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Neuromuscular adaptations to voluntary contraction following postactivation potentiation

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A thesis submitted in partial fulfillment of the requirements for the degree in Doctor of Philosophy

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by

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Abstract

Muscle contractile properties are history-dependent, and following a conditioning contraction, muscle tissue may be fatigued (slower, weaker) or potentiated (faster, stronger). Postactivation potentiation of evoked contractions, such as the electrically stimulated twitch, has been thoroughly studied. However, the effects of potentiation on voluntary contraction are not well understood, and prior study is largely equivocal.

The following studies propose to determine the effects of potentiation during 1) submaximal contractions at different muscle lengths 2) ballistic contractions following tetanic and voluntary conditioning, and 3) motor evoked potentials following tetanic and voluntary conditioning contractions. Evoked twitch potentiation was assessed with all of the above voluntary measures to compare electrically evoked contractions to those involving the entire neuromuscular system.

Study 1 illustrates that voluntary neuromuscular efficiency of the triceps brachii is greater in a shortened compared to lengthened muscle position. The results of Study 2 indicate that voluntary ballistic peak rate of torque development (RTD) is unchanged following a tetanic conditioning contraction, and is impaired following a voluntary conditioning contraction. This is observed concomitant to a 2-fold increase in twitch torque and peak RTD. Study 3 shows that despite failure of voluntary peak RTD to improve following potentiation, that RTD is enhanced at non-peak time points, implying that performance may adapt differentially throughout the time course of contraction. Study 4 used transcranial magnetic stimulation to provoke a cortical silent period to assess motor cortical inhibition. Following both voluntary and involuntary conditioning contractions, twitch potentiation was observed concurrent to cortical inhibition. This indicates that the conditioning contraction may simultaneously enhance muscular contractile properties and inhibit activity of the motor cortex.

Together, these results indicate a limited opportunity for a conditioning contraction to enhance voluntary contractile properties, despite the substantial enhancement to twitch properties. In addition to the muscular fatigue to which the twitch is subject, the

conditioning contraction has centrally inhibitory effects which constrain voluntary contractile performance. This thesis highlights the importance of considering the entire neuromuscular system when assessing contractile adaptations and performance in relation to contractile history.

Keywords

Postactivation potentiation, voluntary contraction, muscle length, rate of torque development, ballistic contraction, cortical inhibition, silent period.

Co-Authorship Statement

This thesis contains material from published manuscripts (Chapters 2, 3). On all manuscripts, Cameron B. Smith was the first author, and Charles L. Rice was a co-author. Additional co-authorships were as follows: Arthur Cheng (Chapter 2), Matti D. Allen (Chapters 3, 4), Brianna Cowling (Chapter 5), Daniel E. Stevens (Chapter 5). Collection, analysis, and interpretation of all experimental data presented in this document were done by Cameron B. Smith.

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The contribution of the group at the Kinesiology Graduate office cannot be underestimated. Jacqui Saunders, Jenn Symmes, and Lindsay Stark have all shown enormous patience and support, and provided help when needed. I owe particular thanks to Dr. Jim Dickey for his support in my studies when it was needed most.

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List of Abbreviations

ANCOVA – Analysis of covariance

ANOVA – Analysis of variance

Ca^{2+} - Calcium

CaM – Calmodulin

CC – Conditioning contraction

EMG – Electromyography

FDI – First dorsal interosseous

FT – Fast twitch

MEP – Motor evoked potential

MVC – Maximal voluntary contraction

NME - Neuromuscular efficiency

PAP – Postactivation potentiation

pRTD – Peak rate of torque development

PT – Post tetanus

PV – Post voluntary

RFD – Rate of force development

RMS – Root mean square

RTD – Rate of torque development

SD – Standard deviation

skMLCK – Skeletal muscle myosin light chain kinase

SP – Silent period

TMS – Transcranial magnetic stimulation

General introduction

Skeletal muscular contraction is a highly complex process which occurs spontaneously upon the release of Ca^{2+} into the sarcoplasm. The contractile properties of the muscle, such as the speed and strength of contraction, depend in part on the contractile history of the muscle. One example of this dependency is obvious after a series of fatiguing contractions, when the muscle becomes weaker and slower. A less obvious result may be observed by eliciting an evoked twitch after a brief (often ~ 10 s), high intensity contraction, known as a conditioning contraction. Following the conditioning contraction, peak twitch torque is greater and both rate of torque development (RTD) and half relaxation time are faster than for the resting twitch. This phenomenon of stronger, faster contractile properties following a conditioning contraction is known as postactivation potentiation.

Postactivation potentiation of the evoked twitch has been studied at length, however the typical model for twitch study is isometric and involuntary, which is a poor proxy for assessing the performance of a functional task. Currently it is not understood how a conditioning contraction will affect performance of voluntary contractions, which are influenced by a number of variables inherent to voluntary muscle activation and the variety of muscle lengths over which dynamic movements are performed.

Postactivation potentiation

Postactivation potentiation can be defined as an enhancement of muscle contractile properties following a brief, intense conditioning contraction. The conditioning contraction which leads to potentiation may be voluntarily controlled [1, 2], or involuntarily evoked [3, 4]. The enhancement of contractile properties may present itself in one of two

ways, an improved force or rate of force development for a given level of activation, or maintenance of force or RFD at a reduced level of activation (Figure 1). Potentiation is maximal immediately following the conditioning stimulus and decays exponentially, returning to control levels typically within 6-10 minutes [5].

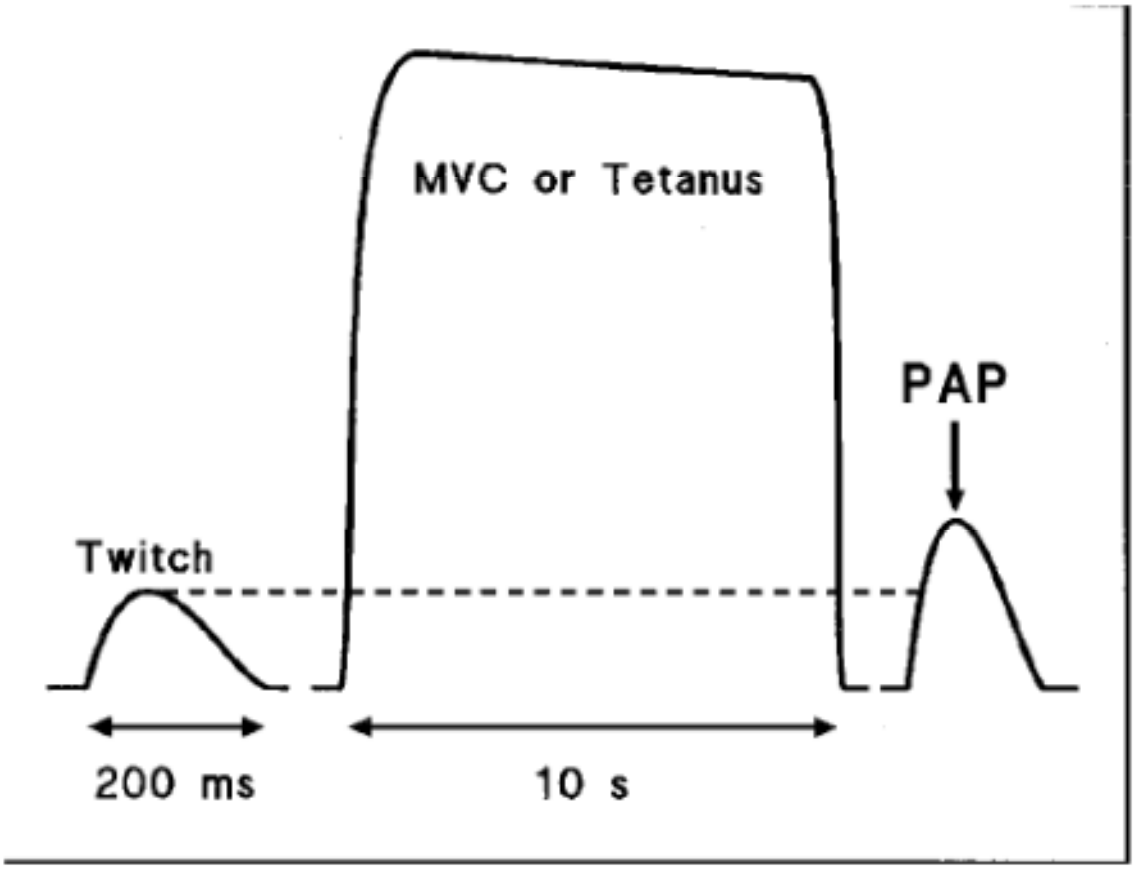

Figure 1. Illustrated representation of twitch potentiation (Sale 2002, reprinted with permission [6])

Figure 1 shows a schematic representation of postactivation potentiation (PAP), with the potentiated twitch following an MVC or tetanus showing a significantly increased force and rate of force development. It is important to note that control and potentiated twitches are evoked with equal stimulation current and equal sarcoplasmic calcium release. Thus, the potentiated muscle displays improved calcium sensitivity.

The effects of potentiation are most apparent at low intramuscular calcium concentrations [7]. Figure 2 illustrates the force-pCa curve before and after a conditioning stimulus. At low intramuscular pCa there is a large increase in calcium sensitivity with potentiation, but that difference diminishes progressively, and becomes absent by ~90% of maximal force. This relationship may also be framed in terms of stimulation frequency, where low frequency stimuli experience the greatest potentiation, and high frequency stimuli are affected the least [7,8]. The failure of potentiation to improve high frequency contractile properties is sensible considering that at high levels of stimulation, sarcoplasmic Ca is already saturated, and thus an increase in calcium sensitivity has little effect.

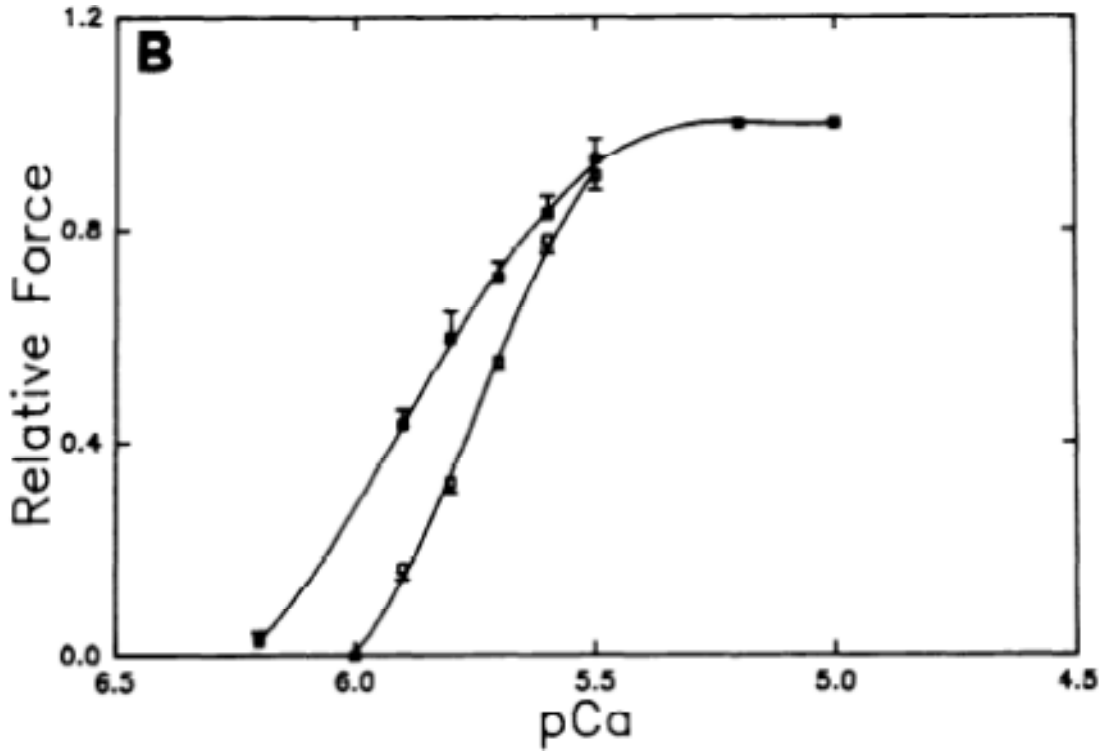

Figure 2. The force-pCa relationship. Force-pCa relationship is shown with unphosphorylated (open squares / bottom line) and phosphorylated (closed squares / top line) myosin filaments (Sweeney 1993 [7])

Mechanisms of postactivation potentiation

Myosin light chain phosphorylation is widely acknowledged as the primary mechanism of potentiation. Calcium released into the sarcoplasm is bound by calmodulin (CaM), which is an intracellular messenger protein. Active CaM then binds to skeletal muscle myosin light chain kinase (skMLCK) which in turn adds a phosphate group to the regulatory light chain component of the myosin molecule. The addition of this phosphate is important for normal contraction (especially in smooth muscle) because it changes the conformational shape of the myosin, steepening the angle of the myosin head in relation to the filament. This new position for the myosin head places it in closer proximity to the actin binding site, encouraging the formation of a cross-bridge. It is particularly noteworthy that the dissociation of the phosphate from the regulatory light chain occurs very slowly (minutes) in comparison to the rate at which muscle relaxation and calcium sequestering occur (ms). For example, a twitch evoked during this refractory period will display a torque and RTD increase of 100-300% compared to the resting twitch. The effect of light chain phosphorylation is greatest immediately after contraction, and decays exponentially over approximately 6-10 min.

The degree of potentiation observed in a particular muscle appears to have some dependence on fiber type composition, with type II fibers experiencing greater enhancement than type I. This causal association was first observed in rat muscle by Moore and Stull [9]. Importantly, only one study since has quantified the relationship between torque potentiation and light chain phosphorylation in human muscle, where Grange and Houston also observed a positive relationship between increasing myosin light chain phosphorylation and increasing torque potentiation [10]. They observed that the degree of twitch potentiation was negatively correlated with the oxidative capacity of the muscle fiber, such that fast-twitch fibers with low oxidative capacity underwent the greatest potentiation. This intermuscular difference was attributed to different enzyme concentration and activity between muscle fiber types. Fast-twitch fibers contained a 3.5 times greater concentration of myosin light-chain kinase compared to slow-twitch fibers, and fast-twitch fibers were dephosphorylated [4] times more slowly. Thus, the pathways of

myosin light chain phosphorylation exist similarly between muscle fibers, but the relative activity of the involved enzymes makes the net effect of potentiation small or absent in slow-twitch muscle fibers. This relationship has been confirmed in humans [11] by correlating twitch contraction time with twitch potentiation for different muscles in vivo, and subsequently assessing fiber type composition using muscle biopsy. Thus, humans with a higher proportion of type II fibers in the knee extensors experience greater potentiation than those with relatively fewer type II fibers.

More recent research has revealed other steps in the neuromuscular pathway affecting twitch potentiation. At the motor end plate, neurotransmitter vesicle size and content are increased following high-frequency trains of stimuli [12]. These changes may fundamentally increase excitation of the sarcolemma for a given axonal input. Furthermore, post-contractile intramuscular calcium kinetics are shown to be altered in parallel to twitch potentiation [13]. In the mouse lumbrical muscle, resting sarcoplasmic calcium concentration has been observed to increase following a potentiating stimulus. This increase is positively associated with twitch potentiation even in the absence of skMLCK, which provides strong evidence for mechanisms contributing to potentiation aside from myosin phosphorylation.

Potentiation and fatigue

It has been well established that contractile potentiation occurs following a brief contraction, while contractile fatigue occurs following repeated or continuous contraction. In fact, it appears that the processes of potentiation and fatigue occur simultaneously, both beginning at the initiation of contraction [14]. To assess the developing effects of potentiation and fatigue, a low-frequency (twitch) and high-frequency (100 Hz tetanus) were assessed periodically during a series of fatiguing contractions [15]. The twitch, which is highly sensitive to potentiation, became progressively stronger, while the fused tetanus, which is indifferent to potentiation, became progressively weaker. The illustration in Figure 3 projects a representative

illustration of the coexistence of potentiation and fatigue, where net contractile performance is determined by the balance between these opposing effects. Because maximum potentiation may be achieved within 10 s of maximal contraction [16], fatigue effects become progressively more dominant as the conditioning duration increases.

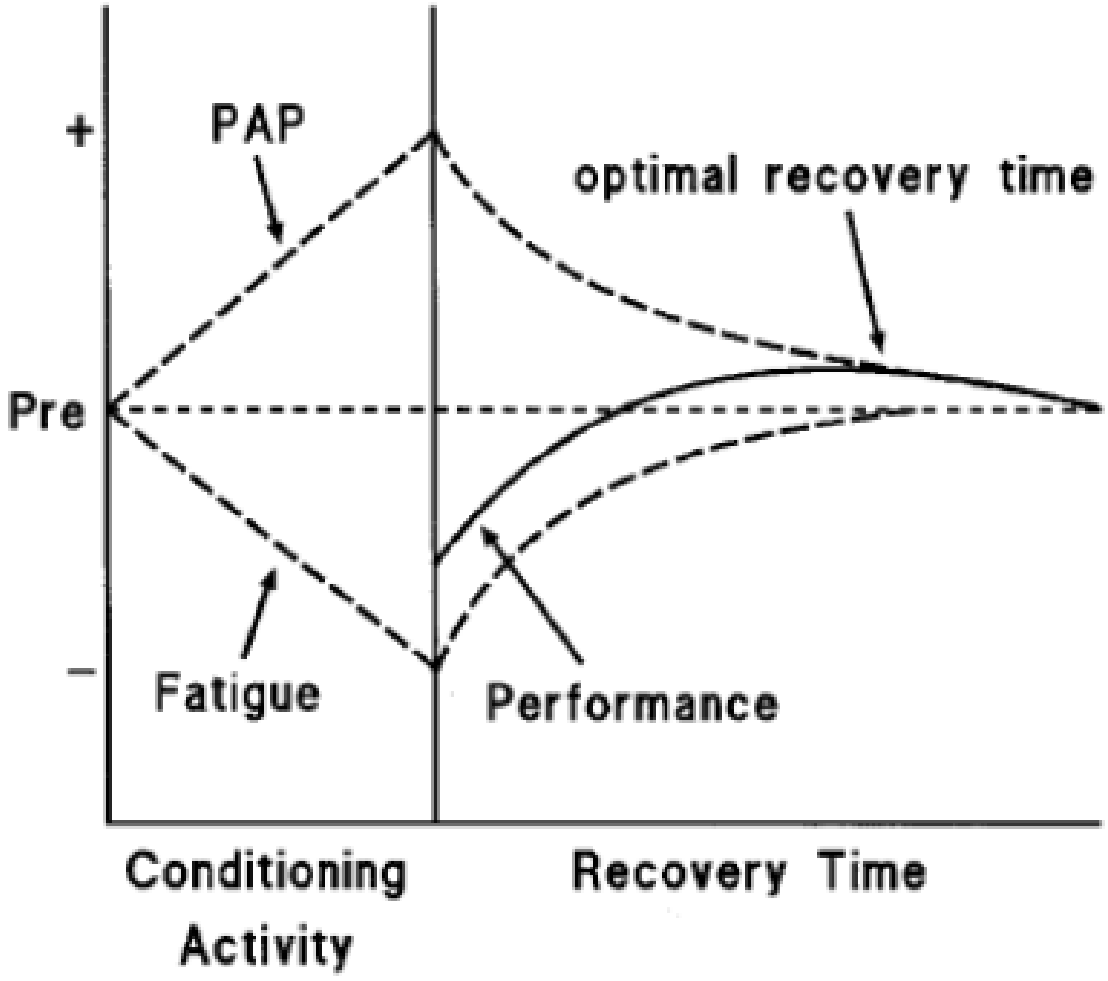

Figure 3. Coexistence of potentiation and fatigue. Depiction of the temporal relationship between potentiation and fatigue, and the resulting contractile performance (Sale 2002, reprinted with permission [6])

The relationship between potentiation and fatigue is now well established for evoked contractions, but whether that relationship persists during voluntary contractions is not known.

Conditioning contraction duration

As discussed in section 1.3, potentiation and fatigue both increase as the conditioning contraction progresses. In order to maximize the net effect of potentiation, the relationship between greater potentiation and minimal fatigue must be optimized. Vandervoort et al. conducted a detailed study assessing twitch potentiation of the human dorsiflexors and plantar flexors following conditioning contractions at a variety of durations [16]. This study identified a 10 s conditioning contraction as the optimal duration for dorsiflexion potentiation, and 10 s – 30 s as optimal for plantar flexors. The authors identify fiber type differences among the triceps surae, where the soleus has an exceptionally high proportion of slow-twitch fatigue resistant fibers, as the reason for contractile property differences. This fiber type difference likely explains the potentiation of the soleus following longer conditioning contractions, which highlights the nature of the relationship between potentiation and fatigue. However, this relationship has not been determined comprehensively for voluntary contractions in any muscle group.

Several studies have made assessments of voluntary potentiation in various models, with equivocal results [17-20]. In particular, Gossen [17] and Baudry [19] have used different durations of CC to measure voluntary potentiation. Baudry observed no improvement in RTD of the adductor pollicis following a 6 s CC, and Gossen observed a reduction in knee extension velocity following a 10 s CC. While several differences exist among all of these study models, it is possible that the 10 s CC duration frequently used causes fatigue of voluntary contraction to which the twitch is not susceptible. The observation of voluntary potentiation at submaximal RTD following a shorter 6 s CC may suggest that voluntary potentiation is optimized at a shortened CC duration [19].

Potentiation and muscle length

Myosin light chain phosphorylation enhances contractile properties by reducing the distance between the myosin head and the actin binding site. However, phosphorylation is not the only variable in determining actin-myosin interfibrillar distance. Because the muscle is an isovolumetric tissue, any change to the length of the muscle is accompanied by a corresponding change to muscle width. This dictates an increased interfibrillar space in the shortened muscle position, and compression between myofibrils in the lengthened muscle position. Thus, in some ways, lengthening the muscle mimics the mechanism of potentiation , and shortening the muscle will have the opposing effect of slowing and weakening contractile properties. Because the studies that have investigated potentiation have primarily used an isometric condition and evoked contractions, it is not well understood how potentiation and muscle length interact, especially during a voluntary contraction.

In addition to the architectural changes occurring with passive muscle length change, there are cross-bridge kinetic changes accompanying active muscle length change. During concentric contraction, shortening-induced force depression is observed [21] and during eccentric contraction, lengthening-induced force enhancement [22] is observed. Of particular interest here is shortening-induced force depression, which is characterized as a reduction in force-generating capability in a muscle following active shortening, compared to a purely isometric contraction at the same muscle length. This depression putatively occurs as a result of cross-bridges in the strongly bound state, which transmit tension in opposition to the direction of contraction. Thus, as a muscle shortens during active contraction, force is progressively weakened by increased interfibrillar spacing as well as strongly-bound cross-bridges, resulting in a significant negative effect in the most shortened positions. If myosin phosphorylation has its greatest positive effect in these short positions, there may be a role for potentiation in counterbalancing these negative effects.

Potentiation and voluntary vs. involuntary contractile properties

Voluntary contraction differs from electrically stimulated contraction in several important regards which make the potentiated twitch a poor indicator of potentiated voluntary behavior. Firstly, the recruitment of motor units occurs differently between voluntary and evoked contraction. Based on orderly recruitment of motor units, the fast-twitch muscle fibers are activated only at the highest levels of descending drive [23]. In order to maximize potentiation, the human must voluntarily recruit all fast-twitch fibers, and recruit them early in contraction. By comparison, the maximal evoked twitch activates all motor units nearly simultaneously, and the high-threshold fast twitch fibers may in fact activate first during electrical stimulation [24].

Central control following a conditioning contraction

As discussed above, activation history of the muscular system influences its subsequent behavior. However, during voluntary contraction the muscular system does not operate in isolation, and is part of the greater neuromuscular system. The 'neural' aspect of the neuromuscular system contains various and complex components, including the motor cortex, descending drive transmitted by spinal synapses, and peripheral motor axons. Modifications to any one of these systems following a conditioning contraction may affect contractile properties. These distinct central components may all be affected in the same way to affect potentiation, or some may become inhibitory while others become facilitatory.

Purpose

The performance of a voluntary task requires coordination among all parts of the neuromuscular system, from the motor cortex to the contractile proteins, and including afferent feedback to the central nervous system. For the potentiated twitch, myosin light chain phosphorylation drastically alters the relationship between electrical input and contractile output, but evoked contractions provide an incomplete model of the integrated neuromuscular system. Understanding voluntary contractile and neural behaviours during myosin light chain phosphorylation is important in clarifying the complex adaptations undertaken by the neuromuscular system following and during voluntary tasks. The series of experiments that follow describe the effect of myosin light chain phosphorylation during voluntary contraction. Thus, the purpose of the study included in Chapter 2 was to assess voluntary neuromuscular efficiency at two different muscle lengths, because functional tasks in which work is done require muscle length change during contraction.

By definition, the primary difference between voluntary and electrically evoked contractions is the source of the stimulus. Fast, explosive voluntary contractions should provide a good opportunity to observe voluntary potentiation, because rate of twitch torque development is known to increase 2-3 fold following a conditioning contraction, but sarcoplasmic [Ca^{2+}] is not saturated until late into torque development [25, 26]. Furthermore, it has not been shown that the conditioning contraction exerts effects on the neuromuscular system proximal to the motor axon, ie. the central nervous system. The purpose of the study presented in Chapter 3 was to assess voluntary and evoked rates of torque development following either a voluntary or a tetanic conditioning contraction.

As a follow-up to Chapter 3, Chapter 4 investigates the time course of ballistic contractions following either voluntary or tetanic conditioning contraction. Because studies often report only *peak* torque, or *peak* rate of torque development, only one small snapshot of the contraction is assessed. The purpose in Chapter 4 was to evaluate the effect of potentiation throughout the entirety of the contraction. Finally, in Chapter 5, the

effects of a conditioning contraction on the CNS were more directly assessed. In this study single TMS pulses were used to evoke a cortical silent period both prior to and following a conditioning contraction, as well as assessing twitch potentiation at these time points. These measures provide an indication of both peripheral (muscle twitch) and central (motor cortical) adaptations occurring simultaneously following a conditioning contraction.

