THE EFFECT OF PRIOR KNOWLEDGE OF TEST ENDPOINT ON THE EXPRESSION OF NON-LOCAL MUSCLE FATIGUE

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ABSTRACT

To clarify if prior knowledge of test endpoint has an effect on the expression of non-local muscle fatigue (NLMF), fifteen male participants (22.4 ± 3.8 years) completed four conditions: 1) KN-fatigue (known endpoint after fatigue), 2) UNK-fatigue (unknown endpoint after fatigue), 3) KN-control (known endpoint without fatigue), 4) UNK-control (unknown endpoint without fatigue). For fatigue conditions, a maximal intensity, unilateral knee extension protocol was completed (two sets of 100s maximal voluntary contractions (MVIC), 60s rest between); control conditions involved rest (260s). The duration of a post-intervention strength-endurance test (contralateral leg extension, ≥30 seconds) was known (KN conditions) or unknown (UNK conditions) by the participant. UNK-fatigue demonstrated the largest anticipatory decreases from pre-MVIC to the start of the strength-endurance test (-18.9% MVIC force, and -25.6% VM RMS EMG). During the strength-endurance test, the UNK-fatigue and KN-control conditions displayed clinically meaningful differences in force (UNK-fatigue 12%↓ over first 30s), which were largest at epoch 6 (UNK-fatigue 21.6%↓ from 25-30s).

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Author

Alan Hamilton

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List of Abbreviations and Symbols

BF	Biceps femoris
CMEP	Cervicomedullary motor evoked potential
CNS	Central nervous system
EMG	Electromyography
ES	Effect size
KN	Known endpoint (contralateral strength-endurance test)
MEP	Motor evoked potential
Mmax	Maximal compound muscle action potential
MVIC	Maximal voluntary isometric contraction
NLMF	Non-local muscle fatigue
RF	Rectus femoris
RMS	Root mean square
SD	Standard deviation
TMS	Transcranial magnetic stimulation
TMEP	Thoracic motor evoked potential
UNK	Unknown endpoint (contralateral strength-endurance test)
VL	Vastus lateralis
VM	Vastus medialis

Chapter 1 Review of Literature

1.1 Abstract

Non-local muscle fatigue (NLMF) occurs when fatigue in one muscle group produces a fatigue response in an unexercised muscle. Research examining NLMF has been inconsistent in showing performance effects, but this has also demonstrated that numerous factors impact its expression. The contraction intensity, duration, type (static versus dynamic), and muscle groups used have all been shown to be important fatigue protocol factors for eliciting NLMF. Further to this, NLMF effects may not be revealed depending on the measurements and post-fatigue test protocols utilized. Examination of force measurements alone can yield meager NLMF results, while inclusion of neuromuscular measurements (i.e. iEMG, TMS, CMEP) may allow for more significant changes and performance mitigation strategies to be seen. Longer, maximal intensity tests tend to be more effective at showing significant findings. Studies have shown distinctive pacing strategies throughout tests of different durations, or when different instructions are provided (prior knowledge manipulation). Typically, longer tests show more pronounced impacts from central fatigue mechanisms. Some researchers argue that at maximal intensities, peripheral mechanisms provide the strongest stimulus for fatigue and potential crossover effects. This is contrasted however by the finding that manipulating prior knowledge of test endpoint affects force output and pacing pattern in repeated maximal voluntary contraction (MVIC) protocols (12 repetitions).

Manipulating a participant's prior knowledge of the test appears to be effective at impacting central mechanisms and modifying performance in localized fatigue studies. Understanding how these factors impact NLMF expression may help clarify the impact of certain test protocols and central fatigue mechanisms.

1.2 Introduction

Muscle fatigue is a multifactorial phenomenon that can present itself in response to various stimuli and can produce both short-term performance impairments and long-term adaptations. Under certain conditions, fatigue in one muscle group has been found to produce fatigue in non-exercised muscles (Halperin, Aboodarda & Behm, 2014b; Halperin, Copithorne & Behm, 2014d; Kawamoto, Aboodarda & Behm, 2014; Martin & Rattey, 2007; Paillard et al., 2010). This phenomenon has most widely been referred to as crossover or non-local muscle fatigue (NLMF). Examining the mechanisms underlying this fatigue phenomenon may help us better understand how central (i.e. cortical, corticospinal, spinal) and peripheral (i.e. neuromuscular junction, muscle fibres) factors modulate fatigue and motor performance. It is currently believed that central factors are largely responsible for the occurrence of NLMF, but much remains unclear concerning the relative contributions of specific processes. If NLMF is a centrally mediated phenomenon, then fatigue and test protocols that exacerbate central factors should reveal more significant NLMF effects. Positive implications for rehabilitation and high-performance training could be realized with a greater understanding of what promotes the greatest NLMF effect and what physiological structures are fatigued in this process.

1.3 Peripheral vs. Central Fatigue

Muscle fatigue is defined as a reduction in the maximal force exerted by a muscle or a muscle group due to central and/or peripheral mechanisms (Enoka & Stuart, 1992). Central fatigue refers to an activity–induced decline in the ability to activate a muscle voluntarily and results from a failure of the central nervous system to excite and drive motor neurons (Gandevia, 2001). This response could be from a spinal or supraspinal source. Peripheral fatigue specifies a reduction in the ability of the muscle fibers to produce force, and a failure of the muscle to respond to neural excitation (Allen et al., 2008; Decorte et al, 2012). Different types of activities can lead to varying stress and fatigue of different mechanisms involved in muscle contraction (Allen et al, 2008). Metabolic by-products such as K^+, H^+, blood lactate, decreased Ca^{2+} sensitivity of contractile proteins, and reduced Ca^{2+} release from sarcoplasmic reticulum provide the most predominant sources of fatigue at the muscle site. During prolonged aerobic exercise, the supply of O_2 may also be insufficient and further contribute to peripheral fatigue (Allen et al, 2008).

Both central and peripheral fatigue can develop with maximal or submaximal intermittent isolated muscle contractions. It has been demonstrated that central motor drive changes as peripheral fatigue develops (Decorte et al, 2012). These changes are evidenced through recruitment of additional motor units, changes in motor neuron firing rate and changes in muscle activation / pacing strategies (Duclay et al., 2011;

Flaxman, Smith & Benoit, 2014; Roelands et al., 2013). Neural structures located within the spinal cord, corticospinal tract and motor cortex, are impacted variably through muscle afferent feedback and biochemical changes experienced within the body and central nervous system (CNS)(Gandevia, 2001). For example, eccentric contractions (compared to concentric or isometric contractions) of the soleus have been shown to impact corticospinal excitability, while the gastrocnemius displayed no such differences between contraction types (Duclay et al., 2011). Metabo- and mechanosensitive group III/IV muscle afferents from exercising muscle groups act to inhibit central processes such as spinal excitability (Amann, 2011; Gandevia, 2001). If inhibitory afferent feedback were the primary contributor to reduced central drive, then the manipulation of cortical factors (i.e. motivation) would not significantly modify the expression of NLMF.

Whether central fatigue is derived from afferent influences or cortical inhibition of spinal or supraspinal centres can be assessed with a number of experimental procedures. The Hoffman reflex (H-reflex) represents afferent excitability of the spinal motoneuron (Enoka & Stuart, 1992) as it is modulated by motor neuron excitability and Ia synaptic transmission from involved muscles including synergist and antagonist muscle groups (Schieppati, 1990). The V-wave is a variant of the H-reflex that depends on the level of efferent and descending neural drive (Duclay et al., 2011). The analysis of motor evoked potentials (MEPs) elicited through stimulation of the motor cortex (transcranial magnetic stimulation [TMS]) or the corticospinal tract (cervicomedullary

motor-evoked potential [CMEP]) can help differentiate changes in excitability at the supraspinal and spinal levels, respectively (Duclay et al., 2011). Changes in MEP size as a result of TMS can reflect changes in both cortical and spinal levels (Rothwell et al., 1991). Direct stimulation of the corticospinal tract through CMEPs however helps determine motor neuron excitability more directly (Martin et al., 2006). Due to their relationship, the MEP/CMEP ratio is used as an index of cortical excitability. Examining the EMG silent period after a maximal MEP can help determine changes in intracortical inhibition, with silent periods longer than 100ms believed to indicate cortical inhibitory mechanisms (Inghilleri et al., 1993).

The relative contribution of central and peripheral factors to overall fatigue is dependent on several factors such as contraction type, muscle groups, exercise intensity, and pacing strategy (Allen et al, 2008; Gandevia, 2001; Halperin & Behm, 2015). Motor control comparisons between different muscle groups must be viewed carefully. Duclay et al. (2011) found a difference in MEP characteristics between soleus and medial gastrocnemius muscle groups. They found that maximal amplitude of MEP and H-reflex and the duration of the silent period were reduced during eccentric MVCs of the soleus but not the medial gastrocnemius. They concluded that modulation of corticospinal excitability during different contraction types occurs mainly due to pre- and post-synaptic inhibitory mechanisms at the spinal level. Researchers have commonly reported differences in voluntary activation and evoked contractile properties for other muscle groups including the quadriceps, dorsiflexors, plantar flexors

and elbow flexors (Behm & St. Pierre, 1997; Behm et al. 2002). Intermuscle differences in motor control are clear and differences in spinal mechanisms appear to play a significant role. A further factor influencing the extent of peripheral versus central fatigue in addition to contraction types and muscle groups is the exercise intensity.

