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# Power reserve following ramp-incremental cycling to exhaustion: Implications for muscle fatigue and function

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# ABSTRACT

In ramp-incremental cycling exercise, some individuals are capable of producing power output (PO) in excess of that produced at their limit of tolerance (LoT) while others cannot. This study sought to describe the: 1) prevalence of a "power reserve" within a group of young men (n=21; mean ± SD: age 25±4 years; $\dot{V}O_{2max}$ 45±8 ml·kg$^{-1}$·min$^{-1}$); and 2) muscle fatigue characteristics of those with and without a power reserve. Power reserve was determined as the difference between peak PO achieved during a ramp-incremental test to exhaustion and maximal, single-leg isokinetic dynamometer power. Pre- versus post-exercise changes in voluntary and electrically-stimulated single-leg muscle force production measures (maximal voluntary contraction, voluntary activation, maximal isotonic velocity and isokinetic power; 1-, 10-, 50-Hz torque and 10/50-Hz ratio), $\dot{V}O_{2max}$ and constant-PO cycling time-to-exhaustion also were assessed. A dichotomy in power reserve was prevalent within the sample resulting in two groups: 1) "No Reserve" (NRES: <5% reserve; n=10) and 2) "Reserve" (RES: >15% reserve; n=11). At the LoT, all participants had achieved $\dot{V}O_{2max}$. Muscle fatigue was evident in both groups, although the NRES group had greater reductions ($p<0.05$) in 10-Hz peak torque (PT), 10/50 Hz ratio, and maximal velocity. Time-to-exhaustion during the constant-PO test was 22±16% greater ($p<0.05$) in RES (116±19 s; PO = 317±52 W) than in NRES (90±23 s; PO = 337±71 W), despite similar ramp-incremental exercise durations and $\dot{V}O_{2max}$ between groups. The differences in muscle fatigue and function between groups suggest that the mechanisms contributing to the LoT are not uniform.

**Keywords**: Peripheral fatigue, central fatigue, muscle function, ramp-incremental exercise

# CO-AUTHORSHIP STATEMENT

This study was designed by M.D. Hodgson, D.B. Copithrone, D. A. Keir and J. M. Kowalchuk with input from the advisory committee (C.L. Rice). The data were collected by M.D. Hodgson and D.B. Copithrone, and analyzed by M.D. Hodgson with the assistance of D.B. Copithrone and J. M. Kowalchuk. M.D. Hodgson wrote the original manuscript for the study and D.B. Copithrone, D. A. Keir, C.L. Rice and J. M. Kowalchuk provided editorial feedback.

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# LIST OF ABBREVIATIONS

| | |
|---|---|
| Ag-AgCl | Silver Chloride Electrode |
| ANOVA | Analysis of Variance |
| ATP | Adenosine Triphosphate |
| $Ca^{2+}$ | Calcium |
| cm | Centimetre |
| CP | Critical Power |
| $CO_2$ | Carbon Dioxide |
| Deg | Degrees |
| GET | Gas Exchange Threshold |
| HRT | Half-Relaxation Time |
| Hz | Hertz |
| iEMG | Integrated Electromyography |
| ITT | Interpolated Twitch Technique |
| $K^+$ | Potassium |
| kg | Kilograms |
| KHz | Kilohertz |
| LT | Lactate Threshold |
| LoT | Limit of Tolerance |
| mA | Milliamps |

| | |
|---|---|
| min | Minute |
| ml | Millilitres |
| ms | Milliseconds |
| MVC | Maximal Voluntary Contraction |
| Nm | Newton-metres |
| $O_2$ | Oxygen |
| $PETCO_2$ | End Tidal Carbon Dioxide Pressure |
| $PETO_2$ | End Tidal Oxygen Pressure |
| $P_{isoPOST}$ | Post Ramp-Incremental Isokinetic Power |
| $P_{isoPRE}$ | Pre Ramp-Incremental Isokinetic Power |
| PO | Power Output |
| $PO_{peak}$ | Peak Cycle Power Output |
| PoT | Potentiated Twitch |
| PT | Peak Torque |
| RER | Respiratory exchange ratio |
| RI | Ramp-Incremental |
| RI-1 | First Ramp-Incremental Protocol |
| RI-2 | Second Ramp-Incremental Protocol |
| RI-95 | Constant-Power Output Protocol at 95% Peak Power Output |
| RISE-95 | Ramp-incremental, step-exercise at 95% exercise protocol |
| RMS | Root Mean Square |

| | |
|---|---|
| RPM | Revolutions per Minute |
| s | Seconds |
| SD | Standard Deviation |
| SE | Step Exercise |
| TPT | Time to Peak Torque |
| V | Volts |
| VA | Voluntary Activation |
| $V_E$ | Ventilation |
| $\dot{V}O_{2max}$ | Maximal Oxygen Uptake |
| $\dot{V}O_{2p}$ | Pulmonary Oxygen Uptake |
| $\dot{V}O_{2peak}$ | Peak Oxygen Uptake |
| W | Watts |
| WR | Work Rate |
| [ ] | Concentration |
| $\Delta P$ | Power Reserve ($P_{isoPOST}$ minus $PO_{peak}$) |
| µs | Microseconds |

# CHAPTER 1

# 1 REVIEW OF LITERATURE

## 1.1 INTRODUCTION

Using breath-by-breath gas-exchange measurements, ventilatory properties (such as the rate of oxygen consumption ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$), ventilation ($V_E$), end tidal oxygen ($PETO_2$) and carbon dioxide ($PETCO_2$), and respiratory-exchange ratio (RER)) can be analyzed to differentiate the exercise domains (light intensity, moderate intensity, heavy intensity, very-heavy intensity/severe intensity). Exercising at a work rate (WR) in the moderate intensity domain (below the lactate threshold (LT) or gas exchange threshold (GET)) is characterized by a $\dot{V}O_2$ increase within the first breath (Phase I/cardiodynamic component) followed by a rapid exponential increase (Phase II) to steady-state (Phase III) (Poole & Jones, 2012). The heavy-intensity domain (between LT/GET and critical power (CP; the asymptote of the power-duration curve for high-intensity exercise – the highest work rate/ $\dot{V}O_2$ that can be sustained for prolonged time (Whipp *et al*., 1986)) is characterized by a secondary $\dot{V}O_2$ elevation superimposed on Phase II (termed the $\dot{V}O_2$ slow component; $\dot{V}O_{2sc}$), which occurs after approximately 90 seconds (Poole *et al*., 1991; Roston *et al*., 1987; Whipp *et al*., 1980; Whipp *et al*., 1986). The upper-limit of the high-intensity domain (CP) is the highest metabolic rate at which $\dot{V}O_2$, lactate, intramuscular creatinephosphate (PCr), and $H^+$ can stabilize (Jones *et al*., 2008), above which becomes the very-heavy or severe-intensity domain. Within the very-heavy intensity domain, $\dot{V}O_2$ will either rise rapidly and exponentially to maximal oxygen consumption ($\dot{V}O_{2max}$), or a $\dot{V}O_{2sc}$ will increase and drive $\dot{V}O_2$ to $\dot{V}O_{2max}$ (Hill *et al*., 2002; Poole *et al*., 1988).

Breath-by-breath gas-exchange can also be used to accurately assess $\dot{V}O_{2max}$ during a variety of exercise protocols using discrete step-increases in work rate (WR) within the very heavy-intensity exercise domain (Hill & Lupton, 1923; Taylor *et al*., 1955; Mitchell *et al*., 1958; Astrand & Saltin, 1961; Duncan *et al*., 1997), continuous step-incremental (SI; Maksud & Coutts, 1971) or ramp-incremental (RI) protocols where WR progressively increases to the limit of tolerance (LoT), as used in the current study (Duncan *et al*. 1997; Whipp *et al*., 1981). $\dot{V}O_{2max}$ is one of the most common physiological measurements made in exercise physiology as it provides an indication of an individual's maximal capacity for uptake, transport, and utilization of oxygen (McConnell, 1988). The traditional "gold standard" criterion for establishing $\dot{V}O_{2max}$ is a plateau in $\dot{V}O_2$ despite an increase in WR. Although the classical $\dot{V}O_{2max}$ reports of Mitchell *et al*. (1958) and Taylor *et al*. (1955) did not implicitly require the data response to plateau (only that at another discrete time the highest $\dot{V}O_2$ achieved does not increase with increasing work-rate), this criterion has consistently been used when assessing $\dot{V}O_{2max}$. However, a true plateau is only demonstrated in approximately 50% of participants (Noakes & St Clair Gibson, 2004; Poole & Jones, 2017), typically requiring other criterion or validation for $\dot{V}O_{2max}$ to be confirmed; these criteria include an increase in heart rate (HR) to maximum values estimated for age (Martiz *et al*., 1961), a respiratory exchange ratio (RER) of 1.15 or greater (Issekutz *et al*., 1962), and/or maximal post-exercise blood lactate levels (>10 $mmol \cdot L^{-1}$; Astrand, 1952). However, Poole *et al*. (2008) suggested that these secondary criteria (used to establish $\dot{V}O_{2max}$) be abandoned as they consistently lead to a significant under-measurement of $\dot{V}O_{2max}$. In an effort to establish a protocol non-reliant on a $\dot{V}O_2$ plateau or secondary criterion,

"verification" protocols were developed to examine whether any difference existed between the $\dot{V}O_{2peak}$ achieved during a RI protocol and a step-exercise (SE) protocol (Day *et al*., 2003, Rossiter *et al*., 2006). In the verification protocol, the RI-protocol was followed by a constant-load, SE-protocol to a WR corresponding to 95% $WR_{peak}$ (RISE-95) or 105% $WR_{peak}$ (RISE-105) (Rossiter *et al*., 2006). During constant-load exercise performed in the very-heavy (VH) intensity exercise domain (above critical power), $\dot{V}O_2$ increases until $\dot{V}O_{2max}$ is achieved, presuming exercise can be tolerated for sufficient duration (Whipp *et al*., 1997). As a result, if the $\dot{V}O_{2peak}$ in the RI and SE are not different despite differing work rates, $\dot{V}O_{2max}$ is confirmed (Rossiter *et al*., 2006; Poole & Jones, 2017).