References

1. Baudry S, Duchateau J. Postactivation potentiation in human muscle is not related to the type of maximal conditioning contraction. Muscle Nerve 2004; 30:328-336.

2. Vandervoort AA, Quinlan J, McComas AJ. Twitch potentiation after voluntary contraction. Exp Neurol 1983; 81:141-152.

3. MacIntosh BR, Willis JC. Force-frequency relationship and potentiation in mammalian skeletal muscle. J Appl Physiol 2000; 88:2088-2096.

4. Requena B, Gapeyeva H, Garcia I, Ereline J, Paasuke M. Twitch potentiation after voluntary versus electrically induced isometric contractions in human knee extensor muscles. Eur J Appl Physiol 2008; 104:463-472.

5. MacIntosh BR, Gardiner PF. Posttetanic potentiation and skeletal muscle fatigue: interactions with caffeine. Can J Physiol Pharmacol 1987; 65:260-268.

6. Sale D. Postactivation potentiation: role in performance. Br J Sports Med 2004; 38:386-387.

7. Sweeney HL, Bowman BF, Stull JT. Myosin light chain phosphorylation in vertebrate striated muscle: regulation and function. Am J Physiol 1993; 264:C1085-95.

8. Abbate F, Sargeant AJ, Verdijk PW, de Haan A. Effects of high-frequency initial pulses and posttetanic potentiation on power output of skeletal muscle. J Appl Physiol 2000; 88:35-40.

9. Moore RL, Stull JT. Myosin light chain phosphorylation in fast and slow skeletal muscles in situ. Am J Physiol 1984; 247:C462-71.

10. Houston ME, Grange RW. Torque potentiation and myosin light-chain phosphorylation in human muscle following a fatiguing contraction. Can J Physiol Pharmacol 1991; 69:269-273.

11. Hamada T, Sale DG, Macdougall JD. Postactivation potentiation in endurance-trained male athletes. Med Sci Sports Exerc 2000; 32:403-411.

12. Xue L, Wu LG. Post-tetanic potentiation is caused by two signalling mechanisms affecting quantal size and quantal content. J Physiol 2010; 588:4987-4994.

13. Smith IC, Gittings W, Huang J, McMillan EM, Quadrilatero J, Tupling AR, et al. Potentiation in mouse lumbrical muscle without myosin light chain phosphorylation: is resting calcium responsible? J Gen Physiol 2013; 141:297-308.

14. Rassier DE, Macintosh BR. Coexistence of potentiation and fatigue in skeletal muscle. Braz J Med Biol Res 2000; 33:499-508.

15. Rankin LL, Enoka RM, Volz KA, Stuart DG. Coexistence of twitch potentiation and tetanic force decline in rat hindlimb muscle. J Appl Physiol (1985) 1988; 65:2687-2695.

16. Vandervoort AA, McComas AJ. A comparison of the contractile properties of the human gastrocnemius and soleus muscles. Eur J Appl Physiol Occup Physiol 1983; 51:435-440.

17. Gossen ER, Sale DG. Effect of postactivation potentiation on dynamic knee extension performance. Eur J Appl Physiol 2000; 83:524-530.

18. Klein CS, Ivanova TD, Rice CL, Garland SJ. Motor unit discharge rate following twitch potentiation in human triceps brachii muscle. Neurosci Lett 2001; 316:153-156.

19. Baudry S, Duchateau J. Postactivation potentiation in a human muscle: effect on the rate of torque development of tetanic and voluntary isometric contractions. J Appl Physiol 2007; 102:1394-1401.

20. Behm DG, Button DC, Barbour G, Butt JC, Young WB. Conflicting effects of fatigue and potentiation on voluntary force. J Strength Cond Res 2004; 18:365-372.

21. Lee SC, Braim A, Becker CN, Prosser LA, Tokay AM, Binder-Macleod SA. Diminished fatigue at reduced muscle length in human skeletal muscle. Muscle Nerve 2007; 36:789-797.

22. Oskouei AE, Herzog W. Observations on force enhancement in submaximal voluntary contractions of human adductor pollicis muscle. J Appl Physiol (1985) 2005; 98:2087-2095.

23. Henneman E, Somjen G, Carpenter DO. Functional Significance of Cell Size in Spinal Motoneurons. J Neurophysiol 1965; 28:560-580.

24. Feiereisen P, Duchateau J, Hainaut K. Motor unit recruitment order during voluntary and electrically induced contractions in the tibialis anterior. Exp Brain Res 1997; 114:117-123.

25. Cannell MB, Allen DG. Model of calcium movements during activation in the sarcomere of frog skeletal muscle. Biophys J 1984; 45:913-925.

26. Isenberg G, Han S, Schiefer A, Wendt-Gallitelli MF. Changes in mitochondrial calcium concentration during the cardiac contraction cycle. Cardiovasc Res 1993; 27:1800-1809.

Potentiation of the Triceps Brachii During Voluntary Submaximal Contractions[1]

Introduction

The capacity of contractile fibers in skeletal muscle to produce torque (or force) is influenced by a variety of factors including contractile history. Postactivation potentiation (PAP) is one outcome of prior muscle activation. It is often characterized by improved calcium (Ca^{2+}) sensitivity and greater-than-normal electrically evoked twitch torque production following a short, high-intensity conditioning contraction [1]. PAP is well documented [2-7], and many of these studies have used electrical stimulation to show that PAP has the ability to enhance contractile torque. However, whether the relatively transient effect of PAP, which decays exponentially and is abolished after approximately 4 - 6 minutes [8], has a significant effect on submaximal voluntary contractile efficiency has not been investigated thoroughly.

Electrically induced twitches differ from voluntary contractions in several aspects related mainly to motor unit activation [9, 10] and contractile sensory feedback [11], which together will affect motor control. With electrical activation of muscle, supraspinal control and afferent feedback are circumvented, both of which are known to be important in normal motor control [12]. In a study by Klein and colleagues [13], contractions of equal torque output were performed with and without a prior conditioning contraction. Reduced motor unit firing rates were observed. This is a change which was attributed to myosin light chain phosphorylation, and it suggested an improvement in contractile efficiency. However, despite reduced firing rates, surface EMG in that study was unchanged

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[1] A version of this chapter has been published. Used with permission from *John Wiley and Sons*.

Smith C.B., Cheng A.J., and Rice C.L. Potentiation of the triceps brachii during voluntary submaximal contractions. Muscle Nerve 2011; 43:859-865.

between pre-MVC and post-MVC states, which could indicate that more motor units were recruited. Thus the extent or possible effect of improved contractile efficiency on motor unit output is not thoroughly understood. Although there have been some studies directed at assessing PAP and contractile performance during ballistic voluntary movements [14-16], previous studies have not evaluated the influence of PAP on torque maintenance during a voluntary sustained contraction. Because PAP has a relatively transient and exponentially decaying effect [8], it is unknown whether PAP can improve isometric torque maintenance over a longer duration than that observed during ballistic voluntary movements of 500 ms or less [15, 16].

Muscle length is also known to affect Ca^{2+} sensitivity and PAP effects [17-19]. The mechanism of potentiation is believed to be due to myosin light-chain phosphorylation [20-22], which in moving the myosin head in closer proximity to actin binding sites allows cross-bridges to be more readily available for binding. Because skeletal muscle is an isovolumetric tissue, changing muscle length is an alternative means of modifying actin-myosin spacing. In the shortened position, interfilament spacing is greater than in the lengthened position, where filaments are positioned closer together [23]. Thus, PAP should have a greater effect when the muscle is in a shortened position compared with the lengthened position, because the myofibrils are already in close proximity in a lengthened muscle and cannot benefit from the optimized actin-myosin interaction resulting from myosin light chain phosphorylation. Indeed, it has been shown with electrical stimulation that potentiation of twitch torque is greater at a short length compared to the same muscle in a lengthened position [19, 24]. During evoked contractions, excitatory input is precisely controlled by the stimulating apparatus. Because voluntary neural input cannot be controlled as precisely, it should be included as a variable in order to make a valid evaluation the effect of PAP on submaximal voluntary torque output. It is known that PAP is not effective at increasing torque output during maximum voluntary contractions, because the muscle is maximally saturated with Ca^{2+} [22]. Therefore, PAP may be more beneficial at submaximal voluntary contractions in which increased Ca^{2+} sensitivity from PAP may increase neuromuscular efficiency. Neuromuscular efficiency (NME: muscle torque output / neural input) is a measure of the relationship between voluntary neural

input and muscular torque output and is expressed in terms of Nm/mV [25, 26]. Previously NME has been used as a measure of contractile efficiency to evaluate neuromuscular failure such as during fatigue, but it has not been used to explore neuromuscular enhancement due to PAP. If NME is improved by PAP this would present an easily accessible, non-invasive means of quantifying voluntary PAP. The evoked twitch, in which PAP has been studied extensively, is a not a physiological contraction and is of limited relevance in determining the functional significance of PAP. Considering that many daily muscle actions are performed at submaximal intensity and at a variety of muscle lengths, the relationship between PAP and joint angle may be functionally significant during contractions at a lower intensity than what is commonly used to assess potentiation.

Fast-twitch muscle fibers are known to potentiate more than their slow-twitch counterparts due to a higher concentration of myosin regulatory light chain kinase [20], thus many studies assess PAP by activating these fibers. However, studies in evoked contractions show the improvement in Ca^{2+} sensitivity from PAP has its greatest effect at low [Ca^{2+}] [27]. Whereas PAP at low intensity of voluntary contraction has not been investigated thoroughly, low intensity contractions occupy a favorable position in the force-pCa^{2+} curve, establishing a reasonable expectation of contractile potentiation following myosin light chain phosphorylation. Furthermore, because the triceps brachii are comprised of an exceptionally high proportion of fast-twitch type II muscle fibers [30], this muscle group presents the greatest opportunity among the limb muscles to have activation of fast-twitch fibers at a relatively low percentage of MVC torque. This feature provides a strong rationale to anticipate an improvement from PAP at submaximal intensities despite their possible preferential reliance on slow-twitch muscle fibers.

Thus, the purpose of this study was to investigate the effect of PAP on the neuromuscular efficiency of the triceps brachii during voluntary submaximal contractions. It was hypothesized that PAP would improve neuromuscular efficiency (Nm/mV) during voluntary contractions and that a greater improvement would be observed at short, compared with long, muscle lengths. To maximize the probability of observing a

measurable result, a highly fast-twitch muscle such as the triceps brachii provides a good model. Biopsy studies show that the triceps brachii is a type II dominant muscle composed of approximately 56-80% FT fibers (average of 66% FT)~) [28-30], and it has shown PAP values as high as 240% [13, 31, 32].

Materials and Methods

1.1.1 Subjects

Twelve healthy male subjects participated in the study. They had a mean age of 24.6 ± 3.5 years, mean height of 178.6 ± 6.6 cm and mean body mass of 79.7 ± 5.2 kg. Subjects were recreationally active, and they were not involved in systematic training of any type prior to this experiment. Prior to the study session, subjects were required to abstain from upper-body exercise and ingestion of caffeine or alcohol for 24 hours. Room temperature for all tests was maintained at approximately 22° C. All methods were conducted in accordance with the guidelines set in place by the ethics review board of the University of Western Ontario. Informed written consent was obtained from all subjects.

1.1.2 Experimental Setup

Subjects were seated in an adjustable chair using inelastic straps to immobilize the shoulders and torso. Hip and knee angles were approximately 80° and 90°, respectively. The right arm was abducted approximately 15° from the torso, and the shoulder was flexed to approximately 45°. The right elbow was placed on a supportive pad, and the arm was immobilized using inelastic straps just proximal to the elbow joint. A System 3 Biodex dynamometer was used to measure elbow extensor torque. The axis of rotation for the dynamometer was aligned with the center of the lateral epicondyle of the right humerus, and the length of the dynamometer arm adjusted to the length of the subject's forearm. With the forearm in the semi-pronated position and secured to the dynamometer

proximal to the wrist joint, the subject grasped the handle at the distal end of the dynamometer arm. In an attempt to minimize contribution of the wrist flexors and extensors, subjects were instructed to maintain a neutral wrist position.

Electrical stimulation was delivered in pulses of 50 μs duration generated from a Digitimer electrical stimulator (model DS7AH, Digitimer, Welwyn Garden City, Hertfordshire, England). The stimulating anode was placed over the upper triceps brachii, just distal to the inferior border of the deltoid muscle. The cathode was placed over the lower triceps brachii, just proximal to the elbow joint. Anode and cathode electrodes were custom fabricated; both measured 8 cm x 2 cm and consisted of several folds of aluminum foil sheets wrapped in paper towel. Before attachment these were soaked in water and treated with conductive gel.

Surface electromyography (EMG) was recorded via a pair of self-adhering surface electrodes (circular recording surface of 0.5cm radius) (Kendall H59P, Mansfield, MA). Each subject's skin was abraded and cleaned with an alcohol swab prior to electrode placement. Inter-electrode distance measured center-to-center was 2cm, with the reference electrode placed 2/3 of the distance from the greater tuberosity of the humerus to the lateral epicondyle and the active electrode placed proximal to the reference. The ground electrode was placed on the acromion process of the subject's right scapula.

All torque data were recorded at a sampling frequency of 100 Hz. Signals were converted from analog to digital using a 12-bit analog-to-digital converter (CED model 1401 Plus, Science Park, Cambridge, UK). Data were both acquired and subsequently analyzed offline using Spike2 v.6.05 software (Cambridge Electronic Design Ltd., Cambridge, UK). Raw EMG was processed online as root mean square (RMS) using a 400-ms time constant. Surface EMG was gained by 200x before being filtered from 10 Hz – 1 kHz.

1.1.3 Experimental Protocol

In a random order, the subject was positioned with the right arm at either 40° or 120° of elbow flexion (0° defined as full extension). To ensure maximal activation of muscle fibers during electrical stimulation, current was increased until isometric twitch torque reached a plateau, and this procedure was repeated at each muscle length. The current used for twitches during the experiment was increased from this level by 10% to ensure supra-maximal stimulation. The stimulation intensity determined for twitches was also used as the current intensity for 100 Hz doublets (two pulses with 10ms inter-pulse duration) to assess voluntary activation [33]. The return of twitch torque to the pre-MVC value was used throughout the experiment as an indicator that the effects of potentiation had dissipated. This recovery time following the conditioning contraction was 6-9 minutes based on each individual's recovery requirements.

To determine peak torque output, two 5s maximal voluntary isometric contractions (MVCs) were performed, with a three minute rest in between. During each of these MVCs, a doublet was delivered at the peak of the MVC and again immediately after the MVC (~1s) to determine voluntary activation using the twitch interpolation method [33]. Subjects were provided with visual feedback of torque output via a computer monitor and were verbally encouraged to contract maximally during all MVCs. The highest peak torque value of the two initial contractions was used as the MVC torque. To establish the baseline EMG value the subject then performed a single contraction of 10 s duration targeted to 25% of MVC torque. For these contractions, a horizontal line was shown on the monitor to indicate the target torque, and the subject was instructed to match torque output to the target line. In order to eliminate any possible order effect or cumulative fatigue, the subject rested for 3 min, which was sufficient time following a submaximal (25%) contraction for twitch torque to return to resting levels. The experimental contractions followed. A single baseline, non-potentiated twitch was recorded, which would be used to calculate twitch potentiation. It was followed by a 5 s MVC (with

interpolated doublet) and immediately followed by a potentiated, post-MVC twitch, a doublet, and a 10s voluntary contraction targeted again at 25% of MVC. Subjects were then allowed 10min of recovery before subsequent contractions. To ensure the muscle was no longer potentiated, twitches were periodically evoked after each contraction condition at 1 min intervals until resting twitch torque returned to the pre-MVC value. Subjects then repeated the same protocol at the other joint angle (40° or 120°). Twitch and MVC torque may differ between muscle lengths, so peak twitch and MVC torque values obtained at each muscle length were expressed relative to values at the same joint angle, and maximal twitch stimulation intensity was determined independently at each joint angle.

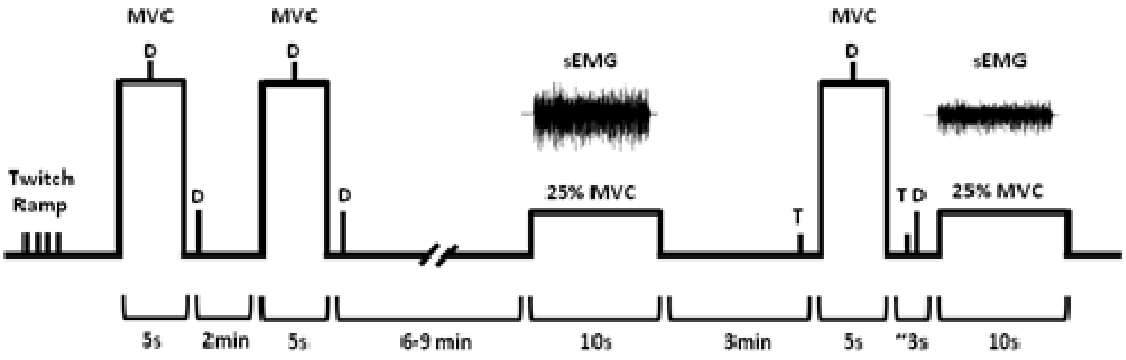

Figure 4. Experimental protocol and example of unprocessed surface EMG recordings. A twitch (T) is evoked before and after each MVC, and a doublet (D) is evoked at the peak, and immediately following each MVC. Examples of raw surface EMG (sEMG) records during each 25% MVC contraction.

1.1.4 Data Analysis

Twitch potentiation was expressed as the percentage increase of the peak twitch torque following the MVC conditioning contraction compared with the peak twitch torque evoked before the MVC contractions. For voluntary contractions, neuromuscular efficiency was expressed as a relative index relating torque output per amount of EMG (Nm/mV). Torque and RMS EMG amplitude values were obtained by calculating the average value recorded over the central 8 s of the 10 s 25% MVC submaximal contraction. Voluntary activation percentage was calculated using the twitch interpolation technique as follows: [1 – (interpolated doublet torque/post-MVC doublet torque)] x 100%.

Mean values for peak twitch torque and neuromuscular efficiency were calculated for both pre- and post-MVC, and at both muscle lengths. Using SPSS software (SPSS 16.0.1 Chicago: SPSS Inc.), interaction and statistical significance were calculated by repeated measures analysis of variance (ANOVA, $P < 0.05$) using muscle length and pre- / post-MVC. Post-hoc testing was done using the Bonferroni correction factor. All values are expressed as mean ± standard deviation except in the figures where error bars represent standard error.

Results

1.1.5 Twitches and MVCs

There was an increase in twitch torque in the post-MVC state for both short (216.9% ±169.3, $P = 0.0017$) and long (77.3% ±32.6, $P < 0.0001$) muscle lengths (Figure 5), but the magnitude of twitch potentiation was greater at the short muscle length than long muscle length ($P = 0.014$) (Figure 5). Maximal voluntary elbow extensor torques were 60.1 Nm ±8.4 and 63.4 ±10.2 at short and long lengths, respectively and there was no length-dependent difference. Elbow extensors were highly activated in all subjects (92.9% ± 5.4), and voluntary activation also did not differ between the short and long muscle length ($P = 0.289$). For each muscle length, initial peak MVC torque was compared to the peak torque of the final MVC performed at the same length; no difference was observed in either torque output or voluntary activation for either the short ($P = 0.283$) or long ($P = 0.083$) muscle length. This suggests that the testing procedures did not induce any cumulative fatigue.

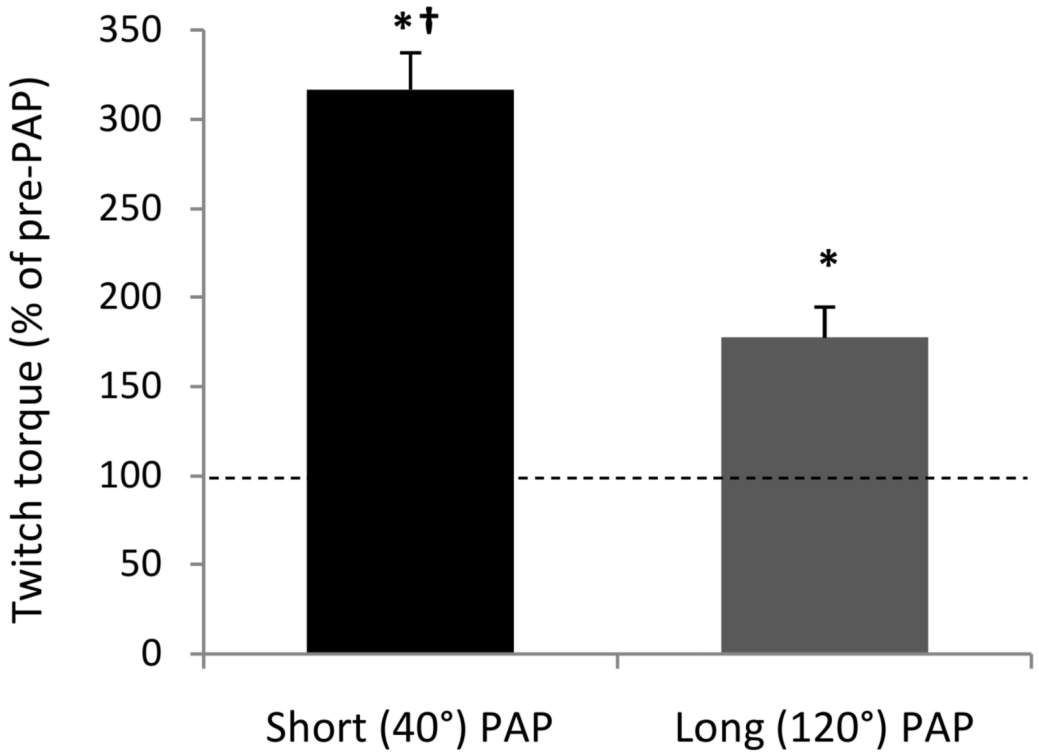

Figure 5. Twitch torque comparison between pre- and post-potentiation, and at short and long muscle lengths. Twitch torque was increased by PAP at both lengths (*), but the effect of PAP was greater at short compared with the long muscle length (†). ($p < 0.05$). The horizontal line at 100% indicates pre-MVC twitch torque.

1.1.6 Submaximal Voluntary Contractions

During voluntary submaximal contractions, pre-MVC NME was not different between short and long muscle lengths (P =0.944). At the short muscle length, NME was improved by 12.2% from the pre-MVC to post-MVC (P =0.002 ; Figure 6), but in contrast, in the lengthened position, NME was unchanged (P =0.734 ; Figure 6). Because torque was unchanged (25% MVC) throughout all submaximal voluntary contractions, changes in this measure are driven by a reduction in the EMG recording. Conversely, for the evoked contractions, the input (electric current) was unchanged during the protocol, and improvements in evoked contractile response were driven by increased torque.

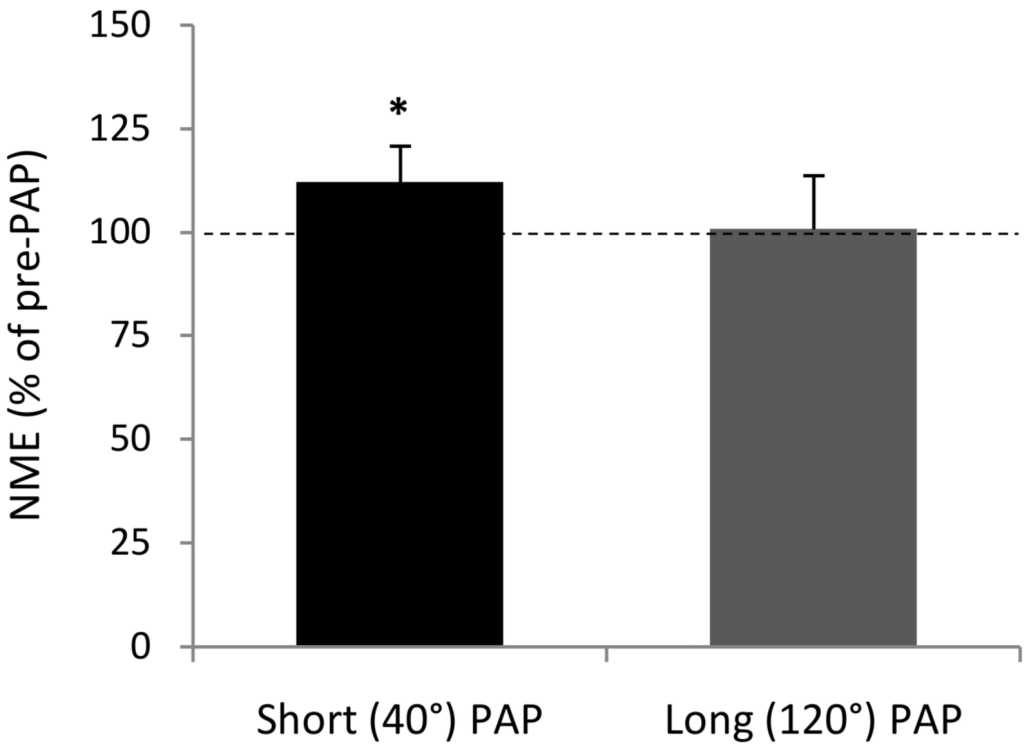

Figure 6. Comparison of neuromuscular efficiency (NME) between pre- and post-potentiation, and at short and long muscle lengths. NME was increased by PAP at short length, but at long length PAP had no effect. ($p < 0.05$). The horizontal line at 100% represents pre-MVC NME.

