NEURAL EXCITATION OF MUSCLE IN RATE OF FORCE DEVELOPMENT AND FUNCTION

by

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ABSTRACT

Movement velocity, and its isometric surrogate rate of force development (RFD), are associated with functional mobility. High levels of neural excitation are necessary for rapid movement to occur. Neural excitation, measured via surface electromyography (EMG), can be quantified using a variety of measures. Early feline experiments revealed a bilinear input:output relationship of the alpha motor neuron that had a primary firing rate range and a secondary firing rate range in response to injected current. Both ranges have been characterized as linear and the secondary range has a greater slope and firing rates that are characteristic of most-rapid contractions or movements. More recent literature showed a bilinear relationship between movement velocity and motor unit firing rate in humans. Older adults and people with Parkinson's disease (PwPD) are two populations that experience decreased rates of force development and neural excitation. It may be the case that not all functional assessments used in these populations require high rates of neural excitation, especially those performed at preferred rather than fastest rates.

PURPOSE: The purpose of this research was threefold: Aim 1) to compare candidate surface EMG measures of neural excitation, Aim 2) to determine the nature of the relationship between EMG measures and peak RFD, with a specific interest in potential bilinearity, and Aim 3) to describe and compare the rate of neural excitation

during common dynamic assessments performed at increasing movement velocities in young adults, healthy older adults, and people with Parkinson's disease. **METHODS:** EMG, isometric force and limb accelerations were recorded during isometric and dynamic movement performed at increasing speeds. The purpose of Aim 1 was to describe the relationship between peak rate of EMG rise and surface electromyogram outcome measures with the strongest measures then used in a comparison of linear and nonlinear models of the relationship between RFD and neural excitation. In the cross-sectional study involving dynamic movements (Aim 2 and 3), analysis of variance was used to test a hypothesized group-by-speed interaction on peak rate of EMG rise (RER) in two lower extremity and two upper extremity movements. The peak RER of the four movement conditions being performed as fast as possible was compared. **RESULTS:** Aim 1.1: Root mean square of the initial 75ms (RMS75) had the strongest relationship while peak RER had the strongest relationship for measures not reliant on EMG onset. Aim 1.2: For RMS75, a linear relationship was the best fit for 14/21 participants. A bilinear relationship was the best fit for 7/21 participants. Neither Log-log nor exponential was best fit for any participants. For Peak RER, a linear relationship was the best fit for 6/21 participants. A bilinear relationship was the best fit for 13/21 participants. Log-log was not the best fit for any participants. An exponential relationship was the best fit for 2/21 participants. Aim 2: Only recumbent cycling revealed a group by speed interaction on peak RER and this finding was consistent in vastus lateralis, soleus, and tibialis anterior muscles. Elbow extension and 4-meter walk revealed group-by-speed interactions for peak

accelerations. Comparing NE during the AFAP condition revealed a group by condition interaction with all groups having differences in peak RER across the movements. In the upper extremity, no group had any significance in RER differences between weighted arm curl and elbow extension. In the lower extremity, YA and PD had significant differences in RER between walking and low-resistance, high velocity bicycling. **CONCLUSION:** Neural excitation is a key determinant of rapid isometric contractions and rapid movement. These findings present evidence to suggest that the known bilinearity of motor unit firing rates is observable in surface EMG measures. Results also provide guidance on the specific movements and rate conditions that are suitable for understanding the role of neural excitation in function and mobility. Assessing movement at a rapid rather than preferred pace will elicit the high levels of neural excitation often associated with functional independence.

Chapter 1

LITERATURE REVIEW

Introduction

Research has found that power is a key element in both skilled movement and general function (Bean et al., 2002; Hazell, Kenno, & Jakobi, 2007; McBride, Triplett-McBride, Davie, & Newton, 2002; Sayers, 2007; Suzuki, Bean, & Fielding, 2001). Within the *power=force x velocity* formula, some have determined that power and velocity are of greater importance to function than the ability to generate maximal force, which is generally described as 'strength' (LaRoche, Cremin, Greenleaf, & Croce, 2010; Sayers & Gibson, 2010) . The rate of isometric muscle force development (RFD) is often used as a surrogate measure for velocity or power in Kinesiology research.

One population with slowed RFD and movement is older adults. From 2000 to 2010 the older adult population (>65 years old) increased by more than 15% and comprises 13% of the United States total population (Howden & Meyer, 2011). Lower strength and RFD, as compared to a young adult population (Barry, Warman, & Carson, 2005; Thompson et al., 2014) is associated with a slowing of movement and functional decline. Older fallers are more likely to have a low RFDs in both ankle plantar and dorsi flexors (LaRoche et al., 2010) and knee extensors (Bento, Pereira,

Ugrinowitsch, & Rodacki, 2010). In 2013 falls accounted for over $34 million in health care costs (Center for Disease Control and Prevention, n.d.).

Physical function is of key importance for older adults, as many fear losing independence more so than death (Prince Marketing Foundation, 2007). A decrease in function can lead to sedentary behavior which in turn leads to a further decline in health and general mood state (Shin, 1999) and increases in anxiety and depression (Tremblay, Colley, Saunders, Healy, & Owen, 2010).

Another population which encounters impaired movement speed is people with Parkinson's disease (PD). PD is the second most common neurological degenerative disorder. It effects about 0.3% of the industrialized world and 1.0% of people over the age of 60 years in the same population. Roughly 8-18 new cases are diagnosed annually per 100,000 people. (de Lau & Breteler, 2006) PD is more prevalent in males and less prevalent in Asian countries. The prevalence of the disease peaks at 70-79 years old and declines after this age (Pringsheim, Jette, Frolkis, & Steeves, 2014).

A PD diagnosis is based on clinical symptomology with the increase in either the amount or severity of symptoms causing a decrease in the quality of life for the patient (Duncan et al., 2014). The main motor symptoms used in diagnosis are: resting tremor, bradykinesia or slowing of movement, rigidity, and postural imbalance. A diagnosis requires at least two of these symptoms (de Lau & Breteler, 2006). In 2006, mitochondrial dysfunction, oxidative stress, and protein mishandling were thought to be the central role in the cause of PD (de Lau & Breteler, 2006) but by 2015

the primary thinking was enteric nervous system dysfunction with focus being on entry to the brain via the vagal nerve (Svensson et al., 2015). Both coffee and tobacco decrease the risk of PD (de Lau & Breteler, 2006) and currently researchers are looking into the potential for various PD subtypes (Marrass & Lang, 2013).

Charcot (1877) as cited in Corcos, Chen, Quinn, McAuley, and Rothwell (1996) stated that with PD there is a "retardation in the execution of movements rather than real enfeeblement of the motor powers." This statement makes clear that the problem with PD is the slowing of the movement rather than weakening of muscles. Corcos et al. found peak maximum voluntary contraction (MVC) and RFD were both lower and both active and passive relaxation time were extended due to the effects of PD. Passive relaxation being the cessation of agonist activity to return to a baseline or zero force level while active relaxation is the cessation of agonist activity and the activation of the antagonist muscle to return to a baseline or zero force level. Of greatest significance was the correlation between percent change in active relaxation time (off medication: on medication) and Unified Parkinson's Disease Rating Scale (UPDRS) ($r=.89$, $p<.05$). (Corcos et al., 1996) This indicates the slowness of active relaxation could be an indicator of a) the severity of the disease and b) a potential lack of function.

Neely et al. compared RFD and force relaxation between people with PD and healthy control participants. Under the instructions to produce force up to 15% MVC for two-seconds then relax for 1 second, they found people with PD to have longer force pulses with slower rates of force development and relaxation (2013). The

slowing of movement translates into a decline in areas of function such as reaction time (Bloxham, Dick, & Moore, 1987), slower and smaller gait movements (Halliday, Winter, Frank, Patla, & Ontario, 1998), and less control to grip objects appropriately (Fellows, Noth, & Schwarz, 1998).

Not only do people with PD differ from healthy controls in MVC and RFD, but they also have impairments in force control mechanisms. Originally discussed by Freund and Budingen (1978) and further examined by Gordon and Ghez (1987), the time to achieve peak force is invariant in rapid isometric contractions regardless of force pulse amplitude. This is due to a positive scaling of RFD with force pulse amplitude. Park and Stelmach (2007) showed with PD, the time to peak force increased as the force level increased compared to healthy adults. The slope of the relationship between RFD and peak force, a control parameter, has been named rate of force development scaling factor (Bellumori, Jaric, & Knight, 2011) and will be discussed in more depth later.

The ability to produce quick movement is paramount to function. With aging and in Parkinson's disease, the ability for quick movement decreases or in some cases is lost completely which leads to ever increasing dysfunction, loss of independence and greater healthcare costs. This project is designed to better understand the neural determinants of quickness and to use this knowledge to identify the changes which occur in both an aged and diseased population. The first aim of this project is to identify a surface EMG measure of neuromuscular activation that correlates to the rate of force development. The second aim of this project is to determine a non-invasive

measure which most accurately describes the underlying neural activation of movement. The last aim is to examine the usefulness of the non-invasive measure during typically used mobility assessments and exercises that are intended to increase speed of movement.

Rate of Force Development

The rate of force development (RFD) is a measure taken from the torque- or force- time curve of a recorded contraction. It is typically obtained during rapid or "explosive" isometric voluntary contractions. RFD has been examined in many different areas of kinesiology and rehabilitation research. RFD has been discussed as an indicator of sports performance (Stone et al., 2006) and as modifiable with both strength training (Aagaard, Simonsen, Andersen, Magnusson, & Dyhre-Poulsen, 2002; Blazevich, Horne, Cannavan, Coleman, & Aagaard, 2008) and motor learning (Gruber & Gollhofer, 2004). RFD has been deemed as a stronger indicator of function than overall strength (Bento et al., 2010; Sayers, Guralnik, Thombs, & Fielding, 2005) and as something affected by both age (Barry et al., 2005; Klass, Baudry, & Duchateau, 2008) and disease (Corcos et al., 1996; Park & Stelmach, 2007; Rose, Løkkegaard, Sonne-holm, & Jensen, 2013).

Force Development in Performance & Adaptability

Sayers (2007) states that power is more pertinent to function and performance than strength. In the Power=Force x Velocity (P=FV) equation, this makes strength,

represented by force, less important that movement velocity. RFD is often used as a surrogate measure of movement velocity and is used to describe rapid/ballistic/explosive isometric contractions. It is a change in force divided by a change in time and often is taken from the first derivative of the force-time curve. The ability to produce high RFD or quick (ballistic/explosive/rapid) movements is associated with sport performance in athletes and mobility and function in older adults, people with PD and other special populations.

The vertical jump is often used as a surrogate for athletic ability, strength and power. McLellen, Lovell, and Gass (2011) explored the role of RFD on vertical jump performance. The aim of their study was to determine the relationship between RFD and vertical jump in untrained, but active male young adults. 23 participants performed six vertical jumps on a force plate. Peak RFD, average RFD, peak force, average force, and time to peak force were measured. They found a significant relationship (r=.68) between peak RFD and vertical jump displacement.

Not only is peak RFD associated with vertical jump height (McLellan et al., 2011), but it is also strongly correlated with sprint cycling performance (Stone et al., 2006), and lower body "explosive force production" is related to rugby performance (Tillin, Pain, & Folland, 2012).

Although older adults may not be participating in high intensity sports, RFD remains important for performing functional tasks of living. The relationship of RFD to function was reinforced by Bento and colleagues (2010) who examined peak force and peak RFD in older adults. 31 older adult women were divided into groups based

on the number of falls in the previous 12 months (0, n=13; 1, n=8; 2+, n=10) and a series of lower body isometric contraction tests. No differences were found in peak force (i.e. strength), but non-fallers had significantly greater knee extensor RFD scores than the other groups.

In their review, Hazell, Kenno, and Jakobi (2007) reinforce Sayers statement of the importance of power with older adults. Optimal training for function occurs when weight is moved at a greater than normal rate. In fact, Hazell et al examined the role of both typical strength training and high velocity power training on functional tasks. They noticed across multiple studies that power training was consistently more beneficial for functional tasks than conventional strength training. For a list of the studies involved see Figure 1 below. Power training provided greater change scores than resistance training (respectively) in balance (+25%, +10%), Chair Rise Time (23%, 9%) and gait speed (10%, 7%). Consistent with the principle of specificity in exercise program design, strength training was only superior to power training for change in strength scores (37%, 32%). According to Hazell's review, the only category in which conventional strength training proved superior to power training was in measures of strength

Figure 1.1 Hazel, 2007

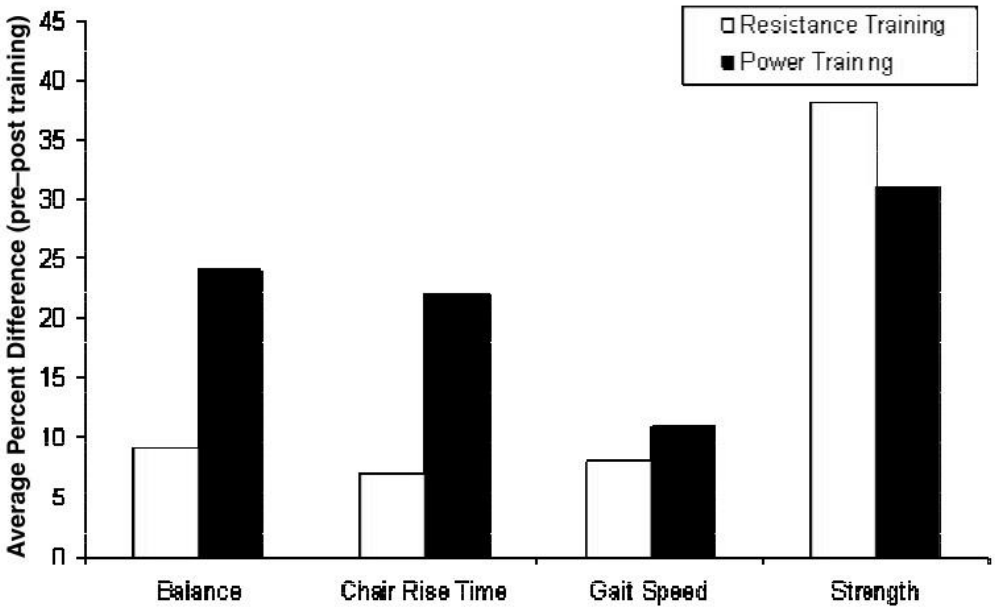


Figure 1 — Differences for activities of daily living and strength reported from a variety of studies on older adults subsequent to 8–16 weeks of resistance or power training. Values are calculated differences and the subsequent averages for resistance-training studies (Brandon, Boyette, Gaasch, & Lloyd, 2000; Fiatarone et al., 1994; Jette et al., 1999; Judge et al., 1994; Schlicht, Camaione, & Owen, 2001; Singh et al., 1997; Skelton & McLaughlin, 1994; Skelton et al., 1995; Westhoff, Stemmerik, & Boshuizen, 2000) and high-velocity-training studies (Bean et al., 2004; Earles et al., 2001; Fielding et al., 2002; Henwood & Taaffe, 2005; Hruda et al., 2003; Kongsgaard et al., 2004; Sayers et al., 2003).

In functional task or activity of daily living (ADL) categories, high velocity power training proved to have greater outcomes. This reinforces the assertion that one's ability to produce high velocity movement increases function. As Hazell discussed, power training yields greater success in function and performance than strength

training (Hazell et al., 2007) which might indicate the adaptability of RFD. RFD can both increase and decrease across a variety of situations.

Barry and colleagues (2005) found lower peak RFD scores in older adults than younger adults prior to training. Klass, Baudry, Duchateau,(2008) also found lower rates of force development in older adults when compared to young adults in isometric dorsiflexion. This was expanded on by Thompson (2014) who sought to explore RFD across different ages. Thompson's research tested 22 young adults, 16 middle aged adults, and 22 older adults. Asking their participants to perform a plantar flexion MVC as rapidly as possible, they recorded the isometric muscular force-time curve (mechanomyogram), from which measured RFD in the first 50ms and between 100-200ms. The variables were analyzed as both absolute values and normalized to peak force. Across all variables RFD was significantly less in the older adult group when compared to both middle aged and young adults. It should be noted that there was no difference between the young adult and the middle-aged group, marking when changes in these variables become more pronounced.

A reduced ability to generate force rapidly also occurs with disability and disease. Parkinson's disease (PD) is a movement disorder which is typically associated with slowing of movement (bradykinesia). This is exemplified by Stelmach and colleagues (Stelmach, Teasdale, Phillips, & Worringham, 1989) who examined the characteristics of force production in individuals with PD. They had seven people with PD, seven healthy older adults, and seven young adults perform isometric elbow flexion while recording force production and neural activation. The

results showed individuals with PD having significantly slower rates of force development than both the healthy older adult and young adult groups. Lower rates of force development are also observed in children with cerebral palsy (Moreau, Falvo, & Damiano, 2012) compared to typically developing children, in the paretic limb following stroke (Fimland et al., 2011), and during recovery from total knee arthroplasty (Maffiuletti, Bizzini, Widler, & Munzinger, 2010) and anterior cruciate ligament repair (Angelozzi et al., 2012).

As discussed, RFD values are part of an individual's ability to perform at high levels in sport and in activities of daily living, for older adults and people with disabilities or injury. Whereas RFD values decrease under conditions discussed, they can also increase through appropriate exercise training methods.

Gruber and Gollhofer (2004) tested the effects of sensorimotor stability training on peak force and RFD in isometric leg press. In this study, sensorimotor training consisted of unilateral stance postural stabilization tasks on unstable surfaces, such as wobble boards and soft pads. After 4 weeks of training, they found no change in peak force, but greater force levels were achieved in both the initial 30 ms and 50ms of the movement. Peak RFD values also increased from 4.95 N/ms to 6.58 N/ms. In a subsequent study (2007), Gruber and colleagues added an element of ballistic training to their protocol to compare sensorimotor stability training to ballistic training and found while both significantly increased RFD, RFD increased more with ballistic training (+48%) than with sensorimotor training (+14%) (Gruber, Gruber, Taube, Schubert, & Beck, 2007).

Along with sensorimotor and ballistic training, various forms of resistance training are commonly used interventions to improve RFD. Different types of resistance training include heavy resistance with repetitions ranging between 75% of one-repetition maximum to 90% of one-repetition maximum (Aagaard et al., 2002), to slow speed contractions (30^{o}/s) (Blazevich et al., 2008), although slow training is most effective for those individuals with below normal RFD values, and finally high-velocity power-resistance training which found increases in peak movement velocity (Henwood, Riek, & Taaffe, 2008). Power resistance training also yields significant changes to contraction velocity in older adults and can be used as a predictor for fall risk (Orr et al., 2006).

The ability to generate force quickly is an indicator for both function and performance. Coaches, athletes, healthcare professional, and trainers can use RFD as a predictive measure for potential performance. Athletes such as cyclists (Stone et al., 2006), rugby players (Tillin et al., 2012), and older adults (Bento et al., 2010) rely on this ability in order to be successful within their given activities. Health care professionals also rely on RFD values to determine return to play times for athletes such as soccer players after injury (Angelozzi et al., 2012). The motor skills (goal-directed movement) of function and performance require the underlying motor ability to generate rapid movement. This motor ability can be trained and is adaptable(Ives, 2014).

Excitation-contraction coupling and RFD

It is widely known that muscular force is developed via the process of excitation-contraction coupling (e-c coupling). Neural input travels from alpha motor neuron to the neuromuscular junction (NMJ) where the neurotransmitter acetylcholine passively diffuses across the NMJ. Action potentials then travel into the muscle fiber via the transverse tubules (T-tubules). As the action potential travels down the T-tubules, calcium is released from the sarcoplasmic reticulum. Calcium floods into the sarcomere where it attaches to the troponin on the tropomyosin uncovering crossbridge binding sites on the actin. The crossbridge heads of the myosin attach to the actin and generate tension in what is called a power-stroke. ATP is used to break the crossbridge connection and re-cock the myosin head to the ready position for its next crossbridge connection and powerstroke.

In studies which have focused on differences or increases in RFD due to muscle factors, the underlying mechanisms include muscle fiber type distributions and myosin heavy chain isoforms, and muscle fiber shortening velocity and the influence of series elastic component stiffness on force output.

Muscle fiber type role in rate of force production

As discussed in the review "Dynamic properties of mammalian skeletal muscles", (Close, 1972) the force velocity curves differ by fiber type with fast twitch fiber having greater shortening velocities. This was supported by Desmedt and Godaux (Desmedt & Godaux, 1978) who found fast twitch muscle to have greater

rates of force development than slow twitch muscle fiber. Clarkson, Kroll, and Mechionda (Clarkson, Kroll, & Melchionda, 1981) examined muscle fiber type and RFD more specifically in both young adult and older adult. Participants performed both an isometric MVC and a fast isometric MVC (FMVC) knee extension and had muscle biopsies done from vastus lateralis. They found significant differences in the fast twitch (FT)-to-slow twitch (ST) fiber ratio along with a difference in absolute rate of force development values. They concluded that a greater FT/ST ratio can produce force more quickly.

The functional unit of each type of skeletal muscle fiber is comprised of both actin and myosin filaments which are involved in crossbridge cycling. Each skeletal muscle fiber type has a different, unique myosin heavy chain isoform which has been seen with histochemical staining (Burke, Levine, Tsairis, & Zajac III, 1973). Gene splicing of drosophila to produce different myosin heavy chain isoforms found that each isoform functioned differently allowing the drosophila to jump to heights different than the wild-type (Wells, Edwards, & Bernstein, 1996). In an intact human model, time to peak torque, peak torque, and muscle biopsies were collected from three different muscle groups (soleus, vastus lateralis, and triceps brachii). The muscle with the highest percentage of myosin heavy chain isoform II also had the fastest twitch time to peak torque. The same muscle also had the highest peak rate of torque development when stimulated at 50Hz. Conversely, the muscle with the lowest percentage of myosin heavy chain isoform II had the slowest twitch time to peak force

and lowest peak rate of torque development when stimulated at 50Hz (Harridge et al., 1996).

Muscle-tendon stiffness in force production

For muscle force to develop, the serial elastic component typically referred to as tendon, stretches as the muscle component shortens. Early work by A.V. Hill (Hill, 1949, 1950) showed the importance of the tendon component to force development. Through a series of studies in which the muscle was rapidly stretched as it was stimulated, it was found that force production occurred more quickly. The pre-stretch of the muscle-tendon unit caused the elongation of the tendon enabling rapid force production to occur. In more recent work, 20 children, mean age 8.9 yrs old, were tested on isometric plantar flexion pre and post a 10-week resistance training protocol. Rate of force development, rate of EMG rise, electromechanical delay, and tendon stiffness were measured. Tendon stiffness increased by 29% and electromechanical delay decreased by 13% and was found to correlate with tendon stiffness (r= -.59) (Waugh, Korff, Fath, & Blazevich, 2014). In another study, thirty-four participants between 20 and 24 years old were tested for muscle-tendon stiffness, MVC, explosive force production, and time to force levels (relative to MVC and absolute). Knee extensors and the patellar tendon were tested. Absolute muscle-tendon stiffness was inversely correlated to time to achieve 150Newtons (0-150N) and time to achieve 300Newtons (0-300N) (r=-.34 and r=-.54, respectively). No normalized significance was found (Hannah & Folland, 2015). In their review, Maffiuletti and colleagues

(Maffiuletti et al., 2016) discuss the influence of muscle-tendon stiffness in rate of force development. While force transmission occurs more quickly through a stiffer muscle-tendon unit, the length of the tendon itself is an important consideration. During plantar flexion, the Achilles tendon and plantar fascia length must both be taken into consideration and force development is expected to occur slowly. Conversely, knee extension with force transmission through the much shorter patellar tendon will occur more rapidly. Therefore, not only does stiffness play a role, but resting length does as well. They concluded that, at this time, more data was needed to determine the role of muscle-tendon stiffness in rate of force development.

Neural determinants of force development

The underlying component of force production of e-c coupling are invariable. Further, Henneman and colleagues (1965) determined that smaller motor neuron and attached muscle fibers (motor unit) are recruited for e-c coupling before larger motor units. Within the invariability of both e-c coupling and the size principle there are a variety of factors that are variable and can greatly influences force production. Relatively recent work in humans demonstrates that high instantaneous motor unit firing rates at the initiation of a muscle contraction are key determinants of RFD (Jacques Duchateau & Baudry, 2014). However, knowledge of the source of such firing rates can be traced back to classic motor neuron studies in felines. One such study (Kernell, 1965) demonstrated that the alpha motor neuron exhibits a bilinear

relationship between firing rate and injected current. In these experimental preparations, there is good opportunity to examine the pure input-output transform of the motor neuron but artificial delivery of excitation as a square-wave or ramp is

Figure 1.2 Kernell, 1965

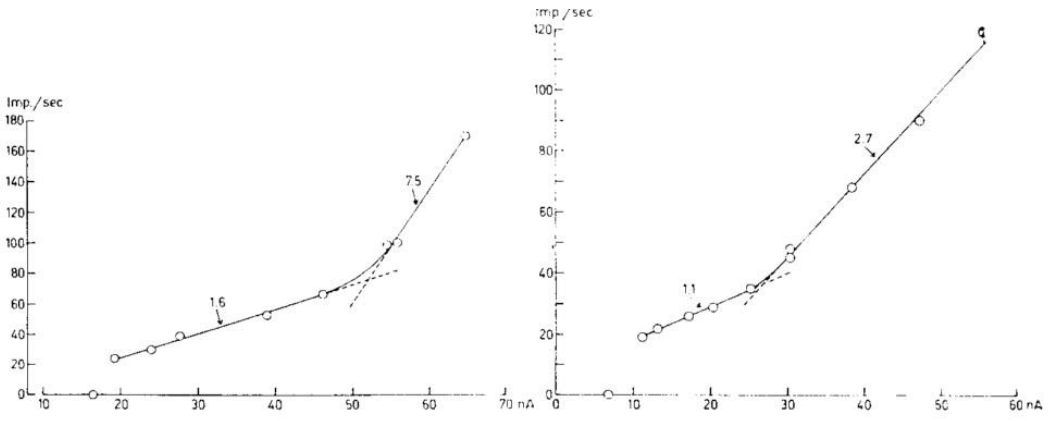


Fig. 2. **Fig. 3.**

Fig. 2. Same cell as Fig. 1. Steady discharge frequencies plotted against current strength. The values were obtained from the discharge which is partly shown in Fig. 1. Current strength was changed in steps at 1.0—1.5 sec intervals, and firing rates were measured over the final 0.5 sec of discharge at each current strength. Straight lines are fitted to the values obtained at weak and strong currents respectively, and the slopes of these lines (imp/sec/nA) are indicated by numbers at arrows.

Fig. 3. Motoneurone of spike size 93 mV at resting membrane potential. Steady discharge frequencies are plotted against current strength, and straight lines are fitted to the values as in Fig. 2. The values were obtained from a continuous discharge (*cf.* Fig. 1), and firing rates were measured at 0.1—0.6 sec following the onset of each current strength.

limited in its representation of human descending drive. Nevertheless, in the current-to-firing rate relationship, at low currents there is a linear relationship with a modest slope (primary range) and at higher currents there is a linear relationship with a significantly greater slope (secondary range). This relationship was further corroborated by Calvin (1978), who recorded higher initial firing rates at higher input

currents. In human tibialis anterior during rapid contractions, Desmedt and Godaux (Desmedt & Godaux, 1977) found the initial secondary range firing to be non-sustaining as the motor unit firing rate rapidly decreased to primary range. In the proposed dissertation work (Aim2), the breakpoint between these two firing rate ranges is of interest.

Different rates of force development elicit strategic changes in how force is developed. During rapid contractions, the relative force level of motor unit recruitment occurs at lower force levels compared to slower ramp contractions (De Luca, Lefever, Mccue, & Xenakis, 1982; Desmedt & Godaux, 1977, 1978). Slower ramp contractions also show peak firing rates to be between 50-60 pulses per second (Christie, Greig Inglis, Kamen, & Gabriel, 2009; Desmedt & Godaux, 1978). Kamen and Knight (Kamen & Knight, 2004) looked at MUFR across different force levels in young and older adult. They found significant differences in maximal MUFR between the two groups with maximal firing rate being calculated as a mean of the fastest five firings once MVC was achieved. They also reported the greatest increase in maximal MUFR in the second of two baseline MVC tests a week apart rather than at the end of a six-week training program. Along with the increase in maximal MUFR a corresponding increase in MVC was also reported.