## 1.2 THE LIMIT OF TOLERANCE

While $\dot{V}O_{2max}$ and the LoT are typically thought to occur simultaneously (i.e., if $VO_{2max}$ is attained, it is unlikely that exercise can be tolerated and sustained for much longer), it is unclear whether the two are connected directly or by some common mechanism (Ferguson *et al*., 2016). The concept of symmorphosis pertains specifically to $\dot{V}O_{2max}$, suggesting that what limits $\dot{V}O_{2max}$ is either the mitochondrial capacity to consume oxygen or the supply of oxygen to the mitochondria depending on the fitness of the individual (Gifford *et al*., 2016). In untrained individuals, $\dot{V}O_{2max}$ is limited by the capacity of the mitochondria to consume oxygen despite an excess of oxygen supply, whereas, among trained individuals, $\dot{V}O_{2max}$ is limited by the supply of oxygen to the mitochondria despite an excess of mitochondrial respiratory capacity (Gifford *et al*.,

2016). In either instance, the amount of energy that the muscle can produce and utilize for power production dictates the LoT. However, this is only applicable if $\dot{V}O_{2max}$ is achieved; if the LoT occurs sub-$\dot{V}O_{2max}$, some other mechanism must be acting to limit exercise performance.

Literature on the LoT has preferentially focused on peripheral fatigue development, with the primary fatigue sites appearing within the muscle cell itself and for the most part not involving the central nervous system or the neuromuscular junction (Fitts, 1994; Kent-Braun *et al*., 2012). In the context of ramp-incremental (RI) exercise, the LoT occurs when peripheral muscle fatigue develops to such an extent that the muscle can no longer produce force beyond that required by the task despite maximal voluntary effort (Allen *et al*., 2008; Jones & Burnley, 2009). This occurs as a result of disturbances in the muscle cell surface membrane, excitation-contraction coupling, and metabolite accumulation (such as Pi, Cr, $H^+$, $Ca^{2+}$, $K^+$, $Na^+$, ADP, and AMP; Fitts, 1994; Kent-Braun *et al*., 2012). Recent literature has suggested that the LoT arises from reaching a "critical fatigue threshold" which downregulates efferent motor output to reduce power output and protect the muscle (Amann & Dempsey, 2008; Amann *et al*. 2006, 2008, 2009, 2011). It has been suggested that a critical fatigue threshold is reached when metabolites have accumulated within the active muscle, thereby increasing muscle group III and IV afferent stimulation that feeds-back centrally to reduce central motor output and thus muscle force development, and contributes to task/performance failure (Amann & Dempsey, 2008; Amann *et al*., 2006, 2008, 2009, 2011). It is thought that this critical fatigue threshold acts to terminate exercise (LoT) to protect the muscle from irreversible structural damage (Amann & Dempsey, 2008; Amann *et al*. 2006, 2008, 2009, 2011).

Alternatively, it has been proposed that from the onset of exercise, a "central governor" of exercise regulates peripheral fatigue development and terminates exercise at submaximal levels to avoid catastrophic failure in the exercising muscle (Noakes & St Clair Gibson, 2004). This model suggests that homeostasis is preserved by regulating neural output (decreasing the firing rate) which subsequently creates the *sensation* of fatigue and terminates exercise from the feeling or emotion of discomfort rather than from the actual manifestation of peripheral fatigue (Noakes & St Clair Gibson, 2004). The central governor, a supposed specific brain centre, acts to provide feed-forward regulation of the duration that a vigorous effort can be maintained in order to conserve homeostasis, protecting vital organs (such as the brain, heart, and skeletal muscle) from hyperthermia, ischemia and other manifestations of catastrophic fatigue (Shephard, 2009). Even the classic experiments of A.V. Hill (1923) suggested that myocardial ischemia was prevented by a "governor" in the heart or brain that would prevent irreversible heart damage during maximal exercise. However, conflict exists in relation to the central governor model and its existence (Marcora, 2008; Shephard, 2009; Inzlicht & Marcora, 2016). Shephard (2009) suggests that the central governor model seems to hold true, although being task-specific for marathon-like, self-paced events rather than shorter, maximal bouts of exercise. In contrast, Inzlicht & Marcora (2016) believe the central governor model teaches "precious little" about exercise regulation, suggesting that self-control simply wanes over time, with participants being less willing to exert effort the longer they have already exerted effort (Baumeister *et al*., 2007). Additionally, it seems improbable that a central governor would evolve to preserve homeostasis that could easily be overturned with a small change of motivation (Inzlicht & Marcora, 2016).

## 1.3 PERIPHERAL AND CENTRAL FATIGUE

During heavy and very-heavy intensity exercise, peripheral skeletal muscle fatigue develops as a result of the high-energy demand and large dependence on anaerobic metabolism (Fitts, 1994; Kent-Braun *et al*., 2012; Westerblad, 2016). Peripheral muscle fatigue development is accelerated at near-maximal exercise intensities due to the reliance on fast-twitch fibres to maintain power-output. The fast conduction velocity and high force production associated with fast-twitch fibres make them ideal for maintaining high power-output, though they are fatigue sensitive (Henneman & Mendell, 1983). Fast-twitch fibres are less oxidatively efficient, a characteristic that is worsened in the high $H^+$ environment that develops during exercise in the heavy and very-heavy intensity domain as a result of metabolite accumulation (Fitts, 1994; Kent-Braun *et al*., 2012). At the LoT, task failure is thought to result from an inability of weakened and slowed muscles to maintain power-output as a result of impaired contractility, excitation-contraction coupling failure, and metabolite accumulation. Impaired contractility has long been thought to result mainly from hydrogen ion ($H^+$) accumulation (muscle acidosis; Fitts, 1994; Kent-Braun *et al*., 2012), with many studies showing a positive correlation between the extent of acidosis and decrease in contractile function (Cady *et al*., 1989; Kent-Braun, 1990). However, there are instances where this correlation is missing, such as the observed decline in force accompanied by a decrease in muscle $H^+$ (Degroot *et al*., 1993). Regardless, muscle acidosis is known to exacerbate the fatigue-inducing effects of other metabolic changes associated with peripheral muscle fatigue, especially increased concentration of inorganic phosphate ([Pi]) and a reduced amplitude of the calcium transient ($Ca^{2+}$) (Fitts, 2016). During heavy and very-heavy intensity exercise, the

increase in Pi is thought to reflect an increased energy cost of exercise (i.e., increased ATP cost of force production) to maintain power output (Broxterman *et al*., 2017). This decrease in power output efficiency is thought to result from the combination of muscle acidosis (high $H^+$) and increased [Pi], which together are associated with an increase in [$HPO4^{2-}$] that has been linked to reductions in muscle power production (peak power by 59% and maximal shortening velocity by 31% (Nelson *et al*., 2014)). Depression of power production has also been associated with reduced myofibrillar $Ca^{2+}$ sensitivity (Place *et al*., 2010), reduced open probability of ryanodine receptors (Place *et al*., 2010), reduced shortening velocity (inhibition of myofibril ATPase; Nelson *et al*., 2014), increased curvature of the force-velocity relationship (lower peak force for a given velocity; Knuth *et al*., 2006), and depolarization of the sarcolemma and excitation-contraction coupling failure ($Na^+/K^+$ pump inhibition increased [$K^+$] combined with reductions in sarcolemma $Ca^{2+}$ release; Allen *et al*., 2008; Fitts, 1994; Kent-Braun *et al*., 2012)),

As peripheral muscle fatigue develops, modifications to central motor output (central fatigue) act to either i) increase efferent output to increase the firing rate and/or the amount of recruited muscle fibres to maintain power output, or ii) decrease efferent output to protect the muscle from irreversible structural damage (Gandevia, 2001). As metabolites accumulate (peripheral fatigue) in the muscle, afferent feedback from group III and IV decrease efferent motor drive to ensure the muscle does not deviate drastically from homeostasis and/or cause permanent muscle damage (Amann & Dempsey, 2008; Amann *et al*. 2006, 2008, 2009, 2011). These afferents are thought to be responsible for

inducing muscle pain and limiting voluntary effort (O'Connor & Cook, 1999). Involuntarily, central motor drive is limited in an effort to protect not only excitation-contraction coupling and actin-myosin interactions, but also to impair performance when its continuation would compromise whole-body homeostatic mechanisms such as temperature regulation, blood pressure, and ventilation (Gandevia, 2001). This is consistent with the decline in motor unit firing rate observed during maximal exercise, a product of competing excitatory and inhibitory influences on the motoneuronal pool to limit peripheral fatigue (Gandevia, 2001).