Discussion

The purpose of this study was to evaluate the effect of potentiation on NME during voluntary submaximal contractions at different muscle lengths. The hypotheses were that potentiation of the triceps brachii would increase NME, and that both PAP and NME would be greater at the short compared with the long muscle length. Both of these hypotheses were confirmed, although the magnitude of improvement in NME was unexpectedly low in comparison with electrically induced twitch potentiation. That is, at short lengths we observed an improvement in twitch torque of ~217% and a voluntary NME improvement of only ~13%. At long muscle lengths, even though twitch torque improved by ~77%, there was no change in voluntary NME. Thus the effectiveness of PAP from a functional aspect seems limited, even at short muscle lengths when PAP is substantial.

1.1.7 MVC and Twitch Responses

Mean elbow extensor MVC torque was comparable to the literature [34, 35]. Using twitch interpolation, the mean activation was on average 93%, and this agrees with prior reports [36-38]. Mean twitch potentiation at short and long muscle length was 216% and 77.3% respectively, which is consistent with previous reports for this muscle group [31, 37]. The great potentiation capability of this muscle group [13, 31, 32] is related to its large percentage (63-67%) of FT fibers [28, 29]. This capability is particularly evident at short muscle length, which is known to facilitate potentiation [18], resulting in PAP increases in twitch torque of over 200% for the elbow extensors.

1.1.8 Submaximal Voluntary Contractions

The observation of reduced motor unit firing rates in potentiated muscle from Klein et al. [13] suggested that the neural input required to maintain muscle torque was reduced by the PAP enhancement of the contractile response. However, that study could not exclude the possibility that additional motor units were recruited to compensate for the reduction in firing rates. Our observation of improved NME during torque maintenance is driven by a reduction in surface EMG post-MVC. Because it has been suggested that the surface EMG signal is determined more by changes in recruitment especially at submaximal levels [39] our results suggest that, in addition to lowered firing rates reported previously [13], PAP also may depress motor unit recruitment or alter recruitment thresholds. However this has not been tested directly at the motor unit level.

While the hypothesis that PAP would improve NME was confirmed, it is noteworthy that the scale of improvement was substantially less for voluntary NME (12% at short, no change at long) than for evoked twitch torque (217% at short, 77% at long). Mechanistically, the factor that most likely determines the difference in improvement between voluntary contractions and evoked twitches relates to improvement in Ca^{2+} sensitivity. This effect is most evident at low [Ca^{2+}], whereas at maximal [Ca^{2+}] levels myosin light chain phosphorylation has no effect [27]. Thus we chose a submaximal intensity of 25% MVC to determine whether or not voluntary torque would demonstrate an improvement in NME. Our result of increased NME at the short length suggests that myosin light chain phosphorylation indeed does reduce the neural input required to sustain 25% of MVC torque. However, there was a smaller increase in voluntary NME than evoked twitch torque with myosin light chain phosphorylation, which indicates less improvement in the voluntary than the twitch contraction.

Light chain phosphorylation is known to increase the Ca^{2+} sensitivity of muscle tissue by placing myosin heads and actin binding sites in closer proximity, so that for a given Ca^{2+} release, cross-bridge attachment occurs at an increased rate [21, 40]. Thus, in the transition from quiescence to contraction, cross-bridges enter the force-generating state more quickly when potentiated, and this alters the proportion of active cross-bridges in the

force-generating state [21], ultimately improving the twitch torque response. Consequently, during voluntary control, the requisite submaximal target torque can be achieved at a lower Ca^{2+} concentration following PAP [41]. The resultant change in the ratio of voluntary input to torque output increases NME while potentiated. However, this improvement is far less than the improvement in evoked twitch, and it is likely that multiple mechanisms underlie that difference. MacIntosh and Willis [42] showed in rat skeletal muscle that after a conditioning contraction, peak force of incompletely fused evoked tetani improved less than evoked twitches. This may occur because of improved Ca^{2+} sensitivity with PAP, which has its greatest effect at low levels of activation. For a single twitch, PAP will be at or near maximum, because initial Ca^{2+} concentration is minimal. For a train of summating pulses however, each pulse introduces additional intracellular Ca^{2+}, and so with each pulse Ca^{2+} concentration rises and the effects of PAP are reduced. Consequently, peak torque of a tetanic contraction will be augmented less by PAP than will a twitch stimulus [42], and similarly, peak torque output of a sustained submaximal contraction may potentiate to a smaller extent than peak twitch torque. In addition to the single stimulus versus the tetanic nature of the contractions, there are potential differences in the fibers being activated between an evoked twitch and a submaximal voluntary contraction. Although both contractions produce submaximal levels of torque, all motor units, including highly potentiable fast-twitch units, are activated during the twitch, whereas the voluntary contraction activates only some of those units. Together, these features may help to explain our results, which showed large evoked twitch potentiation and only modest improvements in NME at the short but not long muscle length.

From the onset of contraction, PAP and fatigue processes exist concurrently [4, 6] and can have opposing effects on contractile performance. Prior experiments in the human dorsiflexors suggest that an MVC of 10 s is optimal to maximize the effects of PAP [43], and at durations beyond 10s, the effects of fatigue become more prevalent and begin to mask PAP. We have shown that the potentiation improves NME less than twitch torque, which suggests that each type of contraction will have a different balance between PAP and fatigue. During pilot testing in this study we found that MVC contractions in the

elbow extensors held longer than 5 s caused twitch potentiation but also induced fatigue, which mitigated any measurable effect of PAP on NME. Our strategy to emphasize the effects of PAP while minimizing fatigue was to shorten MVC duration from 10 s to 5 s. Baudry et al. [15] acknowledged and attempted to describe the differential effect of PAP on twitch compared to voluntary contractions and found that, while twitch potentiation was maximal immediately after MVC, the maximal potentiation of voluntary ballistic contractions was delayed until 1 min after MVC. Even then it was substantially less than evoked twitch potentiation. In relation to the length-dependency of PAP, a previous study has indeed shown that fatigue is greater at long versus short muscle lengths following isometric contraction tasks [44], suggesting that either fatigue is also length-dependent, or that the length-dependency of PAP has the ability to mask fatigue differently between muscle lengths. In this study the finding that muscle length during isometric situations affects PAP raises the question of how these factors may interact during dynamic contractions. We have shown during an isometric contraction that PAP affects torque more favorably in the shortened than in the lengthened position. However, during dynamic contractions it has been shown that additional mechanisms such as thin filament deactivation [45] and shortening induced force depression [46] decrease torque as the muscle shortens. This effect is opposite to what we observe from PAP during isometric contractions, where torque is improved at short muscle length. It is unclear how PAP may affect torque output during non-ballistic dynamic contractions, or whether PAP may function to preserve torque output as the muscle shortens in the presence of torque-reducing mechanisms. Thus, it appears that the relationship between PAP, fatigue, and muscle length is different between evoked twitch and voluntary submaximal contractions, and that further differences may exist for non-ballistic dynamic contractions. The nature of these complex interactions during voluntary control will require further study.

Many previous studies have chosen to perform contractions at a high intensity to maximize recruitment of FT fibers, which are highly potentiable. By contracting at only 25% MVC, likely fewer of the more potentiable motor units are recruited. However, to minimize this possible limitation we utilized the triceps brachii model and aimed instead to activate it at an advantageous portion of the force-Ca^{2+} curve to determine whether

myosin light chain phosphorylation would benefit lower intensity contractions. Although maximal ballistic contractions may activate a large portion of FT fibers and show a large improvement from myosin light chain phosphorylation, there are many functional activities to which ballistic movements are not relevant. Rather than aiming to maximize NME, the rationale here was to show the effect of myosin light chain phosphorylation at different muscle lengths during a type of contraction which is functionally relevant, but under-represented in the study of PAP. The improvement in NME observed in this study is in agreement with those by Klein and colleagues [13], which suggested an overall reduction in neural input during torque maintenance. The corroboration of our results with those above provides support for our conclusion, but a more complete understanding of the neural responses to PAP during varying functional conditions remains to be clarified.

1.1.9 Conclusion

We have demonstrated that NME of the triceps brachii is improved by potentiation, while confirming that muscle length influences PAP similarly for evoked and voluntary contractions. These results support suggestions from previous studies that the neural input required to maintain contractile torque is reduced when muscle is potentiated [13]. However, our results further indicate a substantially limited role for PAP during sustained submaximal voluntary contractions in comparison to evoked twitches, and for contractions performed at long muscle lengths. It appears that PAP provides greater benefit to twitch-like contractions performed with the muscle in a shortened position. We have shown that the relationship between PAP and torque output is distinct between submaximal voluntary contractions and evoked twitches and differs in relation to muscle length. Consequently, these findings underscore the influence of contractile history, contraction type, and muscle length on voluntary motor control.

References

1. Sale D. Postactivation potentiation: role in performance. Br J Sports Med 2004; 38:386-387.

2. Abbate F, Sargeant AJ, Verdijk PW, de Haan A. Effects of high-frequency initial pulses and posttetanic potentiation on power output of skeletal muscle. J Appl Physiol 2000; 88:35-40.

3. Baudry S, Klass M, Duchateau J. Postactivation potentiation influences differently the nonlinear summation of contractions in young and elderly adults. J Appl Physiol 2005; 98:1243-1250.

4. Fowles JR, Green HJ. Coexistence of potentiation and low-frequency fatigue during voluntary exercise in human skeletal muscle. Can J Physiol Pharmacol 2003; 81:1092-1100.

5. Manning DR, Stull JT. Myosin light chain phosphorylation-dephosphorylation in mammalian skeletal muscle. Am J Physiol 1982; 242:C234-41.

6. Rassier DE, Macintosh BR. Coexistence of potentiation and fatigue in skeletal muscle. Braz J Med Biol Res 2000; 33:499-508.

7. Sale DG. Postactivation potentiation: role in human performance. Exerc Sport Sci Rev 2002; 30:138-143.

8. MacIntosh BR, Gardiner PF. Posttetanic potentiation and skeletal muscle fatigue: interactions with caffeine. Can J Physiol Pharmacol 1987; 65:260-268.

9. Feiereisen P, Duchateau J, Hainaut K. Motor unit recruitment order during voluntary and electrically induced contractions in the tibialis anterior. Exp Brain Res 1997; 114:117-123.

10. Trimble MH, Enoka RM. Mechanisms underlying the training effects associated with neuromuscular electrical stimulation. Phys Ther 1991; 71:273-80; discussion 280-2.

11. Gandevia SC, Macefield G, Burke D, McKenzie DK. Voluntary activation of human motor axons in the absence of muscle afferent feedback. The control of the deafferented hand. Brain 1990; 113 (Pt 5):1563-1581.

12. Duchateau J, Enoka RM. Neural control of shortening and lengthening contractions: influence of task constraints. J Physiol 2008; 586:5853-5864.

13. Westing SH, Cresswell AG, Thorstensson A. Muscle activation during maximal voluntary eccentric and concentric knee extension. Eur J Appl Physiol Occup Physiol 1991; 62:104-108.

14. Klein CS, Ivanova TD, Rice CL, Garland SJ. Motor unit discharge rate following twitch potentiation in human triceps brachii muscle. Neurosci Lett 2001; 316:153-156.

15. Baudry S, Duchateau J. Postactivation potentiation in a human muscle: effect on the load-velocity relation of tetanic and voluntary shortening contractions. J Appl Physiol 2007; 103:1318-1325.

16. Baudry S, Duchateau J. Postactivation potentiation in a human muscle: effect on the rate of torque development of tetanic and voluntary isometric contractions. J Appl Physiol 2007; 102:1394-1401.

17. Gossen ER, Sale DG. Effect of postactivation potentiation on dynamic knee extension performance. Eur J Appl Physiol 2000; 83:524-530.

18. Balnave CD, Allen DG. The effect of muscle length on intracellular calcium and force in single fibers from mouse skeletal muscle. J Physiol 1996; 492 (Pt 3):705-713.

19. MacIntosh BR. Role of calcium sensitivity modulation in skeletal muscle performance. News Physiol Sci 2003; 18:222-225.

20. Miyamoto N, Mitsukawa N, Sugisaki N, Fukunaga T, Kawakami Y. Joint angle dependence of intermuscle difference in postactivation potentiation. Muscle Nerve 2010; 41:519-523.

21. Ryder JW, Lau KS, Kamm KE, Stull JT. Enhanced skeletal muscle contraction with myosin light chain phosphorylation by a calmodulin-sensing kinase. J Biol Chem 2007; 282:20447-20454.

22. Sweeney HL, Stull JT. Alteration of cross-bridge kinetics by myosin light chain phosphorylation in rabbit skeletal muscle: implications for regulation of actin-myosin interaction. Proc Natl Acad Sci U S A 1990; 87:414-418.

23. Vandenboom R, Grange RW, Houston ME. Threshold for force potentiation associated with skeletal myosin phosphorylation. Am J Physiol 1993; 265:C1456-62.

24. Wang YP, Fuchs F. Length-dependent effects of osmotic compression on skinned rabbit psoas muscle fibers. J Muscle Res Cell Motil 2000; 21:313-319.

25. Rassier DE, Tubman LA, MacIntosh BR. Length-dependent potentiation and myosin light chain phosphorylation in rat gastrocnemius muscle. Am J Physiol 1997; 273:C198-204.

26. Miller RG, Giannini D, Milner-Brown HS, Layzer RB, Koretsky AP, Hooper D, et al. Effects of fatiguing exercise on high-energy phosphates, force, and EMG: evidence for three phases of recovery. Muscle Nerve 1987; 10:810-821.

27. Milner-Brown HS, Mellenthin M, Miller RG. Quantifying human muscle strength, endurance and fatigue. Arch Phys Med Rehabil 1986; 67:530-535.

28. Persechini A, Stull JT, Cooke R. The effect of myosin phosphorylation on the contractile properties of skinned rabbit skeletal muscle fibers. J Biol Chem 1985; 260:7951-7954.

29. Harridge SD, Bottinelli R, Canepari M, Pellegrino MA, Reggiani C, Esbjornsson M, et al. Whole-muscle and single-fibre contractile properties and myosin heavy chain isoforms in humans. Pflugers Arch 1996; 432:913-920.

30. Johnson MA, Polgar J, Weightman D, Appleton D. Data on the distribution of fibre types in thirty-six human muscles. An autopsy study. J Neurol Sci 1973; 18:111-129.

31. Elder GC, Bradbury K, Roberts R. Variability of fiber type distributions within human muscles. J Appl Physiol 1982; 53:1473-1480.

32. Cheng AJ, Rice CL. Fatigue-Induced Reductions of Torque and Shortening Velocity Are Muscle-Dependent. Med Sci Sports Exerc 2010; 49: 1651-1659.

33. Rice CL, Cunningham DA, Paterson DH, Dickinson JR. Strength training alters contractile properties of the triceps brachii in men aged 65-78 years. Eur J Appl Physiol Occup Physiol 1993; 66:275-280.

34. Shield A, Zhou S. Assessing voluntary muscle activation with the twitch interpolation technique. Sports Med 2004; 34:253-267.

35. Hamada T, Sale DG, Macdougall JD. Postactivation potentiation in endurance-trained male athletes. Med Sci Sports Exerc 2000; 32:403-411.

36. Kawakami Y, Nakazawa K, Fujimoto T, Nozaki D, Miyashita M, Fukunaga T. Specific tension of elbow flexor and extensor muscles based on magnetic resonance imaging. Eur J Appl Physiol Occup Physiol 1994; 68:139-147.

37. Cheng AJ, Rice CL. Voluntary activation in the triceps brachii at short and long muscle lengths. Muscle Nerve 2010; 41:63-70.

38. Klein CS, Rice CL, Marsh GD. Normalized force, activation, and coactivation in the arm muscles of young and old men. J Appl Physiol 2001; 91:1341-1349.

39. Jakobi JM, Rice CL. Voluntary muscle activation varies with age and muscle group. J Appl Physiol 2002; 93:457-462.

40. Christie A, Greig Inglis J, Kamen G, Gabriel DA. Relationships between surface EMG variables and motor unit firing rates. Eur J Appl Physiol 2009; 107:177-185.

41. MacIntosh BR, Willis JC. Force-frequency relationship and potentiation in mammalian skeletal muscle. J Appl Physiol 2000; 88:2088-2096.

42. Metzger JM, Greaser ML, Moss RL. Variations in cross-bridge attachment rate and tension with phosphorylation of myosin in mammalian skinned skeletal muscle fibers. Implications for twitch potentiation in intact muscle. J Gen Physiol 1989; 93:855-883.

43. Sweeney HL, Bowman BF, Stull JT. Myosin light chain phosphorylation in vertebrate striated muscle: regulation and function. Am J Physiol 1993; 264:C1085-95.

44. Vandervoort AA, Quinlan J, McComas AJ. Twitch potentiation after voluntary contraction. Exp Neurol 1983; 81:141-152.

45. Lee SC, Braim A, Becker CN, Prosser LA, Tokay AM, Binder-Macleod SA. Diminished fatigue at reduced muscle length in human skeletal muscle. Muscle Nerve 2007; 36:789-797.

46. Oskouei AE, Herzog W. Observations on force enhancement in submaximal voluntary contractions of human adductor pollicis muscle. J Appl Physiol (1985) 2005; 98:2087-2095.

Voluntary rate of torque development is impaired following a voluntary versus tetanic conditioning contraction[2]

Introduction

Activation history influences the contractile characteristics of skeletal muscle, and the consequences of prior contraction may be force-diminishing (fatiguing) or force-enhancing (potentiating) depending on the intensity and duration of the activity [1]. Due to improved calcium (Ca^{2+}) sensitivity, potentiation is characterized by enhancement in submaximal torque and rate of torque development (RTD) following one relatively brief (5-10 s) conditioning contraction of moderate to high intensity [1, 2]. Many previous human and animal studies have induced potentiation either by a voluntary contraction [post-voluntary (PV)] [3, 4] or an evoked tetanus [post-tetanus (PT)] [5, 6]. Assessing evoked contractions, rather than voluntary, avoids many complications and limitations associated with voluntary control, but this type of activation is non-physiological and disregards the important role of the central nervous system in controlling and modifying normal muscle contraction. The effects of potentiation on evoked single pulses [4, 7], and trains of pulses [5, 8] have been well studied, but the outcomes of potentiation on succeeding voluntary contractions are less clear. Results are few and varied regarding the effects on voluntary dynamic contractile velocity, power, and RTD after potentiation [9-11]. Furthermore, it is not well understood how the inclusion of central nervous control may affect the properties altered during potentiated contraction. Potentiation by a voluntarily controlled conditioning contraction, rather than evoked tetanus, may influence the effect of potentiation in one of two ways: either peripherally, by differently affecting intramuscular processes such as myosin phosphorylation, or centrally, by affecting

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Smith C.B., Allen M.D., Rice C.L. Voluntary rate of torque development is impaired after a voluntary versus tetanic conditioning contraction. Muscle Nerve 2014; 49:218-224.

subsequent behaviour of the motor nervous system proximal to the neuromuscular junction.

Myosin light chain phosphorylation is widely considered the primary mechanism of potentiation [2, 12, 13]. Skeletal muscle myosin regulatory light chain kinase is responsible for phosphorylating the light chain, and is the target of a pathway initiated by Ca^{2+} released into the sarcoplasm during contraction. While phosphorylation persists [~6-10 minutes following maximal voluntary contraction (MVC) [4]], Ca^{2+} sensitivity of the potentiated muscle is increased, which allows faster and more forceful contractions. If Ca^{2+} exposure is the driving force for myosin light-chain phosphorylation, then the source of the action potentials (voluntary drive or tetanic stimulation) should not affect myosin phosphorylation following voluntary contraction or evoked tetanus at the same force/time integral. Previous studies report no effect of a voluntary conditioning task on potentiation of evoked contractions of 1, 2 or 3 pulses [3], and it has been suggested that the primary predictor of twitch potentiation is the number of action potentials which reach the muscle, rather than the source of those potentials [ie. voluntary (CNS) or involuntary (electric stimulator)] [14, 15]. Because the peripheral evoked responses appear to be indifferent to the source of activation, it seems likely that any disparity between PV and PT potentiation is not distal to the motor axon.

Regardless of the peripheral response, PV and PT contractions may have different effects at the CNS level. Following both brief [16] and sustained [17] voluntary contractions, reduced corticomotor excitability has been shown to persist for up to 20 minutes. Furthermore, maximal contractions sustained for 2 minutes [18], or performed in 1 minute intervals repeatedly [19], have been shown to cause significant activation failure. A sustained evoked tetanus fundamentally bypasses supraspinal and spinal voluntary control pathways, inducing potentiation without directly activating associated central influences. Although, there is afferent feedback to the CNS during electrical stimulation, as shown by increased brain activation with fMRI scans [20], it is unknown whether this type of afferent activity has any fatiguing or inhibitory effect, such as that observed following voluntary contractions. Therefore, it is reasonable to suggest that a sustained tetanus and

an MVC may have different effects as conditioning contractions, thus resulting in differences during subsequent potentiated contractions. The evoked twitch is enhanced by up to ~200% by potentiation, but the voluntary measure of neuromuscular efficiency [expressed as (torque / EMG)] is enhanced by only ~12% [21]. Assessing only twitch potentiation may fail to detect central inhibition which is revealed when potentiated voluntary contractions are performed. This supports the idea that for voluntary contractions, additional factors beyond the degree of myosin light chain phosphorylation within the muscle regulate the properties of potentiated voluntary contractions, but this has not been explored comprehensively.

Contractile torque is enhanced by potentiation, but only at submaximal levels of activation. Consequently, to assess potentiation by measuring torque, the level of submaximal activation must be known. One difficulty associated with assessing potentiation of a voluntary contraction is the inability to control precisely the level of activation, unlike a contraction evoked by stimulation. In addition to enhancement of submaximal torque following potentiation, the rate of torque development is also facilitated during high intensity voluntary (ballistic) and electrically induced high frequency (250 Hz) trains [10]. Therefore, ballistic RTD can provide a useful index to assess potentiation during voluntary contractions.

Thus, to explore the possible differences between evoked and voluntarily controlled contractions in postactivation potentiation, each contraction type was assessed as a conditioning and a potentiated contraction of the human dorsiflexors. It was hypothesized that 1) twitch properties would be equally potentiated following evoked and voluntary conditioning contraction, and that 2) ballistic rate of torque development would potentiate more following an evoked than a voluntary conditioning contraction.

Materials and methods

1.1.10 Participants

Eleven healthy men participated in the study. They were aged 22-29 years (25.9 y ± 2.2) with a mean height of 178.5 cm ± 6.0 and mean body mass of 82.3 kg ± 9.4. Based on pilot data, an a priori calculation using statistical software (G*Power, v.3.1.3, Franz Faul, Universität Kiel, Germany) indicated that 11 subjects would provide sufficient statistical power (> 0.8) to show differences in ballistic RTD. Participants were recreationally active and not participating in any systematic training prior to this study. Participants were required to abstain from lower-body exercise 24 hours prior to testing, and from ingestion of caffeine or alcohol 12 hours prior. Room temperature for all tests was maintained at approximately 22° C. All methods were conducted in accordance with the guidelines of the local ethics review board following the Declaration of Helsinki. All participants provided informed verbal and written consent.

1.1.11 Experimental setup

Participants were seated with their right leg in a custom built isometric ankle dynamometer with hip and knee joint angles of approximately 90°. The right ankle joint was positioned at 20° of plantar flexion to minimize torque contribution of the fibular muscles [22], and the foot was secured to a rigid footplate by inelastic Velcro straps over the toes and dorsum of the foot. Torque applied to the footplate was measured by a strain gauge in line with the ankle axis of rotation, and regular calibration produced a consistent linear relationship. The great toe was left unsecured by straps, to eliminate torque contribution of extensor hallucis longus. The lower limb was immobilized using a c-clamp pressing downwards on the distal aspect of the right thigh.

Surface electromyography (EMG) was recorded via pairs of self-adhering surface electrodes (circular recording surface of 0.5 cm radius) (Kendall H59P, Mansfield, MA). Prior to electrode placement, the recording sites were abraded lightly and cleaned using presoaked alcohol swabs (70% isopropyl alcohol). Voluntary muscle activity was

assessed with a pair of recording electrodes placed over the tibialis anterior (TA) in a bipolar arrangement with active and reference electrodes at 10 and 12 cm distal to the tibial tuberosity. Plantar flexor EMG was also recorded via pairs of electrodes, with the reference electrode 2 cm distal to the active, and placed over the centre of the medial gastrocnemius muscle belly. Soleus EMG was collected via electrodes placed ~2 cm apart along the midline of the muscle, ~2 cm distal to the inferior border of the gastrocnemii. An electronic thermistor probe was secured to the skin over the belly of the TA, and skin temperature was recorded at the beginning and termination of testing.

Contractions of the tibialis anterior were evoked through stimulation of the common fibular nerve via a pair of circular carbon rubber electrodes (3 cm diameter) (Empi, St. Paul Minnesota, USA) which had been coated with conductive gel. The cathode was placed on the skin anterior and just distal to the fibular head, and the anode was placed posterior and slightly superior to the fibular head in a position that maximized twitch torque. The electrodes were secured in position using tape. Contractions were evoked by square-wave electrical pulses of 100 μs duration generated by a Digitimer stimulator (model DS7AH, Digitimer, Welwyn Garden City, Hertfordshire, England). Pulses were delivered either as single stimuli (twitch) or as trains of stimuli at a frequency of 50 Hz. The operator applied manual pressure over the anode during all stimulation to ensure proper positioning.

Torque signals were recorded from a custom-built dynamometer at a sampling frequency of 500 Hz, and converted to digital format using a 12-bit analog-to-digital converter (CED model 1401 Plus, Science Park, Cambridge, UK). Surface EMG signals were pre-amplified (x100), low-pass filtered at 1000 Hz with a notch filter at 60 Hz, and sampled at a frequency of 2500 Hz. All torque and EMG data were acquired and saved for offline analysis using Spike2 v.7.0.7d software (Cambridge Electronic Design Ltd., Science Park, Cambridge, UK). Figure 7 depicts a representative sample torque recording, illustrating a conditioning contraction followed by potentiated twitch and ballistic contractions.

