EXERCISE EFFECTS ON MUSCLE CAPACITY AND PHYSICAL FUNCTION IN OLDER OVERWEIGHT WOMEN AND CHRONIC STROKE SURVIVORS.

By

EWAN RHYS WILLIAMS

(Under the Direction of Ellen M. Evans)

ABSTRACT

Purpose: Mobility is critical to maintain physical independence especially for overweight older adults and individuals afflicted by stroke. Leg rate of torque development [RTD] as a measure of peak muscle power and asymmetry of muscle power [%ASYM] have emerged as potential predictors of lower extremity physical function [LEPF] but the plasticity of these outcomes in response to exercise training is unknown. **Methods**: Utilizing secondary data analysis from two separate intervention studies: 1) a 6-month exercise and diet-induced weight loss intervention for overweight inactive older women, and 2) an 8-week power training intervention for chronic stroke survivors, the three primary aims of this dissertation were: a) to determine the relative effect of weight loss with or without exercise training [EX+WL vs. WL] on changes in RTD (Aim 1) and %ASYM (Aim 2) and subsequent associations with changes in LEPF in overweight and obese older women, b) to determine the effect of power training on RTD parameters and subsequent changes in gait and walking performance in chronic stroke survivors (Aim 3). **Results**: For primary aims 1 and 2, weight loss was similar in both groups ($p > 0.95$) averaging -7.1±4.1kg and -9.8±4.2%. Knee flexion RTD improved in EX+WL compared with WL (36% vs. -16%; $p = 0.031$), with no other changes in RTD parameters observed;

changes in RTD were not associated with changes in LEPF. No group changes in %ASYM were observed. Reductions in Leg Flexor %ASYM, alone, were associated with improvements in Up and Go task performance, independently explaining 15.8% of the variance ($p < 0.05$). For primary aim 3, our results suggest power training to be an effective intervention for improving RTD in both the paretic and nonparetic limbs, however, only improvements in the nonparetic limb RTD were associated ($p < 0.05$) with changes in walking speed ($r = 0.66$) and walking task performance ($r = 0.88$).

Conclusion: Our results suggest exercise training can improve RTD, but not %ASYM indices of power in older women undergoing weight loss but the impact on LEPF appears negligible. Furthermore, power training can be an effect intervention post-stroke to improve gait characteristics and walking performance.

KEY WORDS: Aging, Exercise, Overweight, Stroke, Power

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DEDICATION

"Etto ni welir un cerydd dros yr amser presennol yn hyfryd, eithr yn anhyfryd: ond gwedi hynny y mae yn rhoi heddychol ffrwyth cyfiawnder i'r rhai sydd wedi eu cynnefino ag ef."

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CHAPTER 1

INTRODUCTION

1.1 Significance

Mobility, defined as the ability to move unassisted, is a critical component for the maintenance of independent functioning, a great number of activities of daily living (ADL), and preservation of quality of life (Pantelaki et al., 2019). Standards for what is considered a limitation in mobility is lacking; however, certain functional markers, including, but not limited to, rising from a chair or ascending stairs, have been reported as indicative marks of physical functional health (Tinetti et al., 1986). Maintaining physical function is paramount due to its adverse influence on health outcomes such as physical disability, institutionalization and mortality in older adults (Guralnik et al., 1995; Hirvensalo et al., 2000; Shumway-Cook et al., 2002). With aging being a multidimensional construct, delineating physiological variables that fluctuate with aging, and/or cognitive adaptations, that account for a decline in mobility is challenging. However, it is widely accepted that salient factors that affect mobility are declines in muscle mass and force production, often coined sarcopenia and/or dynapenia (Clark & Manini, 2008; Frontera et al., 2000; Lindle et al., 1997).

The mechanisms and implications consequent to these adaptations are relatively understudied or lacking a consensus. However, a growing body of literature has started to identify variables that may warrant further investigation. Muscle power, for instance, has been observed as a stronger predictor of certain physical function task performances in older adults, compared to traditional measures of muscle strength (Kalapotharakos et al., 2010). Muscle power, quantified as the product of force and velocity, has been proposed as a more stringent measure of muscular adaptations, specifically in the aging and clinical populations, due to its sensitivity to the physiological changes that occur in the neuromuscular motor systems (Clark et al., 2011). However, although a number of mechanistic explanations have been suggested for the decline in power observed with age, a definitive characterization of the interaction of factors, remains elusive. However, perhaps more essential is the fact that a lessening of muscle power appears to have significant detrimental effects on quality of life, as the majority of activities of daily living require rapid alterations of muscle activation for task completion (Reid et al., 2015).