## 1.4 POWER RESERVE

The maximum power that human muscle can produce is determined by its structure, fibre type composition, and the present state of the muscle as influenced by previous activity (Sargeant, 1994). At the LoT of an incremental exercise test, it is expected that a truly maximal effort has been given and that no power can be produced above that required by the exercise task. However, recent literature has questioned whether the power output achieved during a ramp-incremental exercise test to the LoT is truly "maximal", or whether the muscle still is capable of generating additional, physiologically significant, power beyond the "peak" level achieved at the LoT but, for whatever reason, is unable to be generated voluntarily (termed "power reserve"; Coelho *et al*., 2015; Ferguson *et al*., 2016*;* Morales-Alamo *et al*., 2015). In the studies of Coelho *et al.* (2015) and Ferguson *et al.* (2016), no power reserve was evident beyond that observed at the LoT associated with the completion of a RI cycle test. A fundamental assumption is that the LoT or "exhaustion" occurs because of central and peripheral

fatigue mechanisms that reduce muscle function to the point that the muscle is unable to produce the force/power required by the task despite maximal voluntary effort (Allen *et al*., 2008; Jones & Burnley, 2009). This lack of a "power reserve" at the LoT has been reported in publications by Burnley, 2010; Macintosh *et al*., 2012; Coelho *et al*., 2015; and Ferguson *et al*., 2016.

However, Marcora & Staiano (2010) and Morales-Alamo *et al*. (2015) demonstrated that a significant power reserve existed at the LoT. In these studies participants were able to generate additional power by as much as three-times greater than that required by the exercise task. Such a large power reserve may result from mechanical, rather than physiological, phenomenon related to the power-velocity relationship, as allowing participants to pedal at a maximal velocity (rather than a fixed cadence) during maximal power testing will result in increased power-production simply as a result of increased cadence (Burnley, 2010). However, when the cycling cadence was fixed in an isokinetic mode, Morales-Alamo et al. (2015) still demonstrated that a power reserve exists at the LoT of a RI protocol, demonstrating that the presence of a power reserve is not just a mechanical phenomenon and that some underlying physiological phenomenon must exist. It seems evident that in some individuals a power reserve exists, while in others no power reserve remains. However, no explanation has been provided for why this difference may exist.

The mechanisms associated with the presence or absence of a power reserve at the LoT of RI cycling test have not been studied directly, though many theories exist to explain this phenomenon. A reduction in maximal voluntary muscle activation (reductions in central motor drive and/or spinal inhibition of cortical drive) is associated

with the LoT of a RI cycling test (Coelho *et al*., 2015). However, the appearance of a power reserve depends on whether the reduction in maximal voluntary muscle activation occurs at the individuals "maximal" exercise capacity, or if the reduction occurs submaximally – in the former, no power reserve would be present, while a power reserve would be evident in the latter. For instance, some of the power reserve may reflect a reduction in supraspinal drive to the motoneurons, which may end exercise sub-maximally to protect the muscle from further peripheral fatigue, though at the expense of a truly maximal performance (Gandevia, 2001). In those without a power reserve, it is suggested that muscle fatigue (peripheral) and reduced muscle activity (central) combine to reduce maximal evocable power (Ferguson *et al*., 2016).

## 1.5 STUDY RATIONALE

Recent literature has suggested that at the LoT (with the associated inability to continue exercise), it is contentious whether a voluntary power reserve exists that is in excess of the power output necessary to maintain the peak external power output required at the termination of a RI exercise test. To the best of our knowledge, no literature has investigated the prevalence of a power reserve within a group of active young men and compared differences in muscle fatigue and muscle function between those with and without a power reserve. Therefore, the primary rationales for completing this study were 1) to determine the prevalence of a power reserve at the LoT during an RI protocol within a group of active young men; and 2) to examine peripheral muscle fatigue development and voluntary activation in participants with and without a power reserve. Based on inconsistencies in the literature (i.e., that a power reserve may or may not be present at LoT), we hypothesized that: 1) there would be a distribution of participants

who did and did not display a power reserve; and 2) decrements in voluntary and electrically-stimulated muscle force production would be greater in participants without compared to with a power reserve. To confirm that participants were motivated and provided a sustained, maximal effort to the end of the RI protocol, we considered attainment of $\dot{V}O_{2max}$ to reflect maximal effort. Therefore, in the present study, $\dot{V}O_{2max}$ was measured and verified by using a RISE95 protocol (Rossiter et al 2006). Additionally, with this protocol, it was hypothesized that $\dot{V}O_{2max}$ would be confirmed in all individuals (confirming a maximal effort) but that during the SE protocol, the exercise duration before reaching the LoT would be greater in individuals expressing a power reserve.

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# CHAPTER 2

# 2 POWER RESERVE FOLLOWING RAMP INCREMENTAL CYCLING TO EXHAUSTION: IMPLICATIONS FOR MUSCLE FATIGUE AND FUNCTION

## 2.1 INTRODUCTION

Ramp-incremental exercise to the limit of tolerance (LoT) is a commonly used protocol for assessing parameters of aerobic function – i.e., lactate threshold; exercise efficiency; $O_2$ uptake kinetics; and peak or maximal $O_2$ uptake ($\dot{V}O_{2max}$; Davis *et al*., 1982; Whipp *et al*., 1981). The mechanism(s) contributing to an inability to continue exercising at intensities associated with the upper limits of a RI protocol (i.e., at the LoT) despite strong verbal encouragement and the participant being highly motivated are not well-understood. A common observation during RI exercise is that the LoT occurs coincident with, or in close proximity to, the attainment of $\dot{V}O_{2max}$ (Keir *et al*., 2016; Rossiter *et al*., 2006). A prevailing theory is that LoT coincides with the development of a specific level of neuromuscular fatigue ("critical fatigue threshold") (Amann & Dempsey, 2008; Amann *et al*., 2008, 2009, 2011) that prevents the muscle from producing higher power outputs. Ferguson *et al*. (2016*b*) recently demonstrated that, in a homogenous group of young, endurance cyclists (age, 22 yrs; $\dot{V}O_{2peak}$, 4.2 L/min), that the instantaneous isokinetic maximal power generating capacity of the muscles during cycling at the LoT in an RI protocol was not different from the task-specific power requirement – i.e., there was no "power reserve" at the LoT. In this study, the authors suggested that the LoT was related to both a reduced central drive for muscle activation and to peripheral, metabolically-induced, muscle fatigue (Ferguson *et al*., 2016*b*), and

was not related to a peripheral fatigue threshold or to differences amongst participants in their physiological and perceptual limits to the exercise task. Alternatively, Coelho *et al.* (2015), using an exercise protocol similar to that used by Ferguson *et al.* (2016), although with a more heterogeneous group of heathy, active, older, participants (age, 42 yrs [range, 29-72 yrs]; $\dot{V}O_{2peak}$, 3.2 L/min), observed a small (~18%) but significant power reserve at the LoT following RI exercise. While the existence of a power reserve could be identified using an isokinetic cycling model (Coelho *et al*., 2015), this method could not discriminate the neuromuscular origins of the contractile impairment and task failure. In addition, Marcora and Staiano (2010) and Morales-Alamo *et al.* (2015) observed a large, significant power reserve (as much as 300%). However, this large power reserve was thought to be the result of mechanical rather than physiological influence, as cadence (which itself can increase power output) was not controlled during the maximal power generation protocol (Burnley, 2010).

Whether a power reserve remains at the point of task failure during RI exercise is contentious (Ferguson *et al*., 2016*a*; Morales-Alamo *et al*., 2016), and its relationship to fatigue development has not been studied in detail. The mechanisms responsible for reductions in muscle force development leading to task failure can originate in peripheral sites within the exercising muscle and/or central sites associated with central motor output and spinal or supraspinal transmission proximal to the neuromuscular junction (Allen *et al*., 2008; Amann & Calbet, 2008; Burnley & Jones, 2007; Fitts, 1994; Noakes & St Clair Gibson, 2004; Secher *et al*., 2008; Walsh, 2000) but the extent to which these mechanisms influence the power reserve is unknown. Importantly, when establishing whether a power reserve exists at task failure it must be assumed that participants are

highly motivated and willing to push themselves to exhaustion during the RI protocol such that the LoT represents a truly maximal, fatiguing effort, typical of that required to engender $\dot{V}O_{2max}$. However, previous work in this area did not confirm $\dot{V}O_{2max}$ with a validation trial and so it is not possible to determine in those displaying a power reserve whether or not a truly exhaustive effort was produced.

Therefore, the purpose of this study was: 1) to determine the prevalence of a power reserve at the LoT during an RI protocol within a group of active young men; and 2) to examine peripheral muscle fatigue development (as identified by quadriceps muscle force decrements in response to low- and high-frequency electrical stimulation) and voluntary activation (as determined by maximal voluntary contraction (MVC) with twitch interpolation, and maximal isotonic contraction velocity) in participants with and without a power reserve. Based on inconsistencies in the literature (i.e., that a power reserve may or may not be present at LoT), we hypothesized that: 1) there would be a distribution of participants who did and did not display a power reserve; and 2) decrements in voluntary and electrically-stimulated muscle force production would be greater in participants without compared to with a power reserve. To confirm that participants were motivated and provided a sustained, maximal effort to the end of the RI protocol, we considered attainment of $\dot{V}O_{2max}$ to reflect maximal effort. Therefore, in the present study, $\dot{V}O_{2max}$ was measured and verified by using a RISE95 protocol (29). Additionally, with this protocol, it was hypothesized that $\dot{V}O_{2max}$ would be confirmed in all individuals (confirming a maximal effort) but that during the SE protocol, the exercise duration before reaching the LoT would be greater in individuals expressing a power reserve.

## 2.2 METHODS

*Participants*

Twenty-one young, healthy and recreationally active men participated in the study (mean ± SD; age 25 ± 4 years; body mass 81± 10 kg; height 184 ± 7 cm; $\dot{V}O_{2max}$ 45 ± 8 $ml \cdot kg^{-1} \cdot min^{-1}$). Participants were non-smokers with no known musculoskeletal, respiratory, cardiovascular or metabolic conditions, and none were taking medications that might influence cardiorespiratory or metabolic responses to exercise.