Motor unit firing rates in the secondary firing range (> 50-60 pulses per second), and specifically doublet discharge (interfiring interval of <5ms), are required in rapid and forceful movements (Baldissera, Cavallari, & Cerri, 1998; Heller, 2010). The higher firing rate causes a higher rate of calcium release which allows more

crossbridge connections to occur which, in turn, yields a more powerful powerstroke (Cheng, Place, Bruton, Holmberg, & Westerblad, 2013). In elderly (Christie & Kamen, 2006; Klass et al., 2008) and special populations (Chou, Palmer, Binder-Macleod, & Knight, 2013), slower rates of muscular force development are explained by less secondary range discharge behavior. As Duchateau and Baudry (2014) discuss in their brief review, maximal motor unit firing rate determines maximal rate of force development.

Secondary firing range and more specifically doublet discharge mechanism research is based primarily on low-level current inputs and force levels. Neuromodulation acts by affecting motor neuron membrane potential which allows for a persistent inward currents (PICs) which results in sustained and/or repeated depolarization (Kiehn & Eken, 1998). PICs have several different effects on motor neuronal firing including the self-sustained firing which is most commonly seen in lower threshold motor units (Gorassini, Bennett, & Yang, 1998; Lee & Heckman, 1998). During self-sustained firing, neuronal dendritic properties initiate their own action potentials. Another phenomenon associated with PICs is "warm up." In this phenomenon, the MU shows a rapid increase to a plateau firing rate(Fuglevand, Dutoit, Johns, & Keen, 2006). The element of PICs which is most related to secondary range discharge behavior is a firing pattern Heckman and colleagues (Heckman, Johnson, Mottram, & Schuster, 2008) refer to as "amplification followed by saturation." Like "warm up" there is a rapid increase of firing rate (amplification) followed by saturation, which is a decrease in firing.

Neuromuscular Excitation

Measurement

The surface electromyogram is used in a wide variety of research topics including the study of control mechanisms in locomotion and single joint control tasks, determinants of strength, power and fatigue, the development of skill in motor learning, the restoration of movement in rehabilitation, as a control signal in the guidance of active prostheses, and many more. The surface electromyogram is a recording that includes the sum of motor unit action potentials that are observed in the recording volume. The surface electromyogram is also influenced by other physiological and technical factors that make it difficult or inappropriate to interpret underlying motor unit discharge behaviors. For example, an increase in motor unit action potentials detected by the sEMG electrode would increase the amplitude of the electromyogram. While it is known that the amplitude of neuromuscular excitation has increased, it remains unknown, from general surface methods, whether this increase is due to an increase in motor unit firing rate (rate coding) or new motor unit recruitment. Factors that need to be considered in the interpretation of the surface electromyogram include, but are not limited to, motor unit rate coding, motor unit recruitment, crosstalk – contamination of the sEMG with excitation of a nearby muscle, co-contraction, and amplitude cancellation. (Farina, Merletti, Enoka, & Neuromuscolare, 2004) Although there is much support for the generally linear relationship between neuromuscular activity and muscle force or tension (Lippold,

1952) (Lawrence & De Luca, 1983), there are important deviations from this rule.

More specific to the present scope of inquiry on rapid force production and movement, measures from the surface electromyogram can also provide information about the rate at which neuromuscular excitation occurs. Under instructions to contract muscle as rapidly as possible in isometric conditions, and in some rapid dynamic movements, the sEMG includes discrete bursts of neural excitation. The rate of neural excitation is represented in the initial portion of these bursts, where the amplitude, area or slope from the rectified signal is typically the dependent measure of interest. However, in addition to the complexities of EMG interpretation, incomplete development of the variables used to quantify rates of neural excitation, and inconsistency across the literature further challenges scientific inquiry that is based on surface electromyography.

Cross Sectional Comparisons

Examining the rates of neuromuscular activation in populations affected by slowing is of interest in order to more accurately predict those at risk for functional decline and loss of independence. In isometric conditions, the rate of neural activation has been examined in healthy older adults (Klass et al., 2008), and people with stroke (Chou et al., 2013). In one study comparing isometric force production in older female fallers and non-fallers, there were no differences in integrated EMG of the initial 200ms of activation (LaRoche et al., 2010). In another study, 40 older adult women were classified as either high active or low active. During an isometric knee-

extension reaction time task, the high-active women were found to have a greater peak EMG amplitude and peak rate of neural activation (rate of EMG rise - RER) than the low-active women (Laroche, Knight, Dickie, Lussier, & Roy, 2007). In a study comparing rapid elbow flexion among people categorized as less- or more-affected by Parkinson's disease, Wierzbicka and colleagues (Wierzbicka, Wiegner, Logigian, & Young, 1991) found that the participants more effected by PD used multiple discrete bursts of activation to reach the desired force level. Although these few studies shared a common interest in neural excitation and rapid force production or movement, the variety of possible sEMG-based dependent measures and their mixed utility with healthy adults or patients results in a challenging situation for the researcher. While the existing literature supports the use of sEMG to quantify rates of neural excitation, it is a general aim of the proposed research to contribute to the further development of methodological approaches by the technical approaches to quantification of excitation rate. Furthermore, we wish to test the generalizability of sEMG measures developed in isometric testing conditions to dynamic movements that exist in clinical tests of mobility or exercises that are recommended to improve speed and power. This would be an extension of work by Clark and colleagues (D. Clark et al., 2014) who showed a relationship between the RER variable and walking speed in older adults.

Neuromuscular Excitation Rates and Interventions

Changes in neuromuscular activation due to interventions is a common use for EMG. Research shows that root means square amplitude over the initial 30, 50, and

100ms of a maximum voluntary contraction increases in young adults after resistance training, but only increases in older adults in the initial 50ms of the contraction whereas the rate of EMG rise for the initial 30, 50, and 75ms increased for both populations post training (Barry et al., 2005). Gruber and Gollhofer (Gruber & Gollhofer, 2004) examined the effects of sensorimotor training on mean average voltage over the initial 30, 50, and 100ms then over 100-200ms, 200-300ms, 300-400ms, and 400-500ms. Post training the only differences seen were in the initial 30 and 50ms. Aagaard et al. (Aagaard et al., 2002) found 14 weeks of heavy resistance training to yield a significant increase in peak rate of force development in knee extension. To examine quadriceps neural activation pre- and post-training, they calculated peak EMG amplitude; mean average voltage (MAV) for the initial 30, 50, 100, and 200ms; and rate of EMG rise for the initial 30, 50, and 75ms. MAV 30 showed significant increases in a single hamstring, MAV 50 in two hamstrings, and MAV 100 all three hamstrings whereas both rate of EMG rise 30 and 50 showed significant increases in all three hamstrings. Representing general progress in our understanding of power and the underlying neural determinants, an important finding in this study is that while measures of neural excitation rate improved, there were no changes in peak EMG amplitude from pre to post training.

Neuromuscular Excitation Rate and Dynamic Movement

Common methodology of measuring neuromuscular activation during activities is to look at profiles. Winter and Yack (Winter & Yack, 1987) sought to

define EMG patterns or profiles during normal human walking. Using 20-35-year-old subjects, they measured neural activity of 16 muscles during a normal stride cycle. The EMG data was processed to a linear envelop and plotted against the stride cycle. This was used to determine the degree of neuromuscular activity during each phase. Similarly, Jorge and Hull (Jorge & Hull, 1986) used EMG to determine on-off profiles for lower body musculature during cycling revolutions. As seen on the left. Dark areas represent a muscle "on" phase and open areas represent muscle "off" phase.

Figure 1.3 Jorge and Hull, 1986

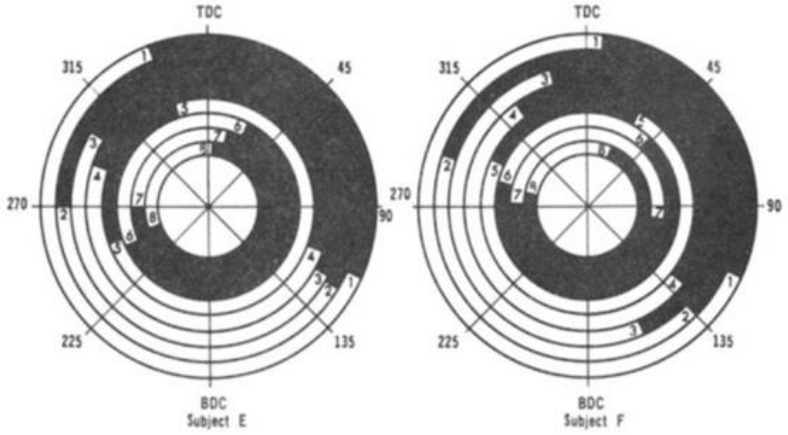


Fig 3. Jorge and Hull, 1986: Regions of on-off muscle activity for 2 individual test subjects. Muscles are 1. Glute max 2. Rectus femoris 3. Vastus medialis 4. Vastus lateralis 5. Tibialis anterior 6. Gastroc 7. Biceps femoris 8. Semimembranosus. Dark areas indicate muscle activity whereas open areas indicate muscles are "off"

Common Neuromuscular Excitation Rate Measures

As discussed earlier, movement quickness is of vital importance to function, mobility, and performance. For movement to happen quickly, the nervous system is

required to excite muscle tissue at a high rate. There are a variety of EMG variables that have been used to measure this activity with few of them being consistent across research. Early neuromuscular activation measurement often consisted of integrated EMG (iEMG) also knows as "area under the curve"). iEMG is calculated by mathematically integrating the linear envelop which assesses total muscle activation for the given time period (Kamen & Gabriel, 2009). To quantify the onset of excitation more specifically, "q30" is the iEMG of the initial 30ms of the rectified EMG burst. Root mean square (RMS) amplitude and mean average voltage (MAV) are variables that are often sliced into different time intervals ranging from the initial 30 to 200-300ms of the activation. Both variables are used to determine a mean amplitude of the rectified sEMG over a given window of time. RMS requires calculating the mean value of the squared data within a given window, then finding the square root of that mean. MAV, similarly, is a mean value of data within a given window after the data has been fully rectified. RMS is considered a "better" variable due to the possibility of amplitude cancellation in MAV calculation. (Kamen & Gabriel, 2009) EMG profiles are a common variable used during measuring of specific activities to determine muscle on-off. An important consideration in the calculations of excitation rate measures from the rectified signal is that the sEMG is often low-pass filtered by a variety of techniques and this has implications for the results. The activity of interest includes a specific landmark, such as heel strike in gait or top-dead-center in cycling, to match the linear envelop for specific muscles to determine neuromuscular activity or inactivity. In dynamic movements, analysis often results in

determination of EMG-off and EMG-on criteria or thresholds (Jorge & Hull, 1986; Winter & Yack, 1987).

RMS, MAV, iEMG, and EMG profiles are commonly used to determine neuromuscular activation. Each variable has been used to explain different types of neuromuscular activation making it difficult to compare outcomes across research. Furthermore, underlying neural mechanisms are difficult to infer from sEMG (Farina et al., 2004). In the past, researchers have indirectly linked sEMG to underlying mechanism (Corcos, Gottlieb, & Agarwal, 1989; Gordon & Ghez, 1987), but the relationship has not been directly investigated for these variables.

Physiological Determinants of Age-related Slowing

Physical slowing is a key element in the loss of function and independence associated with aging. To promote evidence-based development of exercise strategies to address this problem, it helps to understand the underlying physiological contributors. This section will focus on age-related changes in central nervous system functions and neuromuscular physiology related to rapid movement.

Central Nervous Changes, Aging, and Reaction Time

Although reaction time and information processing are not central to the proposed work, this topic has high ecological significance to the overall purpose. In

activities of daily living rapid contractions are often required in the broader task of responding to an external stimulus or perturbation. Thus, the successful outcome of the motor response not only depends on motor output but also sensory detect and information processing.

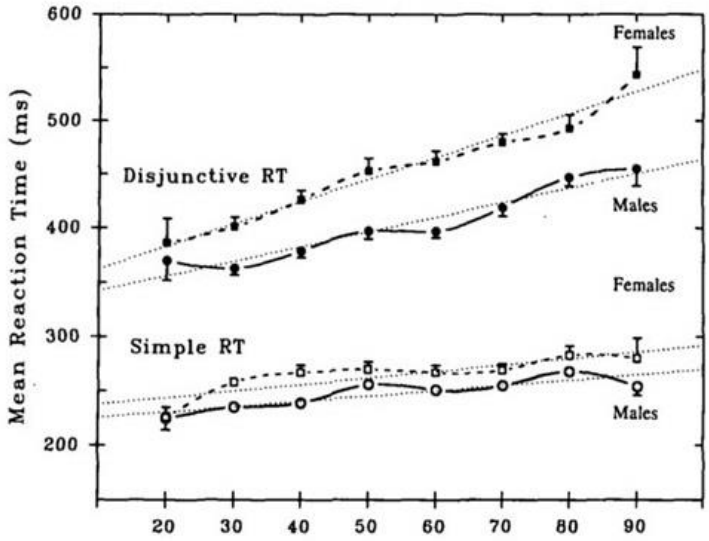
Sensorimotor function and information processing rates can be evaluated via simple reaction time (SRT) which measures the efferent pathways along with stimulus detection, disjunctive reaction time (DRT) which includes the somatosensory processing leading to stimulus identification along with the efferent pathways, and choice reaction time (CRT) which encompasses full information processing system of stimulus identification, response selection, and movement programming. (Schmidt & Lee, 2014) Many cross-sectional studies involving young and older adults have been done to understand the changes in reaction time. Fozard and colleagues (1994) sought to examine changes in reaction time both cross-sectionally and longitudinally. There were 1265 (833 m, 432 f) participants with at least one visit for cross-sectional analysis. Of those, 446 males and 134 females made at least three visits over four years and 264 males and 23 females made at least five visits over eight years for longitudinal analysis. Participants performed auditory simple and disjunctive reaction time tasks with between 6-13 seconds between each "go" stimuli. This time was chosen as part of a parallel study on brain wave activity recorded through Electroencephalogram. Cross-sectional analysis was performed using each participant's first visit. Both SRT and DRT significantly increased across decades 2-

9. Data also revealed significant differences in error by omission (failure to respond to the stimuli within 800ms) across the same decades.

Participants that made three visits over four years were used for longitudinal analysis. An ANOVA revealed significant age-related slowing in reaction time; SRT changed from 229.1ms to 292.6ms, a 28% increase. Similar changes were seen using both mean and median values. Total errors also significantly increased with age. DRT changes were also significant over time. Mean DRT time increased from 374.7ms to 459ms, a 22.5% increase.

Consistent with Hicks law (1952), CRT will have an exponentially greater reaction time as the number of choices increases. This is universal across ages but RT increases are greater in an aging population (Simon & Pouraghabagher, 1978) than in young adults. Simon and Pouraghabagher (1978) had 32 young adult subjects and 32 older adult subjects perform visual CRT task.

Figure 1.4 Fozard et al. 1994



Sample:	DRT	F	=	13	88	71	49	66	103	48	7
		M	=	14	137	126	138	174	128	122	14
	SRT	F	=	13	88	71	50	69	103	51	8
		M	=	14	139	125	140	177	130	121	18

Figure 2. Mean of median auditory reaction times for each participant's first visit as a function of age, sex, and task type expressed with standard error bars, spline fitting, and first order regression lines. Age intervals are by decade, ± 5 years (e.g., the sixth decade contains participants from 55–64 years of age). Sample sizes for the second through ninth decades were 27, 227, 197, 190, 246, 233, 172, 26.

Subjects received both visual and auditory stimulus and were told to respond to only the visual stimulus. The older adult group showed slower response times (584ms vs 456ms) than the young adults. There was also an intact stimulus (clear view of visual stimulus) and a degraded stimulus (a translucent plexiglass obstructed the visual stimulus) component to their experiment which showed older adults had significantly slower RT time than the young adults for the degraded stimulus as compared to the

clear stimulus (24% slower vs 13 % slower). Their research indicates a slowing of central processing centered mainly in stimulus detection.

The cause of slowed central processing may be due to a decrease in cerebral gray matter that occurs with aging (Courchesne et al., 2000; Jernigan et al., 2001; Raz et al., 1997). Some studies have found a greater reduction specifically in the prefrontal cortex (Jernigan et al., 2001; Raz et al., 1997) which would indicate a change in the response selection stage of information processing.

The reduction in cerebrum area may be a cause for functional reorganization of the cerebrum and further result in a larger area of activation during movement in older adults that was seen in fMRI studies and discussed in reviews (Talelli, Ewas, Waddingham, Rothwell, & Ward, 2008; Ward, 2006). Structural decrements and activation increases could also account for changes in central nervous control mechanisms of rapid movement as seen in both isometric (Bellumori, Jaric, & Knight, 2013) and dynamic (Ketcham, Seidler, Gemmert, & Stelmach, 2002) movements.

Peripheral Nervous changes in Aging

Downstream neural changes also occur with aging which result in both muscular and alpha motor neuron changes. These changes can be considered a cascade of events which maybe the underlying causes of *dynapenia*, which is the age-related loss of strength and power (B. C. Clark & Manini, 2008). These changes may begin with the motor unit denervation process that stimulates a host of both downstream and

upstream events. Lexell (Lexell, 1995) defines denervation as "a loss of contact between a nerve and muscle fiber" which occurs at the motor unit level.

Age related motor unit denervation has been seen in a rat model (Aare et al., 2016) but is more difficult to observe in humans. The observation of human MU denervation is reflected in the downstream and upstream changes more easily observed as motor unit number estimation (MUNE), motor unit size estimation and remodeling, motor unit action potential (MUAP) size, and spinal motor neuron changes.

Campbell, McComas, and Petito (Campbell, McComas, & Petito, 1973) tested 94 subjects between ages 3 and 96 years old. They found a decrease in functioning motor units in older adults along with an increase in motor unit size as observed through changes in MUAP amplitude.

Stalberg and Fawcett (1982), who built upon McComas and Petito's research, reported motor unit changes with aging during single fiber electromyogram (SFEMG) recordings. They measured muscle fiber density through both peak amplitude and area under the curve during a 60ms window around the peak amplitude. All measurements were taken during low level contractions. They tested 224 subjects across all decades of life ranging from 12 years old to 79 years old. Biceps brachii, vastus lateralis, and the tibialis anterior were tested across multiple recording sites in each muscle resulting in a total of 4709 recordings. Stalberg and Fawcett found a strong positive correlation between age and muscle fiber density. They found gradual increases in both amplitude and area until age 60 wherein both measures showed marked increases. They concluded the significant increase in area and area was due to

significant motor unit size. The increase in motor unit size happens in conjunction with a decrease in physiological cross-sectional area (Frontera et al., 2000).

Figure 1.5 Campbell et al., 1973

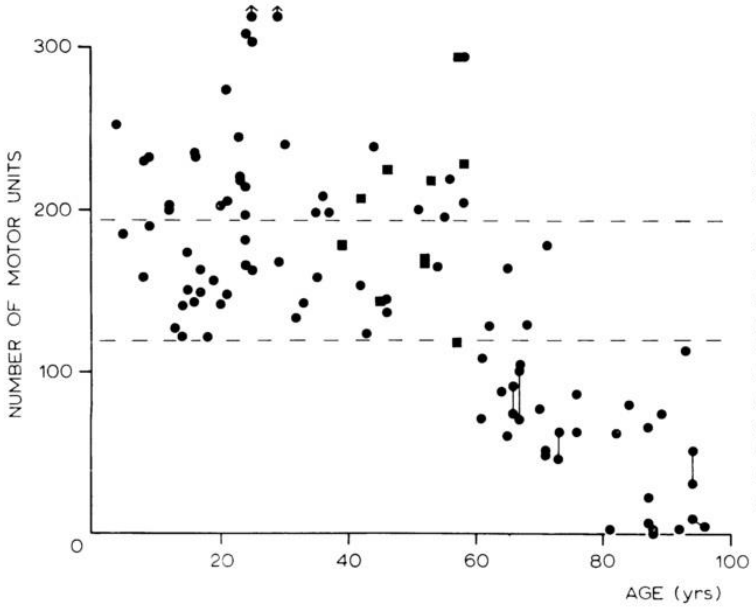


FIG. 2. *Numbers of functioning EDB motor units in 94 subjects aged between 3 and 96 years (101 legs altogether). Vertical lines link results in both legs of same subject. Squares denote values obtained in 'normal' legs of 10 hemiplegic patients (see methods). Upper interrupted horizontal line shows mean number of units in control subjects aged 3–58 years (197 units); lower interrupted line indicates smallest value in same subjects (121 units).*

The changes seen in aging motor units indicate structural changes are occurring within the motor unit itself. The decrease in strength and power associated with dynapenia would point to changes to fast-fatiguing motor units (FF) which has been observed in rats (Kadhiresan, Hassett, & Faulkner, 1996). Kadhiresan and associates (1996) found a 34% decrease in the total number of FF and a 14% decrease in the number of fibers within each remaining FF when comparing adult rats to elderly rats. They also recorded no change in the number of slow motor units but a drastic increase of almost 300% more fibers per motor unit (57 fibers in adult rats; 165 fibers

in elderly rats) within these same slow motor units. Further, Lexell and Downham (1991) found a change in fiber-type distribution within the muscle. They took muscle biopsies from 24 participants between the ages of 15 and 83 and performed histochemical staining and fascicle counting to look at the distribution. They found the younger participants were more likely to have a mosaic patterned distribution of muscle fiber type while the older adults showed larger "clumped" sections of specific fiber-types.

Age differences in motor unit populations can also be observed in the spinal cord. Human cadaver preparations revealed consistent numbers of spinal motor neurons until the age of 60 and a significant decrease in the number of spinal motor neurons thereafter (Tomlinson & Irving, 1977). Furthermore, while there is a reduction in total motor unit number, the size of the remaining motor neurons in older adults is greater. It is generally believed that this shift is part of a motor unit remodeling process (see Piasecki et al., 2016 for review) in which functioning motor units are generally believed to reinnervate the muscle fibers that lost innervation from their affiliated motor neuron (Yuan, Goto, Akita, Shiraishi, & He, 2000).

Physiological changes which occur with aging initiate a downward slope of movement function and independence. From cerebral size and activation changes to a neuromuscular decrease in motor unit number and corresponding increase in motor unit size, these alterations can slow down aging individuals. A clear shift from FF motor units to slow motor units as seen by Kadhiresan et al. and the new distribution pattern of motor units act in concordance with dynapenia. These are important factors

to consider together with the proposed work on rates of neural excitation of muscle tissue.

Pathophysiology of Bradykinesia in Parkinson's Disease

Parkinson's disease (PD) is part of a group of conditions classified as movement system disorders. It is the result of a loss of dopamine-producing brain cells in the substantia nigra of the basal ganglia (Office of Communications and Public Liason, 2014). The basal ganglia is a complex set of nuclei that help initiate and control movement. Its components comprise both direct and indirect pathways which are either excitatory or inhibitory, respectively. In the direct pathway, the role of the substantia nigra is to inhibit an inhibitory complex (disinhibit) called the globus pallidus interna (GPi). By disinhibiting the GPi, the desired movement is projected through the basal ganglia to the thalamus for downstream processing and movement production. Dopamine deficiency results in the substantia nigra being unable to disinhibit which yields the GPi inhibiting the motor systems. The role of the substantia nigra in the indirect pathway is to disinhibit the globus pallidus externa (GPe) which, in a downstream cascade of reactions, allows the GPi to inhibit the thalamus and subsequently the motor system. Dopamine deficiency leads to the inability of the GPe to be disinhibited which results in the reduced inhibition of the thalamus and motor systems. (Obeso et al., 2000; Shumway-cook & Voollacott, 2011)

The basal ganglia has projections to the supplemental motor area (SMA) which is a key area of the brain for internally initiated movement. Research has shown that people with PD have greater difficulty with self-initiated tasks (Burleigh-Jacobs, Horak, Nutt, & Obeso, 1997). Examination of this phenomenon was done using a pre-movement EEG measure (Bereitschaftspotential, BP). The BP is divided into BP1, which is the early component and associated with the SMA, and BP2, which is the later component and associated with the prefrontal cortex, which controls externally cued movement.

Dick and colleagues (1989) examined BP1 during a self-initiated finger flick activity in people with PD. The finger extension was performed on their own time and not in response to any external (auditory or visual) or internal (counting, breathing…etc) cues. EEG data were collected for 2.9 seconds prior to and 1.2 seconds after neuromuscular activation of the movement as determined by EMG onset measures. Outcome measures used were peak amplitude of BP negativity, BP amplitude 650 ms prior to EMG onset as a representative of BP1, and BP2 which was calculated as BPpeak-BP650. They found BP1 amplitude to be smaller in the patient population than in the healthy controls, no significant differences in BPpeak between healthy control and people with PD, and a larger than normal BP2 in people with PD.

SMA function in PD was more closely examined by Jenkins and colleagues (1992). Knowing there is a decrease in SMA activity in individuals with PD, they examined the role of treatment with apomorphine, a dopamine agonist, in SMA activity in individuals with PD. Participants moved a joystick to a pace guided by a

tone which occurred every 3 seconds. The movements allowed were forwards, backwards, right, or left. Participants were not given directional instructions other than to not build up a repetitive sequence. Even though they were paced, the research group determined the lack of directional instruction caused the activity to be self-initiated. Subjects were tested both after a medicine washout period (eight hours for l-dopa; 1-2 hours for apomorphine) and on medicine. PET scans were performed during rest, activity off medicine, and activity on medicine. All participants had a Hoehn Yahr score of 5 off medication and 3 on medication. After treatment, fMRI was greater in SMA, indicating increased blood flow. Adjacent cerebral areas such as the sensorimotor and premotor cortices did not see similar increases in blood flow. This study helps to demonstrate that while the basal ganglia is the primary brain area affected by PD, the secondary effects involve other brain areas that are associated with critical mobility functions, in this case, movement initiation. This finding was further corroborated in 2005 by Rodriguez-Rojas and colleagues who used fMRI to indirectly measure neural activity via hemodynamics of SMA activity pre and post dopaminergic treatments. Significant increases in SMA neural activity post treatments during hand movement activities in individuals with PD were reported (Rodriguez-Rojas et al., 2005).

Bradykinesia as a primary symptom concerns both movement changes and information processing changes. To determine dysfunction in motor pathways simple reaction time (SRT) tests can be used as the only requirement is stimulus detection, whereas a “go/no go” reaction time requires both stimulus detection and stimulus

identification, and choice reaction time involves stimulus detection and identification along with response selection. All reaction times tasks involve movement programming and program release.

Reaction times deficits in people with PD were first seen in 1925 (Wilson, 1925). Evarts and colleagues (1981) found both reaction time (RT) and movement time (MT) were more impaired in people with PD when compared to healthy older adults and young adults. Within those findings, they also found MT impairment to be more severe than RT. The PD group also showed the greatest variance both between subjects and within (right hand vs left hand) subjects. Pascual-Leone and colleagues (1994) examined the sensitivity of the motor pathways in reaction time tasks. Ten people with PD had significantly longer SRT than ten age-matched healthy subjects. When subthreshold transcranial magnetic stimulation (TMS) was applied the SRT for the patient population improved to equal that of the healthy population

To determine if people with PD exhibited a slowing in RT that was separate from MT slowing, Evarts et al. recruited people with PD who had MTs at or below the mean MT of older adults (49ms). In this sample, they found significantly slower reaction times even though MTs were not significantly different. In the same study, a subgroup of people with PD with RTs at or below the older adult means (256ms) were recruited for comparisons of MT. Again, there was a significant increase in MT in the PD group. (Evarts et al., 1981) Ultimately, Evarts et al. showed that slowing can occur in MT or RT or both. Cooper and colleagues surmised further that key elements involved with bradykinesia are the complexity of the task and the compatibility

between the stimulus and the response (Cooper, Sagar, Tidswell, & Jordan, 1994) which is also supported by Kutukcu's examination of choice reaction time in people with PD (Kutukcu, Marks, Goodin, & Aminoff, 1999).

Evidence demonstrates that the physiological reason behind bradykinesia is multifaceted. The decline in dopamine production in the substantia nigra (SN) causes motor coordination deficits that involve multiple, integrated, brain areas. These deficits manifest themselves in over-inhibition or improper disinhibition of movement. The dysfunctional movement signaling from the basal ganglia projects forward into difficulties with self-initiated movement in SMA which results in a disruption, or slowing, of movement. Furthermore, the destruction of dopaminergic cells in the SN cause a depletion of dopamine within the entire system. Dopamine depletion could greatly affect arousal and alertness levels during stimulus processing (Rihet, Possamaï, Micallef-Roll, Blin, & Hasbroucq, 2002) which aligns with the delays in reaction time seen in people with PD and the reduced effectiveness of TMS at improving RT. The interaction between a minimized arousal signal or decrease in stimulus processing and a degradation of the ability to initiate and coordinate movement could be a main cause of bradykinesia in people with Parkinson's disease.