1.1.12 Experimental protocol

Once secured in the dynamometer, maximum isometric twitch torque was determined by increasing stimulation current until isometric twitch torque reached a plateau. The current was then increased a further 10–15% to ensure supramaximal stimulation was achieved. Maximum twitch currents ranged from 45 to 80 mA. Participants then performed two isometric MVCs of ~3 s duration, during which strong verbal encouragement and on-line visual feedback were provided. Supramaximal twitches were administered: ~3 seconds prior to MVC, at peak torque output during the MVC, and immediately upon relaxation post-MVC. This sequence allowed assessments of twitch potentiation following MVC, and voluntary activation using the interpolated twitch technique as follows: [(1-(interpolated twitch/potentiated twitch))*100%] [23].

Participants rested for 6-9 minutes following the MVCs to allow potentiation to dissipate. This was confirmed by the return of twitch torque to resting amplitude. Maximum evoked 50 Hz torque was then determined by increasing stimulation current until torque reached a plateau despite increased current. For this current ramping process, stimulus trains of 250 pulses at 50 Hz (5 s) were used. The current for maximal 50 Hz torque responses ranged from 45 to 80 mA. Following another 6-9 minutes of rest and once twitch torque had returned to resting amplitude, participants performed baseline ballistic contractions. Specific instructions to focus on achieving the fastest possible rate of torque development and to relax immediately upon reaching peak torque were provided, along with strong verbal encouragement and visual feedback during contraction. Subjects then became accustomed to the contractions by performing between 2 and 6 baseline ballistic contractions. Peak RTD was calculated from the torque recording as the peak instantaneous slope between the initial deviation from baseline and the peak torque.

After twitch torque had returned to resting amplitude, a 10 s potentiating contraction was completed using either an evoked contraction at 50 Hz, or a voluntary contraction targeted to the same torque. Immediately following a potentiating contraction, 2 twitches were evoked followed immediately by 2 voluntary ballistic contractions. The delays between the end of conditioning contraction and onset of twitch or ballistic contractions

were ~1 s and ~4 s respectively. Participants then rested for 6-9 minutes to allow potentiation to dissipate, which was confirmed by a return of baseline twitch torque. This procedure was repeated 4 times in random order (i.e. voluntary or evoked conditioning contraction), so that 2 of the potentiating contractions were evoked (i.e., involuntary), and 2 contractions were under voluntary control.

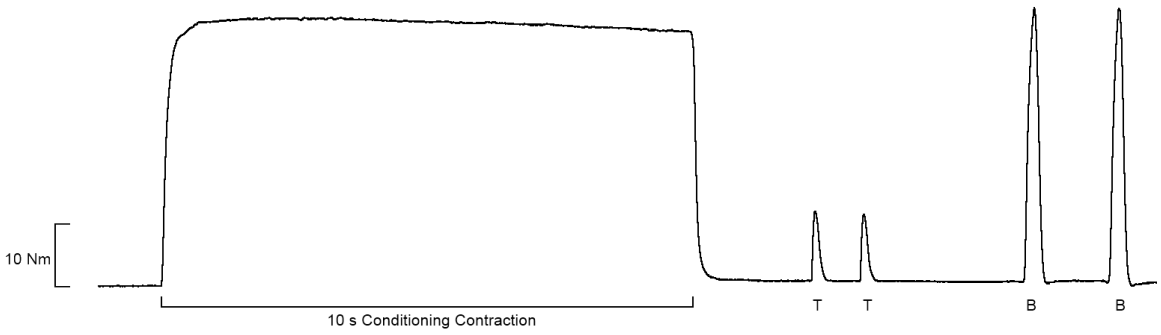

Figure 7. A representative sample torque recording is depicted. This tracing shows a 10 s conditioning contraction followed by 2 evoked twitches (T) and two voluntary ballistic contractions (B).

1.1.13 Statistics

All statistical analyses were conducted using statistical software (SPSS v.19.0.0; SPSS Inc., Chicago, Illinois). Mean values for contractile properties (twitch torque and RTD, ballistic RTD) were compared across 3 conditions (baseline, PT, PV) using repeated measures analysis of variance (ANOVA). Because input for tetanus is controlled precisely by the stimulating apparatus, but ballistic contractions are under voluntary control, analysis of covariance (ANCOVA) was performed for ballistic RTD to determine differences between PT and PV contraction while accounting for variance in baseline ballistic RTD. Where differences were found for ballistic contractions, EMG activity was compared between PT and PV using the paired student's T-test. Significance was set at $P < 0.05$, and post-hoc analysis was performed using the Bonferroni correction. All values in text and figures are represented as means ± standard deviations.

Results

Peak torque during MVC was 57.3 Nm ±12.5, and voluntary activation was calculated as 96.8 % ±3.4. Mean torque during the entirety of the sustained MVC was 48.6 Nm ±12.5, of which the 10 s potentiating contractions represented 78%. Conditioning contraction torques were well-matched and averaged 37.9 Nm ±8.1 for the evoked tetani, and 38.4 Nm ±7.8 for voluntary potentiating contractions. Skin surface temperature between the beginning (30.6 °C ±0.8) and completion (30.6° C ±0.9) of testing was unchanged (P = 0.61).

Twitch properties were measured at baseline and following conditioning contractions and are summarized in Table 1. Immediately following MVC (in a potentiated state), twitch torque was increased by 72.8% ±22.5 (P < 0.001), and twitch peak RTD increased by 107.0% ±30 (P < 0.001). Baseline RTD for voluntary ballistic contractions was 422.0 Nm/s ±88.9.

Table 1. Twitch and ballistic contractile properties

	Twitch		Ballistic
Condition	Torque (Nm)	Peak RTD (Nm/s)	Peak RTD (Nm/s)
Baseline	5.2 ±1.7	115.4 ±35	422.0 ±89
Post-tetanus	9.5 ±2.3*	256.8 ±53*	390.2 ±59*
Post-voluntary	8.9 ±3.1*	240.3 ±75*	356.4 ±69*†

Values are mean ± SD. * indicates significant difference from baseline, † indicates significant difference from post-tetanus ($P < 0.05$).

Twitch torque immediately after the 10 s potentiating contraction was increased in both conditions, however the magnitude of the increase was not statistically different between conditions (Figure 8A). Twitch torque increased by 82% to 9.5 Nm ±2.3 (P=0.03) following evoked tetanus and by 70% to 8.9 Nm ±3.1 (P=0.04) following voluntary contraction. Twitch RTD following evoked tetanus was increased by 122% to 256.8 Nm/s ±52.6, and increased following voluntary target by 108% to 240.3 Nm/s ±75.4 (Figure 8B). These increases were not statistically different between conditions.

Ballistic contractions performed following a 10 s evoked tetanus reached a mean peak torque equal to 75% of MVC. Contrary to the potentiated twitches, RTD of voluntary ballistic dorsiflexions was reduced following the 10 s conditioning contraction (Table 1). Peak RTD decreased 16% from baseline to 356.4±69.1 Nm/s (P = 0.04) following the voluntary target contraction and 8% from baseline to 390.2±59.3Nm/s (P = 0.001) following evoked contractions. To further control for variation in individual neural drive during ballistic contractions at baseline, an ANCOVA was performed which indicated that PT ballistic RTD was significantly greater than PV RTD (P = 0.004) (Figure 9). To evaluate neuromuscular activity during torque development, surface EMG of the tibialis anterior was rectified and averaged between the onset of EMG and the time point of peak RTD. EMG activity during the PV ballistic contraction was 0.18 mV ±0.08, which was significantly lower than during PT contraction at 0.21 mV ±0.09 (P = 0.03). Figure 10 illustrates the strong directionality of the difference in EMG activity between potentiated contractions, and that it parallels the similar change in RTD.

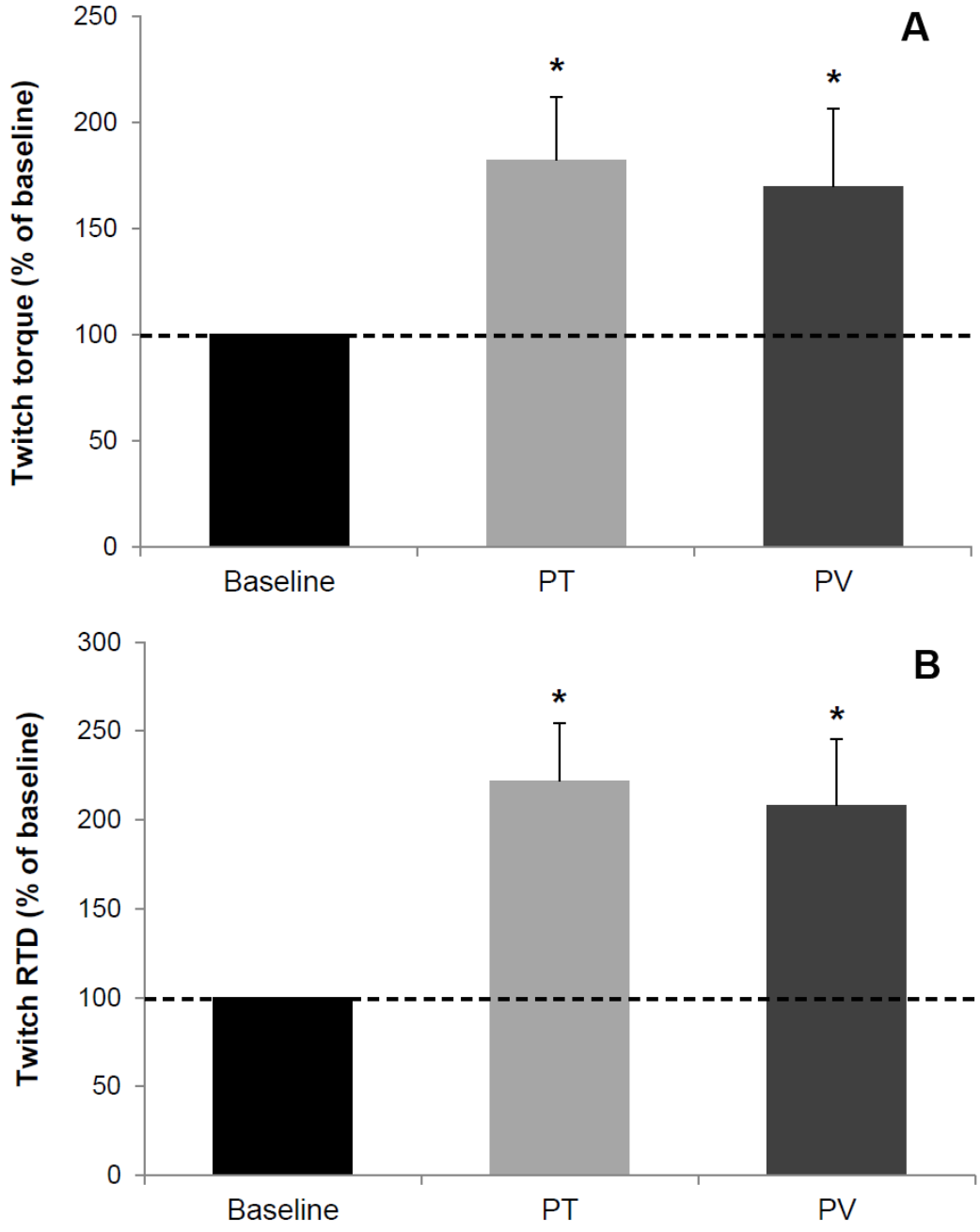

Figure 8. Potentiated twitch torque and RTD A) Twitch torque comparisons between baseline, post-tetanus (PT), and post-voluntary (PV) conditions. B) Twitch rate of torque development comparison between baseline, post-tetanus and post-voluntary conditions. *denotes significant difference from baseline (P<0.05).

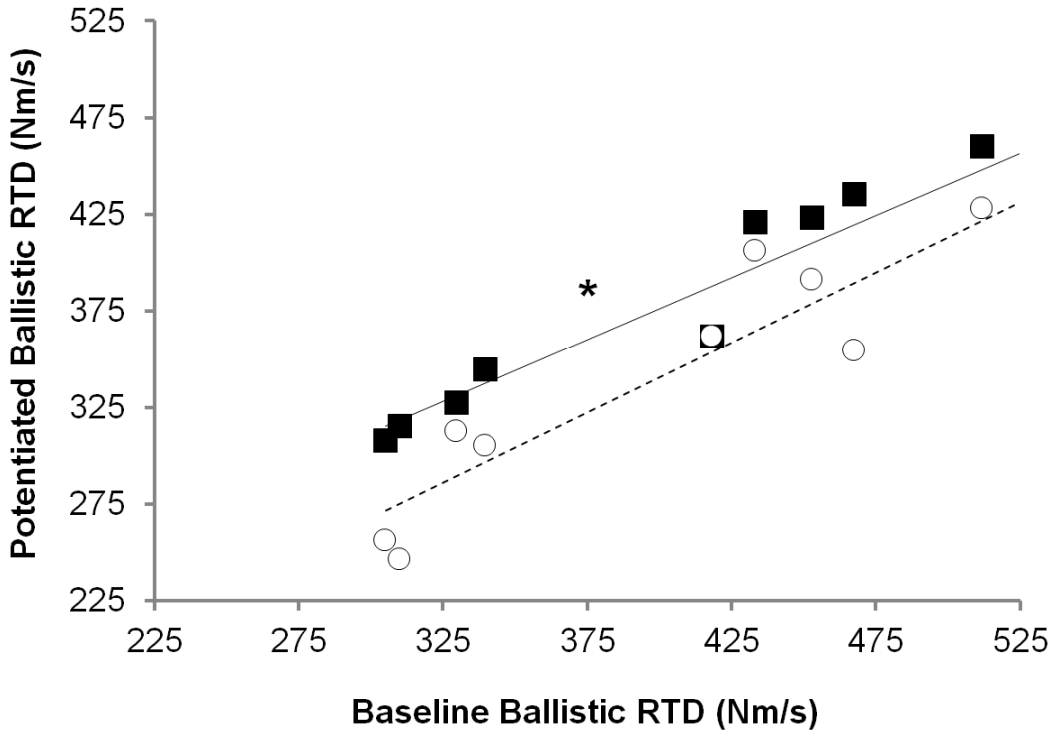

Figure 9. Ballistic RTD post-tetanus (■) post-voluntary (○) vs. baseline RTD. Analysis of covariance indicates that the Y-intercept of post-tetanic RTD (solid line) is greater than post-voluntary RTD (dashed line) ($P<0.05$).

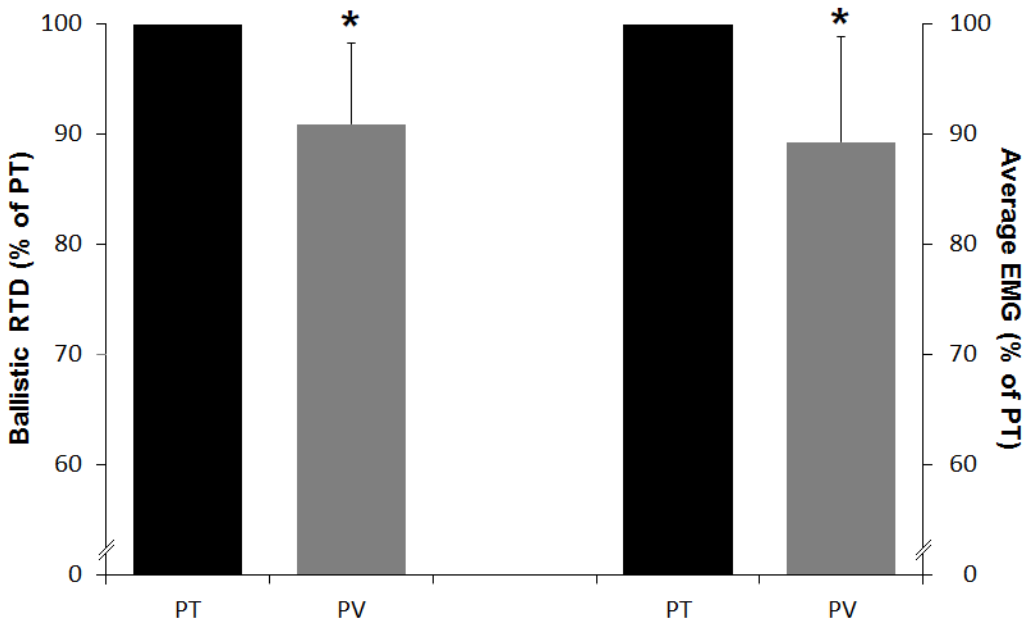

Figure 10. Ballistic rate of torque development and associated EMG, expressed as a percentage of PT value. Both RTD and EMG are significantly (*) and similarly reduced compared to PT.

Discussion

The purpose of this study was to explore the role of central and peripheral components in the potentiation of twitch and ballistic contractions following an evoked (PT) or voluntary (PV) conditioning contraction. The hypotheses were that evoked and voluntary conditioning contractions would have equal potentiating effects on an evoked twitch, and that voluntary ballistic RTD would be greater following the evoked than the voluntary conditioning contraction. As expected, twitch torque and twitch RTD were each potentiated above baseline following both PT and PV, and the magnitude of potentiation was the same for each condition. For potentiated ballistic contractions, RTD was greater following a tetanic conditioning contraction than a voluntary contraction. However, in contrast with an increase in twitch RTD compared to baseline, ballistic RTD was depressed compared to baseline following both types of conditioning contractions.

1.1.14 MVCs and baseline measurements

The MVC torque and voluntary activation levels we observed were consistent with what others have reported in the dorsiflexor group [24-26]. Following the 3 s MVC, a potentiated twitch was evoked which showed torque potentiation (~73%) and RTD potentiation (~107%) both of which agree with previous reports for this muscle [4, 27]. Torque achieved during the 50 Hz evoked tetanus was equal to ~78% of MVC torque, which was matched well during voluntary targeted contractions.

1.1.15 Potentiated measurements

We found equal potentiation of twitch torque and twitch RTD following both evoked and voluntary conditioning contractions, and both agree with previous reports [3, 15]. Although the 10 s conditioning contractions were very strong (78% of MVC), they were not strictly maximal, but were sufficient to induce substantial potentiation. Potentiation is apparent at contractions of 50% MVC [4], and by ~70% MVC most motor units in the tibialis anterior are activated [28, 29]. In addition, prior investigations have shown that the number of pulses rather than firing frequency is predictive of potentiation magnitude, so these

submaximal contractions of 10 s duration should fully potentiate high-threshold motor units even if they are activated at sub-maximal firing rates [14, 26]. Furthermore, the order of MU activation can be different during voluntary compared with electrically excited activation, at least at submaximal levels [30, 31], but because we are activating the muscle at very high levels likely all units are fully or equally recruited in both conditions [28, 29] permitting a valid comparison. Prior studies [30, 31] suggest that an activation discrepancy between voluntary and tetanic contractions should cause differences in the opposite direction to what we observe, which supports our assertion that the conditioning contractions were of sufficiently high intensity.

Potentiated ballistic contractions showed reduced RTD compared to baseline, and between contraction types RTD was slower for PV than PT. Figure 9 shows the ballistic RTD for both PV and PT plotted against baseline RTD for each subject, along with the regression line for both PT and PV. The slopes of the 2 lines are not statistically different, suggesting a similar effect across all subjects, and the y-intercept for PV is significantly less than for PT This implies some inhibiting effect following the 10 s voluntary contraction which is absent or reduced following the 10 s tetanus. Potentiated ballistic contractions are under voluntary control, and spinal and supraspinal components are integral in the performance of voluntary tasks. The performance of a 10 s, ~78% MVC contraction likely includes inhibitory effects at the spinal or corticomotor level which would affect the subsequent voluntary contraction [32]. Although the precise site of inhibition is not clearly understood, it appears unlikely that corticomotor inhibition is mediated by afferent input. Using transcranial magnetic stimulation, motor evoked potential size and silent period duration (measures of cortical excitability) indicate cortical inhibition following both fatiguing [33] and non-fatiguing [17] contractions. Furthermore, using electrical transmastoid stimuli, these measures recover after activity despite the maintenance of ischemia [18]. The observations of consistent inhibition and recovery of cortical measures despite peripheral conditions which would provide wide variance in afferent feedback suggest central rather than peripheral mediation of post-activity corticomotor depression. Because tetanic contraction requires no central involvement, these inhibitions should be absent from post-tetanic contractions.

One unique quality of a maximal ballistic contraction is that high-threshold motor units are recruited very early in the task; during dynamic tasks, high-thresholds may even become active before the initiation of movement [34, 35]. In this way, the characteristics of the contraction are highly dependent on the early coordination of muscle activation. Inhibition at the spinal level may impair early activation of high-threshold motor units, which are also the largest and fastest motor units [36] and would be expected to contribute substantially to maximal rate of torque development. We found that the decreased peak RTD following voluntary conditioning was accompanied by reduced average rectified EMG activity preceding peak RTD when compared with the EMG recorded during PT ballistic contraction. These EMG results provide further evidence and agree with other studies cited above that, following a voluntary conditioning contraction there is central inhibition of motor unit activity that is at least partly responsible for the reduction in ballistic potentiation.

Karatzaferi et al.[11] have shown a reduction in maximal shortening velocity associated with myosin phosphorylation in permeablized rabbit psoas fibers. While the conditions of the rabbit psoas fiber are quite artificial and mimic extreme fatigue conditions, the results indicate that myosin phosphorylation itself is associated with inhibited maximal shortening velocity. These results, in a decidedly different model, agree with the reduction in isometric RTD observed following tetanic and voluntary conditioning contractions in our study and by Baudry and Duchateau [10]. A common mechanism may be at work to impair both shortening velocity and isometric RTD, or these may be separate mechanisms, in which case human muscle may be subject to additional constraining effects during shortening contraction. Thus, it seems that immediately following the conditioning contraction, when potentiation has its greatest positive effect on torque production, there is a negative effect on peak rate of torque development and maximal shortening velocity. Although it is not clear how these responses may work, two possibilities are likely: the maximal nature of the contraction, and the altered attachment/detachment rates with myosin phosphorylation.

Potentiation is understood to have its greatest effect at low [Ca^{2+}], such as during a twitch or low frequency tetanus where it substantially improves peak torque; however, myosin phosphorylation offers little or no improvement at high [Ca^{2+}], as exemplified by its inability to increase maximal contractile power [13, 37]. Presumably, at high [Ca^{2+}], there is always sufficient calcium to cause complete activation of all possible cross-bridges, and improving calcium sensitivity offers no further activation. Therefore, because the ballistic contractions performed in this experiment required maximal efforts, there may have been little opportunity for myosin phosphorylation to increase peak RTD above baseline. Recently a greater enhancement of dynamic concentric torque following evoked conditioning contraction over voluntary contraction was shown in knee extensors [15]. Our study agrees with these results fundamentally, and we also avoid the following potential limitations of the dynamic model. It has been shown that following myosin phosphorylation there is an increased rate of cross-bridge attachment, but no change in the rate of detachment [2]. During isometric contraction, this results in improved torque development, as cross-bridges attach quickly and force summates. However, shorter attachment time with unchanged detachment means that each cross-bridge spends a greater *proportion* of time in the non-force generating state. To clarify, if a hypothetical myosin filament takes 1 ms to attach and generate force, and 1 ms to detach, it spends 1/2 its time in the force generating state. If this hypothetical filament then shortens its attachment time to 0.5 ms, with unchanged 1 ms detachment, it now spends only 1/3 of its time in the force generating state, despite a faster cross-bridge cycle. Furthermore, during rapid dynamic concentric contractions, the cross-bridges which are bound but not detached may exert a form of drag which would limit maximal shortening velocity [11, 38] and may explain the observation of decline in dynamic contractile properties following potentiation [10, 15]. Because the isometric model we have studied allows no joint movement, torque production is not affected by these factors inherent to dynamic contraction. Thus our results provide evidence that the reductions in ballistic contractile properties relate to processes occurring during conditioning contraction and not to the model of study.

These findings show that evoked and voluntary conditioning contractions have differing effects on the potentiated voluntary contractile properties. Furthermore, enhanced evoked twitch characteristics may not be a good predictor of voluntary performance following prior activation, as they fail to account for important changes in excitability that occur after as little as 10 s of voluntary activity. It appears that the remarkably large improvements in twitch torque and rate of twitch torque development following potentiation are not reflected during voluntary contractions, and in some cases may be reduced. Thus, when assessing primarily peripheral effects such as twitch potentiation, there does not appear to be any effect of contraction type; however, conditioning contraction type does seem to influence potentiation of subsequent voluntarily controlled contractions. To provide insight into functional outcomes of potentiation, it is important to understand voluntarily potentiated contractions to provide a more inclusive representation of changes in the integrated neuromuscular system.

References

1. Sale D. Postactivation potentiation: role in performance. Br J Sports Med 2004; 38:386-387.

2. Sweeney HL, Stull JT. Alteration of cross-bridge kinetics by myosin light chain phosphorylation in rabbit skeletal muscle: implications for regulation of actin-myosin interaction. Proc Natl Acad Sci U S A 1990; 87:414-418.

3. Baudry S, Duchateau J. Postactivation potentiation in human muscle is not related to the type of maximal conditioning contraction. Muscle Nerve 2004; 30:328-336.

4. Vandervoort AA, Quinlan J, McComas AJ. Twitch potentiation after voluntary contraction. Exp Neurol 1983; 81:141-152.

5. MacIntosh BR, Willis JC. Force-frequency relationship and potentiation in mammalian skeletal muscle. J Appl Physiol 2000; 88:2088-2096.

6. Requena B, Gapeyeva H, Garcia I, Ereline J, Paasuke M. Twitch potentiation after voluntary versus electrically induced isometric contractions in human knee extensor muscles. Eur J Appl Physiol 2008; 104:463-472.