*Ethical Approval*

The study was conducted according to the Declaration of Helsinki and all procedures were approved by *The* University of Western Ontario Ethics Committee for Research on Human Subjects. Procedures and risks were explained to each participant before they volunteered and gave informed written consent to participate in the study.

*Experimental Protocol*

*Exercise testing*. All tests were conducted in an environmentally controlled laboratory at a similar time of day, 2 to 3 hours after a standardized meal (composed of 500 ml of water and 2–3 g/kg body mass of low glycemic-index (approved cereal, pasta, oatmeal, legumes, etc.) carbohydrates). Subjects were reminded of the required standardized meal the night before reporting to the laboratory, and all subjects confirmed dietary adherence prior to commencing any protocol. Exercise protocols were performed on an electromagnetically-braked cycle ergometer (Velotron; RacerMate, Seattle, WA). Participants were instructed to abstain from vigorous physical activity in the 24 hours

preceding each test and to avoid caffeine consumption on the day of testing. All testing sessions were separated by a minimum of 48 hours.

The experiment consisted of three visits to the laboratory separated by a minimum of 48 hours (see Fig.1). The first visit served as a familiarization session for the RI exercise test protocol (Fig. 1A). On the second visit an RI test to the LoT was performed and included voluntary and electrically-stimulated neuromuscular testing both before and immediately after the RI test (see below) to establish muscle performance and fatigue characteristics at LoT in individuals identified with and without a power reserve (Fig. 1B). On the third visit a RISE95 exercise test was completed (see below) (Rossiter *et al*., 2006) to verify the attainment of $\dot{V}O_{2max}$ and to establish exercise tolerance (as measured by time-to-fatigue) during the constant-PO (SE) component of the RISE95 protocol in individuals identified with and without a power reserve (Fig. 1C).

The RI test protocol consisted of 4 min leg cycling at a baseline PO of 50 W, followed by a progressive increase in PO at 25 W/min to the participant's LoT. Participants maintained a cadence of 70 rpm throughout the exercise protocol and the test was terminated (LoT) when participants were unable to continue the exercise and/or the cycling cadence fell below 55 rpm despite strong verbal encouragement by laboratory personnel. The RISE95 test consisted of an initial RI test (at 25 W/min) to the participant's LoT followed by 5 min recovery (2 min resting recovery and 3 min cycling at 50 W baseline), and then a constant PO step-exercise (SE) test at a PO equal to 95% $PO_{peak}$ reached at the LoT in the preceding RI test (Rossiter *et al*., 2006).

On the second visit, participants completed the RI protocol to the LoT but with assessment of neuromuscular function made immediately before and within ~ 35 s after

the RI test. Measures of neuromuscular function consisted of voluntary and electrically-stimulated static and dynamic single limb quadriceps contractions.

It should be noted that although comparisons between whole-body cycling and knee extensions cannot be made directly, it has been reported that during whole-body cycling the largest proportion of the total positive mechanical work is achieved by the knee extensor muscles (39%; in comparison to 27% hip extensors, 4% hip flexors, 10% knee flexors, and 20% ankle plantar flexors) (Ericson, 1986). In this regard, isolating the knee extensor muscles for neuromuscular testing provides insight into the relative influence of fatigue development on the LoT and the presence or absence of a power reserve.

*Neuromuscular testing.* Neuromuscular testing was performed on the second visit, before and immediately following the RI test. All post-RI stimulation and joint angle settings were identical to those established pre-exercise, allowing post-testing to commence within ~ 35 s of the participants reaching their LoT, with all neuromuscular testing completed within ~ 3 min of the RI protocol. Participants performed a series of quadriceps muscle function tests (described below and Fig. 2) of the left leg while seated in a Humac-Norm Cybex dynamometer (Computer Sports Medicine, Stoughton, MA), with the joint angles of the hip, ankle and knee adjusted to match, as close as possible, the joint angles associated with upright cycling. The lever length of the Humac-Norm Cybex dynamometer was adjusted so that the resistance pad rested comfortably on the leg just proximal to the malleoli with the center of rotation aligned with the rotational axis of the knee. Participants were secured firmly in the seated position using shoulder and waist

straps. Two custom-made aluminum foil electrodes (~20 x 5 cm) wrapped in paper towel and soaked with a conductive brine were taped tightly over the anterior thigh musculature. One electrode was placed over the proximal thigh 10 cm distal to the inguinal fold, and the second electrode was placed on the distal thigh 7 cm superior to the patella (Roos *et al*., 1999). The electrodes were attached to a constant current muscle stimulator (DS7AH; Digitimer, Welwyn Garden City, Hertfordshire, UK) to elicit electrically-stimulated contractions. The order for neuromuscular assessment was similar pre- and post-RI exercise except that post-RI voluntary MVC measures were measured last thereby minimizing any effects of fatigue recovery on the post-exercise voluntary dynamic (isokinetic & isotonic torque) and electrically-stimulated force-frequency measures.

Isokinetic torque (Nm), isometric torque (Nm) and maximal velocity of isotonic knee-extensions (deg/s) were recorded before and after each exercise protocol. Torque data were collected and displayed on a computer using Spike 2 version 7.02 (Cambridge Electronic Design, Cambridge, UK). Torque and velocity were sampled at a frequency of 500-Hz.

*Isometric torque:* Doublet stimulation (pulse separation 10 ms; pulse width 200 us; 400 V, range 250–650 mA) was used to establish the maximal knee-extensor twitch torque (Nm), defined as the point at which increases in stimulation intensity (mA) no longer resulted in an increase in torque production. Stimulation intensity was then increased by 20%. A minimum of two maximal voluntary contractions (MVCs) lasting 3 s were completed, and a third MVC was completed if the first two MVCs differed by more than

10%. Two minutes of rest was provided between each attempt. Participants were provided with visual feedback and strong verbal encouragement during all MVCs. A supramaximal doublet was elicited during (superimposed twitch) and succeeding (potentiated twitch) each MVC. This was used to calculate voluntary activation (VA superimposed twitch/potentiated twitch) (Belanger & McComas, 1981). All post-RI stimulation settings were identical to that established pre-exercise.

The quadriceps muscle twitch and tetanic torques were assessed at stimulation frequencies of 1-, 10- and 50-Hz each for 1 s [see Edwards *et al*., 1977] using a 50-μs pulse width (400 V, range 250–475 mA) at an intensity that achieved ~50% MVC at 50-Hz. The 1- and 10-Hz stimulation were elicited at the same stimulator settings as the 50-Hz stimulation. Post-exercise stimulation intensities (mA) were identical to those used at pre-exercise.

*Isokinetic torque:* Maximal isokinetic torque production was assessed with a series of five isokinetic knee extension maneuvers at two velocities (separated by 15 s) matched to simulate the set velocity markers during cycling (set-cadence: 70 rpm = 220.1 deg/s; cut-off cadence: 55 rpm = 120 deg/s). A sixth knee extension maneuver was made if any of the peak torque values varied by more than 10% during the five knee extensions. Participants were instructed to extend their left leg rapidly and with maximal effort throughout the set range of motion. The average torque achieved throughout each of the five knee extension maneuvers was recorded and the average of all knee extensions for each participant was calculated and reported. Maximal isokinetic knee extension power (W) was calculated as the product of angular velocity (in radians/s) and maximal torque

(Nm).

*Isotonic torque*: Maximal knee extension isotonic velocity was assessed against a resistance equivalent to 20% of the pre-exercise MVC torque. Participants were told to extend their leg as rapidly as possible during five knee extension maneuvers, with each separated by 2 s rest. A sixth kick was performed if peak velocity varied by more than 10% during the five kicks. The average values of the five knee-extension maneuvers were calculated and reported. Velocity was recorded in radians per second. Isotonic power (W) was determined as the product of angular velocity (radians/s) and torque (Nm).

*Gas exchange*. During each trial, breath-by-breath gas-exchange measurements were made as follows: inspired and expired volumes and flow rates were measured using a low-dead-space bidirectional turbine (VMM 110; Alpha Technologies, Laguna Hills, CA) and pneumotach (4813; Hans Rudolph, Shawnee, KS). Respired air was sampled continuously at the mouth and analyzed by mass spectrometry (AMIS 2000; Innovision, Lindvedvej, Denmark) for fractional concentrations of $O_2$ and $CO_2$. The volume turbine was calibrated before each test using a syringe of known volume (3 liters) over a range of flow rates, and the pneumotach was adjusted for zero flow. The mass spectrometer was calibrated using precision-analyzed gas mixtures. The time delay between an instantaneous square-wave change in fractional gas concentration at the sampling inlet and its detection by the mass spectrometer was measured electronically by computer. Respiratory volumes, flow, and gas concentrations were recorded at a sampling frequency of 100-Hz and transferred to a computer, which aligned gas concentrations

with volume signals as measured by the turbine. Flow from the pneumotach was used to resolve inspiratory-expiratory phase transitions, and the turbine was used for volume measurement. The computer executed a peak-detection program to determine end-tidal $PO_2$, end-tidal $PCO_2$, and inspired and expired volumes and durations to build a profile of each breath. Breath-by-breath alveolar gas exchange was calculated using the algorithms of Swanson (1980).