A wide-range of contraction intensities, from low submaximal to maximal have been employed to study fatigue development. Sogaard and colleagues (2006) utilized a sustained, submaximal elbow flexion fatigue protocol (15% MVIC) to assess peripheral and central fatigue processes. Due to progressive decreases in resting twitch force and increases in superimposed twitch, they concluded that both peripheral and central fatigue increase progressively at low intensities. The researchers evoked superimposed twitches during brief MVICs throughout the fatigue protocol via motor nerve stimulation as well as motor cortical stimulation. As the superimposed twitch increased when evoked by both motor nerve and motor cortical stimulation, the main component of central fatigue appears to be suboptimal output from the motor cortex. Other studies utilizing both low and high intensity contractions indicated that low-force (20-50% MVIC), long-duration fatiguing contractions induce greater central fatigue than high-force (75-80% MVIC)(Behm & St. Pierre, 1997; Yoon et al, 2007). Martin et al. (2006) utilized TMS of the motor cortex and CMEPs to examine the output of motor neuron pools to corticospinal inputs at different voluntary contraction intensities during an isometric elbow flexion exercise. The researchers noted similar reductions in CMEPs and MEPs with increasing contraction strength. They therefore concluded that at higher

intensities, motor neuron properties and not the motor cortex limit motor neuron output (i.e. TMS did not overcome the decrease in central drive). There are a number of other phenomena that illustrate the influence of central drive on muscle force output.

1.4 Non-Local Muscle Fatigue (NLMF)

Research investigating the NLMF phenomenon has had limited success at clarifying, and even producing it. In a review of related research by Halperin and Behm (2015), only 30 of 57 studies examining NLMF were reported to have found an effect. The inconsistent results found in the literature have made it difficult to develop comprehensive and prevailing theories surrounding NLMF. As a result, conflicting theories governing the key physiological processes and inputs involved in the expression of NLMF are common (Decorte et al., 2012; Marcora et al., 2009; Martin & Rattey, 2007; Takahashi et al., 2011). It is likely that differences in fatigue and test protocol variables such as intensity, duration / volume (i.e. number of sets and repetitions, length of time holding contraction), contraction type (i.e. isometric, concentric, eccentric), rest intervals and pacing strategies have contributed to the mixed NLMF findings. Gaining a better understanding of these variables can help clarify the processes behind NLMF and hopefully result in more predictable expression and manipulation of it.

1.4.1 Contraction Types

Isometric contractions are commonly used as part of fatigue or test protocols in research but have produced mixed NLMF results when utilized. Some studies have demonstrated NLMF effects such as force reduction (Kennedy et al, 2013; Martin & Rattey, 2007; Rattey et al, 2006) while others have not (Paillard et al, 2010; Zijdewind et al, 1998). Paillard et al. (2010) utilized voluntary as well as electrically stimulated isometric contractions of knee extensors to assess changes in contralateral force and postural control. They followed a low-intensity (10% MVIC), high repetition (10 sets, 10 seconds between sets; 50 repetitions per set, 4 seconds contraction, 2 seconds rest) protocol and found no significant change in contralateral strength following the voluntary or electrically–stimulated exercise. A crossover fatigue effect was noted in the study however; as postural control of the contralateral leg was reduced following both fatigue protocols. The similar crossover balance-related results from voluntary and electrically evoked contractions also indicate that afferent feedback from peripheral fatigue processes could play a substantial role in NLMF expression without cortical influences.

Static-stretching (isometric hold of stretch) has been shown to induce performance decrements similar to exercise-induced fatigue, particularly when longer-duration and higher-intensity stretching protocols are used. Recent research has examined the impact of static-stretching on NLMF. Marchetti et al. (2016, under review)

were able to show a crossover fatigue effect following a prolonged stretching protocol for the pectoralis major (6 sets of 45s/15s, 70-90%). The EMG of the triceps decreased during a compound movement (bench press MVIC) subsequent to the stretching protocol. Unfortunately, no other measures were reported to further determine the occurrence of performance decrements.

Following a similar stretching protocol for the ankle plantar flexors (6 sets of 45s/15s, 70-90% discomfort), da Silva et al. (2015) found a decrease in jump height and impulse for the contralateral, non-stretched limb. They concluded that the static-stretching induced a central nervous system inhibitory effect but were unable to further isolate the specific mechanism.

1.4.2 Contraction Intensity

It is unclear what contraction intensity is most effective at evoking an NLMF effect. Kawamoto et al. (2014) demonstrated similar results between two different dynamic unilateral knee extension fatigue protocols (70% vs. 40% MVIC). Both fatigue protocols that the non-dominant knee extensors completed produced decreases in force and time to exhaustion in the non-exercised knee extensors. Kennedy and colleagues (2013) also demonstrated that a maximal bilateral continuous isometric handgrip fatigue protocol produced greater decreases in ankle plantar flexion MVIC and voluntary activation than a submaximal (30% MVIC) fatigue protocol. In contrast, Rattey et al.

(2006) completed a fatigue protocol where the dominant leg performed a continuous, maximal isometric knee extension for one set of 100 seconds. Following this protocol, the non-dominant leg (non-exercised leg) exhibited no significant changes in twitch force, M-wave properties or MVIC force. A decrease in voluntary activation, twitch values and EMG activity of the dominant leg following the exercise indicated that localized fatigue had occurred with both central and peripheral contributions.

1.4.3 Fatigue Duration

Exercise volume has also been shown to impact the occurrence of NLMF. A study by Doix and colleagues (2013) demonstrated no NLMF effect in the contralateral knee extensors following a 100-s MVIC, but two sets of a 100-s MVIC was sufficient to produce NLMF effects. Halperin et al. (2014d) demonstrated that two continuous 100-s unilateral MVICs (1 min rest between) of the elbow flexors or the knee extensors produced significant decreases in force, EMG activity and voluntary activation in the non-exercised knee extensors. The protocol was insufficient to elicit NLMF in the non-exercised elbow flexors however and highlights the existence of muscle specific differences.

1.4.4 Intermittent vs. Continuous Fatigue Protocols

It is unclear whether continuous or intermittent isometric contractions affect fatigue mechanisms differently and more research needs to be done to clarify. Current research has not been able to definitively address how differing contraction types and intensities influence circulation and hemodynamic responses throughout the body (Gurley et al. 2012; Jensen et al. 1995; Thompson et al. 2007). Current research suggests that lower body endurance activities (i.e. running, cycling), at various intensities and durations, do not produce NLMF (Decorte et al, 2012, Halperin & Behm, 2015). For example, Ross et al. (2010) found no difference in participants' handgrip MVICs following a 20 km run. Decreases in knee extensor EMG activity, voluntary activation and MVIC force were observed in the final 5 km of the run. The researchers concluded that impaired voluntary activation and neural drive were responsible for the decrease in leg strength rather than contractile properties. Elmer and colleagues (2013) also found no changes in handgrip force following a one-leg cycling fatigue protocol. In the same study, the contralateral (non-exercised) leg was also tested and revealed no loss in maximum cycling power (Elmer et al., 2013).

1.4.5 Contralateral Fatigue Tests

Differences in post-fatigue tests of the non-exercised limb could also contribute to some studies not finding a NLMF effect. In a review of relevant literature, Halperin et

al. (2015) found that most NLMF studies utilized one of several testing protocols: 1) single MVIC, 2) repeated MVICs with long rest periods (≥ 30s), and 3) submaximal exercise to exhaustion. Subsequently, Halperin et al. (2014b) completed a study where they utilized two different testing protocols to assess NLMF in elbow flexors: a single MVIC and a strength-endurance protocol of 12 MVICs with 10s rest between repetitions. The single MVIC failed to demonstrate NLMF effects, but the last 5 repetitions of the strength-endurance protocol did reveal force decrements. Amann and colleagues (2013) also utilized two different tests to examine fatigue processes following a high-intensity unilateral knee extension fatigue protocol. A MVIC post-test remained unchanged for contralateral knee extensors, but time to failure during the endurance test decreased significantly. The results of Kawamoto et al. (2014) demonstrated NLMF through both a MVIC and submaximal (70% MVIC) time to exhaustion post-fatigue test however. The researchers could have achieved these results due to the high volume of exercise performed during the fatigue protocol (4 sets, each to task failure). The volume of the fatigue protocol was sufficient to generate NLMF at both 40% MVIC and 70% MVIC contraction intensities. Currently, greater NLMF effects have been observed when time to exhaustion tests (21% [range: 2-49%]) have been utilized, compared to force / power measurements (~5% [0-10%]) (Halperin et al. 2015).

1.4.6 NLMF Limb Differences

In the Halperin and Behm (2015) review of NLMF literature, 82% of relevant studies testing the lower limbs found NLMF while only 24% of studies using upper body measures demonstrated NLMF. Halperin and colleagues (2014d) illustrated this disparity in NLMF occurrence between upper and lower body limbs. They tested contralateral knee extensor performance following a high-intensity unilateral fatigue protocol of the dominant elbow flexors or knee extensors and found decreases in force and muscle activation from both fatigue conditions. In the same study, the exact same fatigue protocols were followed again but the elbow flexors were tested and no NLMF effects on force or EMG were evident. Zijdewind et al. (1998) found only minor crossover effects in the contralateral hand following an ipsilateral, isometric fatigue protocol (30% MVIC) of the first dorsal interosseus (FDI) muscle. Similar to Halperin et al. (2014), Kennedy and colleagues (2013) demonstrated that fatigue induced in upper body limbs can produce NLMF in lower limbs. The researchers asked participants to hold a maximal or submaximal bilateral isometric handgrip until force decreased to 80% of pre-fatigue values (Kennedy et al., 2013). They then tested the ankle plantar flexors and found a reduction in MVIC force and voluntary activation.

The disparity between upper and lower limb muscles may be partially explained by differences in flexor and extensor muscle afferents and motoneurons. Studies examining fatigue and NLMF commonly utilize knee extension for the lower body, and

elbow flexion for the upper body. Martin and colleagues (2006) demonstrated that during fatigue of the bicep and triceps muscle groups, group III and IV muscle afferent feedback from homonymous or antagonist muscles inhibited extensor motoneurons but facilitated flexor motoneurons. The researchers therefore concluded that extensor muscles might require greater cortical drive during fatigue to overcome the stronger inhibitory stimulus of muscle afferents.