Assessing Function and Mobility

Assessing function and mobility in older adults and people with PD can be accomplished many ways. The NIH Toolbox assesses motor function using walking endurance tests, gait speed tests, dexterity tests, strength tests, and balance tests. The

Senior Fitness Test™ assesses fitness and function using muscular strength and endurance measures along with cardiovascular and range of motion assessments. Multifactorial approaches can also be used to determine functional status. Often, multifactorial approaches encompass not just physical assessments but also a medical history and both cognitive and psychological assessments. One such multifactorial approach (Delbaere et al., 2010) assessed 80 mobility limited older women then had them report falls over the following twelve months. They found in a medical history, a history of previous falls (Odds ratio: 2.27) and dizziness (odds ratio: 1.49) to be the greatest predictors of future falls. To assess physical abilities, Delbaere et al. examined unipedal stance balance, 6-meter walk, and the Physiological Profile Assessment (PPA) (Lord, Menz, & Tiedemann, 2003), which includes proprioception, postural sway, reaction time, and leg strength measures. They found the PPA (odds ratio: 1.31) to be the strongest predictor of future falls. Paul et al. (2013) used a different multifactorial approach to assess 205 community-dwelling people with PD followed by monthly inquiries regarding falls during 6-month follow up period. They found fall history (odds ratio: 2.33), freezing of gait (odds ratio: 2.52), and self-selected gait speed (odds ratio: 4.27) to account for 80% of the outcome prediction in a multiple logistical regression model. As discussed previously, both high RFD and elevated neural excitation of muscle are necessary for fast, powerful movements which are necessary for function and performance.

Assessments and Determinants of Function

With such a wide range of methods to assess function, understanding the determinants is important. Comparing strength and power measures to the self-reported Functional Status Survey (FSS) found lower body power to have only a slight stronger correlation to FSS scores than lower body strength ($r = -.49$ vs $r = -.47$) in 80 older women with impaired function (Foldvari et al., 2000), but physical assessments have shown greater differences than surveys.

The roles of strength and power have been examined in assessments such as gait speed (Cuoco et al., 2004) and balance (Mayson, Kiely, LaRose, & Bean, 2008). Forty-five disabled older adults were assessed for strength (1RM) and power (40% of 1RM). Power was found to have the stronger relationship to habitual gait speed (HGS) than strength ($r = .59$ vs $r= .26$). The researchers also found a curvilinear relationship between lower body power and HGS (Cuoco et al., 2004) similar to Buchner et al (1996) who found a curvilinear relationship between lower body strength and HGS and interpreted it as strength having a ceiling effect on HGS. An examination of the neural determinants of HGS found power training to increase peak amplitude of knee extensors during HGS with no corresponding increases in the gait speed, again, indicating a ceiling effect of neural excitation on HGS (Beijersbergen, Granacher, Gäbler, DeVita, & Hortobágyi, 2017). Using both simple and composite assessments, Mayson et al. (2008) examined the relationship of lower body strength (1RM) and movement velocity (extrapolated from power measured at 40% of 1RM) during a seated leg press to balance. Mobility-limited older adults performed a

unipedal stance (simple assessment), the Berg Balance Assessment, Dynamic Gait, and the Performance Oriented Mobility Assessment (POMA) (composite assessments). Strength was found to have a significant association with the simple balance assessment (odds ratio: 1.06) while movement velocity was significantly related to the composite assessments: Berg, Dynamic Gait, and POMA (Odds ratios: 14.23, 35.80, 33.92, respectively).

Effects of Interventions on Function

In a recent review of exercise prescription for older adults, Barker (Barker, 2017) states the importance of power, or the ability to generate force quickly. Barker reinforced, as discussed above, the role of power in most functional mobility skills by stating most skills require power and the ability for rapid neuromuscular activation. Many previous studies, primarily focusing on both strength and power, have examined the role of intervention on functional assessments.

Strength, aerobic, and combination interventions were prescribed to 75 community-dwelling older adults. There were assessed for strength and aerobic fitness along with gait and balance pre- and post- six months of intervention. While strength improvements were reported in both the strength group in hip flexion, extension, adduction, abduction, knee flexion and extension, the aerobic and combination groups only reported strength increases in knee extension. There were no improvements in gait speed, step length, or stair climb. Similarly, there were no improvements in the balance measures (unipedal stance, tandem stance, narrow beam

walk, unstable surface stance). Interestingly, while no improvements were seen in the functional measures, exercise had a protective effect on fall risk (relative hazard: .53) over the non-exercise control. (Buchner et al., 1997)

Traditional resistance training was compared to high velocity resistance training by Bottaro et al (2007). Over a 10-week period, twenty older adults participated in a full body resistance training program. They were randomly divided into a power training group (PT) who performed the concentric movement in 1-second and a traditional training group (TRT) who performed the concentric movement in 2-3 seconds. All eccentric movements were performed in 2-3 seconds. Functional status was assessed using a 30-second arm curl, a 30-second sit-to-stand, and an 8-foot up and go assessments, three components of Rikli and Jones (Rikli & Jones, 2001) Senior Fit Test™. Both groups reported similar significant strength gains of about 25% in upper and lower body 1RM strength measures. Power increases were also significant for both groups, but the PT group reported 31% and 37% increases in peak power in lower and upper body, respectively. The TRT group increased 8% and 13% in lower and upper body peak power, respectively. While both groups experienced both strength and power increases, only the PT showed significant improvements in the three functional assessments of arm curl, sit-to-stand, and 8-foot up and go (percent changes: 50%, 43%, and 15%, respectively). Bottaro et al.'s experiment along with Hazell's (Hazell et al., 2007) reinforce the importance of high-velocity power training over traditional strength training for improving functional status in older adults.

More recent exercise intervention research for people with PD have focused on power, but more specifically, the velocity component within the 'power=force x velocity' equation. Power training, yoga, and recumbent cycling have all been used to improve function in people with PD. In previous research Ni et al (Ni, Signorile, Balachandran, & Potiaumpai, 2016) found power training to alleviate bradykinesia symptoms. A follow up experiment compared the effects of power training to high-speed yoga (Ni, Signorile, Mooney, et al., 2016) in balance and gait tasks. Thirty-seven participants with PD completed 12 weeks of either power resistance training (rapid concentric, 2-3 second eccentric contractions), high-velocity yoga, or a no exercise. Along with lower extremity strength and power assessed pre- and post-intervention, balance was measured with Berg Balance Scale (BBS), Mini-Balance Evaluation Systems Test (Mini-BEST), unipedal stance, postural sway, TUG, and functional reach. Gait speed was recorded at both HGS and maximal speed during a 10-meter walk. Both strength (.2 kg/body weight (kg), .3 kg/body weight (kg)) and power (2.6 W/body weight (kg), 1.8 W/body weight (kg)) significantly increased post training for the power training and yoga groups, respectively. Both the power training and yoga groups reported significant increases in gait speed at HGS (.12 m/s, .14 m/s) and fastest (.16 m/s, .22 m/s) speeds. Balance scores significantly improved for both groups in the BBS, Mini-BEST, TUG, and functional reach (less affected side). The power training group also had significant improvements on the more affected side in the functional reach and unipedal stance while the yoga group reported significant improvements on the less affected side in the unipedal stance. All significant

improvements were also significantly different than the control group, but two interventional groups did not significantly differ from each other. Ni et al.'s experiment indicates velocity-based training need not focus on power, merely speed to improve function in people with PD.

Another experiment focusing on movement velocity, examined the effects a high-speed low-resistance interval recumbent cycling intervention on function for 14 people with PD (Uygur, Bellumori, & Knight, 2017). The cycling intervention was comprised of twelve training sessions over six weeks. The intervention incorporated 5-minute warm up and cool down periods and 20 minutes of intervals. The intervals were 15 seconds of pedaling as fast as possible and 45 seconds of pedaling at a preferred cadence. The researchers tested 10-meter walk time and the number of steps taken, TUG, functional reach, four-square step test, and nine-hole peg test (an upper extremity dexterity measure). Significant improvements were seen in all measures.

Neural Excitation and Function

The importance of power as it relates to function and mobility is clear. The relationship between high RFD, rapid movement and high levels of neural excitation have been discussed above, but the role of neural excitation in function should be established. Clark, Patten and colleagues performed a series of studies examining differences in neural excitation in healthy older adults and those with functional mobility limitations.

Clark et al. established power differences between healthy middle-aged (MH) and older adults (OH) and mobility-limited older adults (OML). They recorded sEMG and calculated power during the middle 15-degrees of a 90-degree knee flexion/extension isokinetic movement. Healthy middle-aged and OH had significant increases in power production when compared to previous velocity (60^{o}/s, 90^{o}/s, 180^{o}/s, and 240^{o}/s) whereas the OML only saw an increase in power from 60^{o}/s to 90^{o}/s indicating they had a ceiling of power production. Similarly, both MH and OH had increases in RMS amplitude of the same middle 15-degrees of the movement at each step of the increasing movement velocities whereas there was no relationship between velocity and RMS amplitude for OML. (D. Clark et al., 2010)

Clark et al. also examined the rate of neural excitation (RER) of pre-movement time during a seated leg press task. MH, OH, and OML 1RM was assessed and the leg press performed at the lowest resistance (260N) and 70% of 1RM. Mobility limited older adults produced significantly less power than both MH and OH in both conditions while the OH produced significantly less power than MH at 70% of their 1RM. Pre-movement time was significantly longer and RER was significantly lower in OML when compared to MH and OH. (D. Clark et al., 2011)

Understanding the association of a decrease in power and neural excitation to function, Clark et al proceeded to examine the relationship between triceps surae RER and maximal gait speed. They assessed 20 healthy older adults with no significant differences in HGS. Using the differences between maximal gait speed and HGS, the OA were divided into fast (>.6 m/s) and slow (<.6 m/s). The slow group had a

significantly lower RER than the fast group and across all participants RER was positively associated maximal walking speed for both 10m and 400m gait tests and usual speed for 400m gait test. (D. Clark, Manini, Fielding, & Patten, 2013)

Beirjebergen and colleagues (2016) reported lower body power training to be associated with increases in maximal walking speed but not HGS. Subsequently, they also examined neural excitation of muscle during usual and fast gait speed after 10 weeks of power training. They reported an increase in neural excitation of planter flexors and knee extensors during both usual and fast gait speeds, but only increases in fast gait speed post-training. (Beijersbergen et al., 2017)

Research indicates, while there are a variety of methods to assess functional mobility, power is a paramount factor in their outcomes. Within power, one's ability to move quickly is an indicator of their functional status. Greater neural excitation of muscle is associated with fast movement and better functional ability. Power or high-velocity interventions have a greater effect on improving function in both older adults and people with PD. Power/velocity training, while increasing neural excitation, has little effect on habitual gait speeds but does improve fastest gait speeds. This implies the use of fastest gait speed may be a more useful measure to determine functional mobility than usual or habitual gait speed.

Summary

Research tells us that the ability to perform rapid movement is paramount to performance in sport and activities of daily living. Two populations that experience a

decline in movement velocity are older adults and individuals with Parkinson's disease. Connections have been made in the literature between human motor unit discharge behavior during rapid movements and animals studies under non-volitional stimulation conditions. What has yet to be accomplished is a more complete translation of these animal studies to a human model under volitional movement conditions. This body of work seeks to further the translation by present a more complete understanding of how global surface electromyograph measurement and underlying motor unit discharge behavior relate to movement velocity across the spectrum of movement velocities. This information will be beneficial to clinicians and researchers alike, creating a basis for understanding how neural activation affects rate of force development and subsequently detecting neural excitation deficiencies during assessment of slowed populations.

Specific Aims

Slowing of movement in older adults (OA) and people with Parkinson's disease (PD, bradykinesia) leads to decreased function, impaired mobility and less independence(Konno, Katsumata, Arai, & Tamashiro, 2004; Potter, Evans, & Duncan, 1995; Viccaro, Perera, & Studenski, 2011). Mechanical power predicts function better than strength(Hazell et al., 2007; Sayers, 2007), and power training improves function in both populations due to improvements in neural excitation and muscle contractility (Alberts, Linder, Penko, Lowe, & Phillips, 2011; Dibble, Hale, Marcus, Gerber, & LaStayo, 2009; Miszko et al., 2003; Orr et al., 2006; Sayers & Gibson, 2010). Power is the product of force and velocity. The proposed work focuses on movement velocity and its isometric surrogate, rate of muscular force development (RFD). RFD is slower in older adult fallers and people with PD when compared to older adult non-fallers (LaRoche et al., 2010; Stelmach et al., 1989). The proposed work examines the role of neural excitation of muscle (NE) in control of RFD and movement velocity. The neural contributors to RFD include motor unit recruitment, motor unit rate coding and antagonist muscle involvement. Increases in descending neural excitation from the brain increase motor unit recruitment and firing rates, which both contribute to a greater amplitude of the surface electromyogram (sEMG) and higher RFD. Early feline experiments demonstrated a bilinear motor neuron firing rate response to injected current, which is analogous to descending excitation. In this relationship there is a breakpoint, above which the relationship between current and firing rate has

a greater linear slope (secondary range) than below the breakpoint (primary range) (Kernell, 1965). Motor unit firing rates in the secondary range (including doublets (Binder-Macleod & Lee, 1996; Desmedt, 1980; Desmedt & Godaux, 1977; Heller, 2010; Van Cutsem, Duchateau, & Hainaut, 1998)) potentiate muscle twitch force and its summation, thereby increasing RFD (J. Duchateau & Hainaut, 1986). There is less secondary range firing behavior in older adults(Klass et al., 2008) and in the paretic limb of people with stroke (Chou et al., 2013). Power training improves secondary range firing behavior in young adults (Van Cutsem et al., 1998). However, we do not know if the breakpoint between primary and secondary range behavior is represented in the surface electromyogram of humans and whether common movement assessments for older adults and people with PD elicit these high rates of neuromuscular activation.

Aim 1 is to describe of the relationship between neural excitation of muscle, derived from the surface electromyogram (sEMG), and peak rate of force development. In young adults, sEMG will be obtained during isometric muscle contractions performed at increasing rates. *H1.1* Correlation will support one measure of neural excitation over others in its relationship with peak rate of force development. *H1.2* A Bi-linear fit will be the best fit in the relationship between the sEMG measure of neural excitation of muscle with the strongest correlation and peak RFD, when compared to models of best fit for similar physiological relationships.

Using expected differences between young, OA and PD groups:

Aim 2 is to examine the rate of EMG rise surface EMG measure in healthy young and older adults and people with Parkinson's disease across increasing movement frequency/velocity conditions. *H2.1*: There will be group by velocity interaction in rate of EMG rise of four common movements; arm curl, elbow extension, recumbent cycling, and over ground walking. *H2.2:* Movements performed as fast as possible will affect the peak rate of EMG rise of young adults, older adults, and people with Parkinson's disease differently. *H2.3:* Four meter walk test performed as fast as possible will elicit greater peak rate of EMG rise than that elicited while walking at a preferred pace.

Aim 3 is to determine whether commonly used movement assessments, performed at increasing velocities show evidence of secondary range behavior of neural excitation of muscle often associated with high levels of function. *H3:* Four common movements (arm curl, elbow extension, recumbent cycling, and over ground walking) will display evidence of non-linear excitation behavior via the significance of a secondary quadratic term.

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Chapter 2

COMPARISON OF NEURAL EXCITATION MEASURES FROM THE SURFACE ELECTROMYOGRAM

Abstract

Peak mechanical power and peak rate of isometric force development predict functional mobility and performance in healthy, athletic and clinical populations. Surface electromyography (EMG) is used to quantify the amplitude and rate of neural excitation (NE) of muscle. Several EMG measures are used to quantify the average magnitude of NE (e.g. RMS amplitude), the total amount of NE within a specified window of time (area under the curve measures), or the rate of NE (slope of rectified EMG). The present aim was to provide empirical guidance for the use of candidate EMG measures to quantify neural excitation during rate dependent force production tasks. Twenty-one apparently health young adults performed isometric dorsiflexion to 40% of their maximum voluntary contraction (MVC) force at increasing rates of force development while EMG was recorded from tibialis anterior. Force and EMG data were processed and analyzed in custom LabVIEW and MATLAB programs and Spearman's rho was used to determine strength of the relationship between EMG measures and rate of force development (RFD). RMS amplitude of the initial 75ms of EMG had the strongest correlation with peak RFD (ρ=0.80) among measures computed at the instance of EMG onset. Peak rate of EMG rise (RER) had the

strongest relationship with peak RFD (ρ=0.69) among measures that were not dependent on EMG onset determination. The strength of the relationship between RER and RFD supports its use during movements such as gait or bicycling, or in conditions such as Parkinsonian tremor, where muscles may not return to resting EMG levels.

Introduction

The neural excitation of muscle is examined with surface electromyography (EMG) to understand neuromuscular control mechanisms (Gordon & Ghez, 1984) and patterns of muscle involvement during movement (Sanderson, Martin, Honeyman, & Keefer, 2006). Numerous studies have examined how such factors are modified by development (McKinlay et al., 2017), aging (Klass, Baudry, & Duchateau, 2008), physical activity (Laroche, Knight, Dickie, Lussier, & Roy, 2007) fatigue (Bigland-Ritchie, 1981), chronic conditions (Chou, Palmer, Binder-Macleod, & Knight, 2013), injury (Wang et al., 2015), intervention (de Paula, Moreira, Huebner, & Szmuchrowski, 2017) and exercise training (Aagaard, Simonsen, Andersen, Magnusson, & Dyhre-Poulsen, 2002). The amount of myoelectric activity detected with EMG represents the sum of the motor unit action potentials (MUAP) in the recording volume. The number of MUAPs is primarily determined by motor unit recruitment and rate coding mechanisms but multiple factors confound their direct expression in the electromyogram. Such factors include, but are not limited to, the filtering effects of soft tissue, electrode movement in dynamic conditions and amplitude cancellation. Relatively high variance in EMG measures necessitates the use of optimal methods and careful selection of dependent measures.

Kinesiologists have become increasingly interested in mechanical power and rates of muscle force development (RFD) as predictors of function and mobility (Hazell, Kenno, & Jakobi, 2007; McBride, Triplett-McBride, Davie, & Newton, 2002), (Paavolainen, Häkkinen, Hämäläinen, Nummela, & Rusko, 1999; Sayers &

Gibson, 2010). Accordingly, studies have focused on the *rate* of neural excitation during rapid isometric contractions (Aagaard et al., 2002; Chou et al., 2013; Clark et al., 2014; Van Cutsem, Duchateau, & Hainaut, 1998). Across such studies, a variety of measures is used to quantify *initial* neural excitation rate at the onset of an EMG burst and/or *peak* neural excitation rate. Amplitude and area under the curve (definite integral, AUC) measures are often calculated over different periods of myoelectric activity (e.g. 30, 50, 75 and 100ms) and a peak rate of EMG rise (RER) measure calculated from the derivative of the smoothed and rectified electromyogram is used with increasing frequency (Aagaard et al., 2002; Chou et al., 2013; Clark et al., 2014; de Paula et al., 2017). Peak RER offers the advantages that there is no requirement to determine EMG burst onset and it can be applied in conditions with no quiet EMG baseline. Root Mean Square (RMS) amplitude and AUC measures have been used extensively to quantify the *magnitude* of neural excitation in the study of maximal strength and gait analysis and technical guidance can be found in references on EMG practice (Kamen & Gabriel, 2009; Konrad, 2005; Winter, 2009). However, the use of EMG measures to quantify the *rate* of neural excitation in rate-dependent muscle contractions is less-well developed and no reference on EMG practice currently describes rate-specific measures categorically. The aim of this study was to describe the relationship between peak rate of force development and a series of sEMG outcome measures to potentially provide empirical guidance for the selection and use of dependent measure to quantify neural excitation during rate dependent force production measures. Submaximal rapid isometric muscle contractions were

performed in ankle dorsiflexion across a wide range of rates of force development. Surface electromyograms were obtained from the tibialis anterior muscle. Candidate EMG measures were evaluated based on their correlations with peak RFD, average RFD and time to peak force. We anticipated that some measures would bear greater correlations with mechanical output while some sets of measures would have trivial differences due to their mathematical similarity.

Methods

Participants

Twenty-one healthy young adults, ten females and eleven males, (mean $\pm$ SD: age=21.8 $\pm$2.8 years; body mass = 72.8 $\pm$ 19.7 kg; height=1.7 $\pm$ .1 m) participated in this study. Participants were recruited from the university student body. All participants were free of neurological deficit/disorder and lower body dysfunction. All participants signed a university approved informed consent before beginning the study.

Procedures

Data were collected during a single testing session using DASYlab v.13 software (National Instruments, Austin, TX) to control acquisition and provide real time bio-feedback of isometric force production. Participants were seated on a custom wooden bench that was equipped with a force measuring device for ankle dorsiflexion.

The bench places both the knee and ankle angles of the tested lower extremity at 110°. The foot of the tested extremity was fastened with a non-elastic buckle strap to a plate affixed to a strain gauge force transducer (Model sm-100, Interface Force Inc., Scottsdale, AZ). Force was amplified and hardware filtered (low pass, 50Hz) at the time of recording (Model SGA, Interface force Inc, Scottsdale, AZ). The skin above the tibialis anterior was shaved and cleansed with ethyl alcohol. A pre-amplified double differential surface electrode was secured to skin above the mid-belly region of the tibialis anterior muscle (MA-300, Motion Lab Systems, Baton Rouge, LA). Signals were digitized at 2 kHz with 24-bit resolution (CDAQ-9178 and module NI9239, National Instruments, Austin TX). Participants were asked to perform isometric dorsiflexion contractions at low force levels to evaluate the quality of electrode placement and adjust amplifier gains. Participants then performed three maximum voluntary isometric contractions (MVC) separated by two minutes of rest. The maximum force achieved was used to present relative force levels (%MVC) in visual feedback. Participants viewed their relative isometric force in real time on a computer monitor (61cm diagonal screen size) positioned at eye level and at a distance of approximately 1.3m. Participants produced force to overlay a plot of their force (blue line) onto a static plot showing a set of linear ramp force-time curves (red line).

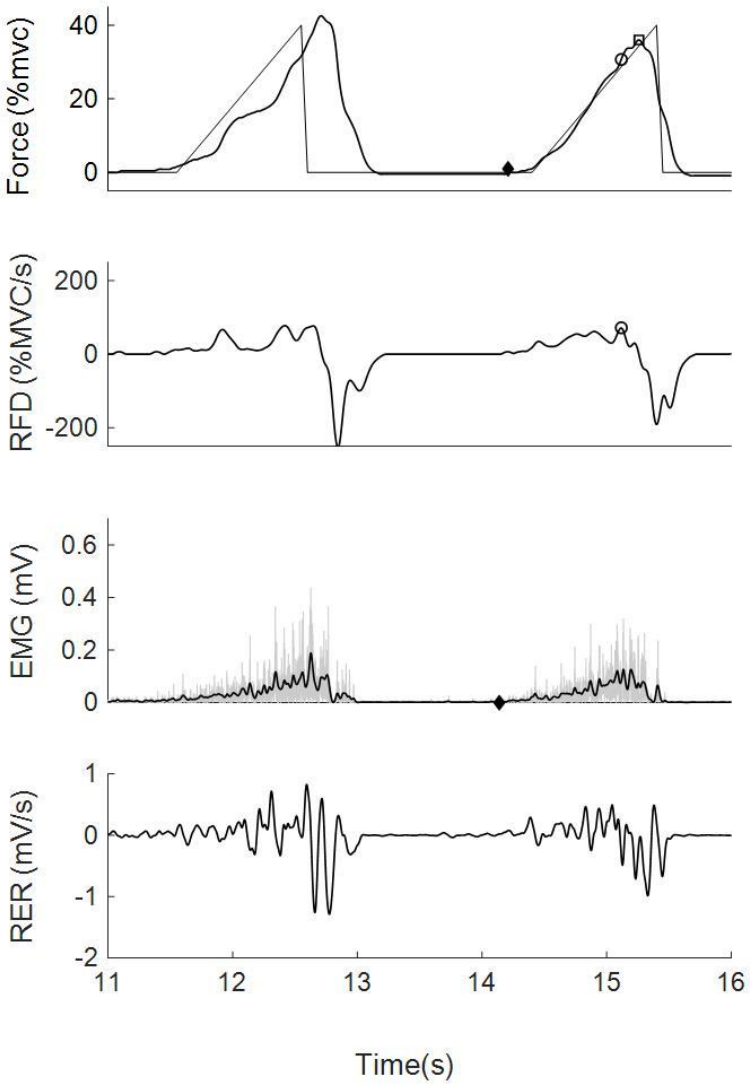

Figure 2.1 Example recording from the 40%MVC/s ramp condition. The Force plot shows the subject's force superimposed on the trajectory they were instructed to match. Diamond = force onset, circle = location of peak RFD, square = peak force. In the RFD plot the circle marks peak RFD. The EMG plot shows rectified (absolute value) EMG with (black line) and without (gray line) smoothing by a low pass filter (diamond marks EMG onset). RER is the derivative of the smoothed RMG. Based on visual inspection of the transition from rest to the prescribed RFD, only the right ramp was selected for analysis

Each set of ramps includes the different experimental conditions (described below). During the ramp conditions, the vertical resolution was .215%MVC/cm and horizontal resolution was 1.67s/cm. Participants also produced open-loop rapid force pulses guided by visual feedback from a vertical bar graph of their relative force level. During the rapid pulses, the vertical resolution is .175% MVC/cm. Instructions were to 'hit the approximate 40% MVC force level as quickly as possible without focusing on accuracy'. Subjects were encouraged to focus on speed rather than accuracy because previous work has shown that instructions for accuracy can reduce the rate of force development (Fitts, 1954).

Experimental Conditions

A trial consisted of either five to seven ramp force-time curves to 40% MVC with rates of force development of 20% MVC/s, 40% MVC/s, 80%MVC/s, 160%MVC/s, and 200% MVC/s or rapid force pulses performed "as quickly as possible". The ramps are asymmetrical with the linear increase in force followed by an instantaneous return to zero %MVC. Ramps were separated by two seconds and rapid force pulses were separated by one second. All trials were thirty seconds in duration with at least one minute between trials. For analysis, the participant's ability to transition from a resting force level to a linear increase in force with the prescribed slope was important. Therefore, based on visual inspection by the investigator, participants performed each rate of force development condition until five ramps of adequate performance were obtained. Participants then proceeded to the next

condition. The ramp force conditions were counterbalanced across participants. Two trials of rapid force pulses were performed last.

Data processing

Force and EMG data were processed using LABview v 2014 (National Instruments, Austin, TX) and visually inspected using programs written in Matlab (Mathworks, Natick, MA). Absolute strength scores are reported in Newtons (N) and, for analysis, the forces were converted to a percentage of MVC force (%MVC). Rate of force development was calculated from the force-time curve as the slope from a linear fit line of all data points within a .1s moving window (± .05s around each data point).

Electromyograms were adjusted for gain, de-trended and rectified (absolute value). Absolute EMG maxima from the MVC contractions are reported in millivolts (mV) and, for analysis, the EMG recordings were converted to a percentage of the RMS amplitude of EMG surrounding peak MVC force (%EMGmx, ± .250s window). Magnitude EMG measures were normalized to the EMGmx. A zero-lag 4^{th} order low-pass Butterworth filter with a 20Hz cutoff was used to create a linear envelope of the EMG and EMGmx was recalculated to reflect the smoothing (EMGmxs). Like RFD, rate of EMG rise (RER) was calculated using the slope from a linear fit line of all data points within a .1s moving window of the smoothed EMG (± .05s around each data point) and normalized the EMGmxs. This maintains the consistency of EMG treatment within the normalization process. User-interactive routines were written to

graphically display the signals of interest and calculate the dependent measures after selection of suitable ramps or pulses for analysis. Automatically determined landmarks were confirmed or corrected. The user selected ramp contractions for analysis based on the quality of the transition from a flat baseline to the rising slope of the given condition. Although subjects had practiced, they sometimes initiated force production too abruptly resulting in EMG spikes and RFD responses that were not consistent with the specified condition. These ramps were excluded from analysis to facilitate interpretation of EMG onset variables.

Force, RFD, EMG, and RER signals were plotted for visual inspection during analysis of all contractions. Markers identifying force initiation, peak force, peak RFD, EMG onset, peak EMG, and peak RER were inspected for accuracy and manually adjusted if necessary. The threshold for the onset of both force production and EMG onset was determined as the mean plus three standard deviations of an initial quiet period (Clark et al., 2011). Force measures include: peak force (PF), peak RFD (RFDPk), and average RFD (RFDavg). All EMG measures were taken from points prior to peak force and include: peak EMG amplitude (from unfiltered and smoothed data, EMGPk, EMGPks), peak RER (RERPk), RMS amplitude computed over the 30, 50 and 75ms following EMG onset (RMS30, RMS50, RMS75) and computed backwards from the instance of RFDPk (RMS30b, RMS50b, RMS75b), EMG AUC in the initial 30, 50 and 75ms following EMG onset (Q30, Q50, Q75) and computed backwards from the instance of RFDPk (Q30b, Q50b, Q75b). The 75ms upper limit of EMG calculations was based on evidence that neural excitation has the

prevailing influence on RFD to this point and contractile factors begin to dominate thereafter (Maffiuletti et al., 2016). The variables computed backwards from RFDPk were explored in search of alternate measures that would not require the determination of EMG onset, as this determination is known to be sensitive to the methodological approach in healthy individuals (Maffiuletti et al., 2016) and likely to be a greater challenge in people with movement disorders. RMS and Q were also calculated from EMG onset to PF (RMS-PF, Q-PF) and from onset to RFDPk (RMS-RFD, Q-RFD). Timing variables include: electromechanical delay (EMD), time to peak RER (TRERPk), time to peak EMG (TEMGPk and TEMGPKs), time to peak RFD (TRFDPk) and time to peak force (TPF).