7. Houston ME, Green HJ, Stull JT. Myosin light chain phosphorylation and isometric twitch potentiation in intact human muscle. Pflugers Arch 1985; 403:348-352.

8. Baudry S, Klass M, Duchateau J. Postactivation potentiation influences differently the nonlinear summation of contractions in young and elderly adults. J Appl Physiol 2005; 98:1243-1250.

9. Gossen ER, Sale DG. Effect of postactivation potentiation on dynamic knee extension performance. Eur J Appl Physiol 2000; 83:524-530.

10. Baudry S, Duchateau J. Postactivation potentiation in a human muscle: effect on the rate of torque development of tetanic and voluntary isometric contractions. J Appl Physiol 2007; 102:1394-1401.

11. Karatzaferi C, Franks-Skiba K, Cooke R. Inhibition of shortening velocity of skinned skeletal muscle fibers in conditions that mimic fatigue. Am J Physiol Regul Integr Comp Physiol 2008; 294:R948-55.

12. Ryder JW, Lau KS, Kamm KE, Stull JT. Enhanced skeletal muscle contraction with myosin light chain phosphorylation by a calmodulin-sensing kinase. J Biol Chem 2007; 282:20447-20454.

13. Vandenboom R, Grange RW, Houston ME. Threshold for force potentiation associated with skeletal myosin phosphorylation. Am J Physiol 1993; 265:C1456-62.

14. Mettler JA, Griffin L. What are the stimulation parameters that affect the extent of twitch force potentiation in the adductor pollicis muscle? Eur J Appl Physiol 2010; 110:1235-1242.

15. Miyamoto N, Kanehisa H, Kawakami Y. Potentiation of Maximal Voluntary Concentric Torque in Human Quadriceps Femoris. Med Sci Sports Exerc 2012.

16. Teo WP, Rodrigues JP, Mastaglia FL, Thickbroom GW. Post-exercise depression in corticomotor excitability after dynamic movement: a general property of fatiguing and non-fatiguing exercise. Exp Brain Res 2012; 216:41-49.

17. Sacco P, Thickbroom GW, Thompson ML, Mastaglia FL. Changes in corticomotor excitation and inhibition during prolonged submaximal muscle contractions. Muscle Nerve 1997; 20:1158-1166.

18. Taylor JL, Butler JE, Allen GM, Gandevia SC. Changes in motor cortical excitability during human muscle fatigue. J Physiol 1996; 490 (Pt 2):519-528.

19. Babault N, Desbrosses K, Fabre MS, Michaut A, Pousson M. Neuromuscular fatigue development during maximal concentric and isometric knee extensions. J Appl Physiol 2006; 100:780-785.

20. Blickenstorfer A, Kleiser R, Keller T, Keisker B, Meyer M, Riener R, et al. Cortical and subcortical correlates of functional electrical stimulation of wrist extensor and flexor muscles revealed by fMRI. Hum Brain Mapp 2009; 30:963-975.

21. Smith CB, Cheng AJ, Rice CL. Potentiation of the triceps brachii during voluntary submaximal contractions. Muscle Nerve 2011; 43:859-865.

22. Marsh E, Sale D, McComas AJ, Quinlan J. Influence of joint position on ankle dorsiflexion in humans. J Appl Physiol 1981; 51:160-167.

23. Allen GM, Gandevia SC, McKenzie DK. Reliability of measurements of muscle strength and voluntary activation using twitch interpolation. Muscle Nerve 1995; 18:593-600.

24. Belanger AY, McComas AJ. Extent of motor unit activation during effort. J Appl Physiol 1981; 51:1131-1135.

25. Kent-Braun JA, Ng AV. Specific strength and voluntary muscle activation in young and elderly women and men. J Appl Physiol 1999; 87:22-29.

26. Connelly DM, Rice CL, Roos MR, Vandervoort AA. Motor unit firing rates and contractile properties in tibialis anterior of young and old men. J Appl Physiol 1999; 87:843-852.

27. Hicks AL, Cupido CM, Martin J, Dent J. Twitch potentiation during fatiguing exercise in the elderly: the effects of training. Eur J Appl Physiol Occup Physiol 1991; 63:278-281.

28. Erim Z, De Luca CJ, Mineo K, Aoki T. Rank-ordered regulation of motor units. Muscle Nerve 1996; 19:563-573.

29. Van Cutsem M, Feiereisen P, Duchateau J, Hainaut K. Mechanical properties and behaviour of motor units in the tibialis anterior during voluntary contractions. Can J Appl Physiol 1997; 22:585-597.

30. O'Leary DD, Hope K, Sale DG. Posttetanic potentiation of human dorsiflexors. J Appl Physiol 1997; 83:2131-2138.

31. Jubeau M, Gondin J, Martin A, Van Hoecke J, Maffiuletti NA. Differences in twitch potentiation between voluntary and stimulated quadriceps contractions of equal intensity. Scand J Med Sci Sports 2010; 20:e56-62.

32. McNeil CJ, Giesebrecht S, Gandevia SC, Taylor JL. Behaviour of the motoneurone pool in a fatiguing submaximal contraction. J Physiol 2011; 589:3533-3544.

33. Sacco P, Thickbroom GW, Byrnes ML, Mastaglia FL. Changes in corticomotor excitability after fatiguing muscle contractions. Muscle Nerve 2000; 23:1840-1846.

34. Desmedt JE, Godaux E. Ballistic contractions in man: characteristic recruitment pattern of single motor units of the tibialis anterior muscle. J Physiol 1977; 264:673-693.

35. Harwood B, Rice CL. Changes in motor unit recruitment thresholds of the human anconeus muscle during torque development preceding shortening elbow extensions. J Neurophysiol 2012.

36. Henneman E, Somjen G, Carpenter DO. Functional Significance of Cell Size in Spinal Motoneurons. J Neurophysiol 1965; 28:560-580.

37. Abbate F, Sargeant AJ, Verdijk PW, de Haan A. Effects of high-frequency initial pulses and posttetanic potentiation on power output of skeletal muscle. J Appl Physiol 2000; 88:35-40.

38. Cuda G, Pate E, Cooke R, Sellers JR. In vitro actin filament sliding velocities produced by mixtures of different types of myosin. Biophys J 1997; 72:1767-1779.

Temporal effects of evoked and voluntary conditioning contractions on potentiated rate of torque development in human skeletal muscle

Introduction

Muscle contractile properties are influenced by activation history, and depending on the prior activity, can affect functional properties such as torque or rate of torque development (RTD) in a negative (eg. fatigue) or positive (eg. potentiation) direction [1, 2]. Typically these factors are assessed by measuring their peak responses of contractile properties [3-7], but properties at non-peak times also may be altered by prior activity. By definition, reporting instantaneous peak values disregards the great majority of other non-peak measurements made during a contraction. These often overlooked time points, especially between onset of contraction and peak torque or peak rate of torque development (pRTD), can influence the 'explosive' quality of maximal torque and RTD [8, 9]. Furthermore, the type of excitation (electrically evoked vs. voluntary) has been shown to influence potentiation and pRTD following otherwise similar conditioning contractions [10]. To date, study has focused primarily on potentiation of evoked contractions [6, 7, 11, 12] rather than voluntary contraction [13, 14], but the influence of the conditioning contraction type (evoked vs voluntary) on the time course of subsequent voluntary contraction is not well understood-.

Post-activation potentiation, widely thought to be primarily a result of myosin light chain phosphorylation, has been shown repeatedly to improve evoked twitch contractile properties, such as faster RTD, shorter time to peak torque, and shorter half-relaxation time compared to the baseline twitch [15,16]. However, studies of potentiated voluntary contractions have been more equivocal, showing differing results depending on the measurement and model chosen. Recently, we showed that the instantaneous pRTD during voluntary ballistic contraction was reduced by ~16% following a voluntary

conditioning contraction, but it was unchanged from baseline following an evoked conditioning contraction despite being matched for torque and time with the voluntary contraction. These ballistic pRTD measurements were made concurrent with twitch potentiation which showed, regardless of conditioning contraction type, a 122% increase in pRTD. Therefore, it seems that whereas the peripheral contractile tissue is indeed potentiated following either type of conditioning contraction, there is a limitation during the potentiated voluntary effort which counteracts an improvement in the maximal contractile properties of the muscle tissue.

One possible limit to potentiation of voluntary pRTD is that during the ballistic contraction, subjects may be able to achieve the true physiological maximal pRTD without the help of potentiation. The twitch pRTD has repeatedly shown a remarkable capacity to potentiate by as much as 200%. However, ballistic pRTD at baseline is already considerably greater than twitch pRTD (~100 Nm/s vs. ~400 Nm/s). Thus, while the maximal twitch pRTD may be maximal for a single pulse of stimulation, it is far from what the muscle can maximally achieve. If there is a ceiling effect preventing an increase in ballistic pRTD, perhaps improvements in contractile performance are apparent at non-peak time points. Assessing RTD at a range of time points would also reveal any changes to the shape of the RTD curve over the time-course of contraction. Considering that myosin light chain phosphorylation enhances the rate at which cross-bridges enter the force generating state, it follows therefore that improvement in the rate of force-generation should be apparent prior to pRTD. An increase in RTD at non-peak times would represent an increase in the acceleration of contraction, and could occur even without an increase in pRTD or 'top speed', following a conditioning contraction.

A second possibility is that central nervous processes are responsible for limiting potentiation of ballistic pRTD. Observations of reduced corticomotor excitability lasting up to 20 minutes have been made following both brief and sustained voluntary contractions [17-19]. Furthermore, significant activation failure has been observed following sustained (2 min) or repeated (in 1 min intervals) maximal contractions [20]. If corticomotor inhibition were the limiting factor to ballistic pRTD following a voluntary

conditioning contraction, this inhibition should be absent following an evoked conditioning contraction, which fundamentally bypasses the pathways of central activation. Thus, a comparison of the time course of ballistic RTD following either a voluntary or an evoked conditioning contraction should reveal any effects of central inhibition on voluntary RTD.

The functional relevance of understanding contractile properties throughout the time course of contraction, especially for ballistic-type tasks that allow limited time to develop torque has been described importantly by Andersen and Aagaard [21] and in subsequent studies. Their method reported RTD values in the human knee extensors cumulatively at 10 ms intervals (ie. 0-10, 0-20… 0-250), providing a view of total torque production at time points up to 250 ms [21]. The cumulative analysis of RTD is important, but information about torque produced during each interval may be obscured by the inclusion of prior time points as the contraction progresses. For example, changes in RTD will readily be apparent between 0-10 ms and 0-20 ms, but will be almost undetectable between 0-200 ms and 0-210 ms because these time points are determined by 95% of the same data. Thus, it may be of interest and value to investigate changes in the torque-producing abilities of the muscle throughout discrete time points of the contraction.

Therefore, to assess the effect of a conditioning contraction on the time course of contractile properties, and the effect of contraction type (voluntary or tetanic), ballistic and twitch contractile properties of the human dorsiflexors were assessed following both a voluntary and a tetanic conditioning contraction. It was hypothesized that 1) ballistic pRTD would be not increase regardless of conditioning contraction type, 2) acceleration of RTD (rate of RTD rise) would be faster at the onset of contraction, and 3) pRTD would be achieved earlier during contractions following tetanic conditioning compared to either baseline or post-voluntary conditioning contractions.

Materials and methods

1.1.16 Participants

Eleven healthy men participated in the study. They were aged 22-29 years (25.9 y ± 2.2) with a mean height of 178.5 cm ± 6.0 and mean body mass of 82.3 kg ± 9.4. Based on pilot data, an a priori calculation using statistical software (G*Power, v.3.1.3, Franz Faul, Universität Kiel, Germany) indicated that 11 subjects would provide sufficient statistical power (> 0.8) to show differences in ballistic RTD. Participants were recreationally active and not participating in any systematic training prior to this study. Participants were required to abstain from lower-body exercise 24 hours prior to testing, and from ingestion of caffeine or alcohol 12 hours prior. Room temperature for all tests was maintained at approximately 22° C. All methods were conducted in accordance with the guidelines of the local ethics review board following the Declaration of Helsinki. All participants provided informed verbal and written consent.

1.1.17 Experimental setup

Participants were seated with their right leg in a custom built isometric ankle dynamometer with hip and knee joint angles of approximately 90°. The right ankle joint was positioned at 20° of plantar flexion to minimize torque contribution of the fibular muscles [23], and the foot was secured to a rigid footplate by inelastic Velcro straps over the toes and dorsum of the foot. Torque applied to the footplate was measured by a strain gauge in line with the ankle axis of rotation, and regular calibration produced a consistent linear relationship. The great toe was left unsecured by straps, to eliminate torque contribution of extensor hallucis longus. The lower limb was immobilized using a c-clamp pressing downwards on the distal aspect of the right thigh.

Surface electromyography (EMG) was recorded via pairs of self-adhering surface electrodes (circular recording surface of 0.5 cm radius) (Kendall H59P, Mansfield, MA). Prior to electrode placement, the recording sites were abraded lightly and cleaned using presoaked alcohol swabs (70% isopropyl alcohol). Voluntary muscle activity was

assessed with a pair of recording electrodes placed over the tibialis anterior (TA) in a bipolar arrangement with active and reference electrodes at 10 and 12 cm distal to the tibial tuberosity. Plantar flexor EMG was also recorded via pairs of electrodes, with the reference electrode 2 cm distal to the active, and placed over the center of the medial gastrocnemius muscle belly. Soleus EMG was recorded via electrodes placed ~2 cm apart along the midline of the muscle, ~2 cm distal to the inferior border of the gastrocnemii. An electronic thermistor probe was secured to the skin over the belly of the TA, and skin temperature was recorded at the beginning and termination of testing.

Contractions of the TA were evoked through stimulation of the common fibular nerve via a pair of circular carbon rubber electrodes (3 cm diameter) (Empi, St. Paul Minnesota, USA) which had been coated with conductive gel. The cathode was placed on the skin anterior and just distal to the fibular head, and the anode was placed posterior and slightly superior to the fibular head in a position that maximized twitch torque. The electrodes were secured in position using tape. Contractions were evoked by square-wave electrical pulses of 100 μs duration generated by a Digitimer stimulator (model DS7AH, Digitimer, Welwyn Garden City, Hertfordshire, England). Pulses were delivered either as single stimuli (twitch) or as trains of stimuli at a frequency of 50 Hz. The operator applied manual pressure over the anode during all stimulation to ensure proper positioning.

Torque signals were recorded from a custom-built dynamometer at a sampling frequency of 500 Hz, and converted to digital format using a 12-bit analog-to-digital converter (CED model 1401 Plus, Science Park, Cambridge, UK). Surface EMG signals were pre-amplified (x100), low-pass filtered at 1000 Hz with a notch filter at 60 Hz, and sampled at a frequency of 2500 Hz. All torque and EMG data were acquired and saved for offline analysis using Spike2 v.7.0.7d software (Cambridge Electronic Design Ltd., Science Park, Cambridge, UK). Figure 12 depicts a representative sample torque recording, illustrating a conditioning contraction followed by potentiated twitches and ballistic contractions.

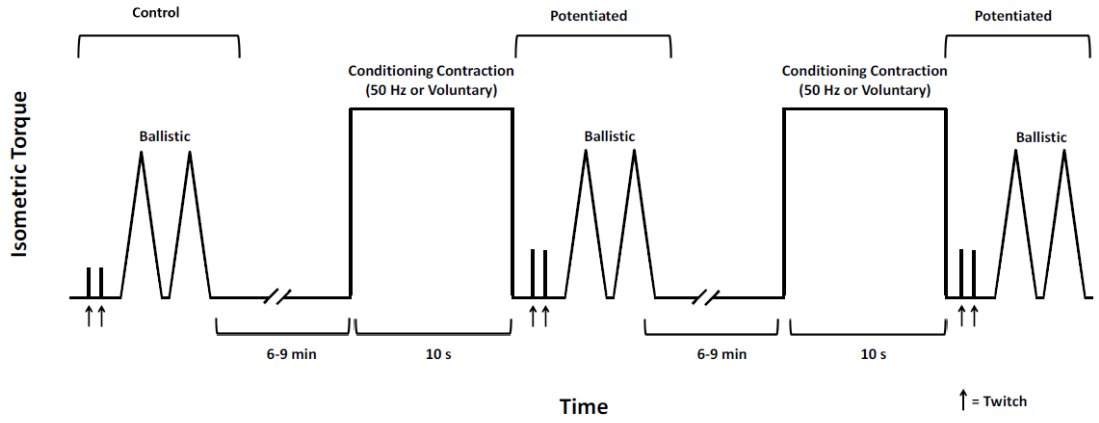

Figure 11. Illustrated representation of protocol timeline

1.1.18 Experimental protocol

Once secured in the dynamometer, maximum isometric twitch torque was determined by increasing stimulation current until isometric twitch torque reached a plateau. The current was then increased a further 10–15 % to ensure supramaximal stimulation was achieved. Maximum twitch currents ranged from 45 to 80 mA. Participants then performed two isometric MVCs of ~3 s duration, during which strong verbal encouragement and on-line visual feedback were provided. Supramaximal twitches were administered: ~3 seconds prior to MVC, at peak torque output during the MVC, and immediately upon relaxation post-MVC. This sequence allowed assessments of twitch potentiation following MVC, and voluntary activation using the interpolated twitch technique as follows: [(1-(interpolated twitch/potentiated twitch))*100%] [22].

Participants rested for 6-9 minutes following the MVCs to allow potentiation to dissipate. This was confirmed by the return of twitch torque to resting amplitude. Maximum evoked 50 Hz torque was then determined by increasing stimulation current until torque reached a plateau despite increased current. For the process of ramping electrical current, stimulus trains of 250 pulses at 50 Hz (5s) were used. The electrical current for maximal 50 Hz torque responses ranged from 45 to 80 mA. Following another [6-9] minutes of rest

and once twitch torque had returned to resting amplitude, participants performed baseline ballistic contractions. Specific instructions to focus on achieving the fastest possible rate of torque development and to relax immediately upon reaching peak torque were provided, along with strong verbal encouragement and visual feedback during contraction. Subjects then became accustomed to these ballistic contractions by performing between 2 and 6 baseline contractions. Peak RTD was calculated from the torque recording as the peak instantaneous slope between the initial deviation from baseline and the peak torque.

After twitch torque had returned to resting amplitude, a 10 s potentiating contraction was completed using either an evoked contraction at 50 Hz, or a voluntary contraction targeted to the same torque. Immediately following a potentiating contraction, 2 twitches were evoked followed immediately by 2 voluntary ballistic contractions. The delays between the end of conditioning contraction and onset of twitch or ballistic contractions were ~1 s and ~4 s respectively. Participants then rested for another 6-9 minutes to allow potentiation to dissipate, again confirmed by a return of baseline twitch torque. In random order (i.e. voluntary or evoked conditioning contraction), this procedure was repeated 4 times so that 2 of the potentiating contractions were evoked (i.e., involuntary), and 2 were controlled voluntarily. Figure 11 shows a schematic illustration of the experimental protocol timeline, and Figure 12 shows exemplar data recorded during one CC and the subsequent twitches and ballistic contractions.

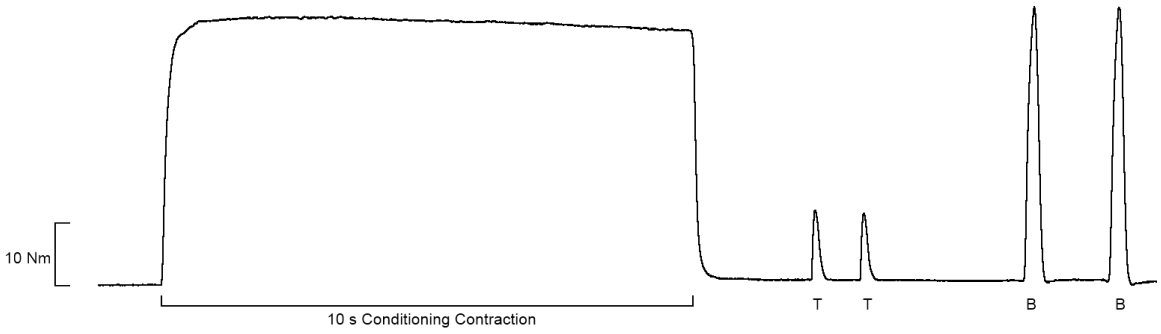

Figure 12. Exemplar torque recording illustrating a 10 s conditioning contraction followed by two evoked twitches (T) and two voluntary ballistic contractions (B)

1.1.19 Statistics

All statistical analyses were conducted using statistical software (SPSS v.19.0.0; SPSS Inc., Chicago, Illinois) with α set to 0.05. MVC and skin temperature were compared using a student's t-test. Mean contractile properties (twitch torque and pRTD, ballistic pRTD) were compared between baseline, post-voluntary, and post-tetanus using a one-way repeated measures ANOVA. To assess the time-course of RTD during contraction, RTD for each condition was averaged during 10 ms binned intervals up to 250 ms (0-10 ms, 10-20 ms… 240-250 ms). Binned RTD values for baseline, post-voluntary and post-tetanus were then analyzed using a two-way repeated measures ANOVA (condition x time). Following each ANOVA in which a significant main effect or interaction was found, post-hoc analysis was performed using the Bonferroni correction method. All values in text and figures are represented as means ± standard deviations.

Results

Instantaneous peak MVC dorsiflexion torque was 57.3 Nm ±12.5, and mean torque throughout the sustained plateau of the MVC was 48.6 Nm ±12.5. Voluntary activation during MVC was estimated to be 96.8% ±3.4. The 10 s potentiating contraction torques were -closely matched at ~80% of mean MVC torque, averaging 37.9 Nm ±8.1 for the evoked tetani and 38.4 Nm ±7.8 for voluntary CC. Skin surface temperature was unchanged between the beginning (30.6 ±0.8° C) and end (30.6 ±0.9° C) of testing ($P = 0.61$). Potentiated twitch following the 3 s MVC was increased by 72.8% ±22.5 ($P < 0.001$) from control, and twitch pRTD increased by 107.0% ±30 ($P < 0.001$).

Table 1 shows contractile properties for control and potentiated contractions. Twitch torque immediately after the 10 s CC was increased in both conditions, however the magnitude of the increase was not statistically different between conditions. Twitch torque increased by 82% to 9.5 Nm ±2.3 ($P = 0.03$) following evoked tetanus and by 70% to 8.9 Nm ±3.1 ($P = 0.04$) following voluntary contraction. Twitch RTD following evoked tetanus was increased by 122% to 256.8 Nm/s ±52.6, and increased following voluntary target by 108% to 240.3 Nm/s ±75.4. These increases were not statistically different between conditions ($P>0.05$).

Table 2. Contractile properties

Condition	MVC Torque (Nm)	Twitch Torque (Nm)	Twitch pRTD (Nm/s)	Ballistic pRTD (Nm/s)
Control	57.3 ±12.5	5.2 ±1.7	115.4 ±35.4	422.0 ±88.9
PT	-	9.5 ±2.3*	256.8 ±52.6*	390.2 ±59.3*
PV	-	8.9 ±3.1*	240.3 ±75.4*	356.4 ±69.1*†

Values expressed as mean ± standard deviation
PT = Post-tetanus
PV = Post-voluntary
* denotes significant difference vs. control
† denotes significant difference vs. PT ($P < 0.05$)

Contrary to the potentiated twitches, pRTD of voluntary ballistic dorsiflexions was reduced following the 10 s conditioning contraction (Table 1). Peak RTD decreased 16% from control to 356.4 Nm/s ±69.1 ($P = 0.04$) for PV and 8% from control to 390.2 Nm/s ±59.3 ($P = 0.001$) for PT. Furthermore, ANCOVA revealed that, relative to control for each individual, PV pRTD was significantly less than PT pRTD ($P = 0.004$).

For twitch and ballistic contractions, time course of RTD was calculated by averaging RTD in 10 ms intervals (0-10 ms, 10-20 ms…) up to 110 ms for twitch and up to 250 ms for ballistic contractions. At each time point comparison was made between control, PV and PT. A significant interaction effect was observed between condition and time for ballistic RTD. Notably, differences were observed very early in contraction (the first 30-40 ms), where twitch RTD was increased for both PT and PV, and peak RTD occurred 10 ms earlier in contraction (Figure 13). For ballistic contractions, PT RTD was greater than control for the first 30 ms and peak RTD occurred 10 ms earlier (at 50 ms). However, PV RTD was unchanged from control for the first 50 ms of contraction, and peak occurred at the same time point as control (at 60 ms) (Figure 14). Some differences between conditions were observed at time points following the peak RTD; however, the slightly slower RTD times later in contraction may be a necessary consequence of the faster RTD occurring early in contraction. In order to more clearly depict the early increase in RTD for PT and PV contractions, Figure 15 depicts the time course of ballistic RTD normalized to the control contraction at each time point.