1.4.7 Central Excitability Modulation

Recent research examining NLMF has been able to show changes in central excitability of the non-exercised limb, even in the absence of a drop in MVIC force. Aboodarda et al. (2015a) were able to show a decrease in normalized EMG activity of the vastus lateralis during an MVIC following bilateral elbow flexor fatigue, even though no decrease in force was seen. Lower supraspinal motor output appeared to be the primary factor as spinal motor neuron responses were higher and peripheral excitability (compound muscle action potential) showed no change.

In another study, Aboodarda et al. (2015b) demonstrated a significant increase in MEPs and decrease of CMEPs during MVICs of non-exercised contralateral biceps brachii, following a unilateral elbow flexion fatigue protocol. Examination of MVIC force and EMG measures did not reveal any significant crossover fatigue effects however. The

increased supraspinal responsiveness (MEP/CMEP) was noted to be a key factor in mitigating significant crossover effects on performance.

Sambaher et al. (2016) utilized a bilateral knee extensor fatigue protocol to assess crossover fatigue effects on the dominant elbow flexors. They found changes in corticospinal excitability, as a lower MEP/CMEP ratio and a trend towards higher CMEP values were demonstrated following the fatigue intervention. The researchers also noted that during a repeated MVIC post-intervention test protocol (12 repetitions, 5s MVICs, 10s rest), decreases in force were more pronounced in the knee extensor fatigue condition compared to rest.

Research has made great progress in clarifying the complex interaction of peripheral and central processes to fatigue but it is still unclear what provides the greater influence overall. Some researchers believe that afferent feedback from the muscle site may be providing the strongest influence over central processes and physical performance decline (Allen et al.; Decorte et al., 2012; de Koning et al., 2011).

Meanwhile, other researchers that have investigated pacing during prolonged exercise have concluded that cortical output appears to be the most significant factor in limiting physical endurance performance (St. Clair-Gibson & Noakes, 2004; Marcora et al., 2009). Research clearly demonstrates the immense specificity and complexity of motor control. This in turn supports how differences in experimental fatigue and test

protocols can result in very different neural and metabolic processes being stimulated or stressed.

Cortical, spinal, or peripheral fatigue may be targeted more depending on numerous experimental and environmental factors as discussed through this review. As researchers continue to gain a better understanding of the wealth of factors involved and how they interact, they can better isolate and control them in future research. Perhaps this will help bridge some of the conflicting conclusions and understanding of current research. Research examining the impact of pacing and mental strategies on physical performance may also help highlight the relative contribution of cortical, spinal and peripheral sources to fatigue.

1.5 Pacing

According to Roelands et al. (2013), "pacing is the distribution of speed, power output or energetic reserves…(and is) influenced by a number of factors including central and peripheral fatigue development." They further detail 'pacing strategy' as the self-selected strategy or tactics that the athletes adopt. Pacing has been observed in numerous sporting events and exercise activities over time. Researchers have traditionally observed a spontaneous pattern, and utilized a U-shaped curve model (fast start, slower middle part, end sprint) to illustrate pacing in events ranging in duration

from 2 min to several hours (Foster et al., 2012). It is typically accepted that during short-duration, high-intensity activities where maximal efforts are necessary, the speed / power output gradually declines as a function of the length of the activity (Chidnok et al., 2013). Studies utilizing unknown fatigue endpoints and pacing deception in particular have shown this is not always the case however, which will be discussed in greater detail in following sections (Billaut et al., 2011; Halperin et al., 2014a; Halperin et al., 2014c).

There is evidence that pacing strategies are based on numerous internal and external factors that are established before the initiation of exercise, and are continually regulated throughout (Halperin et al., 2014a; Halperin et al., 2014c; Roelands et al., 2013). Intramuscular substrate availability (Lima-Silva et al. 2011; Rauch et al. 2005), core temperature (Tucker et al. 2006b; Tucker et al. 2004), motivation (Blanchfield et al. 2013; Stone et al. 2012), and knowledge of end point (Ansley et al. 2004; Billaut et al. 2011) have all been demonstrated to influence pacing. St. Clair-Gibson and Noakes (2004) support that pacing strategies involve neural processes in the brain to control exercise activity - internal sensory signals and information from the environment are actively integrated there to provide pacing input. De Koning et al. (2011) contend that intramuscular substrate / metabolic changes are most likely to determine changes in power output in shorter duration events (1-30 min). They also stated that core temperature elevation and availability of carbohydrates could play a significant role in pacing, but in mid- (20-120 min) and long-duration events (>90 min) respectively.

Only a few studies have examined pacing during short duration and high intensity cyclic exercise (i.e. running, cycling), and they demonstrate a central and fairly subconscious implementation of pacing strategy (Ansley et al. 2004; Billaut et al. 2011; Wittekind et al. 2011). These studies indicated that shorter known endpoints tend to produce greater initial power, without a significant drop off in performance when encouraged to continue with further repetitions. Known endpoints of longer duration (i.e. two times the duration of shorter time, 10 sets vs. 5 sets) and unknown endpoints both appear to limit truly maximal output at higher intensities.

Billaut et al. (2011) engaged participants in a protocol where there were three conditions: 1) control condition where ten sets of 6 s maximal sprint with 24 s rest were completed with prior knowledge of repetitions; 2) unknown condition where subjects were not told how many sets they would be performing but were stopped at ten; and 3) deception condition where subjects were told they would complete five sets and were then encouraged to continue until ten. Participants in the deception condition produced more total work, power and lower body EMG during the first five sprints compared to the other two conditions. The unknown condition also exhibited a relatively early decrease in work and EMG. The study was effective at showing that both deception and lack of knowledge about endpoint influences performance, particularly during the initial portion of exercise.

Research is even more limited concerning pacing strategies during maximal muscle contractions (Shephard 2009; Weir et al. 2006). Halperin et al. (2014a; 2014c) completed two studies examining the impact of known vs. unknown endpoints on force production and EMG activity during an elbow flexion MVIC fatigue protocol. For the unknown condition, participants were not told how many MVICs to perform but were stopped after 12, which was the same number as a known control condition. There was also a deception type unknown endpoint where participants were told they would perform 6 MVICs, but were then encouraged to continue until 12 were completed. Both genders produced greater forces during the first 6 MVICs in the deception condition compared to unknown. Males also exhibited greater biceps brachii EMG activity during that time. No significant differences in average force were found over the last 6 MVICs for females across conditions but they did remain a little higher in the deception condition for males. Together, these results indicate that deception can enhance performance even when the effort is already supposed to be maximal, while an unknown endpoint can inhibit performance.

It is clear based on current findings that prior knowledge of endpoint is an important factor in pacing strategies and in realizing maximal physical output. Marcora et al. (2009) suggests that an unknown exercise endpoint restricts our ability to select a pacing strategy, and may lead to decreases in motivation, the creation of more psychological strain and performance impairment. In their central governor model, St. Clair-Gibson and Noakes (2004) propose that before and continuously during exercise,

the brain subconsciously calculates the metabolic cost required to complete an exercise task given prior experience, and under the influence of environmental conditions and the current physical state (St. Clair-Gibson & Noakes, 2004). As part of their model, they propose that the most important input to the central calculation is the known duration of the activity and that two different strategies are employed depending on whether exercise endpoint is known or unknown. They support the existence of two different strategies by noting that in studies where the exercise endpoint is known, performance tends to be more consistent than in studies where the endpoint is not known. Given the framework of their theory, it is reasonable to hypothesize that an inefficient pacing template is more likely to be used in an unknown endpoint situation and impact performance negatively.

Research tends to support a strong influence of endpoint knowledge on local physical performance (i.e. performance within the muscle group being exercised and tested) as numerous studies have demonstrated that physical performance changes under different knowledge of endpoint conditions (Billaut et al., 2011; Halperin et al., 2014a; Halperin et al., 2014c). Billaut et al. (2011) found that when participants did not know how many sprints they would perform, they performed less total work than when they were told the number of sprints prior to performance. As previously discussed, studies where participants are deceived as to the true endpoint also reveal higher performance outputs when shorter performance periods are expected (Billaut et al., 2011; Halperin et al., 2014a; Halperin et al., 2014c). While research shows that prior

knowledge of endpoint affects localized physical performance, further research is needed to clarify whether endpoint knowledge will impact NLMF expression similarly.

In addition, fatigue protocols that successfully elicit NLMF are typically performed over a longer period of time (i.e. >2 min) than the subsequent tests (i.e. 5s MVIC, 30s MVIC). Learned pacing may therefore play a greater role in NLMF expression in unknown endpoint conditions. The prior fatigue protocol may influence the pacing strategy during the subsequent crossover test in a way that is not optimal for the shorter tests. If a person is told the duration of the test, they may be better able to override the more immediately used pacing strategy. If a person is not told the duration of the test however they may revert subconsciously back to the longer pacing strategy that was necessary in the previous physical effort. Further, if our motivation and central drive is already weakened through a prior fatigue protocol, it may exacerbate central factors involved in NLMF, interfere with pacing strategies and lead to greater expression of NLMF.

As fatigue develops, our sense of effort increases when trying to maintain a similar performance output (Marcora et al., 2009). Indeed, increasing sense of effort tends to correlate with other markers of fatigue (de Morree et al., 2012; 2014). Understanding the interaction of fatigue processes and sense of effort may help highlight the relative contribution of those processes under different fatiguing conditions.