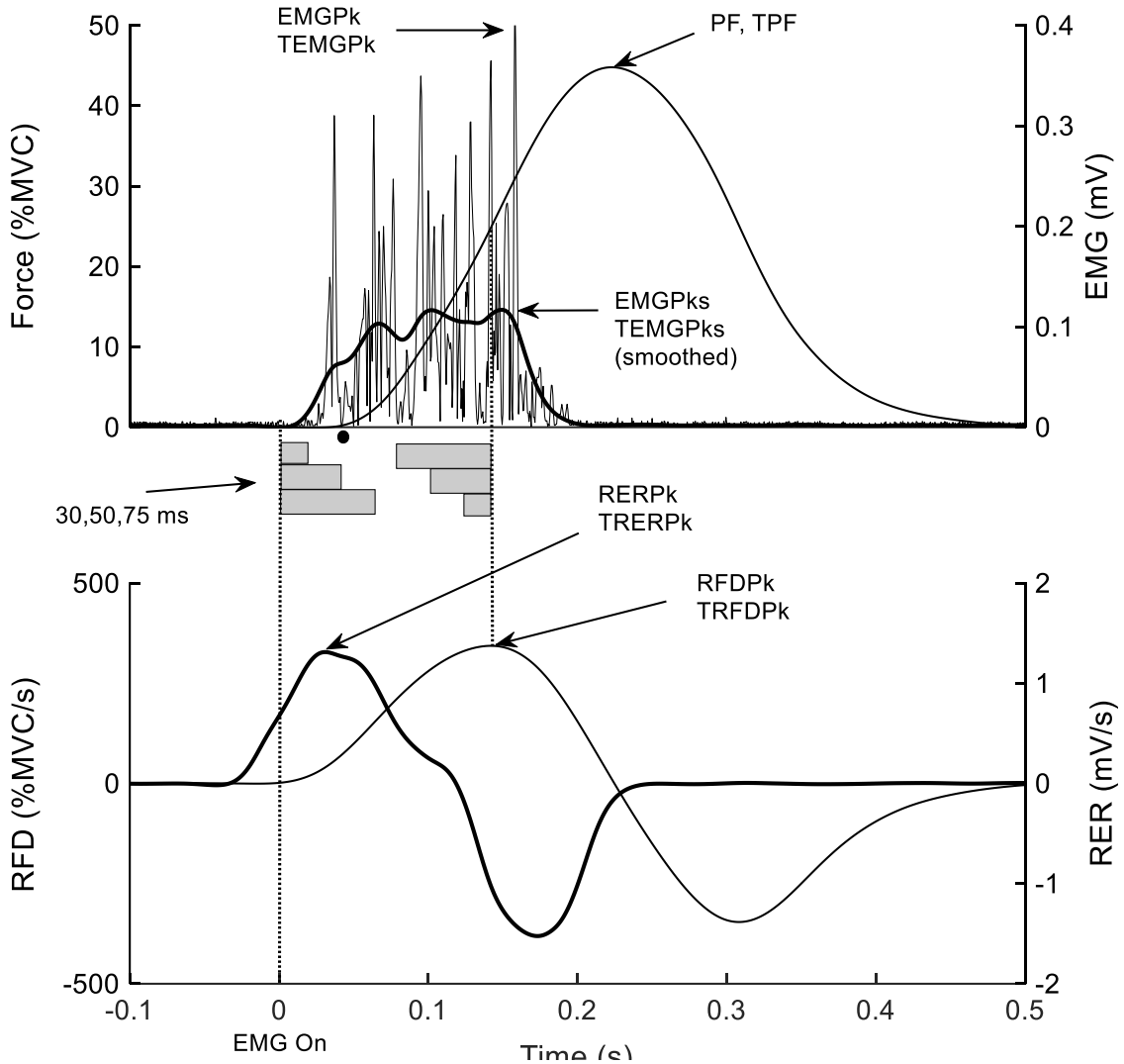

Figure 2.2 Representative rapid muscular contraction to 40 %MVC performed under instructions to produce force "as fast as possible". Top: Isometric force (thin unimodal line), rectified EMG burst (thin line) and rectified and smoothed EMG burst (thick line). Bottom: Rate of force development (thin line) and rate of EMG rise (RER, thick line). Magnitude and timing (T) measures: peak force (PF, TPF), peak rate of force development (RFDPk, TRFDPk), peak rate of EMG rise (RERPk, TRERPk), peak EMG (EMGPk, TEMGPk) and peak smoothed EMG (EMGPks, TEMGPks). TPF and TRFDPk are relative to force onset (dot). EMG timing is relative to EMG burst onset at 0 s. Gray bars illustrate the 30, 50 and 75 ms windows within which EMG RMS and Q measures were computed forward from EMG onset and backward from TRFDPk.

Statistical analysis

SPSS v24 (IBM, Armonk, NY) was used for analysis. Spearman's ρ correlations used to describe all relationships between measures because visual inspection revealed many instances of skewed distributions and heteroskedasticity. Considering the assumed application to research on rapid muscle contractions, analyses were conducted separately for all contractions (n=1081), and for the subset of contractions with an average RFD greater than 220 %MVC/s (n=249), which will be referred to as rapid, hereafter. In text, values are reported as a means ± standard deviations.

Results

The mean grip strength of the participants was 378.4 ± 102N. The mean dorsiflexion strength was 154.7 ± 33.2N. Both strength measures are consistent with other reports (Carroll, Joyce, Brenton-Rule, Dalbeth, & Rome, 2013; Massy-Westropp, Gill, Taylor, Bohannon, & Hill, 2011) and support the neuromuscular health of the sample. In the subset of rapid contractions RFDavg was 283 ± 44 %MVC/s, RFDPk was 385 ± 55 %MVC/s and TPF was 161 ± 25ms. The RFD measures are within the range of values shown for rapid dorsiflexion to 40 %MVC in Figure 1 of van Cutsem et al. (Van Cutsem et al., 1998) and the present time to peak force is slower than their pre-training value of 135.8ms which was obtained from the five fastest contractions in each of their subjects.

For each fixed-duration of computation (30, 50, 75 ms), RMS and Q measures were strongly correlated with each other in all contractions (ρ>.988) and in the subset of rapid pulses (ρ>.981). This redundancy is to be expected because integral measures computed over fixed periods of time are expressions of mean amplitude. For efficiency, only the fixed-duration RMS measures, rather than Q, will be emphasized from here forward.

Figure 3 shows the temporal progression and variance of events in the rapid contractions. Note that, for this figure only, TRFDPk and TPF are calculated relative to EMG onset rather than from force onset. Thus, all measures share a common zero time. Horizontal lines mark the 30, 50 and 75 ms windows within which the RMS measures were calculated. The median EMD for the rapid contractions was 35.5ms. Although differences between correlations were small, EMD was best predicted by RMS values calculated for the 50ms window, which is more likely to include RERPk (median TRERPk = 29.5 ms), than the 30 ms window. For RMS30, RMS50 and RMS75, correlations with EMD were -.511, -.515 and -.425, respectively. Compared to RMS50, RERPk was a relatively poor predictor of EMD (ρ=-.233) despite its temporal proximity.

Median TRFDPk was 123ms and 69ms in all and rapid contractions respectively. As RFDAvg increased, there was greater temporal coupling between RERPk and RFDPk with the standard deviations of the time between RERPk and RFDPk decreasing from 384ms in all contractions to 16ms in rapid. In rapid contractions, RERPk preceded RFDPk by a median value of 73.5ms. This duration is

a relevant consideration for the variables that are calculated backwards from the instance of RFDPk (RMS30B, RMS50B, RMS75B in Table2).

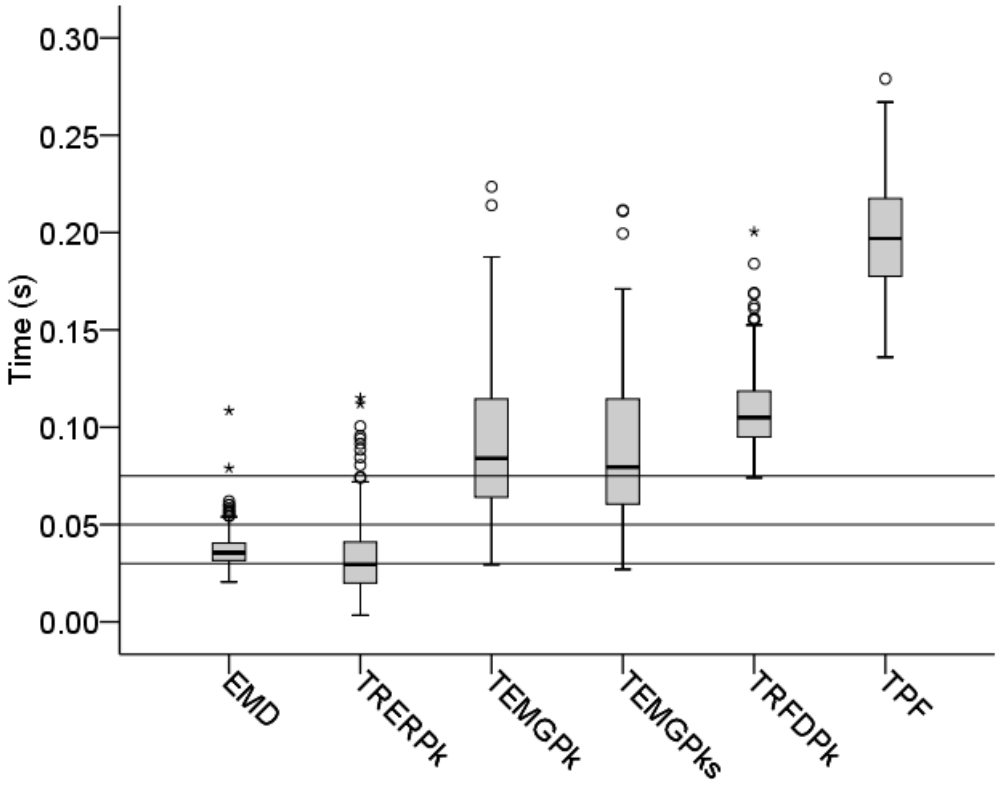

Figure 2.3 Box and whisker plot showing the progression of surface electromyography (EMG) and force events from 249 isometric muscle contractions with rates of force development (RFD) greater than 220 %MVC/s. All times are specified relative to the onset ofBox and whisker plot showing the progression of surface electromyography (EMG) and force events from 249 isometric muscle contractions with rates of force development (RFD) greater than 220 %MVC/s. All times are specified relative to the onset of the EMG burst. Each measure has a skewed distribution with a tail extending towards slower times. Variables are: electromechanical delay (EMD), time to peak rate of EMG rise (TRERPk), time to peak EMG (TEMGPk), TEMGPk using smoothed data (TEMGPks), time to peak RFD (TRFDPk) and time to peak force (TPF). That some values of TRERPk are less than EMD is a result of RER being computed from a .1s window of data. Horizontal reference lines at 30, 50 and 75 ms are shown to facilitate interpretation of EMG RMS and Q measures that were computed for these windows of time (see methods text for details). [created in SPSS]

Table 1 contains Spearman's ρ values for relationships between each EMG measure and RFDPk, RFDavg and TPF for all contractions and for rapid contractions. Although RFDAvg and TPF are not mathematically independent (TPF is part of the RFDavg computation) both are reported to confirm the notion that they are interchangeable. In all contractions and in rapid contractions, the correlations between RFDAvg and TPF were ρ=-.987 and ρ=-.797, respectively. In all contractions and in rapid contractions, the correlations between RFDPk and TPF were ρ=-.974 and ρ=-.697, respectively. Using an average of the Fisher transformed correlations involving all EMG variables, the magnitude of correlations is substantially less for the subset of rapid contractions (ρ=.371 vs. ρ =.617) due to a restricted range effect (Bland & Altman, 2011). Nevertheless, the relative strength of these correlations remains important to consider for research specifically involving rapid isometric contractions. Furthermore, if generalizations to clinical populations such as stroke are made, the correlations from data including the slower RFD contractions are more important.

For the set of all contractions, inverse correlations between Q-PF and the RFD variables were quite strong for reasons unrelated to neural excitation rate. The slowest ramp contractions required a prolonged period of neural excitation resulting in greater area under the rectified EMG curve due to increased duration rather than amplitude. Correlations between RMS-RFD and mechanical rate measures were consistently

greater than those involving RMS-PF. In the present dataset, RMS75 tended to have the strongest correlations with RFD and TPF measures. RERPk has the greatest support among the variables that did not require determination of EMG onset and was superior to the experimental variables that were computed backwards from the instance of RFDPk (e.g. RMS50B). Within each set of contractions, EMGPk (both unfiltered and smoothed) had a relatively poor correlation with RFD or TPF and bears the greatest variability in its timing (Figure 3).

Table 2.1 Spearman's correlations between EMG measures and Peak RFD, Average RFD and Time to Peak Force (TPF) computed for each force pulse. Correlations were calculated for all data (1081 pulses) and for the subset of rapid force pulses (249 pulses). RFD was normalized to maximal voluntary contraction force and all EMG variables were normalized to maximal EMG (see text for details). For each set of results the EMG variables are sorted in descending order based on their correlation with RFD Pk. RMS variables computed over fixed durations (30, 50 and 75 ms) were computed either forwards from EMG onset (RMS50, RMS50 and RMS75) or backwards from Peak RFD (RMS50B, RMS50B and RMS75B). RMS and Q variables were also computed from EMG onset to peak RFD (-RFD) or from EMG onset to peak force (-PF).

All Data (n=1081)				RFD Avg > 220 %MVC/s (n=249)			
EMG	RFD Pk.	RFD Avg.	TPF	EMG	RFD Pk.	RFD Avg.	TPF
RMS75	***0.80***	***0.81***	***-0.81***	***RMS75***	***0.52***	***0.51***	***-0.54***
RMS-RFD	0.74	0.72	-0.72	RMS50	0.51	0.53	-0.56
RMS50	0.71	0.72	-0.72	***RERPk***	***0.48***	***0.41***	***-0.40***
RERPk	***0.69***	***0.67***	***-0.66***	RMS-RFD	0.45	0.38	-0.33
RMS30	0.60	0.61	-0.62	RMS50B	0.43	0.36	-0.27
RMS75B	0.58	0.55	-0.54	RMS30	0.43	0.45	-0.50
RMS50B	0.58	0.55	-0.54	RMS-PF	0.41	0.34	-0.22
RMS30B	0.55	0.53	-0.52	RMS30B	0.39	0.33	-0.21
RMS-PF	0.52	0.51	-0.49	RMS75B	0.38	0.30	-0.22
EMGPk	0.23	0.21	-0.19	EMGPk	0.32	0.25	-0.17
Q-RFD	-0.25	-0.27	0.28	Q-RFD	0.22	0.14	-0.01
Q-PF	-0.78	-0.80	0.82	Q-PF	0.10	0.01	0.19

Table 2 contains the correlations among the candidate EMG measures for all contractions (above the diagonal) and for rapid pulses (below the diagonal). Throughout Table 2, several correlations among variables are strong as one would expect given their similarity. RMS75 and RERPk, the two variables bearing stronger correlations with contraction rate, are correlated at ρ=.75 and ρ=.86 for all and rapid

contractions, respectively. While related, these two variables also carry some amount of unique variance.

Table 2.2 Spearman correlations between all measures. Correlations based on all contractions are below the diagonal and correlations for the subset of rapid contractions (RFDAvg > 220 %MVC/s) are above the diagonal.

	RMS30	RMS50	RMS75	RMS-RFD	RMS-PF	Q-RFD	Q-PF	RER Pk	EMG Pk	RMS30B	RMS50B	RMS75B
RMS30		0.81	0.71	0.60	0.53	0.42	0.30	0.51	0.44	0.44	0.48	0.51
RMS50	0.88		0.89	0.72	0.62	0.49	0.33	0.68	0.53	0.49	0.58	0.62
RMS75	0.82	0.94		0.86	0.75	0.62	0.45	0.86	0.68	0.59	0.74	0.77
RMS-RFD	0.68	0.74	0.80		0.95	0.89	0.74	0.93	0.88	0.86	0.96	0.98
RMS-PF	0.60	0.61	0.64	0.88		0.91	0.87	0.86	0.90	0.86	0.93	0.96
Q-RFD	0.01	-0.05	-0.10	0.30	0.31		0.89	0.78	0.82	0.85	0.89	0.94
Q-PF	-0.33	-0.45	-0.52	-0.28	0.03	0.54		0.62	0.76	0.74	0.75	0.80
RER Pk	0.62	0.70	0.75	0.87	0.83	0.15	-0.25		0.80	0.73	0.88	0.91
EMG Pk	0.39	0.38	0.39	0.66	0.84	0.41	0.26	0.68		0.79	0.88	0.89
RMS30B	0.50	0.54	0.58	0.89	0.81	0.47	-0.09	0.75	0.66		0.91	0.88
RMS50B	0.53	0.57	0.61	0.93	0.84	0.48	-0.10	0.80	0.70	0.95		0.97
RMS75B	0.54	0.58	0.63	0.95	0.86	0.50	-0.09	0.82	0.71	0.93	0.98	

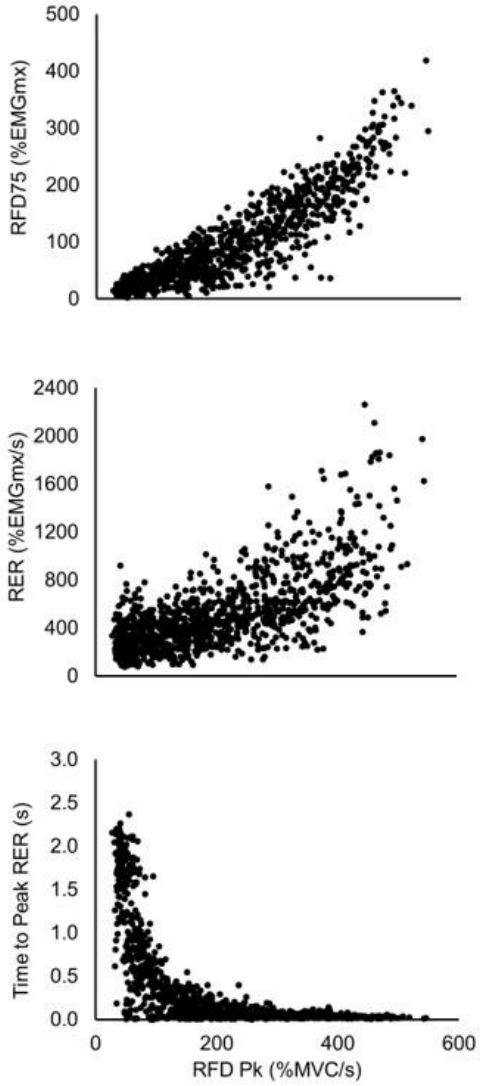

Figure 2.4 Scatter plots of RMS75, peak RER and time to peak RER against peak RFD. Greater variance in peak RER partly explains the stronger correlations observed with RMS75. Although subtle, the slight upturn in initial (RMS75) and peak (RER) neural excitation rates is consistent with what is known about the secondary firing rate range of the alpha motor neuron (Calvin, 1978; Kernell, 1965). The considerable reduction in variance in time to peak RER above 220 %MVC/s is representative of other timing variables including time to peak force and the time between peak RER and peak RFD. The reduced variance in neuromuscular function that is achieved in maximal-rate contractions is the key property described by Freund et al. (1978) to promote this model for the study of integrated systems physiology.

Discussion

The present findings are based on isometric dorsiflexion contractions to a force level of 40%MVC, which were performed by apparently healthy young adults. Subjects produced force at rates from 20%MVC/s to "as fast as possible". The fastest contractions observed in the present data approximate 500%MVC/s (Figure 4). Greater rates of force development could be achieved with rapid contractions to higher force levels. Nevertheless, the current sample includes a wide range of rates of force development that researchers may encounter in special populations and healthy active adults.

The primary metric used to evaluate the quality of candidate EMG measures was their Spearman's correlation with peak RFD. Several of the correlation coefficients cited to support certain variables cannot be considered strong ($\rho \approx .5$). This is not surprising because EMG measures are known to have high variability and the neural excitation of the agonist muscle is not the sole determinant of rates of force production. One must also consider contributions such as: muscle fiber shortening velocity, muscle strength, interactions between contractile and elastic tissues, and the involvement of synergist and antagonist muscles (Maffiuletti et al., 2016). While acknowledging that the candidate EMG measures only explained a portion of the variability in contraction rate, it was the relative strength of correlation coefficients that formed the basis of our conclusions.

Using the full set of data, relatively strong correlations were observed between several EMG measures and the three measures used to quantify contraction rate (peak RFD, average RFD and time to peak force). A subset of rapid contractions (RFDAvg >220 %MVC/s) was analyzed separately because most hypotheses related to RFD involve maximal rate contractions (sometimes described as most-rapid, ballistic or explosive force production). In the subset of rapid contractions, the correlations were lower overall but there was general consistency among the ranking of measures that we highlight. RMS75 and RERPk are emphasized due to relatively high correlations with peak RFD and because of meaningful differences in their computation. RMS75 is an amplitude measure that requires the determination of EMG onset. Peak RER is a true rate measure because it is calculated as the derivative of the rectified and smoothed electromyogram. A continuous RER signal can be computed for the entire electromyogram of interest and calculation of peak RER does not require the instance of EMG onset to be determined. Thus, issues related to EMG thresholds and technical or physiological challenges related to baseline can be avoided.

The ultimate consideration in selecting EMG variables is their suitability for a given hypothesis. For example, EMG measures that require accurate determination of EMG onset, such as RMS75, will be especially challenging in individuals with Parkinsonian tremor or spasticity. There are also movement conditions such as gait or bicycling in which a muscle may not consistently exhibit a quiet baseline. In these cases, a measure like RERPk has a distinct advantage. Among the tested measures that do not require EMG onset (peak EMG amplitude and variables computed

backwards from the instance of peak RFD), correlations between peak RER and peak RFD were superior. Compared to RMS and Q measures, RER appears less frequently in the literature. Nevertheless, an increasing number of studies support the validity of this measure. For example, decreases in RER have been associated with reduced RFD due to fatigue (Morel et al., 2015) and eccentric exercise (Farup, Rahbek, Bjerre, de Paoli, & Vissing, 2016). However, in the same manner that RMS and Q measures have been computed for fixed windows of time with respect to EMG onset, some have similarly calculated average RER (Farup et al., 2016). While this does not diminish the results of the cited study, this manner of calculation eliminates the advantage of RER as a measure that does not require EMG onset determination.

The present results favored calculations of RMS amplitude or integral (Q) measures over the longer tested duration (75 vs. 30 and 50 ms) following EMG onset. This was not surprising considering prior studies that linked this period of time with a greater neural contribution to RFD (Maffiuletti et al., 2016). RMS amplitude was superior to Q for measures that were bounded in time by the achievement of RFDPk or PF. The slower ramp contractions represented a special case for Q in which increased area under the curve was due to prolonged neural excitation rather than greater neural excitation (see negative correlations with RFD for Q-RFD and Q-PF in Table 1). This is a meaningful consideration for conditions such as stroke in which severe restrictions in peak motor unit firing rates have been observed (Chou et al., 2013). Without the ability to produce high instantaneous firing rates in rapid contractions, some individuals with stroke exhibited prolonged motor unit firing (more total spikes) to

reach a target force. With a varied duration of calculation in such conditions, a greater area under the rectified EMG can represent either greater firing rates and/or recruitment (high amplitude EMG, short duration) or impairment (low amplitude EMG, long duration). In contrast, RMS-RFD, RMS-PF or RERPk are temporally unconstrained measures that would more faithfully represent the quality of neural excitation.

Even though RMS75 (and Q75) were more strongly correlated with peak RFD than corresponding measures computed over 30 or 50ms, we do not suggest that these latter measures are flawed or that a minimal set of measures must be used. Some have effectively used a comprehensive sets of serial measures calculated from onset to 30-100ms (or greater) to test hypotheses about the temporal patterns in neural excitation with respect to RFD and how they might change with training in young (Aagaard et al., 2002) and older (Barry, Warman, & Carson, 2005) adults. While methodological recommendations would be simplified by empirical support for a small set of measures, the absence of a clearly distinct set of measures can also be viewed positively. Numerous studies have examined the role of neural excitation in rapid contractions using a variety of measures represented by those selected for this project. Strong correlations among EMG measures can provide some confidence that non-significant findings in various studies were not necessarily due to the selection of the wrong measure. For example, the choice between RMS or Q seems inconsequential for calculation over fixed window sizes. However, peak EMG amplitude does appear

to be a questionable measure compared to the others if one is interested in the determinants of RFD.

One interesting observation is that multiple EMG measures exhibited a slight upturn in neural excitation as RFD increased beyond 300-400 %MVC/s (see exemplar variables RMS75 and RERPk in Figure 4). While non-linearities in the EMG to force relationship are well-established, less attention has been given to the full continuum of the EMG to RFD relationship. The upturn observed in the EMG data parallels the bilinear response of the alpha motor neuron to increases in current injection (Calvin, 1978; Kernell, 1965), based on which the primary and secondary firing rate ranges were named. The secondary range is where very high initial motor unit firing rates, including doublets, contribute to the acceleration of force production ((Baldissera, Cavallari, & Cerri, 1998; John E Desmedt & Godaux, 1977; Hill, 1949) or limb movement (Harwood & Rice, 2014). Although multiple factors contribute to the surface electromyogram in addition to initial motor unit discharge rates, some have shown evidence of comparable changes in the first three inter-spike intervals and the initial phase of the rectified EMG burst in response to dynamic training (Van Cutsem et al., 1998). Some, but not all, of the subjects in the present study presented evidence of nonlinearity in the full EMG-RFD relationship and this is an interesting area for further study.

The use of a wide range of RFD conditions in the present study also provided the opportunity to observe key features of the transition from slow, closed-loop, force production to fast, open-loop, force production. When Freund *et al*(Freund &

Budingen, 1978) explained their interest in maximal rate isometric and isotonic conditions, they cited the benefit of a system's invariance when it is operating against the limits of its function. The bottom panel of Figure 4 shows one of multiple measures (time to peak RER) that exemplified the transition to relatively invariant system behavior as the rate of force development increased. While multiple studies have demonstrated invariant or nearly invariant time to peak force in rapid force pulses of varied amplitudes (J E Desmedt & Godaux, 1975; Freund & Budingen, 1978; Gordon & Ghez, 1987), there has been little systematic inquiry into the rate of force development at which neuromuscular control mechanisms achieve this state of invariance or the implications for optimal human performance and disease. Other measures with similar patterns of diminished variance included time to peak force, time to peak RFD and the time between peak RER and peak RFD. It might be the case that the ability to generate high initial firing rates is a necessary component of this invariance.

Limitations

Generalizations of the present findings beyond healthy young adults and outside of the tibialis anterior muscle should be made with caution. The onset-based measures, including electromechanical delay depend on the chosen method of threshold determination which may vary considerably across published studies. In the slowest contractions of the present study, initial neural excitation was less pronounced and more user intervention in the determination of EMG onset was required.

Conclusion

We examined multiple EMG measures to determine whether specific measures would have greater correlations with peak rate of force development. We were particularly interested in establishing whether peak rate of EMG rise (RER), taken from the derivative of the rectified and smoothed electromyogram, would have relationships with peak RFD that are comparable with measures computed in specific windows following EMG onset. Such knowledge would support RER applications to the study of rapid contractions in conditions such as Parkinson's disease where tremor sometimes hinders the determination of EMG onset. While RMS75 and Q75 had stronger correlations with peak RFD, RER was supported as the best non-onset-based alternative among the measures tested.