Recent literature suggests that rapid torque (or force) development or rate of torque development (e.g. [RTD]; delta torque/delta time) of primary muscle groups involved in LEPF are independent predictors of physical function tasks in older adults (Olmos et al., 2019, 2020; Osawa et al., 2018). Additionally, greater knee flexor RTD has been observed in non-fallers compared to fallers, suggesting rapid activation patterns may play an important role in balance recovery after a trip or external perturbation (Bento et al., 2010; Pijnappels et al., 2008). However, the underlying mechanisms and subsequent trainability of RTD parameters with respect to LEPF in older adults remain incompletely characterized (Conlon et al., 2017; Moura et al., 2020). Thus, further investigation is warranted regarding the plasticity of RTD and the subsequent influence on LEPF performance.

The degree of muscle capacity asymmetry [ASYM] has also been suggested as a potential contributing factor to LEPF performance. Although, some degree of ASYM is common in individuals, reports suggest the lower limb strength ASYM >10% may be clinically meaningful in older adults and may represent an early detectable risk factor for future impaired functional capacity (Carabello et al., 2010). Previous studies have reported an increase in strength ASYM of the leg extensors to be associated with impaired postural balance (Portegijs et al., 2005), increased incidence of falls (Laroche et al., 2012; Skelton et al., 2002), and a reduction in LEPF (Straight et al., 2016). However, a consensus in the literature is lacking regarding change in ASYM via various interventions and the relative importance for LEPF (Fimland et al, 2011).

An accumulating body of evidence has highlighted the importance of muscle power on physical function and mobility in older adults. However, the confounding effect of additional clinical factors that often accompany and/or impact the aging population have been relatively unexplored. Subsequent to this, explorations into methods of improving key factors that potentially impact LEPF in these populations are vague. Exercise and physical activity multimodal interventions are considered one of the main strategies to counteract reductions in LEPF in older adults, especially in “at risk” populations (Groessl et al., 2019). However, the impact of exercise on determinants of muscle quality, power and clinically relevant LEPF task performance is less understood.

Relatedly, the prevalence of obese older adults’ living in the United States has drastically increased over the past three decades, with over 40% currently afflicted (Hales et al., 2017). Obesity negatively impacts LEPF and is associated with loss of independent living in part due to reduced muscle quality and capacity (Villareal et al., 2005; Vincent et al., 2010). Concurrent exercise/physical activity and weight loss interventions are known to be effective to prevent functional decline, with the combination resulting in greater improvements in muscle strength, physical function, and mobility than either treatment alone (Jiang & Villareal, 2019; Villareal et al., 2011). However, the inclusion of power modulations, specifically RTD parameters, in response to these interventions are lacking and may be salient contributing factors to improvements in LEPF observed in response to exercise training and weight loss in older adults.

As with obesity, the incidence of stroke, defined as a sudden onset of a focal neurological deficit caused by a cerebrovascular occlusion or rupture, is increasing globally, and is further exacerbated with age. Affinity of physiological and neurological deficits following stroke vary by data collection agency; however, unfortunately, ~60-85% of stroke survivors exhibit motor coordination deficits and ~40+% have total hemiparesis (Algurén et al., 2010; Perry et al., 1995). Despite this, it is suggested that ~90% of stroke survivors regain walking ability within 6 months post stroke; yet, poor balance, limb weakness and asymmetrical motor control remain issues in the vast majority of ambulatory stroke survivors. Recent literature indicates positive effects of high-intensity and high-velocity lower limb training programs on walking-speed (Hunnicutt et al., 2016; Morgan et al., 2015), and general locomotor function (Aaron et al., 2017) in chronic stroke survivors. However, as with obese older adults, the inclusion of power modulations, specifically RTD parameters following this form of exercise, and the impact on ambulation characteristics is unknown.

To date, research targeting muscle capacity, lower extremity physical functioning (LEPF), and fall risk in the older adult and/or chronic stroke populations are limited by translation of clinical and/or research measures and resources. For instance, muscle power required for single-joint movements, often observed in the literature, does not accurately represent the essential forces to correctly perform most purposeful complex synergies involved in daily activities. As such, complete mechanography of patients would be an ideal assessment. However, considering the aforementioned physiological changes in these populations, such protocols are typically deemed risky. Furthermore, attaining force plates, motion capture and the expertise to analyze said data is traditionally unattainable in the clinical settings. Thus, exploring methodologies that are clinically feasible but have high specificity are imperative to understanding the influence of aging and clinical conditions on risk for reductions in LEPF and subsequently falls.

1.2 Primary Aims

Therefore, in this context, the overarching aim of this portfolio, which included 3 manuscripts devised from secondary analyses afforded by two separate project datasets, is to evaluate the effects of a) muscle force production (i.e., RTD) and b) contralateral activation patterns (i.e., %ASYM) on clinically relevant LEPF in two clinical populations (overweight older women and chronic stroke patients), using clinically available equipment and methodologies, following an exercise, exercise and weight loss, or weight loss intervention.