1.6 Ratings of Perceived Exertion

Ratings of perceived effort (RPE) have been utilized widely through physical performance research and they have been proven to be reliable indicators of both aerobic (Robertson & Noble, 1997) and resistance exercise intensity (Lagally et al. 2002). Researchers have demonstrated reliably that RPE increases along with EMG activity when force intensity or fatigue increases (de Morree et al. 2012). Further to this, de Morree et al. (2012) found a significant correlation between RPE and movement-related cortical potential (MRCP) during a dynamic unilateral elbow flexion fatigue protocol (at 20% 1-RM and 35% 1-RM intensities). The study provides evidence that perception of effort correlates with central motor command during physical exertion.

Mental exertion has been found to alter muscle endurance performance when performed simultaneously (Yoon et al. 2009), or prior to (Pageux et al., 2013) physical exertion at low-intensity (isometric contraction at 20% MVIC). The study completed by Pageaux et al. (2013) found that mental exertion prior to a physical endurance task (continuous isometric bilateral knee extension at 20% MVIC) resulted in higher RPEs and shorter times to exhaustion. In contrast, research by Rozand et al. (2014) indicates that mental exertion does not alter maximal muscle activation or neuromuscular function of knee extensors. These findings are consistent with similar research testing maximal force production following mental exertion (Pageaux et al. 2013). Bray et al. (2012)

found that handgrip MVIC declined with cognitive effort however. Although there were differences in protocols, this could also demonstrate a possible difference in how upper and lower limbs respond to mental fatigue.

In the Rozand et al. (2014) study, three different mental exertion conditions were employed of varying intensity, all lasting 27 minutes. Perhaps longer periods of mental exertion would eventually lead to NLMF in maximal performance tests. Several authors have proposed that a brain-based energy resource governs performance of cognitive, emotional, and physical effort regulation (Bray et al., 2012; Gailliot et al., 2007). Further research is needed to clarify this theory, and whether certain kinds of mental exertion would utilize pools of neural resources to limit maximal force production.

Marcora et al. (2009) found that performing a demanding cognitive task prior to a high intensity cycling endurance task resulted in shorter times to failure and higher RPE scores. As no differences in cardiorespiratory or musculo-energetic factors were noted between control and cognitive fatigue groups, the researchers concluded higher perception of effort was the key performance-limiting factor.

Perceived exertion appears to be an important indicator of mental exertion (Bray et al., 2012; Marcora et al., 2009; Pageaux et al., 2013; Rozand et al., 2014). Researchers have used the RPE measure to help reveal the impact of various factors on mental exertion and pacing (Bray et al, 2012; de Morree et al., 2012; de Morree et al., 2014). Although prior knowledge of exercise endpoint has been shown to impact performance

(Billaut et al., 2011; Halperin et al., 2014a, Halperin et al., 2014c), it has not been shown to correlate with higher RPE measures (Billaut et al., 2011). Currently, it is unknown whether prior knowledge of endpoint will correlate similarly under NLMF conditions. If NLMF is largely a centrally mediated phenomenon and not knowing the exercise endpoint aggravates central factors, it is possible that NLMF may be more magnified under unknown endpoint situations.

1.7 Conclusions

The use of a wide-range of methodologies in the study of fatigue and NLMF has highlighted the task specificity of fatigue (i.e. different conditions induce different fatigue effects). Much clarification is still required however concerning the processes involved in fatigue and the NLMF phenomenon in particular. Higher intensity exercise appears to be more effective at producing NLMF (Kawamoto et al., 2014; Halperin & Behm, 2015 under review). Researchers also tend to agree that the afferent output associated with peripheral fatigue processes are primary contributors to local-muscle fatigue at higher exercise intensities (Allen et al., 2008). This finding supports the notion that stimulation of peripheral mechanisms, which can impact central processes (i.e., afferents, endocrine, blood borne metabolites) could play a large role in the development of NLMF.

Research tends to indicate that central processes play a relatively larger role in local-muscle fatigue during lower intensity, longer duration exercise however (Behm & St. Pierre, 1997; Yoon et al., 2007). Central fatigue may therefore provide a stronger inhibitory influence on performance and impact NLMF more significantly in these cases. Together, NLMF is more commonly observed when high intensity and high volume (long contraction duration [i.e. 100s], higher repetitions [$\geq$ 10]) fatigue protocols are followed (Doix et al., 2013; Halperin & Behm, 2015 under review). Longer testing protocols (i.e. repeated maximal contractions with short rest intervals, continuous contraction until failure) appear to be more effective at revealing an NLMF effect than single MVIC tests (Halperin et al., 2014b; Halperin & Behm, 2015). Single MVIC tests have been able to show an NLMF effect under certain conditions, but less frequently and typically where higher intensity and volume fatigue protocols have been followed (Kawamoto et al., 2014).

Intense or prolonged mental effort has been shown to increase RPE (Marcora et al., 2009), which could impair mental vigilance and promote stronger NLMF effects through central factors. Longer testing protocols may provide stronger evidence of NLMF (Halperin et al., 2014b) and help highlight central factors of mental vigilance as well. Prior knowledge of exercise endpoint is a central factor that has been shown to impact sensation of fatigue and performance (Billaut et al., 2011; Halperin et al., 2014a; Halperin et al., 2014c). Currently, the literature has not examined if prior knowledge of exercise endpoint modifies NLMF expression. If prior knowledge of endpoint modifies

NLMF than it gives support to the role of central factors (i.e. cortical) as a mediator in the phenomenon.

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Chapter 2 Research Paper

2.1 INTRODUCTION

Muscle fatigue is a multifactorial phenomenon that can present itself in response to various stimuli and can produce both short-term performance impairments and long-term adaptations. Under certain conditions, fatigue in one muscle group has been found to produce fatigue in non-exercised muscles (Halperin, Aboodarda & Behm, 2014b; Halperin, Copithorne & Behm, 2014d; Kawamoto, Aboodarda & Behm, 2014; Martin & Rattey, 2007; Paillard et al., 2010). This phenomenon is referred to as crossover or non-local muscle fatigue (NLMF).

Examining the mechanisms underlying the NLMF phenomenon may help us better understand how central (i.e. cortical, corticospinal, spinal) and peripheral (i.e. neuromuscular junction, muscle fibres) factors modulate fatigue and motor performance (i.e. force, endurance time). Central fatigue refers to an activity–induced decline in the ability to activate a muscle voluntarily and results from a failure of the central nervous system to excite and drive motor neurons (Gandevia, 2001). Peripheral fatigue specifies a reduction in the ability of the muscle fibers to produce force, and a failure of the muscle to respond to neural excitation (Allen et al., 2008; Decorte et al, 2012).

It is typically accepted that during short-duration, high-intensity activities where maximal efforts are necessary, the speed / power output gradually declines as a function of the length of the activity (Chidnok et al., 2013). Studies that manipulate participants' prior knowledge of test endpoint have shown this is not always the case however (Billaut et al., 2011; Halperin et al., 2014a; Halperin et al., 2014c). Research tends to support a strong influence of endpoint knowledge on local physical performance (i.e. function of muscle group being exercised and tested). Studies where participants are deceived as to the true endpoint reveal higher force and EMG outputs when shorter exercise periods are expected (Billaut et al., 2011; Halperin et al., 2014a; Halperin et al., 2014c). While research has shown that prior knowledge of endpoint affects localized physical performance, further research is needed to clarify whether endpoint knowledge will impact NLMF expression similarly.

To the best of our knowledge, no previous studies have examined the impact of knowledge of task endpoint on pacing with NLMF. It is currently believed that central factors (i.e. psychological) are largely responsible for the occurrence of NLMF, but much remains unexamined. If NLMF is a centrally mediated phenomenon, then a variable that could exacerbate central fatigue such as lack of knowledge of task endpoint, should affect NLMF responses.

In addition, fatigue protocols that successfully elicit NLMF are typically performed over a longer period of time (i.e. >2 min) than the subsequent tests (i.e. 5s MVIC, 30s

MVIC) (Kawamoto et al., 2014; Martin & Rattey, 2007; Takahashi et al., 2011). Learned pacing may therefore play a greater role in NLMF expression in unknown endpoint conditions. In their central governor model, St. Clair-Gibson and Noakes (2004) propose that before and continuously during exercise, the brain subconsciously calculates the metabolic cost required to complete an exercise task given prior experience, and under the influence of environmental conditions and the current physical state (St. Clair-Gibson & Noakes, 2004). Given the framework of their theory, an inefficient pacing template is more likely in an unknown endpoint situation, which would impact performance negatively (St. Clair-Gibson & Noakes, 2004)

If central drive is already affected from a prior fatigue protocol, further effects on motivation through knowledge of task endpoint manipulation may exacerbate central factors involved in NLMF. It is hypothesized that an unknown test endpoint will interfere with the implementation of pacing strategies and will lead to greater expression of NLMF. Positive implications for rehabilitation and high-performance training could be realized with a greater understanding of what promotes the greatest NLMF effect and what physiological structures are fatigued in this process.

2.2 METHODS

2.2.1 - Experimental Approach to the Problem

A randomized cross over study design was employed to examine the acute effects of unilateral knee extensor muscle fatigue on the performance of the contralateral homologous muscle. To determine if pacing factors impact NLMF expression in contralateral homologous muscle, this study examined 1) maximal force of the contralateral leg extensors pre- and post-intervention (a high-intensity unilateral knee extension fatigue protocol, or rest), 2) different prior knowledge of exercise endpoints within a strength endurance test of contralateral leg extensors post-intervention, and 3) level of activation of the vastus lateralis (VL), vastus medialis (VM), rectus femoris (RF) and biceps femoris (BF) muscle groups of both legs throughout intervention and test protocols. Participants were scheduled for four separate testing sessions, each lasting approximately 45 minutes and separated by at least 48 hours. Experimental conditions were presented randomly and included 1) KN-fatigue: Known test endpoint with pre-fatigue of contralateral knee extensors, 2) UNK-fatigue: Unknown test endpoint with pre-fatigue of contralateral knee extensors, 3) KN-control: Known test endpoint with no prior exercise of contralateral knee extensors and 4) UNK-control: Unknown test endpoint with no prior exercise of contralateral knee extensors.