*Data Analyses*

Breath-by-breath $\dot{V}O_{2p}$ data were collected and analyzed for the RI and RISE95 protocols. $\dot{V}O_{2peak}$ was determined as the average of the final 15 s of the RI (ramp-incremental) protocol. By relating the three $\dot{V}O_{2peak}$ values (associated with the RI protocols from visits two and three and the 95% PO (SE) protocol) with the respective final POs it was possible to verify whether criteria for establishing $\dot{V}O_{2max}$ had been achieved – i.e., no significant difference in $\dot{V}O_{2peak}$ despite differences in $PO_{peak}$.

To quantify the degree of neuromuscular fatigue, both voluntary and electrically-stimulated muscle torque and power measures were analyzed and compared pre- vs. post-exercise for each participant. Voluntary measures included peak MVC torque, voluntary activation (VA), maximal isotonic and isokinetic power. Electrically-induced measures included the peak torque elicited during the 1-, 10- and 50-Hz tetanic contractions, comparison of pre-to-post fatigue potentiated doublet (PoT) torque succeeding the MVC, and a ratio of low-to-high frequency (10/50-Hz) was computed. The 50-Hz HRT (half relaxation time) and 10-Hz HRT were expressed in normalized values (ratio of amplitude to time) to account for the decreased amplitude associated with fatigue. All changes were

expressed in absolute and relative (% pre-RI) units. The magnitude of change in all voluntary and electrically-stimulated muscle contraction variables were compared pre- to post-exercise within groups, and total percent change post-exercise between groups. Power reserve was calculated as the percent difference between $PO_{peak}$ and $P_{isoPOST}$ (Ferguson *et al*., 2016):

$$\textit{Equation 1}: ([\ P_{isoPOST} - PO_{peak}\ ] / PO_{peak}) \cdot 100$$

*Statistical Analysis*

Data are presented as means ± SD. Frequency distribution analysis was performed to determine the prevalence of isokinetic power reserve within the population. Paired t-tests were used to analyze pre-post difference within groups. A one-way ANOVA was used to compare all electrically-stimulated and voluntary fatigue variables between groups. All statistical analyses were performed using SigmaPlot version 11.0 (Systat Software, San Jose, CA). Statistical significance was accepted at $\alpha < 0.05$.

## 2.3 RESULTS

*Power Measurements*

In all subjects (n=21) the mean $PO_{peak}$ (measured at the cycle flywheel) from ramp-incremental (RI) exercise was 343 ± 64 W at 70 rpm. The post-RI isokinetic knee-extension power at 70 rpm ($P_{isoPOST}$, 408 ± 91 W) was reduced ($p<0.05$) by 302 ± 126 W compared to pre-RI isokinetic power ($P_{isoPRE}$, 710 ± 218 W); the mean difference between $PO_{peak}$ and $P_{isoPOST}$ (ΔPReserve) was 64 ± 71 W yielding an average isokinetic cycle

power reserve of 14 ± 13%. Isokinetic knee-extension power at 55 rpm (which was set as the lower cut-off limit for stopping the RI test) was reduced 179 ± 5 W ($P_{isoPRE}$, 675 ± 150 W; $P_{isoPOST}$, 497 ± 155 W).

A dichotomy in ΔPReserve within the subject sample was observed in which there was a grouping of subjects with very little difference between the end-RI $PO_{peak}$ and the $P_{isoPOST}$ at 70 rpm (< 5% power reserve) and a group with a much larger difference between the two peak torque values (>15% power reserve), with no subjects found in the 5% to 15% region (see Fig. 3). Based on this separation, subjects were placed into two groups: 1) those with a power reserve of < 5% ("NRES"; n, 10; ΔPReserve, 2.7 ± 1.3%; range, 0.4 to 4.6%) and 2) those with a power reserve of > 15% ("RES"; n, 11; ΔPReserve, 24.4 ± 10.0%; range, 15.2 to 43.7%). There were no between group differences in $P_{isoPRE}$ and $PO_{peak}$ (Table 1), but due to a higher ($p<0.05$) $P_{isoPOST}$ in RES (448 ± 87 W) compared to NRES (364 ± 77 W), ΔPReserve was greater ($p<0.05$) in RES (24.4 ± 10.0%) compared to NRES (2.7 ± 1.3%).

*$\dot{V}O_2$ measurements*

There were no differences in absolute $\dot{V}O_{2peak}$ amongst the RI protocol (visit 2) (3.64 ± 0.68 L/min; $PO_{peak}$, 343 ± 62 W), the RI phase of the RISE95 protocol (visit 3) (3.64 ± 0.66 L/min; $PO_{peak}$, 348 ± 62 W) and the constant-PO (SE) phase of the RISE95 protocol (visit 3) (3.55 ± 0.65 L/min; $PO_{peak}$, 331± 59 W) despite differing peak POs amongst the RI and SE protocols, thereby satisfying the criteria for confirming $\dot{V}O_{2max}$. There were no differences for $\dot{V}O_{2max}$ between the RES and NRES groups.

*Muscle Contractile Measurements*

The voluntary and electrically-stimulated neuromuscular responses measured in RES and NRES pre- and post-RI exercise are presented in Table 2. In both RES and NRES, the MVC, maximal isotonic knee-extension velocity, 1-Hz twitch, doublet PoT, 10-Hz PT, 50-Hz PT, and 10/50-Hz ratio were reduced ($p<0.05$) post- compared to pre-RI values. Voluntary activation of the MVC was similar in both groups and unchanged after RI exercise. The 1-Hz TPT and 10-Hz HRT were increased ($p<0.05$) post-RI in both groups, while the 1-Hz HRT was increased ($p<0.05$) post-RI in the RES only.

Muscle tetanic torque development with electrically-induced 10-Hz stimulation was reduced to a greater extent ($p<0.05$) in NRES (63 ± 9%) than in RES group (45 ± 15%) post- compared to pre-RI. Because no significant changes in muscle tetanic torque were seen with 50-Hz stimulation in either group pre- vs post-RI exercise, the 10/50-Hz ratio was reduced ($p<0.05$) more in NRES (51 ± 12%) than in RES (36 ± 16%) post-RI (Fig. 4). Also, maximal voluntary isotonic velocity was reduced to a greater extent ($p<0.05$) in NRES (-17 ± 7%) compared to RES (-9 ± 7%).

*Exercise Endurance Time*

During the constant-PO, verification (SE) portion of the RISE-95 protocol, the time to the LoT was 22 ± 16% greater ($p<0.05$) in RES (116 ± 19 s) than in NRES (90 ± 23 s), despite similar RI exercise durations and $\dot{V}O_{2max}$ between groups.

**Table 1:** Physical characteristics and aerobic responses to the exercise tests. (*) represents a significant difference between $PO_{peak}$ and $P_{isoPOST}$. (¥) represents a significant difference between $P_{isoPRE}$ and $P_{isoPOST}$. (§) represents a significant difference between NRES and RES. Statistical significance was accepted at alpha < 0.05.

| | ***NRES*** | ***RES*** |
|---|---|---|
| n | 10 | 11 |
| Age, years | 24 ± 1 | 26 ± 4 |
| Mass, kg | 78 ± 11 | 84 ± 9 |
| Height, cm | 182 ± 8 | 185 ± 7 |
| $\dot{V}O_{2max}$, $L \cdot min^{-1}$ | 3.69 ± 0.77 | 3.61 ± 0.61 |
| $\dot{V}O_{2max}$, $ml \cdot kg^{-1} \cdot min^{-1}$ | 47.3 ± 8.27 | 43.2 ± 6.85 |
| $HR_{peak}$, $beats \cdot min^{-1}$ | 190 ± 7 | 187 ± 8 |
| $P_{isoPRE}$ | 640 ± 257 | 774 ± 162 |
| $PO_{peak}$ | 355 ± 74 | 333 ± 55 |
| $P_{isoPOST}$ | 364 ± 77¥ | 448 ± 87¥*§ |
| ΔPReserve | 9 ± 8 | 114 ± 14§ |
| Power Reserve, % | 3 ± 1 | 24 ± 9§ |

Terms: $HR_{peak}$, peak heartrate achieved during RI-protocol; $VO_{2max}$, maximal oxygen uptake; $P_{isoPRE}$, Pre-RI isokinetic power; $PO_{peak}$, RI maximal power output; $P_{isoPost}$, Post-RI isokinetic power; ΔPreserve, Power Reserve ($P_{isoPOST}$ minus $PO_{peak}$);

**Table 2**: Absolute peak muscle responses before and after exercise and relative change in muscle response during voluntary and electrically-stimulated contractions measured after RI-1. (¥) represents a significant difference between $P_{isoPRE}$ and $P_{isoPOST}$. (§) represents a significant difference between NERS and RES. Statistical significance was accepted at alpha < 0.05.