Primary Aim 1: To determine the relative effect of weight loss with or without concomitant exercise training on RTD parameters in overweight/obese inactive older women, and the association of these adaptations on LEPF task performance. Hypothesis: It was hypothesized that a) weight loss combined with exercise training would improve RTD parameters to a greater degree than weight loss alone and the effect would be independent of changes in weight and b) changes in RTD parameters would be positively related to changes in LEPF.

Primary Aim 2: To investigate the relative effect of weight loss, with or without exercise training on between and intra-leg power ASYM in overweight/obese inactive older women. And subsequently, to explore the association between changes in ASYM and changes in clinically relevant LEPF performance tasks. Hypothesis: It was hypothesized that a) exercise training would reduce all indices of ASYM and b) reductions in ASYM would be associated with improvements in LEPF.

Primary Aim 3: To determine the effect of POWER training on knee extensor RTD parameters and explore the association among any adaptations in RTD parameters and gait characteristics and walking task performance, in chronic stroke patients. Hypothesis: It was hypothesized that a) the intervention would improve bilateral RTD parameters and b) changes in RTD parameters would be positively associated with improvements in walking speed.

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CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

Mobility is largely considered a key determinant of health and quality of life among both the aging and clinical populations (Fagerström & Borglin, 2010; Groessl et al., 2007; Trombetti et al., 2016). Indirectly, limited ability to perform lower extremity physical function [LEPF] performance tasks have a multitude of adverse risk factors, including, but not limited to, cognitive decline, reduced independence, and an augmented risk of fractures and falls (Feskanich et al., 2002; Matthews et al., 2012; Patel et al., 2010). Directly, a reduction in mobility and LEPF has been shown to result in higher rates of morbidity, disability, hospitalization and ultimately mortality (Guralnik et al., 1995; Hirvensalo et al., 2000; Shumway-Cook et al., 2002). Standards for what is considered a limitation in mobility is lacking; however, certain functional markers, including, but not confined to, rising from a chair or ascending stairs, have been reported as indicative marks of physical functional health (Tinetti, 1986). With aging being a multidimensional construct, delineating associated antagonistic variables that fluctuate with aging, or cognitive adaptations, and account for a decline in LEPF is challenging. However, it is widely accepted that one constant feature that may affect mobility and LEPF is a decline in muscle mass, strength, and force production, often termed sarcopenia or dynapenia (Morley et al., 2011).

Muscle mass is a primary determinant of sarcopenia. However, a dichotomous relationship appears to be present between muscle mass and strength (Morse et al., 2005), with the magnitude of loss in one disassociated with the loss in the other (Reid et al., 2012). Consequently, more encompassing alternative markers of muscular performance have recently gained traction in the research. Muscle power, quantified as the product of force and velocity, has subsequently been proposed as a more stringent measure of muscular adaptations, specifically in the aging and clinical populations, due to its sensitivity to the physiological changes that occur in the neuromuscular motor systems (Clark et al., 2011). Mechanistic determinants behind changes in muscle power remain elusive with multiple plausible explanations, ranging from single muscle fiber contractile properties (Frontera et al., 2008), intermuscular adipose tissue infiltration (Yoshida et al., 2012), and neuromuscular activation (Aagaard et al., 2010) all being explored, as examples. However, perhaps more important, a lessening of muscle power appears to have significant detrimental effects on quality of life, as the majority of activities of daily living require rapid alterations of muscle activation for LEPF task completion; thus, strategies to preserve or enhance muscle power are warranted (Reid et al., 2015).

Delineation of direct inferences and contributing factors on the deterioration of muscle power in aging and the subsequent impact on LEPF is complex, however, bilateral variances in activation patterns have been suggested to play a role. Whilst some degree of muscle capacity asymmetry [ASYM] is common in individuals, reports suggest lower limb strength ASYM >10% may be clinically meaningful in older adults and may represent an early detectable risk factor for future impaired functional capacity (Carabello et al., 2010). A consensus is lacking; however, it has been reported that greater between-limb %ASYM muscle capacity is associated with impaired postural balance (Portegijs et al., 2005), increased incidence of falls (Laroche et al., 2012; Skelton et al., 2002), and a reduction in LEPF (Straight et al., 2016). Considering the potential impact, deliberation of muscle power activation patterns, commonly expressed as %ASYM also warrants investigation.