Maximum voluntary isometric contraction (MVIC) tests (knee at 83^{o}, 0^{o} being full extension; 5 s hold time) were conducted prior to and following intervention protocols

by the non-dominant (non-exercised) and dominant (exercised) legs. The known or unknown test endpoint noted in the experimental conditions refers to the type of strength-endurance test the non-dominant (non-exercised) leg completed post-intervention. For the known endpoint conditions (KN), the participant was notified prior to the start of the test that they would have to hold a knee extension MVIC for 30 seconds. The participant was able to view a timer throughout the test so they were aware of the approaching endpoint. For the unknown endpoint conditions (UNK), the participant was instructed to hold a knee extension MVIC until they reached a certain point of fatigue, at which time they would be told by the researcher to stop. Unbeknownst to the participant, the point of fatigue where participants were stopped during the unknown test was set at 60% of the initial MVIC.

2.2.2 - Participants

Fifteen recreationally trained male participants were recruited for the purposes of this study (22.4 ± 3.79 years; 1.80 ± 0.052 m; 77.87 ± 10.40 kg). Recreationally trained was defined as participating in at least 2 activity sessions a week for the past 6 months. Prospective participants who reported neurological or musculoskeletal complications involving knee structures such as surgery or injury, or cardiovascular conditions such as high blood pressure would have been excused from the experiment. All participants filled out the Physical Activity Readiness Questionnaire+ (PAR-Q+) form (CSEP, 2011) and

provided written informed consent in accordance with ethics approval to further confirm suitability for the study. Ethical approval for the study was obtained from the Human Research Ethics Authority of the Memorial University of Newfoundland (#15.066). Participants were instructed to avoid strenuous activity and abstain from alcohol, caffeine or nicotine consumption for a 24-hour period prior to participation. Leg dominance was determined by asking what foot the individual kicks a ball with (Oldfield, 1971).

2.2.3 - Protocol

Each session started with the placement of surface electromyography (EMG) electrodes on the vastus lateralis (VL), vastus medialis (VM), rectus femoris (RF) and biceps femoris (BF) muscles of the non-dominant leg. Self-adhesive Ag/AgCl electrodes (Meditrace^{TM} 130 ECG conductive adhesive electrodes) were placed according to previously supported protocols (Hermens et al. 2000, Paddock and Behm, 2009, Kawamoto et al., 2014). The surface electrodes were placed at the mid-point of the anterior superior iliac spine and the patella for the RF, 80% along the line from anterior superior iliac spine to the joint space in front of the anterior border of the medial ligament for the VM, and 66% on the line between anterior superior iliac spine and lateral side of the patella for the VL. The mid-point between the gluteal fold and popliteal space was used for the BF. The electrodes were placed 2 cm apart (centre to

centre) and parallel to the direction of the muscle fibres. The ground electrode was placed on the lateral femoral epicondyle. The skin was prepared prior to electrode placement by shaving the area, rubbing with sandpaper and cleansing with an isopropyl alcohol swab to ensure minimal skin resistance.

To ensure an adequate signal-to-noise ratio, an inter-electrode impedance of <5 kOhms was obtained prior to testing. The EMG signal acquisition system (Biopac System Inc., DA 100: analog-digital converter MP150WSW; Holliston, Massachusetts) recorded all signals at a sampling rate of 2000 Hz. All EMG signals were filtered with a Blackman - 61 dB band-pass filter between 10-500 Hz, amplified (bi-polar differential amplifier, input impedance = 2MΩ, common mode rejection ratio > 110 dB min (50/60 Hz), gain x 1000, noise > 5μV), and analog-to-digitally converted (12 bit) for storage and analysis on a personal computer. A commercially designed software program (AcqKnowledge III, Biopac Systems Inc.) was used for the establishment of signal parameters and for data analysis.

Participants were then seated in a knee extension machine (Modular Leg Extension, Cybex International, Medway, MA, USA) with the hips and knees fixed at 90^{o} and 83^{o} respectively. A knee flexion position of 83^{o} was based on the constraints of the leg extension device. A 5-point harness was placed around the waist and shoulders of the participants and they were instructed to cross their hands across their chest to minimize upper body involvement. The dominant and non-dominant ankles were

inserted into padded ankle cuffs and attached to strain gauges (Omega engineering Inc., LCCA 250, Don Mills, Ontario) with non-extensible straps. The straps and strain gauge were secured to the leg extension machine through a custom-built apparatus that allowed a 90^{o} angle to be maintained between the straps and the participants' lower shin. Once properly positioned on the knee extension machine, subjects performed a warm-up consisting of two sets of 10 dynamic bilateral knee extensions with a load approximately equal to 30% of the participant's total body mass. Following this procedure, they performed five submaximal unilateral isometric knee extensions lasting five seconds each, with both the right and left legs (at 83^{0}; 0^{0} being full extension). The desired intensity for these isometric contractions was described as a force equal to 6-8/10 on a scale of one to ten, where 10/10 is maximal effort.

Immediately after this warm-up, participants performed a MVIC protocol with both legs. Each leg performed two unilateral isometric knee extension MVICs and if the difference between the two MVICs was more than 5%, a third MVIC was performed. Each MVIC was performed for 5 s with 2 min rest between. Knee flexion MVICs (5 s hold) were then performed for the non-dominant leg for normalization of bicep femoris EMG. Following the MVIC pre-tests, a fatigue protocol or rest (260s) was presented as an intervention depending on the experimental condition. The dominant leg was used for all fatiguing protocols and the participants were encouraged to keep the contralateral leg relaxed during leg contractions. The EMG of the contralateral leg was monitored

throughout the fatigue protocol to ensure it was staying relaxed (< 5% MVIC EMG). Data for both legs were saved throughout the fatigue protocol and tests for later analysis.

The fatigue protocol utilized for this study has been shown to elicit NLMF in contralateral knee extensors (Doix et al., 2013, Halperin et al. 2014b). The dominant leg performed a continuous knee extension MVIC for two, 100-second sets, separated by one minute of rest.

Immediately upon completion of the fatigue protocol or rest period (control), the contralateral leg performed a series of MVICs for 5 seconds each followed immediately by the strength-endurance test according to the experimental condition. When the strength-endurance test was performed with a known endpoint, a monitor was used to allow subjects to see the time, but they were blinded to their force output. When participants did not have prior knowledge of test endpoint, they were kept blinded to the test duration and force output. Participants were told to "go hard" at 5-second intervals throughout all fatigue protocols and tests to ensure consistent encouragement. The test endpoint condition was presented randomly and explained to the participant following the brief post-intervention MVICs and immediately before the strength endurance test. The hypotheses and expectations based on prior research were not explained to the subjects with the hope of reducing unconscious bias.

2.2.4 - Measurements and Data Analysis

MVIC tests pre and post-intervention were included to allow for comparisons of peak force production based on previous research (Hearn et al., 2009; Kawamoto et al., 2014). For each muscle, the mean amplitude of the root mean square (RMS) of the EMG signal was calculated over a 2-second window that included the peak force output in the middle of the window (1-second prior, 1-second after). For condition comparisons, the peak force or EMG RMS from pre-MVICs were used to normalize values from post-MVICs (post / pre) and strength-endurance tests (epoch mean / pre-MVIC).

The known and unknown endpoint tests were directly compared over the initial 30 seconds of the strength-endurance test. EMG RMS signal and force output data from sequential 5-second epochs were used for analysis (mean from each epoch). The duration of the unknown endpoint test was monitored and compared between fatigue and rest conditions. If an individual's MVIC force decreased to less than 60% of initial MVIC in less than 30 seconds they were not informed and were encouraged to continue the contraction for the 30-second period.

2.2.5 - Statistical Analyses

To expose meaningful differences, a magnitude-based approach for analysis and reporting of results was utilized. Effect sizes are reported along with the percent

likelihood that the observed effect size is larger than a small effect size (meaningful difference). In accordance with previous research, Cohen's d values of 0.2, 0.6 and 1.2 were used as thresholds for small, medium and large effect sizes (Drinkwater, Pritchett & Behm, 2007). The percent likelihood that the observed effect size was larger than the smallest worthwhile change (ES: 0.2) was calculated based on previous methods (Drinkwater, Pritchett & Behm, 2007; Hopkins, 2004; Page, 2014). Chances of a meaningful difference were classified qualitatively as follows: <1%, almost certainly not; <5%, very unlikely; <25%, unlikely; 25-75%, possible; >75%, likely; >95%, very likely; and >99% almost certain.

The normality and homogeneity of variances within the data were confirmed with the Shapiro-Wilk and Levene's tests, respectively. An independent samples t-test was also employed to determine if a significant difference in duration (time to reach 60% pre-MVIC force) between the two unknown endpoint conditions occurred. An alpha of 5% was used to determine statistical significance.

2.3 RESULTS

2.3.1 – MVIC Tests

2.3.1.1 – Normalized MVIC Peak Force Measures

Demonstrating a crossover potentiation of force, knee extension MVIC force of the non-exercised, non-dominant limb was “likely” to be higher during the UNK-fatigue condition compared to both control conditions (85% vs. KN-control, ES: 0.58; 93% vs. UNK-control, ES: 0.96). The dominant leg demonstrated 44.3% higher force in the KN-control condition compared to KN-fatigue, and 30.4% higher than UNK-fatigue, confirming substantial localized muscle fatigue. The UNK-control condition also demonstrated higher peak force measures compared to both fatigue conditions (34.1% > than KN-fatigue; 21.1% > than UNK-fatigue).