| | ***NRES*** | | ***RES*** | |
|---|---|---|---|---|
| | *Pre-RI* | *Post-RI* | *Pre-RI* | *Post-RI* |
| MVC, Nm | 287 ± 93 | 224 ± 77 | 326 ± 51 | 258 ± 41 |
| MVC, % pre-RI | | -22 ± 14¥ | | -20 ± 9 ¥ |
| VA, % | 89 ± 3 | 85 ± 7 | 89 ± 8 | 88 ± 8 |
| VA, % pre-RI | | -4 ± 7 | | -2 ± 4 |
| Maximal Velocity, deg•s$^{-1}$ | 293 ± 40 | 252 ± 30 | 319 ± 41 | 290 ± 34 |
| Maximal Velocity, % pre-RI | | -17 ± 7¥ | | -9 ± 7¥§ |
| 1-Hz Twitch PT, Nm | 74 ± 18 | 47 ± 17 | 72 ± 18 | 51 ± 12 |
| 1-Hz Twitch PT, % pre-RI | | -37 ± 16¥ | | -27 ± 17¥ |
| PoT Doublet, Nm | 111 ± 33 | 89 ± 26 | 126 ± 15 | 108 ± 14 |
| PoT Doublet, % pre-RI | | -20 ± 7¥ | | -13 ± 14¥ |
| 10-Hz Tetanus PT, Nm | 64 ± 14 | 24 ± 7 | 56 ± 18 | 30 ± 10 |
| 10-Hz Tetanus PT, % pre-RI | | -63 ± 9¥ | | -45 ± 15¥§ |
| 10-Hz Tetanus Normalized HRT, ms/Nm | 3 ± 1 | 7 ± 3 | 2 ± 1 | 6 ± 2 |
| 10-Hz Normalized HRT, % pre-RI | | 130 ± 101¥ | | 203 ± 103¥ |
| 50-Hz Tetanus PT, Nm | 166 ± 32 | 128 ± 28 | 135 ± 34 | 114 ± 33 |
| 50-Hz Tetanus PT, % pre-RI | | -23 ± 9¥ | | -16 ± 13¥ |
| 50-Hz Tetanus Normalized HRT, ms/Nm | 1 ± 1 | 1 ± 1 | 0.8 ± 0.1 | 0.9 ± 0.3 |
| 50-Hz Normalized HRT, % pre-RI | | 29 ± 46 | | 28 ± 48 |
| 10/50-Hz ratio | 0.40 ± 0.09 | 0.19 ± 0.06 | 0.43 ± 0.12 | 0.28 ± 0.12 |
| 10/50-Hz, % pre-RI | | -51 ± 12¥ | | -36 ± 16¥§ |

Terms: MVC, maximal voluntary contraction; PT, peak torque; HRT, half relaxation time; TPT, time to peak torque; PoT, potentiated twitch; VA, maximal voluntary activation; RI, ramp-incremental; Hz, Hertz (stimulations per second); Nm, newton-meters.

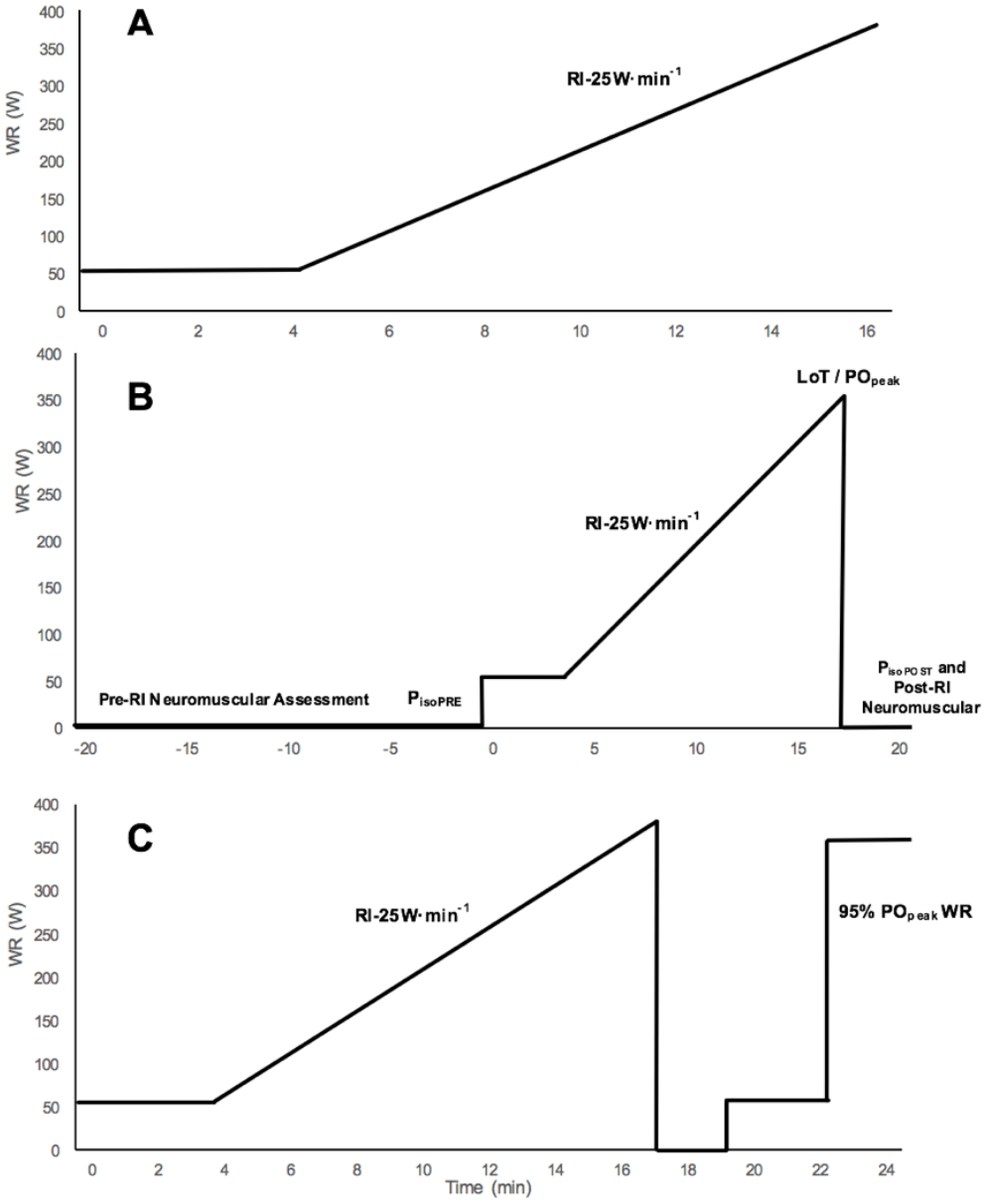


**Figure 1.** Schematic of Exercise Protocol. *A* (Visit 1; familiarization): Ramp incremental (RI) exercise test (50 W baseline, 25W·min$^{-1}$ ramp). *B* (Visit 2): RI-muscle fatigue intervention. T = -20 to -5 illustrates the pre-RI neuromuscular assessment, T = 0 to 17 illustrates the RI-muscle fatigue intervention, and T = 17 to 20 illustrates $P_{isoPOST}$ and post-RI neuromuscular assessment. *C* (Visit 3): RI and 95% $PO_{peak}$ for $\dot{V}O_{2max}$ validation and time to exhaustion (muscle function).

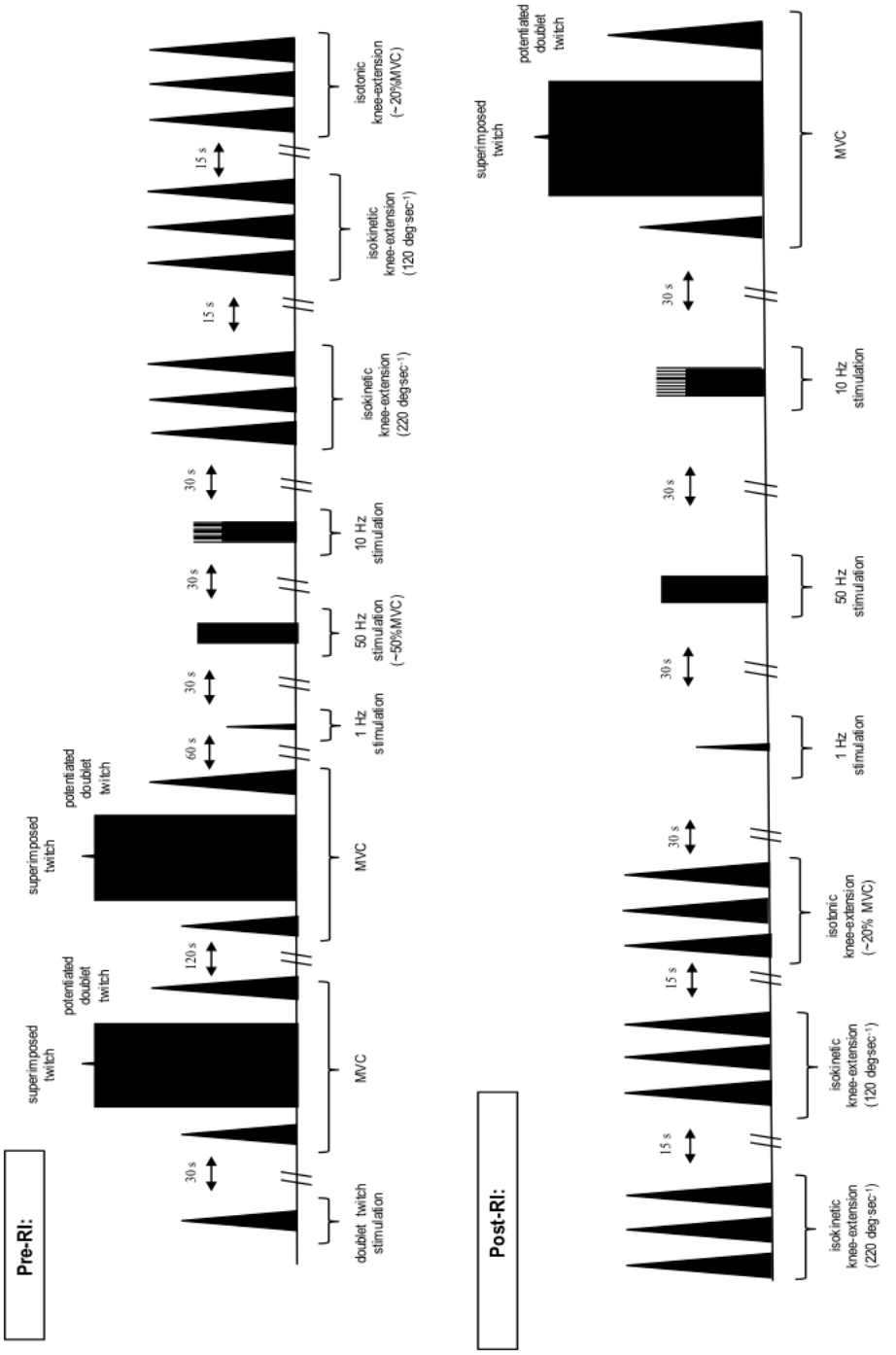


**Figure 2**. Schematic of Neuromuscular Testing. Pre-RI: doublet stimulation to maximal knee-extensor twitch torque, MVC, 1-Hz, 50-Hz, 10-Hz, isokinetic knee-extensions (maximal power/$P_{isoPRE}$), and isotonic knee-extensions (maximal velocity). Post-RI: isokinetic knee-extensions ($P_{isoPOST}$), isotonic knee-extensions, 1-Hz, 50-Hz, 10-Hz, MVC.