Rate of torque development (RTD: ∆Torque/∆Time), which emphasizes torque production during the initial 200ms of a given muscle contraction (Aagaard et al., 2002), has recently become a popular method for assessing muscle power in both the clinical and athletic populations due its ease of assessment. Despite this, discrepancies in measurement techniques have resulted in inconclusive and inconsistent results in the literature. Recently, Maffiuletti et al. (2016) published a review article examining and suggesting recommendations for techniques to provide a more valid and widespread quantification of RTD. However, beyond the practical recommendations regarding technique, the relationship between RTD, mobility, and/or LEPF in the older adult and certain clinical populations remains inadequately characterized and may have great clinical importance. This report subsequently seeks to review studies that examined RTD parameters in relation to mobility and LEPF in older adults or chronic stroke patients, both know to have reduced muscle power and LEPF impairments, to help inform and develop interventions to facilitate physical functional independence.

Studies were identified via literature searches on relevant electronic databases through December 2020 using the following search terminology: “Rate of Torque Development”, “Rate of Force Development”, “Physical Function”, “Mobility”, “Asymmetry”, “Older Adults”, “Overweight or Obese”, “Stroke”. For the purpose of this review, older adults were considered cohorts ≥65 years old and all studies examining stroke and RTD were included due to their clinical restrictions.

2.2 Rate of Torque Development

Measurement and Methodological Considerations

Due to the sensitivity and subsequently reduced reliability, a strict methodological approach is required in order to collect meaningful and worthwhile RTD data. Although alternative methods have been utilized, RTD has most often been assessed in isolated single-joint tasks such as ankle dorsi-/plantar flexion (Gruber et al., 2007), knee extension/flexion (Callahan et al., 2007; De Ruiter et al., 2004; Y Osawa et al., 2018; Thompson et al., 2013), hip abduction/adduction (Morcelli et al., 2016), and elbow flexion/extension (Barry et al., 2005) on a commercially available isokinetic dynamometer or a custom-built dynamometer rotating around a singular axis. Such mechanisms reduce the confounding influence of joint angle and angular velocity changes by restraining and restricting the participant's extraneous movement or muscular incorporation, although some biological interference is arguably inevitable.

As with any sensitive mechanistic measurement, acquisition and filtering accuracy and consistency are particularly important. However, dynamometer variations and compliance make for a less than ideal environment. A consensus for the distinct assessment timeframe for RTD is lacking; however, 0 – 200ms is considered a ballistic movement (Suchomel et al., 2018). As such, it is important that the recording apparatus has low noise and high frequency signaling capabilities to accurately measure motor response time. Considering human skeletal muscle has the capability of producing >10 maximum isometric forces per second (De Ruiter et al., 1999) and motor response times can range from <7ms and <13ms for involuntary and voluntary responses, respectively (Tillin et al., 2010), a sample rate of ≥1kHz is ideal (Maffiuletti et al., 2016).

Considering the nature of RTD measurements, differing analysis techniques can vary the results extensively. Initially, differing onset detection methods exist, with both absolute unit thresholds and relative percentages to an individual's maximal voluntary contraction [MVC] appearing to be the most reliable processes. Furthermore, Tillin et al. (2012a, 2013b) recommend that manual detection methods be exploited due to the high inherent noise levels observed in dynamometers. Ensuring consistency during this initial phase is inevitably vital for a technique that is dependent on the first 200ms. Once onset is defined, a number of outcome measures can be obtained from the force time curve. Force at specific timepoints and peak RTD (i.e., the steepest part of the curve) appear to be the most common outcomes reported (Rousanoglou et al., 2010; Tillin et al., 2010). However, considering change in momentum of a body is directly proportional to impulse measurements during functional activities, impulse is arguable the most functionally relevant, yet is rarely included. Furthermore, data normalization techniques can significantly adjust the reported results. Both body mass and muscular CSA (cross-sectional area) have been reported as useful normalization outcomes. However, the ideal function has yet to be disclosed or discovered. Irrespective of this lack of convention with regard to normalization of RTD data, all measures should be corrected for gravitational forces in some way, whether by limb weight or dynamometer calibration.

Excluding task specifics, acquisition, and filtering, it appears that feedback and methods differ and potentially influence RTD data the most. Naturally, instructions play a pivotal role in any study application. However, the distinct vocabulary used prior to and during the RTD trial has emerged pinnacle. Explorations comparing the contractions following varying commands suggest the use of “contract as hard and as fast as possible” to be the most successful instruction (Bemben et al., 1990; Sahaly et al., 2001). However, few studies identify their methodological instructions, and of those who do, few utilize these protocols.

Physiological Deliberations

For the majority of voluntary skeletal muscle movements, both neural and muscular factors contribute to the performance of rapid contractions. However, considering the complexity of human physiology and equating the relative contribution of neural and muscular factors is very difficult, yet central to the appreciation of the association of RTD within select subject groups.