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Chapter 3

EXAMINATION OF THE RELATIONSHIP BETWEEN NEUROMUSCULAR EXCITATION AND RATE OF FORCE DEVELOPMENT

Abstract

In feline alpha motor neurons, a bilinear relationship exists between injected current and the neuron's firing rate. In a similar set up, researchers have shown there is a linear relationship between a current injected to the motoneuron and rate of force development (RFD). In humans, the bilinear relationship between elbow extension velocity and motor unit firing rate has been observed in anconeus muscle. However, the relationship between isometric RFD and neuromuscular excitation (NE) has been examined separately in slow ramp contractions and rapid force pulses, which leaves the understanding of the continuous relationship incomplete. The aim of this experiment was to determine the nature of the relationship between peak RFD and NE across a continuum of increasing RFD in healthy young adults. Twenty-one healthy young adults performed isometric dorsiflexion contractions to 40% of maximal voluntary contraction (MVC) force at increasing rates of force development while myoelectric activity of the tibialis anterior (TA) was recorded with surface electromyography (EMG). Onset (RMS75) and peak rate of EMG rise (RER) EMG measures were computed from the EMG as measures of neuromuscular excitation.

Akaike Corrected Information Criterion was used to calculate the best fit model between linear, bilinear, log-log transformation, and exponential. Akaike Information Criterion differences and weight determined the likelihood and confidence of each model. An analysis of peak RFD and peak RER revealed six individuals had a linear best fit and fifteen had a nonlinear best fit. More specifically, individual data showed linear to be the best fit for six, bilinear to be the best for thirteen, and exponential to be the best fit for two. Analysis of peak RFD and RMS75 revealed linear to be the best fit for fourteen and the remaining seven showed a bilinear best fit. The human RFD:RER relationship mirrors the bilinearity motor neuron firing behavior of felines in some but not all subjects. RER reveals the bilinearity more than RMS75. These findings may have implications for examining this relationship in special populations and simplifying determination of functional loss.

Introduction

Important aspects of the relationship between neuromuscular excitation and rate of force development (RFD) remain unknown in humans. Neuromuscular excitation (NE) can be examined with surface electromyography and represents the "composite electrical sum of all of the active motor units" (MU)(Robertson, Caldwell, Hamill, Kamen, & Whittlesey, 2004), primarily determined by the MU recruitment and rate coding mechanisms of force control (Gary Kamen & Gabriel, 2009). Feline preparations revealed a bilinear relationship between current injected into the lumbo-sacral nerve plexus (representing neural drive) and spinal motor neuron firing rates (Baldissera, Cavallari, & Cerri, 1998; Calvin, 1978; Kernell, 1965). The bilinear relationship consists of a primary firing rate range with a modest slope and a secondary firing rate range with a greater slope. Primary range firing rates are known to be sustainable and are similar to maximal firing rates observed in human studies on maximal strength or controlled (non-ballistic) force production (Connelly, Rice, Roos, & Vandervoort, 1999; G. Kamen & Knight, 2004), whereas secondary range firing rates are short lasting and typically occur at the onset of rapid muscle contractions (Desmedt & Godaux, 1977; Van Cutsem, Duchateau, & Hainaut, 1998) or in applications of peak velocity (Sogaard, Sjogaard, Finsen, Olsen, & Christensen, 2001).

Feline models also indicated a positive linear relationship between a current injected into a spinal motor neuron and RFD (Baldissera & Campadelli, 1977). Related to a more intuitive movement outcome, this relationship was further supported by the finding that increasing injected current reduces the time to achieve peak force

(Kernell, Eerbeek, & Verhey, 1983). Baldissera et al. conducted a key study in feline motor neurons involving both sinusoidal neural input with increasing frequency and ramp input conditions with increasing slope that illustrates how the alpha motor neuron switches from primary range to secondary range firing rates to overcome the low-pass filter effects of muscle (Baldissera et al., 1998). The central question in the present study is whether there is evidence of such bilinearity in measures taken from the surface electromyogram.

Considering the linear relationship between current that is injected to a motor neuron and RFD in animal studies, the volitional control of RFD in humans can similarly be used as an independent variable to manipulate the descending drive to the spinal motor neuron pool. The resulting neuromuscular excitation can be quantified using surface electromyography (EMG). Acknowledging other contributing factors such as muscle fiber type, muscle mechanics and antagonist involvement, RFD is mostly determined by the strength of descending drive and used to predict function or performance ability (Maffiuletti et al., 2016). In the condition of stroke, for example, impaired descending drive limits peak initial firing rate and the resulting maximal rate of force development (Chou, Palmer, Binder-Macleod, & Knight, 2013).

Few have examined the relationship between NE and RFD through the full range of volitional RFD in humans (Harwood, Davidson, & Rice, 2011). Rather, much of our knowledge on this topic is from studies that examined the extremes of the RFD:NE relationship, using either slow ramp or maximal rate muscle contractions. In studies on the adaptations to resistance exercise training, for example, increases in

maximal RFD were associated with increases in the rate of EMG rise (Aagaard, Simonsen, Andersen, Magnusson, & Dyhre-Poulsen, 2002) and initial MU firing rates (Van Cutsem et al., 1998) that are similar to the secondary range firing rates observed in felines. Computer simulations also support the role of secondary range motor unit discharge behavior in the rapid production of muscular force (Heller, 2010). However, few studies (Harwood et al., 2011) have detailed the middle range RFD conditions where the transition from primary range behavior to secondary range behavior is likely to occur.

The aim of this study is to provide a more complete description of the relationship between surface EMG measures of neural excitation and RFD, with a specific interest in determining whether the known underlying nonlinearities in motor unit discharge behavior are observable. We hypothesize that a non-linear relationship, and more specifically, a bilinear relationship will be observed. Such knowledge may support the application of electromyography to the study of neuromuscular function during rapid movements in health, pathology and human performance.

Ankle dorsiflexion was chosen as the model because the role of tibialis anterior (TA) in ambulation and because it has a substantial history in relevant motor control research (Connelly et al., 1999; Desmedt & Godaux, 1977; Feiereisen, Duchateau, & Hainaut, 1997; Van Cutsem et al., 1998). Studies have examined motor unit discharge behavior during ramp (Van Cutsem, Feiereisen, Duchateau, & Hainaut, 1997) and ballistic contractions (Desmedt & Godaux, 1977), and recruitment order (Feiereisen et al., 1997). TA MU discharge behavior has been examined with aging (Connelly et al.,

1999), and in people with stroke (Chou et al., 2013). Exercise training can increase initial MU firing rates in the TA with corresponding increases in RFD and evidence of the neural adaptation in the EMG burst (Van Cutsem et al., 1998). In related studies on NE and motor control, neuromuscular activity in the TA was more strongly correlated to center of pressure and balance measures than EMG from the triceps surae (Di Giulio, Maganaris, Baltzopoulos, & Loram, 2009).

Based on evidence of bilinearity in previous motor control research, a strict bilinear model of the data was our first model. Two other models were tested using guidance from the analysis of blood lactate concentration curves. The nonlinear relationship between blood lactate concentration and exercise workload was first reported in 1930 (Owles, 1930). Beaver, Wasserman, and Whipp determined that the best mathematical fit for this relationship used log-log transformation (Beaver, Wasserman, & Whipp, 1985). Later researchers found that an exponential model is most representative of the underlying physiology (Hughson, Weisiger, & Swanson, 1987). For our purposes, the null hypothesis states a linear relationship between surface EMG measures of NE and RFD, establishing our fourth model. Therefore, the models tested in the present study were linear, bilinear, log-log transformation, and exponential. One potential advantage of a bilinear fit is that the intersection between the two lines identifies a specific physiological change point of interest, similar to the lactate threshold. If bilinearity in EMG is directly related to the underlying firing rate behavior, this change point might approximate where the discharge behavior switches from the primary range to the secondary range.

Methods

Twenty-one healthy young adults, ten females and eleven males, (mean ± SD: age=21.7 ±2.7 years old, body mass = 73.6 ± 20.2 kg, height=1.7 ± 0.1 m, maximal grip strength = 39.5 ± 10.2 kg) participated in this study. All participants were university students and free of neurological deficit or disorder, lower body dysfunction, and recent (<6 months) lower body injuries. All participants signed a university approved informed consent before beginning the study.

Procedures

Data were collected during a single testing session. Participants were seated on a custom wooden bench that placed the knee at 70° flexion from full extension and the ankle into 20° of plantar flexion from neutral. The left foot was fastened with a non-elastic buckle strap to a plate that was affixed to a strain gauge force transducer (Model SM-100, Interface Force Inc., Scottsdale, AZ). Force was amplified, and hardware filtered (low pass, 50Hz) at the time of recording (Model SGA, Interface force Inc, Scottsdale, AZ). The skin above the tibialis anterior was shaved, abraded, and cleansed with ethyl alcohol. A pre-amplified double differential surface electrode was secured to skin above the mid-belly region of the tibialis anterior muscle (MA-300, Motion Lab Systems, Baton Rouge, LA). Signals were recorded at 2kHz and

digitized with 24-bit resolution (CDAQ-9178 and module NI9239, National Instruments, Austin TX). Participants were asked to perform isometric dorsiflexion contractions at low force levels to evaluate the quality of electrode placement and adjust amplifier gains. Participants then performed three maximum voluntary isometric contractions (MVCs) separated by two minutes of rest. The maximum force achieved was used to present relative force levels (%MVC) in visual feedback. Participants viewed their relative isometric force in real time on a computer monitor (61 cm diagonal screen size) positioned at eye level at approximately 1.3m away. Participants were asked to produce force to match a static plot showing a set of linear ramp force-time curves (figure 1).

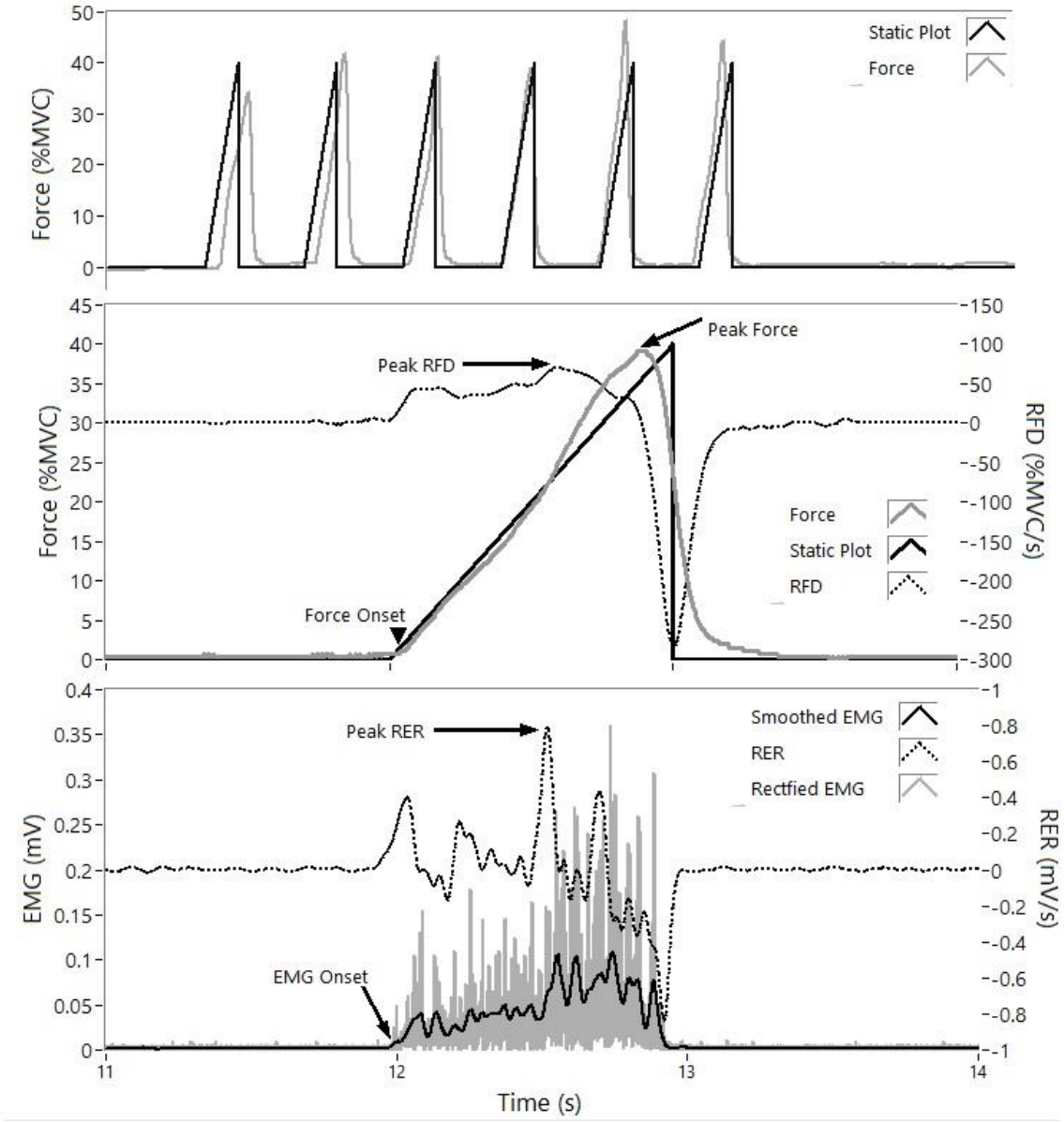

Figure 3.1 A sample force-trace for 40%mvc/s and processing. The top graph the static plot (black line) and force produced by the participant (gray line). The middle graph is zoomed to 11-14 seconds of the top graph with the addition of the df/dt (RFD, dotted line). Time of force onset along with peak RFD and peak force values and times were recorded. The bottom graph is the rectified (gray line), smoothed (black line), and dEMG/dt (RER, dotted line). Time of EMG onset and peak RER time and value were recorded.

Each set of ramps included the different experimental conditions (described below). During the ramp conditions, the vertical resolution was 0.215 %MVC/cm and horizontal resolution was 1.67s/cm. Participants also produced rapid force pulses using a vertical bar graph of their relative force level as feedback. During the rapid pulses, the vertical resolution was 0.175 %MVC/cm. Participants were given instructions to 'hit the approximate force level as quickly as possible without focusing on accuracy' since instructions for accuracy can reduce the rate of force development in these tasks (Gordon & Ghez, 1987). DASYlab v.13 (National Instruments, Austin, TX) was used to control data acquisition and provide all real-time biofeedback of isometric force production.

Experimental Conditions

A recording contained either ramp contractions or rapid force pulses to 40%MVC. There were five different prescribed rates of force development conditions (20% MVC/s, 40% MVC/s, 80%MVC/s, 160%MVC/s, and 200% MVC/s). Rapid force pulses were performed "as quickly as possible" to 40% MVC. The ramps were asymmetrical with the linear increase in force followed by an instantaneous return to zero %MVC resulting in a sawtooth pattern (figure 1). Ramps were separated by 2 seconds. Pulses were separated by 1 second. Recordings were thirty seconds in duration with at least one minute between. Due to the use of an EMG measure computed from the onset of each EMG burst, the participant's ability to transition

from a resting force level to a linear increase in force was important. Therefore, based on visual inspection by the investigator, participants practiced each rate of force development condition until five ramps of adequate performance were obtained. Participants then proceeded to the next condition. The ramp force conditions were counterbalanced across participants. Acknowledging the potential for an order effect, but trying to diminish the potentiation effects of rapid movement (Bernard et al., 2003) the participants' final condition was always two recordings of rapid force pulses.

Signal processing

Force and sEMG data were processed using LabVIEW v. 2014 (National Instruments, Austin, TX). A time-varying rate of force development signal was calculated from the recorded force-time curve as the slope from a linear fit line of all data points within a .1s moving window (± .05s around each data point). All values derived from the force-time curve were normalized to MVC force. After adjusting for gain, removing DC offset, and bandpass filtering between 10-990Hz, the EMG was absolute value rectified. The root mean square amplitude of the initial 75ms (RMS75) of neuromuscular excitation was calculated. A linear envelope of the rectified EMG was created by applying a zero-lag 4^{th} order low-pass Butterworth filter with a 20Hz cutoff. Like the RFD signal, a time-varying rate of EMG rise (RER) signal was calculated from the linear envelope using the slope from a linear fit line of all data points within a .1s moving window (± .05s around each data point) of the sEMG signal. The EMG recordings were normalized to the RMS amplitude of EMG in the

maximal MVC trial (± .250s window surrounding MVC) which was filtered similarly. User-interactive routines were written to graphically display the signals of interest and calculate the dependent measures. The force, RFD, linear envelope of sEMG, and RER signals were plotted for visual inspection during analysis of all contractions. Peak RER was used as a representative of peak neuromuscular excitation whereas RMS75 is representative of the amplitude of neural excitation during the initiation of the contraction.

2.4. Model Selection

Although some conventions would place NE on the abscissa as the physiological determinant of RFD (ordinate), RFD is represented on the abscissa in this study for consistency with the early feline models and knowing that volitional RFD in the experimental conditions is a surrogate for descending drive. The referent model (model 1) is a strict linear relationship, which is defined as:

$$y=ax+b$$

where 'a' is the slope of the line, 'x' is the peak RFD, and 'b' is the y-intercept.

Model 2 is based on a strict bilinear relationship that has been seen in early neurophysiology research. This relationship is defined as:

$$y = \begin{cases} a_0 + a_1 x & if\ x \leq x_0 \\ b_0 + b_1 x & if\ x > x_0 \end{cases}$$

where

$$x_0 = \frac{a_0 - b_0}{a_1 - b_1}$$

where ‘y’ represents the estimated peak rate of neuromuscular excitation, ‘x’ represents the peak rate of force development, ‘a_0’ represents a constant of the first linear relationship, ‘a_1’ represents the slope of the first linear relationship, ‘b_0’ represents a constant of the second linear relationship, ‘b_1’ represents the slope of the second linear relationship, and x_0 is the change point where the two relationships intersect.

Model 3 is a bilinear fit following a log-log transformation. For this model, the log values were found for both peak RFD and peak RER prior to fitting it into the same bilinear relationship listed above.

Model 4 is based on an exponential relationship. This relationship is defined as:

$$y=ae^{(bx)}+c$$

where ‘y’ represents the estimated peak rate of neuromuscular activation, ‘x’ represents the peak rate of force development, ‘a’ is the y-intercept, ‘b’ is the growth factor, and ‘c’ is a constant.

Data analysis

Using a custom LabVIEW program (National Instruments, Austin, TX), the four-candidate models were fitted iteratively with lines of best fit until the least mean square error was found. The corrected Akaike Information Criterion (AICc) (Shono, 2000), the bias-corrected, small sample-size form of Akaike Information Criterion (AIC) (Akaike, 1973) was used to inform model selection. AIC is calculated from the mean square error of the line of best fit for each model. The formula is:

$$AIC=n\log(MSE) +2K + n(1 + \log(2\pi))$$

where ‘n’ is the total number of points used to determine the line of best fit and ‘K’ is the number of fitted parameters. The bias-corrected AICc is:

$$AICc=AIC + 2K(K + 1)/(n-K-1)$$

where again ‘n’ represents the total number of points used to determine AIC and ‘K’ is the number of fitted parameters. As ‘n’ increases AICc approaches AIC.

The model with the lowest AICc was selected as the "best" model of the four tested. Burnham and Anderson (Burnham, Anderson, & Burnham, 2002) classified the differences of selected models from the AICc minimum ($\Delta_i = AICc_i - AICc_{min}$) as follows: $\Delta_i > 10$, there is no support for the model and it may be excluded from further consideration. $\Delta_i < 2$ have substantial support and $4 > \Delta_i > 7$ is considered to have less support. The Akaike weight (w_i) of each model is calculated to determine the evidence of the model being the best fit of the available models. It is the likelihood of each model divided by the sum of the likelihoods of all models. Akaike weight is calculated as:

$$w_i = (\exp(-.5\Delta_i))/(\Sigma^4_{k=1}\exp(-.5\Delta_k))$$

where '$\exp(-.5\Delta_i)$' is the likelihood of a given model (Wagenmakers & Farrell, 2004). For our purposes, w_i will be multiplied by 100 and expressed as a percentage of the total weight of the models (100%). Examination of the Akaike weights by dividing the best by another chosen weight ($w_{best\ fit}/w_i$) is used to reveal the relationship between the two models.

Results

The mean grip strength for the participants was 378.4 $\pm$ 102N. The mean dorsiflexion strength was 154.7 $\pm$ 33.2N. Both strength measures are consistent with

other reports (Carroll, Joyce, Brenton-Rule, Dalbeth, & Rome, 2013; Massy-Westropp, Gill, Taylor, Bohannon, & Hill, 2011) and support the neuromuscular health of the sample.

Model testing at the level of the individual is more appropriate for the stated hypothesis considering that aggregate data might hide nonlinearity if y-intercepts, slopes and parameters of curvature are not consistent across individuals. This approach is consistent with the individual computation of blood lactate curves (Hughson et al., 1987).

Using RER to quantify neural excitation, the linear fit was best in six participants while a non-linear fit was best in fifteen. A chi square test indicated that this is a significant (X^2=3.86, p=.05) departure from an equal distribution across linear and nonlinear models. More specifically, linear model was the strongest for six participants and had substantial support (Δ_i <2) or support (4<Δ_i <7) for nine other participants. The bilinear model was the strongest fit for thirteen participants and had substantial support or support for five participants. The remaining three participants had an AIC difference less than 10, thus a bilinear fit must still be considered. Log-log transformation was the strongest fit for no participants and had one participant with an AICc differences below the threshold for consideration. Exponential was the strongest fit for two participants and had substantial support or support for thirteen other participants. An exponential fit should still be considered for another three participants. The breakdown of individual participant means square errors and AICc values can be viewed in table 1. Each bilinear fit has a change point separating the

primary range from the secondary range. The mean primary range slope was 0.51, the mean secondary range slope is 3.21, and the mean peak RFD where neuromuscular excitation changes from primary to secondary range is 203.9 %MVC/s. Table 2 reports the primary slope, change point, and secondary slope for each participant with a bilinear fit as the strongest.

Table 3.1 : Individual participants peak RFD and peak RER mean square error and AICc values for the four models. Linear fit was strongest for 6/21 participants. Fifteen participants had a non-linear fit. Of the non-linear best fits: Bilinear was strongest for 13/21, Log-log strongest for 0/21, and Exponential strongest for 2/21. *=strongest fit

	Linear		Bilinear		Log-Log		Exponential	
Subject	MSE	AICc	MSE	AICc	MSE	AICc	MSE	AICc
1	21369	537.9	11011	519.2*	199270	640.8	13272	524.5
2	1995	730.54	1706	728.2*	1736	729.4	1836	731.1
3	13572	593.0	9783	586.2*	167267	722.5	10867	588.9
4	5925	495.6	4109	488.9*	36356	582.6	5219	496.7
5	25358	856.6	15509	832.8	74819	936.7	15459	830.3*
6	23215	657.4*	22862	665.5	185596	772.3	23904	665.4
7	27082	834.9	23101	833.4*	165532	959.4	25242	836.7
8	9185	681.9	7549	679.5	55121	792.8	7814	679.1*
9	7056	877.5	5928	873.0*	33399	1002.6	7048	883.7
10	4284	492.8	3467	492.5*	53282	612.8	3884	495.1
11	16741	767.1	12291	756.2*	220095	932.2	14198	762.7
12	16105	350.7*	14956	358.4	156839	424.2	15419	356.5
13	27222	756.9*	25592	762.1	466505	930.4	35247	778.3
14	15268	536.3	11894	534.6*	177698	650.9	12842	535.4
15	11400	535.9*	10141	539.8	52245	611.9	10677	539.6
16	23703	787.6*	22351	792.7	190012	923.0	23444	793.3
17	5978	784.3	4088	767.1*	44508	929.4	4467	770.9
18	26702	534.3*	26262	542.7	123688	606.2	26652	540.8
19	30785	645.5	17689	627.2*	262340	759.4	21659	634.8
20	51723	725.7	42538	724.1*	521499	857.0	47552	727.7
21	12565	810.3	9164	798.1*	128431	972.3	11194	809.0

Table 3.2 shows the primary range slope, change point, and secondary range slope for all participants showing in whom a bilinear best fit was best. A paired t-test revealed a significant difference between the primary and secondary slopes ($t = -6.668$, $p<0.001$).

Subject ID	Primary slope	Change point (RFD%MVC)	Secondary slope
1	0.499	285.1	3.624
2	0.196	162.1	0.894
3	0.737	232.0	2.941
4	-0.174	154.0	1.954
7	-0.765	154.7	1.858
9	-0.186	120.5	1.793
10	0.102	126.3	1.796
11	1.334	256.7	6.024
14	1.249	222.0	3.986
17	0.675	181.8	2.063
19	1.611	367.3	7.994
20	1.692	256.8	4.386
21	-0.279	131.9	2.459
MEAN	**0.515**	**203.9**	**3.213**
Standard Deviation (±)	**0.784**	**73.8**	**1.994**

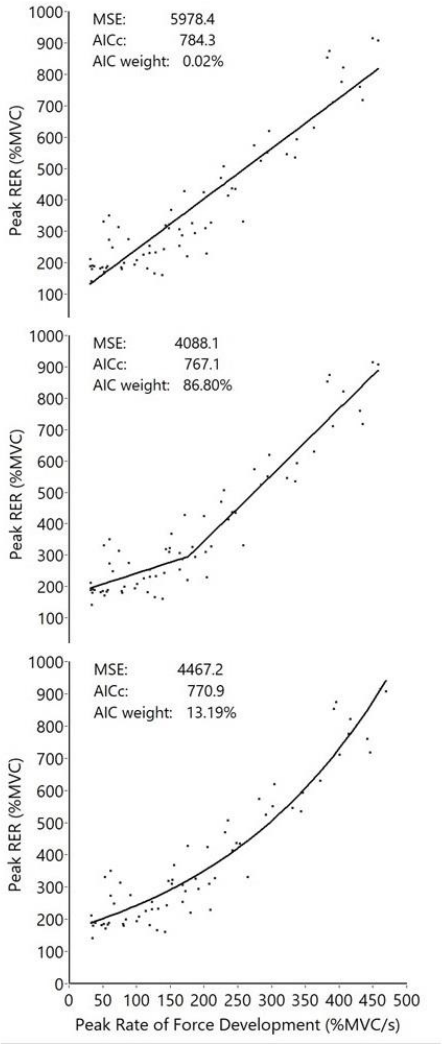

Figure 3.2 Linear, bilinear, and exponential fit for participant number 763. The MSE, corrected AIC, and AIC weight (% likelihood of each fit being the best fit) are listed on each figure. The bilinear fit was best for this participant and the change point was at an RFD of 169.8%MVC/s. Notice the AIC differences between bilinear and exponential (3.8) and bilinear and linear (17.2). With a difference of 3.8, exponential still has strong support for the likelihood of it being a fit whereas an AIC difference of 17.2 is above the threshold of 10 (see methods for more detail) for support and is eliminated from likelihood.

Models based on neuromuscular excitation at movement initiation (RMS75) were examined similarly. The AICc, and AIC Weight for each fit for individuals are reported in table 3. The linear fit was the best fit for fourteen participants with three others having substantial support or support for a linear fit. A bilinear fit was the best fit for seven participants and had substantial support or support for another nine participants. Bilinear fit should still be considered possible for the remaining five participants. Log-log transformation was eliminated from consideration for all participants as the lowest AICc difference was outside of the consideration range ($\Delta_{\text{Log-log}} > 196$, $\Delta_{\text{consideration}} < 10$), and an exponential fit had substantial support or support for seven participants and for another seven, exponential fit should be considered.

Table 3.3 The corrected AICc and AIC weight for different models of fit for peak rate of force development (RFD) and the RMS EMG of the initial 75ms of neuromuscular excitation. Log-log transformation was eliminated from consideration due to all AIC differences being greater than 10 (see methods for details) and is not reported here. *denotes strongest fit

	Linear		Bilinear		Exponential	
	AICc	AIC Weight	AICc	AIC Weight	AICc	AIC Weight
1	273.0	0.3	261.6*	98.9	271.4	0.7
2	272.7	14.5	270.0*	57.1	271.4	28.4
3	336.0*	58.9	336.7	40.4	344.7	0.7
4	222.5*	90.3	228.7	4.1	228.0	5.6
5	467.8	0.1	453.9*	94.4	459.6	5.5
6	367.7*	94.1	373.3	5.9	388.3	0.0
7	450.6*	91.5	455.4	8.5	476.4	0.0
8	301.5*	97.2	309.3	2.0	311.2	0.8
9	436.0*	81.3	438.9	18.6	448.2	0.2
10	272.5*	81.1	277.3	7.4	276.4	11.5
11	428.7*	92.2	435.5	3.1	434.6	4.7
12	181.4*	96.0	190.3	1.1	188.4	2.9
13	400.2*	84.9	403.7	15.0	414.7	0.1
14	309.7*	98.6	318.2	1.4	326.1	0.0
15	296.9*	96.2	304.2	2.5	305.4	1.3
16	380.8	0.0	359.8*	92.8	364.90	7.2
17	383.0	28.4	381.3*	67.8	387.0	3.8
18	286.8*	97.7	295.9	1.1	295.6	1.2
19	348.8	0.0	326.4*	99.6	337.1	0.5
20	350.8*	95.8	357.1	4.2	380.3	0.0
21	378.8	7.3	373.7*	90.7	381.3	2.0

Discussion

The aim of this study was to provide a more complete description of the relationship between surface EMG measures of neuromuscular excitation (NE) and rate of force development (RFD) during isometric muscle contractions, noting known

nonlinearity of underlying motor unit discharge behavior. A nonlinear relationship between peak NE and RFD was observed in 15 of 21 participants and in 13 of these participants the best fitting model was bilinear. While nonlinearity was not the best fit model in all participants, that 71% of the participants demonstrated nonlinearity best fit and all participants had some level of support specifically for bilinearity warrants further inquiry into this detail of neuromuscular excitation. That the AIC differences allow a bilinear fit to remain in consideration even when a linear fit was best, strengthens the hypothesis of the existence of a movement velocity threshold.