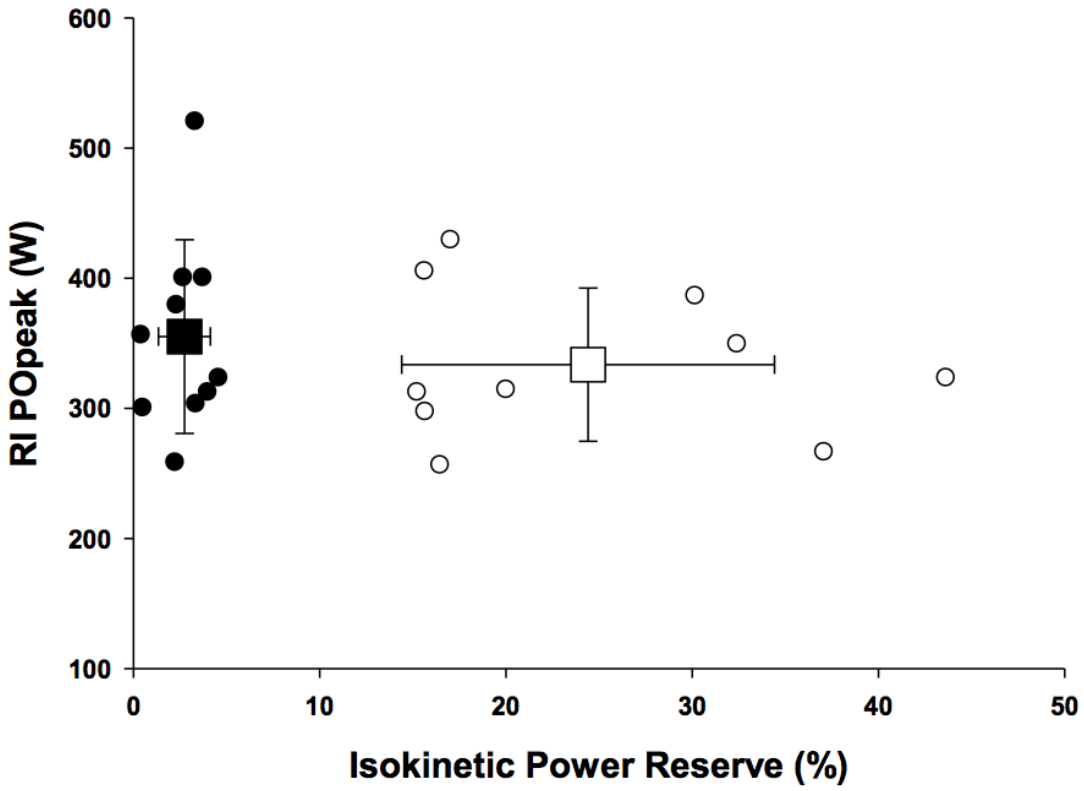


**Figure 3.** Distribution of the prevalence of isokinetic power reserve vs. RI $PO_{peak}$ within a single group of recreationally active young men. The absence of isokinetic power reserve between 5% and 15% allowed for differentiation of two distinct populations: 1) NRES (closed circles; <5%; n = 10) and 2) RES (open circles; >15%; n = 11). The open square represents the mean $PO_{peak}$ and ΔPReserve for RES, while the closed square represents the mean $PO_{peak}$ and ΔPReserve for NRES.

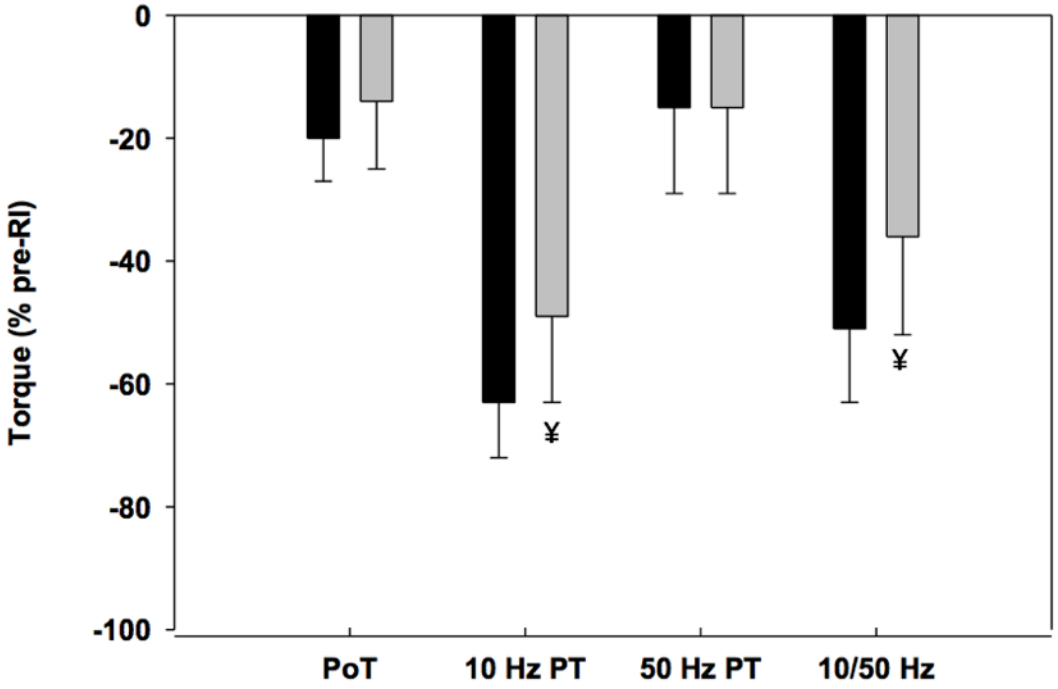


**Figure 4.** Group mean pre- to post-exercise muscle response (as represented by % change in torque measurements during 1-s at 1-Hz (1-Hz PT), 1-s at 50-Hz (50-Hz PT), and 1-s at 10-Hz (10-Hz PT) electrical stimulation, potentiated twitch (PoT), and 10/50-Hz ratio. *Black* represents NRES while *grey* represents RES. Significant differences (¥) exist between groups in 10-Hz PT and 10/50-Hz. Statistical significance was accepted at alpha $< 0.05$.

## 2.4 DISCUSSION

During RI-exercise, the limit of tolerance (LoT) and an inability to continue exercise has been attributed to an inability of muscle to meet the torque or power requirements of the task, despite maximal effort by the participant. It has been reported that at the LoT following an exhaustive RI exercise test some individuals still are capable of volitionally producing power far greater than the PO associated with the termination of the RI test (i.e., evidence of a power reserve) whereas others are unable to voluntarily generate additional power beyond that required of the RI $PO_{peak}$ (i.e., no power reserve). While the factors that contribute to the LoT remain debated, these sub-groups of individuals indicate that the mechanisms leading to a LoT are not uniform. The current study compared the peak PO achieved at the LoT at the end of a RI exercise protocol with the maximal volitional isokinetic knee-extensor power measured within ~ 35 s after the RI to establish the prevalence of power reserve in a group of 21 participants. Additionally, pre- vs post-RI exercise differences in voluntary and electrically-stimulated muscle contractions were compared to test the hypothesis that those participants with a power reserve would experience greater decrements in muscle function and greater muscle fatigue. The main findings were that: i) approximately half of the participants studied had a power reserve (defined as a greater than 15% difference between $PO_{peak}$ and $P_{isoPOST}$); ii) at LoT, both the RES and NRES group displayed reductions in voluntary and electrically-stimulated quadriceps muscle torque, and the magnitude of decrement in force development was greater in the NRES than in the RES group; and iii) exercise time to the LoT during the bout of constant-PO exercise at 95% $PO_{peak}$ was shorter in the NRES than in the RES group. These data indicate that at the LoT following an RI

exercise test, the presence or absence of a power reserve may be consequent to differences in peripheral muscle fatigue development and subsequent differences in muscle function.