Association between RTD and neural characteristics, including motor unit activation and discharge rates, have been assessed by surface EMG in several study groups, in vivo (De Ruiter et al., 2004; Fimland et al., 2011; Klass et al., 2008). Irrespective of subject population, results indicate that rapid force production, especially at onset, is predominantly determined by muscle activation rate rather than speed-related muscle contractile properties (Andersen & Aagaard, 2006; De Ruiter et al., 2004). However, it appears this relationship may be inverse with contractions >75ms (Folland et al., 2014). Despite these seemingly sound results, due to the vast inter-individual variability in MVC performance and mechanistic restraints in neural determinant assessment, more foundational research is needed to quantify the relationship between these variables and RTD.

Neural determinants alone would not completely explain the observed inter-muscular and inter-individual differences; thus, a number of muscular factors have been considered as influential elements. Bearing in mind muscular assessment typically involves invasive measures, the majority of ensuing factors are based on reasonable theoretical knowledge or empirical data outside of distinct RTD studies. Potential muscular determinants for consideration include: muscle size and architecture (Blazevich et al., 2009), muscle fiber type composition (Taylor et al., 1997), myofibrillar mechanisms (Hamada et al., 2000), and musculotendinous stiffness (Waugh et al., 2013). Certainly, further research and exploration is required; however, all the aforementioned factors change with age and neurological alterations and, thus, would imply plausible causation for explorations of RTD in the older adult and chronic stroke populations.

RTD Trainability

Practical implications of RTD are extensive in both the clinical and athletic populations; thus, understanding methods of amending or improving RTD is logically important. Both heavy-resistance strength training and explosive training (e.g., plyometric) appear to have strong stimulatory influence on RTD through their impact on muscle activation dynamics (Aagaard et al., 2002; Tillin & Folland, 2014), at least in recreationally trained male individuals. Conversely, a similar intervention design including aerobic, or muscle endurance training observed no changes in EMG amplitude or RTD parameters in a similar sample (Vila-Chã et al., 2010). These adaptations have been reported in both the young and older populations (Christie & Kamen, 2010; Patten et al., 2001). However, the plausibility of such regimes in untrained or inactive older adults or chronic stroke patients remains relatively unstudied.

2.3 Implications for Selected Cohorts with Compromised Muscle Power

RTD and Overweight/Obese Older Adults

The prevalence of obese older adults living in the United States has drastically increased over the past three decades, with close to a third currently affected (Hales et al., 2015). The list of impediments related to being obese for the older adult is extensive, with most contributing to limitations in mobility and deteriorations in physical function (Vincent et al., 2010). Although the exact mechanism underlying the associations remains elusive, obesity appears to correlate with impairments in muscle function and poor muscle quality (Valenzuela et al., 2020). Some studies have reported increases in absolute force and power production with higher body mass index [BMI], yet when normalized to body weight or other variables of body composition (i.e., relative characteristics), deficiencies in muscle function are actually observed (Tallis et al., 2018). However, considering the increased mass outside an obese individual's base of support, the ability to generate force rapidly to counteract this may be more essential than that of an age-matched healthy individual (Matrangola & Madigan, 2011; Robinovitch et al., 2002), especially in older adults.

RTD "performance" appears to be primarily determined by an individual's capacity to produce maximal voluntary contraction as a result of an increase in motor unit discharge rate (Klass et al., 2008). Nevertheless, reported large inter-muscular (e.g., leg extensors vs. flexor digitorum muscles) variations in RTD cannot be completely explained by muscle activation rates alone (Andersen & Aagaard, 2006). Thus, muscle composition, architecture and musculotendinous aspects have all subsequently been suggested to be contributing factors (Erskine et al., 2014; Folland et al., 2014). With an application to older adults, the effect of aging on muscular properties is extensive, with decreases in motor unit activation rate (Ling et al., 2009) and changes in muscle function (Larsson et al., 2019) being well documented in older adults (Bento et al., 2010; Van Driessche et al., 2019). Likely due to these adaptations, recent articles have reported RTD as an independent predictor of physical function tasks such as timed "up and go" as well as self-selected and maximal walking velocity in healthy weight older adults (Hester et al., 2019; Osawa et al., 2018). Along with accounts observing RTD as an independent predictor of physical function tasks and self-paced walking velocities in older adults (Olmos et al., 2020), RTD has also been reported to influence balance recovery ability following a trip perturbation (Pijnappels et al., 2005).