In a similar study that examined motor unit discharge rate and surface EMG during dynamic contractions, the expected bilinearity was observed in the motor unit results but not in surface EMG (Harwood et al., 2011). The absence of bilinearity in surface EMG was not surprising considering that it has not been observed in other EMG studies with rate manipulations (e.g. Le Bozec et al., 1980) and that surface EMG measures are more sensitive to changes in motor unit recruitment than firing rate (Christie et al., 2009). The observations of bi-linearity in the present study may have been promoted by experimental design parameters including data analysis at the individual level, the use of RER to quantify EMG, and a large number of trials across a wide range of RFD conditions.

Consistent with bilinear motor unit firing behavior observed in anconeus (Harwood et al., 2011), the present results support a change point in the relationship between volitional RFD (as a surrogate for descending drive) and the rate of neuromuscular excitation as measured with surface EMG. Above this change point,

the relationship bears a greater slope, which parallels the bilinear behavior of the motor neuron observed in both feline (Kernell, 1965) and human (Harwood et al., 2011) studies. Variance in the location of the change point in our participants suggests that there may be an individual-specific threshold for secondary range firing behavior. In feline studies that used both sinusoidal and ramp input to the motor unit, a property of the motoneuron called 'dynamic sensitivity' was credited with overcoming the low-pass filter effects of muscle tissue and optimal mechanical output depended on the matching of neuron to contractile properties (Baldissera et al., 1998). It might be the case with humans *in vivo* that the change point will vary according to contractile and elastic properties of the involved tissues and it will be subject to the influence of muscle length and velocity. The observed variance in the change point also confirms the importance of examining bilinearity in individual subject data rather than in group data.

Despite any similarity to the bilinearity observed in motor unit data published elsewhere, it is important to understand that none of the present data provide direct evidence that secondary range motor unit firing behavior is visible in the surface electromyogram. One must also consider the contributions of motor unit recruitment and technical factors. Nonlinear summation of electrophysiological potentials from higher threshold motor units is a possibility. In both the first dorsal interosseous (Masakado et al., 1994) and tibialis anterior (Fling, Knight, & Kamen, 2009) muscles, the macro-EMG technique supports a moderate positive correlation between a motor unit's recruitment threshold and its electrophysiological size. There is also the

possible effect of amplitude cancellation (AC), which might actually make it less likely to observe secondary range behavior in the surface electromyogram. However, while simulation studies have provided some information about the effects of excitation (force level) on AC, the complex interplay between excitation rate, recruitment and AC makes the clear generalization of AC studies to the present findings tenuous.

Recruitment dynamics are nonlinear. During slow ramp contractions of TA, recruitment of recorded motor units occurs up to 88% of MVC with a greater relative number of them being recruited early (Feiereisen et al., 1997). Furthermore, there is a strong influence of RFD on recruitment threshold force. During rapid isometric (ballistic) contractions, the recruitment threshold force of motor units in TA is reduced by 70% compared to the corresponding ramp threshold force (Desmedt & Godaux, 1977). In simulation studies that represent ramp and not ballistic conditions, Keenen (Keenan, Farina, Maluf, Merletti, & Enoka, 2005) examined the effects of excitation level on AC. The greatest difference between normalized EMG with and without simulated AC occurred at 40% excitation. At what force level 40% excitation occurs is difficult to determine as the NE:Force level relationship was not assessed in the simulation. Futhermore, according to Farina et al. (Farina, Merletti, & Enoka, 2014), AC increases as neural drive and/or amplitude increases. So, if AC is more likely to exist in the present rapid contractions to 40%MVC, the question remains; how would AC affect the non-linear relationship in only some participants?

Through this project, it became increasingly clear that the detection of nonlinearity or bilinearity is highly sensitive to the EMG measure used. Pilot data were used to guide our selection of the measures. Among candidate variables, the root-mean-square amplitude of the first 75 ms of the EMG burst (RMS75) and the peak rate of EMG rise (RER) were chosen based on having the greatest correlations with peak RFD. Despite a moderate Spearman's correlation of ρ=.75 between RMS75 and RER in the current dataset, the results of model fitting was markedly different for the two measures. This observation alone indicates that the ability to detect nonlinearity in this relationship is highly sensitive to the chosen measure. It may also be the case that there is a more sensitive measure than peak RER. Considering the present findings, one might expect that populations with diminished RFD would not exhibit similar nonlinearity in the RFD:NE relationship; the nonlinearity might be absent, or the slope of the secondary range behavior might be less.

The relationship between rapid contractions and neural excitation was discussed by Corcos and colleagues (Corcos, Gottlieb, & Agarwal, 1989) as part of a speed-sensitive strategy. From their surface EMG measures, they surmised that high initial motor unit firing rates are necessary for rapid movement. This prediction is partly supported by findings of diminished peak firing rates and neural excitation in older adults (Klass, Baudry, & Duchateau, 2008) and people with stroke (Chou et al., 2013) who both experience reduced RFD. Considering the extensive studies that have been done on the control of slow and fast rates of movement or force development in health and disease, it may be surprising that few, if any, studies have reported

bilinearity in the EMG to rate relationships. In addition to the influence of variable selection, it is likely also the case that few studies have been designed based on hypothesized bilinearity and with adequate data points obtained above and below the possible break point. Without adequate sampling, curve fitting with EMG measures that are expected to be highly variable would be challenging. In fact, the present study was limited by restricting contractions to 40% MVC. If conditions included maximally rapid contractions to a variety of greater force levels, the present description would be more complete and greater support for bilinearlity may have been observed.

Determining why most, but not all, individuals have a nonlinear RFD-NE relationship requires further consideration. Exploratory analysis comparing linear to non-linear groups was performed for sex, grip strength normalized to body mass, dorsiflexion MVC normalized to body mass, BMI, body mass, and participation of high intensity activity in the previous year. Due to the small sample size (N=21), Fisher's Exact Test was used for the influence of sex and activity. Independent t-tests comparing linear and non-linear groups were used for BMI, body mass, normalized MVC, and normalized handgrip. The Fisher's exact test revealed no differences in best fit by sex ($p=.633$) or participation in recent high intensity activity ($p=.523$). Independent t-tests showed there were no differences in BMI ($t=1.004$, $p=.359$), body mass ($t=1.730$, $p=.100$), normalized MVC ($t=0.686$, $p=.501$), or normalized handgrip ($t=-1.019$, $p=.321$). Another factor that might explain the mixed observations of nonlinearity across participants is heterogeneous compliance of the muscle tendon (M-

T) unit. During slower movements, a more compliant tendon results in a lower rate of force development (Earp et al., 2011; Wilkie, 1950) by allowing for greater lengthening prior to force development. As greater lengthening occurs, greater NE may be required to achieve the prescribed RFD in the lower RFD conditions.

A limitation of this study is that contributions from antagonist musculature were not measured. Older individuals exhibit greater co-activation indices across the ankle joint with a corresponding decrease in RFD when compared to healthy young adults (Thelen, Schultz, Alexander, & Ashton-Miller, 1996). Corcos et al. (Corcos et al., 1989) have shown that the size of the antagonist burst also scales with movement speed. Depending on the nature of the antagonist involvement, co-contraction could be a factor that influences the relationship between neural excitation of the agonist and the resulting RFD. Moving forward, identifying the role of co-contraction in the RFD:NE relationship is important and will influence the interpretation and estimation of underlying neural activity based on peak RFD.

The aim was to provide a more complete description of the relationship between surface EMG measures of neural excitation and RFD, with a specific interest in determining whether the known underlying nonlinearities in motor unit discharge behavior are observable. Results support a bilinear relationship between rate of EMG rise and RFD in the 100% of the subjects and we have found that this observation is highly sensitive to the selection of the EMG measure. These results support continued systematic work on this topic. If such bi-linearity can be reliably observed and directly connected to underlying motor unit firing patterns, researchers and

practitioners will be better equipped to determine the extent to which individuals use secondary range discharge behavior in mobility and peak performance.

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Chapter 4

RATE OF NEURAL EXCITATION DURING MOVEMENTS AT DIFFERENT SPEEDS IN OLDER ADULTS AND PEOPLE WITH PARKINSON'S DISEASE

Abstract

Movement slowing in older adults and People with Parkinson's disease (PwPD) is an indicator of functional decline. High levels of neural excitation are necessary for rapid movement and function. Neural excitation during some assessments may not elicit the necessary speed and underlying neural excitation to enter the elevated neural excitation range associated with high velocity function. The purpose of this study was to determine how movement speed effects the rate of neural excitation in young adults, healthy older adults, and PwPD. A secondary purpose was to compare neural excitation in four movements performed "as fast as possible". Three groups of 10 each of young adults, older adults, and PwPD performed arm curl, transverse elbow extension, recumbent cycling, and a 4-meter walk at increasing movement velocities while surface electromyography (EMG) and accelerometry were recorded. Movement velocity affected the peak rate of EMG rise (RER) of the three groups similarly for arm curl, walking, and elbow extension. Recumbent cycling showed movement velocity effecting peak RER of each group differently. Recumbent cycling elicited the greatest peak RER for young adults and PwPD while walking RER was greatest for

older adults when all four movements were compared. No group had significant differences between arm curl and elbow extension RER. Young adults and PwPD had RER differences between cycling and walking while older adults did not. When comparing walking at a preferred pace to as fast as possible, all groups revealed walking "as fast as possible" to elicit significantly greater RER than walking at a preferred pace.

Introduction

Slowing of physical movement is one part of the functional decline experienced by both aging adults and people with Parkinson's disease (PwPD). Older adults show a marked decrease in gait velocity at about 65 years of age (Shumway-Cook et al., 2007) and slow/small movement (i.e. bradykinesia) is 'one of the most striking features of motor disability' in PwPD (Hallett & Khoshbin, 1980). The rate of isometric muscular force development (RFD) and movement velocity are important determinants of function and mobility (Bento, Pereira, Ugrinowitsch, & Rodacki, 2010; LaRoche, Cremin, Greenleaf, & Croce, 2010; Studenski et al., 2011) with higher RFD and faster velocities associated with better function. In cross-sectional studies, older adults and people with Parkinson's disease (PD) typically exhibit lower RFD. For example, in isometric ankle dorsiflexion, RFD was 48% less in older adults compared to young adults with corresponding group-differences in integrated EMG and motor unit discharge rates [5]. In isometric elbow flexion, RFD was 70% less in PwPD compared to elderly adults (Stelmach, Teasdale, Phillips, & Worringham, 1989). In addition to reductions in RFD, muscle shortening velocity decreases have been reported in older adults during elbow flexion (Labarque, Op 'T Eijnde, & Van Leemputte, 2002) and plantar flexion (Narici, Maganaris, & Reeves, 2005) (full

review on contraction velocity with aging see Raj, 2010 (Raj, Bird, & Shield, 2010)) Furthermore, Corcos's speed sensitive strategy implied the necessity of high initial neural excitation and the scaling of the slope of the initial excitatory burst as important factors is movement velocity (Corcos, Gottlieb, & Agarwal, 1989). While the contractile properties of muscle and the influence of elastic tissues remain important contributors to the production of peak power (Maffiuletti et al., 2016), the application of neuromotor training to healthy aging (Brustio et al., 2015) and findings of disordered neuromuscular control in movement disorders such as PD (Wierzbicka, Wiegner, Logigian, & Young, 1991) indicate a better understanding of neuromuscular excitation and its assessment in rapid movement is necessary.

There is a wide array of methods to assess function and mobility in older adults and PwPD. The NIH Toolbox recommends assessments that measure walking endurance, gait speed, dexterity, strength and balance (Reuben et al., 2013). The Senior Fit Test™ (Rickli & Jones, 2013) measures fitness and function through a series of muscle strength and endurance, cardiovascular, and range-of-motion assessments. Other multifactorial assessments include not just physical skills, but medical history, and psychological status.

Although traditional strength training has been acknowledged as a way to improve function (Kenny et al., 2011), evidence suggests power training will have a greater effect on function than strength (Hazell, Kenno, & Jakobi, 2007). More recently, focus in intervention research has examined the velocity component of the power equation (power=force x velocity). High-velocity yoga was as effective at

alleviating PD symptoms and improving function as high-velocity resistance training (power training) (Ni et al., 2016). Twelve sessions of high-velocity low-resistance interval cycling resulted in significant improvement in dynamic balance, agility, and gait measures in older adults (Bellumori, Uygur, & Knight, 2016). A similar intervention for people with PD resulted in improvements in functional measures such as balance, gait speed, and agility (Uygur, Bellumori, & Knight, 2017). Therefore, velocity-based training can improve functional status in older adults and PwPD, and the ability for rapid movement seems to be a key determinant of functional status.

The underlying neural excitation of muscle related to rapid movement has been examined in both static and dynamic contractions. Clark and colleagues found neural excitation to plateau for mobility-limited older adults at a movement velocity of 90^{o}/s whereas healthy middle-aged and older adults utilized increasing neural excitation up to 240^{o}/s (Clark et al., 2010). They also found pre-motor time during an isotonic leg press to be greater and rate of neural excitation to be lower in the mobility-limited older adults when compared to health middle-aged and older adults (Clark et al., 2011). Examining a rapid standing heel raise, Clark and colleagues also found peak RER of the triceps surae to be lower in healthy older adult with slower fastest gait speeds than those who have faster fastest gait speeds (Clark, Manini, Fielding, & Patten, 2013). Beijersbergen and colleagues (Beijersbergen, Granacher, Gäbler, DeVita, & Hortobágyi, 2017) examined the effects of power training intervention on both habitual/preferred gait speed (HGS) and fastest gait speeds in older adults. The power training increased neural excitation during isometric MVCs, but there were no

changes in HGS. There were, however, significant increases in participants fastest gait speeds. High levels of neural excitation are necessary for function (Mian, Baltzopoulos, Minetti, & Narici, 2007) and associated with faster gait velocities (Clark et al., 2013).

Early neurophysiology research shows the relationship between a current injected into an alpha motor neuron and output motor unit firing rates in feline models to be linear at lower currents (primary range) with a second linear relationship with a greater slope and different y-intercept (secondary range) at greater currents (Kernell, 1965). The bilinear relationship insinuates that the greater the input to the alpha motor neuron the greater the rate of neuromuscular excitation and overall activation. The secondary range of activation, associated with high rates of force development (Heller, 2010; Van Cutsem, Duchateau, & Hainaut, 1998) may equally be necessary for function. The secondary range is known to be diminished or missing in stroke patients (Chou, Palmer, Binder-Macleod, & Knight, 2013), older adults (Klass, Baudry, & Duchateau, 2008), and (Glendinning & Enoka, 1994).

Acknowledging the importance of the secondary range of neural excitation to rapid movement and functional independence, this project seeks to exploit the differences between healthy young (YA) and older adults (OA) and people with PD (PD) to investigate neural excitation during dynamic functional assessments. The aim of this study was to examine the rates of neural excitation across increasing movement velocities during common movements. Our hypothesis is that a group-by-speed interactions will be seen in the four common movements of arm curl, elbow extension,

recumbent cycling, and over ground walking. A second aim of this study was to compare neuromuscular excitation during upper extremity and lower extremity movements performed "as fast as possible". We hypothesized each group would report significant differences between the four movement conditions.

Methods

Participants

Ten healthy young adult (YA) and ten healthy older adults (OA), free of joint and musculo-skeletal dysfunction and neurological disease or deficit including central processing deficits participated in this study. Ten people with Parkinson's disease (PD) (median months since diagnosis: 105.5) with no other significant medical conditions and a Hoehn-Yahr score of 3 or lower also participated. People with PD were told to maintain their regular medication schedule and nine PwPD were on dopamine replacement medication. For the nine on medication, the last pill prior to testing was taken between 35-180 minutes prior to testing. All participants signed a university approved informed consent form. Simple descriptive statistics can be viewed in table 1.

Data Collection

All testing was performed during a single testing session. Height, body mass, and dominant leg leg-length (ASIS to lateral malleolus) were recorded. Dominant hand handgrip strength was assessed (Jamar, Patterson Medical, Warrenville, IL).

Neuromuscular activation was recorded with EMG (Motion Labs System MA-300, Motion Lab Systems, Baton Rouge, LA). Acceleration, being the first derivative of velocity and mirroring the relationship of RFD to isometric force-time curves, is a key measurement. Movement acceleration was recorded with a tri-axial accelerometer (PCB Piezotronics Model 482C series with model #356A17 sensor, Depew, NY). All signals were sampled and digitized at 2 kHz and 24-bit resolution (CDAQ-9178 and module NI9239, National Instruments, Austin TX).

Biceps brachii (BB) neuromuscular activation was recorded during the arm curl. Triceps brachii (TB) neuromuscular activation was recorded during elbow extension. Neuromuscular activation for vastus lateralis (VL), biceps femoris (BF), soleus (SO), medial gastrocnemius (MG), and tibialis anterior (TA) was recorded during recumbent cycling intervals and while walking overground in different speed conditions. In the PD group, the limb that was less affected by tremor was used in testing to minimize potentially confounding effects of tremor on limb acceleration. YA and OA participants were tested in their dominant limb. Prior to electrode placement, the area superficial to the muscles of interest was cleaned and prepared (Konrad, 2006).

For upper body movements, the tri-axial accelerometer was placed 28cm distal to the olecranon process on the posterior side of the lower arm. For lower body movements, the tri-axial accelerometer was placed 3cm proximal to the lateral malleolus of the dominant leg.

Considering the direct relationship between tangential acceleration and the radius of the arc (leg length), lower extremity acceleration data were standardized to the mean

leg length of all participants via dividing by the individual's leg length (acceleration/cm) and multiplying by the mean length. Acceleration was recorded during all movements except recumbent cycling where RPMs were used to describe movement speed.

Experimental Conditions

The movements of interest include: 30 second arm curl from the Senior Fit Test [tm] (SFT) (Rikli & Jones, 2001), high-speed low-resistance recumbent bicycle interval (Bellumori et al., 2016; Uygur et al., 2015, 2017), 4 meter walk test (National Institute of Health, 2016; Peters, Fritz, & Krotish, 2013), and elbow extension (Bellumori, Jaric, & Knight, 2011; Harwood, Davidson, & Rice, 2011).

Arm Curl: The SFT has participants perform a 30s weighted arm curl (8lbs for males, 5lbs for females) with the total number of curls completed equating to a functional and strength status. The categories for total curls completed are: <11 curls are "at risk for loss of functional mobility", 12-17 curls are "normal range", and >17 curls are "above average." For this study, a specific number from each category was selected. The higher ends of 'at risk' and 'above average' were chosen (9 and 27, respectively) along with the median of the 'normal' category (15). The number of curls representing each category was converted to a movement frequency of beats per minute (bpm) and hertz (curls per second). BPM was programmed into a digital metronome to provide a specific pace for participants to follow. The metronome was

set to beat at the end of both the concentric and eccentric actions of the arm curl. The metronome settings were: 36bpm (9 curls/30s), 60 bpm (15 curls/30s), 108 bpm (27 curls/30s), and the matching curls/second frequencies were as following: 0.3Hz, 0.5Hz, 0.9Hz, respectively. The "as fast as possible" (AFAP) had an accompanying unrealistic fast metronome pace of 160 bpm (40 curls/30s) to maintain the consistency of a metronome noise to follow. Participants did not perform the full 30s arm curl test, beginning with the slowest bpm, participants performed 7-10 weighted arm curls at each movement pace with a 60s rest period between each pace.

Elbow Extension: The internally rotated shoulder was flexed to 90^{o} in the sagittal plane and the elbow was flexed to 100^{o} (0^{o} = full extension) to perform transverse plane elbow extension. The upper arm, approximately 2.254cm proximal to the olecranon process, was supported by a stable support which allowed the elbow to extend freely. While standing, participants were asked to extend their elbow at the given velocity and return to the starting position slowly. Although no known specific-velocity elbow extension functional assessment exists, most-rapid elbow extension is among the most frequently used models in the study of neuromotor control and pathology (Berardelli et al., 1996; Brown & Gilleard, 1991). The participants performed this movement at a "preferred" or "comfortable" velocity followed by a "slower than preferred" velocity, followed by a "faster than preferred" velocity, and finally an "as fast as possible" velocity. Participants performed 7-10 elbow extensions at each velocity with 60s rest between conditions.

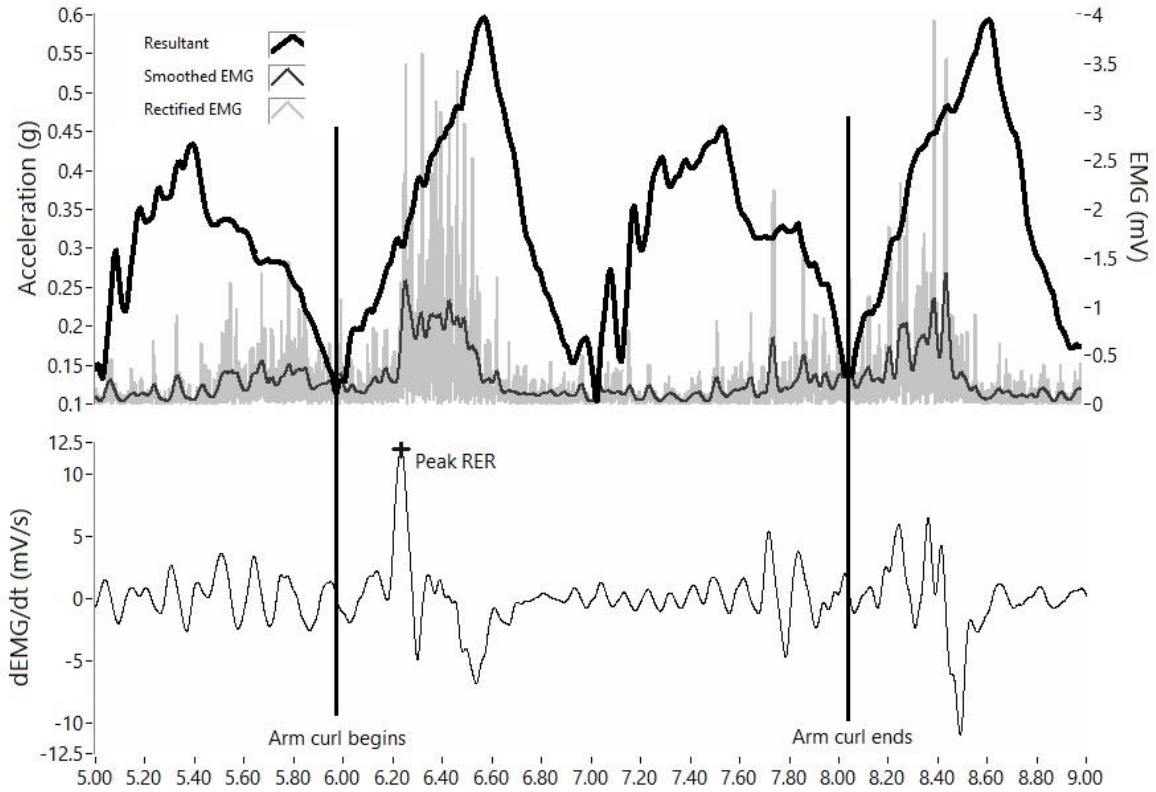
Recumbent bicycling: Participants were seated in a recumbent cycle ergometer (RT2 G3, Monark Exercise AB, Vansbro, Sweden) and allowed to position themselves comfortably. They were instructed to cycle at specific rotations-per-minute (RPM) for 10-15 seconds. The RPMs prescribed were 40, 60, 80, 100, 120, and AFAP. Participants unable to achieve 120RPMs were still asked to pedal AFAP to achieve maximal neural excitation. At least 60s of rest was given between prescribed RPMs.

4-Meter Walk: Participants first performed the NIH 4-meter walk test at their preferred pace (National Institute of Health, 2016). Then, similar to the instructions used by Lavendar et al (Lavender, Mehta, & Allread, 2013) they repeated the test with instructions to walk slower than their preferred pace; as if they were "strolling in the park." They then repeated the test with instructions to walk "faster than their preferred pace, but not as fast as possible". Lastly, they were asked to perform the test walking "as quickly as safely as possible." Each condition was performed twice. Participants were given at least 60s of rest between each trial.

Data Reduction

Acceleration: Triaxial accelerometry data were processed in a custom LabVIEW (National Instruments, Austin, TX) program. Accelerometry data were downsampled to 200Hz and plotted, low-pass filtered (4^{th} order zero-lag Butterworth filter with 20Hz cutoff) and converted from volts to gravitational force (g; A-

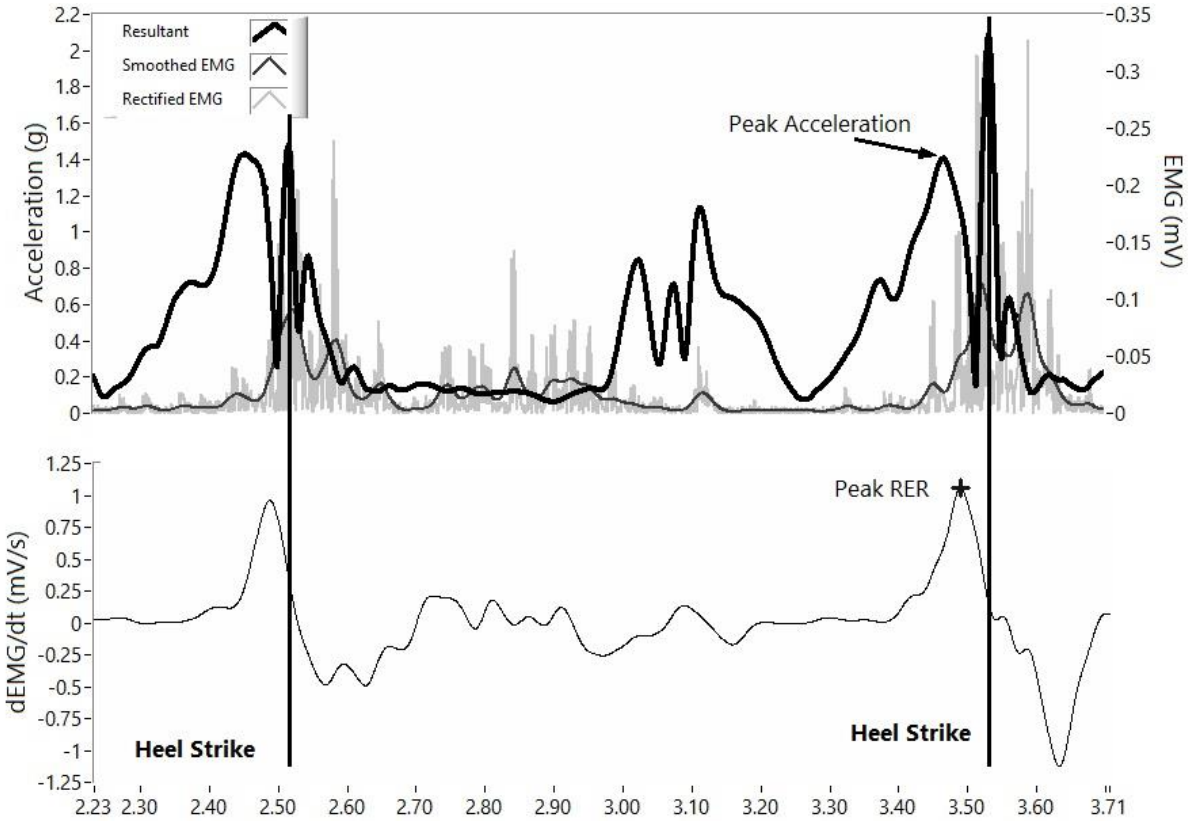
x=530mV/g, A-y=539mV/g, A-z=507mV/g). The magnitude of the resultant vector was calculated by finding the square root of the sum of the squares of the A-x, A-y, and A-z vectors and plotted. Within each movement examined using accelerometry (arm curl, elbow extension, walking), peak resultant accelerations within each cycle of interest were obtained; throughout the entire arm curl, from movement onset to termination in elbow extension (Figure 1), and between consecutive heel strike impact artifacts in walking (figure 2).