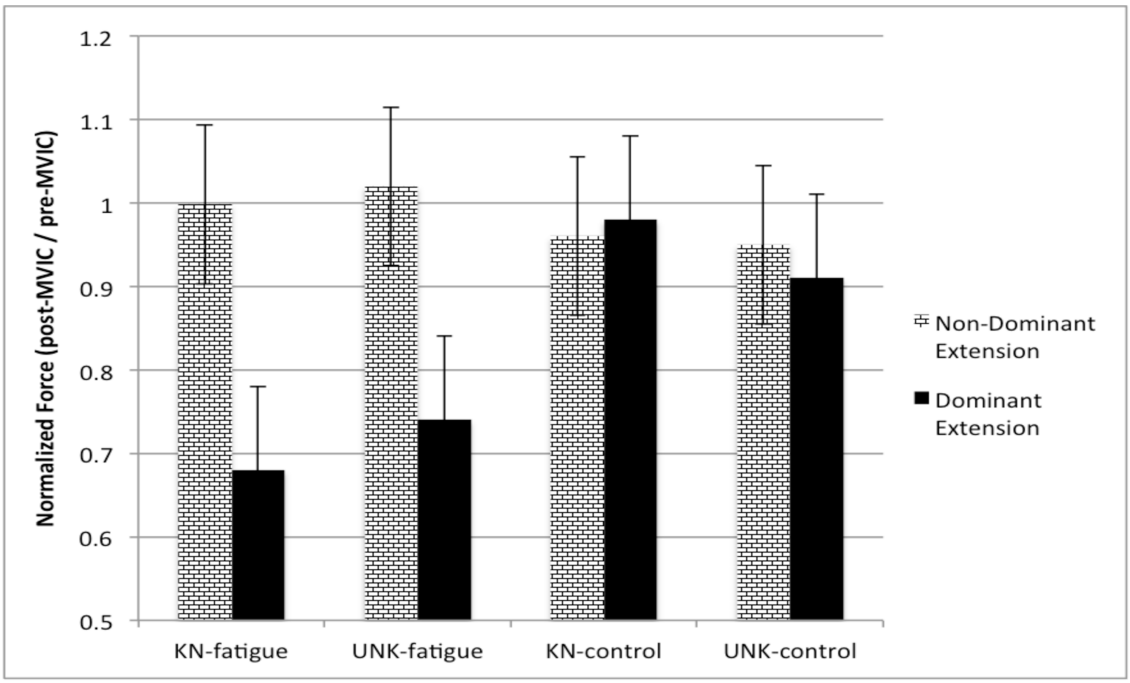

Figure 3.1.1. Mean and standard deviation of the MVIC Force: Peak normalized force across conditions for Dominant and Non-Dominant (non-exercised) leg extensions.

2.3.1.2 – Normalized MVIC EMG RMS Measures

Similar to non-dominant knee extension MVIC force, UNK-fatigue demonstrated higher EMG activity compared to KN-control and UNK-control for all quadriceps muscles (80-95% likely). Although no difference in force was noted between KN-fatigue and KN-control, all muscle groups examined were "likely" to exhibit higher EMG activity during KN-fatigue as well (78-90%). It was also "likely" that the RF and VL muscles would be less active during KN-fatigue compared to UNK-fatigue (96% and 84% respectively).

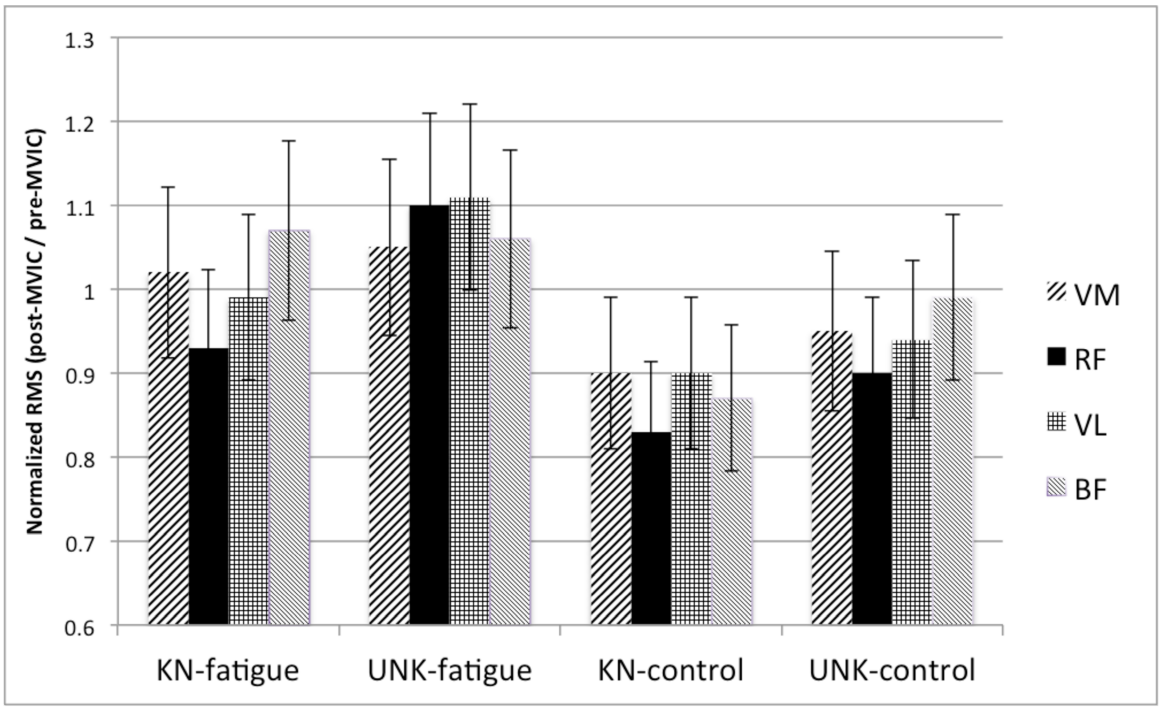

Figure 3.1.2: Mean and standard deviation of the MVIC EMG RMS: Normalized EMG measures (post-MVIC RMS / pre-MVIC RMS) for each muscle group across all conditions.

2.3.2 Contralateral Strength-Endurance Test Measures

2.3.2.1 – Normalized Mean Force

There was evidence for a prior knowledge effect. Prior knowledge of endpoint with crossover fatigue (KN-fatigue) was "likely" to generate higher forces in the final two epochs compared to no prior knowledge with fatigue (UNK-fatigue) (75% & 80% respectively). The strongest crossover fatigue effect was demonstrated when comparing the UNK-fatigue and KN-control conditions, as meaningful differences were "likely" or

"very likely" from epoch 2 through 6 (86-97% likelihood). KN-control produced 12% higher force than UNK-fatigue during the strength-endurance test (average of first 30 seconds), which was greatest at epoch 6 (21.6%). The UNK-fatigue condition also exhibited lower forces in epoch 3 compared to UNK-control (75% likelihood), further supporting a crossover fatigue effect. There was no evidence of crossover fatigue with the known endpoint condition as no meaningful differences were shown between the KN-fatigue epochs and the two control conditions (KN-control and UNK-control). Prior knowledge of endpoint did have an effect on pacing strategy as the KN-control condition demonstrated higher forces in the final epoch compared to UNK-control (90%, likely) (Table 3.2.1a).

Table 3.2.1a: BETWEEN CONDITIONS X TIME FORCE INTERACTION: Effect sizes comparisons between conditions at each fatigue protocol epoch. Asterisks denote that a ≥75% likelihood to demonstrate a meaningful difference.

	KN-Fatigue vs. UNK-Fatigue	KN-Fatigue vs. KN-Control	KN-Fatigue vs. UNK-control	UNK-fatigue vs. KN-control	UNK-fatigue vs. UNK-control	KN-control vs. UNK-control
Epoch 1: 0-5s	-0.21	0	-0.04	0.29	0.25	-0.04
Epoch 2: 5-10s	-0.18	0.18	0.14	0.42*	0.4*	-0.04
Epoch 3: 10-15s	-0.23	0.22	0.16	0.54*	0.44*	-0.06
Epoch 4: 15-20s	-0.19	0.13	0	0.45*	0.26	-0.13
Epoch 5: 20-25s	-0.33*	0.18	-0.05	0.67*	0.34	-0.25
Epoch 6: 25-30s	-0.4*	0.17	-0.07	0.86*	0.29	-0.41*

Both fatigue conditions demonstrated “very likely” or “almost certain” drops in force from epoch 1 to epoch 2. The control conditions did not see the same initial drop in force. It therefore appears that the contralateral fatigue amplified fatigue-induced force losses in the first 10 seconds of the 30-second fatigue trial. Also, KN-control was better able to recover force production at the end of the test (epoch 6).

Table 3.2.1b: WITHIN CONDITIONS X TIME FORCE INTERACTION: Percentage chance that the mean force in the identified epoch was clinically worse than the first epoch. Number signs indicate where differences were not meaningful (<75% likely).

	EPOCH 2	EPOCH 3	EPOCH 4	EPOCH 5	EPOCH 6
KN-FATIGUE	98	100	99	100	99
UNK-FATIGUE	95	99	98	100	100
KN-CONTROL	51#	76	85	80	70#
UNK-CONTROL	35#	73#	98	99	100

2.3.2.2 – Normalized RMS EMG

Vastus Medialis (VM)

Analysis of RMS EMG data for the VM provided stronger indications that crossover fatigue had occurred. Similar to force, level of activity of the VM in KN-fatigue was “likely” to be higher during epochs 4, 5 and 6 compared to UNK-fatigue (83%, 90% and 92% respectively). KN-fatigue was also “likely” to have lower activity than both

control conditions at epochs 2 and 3 (KN-control: 76% and 78%, UNK-control: 91% and 89%). This lower activity was also present during epochs 5 and 6 compared to KN-control (85% and 80%). The UNK-fatigue condition was 94-100% likely to have lower muscle activity than KN-control throughout epochs 2-6. UNK-fatigue also demonstrated lower muscle activity from epoch 1 through 6 compared to UNK-control (78-96% likely). Finally, in agreement with the force rebound previously reported, KN-control was 82% likely to have higher activity than UNK-CONTROL during epoch 6. The VM RMS EMG reveals a contribution to the force rebound that occurred with KN-control but not in UNK-control.