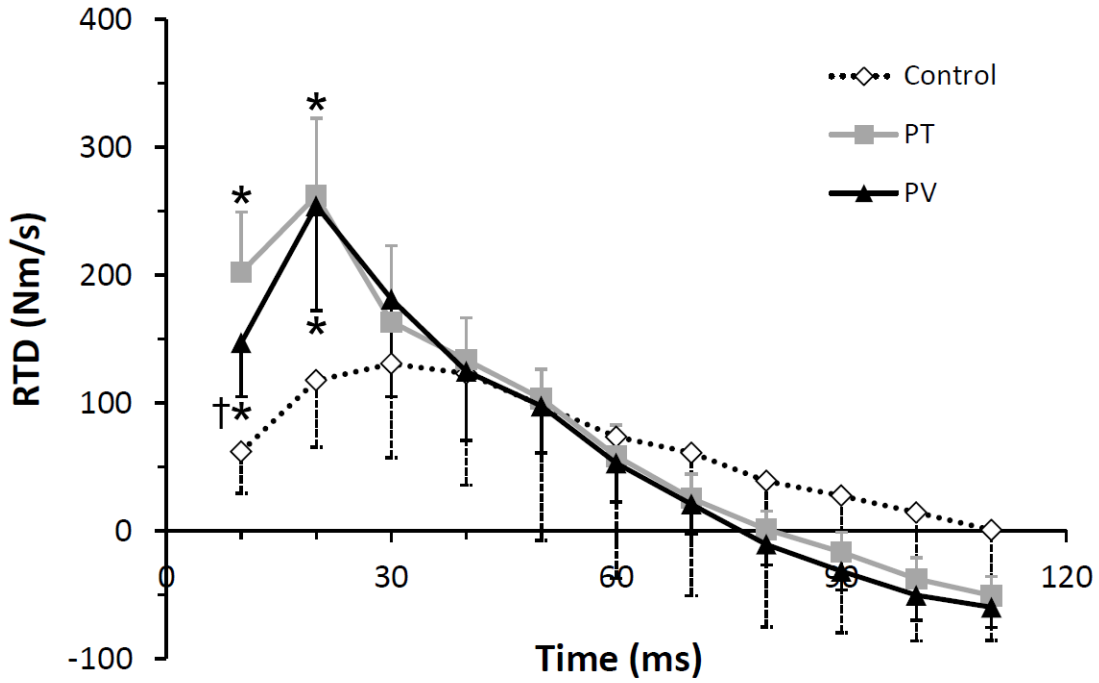

Figure 13. Timeline of evoked twitch RTD control, PT and PV. Twitch RTD is increased compared to control at 10 ms and 20 ms. * denotes significant difference vs. control, † denotes significant difference vs. PT ($P < 0.05$)

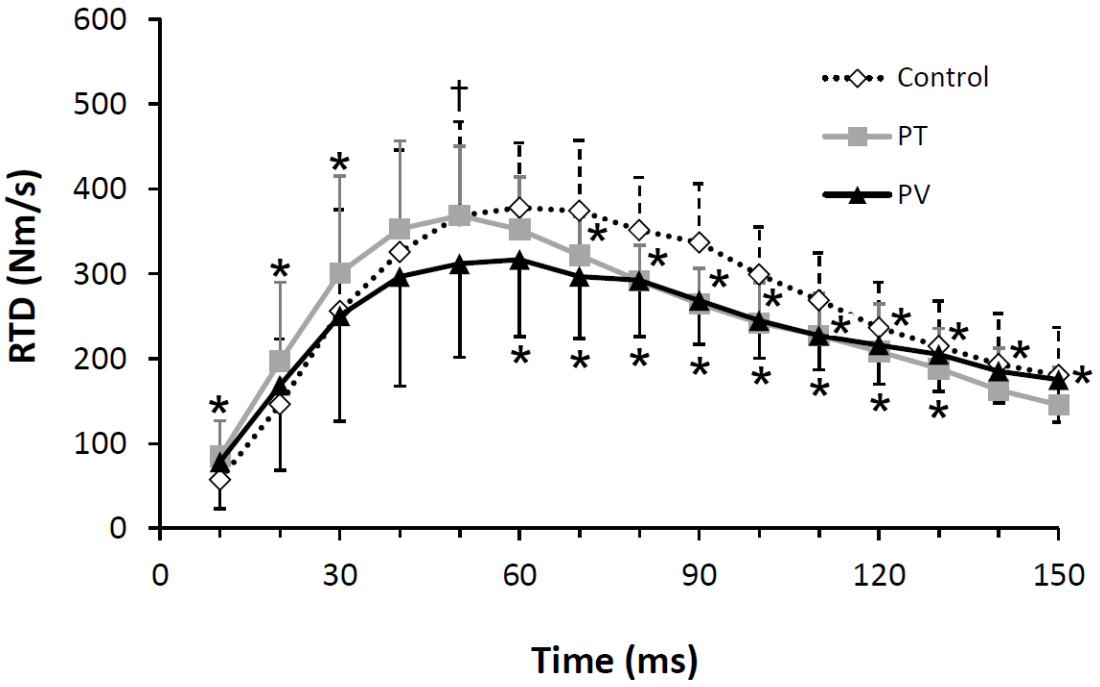

Figure 14. Timeline of voluntary ballistic RTD for control, PT, and PV. Compared to control: PT RTD is increased between 10 ms and 30 ms, and reaches peak 10 ms earlier; PV is similar to control between 10 ms and 40 ms, and is reduced thereafter. * denotes significant difference vs. control, † denotes significant difference vs. PT ($P < 0.05$)

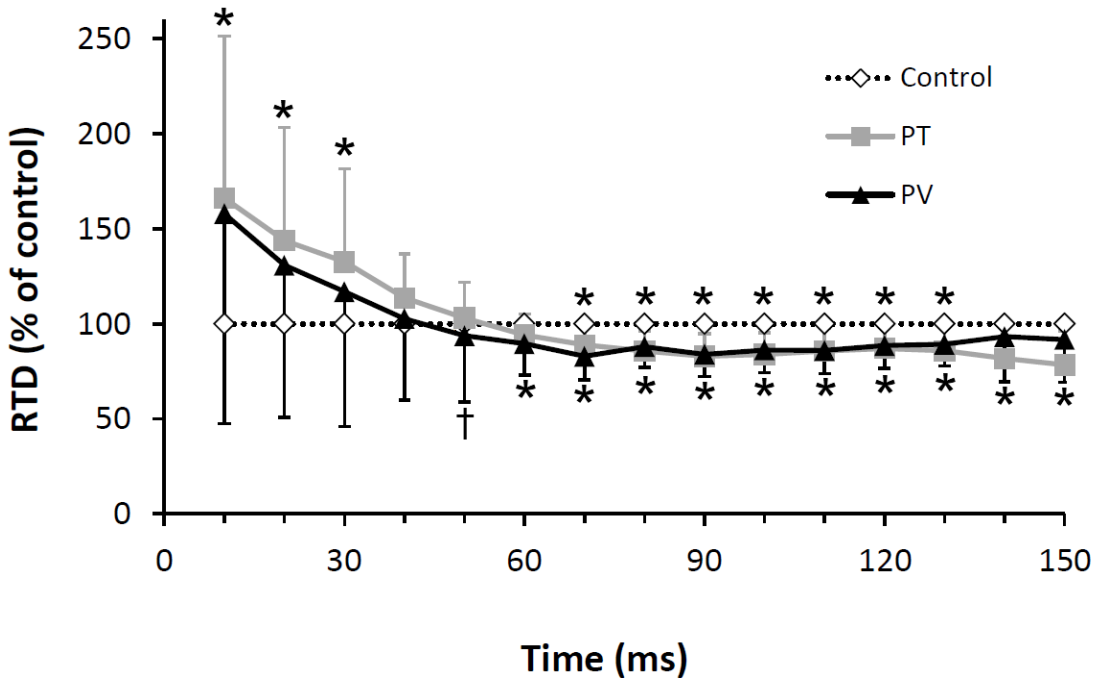

Figure 15. Timeline of ballistic RTD normalized to control. This shows the same data as Fig. 4, but by normalizing to control RTD, the differences are more visually apparent, especially in the first ~50 ms leading up to pRTD. * denotes significant difference vs. control, † denotes significant difference vs. PT ($P < 0.05$)

The coefficient of determination (R2) was calculated between ballistic RTD and MVC torque in discrete 10 ms intervals, as opposed to cumulative intervals previously published [21]. As shown in Figure 16, ballistic RTD is moderately well predicted (R2 ~ 0.5) by MVC torque for the first ~60 ms of contraction, and this relationship becomes stronger following either PT or PV potentiation (R2 ~ 0.6). At time points after ~60 ms this relationship becomes progressively weaker and by 100 ms it does not to appear be meaningful for PT or PV compared to control.

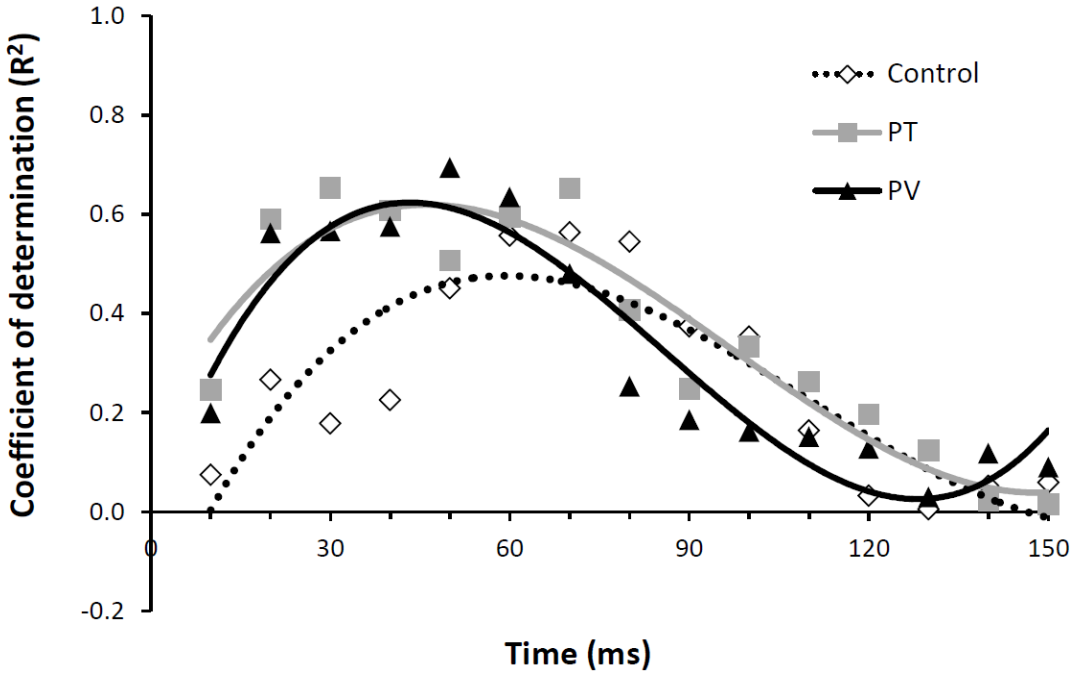

Figure 16. Coefficient of determination between ballistic RTD and maximal MVC torque over time. Early in contraction, RTD is well predicted by MVC torque, but that relationship becomes weaker following pRTD, which occurs around 50-60 ms. Trend line shown is a 3rd order polynomial regression

To evaluate neuromuscular activity during ballistic torque development, surface EMG of the tibialis anterior was rectified and averaged between the onset of EMG and the time point of peak RTD. Voluntary EMG activity during PV ballistic contraction was significantly lower (0.18 ±0.08 mV) than during PT contraction (0.21 ± 0.09 mV) ($P = 0.03$).

Discussion

The main result is that during voluntary ballistic contractions, acceleration of torque development is increased following an evoked conditioning contraction and depressed following a voluntary conditioning contraction, both occurring without any accompanying improvement in the peak rate of torque development. These observations are made concurrent to typical twitch potentiation, which shows dramatically increased torque and RTD (increased by ~100% for each). These findings support the suggestion that a voluntary conditioning contraction imposes a limitation (likely centrally mediated) to subsequent maximal voluntary contraction, and that this inhibition is absent following an evoked conditioning contraction or during an evoked twitch. Furthermore, this study expands on prior work by revealing a potential ergogenic role for PAP in enhancing acceleration of torque development early in contraction.

1.1.20 Control measurements

Contractile properties such as MVC torque and activation level, as determined using interpolated twitch, were consistent with prior results from this muscle group [23]. The voluntary and tetanic CCs were closely matched: mean torque for voluntary was 37.9 Nm ±8.1, and for 50 Hz tetanus was 38.4 Nm± 7.8, which was approximately 80% of MVC torque for both. Following MVC, twitch torque was potentiated by ~73%, and peak twitch RTD by ~107%, which is similar to what others have observed in this muscle group [24, 25].

1.1.21 Ballistic Contractions

The capacity of a muscle to generate torque is typically assessed by measuring either the instantaneous pRTD or the average RTD during a period of contraction. Changes in contractile properties, particularly the maximal speed of a muscle, are often reported as pRTD at an instantaneous time point, ignoring submaximal time points [5, 13]. The results of the present study, as well as others [10, 14] show no improvement (and in some cases a decrement) in maximal voluntary velocity or pRTD with potentiation. However, the

above cited studies base their measures of potentiation on instantaneous values during contraction. By focusing on peak velocity or peak RTD alone, other changes occurring at non-peak time points may be overlooked. For example, it is well known that potentiation has progressively less effect on contractile properties as [Ca^{2+}] increases towards saturation [26, 27], such that twitch torque is enhanced substantially, but maximal torque is unaffected. For this reason, maximal contractions are not often chosen as the model to investigate potentiation. However, muscular contractions are not instantaneously maximal; there is a period of time between onset of contraction and the peak, during which the contraction is effectively submaximal. Assessing RTD during the early non-peak time points of a ballistic contraction may be a unique period of time during which potentiation would have a positive effect on an otherwise maximal contraction. Thus, we have analyzed RTD in 10 ms intervals throughout ballistic contraction, to examine non-peak time points as the contraction develops. Following tetanus, we observed no change in ballistic pRTD. However, RTD was increased during the first 30 ms of contraction, and pRTD occurred 10 ms earlier for PT than for control. This represents an increase in the acceleration of torque development, despite no change in the peak. For PV ballistic contraction, peak RTD was reduced compared to control, but RTD was similar between conditions at all time points leading up to the peak. It is possible that at initial, submaximal time points in ballistic contraction potentiation serves to enhance PT RTD, and preserves PV RTD in the presence of any central inhibitory effects. Calcium diffusion within the sarcoplasm is not complete until at least 20-25 ms of contraction [28, 29], therefore [Ca^{2+}] is submaximal for some fibrils for the first 2-3 time points measured here. Myosin phosphorylation improves Ca^{2+} sensitivity, which is most apparent at low [Ca^{2+}], and therefore it is not surprising that the only significant effects of voluntary potentiation are found early in contraction when [Ca^{2+}] is still increasing. By the time RTD has reached a peak, the myofibrils are saturated with Ca^{2+}, thus abolishing the effects of increased Ca^{2+} sensitivity. This may explain why ballistic pRTD is not improved following a 10 s conditioning contraction.

The cross-bridge cycle duration can be demarcated by two periods: the time required for cross-bridge attachment and power-stroke, and the time required to return to the resting state. Myosin phosphorylation is understood to shorten the time required for the first phase, without affecting the rate of detachment, which consequently shortens the overall cycle [28, 29]. Because a maximal effort saturates the sarcoplasm with Ca^{2+} very quickly [28, 29], there is a limited time during which heightened Ca^{2+} sensitivity can affect contractile properties. By shortening the duration of the cross-bridge cycle, potentiation may allow each myofibril to complete more power-strokes before saturation.

Using the same dorsiflexor model, we previously reported peak ballistic RTD following voluntary and tetanic conditioning contractions; those results indicated that neither type of conditioning contraction enhanced ballistic pRTD, and that pRTD was impaired post-voluntary. The results of the current study support the interpretation that central factors may play an important role on determining the expression of maximal voluntary RTD following a conditioning contraction, essentially counteracting the enhanced function of the contractile tissues due to inherent potentiation.

Our results bear comparison with prior studies of voluntary potentiation, which have shown mixed results. Knee extension velocity following a 10 s conditioning contraction was unchanged [28, 29], whereas in the thumb adductors ballistic RTD was potentiated by nearly 10% following a 6 s MVC [13]. The difference between these two investigations is likely explained by one of two main differences: 1) the longer CC duration in the quadriceps study (10 s vs. 6 s), or 2) the greater content of fatigable type II muscle fibers in the quadriceps (~45%) compared with the adductor pollicis (~20%) [30]. The present study design includes features common to each of the above studies. Similarity to Baudry et al.'s thumb adductor study, our study also utilized ballistic contractions peaking at ~75% MVC torque, and the tibialis anterior has a similar muscle fiber composition (~26% type II), and similarly to the Gossen et al. knee extensor study, we also used a 10 s CC duration. Given that our results showing no improvement in pRTD following either type of conditioning contraction are similar to those of Gossen, it follows

that the lack of voluntary potentiation is likely attributable to the 10 s CC duration rather than fiber type composition or contraction type (isometric v. dynamic).

While 10 s has been shown to maximize twitch potentiation [6], the complexities inherent to voluntary control may require a shorter CC duration for maximum potentiation. The mechanism responsible for impairment of contractile properties, which appears to be absent after 6 s CC but present after a 10 s CC, is consistent with a fatigue process which further impairs function with increasing duration of activity. However, it is not immediately clear whether the impairment is occurring centrally or at the muscle level. We found equal twitch potentiation following the initial 3 s MVC and the 10 s experimental CCs, which suggests that between 3 s and 10 s of CC there are no peripheral (distal to the stimulating electrode) fatigue effects influencing contractile torque. Thus, the site of any impairment to voluntary contraction during the 10 s CC must occur proximal to the stimulating electrode, making them central inhibitory effects likely occurring at the cortical or spinal level. If central inhibition were responsible for impaired RTD, it should be apparent by changes in the voluntary EMG signal. Indeed, a previous study showed that when ballistic dorsiflexion was preceded immediately by 3-4 s of contraction at 25% MVC, mean motor unit discharge rate was lower, and there were fewer initial double discharges (interspike interval <5 ms) than for a ballistic contraction from rest [31]. Additionally, average rectified surface EMG between the onset of ballistic contraction and peak RTD was lower following a 10 s conditioning contraction than during control ballistic contraction. These measures do not directly demonstrate central fatigue, but they do indicate that contractions of 10 s duration or less are sufficient to cause modifications of central activation patterns. Despite these indirect measures, collectively they are consistent with a central fatigue mechanism which inhibits voluntary contractile properties following a conditioning contraction of 10 s or less.

The findings of this study show that a 10 s conditioning contraction enhances RTD during the first 30-40 ms of a voluntary ballistic contraction, despite no increase in peak RTD. Furthermore, the reduction in PV ballistic RTD in comparison to PT and control indicate an inhibitory effect following conditioning contraction, which I propose are

primarily cortico-spinal. The coexistence of potentiation and fatigue within contractile tissue is widely accepted, but it also appears that there may be a second coexistence between peripheral potentiation and central inhibition.

References

1. Behm DG, Button DC, Barbour G, Butt JC, Young WB. Conflicting effects of fatigue and potentiation on voluntary force. J Strength Cond Res 2004; 18:365-372.

2. Rassier DE, Macintosh BR. Coexistence of potentiation and fatigue in skeletal muscle. Braz J Med Biol Res 2000; 33:499-508.

3. O'Leary DD, Hope K, Sale DG. Posttetanic potentiation of human dorsiflexors. J Appl Physiol 1997; 83:2131-2138.

4. Fukutani A, Hirata K, Miyamoto N, Kanehisa H, Yanai T, Kawakami Y. Effect of conditioning contraction intensity on postactivation potentiation is muscle dependent. J Electromyogr Kinesiol 2014.

5. Froyd C, Beltrami FG, Jensen J, Noakes TD. Potentiation increases peak twitch torque by enhancing rates of torque development and relaxation. J Hum Kinet 2013; 38:83-94.

6. Vandervoort AA, Quinlan J, McComas AJ. Twitch potentiation after voluntary contraction. Exp Neurol 1983; 81:141-152.

7. Vandenboom R, Grange RW, Houston ME. Myosin phosphorylation enhances rate of force development in fast-twitch skeletal muscle. Am J Physiol 1995; 268:C596-603.

8. Harwood B, Davidson AW, Rice CL. Motor unit discharge rates of the anconeus muscle during high-velocity elbow extensions. Exp Brain Res 2011; 208:103-113.

9. Maton B, Bouisset S. Motor unit activity and preprogramming of movement in man. Electroencephalogr Clin Neurophysiol 1975; 38:658-660.

10. Smith CB, Allen MD, Rice CL. Voluntary rate of torque development is impaired following a voluntary versus tetanic conditioning contraction. Muscle Nerve 2013; 49:218-224.

11. Baudry S, Duchateau J. Postactivation potentiation in human muscle is not related to the type of maximal conditioning contraction. Muscle Nerve 2004; 30:328-336.

12. MacIntosh BR, Willis JC. Force-frequency relationship and potentiation in mammalian skeletal muscle. J Appl Physiol 2000; 88:2088-2096.

13. Baudry S, Duchateau J. Postactivation potentiation in a human muscle: effect on the rate of torque development of tetanic and voluntary isometric contractions. J Appl Physiol 2007; 102:1394-1401.

14. Gossen ER, Sale DG. Effect of postactivation potentiation on dynamic knee extension performance. Eur J Appl Physiol 2000; 83:524-530.

15. Sale DG. Postactivation potentiation: role in human performance. Exerc Sport Sci Rev 2002; 30:138-143.

16. Houston ME, Grange RW. Torque potentiation and myosin light-chain phosphorylation in human muscle following a fatiguing contraction. Can J Physiol Pharmacol 1991; 69:269-273.

17. McNeil CJ, Giesebrecht S, Gandevia SC, Taylor JL. Behaviour of the motoneurone pool in a fatiguing submaximal contraction. J Physiol 2011; 589:3533-3544.

18. Teo WP, Rodrigues JP, Mastaglia FL, Thickbroom GW. Post-exercise depression in corticomotor excitability after dynamic movement: a general property of fatiguing and non-fatiguing exercise. Exp Brain Res 2012; 216:41-49.

19. Sacco P, Thickbroom GW, Thompson ML, Mastaglia FL. Changes in corticomotor excitation and inhibition during prolonged submaximal muscle contractions. Muscle Nerve 1997; 20:1158-1166.

20. Sacco P, Thickbroom GW, Byrnes ML, Mastaglia FL. Changes in corticomotor excitability after fatiguing muscle contractions. Muscle Nerve 2000; 23:1840-1846.

21. Andersen LL, Aagaard P. Influence of maximal muscle strength and intrinsic muscle contractile properties on contractile rate of force development. Eur J Appl Physiol 2006; 96:46-52.

22. Shield A, Zhou S. Assessing voluntary muscle activation with the twitch interpolation technique. Sports Med 2004; 34:253-267.

23. Belanger AY, McComas AJ. Extent of motor unit activation during effort. J Appl Physiol 1981; 51:1131-1135.

24. Connelly DM, Rice CL, Roos MR, Vandervoort AA. Motor unit firing rates and contractile properties in tibialis anterior of young and old men. J Appl Physiol 1999; 87:843-852.

25. Kent-Braun JA, Ng AV. Specific strength and voluntary muscle activation in young and elderly women and men. J Appl Physiol 1999; 87:22-29.

26. Vandenboom R, Grange RW, Houston ME. Threshold for force potentiation associated with skeletal myosin phosphorylation. Am J Physiol 1993; 265:C1456-62.

27. Abbate F, Sargeant AJ, Verdijk PW, de Haan A. Effects of high-frequency initial pulses and posttetanic potentiation on power output of skeletal muscle. J Appl Physiol 2000; 88:35-40.

28. Cannell MB, Allen DG. Model of calcium movements during activation in the sarcomere of frog skeletal muscle. Biophys J 1984; 45:913-925.

29. Isenberg G, Han S, Schiefer A, Wendt-Gallitelli MF. Changes in mitochondrial calcium concentration during the cardiac contraction cycle. Cardiovasc Res 1993; 27:1800-1809.

30. Johnson MA, Polgar J, Weightman D, Appleton D. Data on the distribution of fibre types in thirty-six human muscles. An autopsy study. J Neurol Sci 1973; 18:111-129.

31. Van Cutsem M, Duchateau J. Preceding muscle activity influences motor unit discharge and rate of torque development during ballistic contractions in humans. J Physiol 2005; 562:635-644.

Coexistence of peripheral potentiation and corticospinal inhibition following a conditioning contraction

Introduction

Muscle contractile history influences subsequent muscle contractile properties, a feature that is frequently observed as contractile slowing and weakening following a moderate to high-intensity fatiguing task. Alternatively, a brief, strong conditioning contraction (CC) may enhance subsequent contractile properties such as torque and rate of torque development by as much as 200%, a phenomenon known as postactivation potentiation [1, 2]. The positive effects of potentiation on involuntary contraction, typically evoked at the peripheral motor axon level, have been consistently and reliably observed [3-6]; however, these artificially evoked contractions do not reflect functional voluntary task performance. Investigations to determine the effect of potentiation on voluntary contractions have failed to demonstrate the remarkable enhancements shown during evoked contraction, and have largely shown equivocal results compared to unpotentiated contractile properties [7-12]. By definition, the primary difference between the voluntary and the involuntary (artificial) contraction is the source of activation: peripheral stimulating electrode vs. central nervous system activation. Thus, if there is an impairment preventing enhancement of the voluntary potentiated contraction, the site of this impairment could be proximal to the peripheral motor axon. This may be consistent with a fatigue or inhibitory process occurring at the motor cortical or spinal level, but adaptations at this level have not yet been studied concurrently with potentiation.

The commonly accepted mechanism of postactivation potentiation is myosin light chain phosphorylation. The light chain becomes phosphorylated during the conditioning contraction and this process can take up to 10 minutes to subside, during which time any evoked twitch contraction will display increased torque and rate of torque development [13, 14]. However, voluntary contractions performed during this time fail to display the same

enhancements, and in some cases voluntary contractile properties are impaired at the same time point that evoked properties are enhanced [9, 12]. Prior study has established that intramuscular processes of potentiation and fatigue occur simultaneously [8, 15], but it appears that there may be a yet unobserved central fatigue that is also concurrent to peripheral potentiation.

Properties of the corticospinal portion of the neuromuscular system are often assessed using transcranial magnetic stimulation (TMS) which produces a motor evoked potential (MEP) [16]. Immediately following the MEP there is a period of time during which voluntary motor function is abolished, and lengthening of this silent period (SP) is associated with fatigue, believed to be a consequence of motor cortical inhibition [17, 18]. If this inhibition is a result of motor cortical activity during a strong voluntary conditioning contraction, then an involuntary tetanic conditioning contraction may allow potentiation of the muscle tissue without any central inhibition.