4.1 Representative data for the 0.5Hz arm curl. The top graph shows the resultant acceleration-time curve (thick black line), the demeaned and rectified EMG (light gray) and the smoothed EMG (dark gray). The vertical black lines signify the beginning and the end of a single arm curl during the continuous weighted arm curl task. The lower figure shows the first derivative of the smoothed EMG (RER), calculated via central tendency slope of a 100ms moving window. Peak RER (dEMG/dtmax) of the curl is marked with a +

EMG: All EMG data were demeaned, rectified, and zero-lag 4th order Butterworth filtered with a 20Hz cutoff in a custom LabVIEW (National Instruments, Austin, TX) program. The rate of EMG rise (RER) signal was calculated using the

slope from a linear fit line of all data points within a .1s moving window (± .05s around each data point) of the EMG signal. The peak RER was taken as the peak value of the RER within the window of movement.



4.2 Representative data for vastus lateralis of a YA walking at a self-prescribed "fast" pace. Each stride is analyzed from heel strike to heel strike of the dominant leg. The thick black line is the resultant acceleration-time curve. The gray line is the rectified EMG and the thin black line is the rectified and smoothed EMG. The bottom figure is the first derivative of the rectified and smoothed EMG calculated via the central tendency slope of a 100ms moving window. Peak RER and acceleration are marked.

Statistical Analysis

Spearman's rho was calculated to describe the strength of the relationship between peak acceleration and peak RER. Correlations were calculated for all data and for aggregated group data.

One-way ANOVAs were performed to test group differences on all descriptive statistics with post hoc analysis for specific relationships. For elbow extension and 4-meter walk, a group by speed mixed-design factorial ANOVA for each muscle of interest was performed. Some participants were unable to perform the faster assigned movement velocities of arm curl and recumbent cycling thereby creating missing data. Therefore, for arm curl and bicycling conditions, a group by speed mixed-model ANOVA for each muscle of interest was performed. Both mixed-design and mixed model ANOVAs were followed with simple main effects and pairwise comparisons for specific interactions. A mixed-design factorial ANOVA was used to compare peak RER during the "AFAP" speed condition across all movements.

Results

Descriptive measures for each group are presented in table 1. Group differences were seen in age [$F(2,27) = 531.3$, $p<0.001$], grip strength [$F(2,27) = 4.373$, $p=.022$], and peak recumbent cycling RPMs [$F(2,27) = 12.68$, $p<0.001$]. YA had significantly greater grip strength than OA ($p=0.020$) and greater peak cycling cadences than both OA ($p=0.001$) and PD ($p<0.001$). Significant group differences

were also observed in peak EMG amplitude of individual muscles during the MVCs (EMGmvc): BB [F (2.27) =3.680, p=.039], BF [F (2,27) =3.864, p=.033], and SO [F (2,27) =4.946, p=.015].

Table 4.1 Descriptive statistics by group; mean (sd) except for RPM which is mean (range). YA was significantly younger than both OA (p<0.001) and PD (p<0.001) with greater grip strength than OA (p=0.018). YA also had significantly greater peak RPMs than both OA (p=0.001) and PD (p<.001). Muscles measured for MVC were Biceps Brachii (BB), Triceps Brachii (TB), Vastus Lateralis (VL), Biceps Femoris (BF), Soleus (SO), Tibialis Anterior (TA), and Medial Gastrocnemious (MG). EMGmvc is the RMS amplitude of a 500ms window around peak EMG during a manually resisted maximum voluntary contraction. YA BB neural excitation was greater than OA (p=.037) and YA SO was greater than PD SO (p=.015) * significantly different from YA.

	YA (9 male, 1 female)	OA (7 male, 3 female)	PD (9 male, 1 female)
Age (years)	21.2 (1.7)	72.3 (3.9) *	69.5 (5.3) *
Leg length (cm)	91.9 (2.2)	91.4 (5.0)	92.7 (4.9)
Body Mass (kg)	73.5 (9.2)	74.2 (12.9)	82.1 (21.0)
Height (cm)	176.3 (9.2)	172.0 (9.0)	176.3 (8.6)
Grip Strength (kg)	47.0 (8.2)	35.1 (10.0) *	39.7 (8.8)
Peak RPM (range)	180 (144-209)	142 (112-171) *	135 (101-173) *
TB EMGmvc (mV)	0.48 (.32)	0.37 (.26)	0.33 (.25)
BB EMGmvc (mV)	1.02 (.53)	0.46 (.28) *	0.66 (.53)
VL EMGmvc (mV)	0.20 (.13)	0.16 (.06)	0.15 (.06)
BF EMGmvc (mV)	0.27 (.16)	0.16 (.06)	0.15 (.06)
SO EMGmvc (mV)	0.15 (.11)	0.08 (.04)	0.06 (.02) *
TA EMGmvc (mV)	0.29 (.14)	0.22 (.10)	0.21 (.14)
MG EMGmvc (mV)	0.16 (.12)	0.13 (.05)	0.09 (.07)

Elbow Extension

Based on tangential (linear) to angular acceleration conversion, peak angular accelerations during the AFAP condition in the present study were 15952 ($\pm$4991), 12967 ($\pm$2437), and 9453 ($\pm$3588) degrees/s^2 for YA, OA, and PD, respectively. These values are similar to those measured in those with moderate karate training (Zehr & Sale, 1993) and more than double than those performing an oscillatory movement in a limited range at submaximal speeds (Gottlieb, Corcos, & Agarwal, 1989)

Using data from all groups, there was a strong correlation between peak acceleration and peak RER of the triceps brachii (ρ=0.790, p<.001). Associations were also strong within each group (YA: ρ=0.859, p<0.001; OA: ρ=0.853, p<0.001; PD: ρ=0.744, p<0.001) (table 2).

For peak rate of EMG rise, there was not a significant group by speed interaction in the elbow extension task. An examination of the main effects revealed a significant speed effect [F (3. 81.4) =102.5, p<0.001]. Post hoc tests revealed peak RER to increase significantly as speed conditions increased (all p<0.001). Peak acceleration during elbow extension had a significant group-by-speed interaction [F (6, 81.1) =6.7, p<0.001]. Simple main effects revealed group effects in the preferred, fast, and AFAP conditions (all F>74.4, all p<0.012) with post hoc showing during preferred, fast, and AFAP, PD had lower peak accelerations than both YA and OA (all p<0.34) and in the fast and AFAP conditions OA had lower peak accelerations than YA (all p<0.001).

The simple main speed effect revealed a speed effect for all groups (all $F>1069$, all $p<0.001$) with all post hoc comparisons showing acceleration increased as speed conditions increased across all groups (all $p<0.001$) (table 3).

Table 4.2 Spearman's rho correlations for peak acceleration to peak RER for aggregate and group data for upper extremity movements. Strong correlations exist for all elbow extension relationships while arm curl shows weak to moderate correlations between peak acceleration and peak RER.

	Curl (n=667)	Extension (n=671)
Aggregate	0.30	0.79
YA	0.41 (n=232)	0.86 (n=225)
OA	0.48 (n=205)	0.85 (n=214)
PD	0.07 (n=230)	0.74 (n=232)

Arm Curl

Using data from all groups, there was a low-moderate correlation between peak arm acceleration and rate of EMG rise in the biceps brachii ($\rho= 0.304$, $p<.001$). Within groups, YA and OA revealed a moderate correlation between acceleration and RER (YA: $\rho= 0.410$, $p<0.001$; OA: $\rho= 0.484$, $p<0.001$) whereas PD revealed no relationship between acceleration and RER ($\rho= 0.072$, $p=0.276$) (table 2).

There was no significant interaction between group and speed in RER of the biceps brachii, but the main speed [$F (3, 77.9) =24.6$, $p<0.001$] effects were significant. All post-hoc comparisons for speed revealed significant increases in peak

RER with increased speed (all $p \leq 0.001$) except for the comparison between 0.9Hz and AFAP ($p=0.573$). (Table 3)

Table 4.3 Mean (SD) of peak RER (%EMGmvc/s) and acceleration (gravitational force, g) during weighted arm curl (Top) and elbow extension (bottom) at different movement rates. Arm curl slow to fast, rates correspond with the "at risk for functional loss", normal, or above average categories, with as fast as possible (AFAP) representing the Senior Fitness Test[tm] 30s Arm Curl instructions. No significant group by speed interaction was revealed for either movement., but both main speed effects were significant.

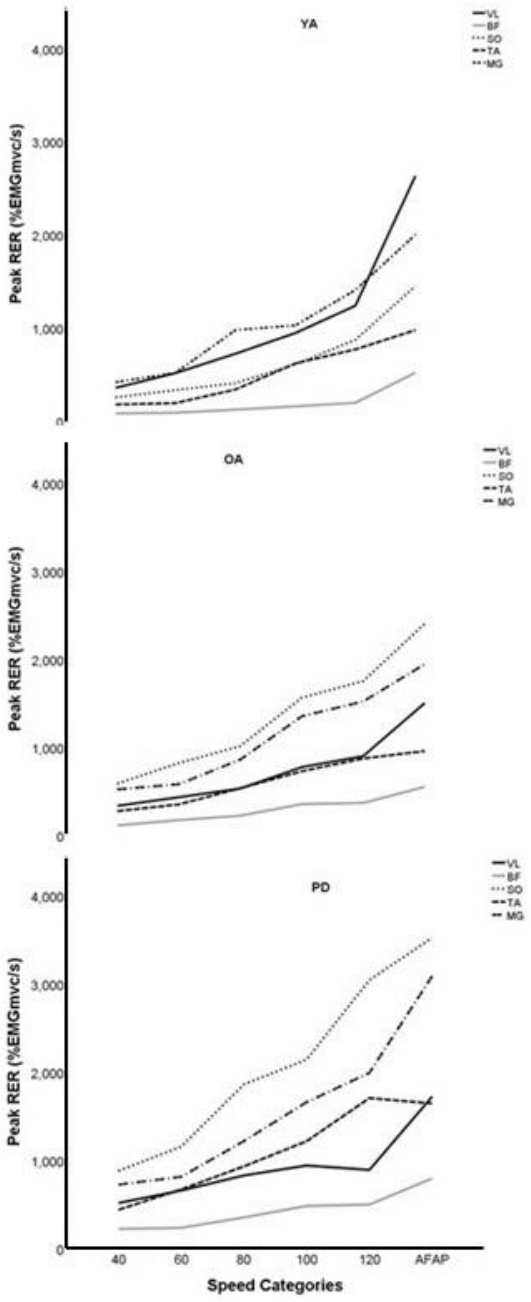
Weighted Arm Curl						
Group	Speed	0.3Hz	0.5Hz	0.9Hz	AFAP	Mean
YA	RER: %EMGmvc/s	760 (577)	960 (731)	1183 (898)	1128 (557)	1008 (190)
	Acceleration: g	0.95 (0.1)	1.2 (0.1)	1.7 (0.3)	2.3 (0.3)	1.54 (0.60)
OA	RER: %EMGmvc/s	688 (214)	894 (357)	1186 (457)	1271 (481)	1010 (268)
	Acceleration: g	1.0 (0.1)	1.5 (0.2)	1.9 (0.3)	2.2 (0.4)	1.65 (0.52)
PD	RER: %EMGmvc/s	888 (404)	1171 (531)	1339 (581)	1206 (485)	1151 (190)
	Acceleration: g	1.0 (0.1)	1.3 (0.2)	1.7 (0.4)	1.9 (0.5)	1.48 (0.40)
Mean	RER: %EMGmvc/s:	779 (101)	1008 (145)	1236 (89)	1202 (72)	
	Acceleration: g	0.98 (0.03)	1.33 (0.15)	1.77 (0.12)	2.13 (0.21)	
Rapid Elbow Extension						
Group	Speed	Slow	Preferred	Fast	AFAP	Mean
YA	RER: %EMGmvc/s	242 (190)	484 (390)	741 (470)	1713 (902)	795 (645)
	Acceleration: g	0.77 (0.4)	1.70 (0.8)	3.20 (1.3)	7.95 (2.5)	3.41 (3.19)
OA	RER: %EMGmvc/s	134 (106)	339 (210)	543 (362)	1110 (571)	532 (420)
	Acceleration: g	0.60 (0.3)	1.61 (0.8)	2.85 (1.0)	6.47 (1.2)	2.88 (2.56)
PD	RER: %EMGmvc/s	308 (319)	621 (489)	406 (476)	1468 (601)	776 (492)
	Acceleration: g	0.71 (0.5)	1.45 (1.0)	7.237 (1.1)	4.71 (1.8)	2.31 (1.74)
Mean	RER: %EMGmvc/s:	228 (88)	481 (141)	663 (105)	1430 (303)	
	Acceleration: g	0.69 (0.09)	1.59 (0.13)	2.81 (0.42)	6.38 (1.62)	

Recumbent Cycling

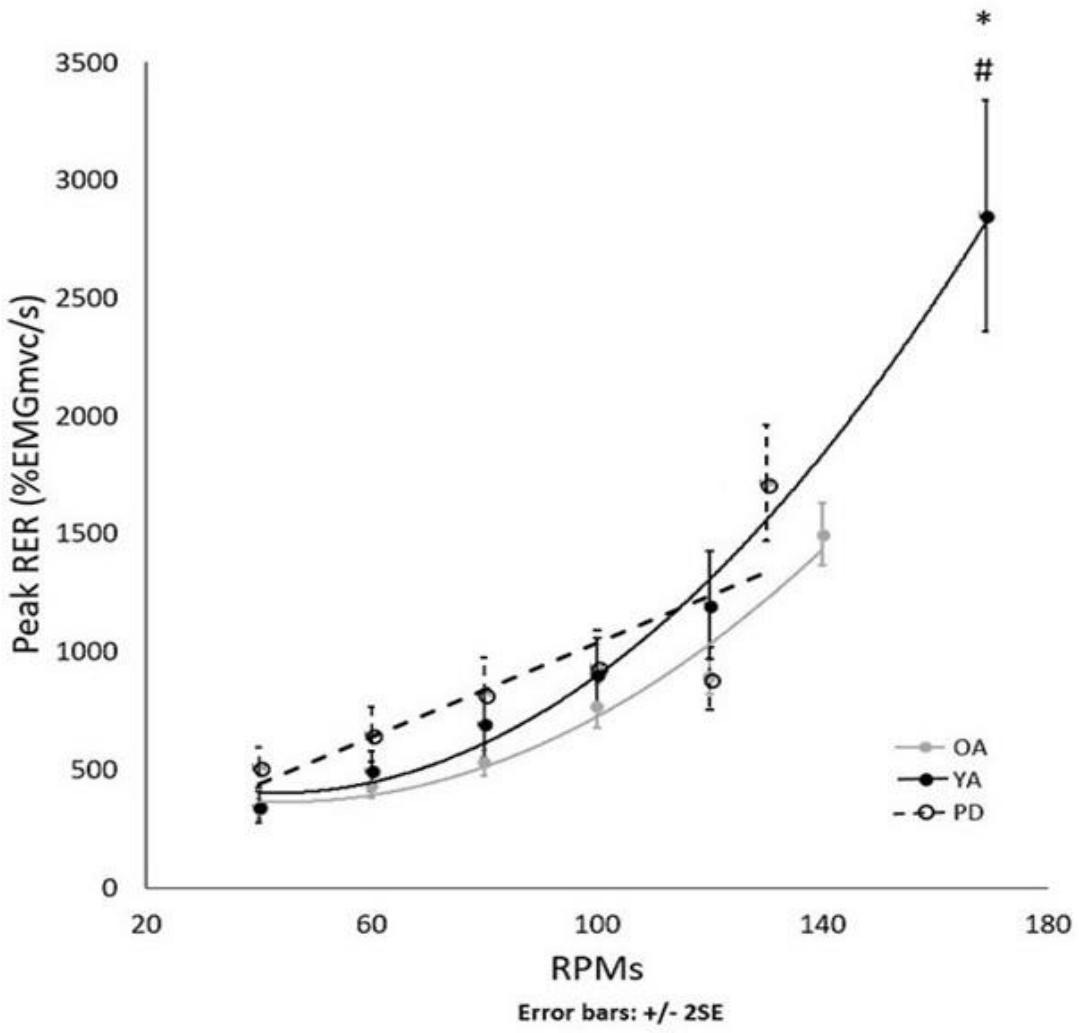
Moderate to strong correlations, ranging between 0.434 and 0.830, existed between recumbent cycling RPMs and peak RER for all lower extremity muscles tested (Table 4). Vastus lateralis, soleus, and tibialis anterior muscles showed a group by speed interaction (All $F>1.9$, all $p<.046$) in peak RER. Speed simple main effects were seen in all three muscles for all groups (all $F>4.0$, all $p<0.002$). VL revealed a group effect in the AFAP condition [$F(10, 129.9) = 14.2$, $p<0.001$] with YA having greater peak RER than both OA and PD (both $p<0.001$). SO revealed group differences at 80, 100, 120, and AFAP rpms (all $F>6.4$, all $p<0.003$) with YA having lower RER than PD at all speeds and lower RER than OA at 100, 120, and AFAP RPMs. In the 120 and AFAP conditions YA was lower than OA and OA was lower than PD (all $p<0.034$). The speed effect for each group across all six speed categories can be viewed in figure 3. The group-by-speed interaction of VL for RPMs represented as continuous rather than categorical can be viewed in figure 4. (table 5)

Table 4.4 Aggregate and group Spearman's correlation coefficients for RER vs. peak RPM during recumbent cycling and RER vs. peak leg acceleration during walking. Correlations are reported for each lower extremity muscle recorded: vastus lateralis (VL), biceps femoris (BF), soleus (SO), tibialis anterior (TA) and medial gastrocnemius (MG). Moderate to strong correlations exist for all relationships during recumbent cycling with weak to moderate correlations during the 4MW.

	VL	BF	SO	TA	MG
RER vs. RPM in Bicycling					
Aggregate (n=30)	0.65	0.54	0.49	0.64	0.72
YA (n=10)	0.71	0.68	0.66	0.83	0.77
OA (n=10)	0.79	0.69	0.72	0.70	0.83
PD (n=10)	0.47	0.58	0.53	0.59	0.64
RER vs. Leg swing acceleration in walking.					
Aggregate	0.358	0.156	0.142	0.321	0.323
YA	0.450	0.251	0.375	0.511	0.444
OA	0.369	0.098	0.289	0.589	0.435
PD	0.412	0.294	0.108	0.191	0.283



4.3 Effect of pedaling speed on peak RER (%EMGmvc/s) in each group for all muscles during recumbent cycling in six different RPM categories. In all groups and muscles except for TA in OA and PD, peak RER during AFAP, was significantly greater than in all other speeds (all $p<0.036$). Typically, peak RER during the slowest speed categories were similar to each other.



4.4 Group x speed interaction of VL peak RER during recumbent cycling. Simple group effects show group differences in the AFAP category. YA peak RER is significantly greater than both OA and PD in "AFAP" and PD RER is greater than OA in "AFAP". * indicates significant differences between YA and OA, # indicates significant differences between YA and PD (all $p<0.001$)

Table 4.5 Peak RER (%EMGmvc/s) values for each muscle and group at increasing RPM conditions during recumbent cycling [mean (SD)]. * indicates value significantly different from YA, † indicates PD peak RER value is significantly different from OA.

	VL			BF			SO			TA			MG		
	YA	OA	PD	YA	OA	PD	YA	OA	PD	YA	OA	PD	YA	OA	PD
40 RPM	342 (249)	333 (159)	511 (326)	78 (44)	111 (57)	217*† (119)	250 (122)	586 (198)	876* (614)	174 (94)	273 (187)	434* (311)	433 (224)	519 (867)	719 (402)
60 RPM	495 (323)	431 (185)	652 (449)	85 (53)	171* (106)	229* (111)	330 (206)	818* (377)	1150* (803)	191 (102)	350 (176)	665*† (612)	572 (329)	579 (224)	809 (414)
80 RPM	695 (547)	530 (200)	883 (592)	119 (78)	221* (120)	347*† (171)	382 (190)	1011* (422)	1856*† (1482)	343 (156)	533 (243)	927*† (733)	939 (466)	858 (335)	1213 (755)
100 RPM	906 (576)	772 (358)	936 (595)	154 (86)	352* (214)	477*† (251)	572 (317)	1560* (733)	2138*† (1449)	609 (245)	726 (352)	1212*† (857)	1066 (447)	1349 (561)	1655* (868)
120 RPM	1198 (862)	897* (271)	886* (396)	192 (122)	365* (190)	493*† (255)	849 (556)	1749* (978)	3040*† (2198)	796 (303)	870 (346)	1701*† (1195)	1413 (574)	1517 (466)	1987*† (1067)
AFAP	285 (1866)	1499* (506)	1717* (943)	515 (388)	549 (207)	789*† (446)	1354 (1030)	2398* (926)	3519*† (2008)	1007 (461)	955 (307)	1640*† (1044)	2036 (835)	1940 (557)	3084*† (3315)

4 Meter Walk

Due to laboratory constraints involving tethered data collections, accurate measures of 4m walk time are not available for 7 subjects (YA: 3 OA: 2 PD: 2). Correlation of 4MW times to peak leg swing acceleration was strong (-0.77). Correlations by group revealed moderate to strong relationships (YA: -0.85 OA: -0.80 PD: -0.69). As leg swing peak accelerations are not commonly reported, correlation to 4MW times is important to validate the measure. Using the 4MW times, walking velocity was calculated (m/s) for both preferred and AFAP for each group. Mean preferred gait speeds were 1.26 ($\pm$0.2), 1.08 ($\pm$0.2), and 1.04 ($\pm$0.2) for YA, OA, and PD, respectively. For AFAP, mean speeds were 2.08 ($\pm$0.1), 1.95 ($\pm$0.4), 1.60 ($\pm$0.2) for YA, OA, and PD, respectively. These times are faster than the 1.0 m/s low cutoff to determine non-mobility limited older adults used by Clark et al (Clark et al., 2013) and close to the times recorded from a 7.62m walk test in YA and OA (Bohannon, 1997).

While the correlation of 4MW times to peak leg swing acceleration were strong, the correlations of peak leg swing acceleration to RER were weak for all muscles in aggregate data (range: 0.156-.0358). Group correlations were weak to moderate and all correlations can be viewed in table 4.

No group-by-speed interaction was revealed for any muscles (table 6). Main group effects were seen in soleus, medial gastrocnemius, and tibialis anterior (All $F > 3.4$, all $p<0.049$). Group soleus and tibialis anterior post hoc analysis revealed YA to have

significantly lower peak RER than both OA and PD and PD to have significantly lower RER than OA (all $p<0.001$). Medial gastrocnemius post hoc showed PD RER to be greater than YA and OA (both $p<0.001$).

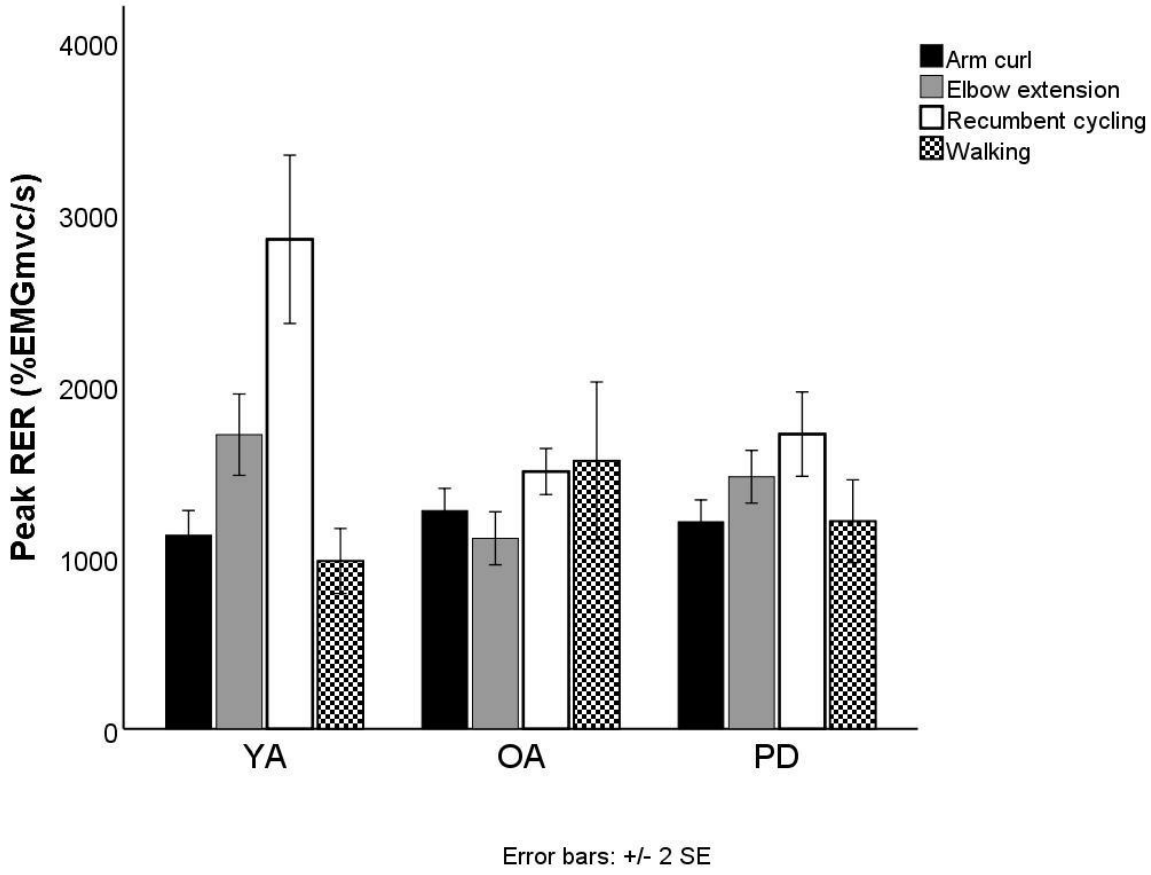
Table 4.6 4-meter walk mean (SD) peak RER (%EMGmvc/s), leg swing acceleration (g), and time (s) for vastus lateralis in each speed condition for all groups. AFAP = as fast as possible. Average pedaling rates in the AFAP condition were 180, 142 and 135 RPM for YA, OA, and PD, respectively.

