Burnley et al., 2001; Burnley et al., 2002b; Koppo and Bouckaert, 2000). However, others have found opposite results (Scheuermann et al., 2001). The higher EMG at the onset of the second heavy exercise bout could indicate that there is an increased demand for O_2 at this point as speculated by Burnley et al. (2002b). However, this present study does not provide further evidence for this explanation as the $\dot{V}O_2$ at the onset of the second exercise bout was no different to that in the priming bout. As this is the first study to examine the effects of exercise priming in intermittent, isometric exercise of a single limb, it is difficult to speculate a reason for the unaltered $\dot{V}O_2$ kinetics observed which contradict those found in cycling exercise. The use of NIRS in this present study may provide some explanation for the unchanged $\dot{V}O_2$ response. This measure of oxygenation may not be sensitive enough to pick up the changes in $\dot{V}O_2$ which may have occurred. Further research may be necessary to investigate the effect of exercise priming in this exercise modality and to add to the results found here. Future studies should manipulate the intensity of the exercise performed and the recovery duration between priming and exhaustive exercise to see if these variables influence the effects of priming.

Consistent with the present study, Burnley et al. (2002b) found a higher arEMG response in the first two minutes of the second exercise bout. These authors, amongst others, additionally observed that there was no change in mean power frequency (MPF), indicating that the increase in muscle activity as shown by the iEMG response was due to a rise in motor unit recruitment as opposed to an increase in firing frequency or preferential recruitment of higher-threshold units. Hughson et al. (2000) speculated that the increase in motor unit recruitment at the onset of exercise may be due to fatigue in the activated fibres meaning that they cannot maintain the demands of the continued exercise. As a result of this, an increase in the number of activated motor units may be the answer to meet these demands. The present study demonstrated a higher level of peripheral fatigue at the onset of the second exercise bout compared to the priming bout but observed no change in the levels of central fatigue at this point. This display of fatigue, accompanied by higher EMG values in the first two minutes of

the second bout than the priming bout could therefore add support for the explanation that the priming exercise increased muscle activity in a subsequent exercise bout with an increase in motor unit recruitment at the onset of exercise as an explanation. Although this may help to explain the findings of the present study, we are aware that the exercise modalities used in the studies are different (Burnley et al. (2002b) and Hughson et al. (2000) involved whole body cycling exercise whereas the present study was single limb isometric knee extension exercise).

The reduction in complexity throughout an exercising bout as found in the present study demonstrates a loss of adaptability in the motor output. The increased variability in force output as exercise progresses to task failure has been attributed to motor unit recruitment and discharge rates (Contessa et al., 2009; Hunter and Enoka, 2003). This mechanistic basis has been further acknowledged when studying the complexity of muscle torque output with fatigue. The number of motor units recruited increases as fatigue develops (Adam and De Luca, 2003). With the development of both peripheral and central fatigue throughout exercise to exhaustion, Pethick et al. (2015) suggested that the loss of complexity observed must have a mechanistic basis which affects the motor unit pool. The exercise in the present study was performed above CT. The motor units recruited above this threshold are more fatigable which means that additional units have to be recruited to maintain torque output (Adam and Luca, 2003). The changes in EMG reflecting muscle activity, and a reduction in complexity throughout the second exercise bout could potentially provide greater evidence for motor unit behaviour as a mechanism for the loss of complexity during exercise to task failure. It also provides an explanation for the effect of exercise priming on muscle torque output complexity.

There has been speculation around the relationship between muscle metabolic rate and muscle torque output complexity (Burnley et al., 2012; Seely and Macklem, 2012). There is evidence supporting motor unit behaviour as a determinant of the $\dot{V}O_2$ response to exercise and more recent studies have recognised its role it in the loss of complexity during exercise, which may suggest there is a link between the two variables. An unavoidable rise in muscle $\dot{V}O_2$ above CT has been observed which coincides with the threshold for a reduction in complexity (Seely and Macklem, 2012) and this correlation has very recently been observed during intermittent, isometric knee extension exercise (Pethick et al., 2019, in press). The

present study also displayed a link between these measures in the un-primed exhaustive exercise bout.