Comparisons of VM RMS EMG measures within each condition showed divergences with force comparisons. The first epoch of KN-fatigue was "likely" (92%) to have lower muscle activity than epoch 6. KN-control demonstrated the most changes throughout the 30-second test with epoch 1 being worse than epochs 4, 5 and 6 (83%, 98% and 100% likelihood respectively). No significant changes in muscle activity throughout the strength-endurance test were revealed for UNK-fatigue or UNK-control conditions.

Vastus Lateralis (VL)

Demonstrating further evidence of a prior knowledge effect, VL RMS EMG activity during KN-fatigue was "likely" (85%) to be higher than UNK-fatigue during epoch

6. The VL also appears to contribute (along with the VM) to the higher force seen in KN-control compared to UNK-control at epoch 6, as KN-control was “almost certain” (99%) to have higher muscle activity during that epoch. KN-control was also “likely” (76%) to have higher activity than UNK-control at epoch 5. Similar to the VM, VL EMG activity during KN-fatigue was “likely” lower than KN-control from epoch 2 to 6 (88-96% likely). Also, UNK-fatigue was “likely” or “almost certain” to be lower than KN-control from epoch 2-6 (90-100%). Interestingly, KN-fatigue was “likely” to be lower than UNK-control at epoch 2 (76%), but higher at epoch 6 (80%).

When considering only time as a factor, the KN-fatigue condition was “likely” to produce higher activity in epoch 1 compared to 2 (77%), but lower activity compared to 6 (93%). Within KN-control, epoch 1 was “likely” to have lower activity than epoch 5 (92%) and “almost certain” to have lower activity than epoch 6 (99%). Regardless of crossover fatigue, both unknown conditions failed to show significant changes (UNK-fatigue and UNK-control).

Rectus Femoris (RF)

Once again, higher activity was seen during KN-fatigue compared to UNK-fatigue at epoch 6 (78% likely). There was limited evidence of crossover fatigue as KN-fatigue was lower than UNK-control at epoch 2 only (84% likely), and UNK-fatigue was only

"likely" to be lower than KN-control during epoch 6 (79%). Overall, performance of the RF appeared to be more stable across conditions than the other muscle groups.

Within conditions, crossover fatigue did appear to have a noticeable effect. The control conditions did not show any significant changes in activity throughout the test. Meanwhile, epoch 1 was "likely" to be greater than epoch 2 for KN-fatigue (77%), and epochs 4 and 6 for UNK-fatigue (77% for both).

Biceps Femoris (BF)

Consistent with other muscle groups, muscle activity was lower during UNK-fatigue compared to KN-control at epochs 5 and 6 (91% and 97% respectively). The KN-fatigue condition provided higher activity compared to UNK-fatigue during epochs 1 through 6 (77-95% likely). BF EMG was lower during UNK-fatigue compared to UNK-control from epoch 1 through 6 (91-99% likelihood).

Within the UNK-fatigue condition, only epoch 2 was "likely" to be lower than epoch 1 (82%). Epochs 5 and 6 were shown to "likely" be higher than epoch 1 (84% and 95%) within KN-control. Finally, epoch 4 in UNK-control was higher than epoch 1 (85% likely).

Table 3.2.2: BETWEEN CONDITIONS X TIME RMS EMG INTERACTION: Effect size comparisons between conditions at each epoch for muscle groups of the contralateral (non-exercised) leg during the strength-endurance test. Asterisks denote a ≥75% likelihood to demonstrate a meaningful difference for that muscle. Shaded cells denote a ≥75% likelihood to demonstrate a meaningful difference in force.

	KN-fatigue vs. UNK-fatigue	KN-fatigue vs. KN-control	KN-fatigue vs. UNK-control	UNK-fatigue vs. KN-control	UNK-fatigue vs. UNK-control	KN-control vs. UNK-control
Epoch 1: 0-5s	VM -0.23 RF 0.1 VL 0.1 *BF -0.47	VM 0.04 RF 0.04 VL 0.38 BF -0.41	VM 0.37 RF 0.3 VL 0.04 BF -0.13	VM 0.29 RF -0.11 VL 0.42 BF 0.02	*VM 0.52 RF 0.18 VL 0.08 *BF 1.02	*VM 0.53 RF 0.21 VL -0.29 BF 0.2
Epoch 2: 5-10s	VM -0.28 RF 0.17 VL 0.13 *BF -0.53	*VM 0.5 RF 0.35 *VL 0.78 BF -0.2	*VM 0.94 *RF 0.64 *VL 0.52 BF 0.08	*VM 0.5 RF 0.17 *VL 0.62 BF 0.36	*VM 0.76 RF 0.38 VL 0.38 *BF 0.87	VM 0.22 RF 0.2 VL -0.16 BF 0.33
Epoch 3: 10-15s	VM -0.3 RF 0.02 VL -0.02 *BF -0.44	*VM 0.47 RF 0.22 *VL 0.77 BF -0.07	*VM 0.86 RF 0.45 VL 0.45 BF 0.16	*VM 0.57 RF 0.25 *VL 0.8 BF 0.33	*VM 0.72 RF 0.26 VL 0.41 *BF 0.59	VM 0.33 RF 0.17 VL -0.22 BF 0.25
Epoch 4: 15-20s	*VM -0.45 RF -0.12 VL 0.05 *BF -0.41	VM 0.2 RF -0.01 *VL 0.75 BF -0.14	*VM 0.54 RF 0.27 VL 0.23 BF -0.01	*VM 0.78 RF 0.24 *VL 0.73 BF 0.42	*VM 0.68 RF 0.28 VL 0.2 *BF 0.57	VM 0.17 RF 0.18 VL -0.26 BF 0.15
Epoch 5: 20-25s	*VM -0.59 RF -0.17 VL -0.32 *BF -0.53	*VM 0.63 RF 0.14 *VL 0.8 BF -0.05	VM 0.36 RF 0.14 VL 0.13 BF 0.1	*VM 0.95 RF 0.32 *VL 1.08 *BF 0.61	*VM 0.6 RF 0.1 VL 0.31 *BF 0.73	VM -0.02 RF 0 *VL -0.41 BF 0.14
Epoch 6: 25-30s	*VM -0.62 *RF -0.39 *VL -0.47 *BF -0.65	*VM 0.53 RF -0.03 *VL 0.84 BF -0.08	VM -0.24 RF -0.31 *VL -0.5 BF -0.29	*VM 1.34 *RF 0.6 *VL 1.4 *BF 0.94	*VM 0.43 RF 0.07 VL 0.1 *BF 0.56	*VM -0.47 RF -0.25 *VL -0.94 BF -0.24

2.3.2.3 – Anticipatory Effect

Comparing peak force values from pre-test MVICs to mean force values during the first epoch revealed that all conditions displayed an "almost certain" drop in force (99-100% likely). Declines in force ranged from 13.9% for KN-control to 18.9% for UNK-fatigue. Similar anticipatory decreases were seen in muscle activity of the VM (95-100% likely), RF (99-100%) and VL groups (94-99%).

Table 3.2.3: ANTICIPATION EFFECT: Means are reported (with SD in brackets) for force and RMS EMG of the contralateral (non-exercised) leg from the pre-MVIC test and Epoch 1 of strength-endurance test. Percent difference and effect size comparisons between pre-MVIC and Epoch 1 values are also provided. Asterisks denote a ≥75% likelihood to demonstrate a meaningful difference.

		pre-MVIC	Epoch 1	Percent Diff.	Effect Size
KN-fatigue	Force	54.25 kg (14.12)	46.69 kg (12.52)	-13.9%	-0.64*
	VM EMG	0.72 mV (0.3)	0.56 mV (0.24)	-22.5%	-0.67*
	RF EMG	0.68 mV (0.2)	0.51 mV (0.22)	-25.4%	-0.79*
	VL EMG	0.84 mV (0.44)	0.6 mV (0.37)	-27.9%	-0.63*
	BF EMG	0.072 mV (0.038)	0.067 mV (0.04)	-7.5%	-0.13
UNK-fatigue	Force	51.79 kg (12.21)	41.99 kg (10.03)	-18.9%	-0.98*
	VM EMG	0.75 mV (0.25)	0.56 mV (0.19)	-25.6%	-1.02*
	RF EMG	0.66 mV (0.18)	0.52 mV (0.16)	-21.7%	-0.87*
	VL EMG	0.75 mV (0.44)	0.58 mV (0.33)	-22.7%	-0.52*
	BF EMG	0.067 mV (0.028)	0.054 mV (0.019)	-18.9%	-0.68*
KN-control	Force	55.21 kg (13.76)	47.51 kg (12.7)	-13.9%	-0.62*
	VM EMG	0.76 mV (0.33)	0.58 mV (0.23)	-23.3%	-0.77*
	RF EMG	0.7 mV (0.22)	0.51 mV (0.2)	-27.5%	-1*
	VL EMG	0.76 mV (0.34)	0.56 mV (0.28)	-33.6%	0.68*
	BF EMG	0.076 mV (0.031)	0.061 mV (0.031)	-20.1%	-0.49*
UNK-control	Force	55.13 kg (12.73)	46.87 kg (14.45)	-15%	-0.54*
	VM EMG	0.72 mV (0.3)	0.6 mV (0.25)	-16.8%	-0.48*
	RF EMG	0.71 mV (0.21)	0.56 mV (0.19)	-20.5%	-0.75*

	VL EMG	0.85 mV (0.45)	0.65 mV (0.4)	-23.7%	-0.51*
	BF EMG	0.069 mV (0.024)	0.063 mV (0.032)	-8.6%	-0.03

2.3.2.4 - Endurance Time

The mean endurance time for the UNK-fatigue condition was 42.05 seconds, compared to 43.83 seconds for UNK-control (Std. dev. = 5.26; Std. dev. = 11.45, respectively). An independent samples t-test confirmed that the difference in endurance time between the two unknown endpoint conditions was insignificant ($t_{(26)} = -0.514$, *p = 0.611*).