RTD and Chronic Stroke Patients

Both the physiological and neurological deficits following stroke vary by data collection agency. However, between 61-86% are living with motor coordination deficits and 37+% of chronic stroke survivors have total hemiparesis (Lui & Nguyen, 2018). Despite this, it is suggested that ~90% of stroke survivors regain walking ability within 6 months after stroke. However, poor balance, limb strength and asymmetrical motor control remains an issue in the vast majority of ambulatory stroke survivors (Roelofs et al., 2018). Evidence suggests that muscle weakness is a key impairment limiting mobility and LEPF following stroke. Compared to healthy adults, few studies have studied RTD in stroke patients, with these studies typically limited to cross-sectional study designs and older chronic stroke survivors. As expected, asymmetries in RTD between the non-paretic and paretic limbs have been observed at both the quadricep and ankle (Fimland et al., 2011; Horstman et al., 2010), which in turn, has been reported to negatively affect gait speed and LEPF (Mentiplay et al., 2018; Takeda et al., 2019) in chronic stroke survivors. Similar results have been reported in acute stroke survivors (Shimose et al., 2019). However, the literature and, thus, outcome measures are sparse in this population; and further research is required.

2.4 Future Direction: RTD Plasticity and Exercise Training

Collectively, the literature supports the notion that RTD parameters have important functional consequences in the overweight inactive older adult and chronic stroke cohorts, both known to have reduced mobility and LEPF abilities. This review also highlights that the physiological determinants of RTD are likely interconnected but incompletely characterized. Certainly, explorations utilizing both invasive measures and non-invasive imaging to understand the relative influence of muscular factors, in combination with the extensive EMG studies that are available, will further guide research regarding RTD parameters.

However, the clinical application of RTD within the current research appears to be lacking; thus, research devoted to the assessment and application of RTD for practitioners is warranted. It is recognized that clinical applications of RTD will be influenced by dynamometer availability. Finally, and most importantly, more research is warranted regarding exercise interventions to determine the plasticity of RTD as a marker of muscle power, ASYM aspects of muscle power, and the subsequent impact on mobility and LEPF. The ultimate long-term public health goal of this work is to contribute, albeit in a limited capacity, to research which influences interventions, programs and clinical recommendations toward the end of preserving or improving mobility or LEPF in inactive obese older adults and chronic stroke patients, two growing sectors of our population.

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CHAPTER 3

Weight Loss and Exercise Effects on Rate of Torque Development and Physical Function in Overweight Older Women

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3.1 Abstract

Purpose: Obesity negatively impacts lower extremity physical function [LEPF] and is associated with loss of independent living in part due to reduced muscle quality and capacity, especially in older adults. Concurrent exercise/physical activity and weight loss interventions are known to be effective to enhance LEPF. However, the inclusion of power modulations, specifically Rate of Torque Development [RTD] parameters in response to these interventions has not been investigated. The aim of this study was to determine the effects of weight loss, with or without exercise training, on RTD parameters and their potential impact on LEPF in overweight physically inactive older women. **Methods**: As a secondary data analysis of a 6-month parent project that involved weight loss involving different dietary regimens with or without exercise, this study involved overweight inactive postmenopausal women (69.1±3.6 yrs; 30.6±4.3 kg/m^2; n=44) who completed the trial within two groups: 1) exercise and weight loss [EX+WL; (N=30)] and weight loss alone [WL; (N=14)]. Leg strength was assessed via dynamometry with RTD parameters [RTD200 = RTD at 200ms, RTDPeak = Peak RTD and T2P = Δ Time to 1st Peak] subsequently measured from the maximal voluntary isometric contractions. LEPF was assessed via 6-min walk, 8-ft up and go, and 30-s chair stand. **Results**: Weight loss was similar in the groups (-7.1±4.1 kg; -9.8±4.2%, $p > 0.95$) whereas EX+WL had greater improvements in most LEPF tasks ($p < 0.001$). EX+WL had a greater increase in RTD200 Flexion compared with WL (36% vs. -16%, $p = 0.031$), with no other changes in RTD parameters observed. No significant regression models were observed predicting change in LEPF performance from changes in RTD parameters (all $p > 0.05$). **Conclusions**: The present findings suggest weight loss, which incorporates exercise training, can improve RTD parameters in overweight/obese physically inactive older women, yet these improvements may not transfer to improvements in physical function task performance.

Key Words: Obesity, Mobility, Leg Power, Concurrent Intervention.

3.2. Introduction

Mobility, commonly termed lower extremity physical function [LEPF], is considered a multidimensional construct and key to the maintenance of independence and quality of life with advancing age. Although numerous variables, all impacted by the aging process, influence LEPF, two well-established salient factors are leg muscle strength and power (Goodpaster et al., 2006; Skelton et al., 1994). In the laboratory or the clinic, quantification of muscle strength typically involves static force production around a single joint. Power, a product of force and velocity, is dependent, in part, on the rate of any given movement and may therefore be more sensitive than the conventional measures of strength (e.g., 1-rep maximum) to physiological fluctuations in the motor system that occur as an individual ages, especially beyond middle-age (Maffiuletti et al., 2016a). Indeed, a developing literature suggests that muscle power is more important than strength for the maintenance of LEPF in older adults (Kalapotharakos et al., 2010; Miszko et al., 2003; Zech et al., 2012).