When comparing the peak PO achieved at the end of the RI protocol with the peak PO generated during maximal voluntary isokinetic knee-extension exercise it became apparent that two distinct groups could be identified, those presenting with a substantial power reserve (> 15%; RES) and those without an appreciable power reserve (< 5%; NRES) (see Fig. 3). This finding is unique because previous work has reported either the presence (Marcora & Staiano, 2010; Morales-Alamo *et al*., 2015) or absence (Coelho *et al*., 2015; Ferguson *et al*., 2016) of a power reserve at the LoT. The difference in findings amongst publications may lie in the interpretation of ΔP at the LoT. In previous literature in which a power reserve was observed, the power generating capacity of muscle was as much as three-times greater (power reserve ~ 300%) than the power required at task failure (Marcora & Staiano, 2010; Morales-Alamo *et al*., 2015); however, this is thought to be the result of mechanical rather than physiological influence as cadence – which itself can increase power output – was not controlled during the maximal power generation protocol (Burnley, 2010). In the present study, we ensured that the cadence was similar to that of the RI protocol. As a result, the RES group was capable of generating, on average, ~25% more power above that required by the task at the LoT (ΔPReserve = 25 ± 10 %). Ferguson et al. (2016) did not find a power reserve, although they stipulated that ΔPReserve needed to exceed 20% to be considered physiologically significant; similar to the cutoff for our RES group. Different interpretations of what is considered a “physiologically significant” reserve (based on ΔPReserve) may explain

why previous studies have not identified in their study sample sub-populations who do and do not display a power reserve (in the current study, ΔPReserve of the entire sample was large (14 ± 13%) and similar to that reported in Ferguson et al. (2016) (12 ± 15%) and Coelho et al. (2015) (18 ± 11%)).

To ensure that any observed power reserve was the result of a physiological reserve and not simply the result of terminating the test prematurely, it was important to verify that participants exercised to their LoT. To accomplish this, the RI protocol was used as both a fatigue-intervention protocol and for identifying and confirming whether $\dot{V}O_{2max}$ had been achieved – i.e., if participants did not reach $\dot{V}O_{2max}$, it is likely that the test was terminated prematurely. For all participants, the $\dot{V}O_{2peak}$ values from the RI (from visit 2) and the values from the RI and SE phases of the RISE95 protocol were not different despite differences in peak PO between the RI and SE protocols, thereby satisfying the criterion for confirming a true $\dot{V}O_{2max}$ and providing support for requirement for a truly exhaustive effort at the LoT.

Between the RES and NRES groups, no differences existed for $\dot{V}O_{2max}$ or $PO_{peak}$. Despite this homogeneity, those participants in the RES group had a larger ΔPReserve because they were able to generate a greater ($p<0.05$) $P_{isoPOST}$. Those in the NRES group exhibited greater reductions in 10-Hz PT and 10/50-Hz indicating that greater peripheral muscle fatigue was accrued in these individuals (Amann & Dempsey, 2008). That peripheral muscle fatigue development after the RI test was consistently greater in the NRES group suggests that it may be a contributory mechanism leading to the LoT unique to those without a power reserve. In this instance, the LoT may have occurred when the muscle became unable to maintain cellular homeostasis or metabolic stability thereby

triggering increased afferent feedback from the muscle and reflex-inhibition of efferent locomotor output (Amann & Dempsey, 2008; Amann *et al*., 2008, 2009, 2011; Edwards *et al*., 1983). Whereas in the RES group, although significant peripheral muscle fatigue was evident (albeit to a lesser degree), the presence of a large reserve may indicate that some other mechanism(s) is/are contributing to fatigue development at the LoT. For example, a reduction of supraspinal drive to the motoneuron (central fatigue; as indicated by the reductions in MVC) could act to protect the muscle from further peripheral fatigue and terminate exercise despite the muscle being capable of producing additional power output and tolerating additional levels of peripheral fatigue (Gandevia, 2001).

It would be expected that those presenting with greater peripheral muscle fatigue development would experience greater impairment of muscle function. Therefore, in addition to voluntary and electrically-stimulated muscle force/torque development, the present study also examined muscle function at the LoT through maximal knee-extension velocity and time-to-exhaustion during an exhaustive bout of constant-load exercise at 95% $PO_{peak}$ immediately following the RI-exercise test. Our data show that relative to pre-RI, maximal velocity was reduced more and time-to-fatigue during the constant-PO SE protocol was shorter in the NRES group consistent with the greater muscle fatigue development in this group. This may provide insight as to why individuals in the RES group possess either i) a capacity for very short-term power production (Coelho *et al*., 2015) or ii) an ability to generate power in significant excess of that required at the LoT, as muscle function was more sufficiently preserved.

Collectively, these data suggest that the mechanism contributing to the LoT may differ between groups. It is evident that at the LoT, participants in the RES group developed

less peripheral muscle fatigue and muscle function was better maintained compared to the NRES group. In this instance, the LoT may result from downregulating efferent output to maintain the muscle environment below the critical fatigue threshold (Amann & Dempsey, 2008). In contrast, the NRES group experienced greater peripheral muscle fatigue suggesting that an alternate mechanism for the LoT exists in this group. The LoT in the NRES group may be a result of reaching the critical fatigue threshold (catastrophic fatigue; Edwards *et al*., 1977), impairing the short- and long-term capacity of the muscle to generate power in excess of that required at the LoT.

## 2.5 CONCLUSIONS

This study determined the prevalence of a power reserve within a seemingly homogenous sample (not pre-selected for specific groups), and a novel, direct association of the differences that exist in muscle fatigue development and muscle function at exhaustion between those with and without a power reserve. At the LoT, peripheral muscle fatigue developed more substantially and muscle function was more severely impaired in the NRES group. Despite this, both groups finished at the same mean peak PO during RI exercise, suggesting that mechanisms contributing to the LoT may differ between groups. In those without a power reserve, a critical fatigue threshold may have been reached, impairing short-term (knee-extensions) and long-term (RI-exercise) capacity to generate power in excess of that required at the LoT. In those with a power reserve, lesser peripheral fatigue development may indicate that the RI-exercise test was terminated below a critical fatigue threshold, preserving the muscle environment and maintaining muscle function, and thus providing a significant capacity for power generation. As has been reported previously, the mechanism(s) associated with muscle

fatigue is/are complex and it is unlikely that a single, all-encompassing mechanism is able to explain exercise tolerance at the higher intensities of RI exercise.

## 2.6 LIMITATIONS

Electrical stimulation is used to bypass central motor drive and to isolate the peripheral factors contributing to impaired neuromuscular function during muscle contractions (Edwards *et al*., 1977; Jones, 1996). In our laboratory, it was not possible to assess muscle contractile properties directly on the cycle ergometer immediately at the LoT after dynamic cycling exercise which required introducing a short delay while the participant was moved from the ergometer to the dynamometer. During this delay, which we limited to ~ 35 s, there may have been some recovery of muscle function (Froyd *et al*., 2013; Gruet *et al*., 2014; Sargeant & Dolan, 1987; Szubski *et al*., 2007; Temesi *et al*., 2017). However, in the present study, significant muscle fatigue was observed in both groups despite this short delay. Also, in four participants (two from each NRES and RES) we assessed recovery of muscle function "immediately" (within ~35 s), and at 5 min and 10 min post-RI exercise to develop a fatigue-recovery timeline and observed that all neuromuscular variables (including maximal isokinetic knee-extension power and 10 Hz stimulated torque and 10/50 Hz stimulated torque ratio) were depressed at each time-point, indicating that with our exercise model, full recovery is delayed and that substantial muscle fatigue remains up to at least 10 min post-exercise.

It was assumed that fatigue during RI cycling exercise could be compared with voluntary and electrically-stimulated muscle force production assessed during knee extension contractions. Despite best efforts to match the biomechanics of whole-body cycling (knee and hip angle, range of motion, etc.) and velocity (70 rpm cycling matched

to 221.1 deg•s$^{-1}$ on the dynamometer) to knee extensions, the contributions of different muscle groups (isolated quadriceps vs. whole-limb) associated with each movement cannot be disregarded (Bini & Carpes, 2014). Additionally, although comparison between the two movements cannot be made directly, it is still evident that i) some participants produced a power output with knee extension contractions equal to the power produced at the LoT in whole-body cycling (NRES) whereas others could produce power with knee-extensions well in excess of the power required at the LoT (RES), and ii) differences in neuromuscular fatigue and muscle function exist between the two groups.

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# APPENDICES

## Appendix A: Ethics Approval Notice

Western Research

Research Ethics

**Western University Health Science Research Ethics Board**
**HSREB Full Board Initial Approval Notice**

**Principal Investigator**: Dr. John Kowalchuk
**Department & Institution**: Health Sciences\Kinesiology,Western University

**Review Type**: Full Board
**HSREB File Number**: 107880
**Study Title**: The relationship between muscle fatigue and power reserve following ramp-incremental cycling to exhaustion .
**Sponsor**: Natural Sciences and Engineering Research Council

**HSREB Initial Approval Date**: May 05, 2016
**HSREB Expiry Date**: May 05, 2017

**Documents Approved and/or Received for Information**:

| Document Name | Comments | Version Date |
|---|---|---|
| Recruitment Items | 107880 Recruitment Advertisement | 2016/04/08 |
| Letter of Information & Consent | Letter of Information Clean | 2016/04/08 |
| Other | EMS Contact Document (Received 18Mar16) | |
| Western University Protocol | (Received 19Mar16) | |

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above named study, as of the HSREB Initial Approval Date noted above.

HSREB approval for this study remains valid until the HSREB Expiry Date noted above, conditional to timely submission and acceptance of HSREB Continuing Ethics Review.

The Western University HSREB operates in compliance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS2), the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use Guideline for Good Clinical Practice Practices (ICH E6 R1), the Ontario Personal Health Information Protection Act (PHIPA, 2004), Part 4 of the Natural Health Product Regulations, Health Canada Medical Device Regulations and Part C, Division 5, of the Food and Drug Regulations of Health Canada.

Members of the HSREB who are named as Investigators in research studies do not participate in discussions related to, nor vote on such studies when they are presented to the REB.

The HSREB is registered with the U.S. Department of Health & Human Services under the IRB registration number IRB 00000940.

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