2.3.2.5 - Force at 30 seconds

The force at the 30-second point of the strength-endurance test was compared across all conditions and no condition effect was found ($F_{(3, 54)} = 1.252$, *p = 0.300*).

2.4 DISCUSSION

The findings of this study demonstrate that prior knowledge of test endpoint had an impact on the expression of NLMF. Significant anticipatory decreases in force and muscle activity were seen across all conditions when comparing pre-MVIC to epoch 1 measures. These anticipatory decreases were largest in magnitude for UNK-fatigue (-18.9% MVIC force, -25.6% RMS of VM). Evidence for NLMF was apparent with force and muscle activation deficits with the strength-endurance test, which contrasted with the force potentiation that occurred with the single MVIC post-test. During the strength-endurance test the UNK-fatigue condition progressively produced lower force (epochs 5 and 6) and muscle activity (VM: epochs 4-6; RF and VL: epoch 6) compared to KN-fatigue through the last 15 seconds of the strength-endurance test. In addition, UNK-fatigue consistently demonstrated lower force and muscle activity (12% lower overall, 21.6% at epoch 6) than KN-control.

The anticipatory drop in force and EMG from pre-MVIC to the first epoch of the strength-endurance test provides strong evidence of a knowledge of task endpoint effect on pacing. Participants understood that the duration of the MVIC and strength-endurance tests would be different (informed of a single 5s MVIC versus 30s for known or unknown for strength-endurance test). It is therefore likely that maximal output was inhibited by a conscious or subconscious decision. Participants anticipated a longer duration of effort and greater discomfort with the strength-endurance test by

suppressing their initial force output. Anticipation of greater discomfort with evoked stimulation has been shown to reduce MVIC and RMS EMG output (Button & Behm, 2008). The extended duration of the contralateral fatigue protocol may have magnified this apprehension, as well as reduced the participant's energy to exert self-control (Baumeister, 2002; Hagger et al., 2010). Both would contribute to less than maximal output during the strength-endurance test. Despite strong encouragement to provide maximal effort, subjects commonly utilize pacing strategies and suppress maximal forces until expectation of a final repetition / effort (Halperin et al., 2014a; 2014c).

Consistent with previous research, the longer duration (strength-endurance) test demonstrated significant NLMF effects versus a single MVIC. At various points throughout the strength-endurance test of the contralateral, non-exercised limb, both fatigue conditions produced less force and muscle activity than the control conditions. In contrast, the MVIC test (single contraction) following the fatigue protocol produced a potentiation of force (UNK-fatigue) and muscle activity (both fatigue conditions). When participants knew they only had a 5 second effort (MVIC), it appears they were able to maintain or even increase their central motor drive (in response to contralateral fatigue). When participants were expecting to perform a longer duration test (30s for KN, or unknown duration for UNK), reductions in muscle activation were more evident.

It is likely that the known endpoint conditions provided higher motivation, which has been shown to enhance self-control and help overcome performance impairments

due to fatigue (Hagger et al., 2010). A prevailing view of self-control is that it is a finite resource like strength or energy, and becomes less effective when depleted (Baumeister, 2002; Hagger et al., 2010). This 'strength model' of self-control places great emphasis on prior task performance and fatigue on our ability to exercise self-control (Hagger et al., 2010). The effects of fatigue and motivation on self-control and task performance are largely suggested to be interactive (Muraven & Baumeister, 2000), which appears to be the case in our study.

Participants' pacing strategies through the strength-endurance test were comparable to those in studies completed by Halperin et al. (2014a; 2014c). Halperin et al. (2014a) noted a more marked decrease in force during the first 6 MVICs (13%) across all conditions, and a plateau in force over the last 6 MVICs (3% decrease). Both of our fatigue conditions reduced force output into epoch 2 before plateauing. The control conditions displayed a more gradual loss of force output into epoch 3 or 4 (UNK-control) before plateauing, and even rebounding in the case of KN-control. Muscle activity remained fairly stable throughout the strength-endurance test, with most significant differences occurring when comparing epoch 1 and 6 for the known endpoint conditions (VM and VL).

Given the maximal and fairly brief (~30s) nature of the strength-endurance test, it can be argued there was limited opportunity for centrally mediated pacing strategies to be employed (Shephard, 2009; Weir et al., 2006). Peripheral feedback has been noted in

previous research to be the key mediator of performance impairments at maximal intensities or shorter durations (Amman et al., 2013; Shephard, 2009; Weir et al., 2006). Our findings of test duration and known versus unknown endpoint effects demonstrate that central factors can provide an impact at this intensity and duration. Similar to our study, Halperin et al. (2014a; 2014c) examined pacing while manipulating the participants' prior knowledge of test endpoint. They found MVIC forces in trained females were significantly higher in a deception condition during the first 6 MVICs, compared to known and unknown conditions (Halperin et al., 2014a). Following a similar procedure with both sexes, they again found that the deception condition was significantly higher during the first 6 MVICs, but only compared to the unknown condition (Halperin et al., 2014c). Both studies found no differences between conditions over the last 6 MVICs of the 12 MVIC protocol. The deception condition they employed was essentially a known endpoint condition with a shorter expected duration (they then kept being deceived and encouraged to continue). Their findings, consistent with those of the present study, reveal that even when every effort is intended to be maximal, higher forces can be produced when an individual is aware of a more immediate and known endpoint.

The similar endurance times between fatigue and control groups for our strength-endurance test is in agreement with Kawamoto et al. (2014), who found no difference in time to task failure between control and contralateral pre-fatigue conditions (40% and 70% MVIC fatigue protocols used). They followed a similar isometric knee extension

endurance test, but task failure was set at 70% pre-test MVIC as opposed to 60% in our study. Although, Amann and colleagues (2013) noted a decrease in endurance time following a contralateral knee extensor fatigue protocol, they used a longer duration cycling test (5-10 minutes) for their endurance protocol.

When examining the influence of different muscle groups, the VM and VL contributed most notably to the aforementioned force changes. Both the VM and VL displayed significant changes that regularly paralleled and in some cases preceded significant changes in force. The greater sensitivity to change observed in muscle activity compared to force suggests that changes in central drive and excitability mitigated other performance impairments. Research has demonstrated that central excitability changes occur in response to developing fatigue, even in the absence of visible performance deficits such as loss of force (Aboodarda et al., 2015a, 2015b; Behm, 2004).

It has long been established in the literature that changes in neural drive due to fatigue are often demonstrated by changes in the amplitude of the RMS EMG signal (Edwards & Lippold, 1956; Moritani et al., 1982). The nonlinear relationship between force and RMS EMG is well documented, especially at high forces, and may help to explain some of the magnitude discrepancies between force and RMS EMG seen in this study (Kamen & Gabriel, 2010; Woods & Bigland-Ritchie, 1983). The varying response of

force and EMG indicates, however, that different changes in neural drive and central excitability occurred in reaction to the conditions.

Higher muscle activity exhibited with post-test MVICs indicate a possible enhancement of central motor drive (Amman, 2011), while lower values throughout the strength-endurance test suggest a decrease in supraspinal motor output (Aboodarda et al., 2015a). While the known versus unknown endpoints were designed to investigate cortical factors, it is difficult to specify what physiological mechanisms were predominant. Aboodarda et al. (2015a) did not observe any change in MVIC force following bilateral elbow flexor fatigue, but normalized VL RMS EMG did decrease significantly. Their analysis included thoracic motor evoked potentials (TMEPs) and maximal compound muscle action potentials (Mmax) in order to more directly examine central excitability changes. They concluded that supraspinal motor output had decreased given that spinal motoneuronal responses (TMEP / Mmax) were higher and peripheral excitability (compound muscle action potential) did not change. In another study, Aboodarda et al. (2015b) again did not find changes in force or EMG of contralateral elbow flexors in response to a unilateral elbow flexion protocol. Their analysis of motor evoked potentials (MEPs) and cervicomedullary motor evoked potentials (CMEPs) indicated an increase in supraspinal responsiveness (higher MEP/CMEP ratio) might have mitigated performance impairments.

Peripheral fatigue and its accompanying afferent feedback can modify central excitability through various mechanisms (Amann et al., 2013). Inhibition by Renshaw cells, Golgi tendon organs, and type III and IV afferents, or decreased excitation of Ia afferents have all been shown to stimulate changes in central excitability and performance (Behm, 2004). It is accepted that force may be sustained through a number of mechanisms, and that they may occur simultaneously (Behm, 2004). Increased motor unit recruitment, modulation of rate coding, the inclusion of catch-like properties, alterations in motor control and neural and post-activation potentiation have been demonstrated as effective neuromuscular strategies for maintaining force output (Behm, 2004). Peripheral feedback mechanisms are likely working in conjunction with cortical influences of mental fatigue and prior knowledge of endpoint to modulate performance in this study.

2.5 CONCLUSION

In accordance with previous research in this area (Doix et al., 2013; Halperin & Behm, 2015), this study demonstrated that a high-intensity and high-volume fatigue protocol can produce NLMF effects. Additionally, the longer-duration test provided clearer indications of performance decrements. Most importantly, the present study revealed that prior knowledge of test endpoint can modify NLMF expression and result in different pacing strategies. Based on our results, changes in central drive and muscle

activity appear to be test specific, and can effectively modulate NLMF related force decrements.

2.6 REFERENCE

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