5.8: Limitations

The methodology of the present study included NIRS which measures the oxygenation of a tissue, in this case the vastus lateralis muscle. This method was used in order to assess oxygen delivery and utilisation by the muscle. NIRS signals can be affected by various factors such as muscle and blood vessel sizes, and light scattering during contractions (Barstow, 2019). NIRS as a method of investigating $\dot{V}O_2$ kinetics may not be sensitive enough to detect subtle changes in $\dot{V}O_2$, thus this provides limitation to our conclusions as the data produced may not be representative of the actual responses occurring within the body. This may therefore provide reason as to why there seemed to be no significant effect of priming exercise on the $\dot{V}O_2$ response to subsequent exhaustive exercise, as there may well have been changes that occurred but were not detected by NIRS.

The present study examined the response to priming exercise performed above CT (40% MVC). This was to ensure the intensity was optimal to produce the fatigue necessary to observe any possible effects of priming, based on previous studies' findings. It was clear when examining the variables measured throughout the exercise and the times to exhaustion that two participants were not producing results in line with the others, with their time to exhaustion markedly greater than the rest of the participants. We concluded upon inspection of their data that these participants were not performing the exercise in the correct intensity domain for this study (above CT). Including them in the data analysis would lead to unrepresentative findings and thus potentially false conclusions. Therefore, following completion of data collection, we removed two participants from the study.
The present study used the contraction intensity of 40% MVC for the exercise regime based on previous studies' results which indicated that this intensity was above the participants' critical torque. As aforementioned, two participants were discarded from the results analyses as we concluded that 40% MVC may not be above critical torque for these participants. Not having individual priming intensities could therefore provide limitation to the present study, as we could not be sure that every participant was exercising in the desired exercise domain when performing at the same relative intensity. An additional study/test prior to this study could have been undertaken to overcome this limitation. This would be in order to calculate a

specific contraction intensity for each individual participant whereby they were performing above critical torque. The present study would then use these individual exercise intensities for the submaximal exercise bouts, and it would be ensured that every participant was performing above critical torque.

The current study did not account for the menstrual cycle in female participants. The menstrual cycle involves changes in hormones, and different phases of the cycle show elevations in specific hormones and reductions in others. The phase of the menstrual cycle could have influenced the performance of the participants, as demonstrated in previous studies involving high-intensity exercise (Jurkowski et al., 1981). Not accounting for these alterations provides limitations to our conclusions, as the menstrual cycle could have influenced the exercise performances and data collected throughout the study.

During the present study, participants were instructed to refrain from caffeine intake for two hours prior to the exercise trial. Although caffeine does not directly impact maximal oxygen capacity, it has been shown to lead to enhancing effects on power output and exercise tolerance (Graham, 2001). As aforementioned, this time frame was based on that used in prior exercise studies with the same/similar exercise modality and regime. However, previous studies indicate that the effects of caffeine on exercise performance can persist for longer than two hours and so this may have been an influential variable and therefore a potential limitation to our results and conclusions.

5.9: Implications/Further direction

As this present study is the first to examine the effects of exercise priming on intermittent isometric single limb exercise, more research is necessary to solidify and understand its effects. This study used a recovery duration of 20 minutes which has previously shown to enable the body and exercising muscle to return to homeostasis. However, this was based on exercise of different modalities and intensities and did not seem to be of sufficient length to show the same result for all measures in the present study. As this is a novel study design, there is a need to more fully understand the effect of various recovery durations imposed and how this affects the performance in subsequent exhaustive exercise of this modality. Future research may also want to consider the exercise intensity at which the contractions are performed in the exercise bouts. The 40% MVC intensity was used in this study based on CT

and complexity research which demonstrated that intensities above CT saw a greater presence of fatigue and effects on muscle torque complexity (Pethick et al. 2015; 2016). Various other intensities above CT could be assessed in order to investigate whether the effects of priming exercise on subsequent exhaustive exercise are influenced.

5.10: Conclusion

In summary, the present study demonstrated that exercise priming does not improve exercise tolerance during intermittent isometric knee extension exercise. Prior exercise did not alter the $\dot{V}O_2$ response to exhaustive exercise. Despite this, a reduction in the complexity of muscle force output was observed as a result of the priming exercise which could be attributed to an increase in arEMG observed at the start of and throughout the second exercise bout. There was a presence of peripheral fatigue at the onset and a progressive development of central fatigue throughout the primed exhaustive bout. The reduction in complexity may therefore be a result of an increase in motor unit recruitment due to fatiguing muscle fibres during the exercise performed above CT. These results suggest that there is a priming effect of prior heavy exercise on subsequent heavy intermittent isometric contractions of the knee extensors performed to exhaustion. However, this exercise priming did not influence muscle $\dot{V}O_2$ kinetics and did not result in an enhanced exercise tolerance/time to exhaustion.

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