Thus, the purpose of this study was to assess SP duration following either a voluntary or an involuntary conditioning contraction, and to investigate the relationship between potentiation and corticospinal properties. It was hypothesized that, following a voluntary conditioning contraction, concurrent SP elongation and twitch potentiation would be observed. Secondly, it was hypothesized that following an involuntary (tetanic) conditioning contraction, twitch potentiation would be observed without a concomitant elongation of SP duration.

Materials and methods

1.1.22 Participants

Nine healthy male subjects volunteered for the study. Participants had a mean age of 25.0 years ± 2.2, mean height of 177.9 cm ± 6.8 and mean body mass of 79.8 kg ± 10.0. All participants self-identified as being right hand dominant. Participants were all recreationally active, but were not involved in systematic training of any type prior to this experiment. Participants were required to abstain from exercise, alcohol, and caffeine for

24 hours prior to testing. Room temperature for all tests was maintained at approximately 22° C. All methods were conducted in accordance with the guidelines set in place by the ethics review board of the University of Western Ontario. Informed written consent was obtained from all subjects.

1.1.23 Experimental setup

A custom-build finger abduction dynamometer was placed on a table, at which participants were seated. The dominant (right in all cases) hand was placed into the dynamometer so that the distal interphalangeal joint of the index finger was aligned with the force transducer on the dynamometer. All other fingers and the thumb were isolated from the index finger using metal dividers. The hand and fingers were strapped to the dynamometer using two custom inelastic nylon straps over the metacarpo-phalangeal joints of the fingers and over the dorsum of the hand. Recording surfaces on the skin were cleaned and lightly abraded using an alcohol swab, and electromyography electrodes (Circular, 0.5 cm recording surface, Kendall H59P, Mansfield, MA) were positioned as follows: the reference electrode was placed on the metacarpo-phalangeal joint of the right thumb, the active electrode placed over the muscle belly of the FDI, and the ground electrode placed over the ulnar styloid process of the right forearm.

Electrically evoked contractions were elicited by square-wave electrical pulses of 100 μs duration generated by a Digitimer stimulator (model DS7AH, Digitimer, Welwyn Garden City, Hertfordshire, England), and were delivered via a bar electrode which was taped firmly in position over the FDI muscle belly, around the active EMG electrode. Contact points on the electrode were 1cm in diameter with 3cm center-to-center distance.

Transcranial magnetic stimulation was evoked over the vertex using single pulses from a Magstim 200 stimulator (The Magstim Company Limited, Spring Gardens, Whitland, Carmarthenshire, SA34 0HR, UK) using a 90 mm circular head coil (Magstim P/N 9784-00).

1.1.24 Experimental protocol

The maximal twitch was determined by progressively increasing stimulator current until no further increase in force was observed. Current was then increased by 10-15% to ensure supramaximal stimulation. Following 2 min rest, participants performed at least one (no more than 3, and only for 1 participant) maximal voluntary contraction to determine maximal finger abduction force. At the peak of the contraction an interpolated twitch was evoked to assess voluntary activation, and a potentiated twitch was evoked immediately following contraction. Participants rested for 3 minutes before maximal electrically evoked 50 Hz force was determined by progressively increasing stimulator current until a plateau in force was reached.

Participants were then allowed 5 minutes of rest before maximal TMS responses were assessed by progressively increasing stimulator intensity until a plateau in MEP intensity was reached, or until the stimulator reached maximum power. Control silent periods were then assessed by delivering a single TMS pulse interpolated during a brief MVC. Participants were carefully instructed to commence maximal contraction effort immediately following the TMS pulse. At least 3 control silent periods were measured, and participants then rested for 5 minutes.

The experimental portion of the protocol involved a 10 s conditioning contraction, followed immediately by an interpolated TMS pulse and 2 electrically evoked twitches elicited at rest. There were 3 types of conditioning contraction: 50 Hz maximal tetanus, voluntary submaximal (matched to tetanus force), and maximal voluntary contraction. In a randomized order, each contraction type was performed 2 times for a total of 6 contractions, with at least 5 minutes of rest between each (Figure 17.)

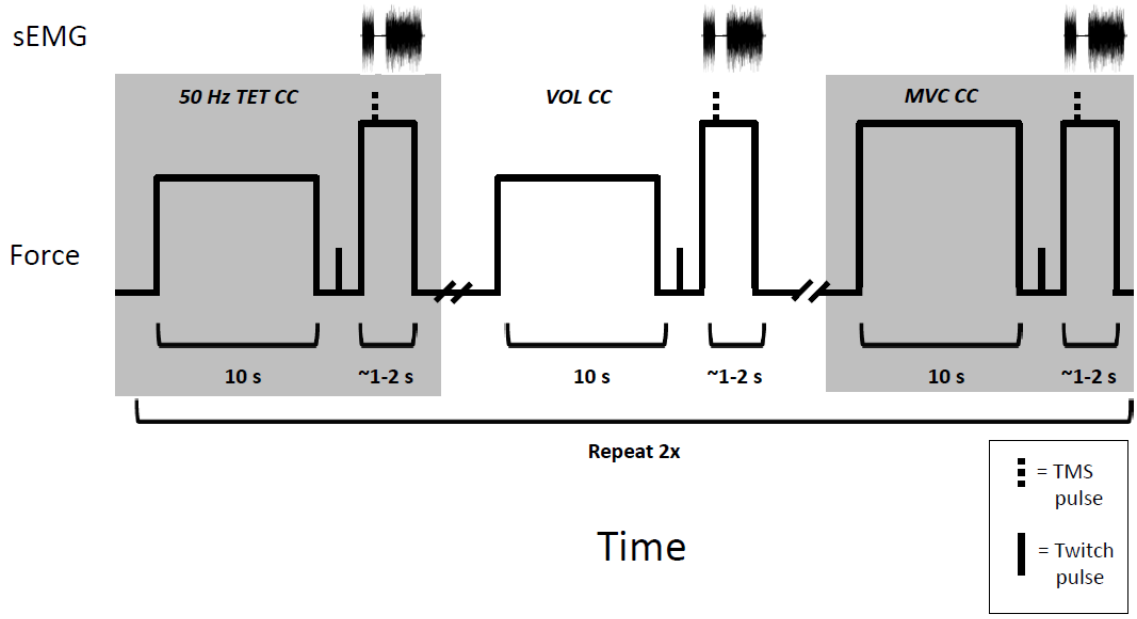

Figure 17. Illustrated experimental protocol depicting 50 Hz tetanic (TET), submaximal voluntary (VOL) and maximal voluntary (MVC) conditioning contractions, followed by potentiated twitch and cortical silent period duration measurements. Each volunteer would perform the protocol as depicted twice. Surface EMG samples are illustrated above the timeline to indicate cortical silent periods

1.1.25 Data processing and analysis

All EMG signals were pre-amplified by 100x before being amplified by 2x and sampled at 2500 Hz. The raw EMG signal was used to assess peak-to-peak MEP amplitude. Prior to silent period measurement, the EMG signal was filtered using a band-pass Butterworth configuration between 25 and 450 Hz. Force signals were amplified by 10x (NL 855 pre amplifier & NL820A Isolator; Digitimer, Welwyn Garden City, Hertfordshire, UK) before being sampled at 2500 Hz (CED model power1401, Science Park, Cambridge, UK).

The silent period was taken as the duration between the TMS stimulus, as recorded by Spike2 software, and the re-establishment of voluntary EMG (See sample recordings, Figure 18.). Restoration of EMG after the silent period was determined by setting horizontal cursors at the upper and lower bound of normal EMG signal noise, and the restoration of voluntary activity was determined by the first deviation outside of these limits.

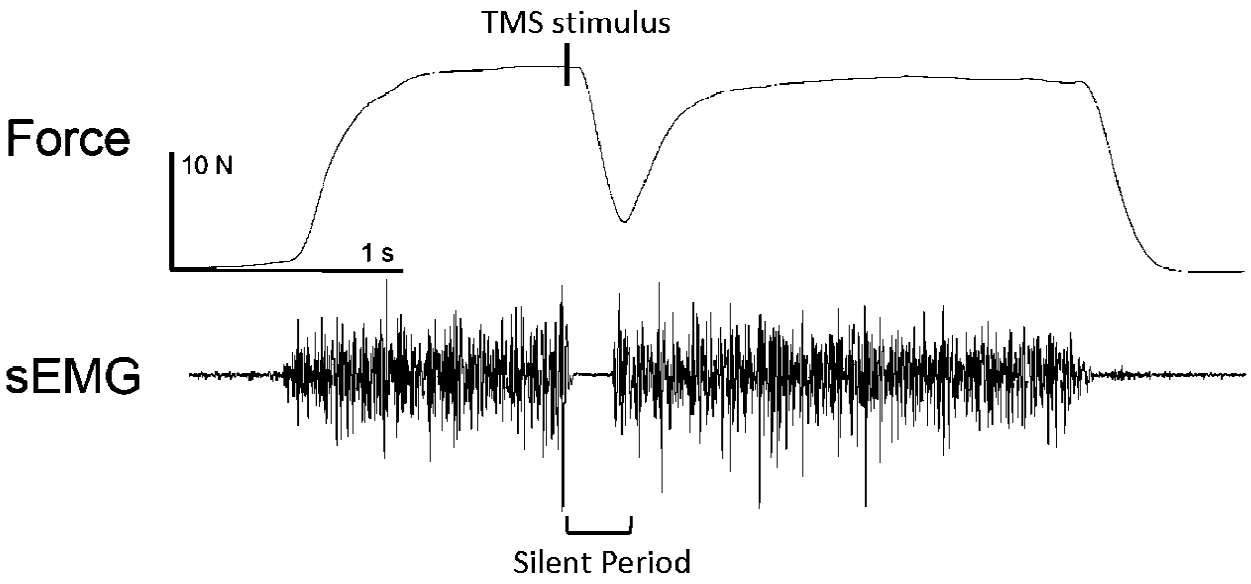

Figure 18. The motor cortical silent period (SP) was defined as the time between the TMS stimulus and the resumption of electrical activity as recorded over the FDI muscle belly

1.1.26 Statistics

All statistical analyses were conducted using statistical software (SPSS, version 19.0.0; SPSS, Inc., Chicago, Illinois) with α set at 0.05. Comparisons of contractile force, RFD and silent period between conditioning contraction type (tetanic, voluntary, MVC) were conducted using a one-way repeated measures ANOVA, using the Bonferroni correction method. All values are reported in text and figures as mean ± SD.

Results

Maximal voluntary force of the FDI was 18.7 N ±2.5, and maximal 50 Hz tetanic CC force was 11.2 N ± 2.5. Thus tetanic stimulation generated ~ 60% of MVC force

Control twitch force was 0.57 N ±0.22, and control RTD was 10.1 N/s ±3.0. Immediately following initial MVC, twitch torque had increased by 117.5% and RTD increased by 49.1% from control. Control SP following a maximal MEP was 359 ms ±54.

Following both types of 10 s conditioning contractions (tetanic and voluntary), twitch force and RFD were potentiated significantly, with no significant difference between conditioning contraction types (Figure 19.). Force was increased following tetanic and voluntary CC by 84.6% ±42 and 94.8% ±64 respectively. Twitch RFD following tetanic and voluntary CC had increased by 45.8 ± 29.6 and 61.1±46.5 % respectively (Figure 20.). To ensure maximal potentiation had been achieved, a third condition was included in which a 10 s MVC was performed as a conditioning contraction. Twitch force and RFD were significantly increased from control following the 10 s MVC by 74.9% ±30 and 41.4% ±22 respectively, and neither of these values differed from the post-tetanic and post-voluntary potentiated twitches.

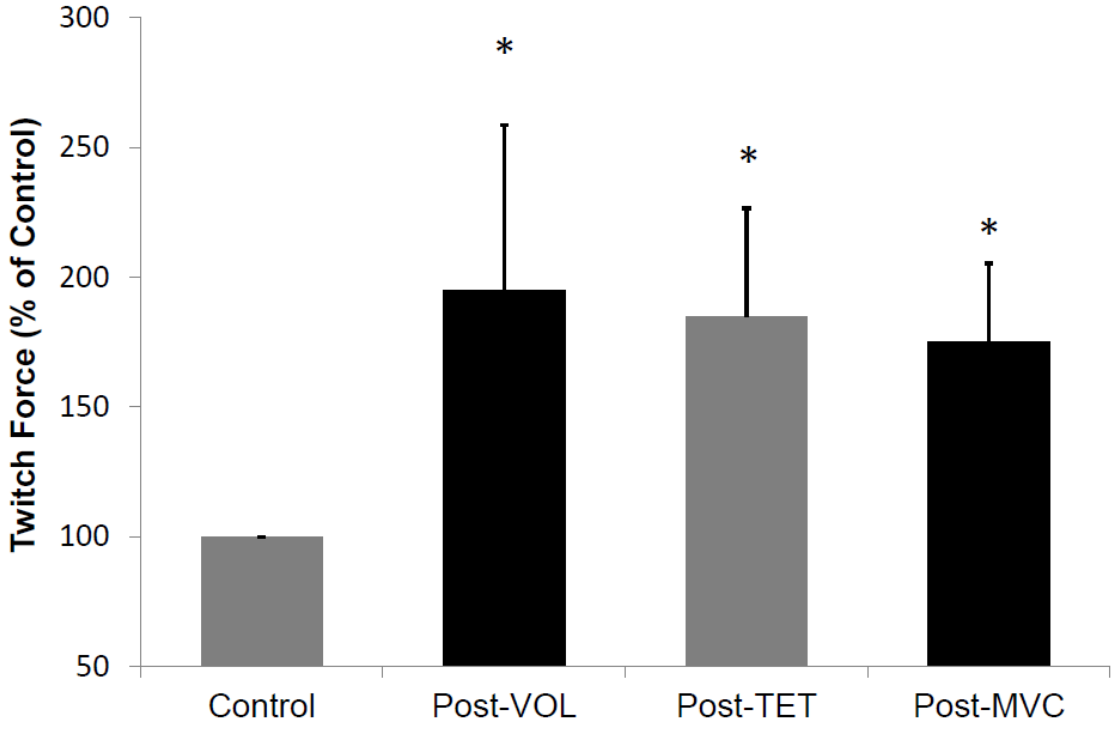

Figure 19. Twitch force (% of control) following submaximal voluntary (post-VOL), tetanic (post-TET), and maximal voluntary (post-MVC) conditioning contractions, normalized to control force for each subject. Force was increased similarly following each type of conditioning contraction. * denotes significant difference from control ($P < 0.05$)

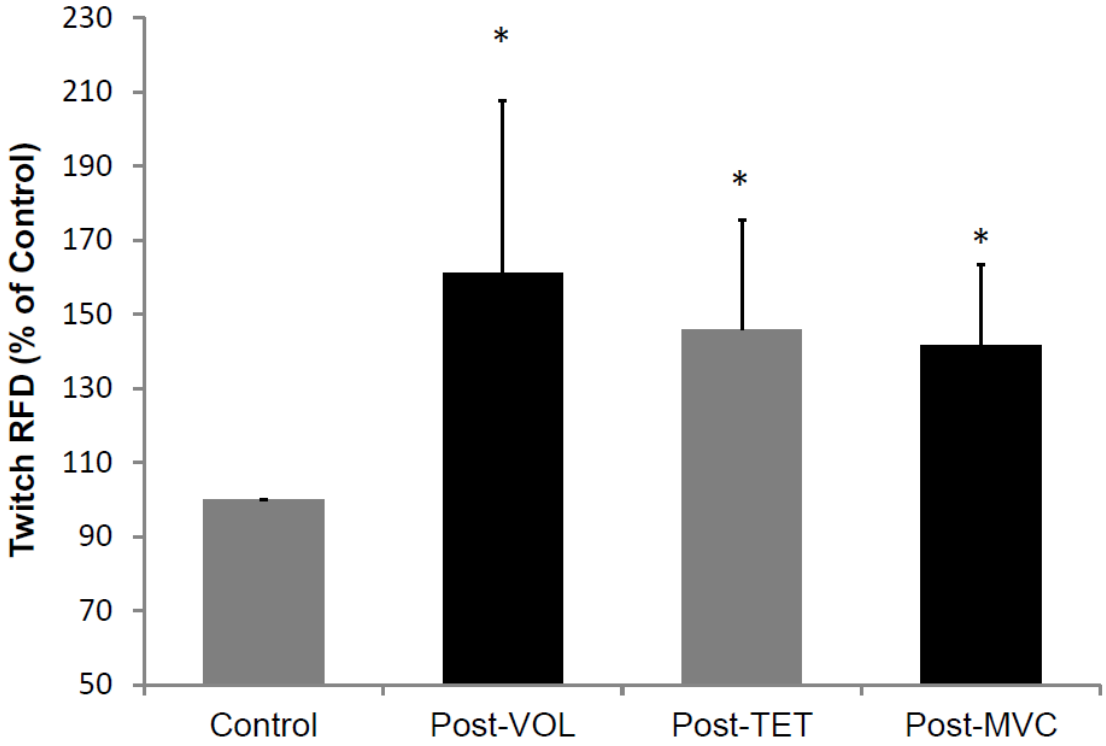

Figure 20. Twitch rate of force development (RFD; % of control) following submaximal voluntary (post-VOL), tetanic (post-TET), and maximal voluntary (post-MVC) conditioning contractions, normalized to control twitch for each subject. RFD was increased following each type of conditioning contraction, with no difference between contraction type. * denotes significant difference from control ($P < 0.05$)

Post-MEP silent period was measured immediately following the potentiated twitches. Compared to control (359 ms ±54), SP was elongated following all types of conditioning contraction as follows: 8.7% ±3.7 post-tetanus, 10.0% ±4.2 post-voluntary, 10.5% ±5.5 post-MVC (Figure 21.). While all types of CC resulted in SP elongation, contrary to the hypothesis we observed no significant differences between CC type.

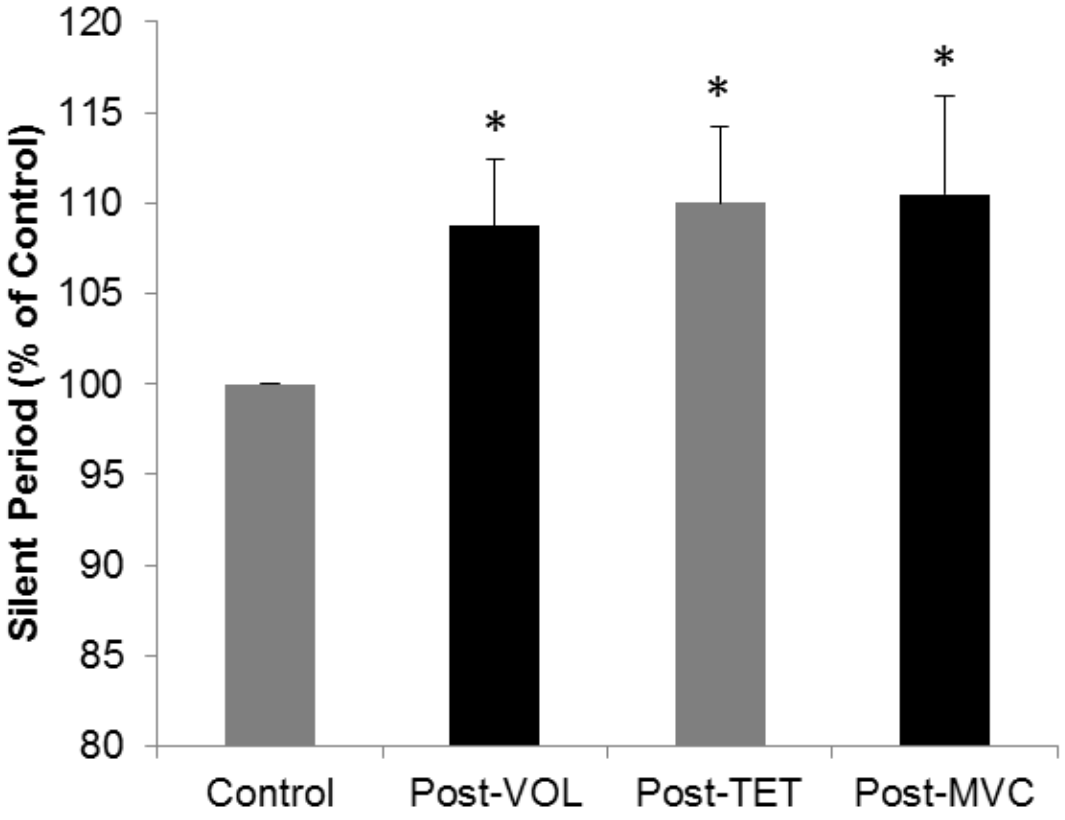

Figure 21. Silent period duration (% of control) following submaximal voluntary (post-VOL), tetanic (post-TET), and maximal voluntary (post-MVC) conditioning contractions, normalized to control force for each subject. SP was elongated following all conditioning contractions, and no difference was observed between conditioning contraction types. * denotes significant difference from control ($P < 0.05$).

Discussion

Based on results from prior studies in our laboratory, it was hypothesized that corticospinal inhibition would be responsible for the absence of enhancement to voluntary contractile properties despite a concurrent large enhancement in evoked contractile properties. This study shows that, following a 10 s voluntary conditioning contraction, SP is elongated from control and evoked twitch torque and RTD are greatly increased. These results support the first hypothesis of simultaneous corticospinal inhibition and peripheral potentiation following a conditioning contraction. However, silent period was similarly elongated following an involuntary conditioning contraction, which disagrees with the second hypothesis that a tetanic contraction would circumvent the process of corcticospinal inhibition.

1.1.27 Voluntary conditioning contractions

Postactivation potentiation has been studied extensively, and is characterized by large increases in twitch torque and RTD. However, studies attempting to demonstrate similar improvements to potentiated voluntary contraction have consistently failed to show substantial improvements, and often show no change or even a decrement to contractile properties [9, 11]. However, changes that occur during contraction are not limited to the muscular components, and central changes are widely observed during brief and sustained contraction [10, 19-22]. Therefore, current results indicate that central inhibition occurs during a voluntary conditioning contraction, thus counterbalancing the positive effects of potentiation during subsequent voluntary contraction.

The main result of this study supports the notion that corticospinal inhibition and peripheral potentiation occur simultaneously following a voluntary conditioning contraction. The data presented here show a remarkably strong and consistent elongation of the SP following either a voluntary or evoked conditioning contraction. While the specific mechanisms of central fatigue are not clearly understood, it has been suggested that SP elongation reflects primarily local intracortical inhibitory mechanisms, because changes to SP can be observed independent to other central fatigue measures such as

voluntary activation [23]. The results here support this interpretation, showing that cortical inhibition (fatigue) appears to be localized to the cortex, while the peripheral contractile tissue of the muscle experiences a local potentiation. This relationship highlights why cortical inhibition concurrent to peripheral potentiation is not apparent unless the central and peripheral components are assessed independently.

The processes of potentiation and muscular fatigue are understood to occur concurrently during conditioning contraction, and the net effect on contractile properties is a balance between potentiation and fatigue [15]. Vandervoort and McComas [14] showed in the tibialis anterior that a 10 s conditioning contraction duration was ideal to maximize the positive effects of potentiation on twitch properties. This duration allowed sufficient potentiation, but was short enough to minimize muscular fatigue. However, prior study in our laboratory has examined voluntary ballistic contractions performed following a 10 s conditioning contraction, and shown a decrease in peak RTD, concurrent to a ~115% increase in twitch RTD (Chapter 4). Whereas a 10 s conditioning contraction duration may minimize muscular fatigue, it does not appear to be sufficiently short to prevent corticospinal inhibition. Elongated SP has previously been observed following 30 s of contraction [24], and our results add to that by showing elongation occurs during 10 s of contraction.

1.1.28 Stimulated conditioning contractions

Although a voluntary conditioning contraction was followed by SP elongation, results also show a similarly strong and consistent SP elongation following an involuntary tetanic conditioning contraction. This result perhaps is surprising and goes against the hypothesis that SP elongation occurs strictly through sustained cortical activity, and that a tetanic contraction would circumvent this process. It seems that this effect has not been reported previously. The current study was designed specifically to assess the inhibitory effect of a voluntary contraction on the corticomotor SP, and thus the apparent afferent effects of tetanic contraction on cortical activity are somewhat speculative.

Afferent feedback from the active muscle seems the most likely mechanism to cause corticospinal inhibition in the absence of cortical activity. The relationship between muscle contractile activity and afferent feedback, and the resultant corticospinal effects, is not precisely understood. Studies from McNeil et al. [25] and Gandevia et al. [22], show that SP duration following fatigue is independent from either group Ia afferent, or group III / IV afferent activity, respectively. In the aforementioned studies, SP duration was assessed during sustained MVC of the human biceps. SP was shown to recover to control duration despite the occlusion of blood to the fatigued muscle, which presumably maintained activity of group III and IV afferent fibers during recovery. The recovery of SP despite continued afferent feedback suggested that group III and IV afferents did not contribute to SP elongation. However, these findings do not fully exclude a role for afferent fibers in the regulation of cortical function, only for those activated by metabolite accumulation following occlusion. For example, it may be possible that the specific afferent pathways responsible for SP elongation are activated during active contraction, but are unaffected by metabolite accumulation. Prior work by S.J. Garland [26] under similarly ischaemic fatigue conditions as the Gandevia group demonstrates activation failure that cannot be explained by muscular fatigue or ischaemia, and implicates small diameter afferent fibers in motoneurone inhibition. Furthermore, corticospinal inhibition has been observed following other methods of pain induction [27], which supports the possibility that muscle afferent response may be specific to the type of stimulus. Given the multiple pathways of inhibition and excitation governing cortical activity, cortical response may vary considerably among muscle groups and experimental protocols. The unequivocal nature of similarly designed studies above may indicate that some stimuli for muscle sensory feedback remain unidentified.