The great majority of daily activities involving LEPF require rapid (<200ms) alterations of muscle activation; therefore, a reduction in activation capabilities may present specific challenges during more complex LEPF movement synergies in older adults. Recent literature suggests that rapid torque (or force) development or rate of torque development (e.g. [RTD]; delta torque/delta time) of primary muscle groups involved in LEPF are independent predictors of physical function tasks in older adults (Olmos et al., 2019, 2020; Osawa et al., 2018). Additionally, greater knee flexor RTD has been observed in non-fallers compared to fallers, suggesting rapid activation patterns may play an important role in balance recovery after a trip or external perturbation (Bento et al., 2010; Pijnappels et al., 2008). However, the underlying mechanisms and subsequent trainability of RTD parameters with respect to LEPF in older adults remain incompletely characterized (Conlon et al., 2017; Moura et al., 2020).

Although the link between muscle quality and LEPF in older adults is relatively well established, there are other key behavioral and physiological factors, beyond muscle strength or power, which contribute to reductions in LEPF in older adults, either directly or indirectly through their impacts on muscle quality. Indeed, the endorsement of habitual exercise/physical activity to prevent physical disability in older adults is well established by federal guidelines (Chodzko-Zajko et al., 2009) although unfortunately ~80% of older adults do not meet the guidelines, especially for strength training (Bennie et al., 2020; Keadle et al., 2016). Relatedly, the prevalence of obese older adults' living in the United States has drastically increased over the past three decades, with over 40% currently afflicted (Hales et al., 2017). Obesity negatively impacts LEPF and is associated with loss of independent living in part due to reduced muscle quality and capacity (Villareal et al., 2005; Vincent et al., 2010). Concurrent exercise/physical activity and weight loss interventions are known to be effective to prevent functional decline, with the combination resulting in greater improvements in muscle strength, physical function, and mobility than either treatment alone (Jiang & Villareal, 2019; Villareal et al., 2011). However, the inclusion of power modulations, specifically RTD parameters, in response to these interventions are lacking and may be salient contributing factors to improvements in LEPF observed in response to exercise training and weight loss in older adults.

Thus, in this context, the primary aim of this study was to determine the relative effect of weight loss with or without concomitant exercise training on RTD parameters in overweight/obese inactive older women. A secondary aim explored the association among changes in RTD parameters and changes in clinically relevant LEPF tasks in response to weight loss and/or exercise training interventions. It was hypothesized that a) weight loss combined with exercise training would improve RTD parameters to a greater degree than weight loss alone and the effect would be independent of changes in weight and b) changes in RTD parameters would be positively related to changes in LEPF.

3.3. Methods

3.3.1 Parent Project

3.3.1a Research Design

The parent project which allowed for this secondary data analysis involved a randomized controlled trial investigating the effect of two different 6-month dietary treatments with or without exercise on body composition, strength, and physical function in older women (Evans et al., 2021). Participants were randomized into three groups: 1) higher protein diet with exercise (PRO+EX), 2) higher protein diet without exercise (PRO), or 3) conventional protein control diet with exercise (CON+EX). The goal of the three treatments was to elicit a ~10% reduction in baseline body weight and all participants were prescribed a similar caloric restriction protocol. Notably the exercise treatments were identical in the PRO+EX and CON+EX groups.

3.3.1b Participants

A total of 44 relatively healthy but overweight or obese older women who completed the larger trial were included in this secondary analysis. For the purpose of this analysis PRO+EX and CON+EX were combined to investigate the impact of exercise and weight loss [EX+WL; (N=30)] compared to weight loss alone [WL; (N=14)]. In brief, inclusion criteria were as follows; aged 65 to 80 yrs, body mass index [BMI] ≥25.0 kg/m^2, and physically inactive (<1 hour per week of physical activity or less than 2 exercise sessions per week) over the past 6 months, non-smoking or tobacco using, independently ambulating, and free from any chronic disease/condition that would preclude safe participation in exercise training or dietary restriction procedures. All participants provided written informed consent to participate in the study, of which all procedures were approved by the universities Institutional Review Board. This study was a registered protocol (NCT01893684; clinicaltrials.gov).