Walking						
			Slow	Preferred	Fast	AFAP
YA	Peak RER		217 (150)	342 (225)	606 (392)	978 (591)
	Peak Acceleration		1.9 (0.7)	2.6 (0.9)	3.5 (1.1)	4.7 (1.0)
	Walk Time (n=7/10)		4.6 (0.6)	3.2 (0.5)	2.4 (0.2)	1.9 (0.1)
OA	Peak RER		550 (616)	684 (624)	1040 (1131)	1561 (1525)
	Peak Acceleration		1.9 (0.7)	2.6 (0.8)	3.5 (1.0)	4.9 (1.4)
	Walk Time (n=8/10)		5.5 (1.2)	3.8 (0.6)	2.9 (0.5)	2.1 (0.4)
PD	Peak RER		663 (485)	852 (588)	923 (454)	1210 (895)
	Peak Acceleration		1.7 (0.7)	2.4 (0.7)	3.0 (1.5)	3.7 (0.9)
	Walk Time (n=8/10)		5.8 (1.2)	4.0 (0.6)	3.3 (0.5)	2.5 (0.3)
Bicycling (Peak RER values)						
	40 RPM	60 RPM	80 RPM	100 RPM	120 RPM	AFAP
YA	342 (249)	495 (323)	695 (547)	906 (576)	1198 (862)	2851 (1866)
OA	333 (159)	431 (185)	530 (200)	772 (358)	897* (271)	1499* (506)
PD	511 (326)	652 (449)	883 (592)	936 (595)	886* (396)	1717* (943)

Assessment Comparisons

Comparisons of all peak RER in the AFAP category across all movement conditions revealed a significant group-by-condition interaction [$F(6, 80.3) = 2.7$,

p=0.019]. Simple group effects note no peak RER differences in arm curl but significant group differences in the other three movements (all $F>13.6$, all $p<0.001$). Post hocs show RER for YA > PD > OA for both elbow extension and recumbent cycling while walking reverses that relationship (OA > PD > YA) (all $p<0.015$). Simple condition effects revealed all groups had significant RER differences across the four movements (all $F>8.0$, all $p<0.001$). For YA peak RER, post hocs showed cycling> elbow extension> arm curl=walking (all $p<0.001$; arm curl: walk, $p=0.231$). OA peak RER in the AFAP condition post hocs revealed the order of RER magnitude walking to be the greatest, followed by cycling, then arm curl, and lastly elbow extension. While there were no significant differences between RER of each movement and the immediate next movement, all other comparisons were significant (all $p<0.003$). Post hoc for the PD group revealed cycling to elicit greater RER than the other three movements (all $p<0.002$). Elbow extension was greater than arm curl ($p=0.013$). (figure 5)

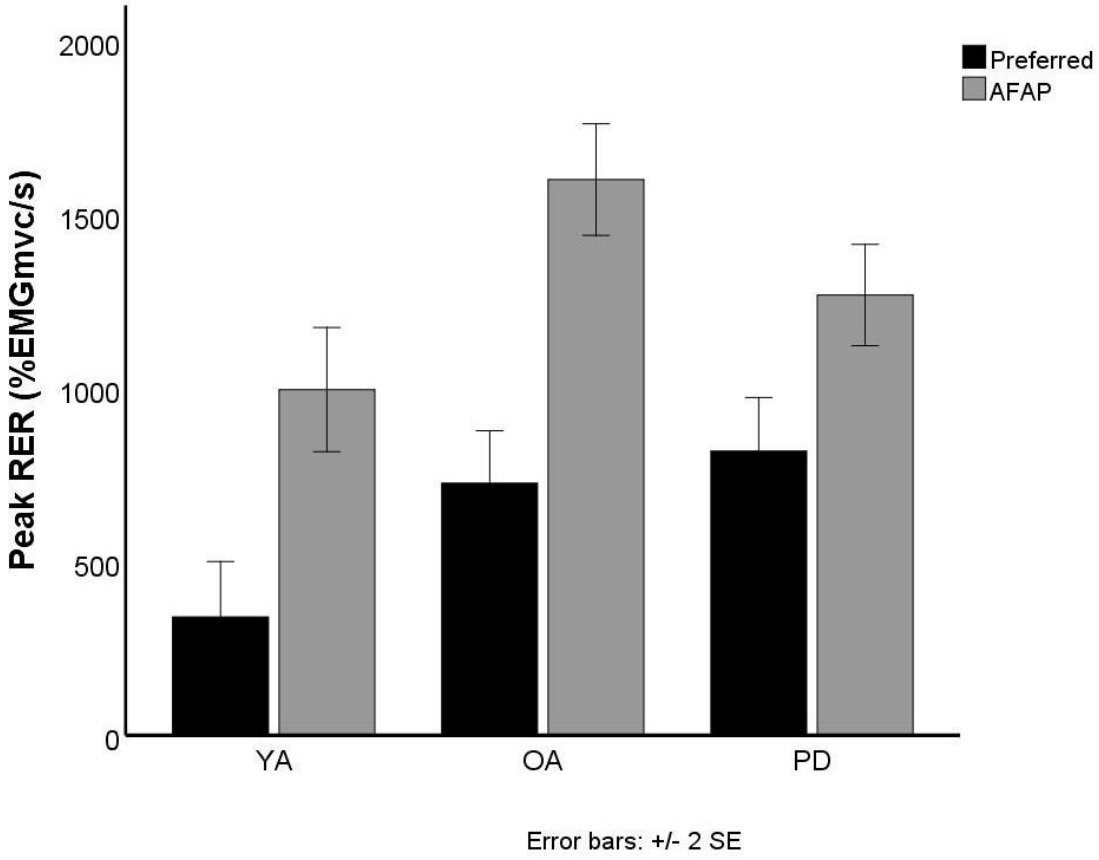


4.5 Group x condition interaction in the AFAP condition. All groups had significant differences in RER between the movement conditions. YA and PD had similar relationships with cycling generating the greatest RER followed by elbow extension. Walk and arm curl had similar RER. OA's greatest RER was in the walk condition followed by cycling, then arm curl and lastly elbow extension although no differences were seen in RER between a movement and the immediate next movement's RER.

Lower extremity comparison of RER in the AFAP category revealed a group-by-condition interaction [$F(2, 26.2) = 4.2$, $p=0.026$]. Speed simple effects revealed both YA and PD had RER differences between the two conditions (both $F>14.4$, both

$p<0.001$) and post hoc analysis revealed recumbent cycling to elicit greater RER than walking for both groups ($p<0.001$).

Paired-t tests were performed for each group individually on walking data to determine differences in peak RER at the preferred compared to AFAP walking categories. The differences between AFAP and preferred peak RER were 656, 876, and 450 %EMGmvc/s for YA ($t=5.5$, $p<0.001$), OA ($t=7.9$, $p<0.001$), and PD ($t=4.2$, $p<0.001$), respectively (figure 6).



4.6 Shows the relationship of Vastus Lateralis peak RER (%EMGmvc/s) at preferred and AFAP walking categories. Paired-t tests indicated that all groups had significantly greater peak RER while walking AFAP compared to walking at a preferred pace.

Based on previous work (Bellumori et al., 2016; Uygur et al., 2017), 60RPMs was set as a "preferred" pace to compare preferred to AFAP. A mixed design ANOVA comparing VL Peak RER the two movement speeds for both walking and cycling revealed group by condition by speed interactions [$F(7,592) = 23.9$, $p<0.001$]

with simple main effects showing all groups in both conditions having greater peak RER in the AFAP speed compared to the preferred speed (all $F>8.2$, all $p<0.001$) and all post-hoc comparisons revealed AFAP peak RER to be greater than preferred peak RER (all $p<0.004$). YA and PD had significant greater peak RER during cycling AFAP than during walking AFAP (both $F> 14.3$, $p<0.001$).

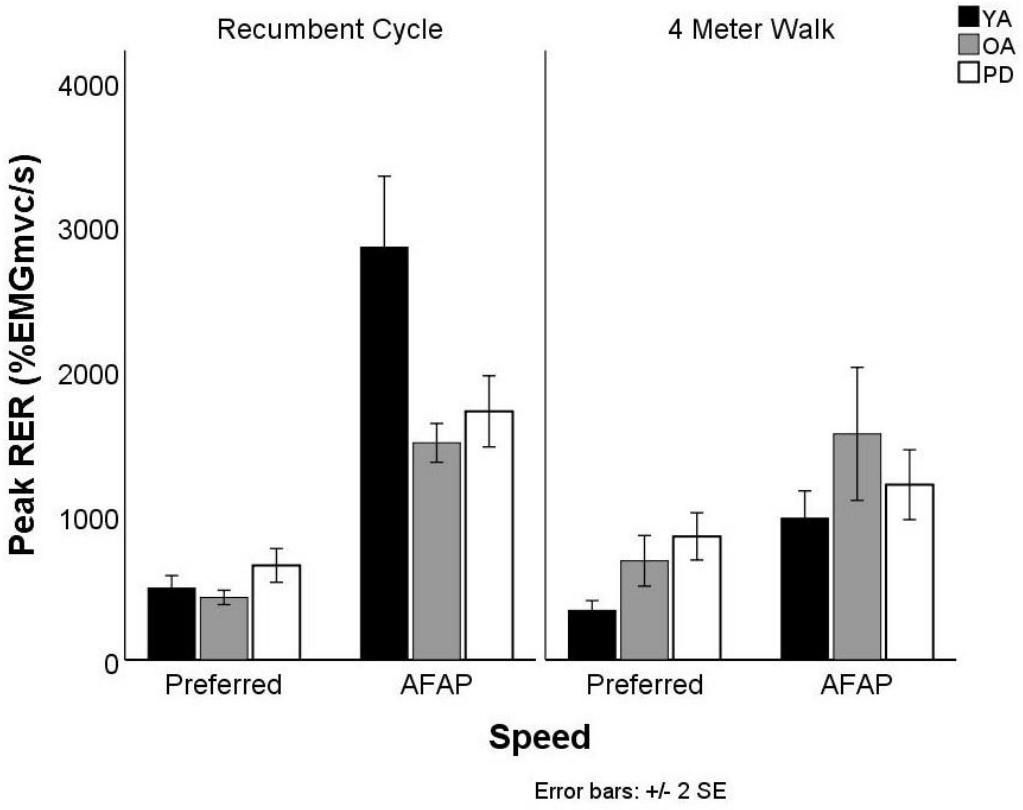
A comparison of upper extremity movements only revealed no group-by-condition interaction, no group effect, nor a condition effect (all $p>0.059$) (figure 7).

Discussion

No group-by-speed interaction for peak RER was revealed for arm curl, elbow extension, or the 4-meter walk (4MW). Recumbent cycling revealed group by speed interactions for RER of vastus lateralis, soleus, and tibialis anterior muscles. These results partially support our first hypothesis of our primary aim. One factor about cycling is that it is performed against less resistance and does not involve balance. The arm curl is performed seated and resisted by 8 and 5 lbs for men and women, respectively and walking is fully weight bearing and associated with dynamic balance.

The expected group differences were realized only partially. In arm curl, PD peak RER was greater than both YA and OA, but contrary to common neuromuscular changes with aging (Campbell, McComas, & Petito, 1973; Lexel & Downham, 1991; Short et al., 2005), there were no difference between YA and OA. While the neuromuscular changes associated with aging did not influence peak RER, people

with PD needed greater levels of RER relative to EMGmvc to accomplish similar acceleration. Known changes in the substantia nigra and dopamine production associated with PD may affect descending drive causing PwPD to need greater neural excitation to accomplish velocity-dependent activities.

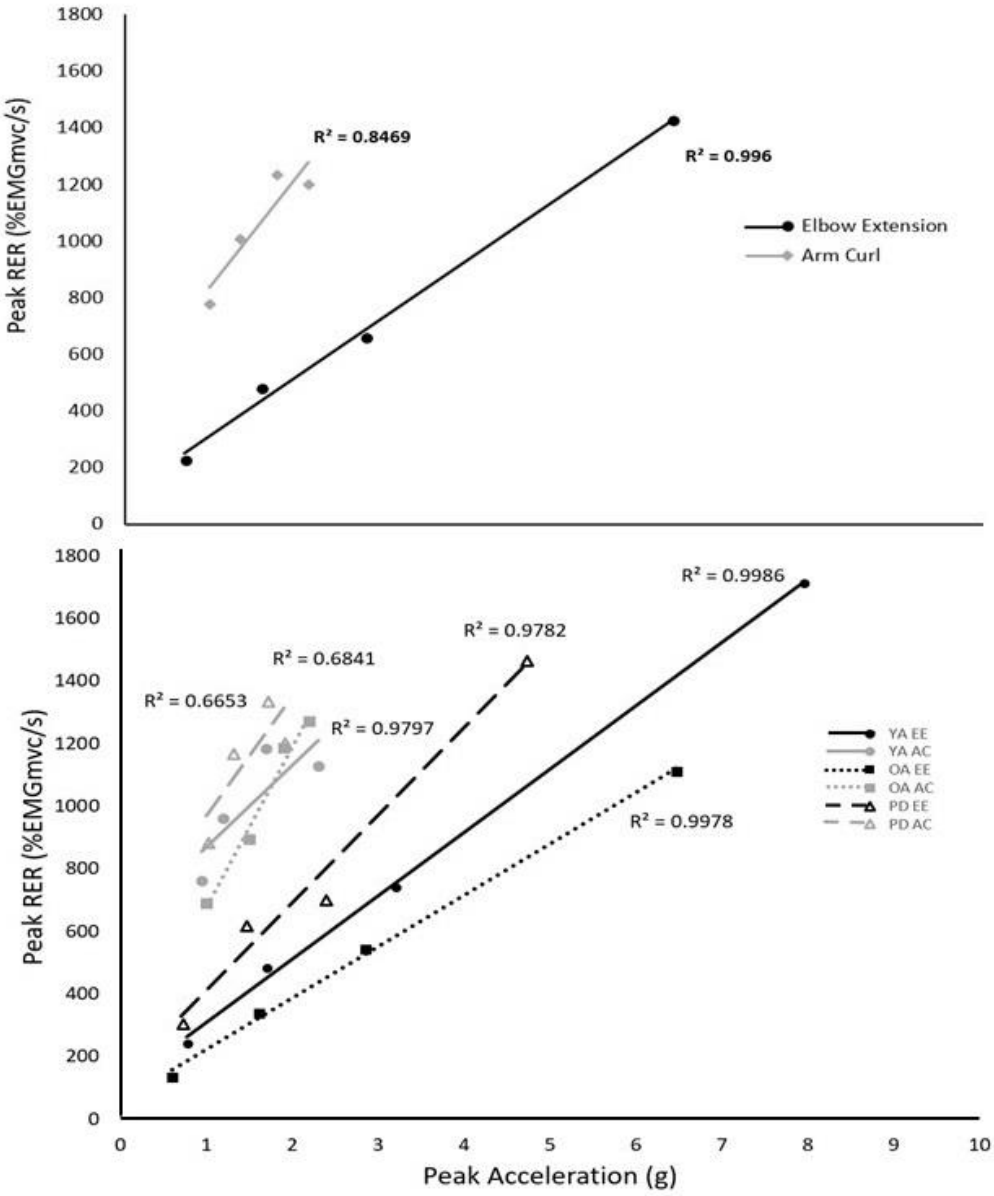


4.7 Shows the relationship of Vastus Lateralis peak RER (%EMGmvc/s) during recumbent cycling and 4-meter walk at preferred and AFAP speed categories. Within each condition, AFAP required greater peak RER than preferred. There were no differences between the two conditions in peak RER at a preferred pace, but YA and PD at significantly greater peak RER during AFAP cycling than during AFAP walking. OA had no significant difference in peak RER in the two AFAP conditions.

Comparing the upper extremity conditions in all groups combined, in the slowest (0.3Hz) condition, arm curl is 41% faster and required 241% greater peak RER than EE. In the preferred (0.5Hz) condition, arm curl had 110% greater RER but was 16% slower than EE. In the fast (0.9Hz) condition Arm curl required 86% greater RER but was 37% slower than elbow extension and in the AFAP condition, arm curl RER peak RER was 16% lower than elbow extension and 67% slower (Figure 7). Recognizing weighted resistance elicits greater neural excitation during non-rapid movement than unweighted exercises (Andersen et al., 2006), the Senior Fit Test arm curl creates high levels of neural excitation by adding weighted resistance and instructions of AFAP indicating maximum levels of neural excitation may be necessary to complete the task. The arm curl assessment can be used to determine function using common equipment.

Corcos (Corcos et al., 1989) discussed elevated neural excitation in rapid movement and van Cutsem (Van Cutsem et al., 1998) determined underlying elevated motor unit firing rate behavior in association with rapid isometric contractions. Although elbow extension peak RER during AFAP was 16% greater with 67% greater acceleration than arm curl AFAP, both movement seem to achieve relatively high rates of neural excitation. While Harwood et al (Harwood et al., 2011) found triceps RMS from onset to peak velocity to plateau during elbow extension, a strong linear relationship between neuromuscular excitation and acceleration with no plateau was observed using the RER measure in the present study. This raises the question of

whether the selection of the neural excitation variable might influence results in a manner that has not been fully considered.



4.8 Aggregated (top) and group (bottom) data plot of both elbow extension and arm curl peak acceleration to peak RER. No group-by-speed interaction existed for either movement which can be see in the bottom figure. Note, the slow arm curl required greater peak RER than the "fast" elbow extension task for both aggregate and individual groups. The AFAP elbow extension required non-significantly greater peak RER than the AFAP elbow curl. In the bottom figure, note the similarities between the groups in both arm curl and elbow extension.

Research informs us that greater neural excitation is associated with higher levels of function and mobility (Clark et al., 2010). The NIH 4-meter walk instructions of walking at a "preferred" pace does not consider the association of gait speed to health and function (Studenski et al., 2011) and the high levels of neuromuscular excitation that are required to produce rapid movement (Duchateau & Baudry, 2014). In VL, the peak RER during AFAP was greater than in the preferred rate condition for all three groups (YA: 186%, OA: 128%, PD: 42%). This study supports Clark et al.'s finding (Clark et al., 2013) of the benefit of using an "as fast as possible" walking condition rather than a "preferred" or "usual" pace.

While recumbent cycling met the expectations of a robust group effect in three of the five muscles, 4MW only revealed a group effect in SO, TA, and MG (all $p<0.049$). For the walking condition, a possible explanation for the muscle-specific elevations in peak RER in OA and PD as compared to YA is an increase in coactivation. during gait. Both older adults (Schmitz, Silder, Heiderscheit, Mahoney, & Thelen, 2009) and PwPD (Dietz, Zijlstra, Prokop, & Berger, 1995) have shown increased co-activation of TA and SO during midstance of gait. As dynamic balance is related to gait speed in OA (Shimada et al., 2003) and PwPD (Yang, Lee, Cheng, Lin, & Wang, 2008), co-activation about the ankle may be a strategy to maintain stability. Figure 8 shows recumbent cycling compared to walking in the "preferred" and "AFAP" speed condition. Note that "AFAP" RER was greater than "preferred" RER in both movements for all groups. Further, in the "AFAP" speed condition for

PwPD, cycling elicited greater RER than walking and may be a more valid means of assessing NE in PwPD over walking. Elimination of balance as a confounding factor may provide a more accurate representation of an individual's neuromuscular excitation capabilities in mobility.

Limitations

The participants in the PD group were recruited from a local community of individuals who were actively engaged in PD specific exercise interventions such as Rock Steady Boxing[tm] and a recumbent cycling interval program (Uygur et al., 2017). Their participation in power and velocity-based exercises may have slowed down or negated the symptoms of PD, thus making their measures more similar to those of the OA in the present study.

Conclusion

Movement slowing is often a first visible sign of functional decline in older adults and people with PD. Understanding the role of the rate of neural excitation of muscle in the movement slowing process might help facilitate more targeted mobility assessments such as a recumbent cycling peak RPM assessment or more frequent inclusion of the seated arm curl. Determining the rate of neural excitation post-assessment might lead rehabilitation practitioners to develop more specific interventions which allow older adults and PwPD to maintain functional independence

for longer. These results are the outcome of recording surface electromyograms during arm curl, elbow extension, recumbent cycling, and walking at difference movement velocities from healthy young and older adults, and people with PD.

The use of prescribed movement velocities is an effective way to study peak rates of neural excitation of muscle. Increasing the prescribed velocities revealed group differences in unloaded elbow extension but not in weighted arm curl. Group by speed differences were observed in lower extremity musculature during cycling while only seen in vastus lateralis in walking. For people with PD, peak RPMs on a recumbent bicycle generate greater peak RER while minimizing the role of balance and may be a more appropriate measure of their bradykinesia. No peak RER significant differences were seen in older adults between AFAP walking and peak RPMs in cycling indicating that either may be useful for measuring function and movement slowing.

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Chapter 5

SUMMARY

Older adults and people with Parkinson's disease (PD) are two populations who experience slowing of movement. With a slowing of movement comes a decline in function and a loss of independence. While a decline in function has often been associated with a decline in strength, Hazell's review found high-velocity low resistance power training to be a more effective means to improve function in older adults (Hazell, Kenno, & Jakobi, 2007), while Ni (Ni, Signorile, Balachandran, & Potiaumpai, 2016) found power training to effectively decrease bradykinesia symptoms in people with PD. Noting the Power=force x velocity equation, Hazell's review effectively compared "power" to "force" (strength) in the context of function. Considering the "velocity" term in the power equation, a comparison of high velocity yoga training to power training yielded similar functional improvements in people with PD (Ni, Signorile, Mooney, et al., 2016). High velocity training also improved function in older adults (Bellumori, Uygur, & Knight, 2016) indicating the importance of quickness in function. The isometric surrogate for quickness, rate of force development (RFD), is determined by the quality of central drive and the resulting neuromuscular excitation (NE), with high levels of both associated with function and mobility (Baldissera & Campadelli, 1977; Bento, Pereira, Ugrinowitsch, & Rodacki, 2010; Mian, Baltzopoulos, Minetti, & Narici, 2007).

One methodological approach used here to study the NE and rate-dependent motor output involved the use of surface electromyography (EMG) during rate-dependent isometric force production. In such work, one must carefully consider the wide variety EMG measures used and the present examination of the NE:RFD relationship included determination of the most appropriate dependent measures. Furthermore, when considering the NE:RFD relationship, one should be aware of the underlying behavior of individual motor neurons. Thus, another part of this dissertation sought evidence in EMG measures of the bilinear relationship between the amount of stimulation of a motor neuron and the resulting firing rate. Early evidence of this bilinear input-output transform was obtained from experiments in which current was injected into a feline lumbar-sacral nerve plexus while alpha motor neuron firing rates were measured (Kernell, 1965). The bilinear relationship reported by Kernell indicated a primary linear relationship, a secondary linear relationship with a greater slope, and a change point where the transition occurs. The feline bilinear relationship was translated to *in vivo* human anconeus muscle during dynamic elbow extension. Both a primary and secondary slope were found with the change point occurring at a velocity of 55%$Velocity_{max}$/s (Harwood, Davidson, & Rice, 2011).

Most studies related to the NE:RFD relationship have used either slow ramp force development conditions (Christie, Greig Inglis, Kamen, & Gabriel, 2009) or ballistic force development conditions (Van Cutsem, Duchateau, & Hainaut, 1998), which left the region that may include a potential change point less-well documented. The first aim of this research was to describe the relationship between NE and peak

RFD. This was accomplished via two steps. The initial step was to determine the best candidate measures of NE for this purpose by describing the strength of the relationships between a series of common and experimental EMG measures and peak RFD. The second step was to determine the best-fit model of the relationship between a NE measure reliant on EMG onset and a measure not reliant on EMG onset with peak RFD. The outcome of the initial step showed the root-mean-square of the initial 75ms of EMG (RMS75) to have the strongest Spearman's rho correlation (ρ =0.80) while peak rate of EMG rise (RER) to have the strongest Spearman's rho correlation (ρ =0.69) of those measures not reliant on EMG onset. The relationship between these measures and peak RFD was fitted with four different models (linear, bilinear, log-log transformation, and exponential). Based on Akaike's Corrected Information Criterion (AICc), the relationship between RER and RFD was linear for six of twenty-one participants, bilinear for thirteen of twenty-one participants, and exponential for two of twenty-one participants. The relationship between RMS75 and RFD was linear for fourteen of twenty-one participants and bilinear for seven of twenty-one participants. This part of the dissertation research provided meaningful indicators of bilinearity in the NE:RFD relationship where little, or no, such information has been reported previously. It is likely that adequate sampling across a wide range of RFD conditions, evaluation of the NE:RFD relationship at the individual rather than group level, and selection of optimal dependent measure (RER in this case) all contributed to this finding.

Having identified potentially sensitive measures and having a sound modeling approach to study the relationship between peak RER and peak RFD, the second aim of this research was to examine NE (via RER) during four common movements (arm curl, elbow extension, recumbent cycling, and 4-meter walk) performed at increasing movement speeds in young adults (YA), healthy older adults (OA), and people with PD (PD). We were interested in determining whether group differences in NE can explain group differences in movement speed. All movements revealed a main speed effect with peak RER increasing as movement speed increased, but only recumbent cycling revealed a group-by-speed interaction. RER of vastus lateralis, soleus, and tibialis anterior increased differently for each group as cycling RPMs increased. All groups had a significant movement condition effect, indicating RER differences across the four movement conditions when performed "as fast as possible." The four meter walk test performed "as fast as possible" elicited greater RER than when performed at a "preferred" pace in all groups.

Aim 3 was to perform a pilot analysis on the four common movements to explore the possibility of observing a bilinear relationship between peak RER and peak acceleration or peak movement rate. Recumbent cycling was found to have the potential for bilinearity by showing significance in the addition of a quadratic term to the data. Subsequent research should apply the more robust modeling methods used in the preceding aims to similarly examine RER changes with increasing bicycling cadence.

Neuromuscular excitation is a key determinant in velocity-dependent function. Clark (Clark et al., 2010, 2014) found older adults with mobility limitations to have lower NE than those without mobility limitations. The studies in this dissertation contribute to this body of work by adding systematic comparisons of noninvasive measures of NE and by providing some evidence of the underlying bilinearity in motor neuron firing that is known to exist in felines and humans. In individuals or populations for whom movement rates are insufficient, one might have more reasons to specifically consider whether secondary range behavior is absent and whether it can be restored? The present research also lends support to the performance of assessing function in an "as fast as possible" condition due to the elevated level of NE, which is associated with functional independence.

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Appendix A

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Appendix F

RESULTS OF NON-LINEARITY IN DYNAMIC MOVEMENT

Methods

Evidence of secondary behavior is determined via a hierarchical multiple regression (HMR) with the inclusion of a quadratic term. The inclusion of the quadratic term assumes a single directional change point in the data with the HMR assessing the significance below the change point and the variance change by inclusion of the quadratic term (points above the change point) and the model in its entirety. The results will be given as a linear r-squared value and significance for points below the change point (r^2-1), an r-squared change value for points above the change point (r^2-2). F-values will be shown for a quadratic regression if significance exists both above and below the change point, linear F-values will be given otherwise.

Results

Evidence of secondary range behavior

For each of the movement conditions, the groups were assessed separately. Examination of scatter plots lead to vastus lateralis, alone, being chosen for lower extremity HMR analysis.

Evidence of non-linearity between peak acceleration and peak RER was seen during recumbent cycling for YA and OA and walking for PD. For all other movements no groups showed evidence of a potential non-linear relationship. Variance for arm curl and walking were low (arm curl: r^2=0.086; walking (YA, OA, PD): r^2=0.292, 0.076, & 0.290, respectively). Movements that showed evidence of a non-linear relationship had r^2-changes of at least 5.0% indicating a specific threshold necessary for a quadratic over a linear relationship. YA elbow extension had the highest variance with change in peak acceleration accounting for 81.4% change in peak RER. The lowest variance was OA during walking. Only 7.6% of the change in peak RER was due to changes in peak acceleration. All r-square and F-values can be seen in table 1.

Table A.1 r-squared and p- values below (r^2-1) and above (r^2-2) the change point in a hierarchal multiple regression of peak RER values with peak accelerations or RPMs (cycling). When r^2-2 was not significant, the model fit was listed as linear, when r^2-2 was significant, the model shows evidence of a non-linear relationship and Quadratic is listed as model. Degrees of Freedom (dof), F-, and p- values are given for the model listed. When neither r^2-1 or 2 were significant, no model or F values were given. Variance (r^2) for the quadratic models can be calculated by adding the r^2 of each segment. Variance for the linear model is simply r^2-1.

Movement (dof)	r^2 -1 (p)	r^2-2 (p)	Model	F(dof), p - values
Arm Curl				
all (1, 114)	0.086, (0.001)	0.025, (0.074)	Linear	10.76, (0.001)
Elbow Extension				
YA (1, 38)	0.814, (<.001)	0.003, (0.442)	Linear	166.74, (<.001)
OA (1, 37)	0.669, (<0.001)	0.009, (0.926)	Linear	74.69, (<0.001)
PD (1, 36)	0.662, (<0.001)	0.002, (0.639)	Linear	70.608 (<0.001)
Cycle				
YA (1, 58)	0.515, (<0.001)	0.059, (0.007)	Quadratic	38.42, (<0.001)
OA (2, 54)	0.769, (<0.001)	0.099, (<0.001)	Quadratic	176.81 (<0.001)
PD (1, 51)	0.311, (<0.001)	0.040, (0.082)	Linear	23.44, (<0.001)
Walk				
YA (1, 31)	0.292 (0.001)	0.046, (0.158)	Linear	12.78 (0.001)
OA	0.076 (0.098)	0.017 (0.427)	None	none
PD (2, 35)	0.290, (<.001)	0.103 (0.020)	Quadratic	11.31 (<0.001)

Discussion

The existence of a bilinear relationship between alpha motor neuron input to output was established in a feline model with injected current (Calvin, 1978; Kernell, 1965) and translated to humans in the movement velocity to motor unit discharge rate relationship (Harwood, Davidson, & Rice, 2011). It was also shown to exist in the peak RFD to peak RER relationship during isometric dorsiflexion (Josephson, Rose,

Knight dissertation manuscript 1.2). The hypothesis of a linear relationship during arm curl was realized while elbow extension, recumbent cycling, and 4-meter walking had mixed results. A confounding factor was the limited variations in speed and overall data. For this reason, the data for each group was aggregated and analyzed. The Simpson Paradox (Julious & Mullee, 1994) must be taken into consideration as the relationship of peak acceleration to peak RER is highly individualized (Josephson, Rose, Knight dissertation manuscript 1.2). Further, the HMR reveals the significance of both elements of dual-system model but cannot determine if adding other terms to the equation are valuable. To accomplish that level of modeling Akaike's Information Criterion is recommended with a greater amount of data per individual (Akaike, 1973; Shono, 2000).

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Appendix G

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ACTION:	APPROVED
APPROVAL DATE:	January 23, 2018
EXPIRATION DATE:	November 18, 2018
REVIEW TYPE:	Expedited Review
REVIEW CATEGORY:	Expedited review per 45 CFR 46.110(b) (2)

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