For each participant in this study, the maximal involuntary tetanic response was determined by progressively increasing stimulation current until no further increase in maximal tetanic force was observed. However, the maximal tetanic force was consistently less than maximal voluntary force. To account for possible discrepancies among the three conditioning contraction types, voluntary CCs were matched for force (~60% MVC) and for intensity (maximal ie. MVC). No significant differences were

observed for SP duration or twitch potentiation for any of the three CC types. Both SP and potentiation are sensitive to the intensity and duration of the conditioning contraction [28]. Silent period elongation following contraction is dependent on contraction intensity [25], and ~65% of MVC has previously been shown as sufficient to cause SP elongation. Furthermore, 60% MVC has been shown to be sufficient for maximal potentiation in hand muscles [29]. In hand muscles which are primarily slow twitch, and for which force gradation is achieved primarily through a rate-coding strategy rather than recruitment [30], the entire motor unit pool is shown to be activated by ~60% of MVC force [31]. These results corroborate our observation that maximal potentiation can be induced by a submaximal contraction of sufficient intensity to recruit all or most of the motor unit pool.

In summary, the findings indicate that following a potentiating conditioning contraction, there is a coexistence of peripheral contractile enhancement and corticospinal inhibition. These results may explain the large discrepancy between evoked contractile properties and voluntary contractile properties following potentiation [11, 12]. We have also observed that an involuntary conditioning contraction induces equal corticospinal inhibition to a voluntary conditioning contraction. That is, corticospinal inhibition may be induced in the absence of any cortical activity. This is a somewhat surprising result, which can likely be attributed to muscle sensory feedback during the CC. Prior study into muscle afferent feedback during voluntary contraction and following fatigue during various tasks and in different muscle groups are equivocal [22, 26, 32, 33], which underscores the high task specificity of fatigue effects, and that the precise nature of muscle sensory feedback is not yet fully understood. It is possible that the afferents implicated here require a minimal force threshold to become active, or that they are stimulated by some characteristic of the contraction itself, rather than being sensitive to metabolite accumulation.

References

1. Sale DG. Postactivation potentiation: role in human performance. Exerc Sport Sci Rev 2002; 30:138-143.

2. Manning DR, Stull JT. Myosin light chain phosphorylation-dephosphorylation in mammalian skeletal muscle. Am J Physiol 1982; 242:C234-41.

3. Baudry S, Duchateau J. Postactivation potentiation in human muscle is not related to the type of maximal conditioning contraction. Muscle Nerve 2004; 30:328-336.

4. Baudry S, Klass M, Duchateau J. Postactivation potentiation of short tetanic contractions is differently influenced by stimulation frequency in young and elderly adults. Eur J Appl Physiol 2008; 103:449-459.

5. Grange RW, Vandenboom R, Xeni J, Houston ME. Potentiation of in vitro concentric work in mouse fast muscle. J Appl Physiol (1985) 1998; 84:236-243.

6. Houston ME, Green HJ, Stull JT. Myosin light chain phosphorylation and isometric twitch potentiation in intact human muscle. Pflugers Arch 1985; 403:348-352.

7. Baudry S, Duchateau J. Postactivation potentiation in a human muscle: effect on the rate of torque development of tetanic and voluntary isometric contractions. J Appl Physiol 2007; 102:1394-1401.

8. Behm DG, Button DC, Barbour G, Butt JC, Young WB. Conflicting effects of fatigue and potentiation on voluntary force. J Strength Cond Res 2004; 18:365-372.

9. Gossen ER, Sale DG. Effect of postactivation potentiation on dynamic knee extension performance. Eur J Appl Physiol 2000; 83:524-530.

10. Klein CS, Ivanova TD, Rice CL, Garland SJ. Motor unit discharge rate following twitch potentiation in human triceps brachii muscle. Neurosci Lett 2001; 316:153-156.

11. Smith CB, Allen MD, Rice CL. Voluntary rate of torque development is impaired following a voluntary versus tetanic conditioning contraction. Muscle Nerve 2013; 49:218-224.

12. Smith CB, Cheng AJ, Rice CL. Potentiation of the triceps brachii during voluntary submaximal contractions. Muscle Nerve 2011; 43:859-865.

13. MacIntosh BR, Gardiner PF. Posttetanic potentiation and skeletal muscle fatigue: interactions with caffeine. Can J Physiol Pharmacol 1987; 65:260-268.

14. Vandervoort AA, Quinlan J, McComas AJ. Twitch potentiation after voluntary contraction. Exp Neurol 1983; 81:141-152.

15. Rassier DE, Macintosh BR. Coexistence of potentiation and fatigue in skeletal muscle. Braz J Med Biol Res 2000; 33:499-508.

16. McNeil CJ, Butler JE, Taylor JL, Gandevia SC. Testing the excitability of human motoneurons. Front Hum Neurosci 2013; 7:152.

17. Roick H, von Giesen HJ, Benecke R. On the origin of the postexcitatory inhibition seen after transcranial magnetic brain stimulation in awake human subjects. Exp Brain Res 1993; 94:489-498.

18. Inghilleri M, Berardelli A, Cruccu G, Manfredi M. Silent period evoked by transcranial stimulation of the human cortex and cervicomedullary junction. J Physiol 1993; 466:521-534.

19. Taylor JL, Butler JE, Allen GM, Gandevia SC. Changes in motor cortical excitability during human muscle fatigue. J Physiol 1996; 490 (Pt 2):519-528.

20. Teo WP, Rodrigues JP, Mastaglia FL, Thickbroom GW. Post-exercise depression in corticomotor excitability after dynamic movement: a general property of fatiguing and non-fatiguing exercise. Exp Brain Res 2012; 216:41-49.

21. McNeil CJ, Giesebrecht S, Gandevia SC, Taylor JL. Behaviour of the motoneurone pool in a fatiguing submaximal contraction. J Physiol 2011; 589:3533-3544.

22. Gandevia SC, Allen GM, Butler JE, Taylor JL. Supraspinal factors in human muscle fatigue: evidence for suboptimal output from the motor cortex. J Physiol 1996; 490 (Pt 2):529-536.

23. von Giesen HJ, Roick H, Benecke R. Inhibitory actions of motor cortex following unilateral brain lesions as studied by magnetic brain stimulation. Exp Brain Res 1994; 99:84-96.

24. McNeil CJ, Martin PG, Gandevia SC, Taylor JL. The response to paired motor cortical stimuli is abolished at a spinal level during human muscle fatigue. J Physiol 2009; 587:5601-5612.

25. McNeil CJ, Giesebrecht S, Khan SI, Gandevia SC, Taylor JL. The reduction in human motoneurone responsiveness during muscle fatigue is not prevented by increased muscle spindle discharge. J Physiol 2011; 589:3731-3738.

26. Garland SJ, Kaufman MP. Role of muscle afferents in the inhibition of motoneurons during fatigue. Adv Exp Med Biol 1995; 384:271-278.

27. Svensson P, Miles TS, McKay D, Ridding MC. Suppression of motor evoked potentials in a hand muscle following prolonged painful stimulation. Eur J Pain 2003; 7:55-62.

28. Taylor JL, Gandevia SC. A comparison of central aspects of fatigue in submaximal and maximal voluntary contractions. J Appl Physiol (1985) 2008; 104:542-550.

29. Fukutani A, Hirata K, Miyamoto N, Kanehisa H, Yanai T, Kawakami Y. Effect of conditioning contraction intensity on postactivation potentiation is muscle dependent. J Electromyogr Kinesiol 2014; 24:240-245.

30. Johnson MA, Polgar J, Weightman D, Appleton D. Data on the distribution of fibre types in thirty-six human muscles. An autopsy study. J Neurol Sci 1973; 18:111-129.

31. Milner-Brown HS, Stein RB, Yemm R. Changes in firing rate of human motor units during linearly changing voluntary contractions. J Physiol 1973; 230:371-390.

32. Butler JE, Taylor JL, Gandevia SC. Responses of human motoneurons to corticospinal stimulation during maximal voluntary contractions and ischemia. J Neurosci 2003; 23:10224-10230.

33. Taylor JL, Petersen N, Butler JE, Gandevia SC. Ischaemia after exercise does not reduce responses of human motoneurones to cortical or corticospinal tract stimulation. J Physiol 2000; 525 Pt 3:793-801.

General discussion and summary

The studies presented in Chapters 2 – 5 of this dissertation uniquely describe the effects of a conditioning contraction and associated potentiation by examining properties of the complete neuromuscular system during a voluntary task. Prior to this series of studies, potentiation was well understood from the perspective of myosin phosphorylation *mechanics* and of artificially evoked contractile properties, but evidence describing the effects of a conditioning contraction on a voluntary task was minimal and conflicting. The purpose of my studies was to describe the effects of a conditioning contraction on the variables affecting a dynamic voluntary task, including intact muscle length change, voluntary contractile properties, and the central nervous system.

Based on the results of this thesis, the primary finding is that an acute conditioning contraction does not enhance voluntary performance of an explosive contractile task, and may even impair performance depending on the goal of the task.

Functional, dynamic tasks require muscle length change in order for work to be done, and in Chapter 2 I showed that the effects of potentiation on voluntary neuromuscular efficiency (NME) are affected by muscle length. This study highlights the main mechanism of potentiation, which is the reduction of actin-myosin spacing via myosin light chain phosphorylation. At short muscle length there was a significant potentiation of NME following a conditioning contraction, but at long muscle length this improvement was absent. Lengthening the isovolumetric muscle tissue requires interfibrillar spacing to decrease, which likely places the actin and myosin filaments close to optimal proximity and thus removes the opportunity for myosin phosphorylation to further improve contractile performance. This creates a situation where, during a shortening contraction beginning in a fully extended joint position, potentiation has little effect at the initiation of contraction in the lengthened position, and then has a progressively greater effect as the muscle shortens. This relationship may preclude potentiation from having an effect during the early period of contraction while torque is

being developed, and may limit the functional role of potentiation to enhance contractile properties. However, the improved calcium sensitivity that accompanies myosin phosphorylation may imply a role for potentiation to preserve contractile properties in the face of fatigue during a series of dynamic shortening contractions, rather than to enhance contraction throughout the range of motion.

In Chapters 3 and 4 I have investigated the effects of both voluntary and involuntary conditioning contractions on the performance of a voluntary ballistic contraction, as well as an evoked muscle twitch. Prior studies have concluded that potentiation would have the greatest positive effect on a ballistic-type voluntary contraction, as studies of involuntary artificial potentiated contraction have shown large improvement in rate of torque development, and little to no improvement of maximal strength tasks. However, I have shown that ballistic contractile properties are not enhanced by potentiation, and are largely depressed. I have shown that concurrent to sizeable potentiation of artificially evoked RTD, voluntary RTD is either unchanged or reduced. I suggest that this disparity is described by an enhancement in contractile performance distal to the motor axon, which explains twitch RTD improvement, and by concomitant inhibition proximal to the motor axon, which explains the absence of voluntary ballistic potentiation.

Further investigation into the time course of RTD reveals more subtle changes to contractile performance following potentiation. Following an involuntary conditioning contraction, where the influence of the central nervous system should be negligible, peak RTD was unchanged. However when RTD was examined at 10 ms intervals, it was evident that RTD increased during the first 40 ms of contraction, reaches a peak 10 ms earlier than the control contraction before falling off. This shows that ballistic RTD following an involuntary CC is in fact compressed to the left rather than being unchanged. Following voluntary CC, peak RTD is reduced, however a time-course analysis shows that RTD is actually increased during the first 30 ms of contraction, and that RTD following voluntary CC is in fact compressed downward and leftward, rather than simply being reduced. Postactivation potentiation is closely associated with Ca^{2+} kinetics, as myosin phosphorylation increases the Ca^{2+} sensitivity of muscle tissue.

Calcium requires 20-25 ms to fully diffuse from the sarcoplasmic reticulum throughout the sarcoplasm, which is a similar time course to the 30-40 ms during which voluntary RTD is improved from control. My interpretation of this temporal pattern is that following a CC, voluntary RTD is enhanced during the first 30-40 ms of contraction while Ca^{2+} is diffusing throughout the cell, and $[Ca^{2+}]$ is still submaximal. After this time period, $[Ca^{2+}]$ is great enough to saturate the contractile filaments, and the muscle loses the benefit of myosin phosphorylation.

Chapter 5 further explores the hypothesis of central inhibition concurrent to peripheral potentiation by using single TMS pulses to create a cortical silent period (SP). The length of the silent period is considered an indicator of cortical excitability or inhibition, such that cortical inhibition results in an elongated SP. Following both voluntary and involuntary conditioning contractions, the cortical SP was elongated compared to a control contraction, which indicates an inhibition of the motor cortex. The observation that both voluntary and artificially evoked conditioning contractions elicited the same degree of SP elongation indicates that cortical inhibition is not primarily caused by fatigue of the motor cortex per se, but rather by afferent feedback from the contracting muscle.

In the general introduction, Figure 3 presented a depiction of the progression of potentiation over time, and the relationships between peripheral potentiation, peripheral fatigue, and contractile performance. Based on the studies I present in this thesis, I propose a modification to this depiction to include central nervous system effects and reflect the differences between voluntary and evoked contractile properties as shown in Figure 20.

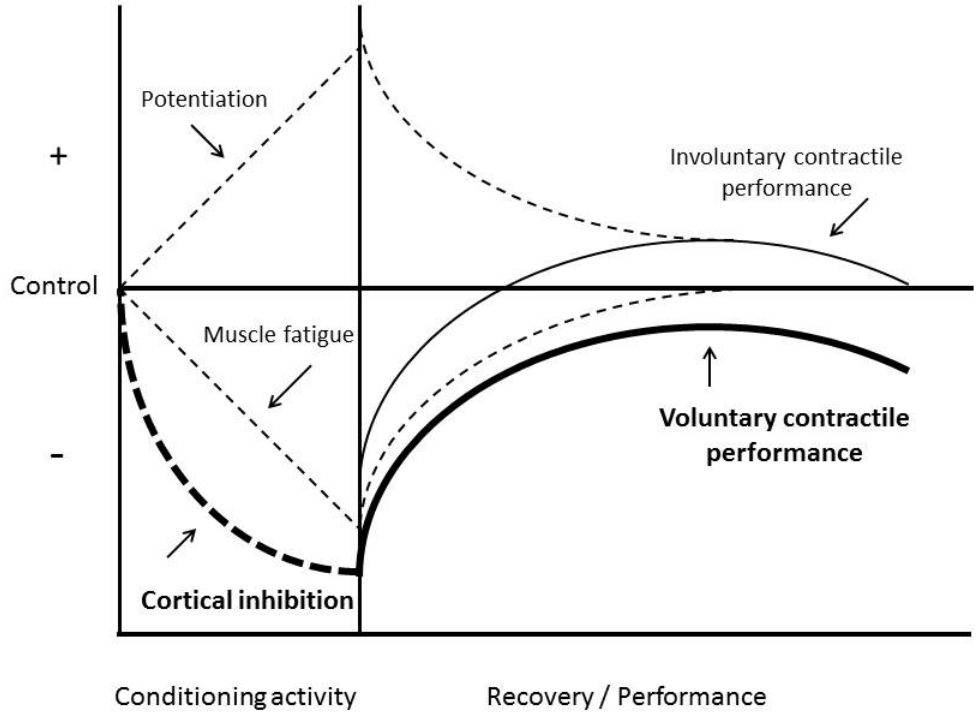

Figure 22. Illustrated depiction of the relationships between potentiation, fatigue, and contractile performance

Adapted from Sale 2002, an illustrated representation of the time course of potentiation, and the relationships to fatigue and performance. Solid lines represent contractile performance, which is the sum of the positive effect of potentiation, and the negative effect of fatigue. The bolded lines, representing cortical inhibition and voluntary contractile performance have been added to Sale's original to reflect the results of this thesis. This modification illustrates that voluntary contractile performance is the sum of potentiation, muscle fatigue *and* cortical inhibition, and is depressed compared to involuntary performance.

Limitations

Chapter 2 describes neuromuscular efficiency (NME; torque / EMG) of the triceps brachii at different muscle lengths in order to comment on potentiation during dynamic contraction. However, the measurements are not taken during dynamic contraction, but rather are isometric contractions at different joint angles. These are indirect measures of muscle length change, and ideally NME would be measured during continuous dynamic contractions and joint rotations. The difficulty with making this type of measurement is that NME as assessed here is the relationship between torque output and neural activity as measured using surface EMG. During an isometric contraction, the position of the muscle tissue deep to the surface electrodes remains fairly constant However, during dynamic contraction, the electrodes stay essentially fixed to the skin over one region of the limb while the muscle moves substantially and so the EMG is recording from different muscle tissue throughout the movement. Using indwelling wire electrodes that follow a portion of the muscle tissue throughout dynamic movement might overcome this limitation.

The studies presented in Chapters 3 and 4 both compare evoked twitch contractions against voluntary ballistic contractions. These contractions are compared because they are both 'maximal' in a sense, but the limitations of the twitch contraction restrict it to peak RTD and peak torque that are submaximal compared to the muscle's full capability . However, the comparisons made in the above studies are meaningful, but a further clarifying comparison would include a series of electrical pulses which would evoke an artificial contraction closer to the maximal capacity of the muscle. Previously Folland et al. [1] have used a 100 Hz octet to evoke this type of contraction.

Many comparisons have been made in this thesis which rely on a conditioning contraction to elicit potentiation within the muscle tissue. I have attributed many of the changes observed to be the result of potentiation, however there are myriad effects which occur concurrent with potentiation, and begin at the onset of contraction. I have made every effort in the study designs to minimize confounding variables such as muscle

fatigue, tendon compliance, muscle temperature, and voluntary activation failure, however I cannot directly rule out all of these possible influences entirely. I argue that in the context of the overall purpose of the thesis, which is to clarify the functional voluntary effects of a conditioning contraction, that any confounding variables which have influenced the results would also be present during the performance of a functional task. Thus, the incidental presence of any secondary effects would not change the fundamental conclusions of these studies and indeed recapitulate the rationale for these studies: that the functioning neuromuscular system is an amalgam of many factors and ultimately has to be evaluated as a complete and complex unit.

In the study presented in Chapter 5, the excitation status of the motor cortex is based on the length of the cortical silent period following a single TMS pulse. This measurement however is indirect, and of course a more direct measurement of cortical behaviour would be ideal. However, the reality of studying the central nervous system activity makes direct measurement difficult or impossible in many cases in vivo, and some level of compromise is almost always necessary. Instead, there are other indirect measures such as the cervicomedullary evoked potential or long interval cortical [1, 2] which, in conjunction with SP, would create a more complete picture of central nervous system adaptations following CC.

Future directions

I have commented briefly on the behavior of potentiated tissue at different muscle lengths, but future study should investigate potentiation during dynamic movement. Furthermore, I have demonstrated that measuring only the peak RTD or peak torque of a contraction may fail to observe important changes occurring at non-peak time points. To understand the behavior of the neuromuscular system during dynamic muscle length change, continuous rather than instantaneous measurements should be sought.

Chapter 4 of this thesis indicates that while potentiated voluntary contractions may not show increased peak RTD, increases do exist during the first 30-40 ms of contraction. Thus, tasks which rely on the early establishment of explosive muscle force or stiffness may benefit from potentiation without an increase in peak RTD. Furthermore, the explosive task examined here was isometric. Thus, future studies should assess contractile properties during a potentiated dynamic movement, focusing on the first ~50 ms of contraction.

In an effort to optimize muscle contractile performance, the studies in this thesis were designed in order to maximize the positive effects of potentiation, while minimizing the negative effects of muscular fatigue. In addition to muscular fatigue, cortical inhibition as a negative influence on voluntary potentiation is suggested. In order to further explore the possibility of enhancing task performance via potentiation, future studies should attempt to minimize central fatigue and inhibition as well as peripheral fatigue. This may include experimenting with CC durations of 6s or less, or a reduction in CC contractile intensity.

As mentioned above, the cortical SP is an indirect measurement of only one component of the central nervous system. Future studies should include measurements of cervicomedullary evoked potentials and long interval cortical inhibition in order to more completely describe CNS activity during potentiation.

Summary

The neuromuscular system is complex and multifarious, and highly adaptable based on its contractile history. Following a conditioning contraction, muscle tissue may be fatigued (slower, weaker) or potentiated (faster, stronger). This thesis investigated voluntary contractile performance following a conditioning contraction. The primary results of my thesis indicate that the neuromuscular system responds in varied ways to a brief, strong contraction, such that muscle tissue becomes faster, and likely due to

enhanced sensitivity to Ca^{2+} influx, while the motor cortex is concurrently inhibited. My results suggest that cortical inhibition may result from feedback from the contracting muscle, rather than overuse of the motor cortex itself (central fatigue). I also show that voluntary potentiation improves neuromuscular efficiency at short muscle length, and enhances voluntary RTD during the first 30-40 ms of contraction. Based on these studies, I propose that postactivation potentiation may have a role to improve voluntary contractile performance during the early phase of contraction, and during a dynamic contraction to preserve contractile performance as the muscle shortens. The negative effects of muscular fatigue and cortical inhibition, which begin at the onset of contraction, preclude potentiation from enhancing maximal voluntary torque or RTD, and that both peripheral and central fatigue must be managed in order to optimize functional task performance.

References

1. Sale D. Postactivation potentiation: role in performance. Br J Sports Med 2004; 38:386-387.

2. Folland, JP., Buckthorpe, MW, Hannah, R. Human capacity for explosive force production: Neural and contractile determinants. Scandinavian Journal of Medicine & Science in Sports 2013.

3. McNeil CJ, Martin PG, Gandevia SC, Taylor JL. The response to paired motor cortical stimuli is abolished at a spinal level during human muscle fatigue. J Physiol 2009; 587:5601-5612.

4. McNeil CJ, Martin PG, Gandevia SC, Taylor JL. Long-interval intracortical inhibition in a human hand muscle. Exp Brain Res 2011; 209:287-297.

Appendix A

Research Western

Use of Human Participants - Ethics Approval Notice

Principal Investigator: Dr. Charles Rice
Review Number: 18097
Review Level: Full Board
Approved Local Adult Participants: 100
Approved Local Minor Participants: 0
Protocol Title: Neuromuscular control of human movement
Department & Institution: Anatomy & Cell Biology,University of Western Ontario
Sponsor: Natural Sciences and Engineering Research Council

Ethics Approval Date: July 22, 2011 **Expiry Date:** August 31, 2015

Documents Reviewed & Approved & Documents Received for Information:

Document Name	Comments	Version Date
UWO Protocol		
Letter of Information & Consent		

This is to notify you that the University of Western Ontario Health Sciences Research Ethics Board (HSREB) which is organized and operates according to the Tri-Council Policy Statement: Ethical Conduct of Research Involving Humans and the Health Canada/ICH Good Clinical Practice Practices: Consolidated Guidelines; and the applicable laws and regulations of Ontario has reviewed and granted approval to the above referenced study on the approval date noted above. The membership of this HSREB also complies with the membership requirements for REB's as defined in Division 5 of the Food and Drug Regulations.

The ethics approval for this study shall remain valid until the expiry date noted above assuming timely and acceptable responses to the HSREB's periodic requests for surveillance and monitoring information. If you require an updated approval notice prior to that time you must request it using the UWO Updated Approval Request form.

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

[redacted]

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Appendix B

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Curriculum Vitae

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- Motor unit properties

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NSERC undergraduate research scholarship recipient 2008

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Data collection
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ARTICLES PUBLISHED IN PEER-REVIEWED JOURNALS

Smith C.B., Cheng A.J., and Rice C.L. Potentiation of the triceps brachii during voluntary submaximal contractions. Muscle Nerve 2011; 43:859-865.

Smith C.B., Allen M.D., Rice C.L. Voluntary rate of torque development is impaired after a voluntary versus tetanic conditioning contraction. Muscle Nerve 2014; 49:218-224.

Stevens D.E., Smith C.B., Harwood B., Rice C.L. In vivo measurement of fascicle length and pennation of the human anconeus muscle at several elbow joint angles. Journal of Anatomy 2014; online DOI: 10.1111/joa.12233

SELECTED ABSTRACT PRESENTATIONS (total career count: 14)

Smith, C.B., Stevens, D.E., Cowling, B., Rice, C.L. Postactivation potentiation and corticospinal inhibition following both voluntary and involuntary conditioning contractions. Applied Physiology, Nutrition, and Metabolism, 2014 39(S42)

Smith, C.B., Allen M.D., and Rice, C.L. Relationship between conditioning contraction type and rate of torque development during potentiated voluntary contractions. Applied Physiology, Nutrition, and Metabolism, 2013, 38(10):1080

Smith, C.B., and Rice, C.L. Twitch potentiation during isometric, shortening, and lengthening contractions in the human triceps brachii. Applied Physiology, Nutrition, and Metabolism, 2012, 37(S34)

Smith CB, Allen MD, Rice CL. Comparison of post-tetanic to postactivation potentiation in human tibialis anterior. Medicine and Science in Sports and Exercise. 2012, 44:688.

Smith, C.B., Harwood, B.J., and Rice, C.L. Motor unit recruitment thresholds of potentiated muscle in humans. Society for Neuroscience 2010 AGM – San Diego

Smith, C.B., Cheng, A.J., and Rice, C.L. Torque-length relationship of the dorsiflexors is altered by muscle shortening, and passive plantar flexor resistance. Applied Physiology, Nutrition, and Metabolism. 2009, 34 (S86).

Smith, C.B., and Rice, C.L. (2009). Postactivation potentiation of the triceps brachii during voluntary contractions. Free communications presentation to the biannual meeting of the Exercise Neuroscience Group Meeting 2009, London, ON.

Smith, C.B., and Rice, C.L. Postactivation potentiation of the triceps brachii during voluntary contractions at two muscle lengths. Applied Physiology, Nutrition, and Metabolism. 2008, 33 (S93).

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Canadian Society for Exercise Physiology – Student member	2009 – present
Society for Neuroscience – Student member	2010 - 2011