3.3.2. Intervention Protocols

3.3.2a Exercise

Participants randomized to exercise interventions, completed a multicomponent exercise session 3 d/wk for 6 months, in accordance with the ACSM guidelines (Chodzko-Zajko et al., 2009). In brief, each session consisted of 1) cardiorespiratory training performed at 70-80% of age-predicted maximal heart rate for 30 minutes during each session, 2) Upper- (chest press, shoulder press, and back row) and lower-body (leg press, knee extension, and knee curl) resistance training exercises, and 3) balance and flexibility exercises. Two sets of 8-10 repetitions at 65% of one-repetition maximum (1-RM) were performed for each resistance training exercise, with muscle strength reassessed every 6 weeks to ensure a progressive overload.

3.3.2b Weight Loss Diets

As detailed elsewhere (Evans et al., 2021) all participants were prescribed a hypocaloric diet that reduced estimated energy needs by ~500 kcal/d to facilitate ~10% weight loss at 6 months. Participants randomized to the EX+WL group received one of two dietary treatments: 1) a higher protein diet (30% protein (1.6 g/kg/d) and 40% carbohydrate), or 2) a conventional protein diet (18% protein (0.8 g/kg/d) and 52% carbohydrate); dietary fat was matched at 30% of daily calories. During the initial phase of the intervention, participants attended at least 2 individual sessions with a registered dietitian nutritionist or supervised nutrition graduate student for instruction. For the remainder of the intervention, participants attended weekly educational/motivational group sessions, as well as individual sessions to facilitate adherence to the dietary regimen.

3.3.3 Outcomes Measures

3.3.3a Weight Status

As with all outcome measures, anthropometric measures were obtained at both baseline and immediately post intervention with standing height (Seca, Model 242) and weight (Tanita, Model WB-110A) being measured using conventional clinical methods.

3.3.3b Lower-Extremity Physical Function [LEPF]

A battery of physical functional tasks was performed at the same time-points, to assess LEPF. Participants performed: a 6-minute walk [WALK], the 8-foot up-and-go [UPGO], and 30-s chair stand [CHAIR], in a randomized order and could rest between tasks as desired. All tasks were selected based upon being clinically well-established, with very good to excellent within-session reliability (Northgraves et al., 2016; Rikli & Jones, 2013).

3.3.3c Muscle Strength and Power

Participants were coached and familiarized with the dynamometer prior to commencement of the testing protocol. Knee extension and flexion maximal voluntary contractions [MVC] were completed on both legs using a calibrated Biodex dynamometer (System 4 Pro, Biodex Medical Systems Inc, Shirley, NY). All participants were seated with the axis of rotation at the knee aligned with the dynamometer arm and back support at 90°. All positional measurements were recorded for replication throughout the study. Participants performed two trials each for knee extension and flexion (4 trials total), at 90° of knee flexion, separated by 30 s of rest. Participants were asked to push or pull with maximal effort against the mechanism for 3 s with active encouragement provided throughout each trial (Andersen & Aagaard, 2006). Raw signal was sampled at 100Hz and exported as raw data files for subsequent data analysis.

3.3.3d Signal Processing for Rate of Torque Development [RTD] Parameters

RTD calculations were completed on the individual's dominant limb, for both the Knee Extensors and Knee Flexors, utilizing the second performance trial to ensure consistency and control for any motor learning. Passive baseline torque (Newton-meters, Nm) was considered limb weight and subtracted from the initial values to create a new baseline of 0Nm for all participants. Torque time trajectories were smoothed with a 5-point moving average (50ms epochs). Percentage change between adjacent time points was calculated with force onset determined as the point at which percentage changes >= 3% or surpassed 4Nm for the Knee Flexors and 7.5Nm for Knee Extensors (Aagaard et al., 2002). RTD was subsequently calculated as the maximum slope of the torque-time relationship (Δtorque/0.05s) within each 50ms epoch. RTD200 was quantified as the RTD at 200ms along the linear slope (Suchomel et al., 2018). Utilizing the same percentage change calculation, first peak, and subsequently the time to first peak [T2P] was considered the first point percent change that was <=3% following onset. Peak RTD [RTDPeak] was considered the highest value across all epochs within the trial. Thus, the three RTD parameters of interest were designated as: RTD200, T2P, and RTDPeak. Finally, absolute peak torque was also calculated from the raw torque-time curve [PeakTor].

3.3.4 Statistical Analysis

All statistical analyses were conducted using SPSS for Windows version 26.0 (SPSS Inc., Chicago, IL). Normality and assumptions were verified using Kolmogorov-Smirnov and Levene tests, respectively. Paired sample *T-tests* were used to determine within-group changes for weight status, PeakTor, RTD and LEPF outcomes of interest. Separate two-way mixed model analyses of variance (ANOVA; EX+WL/WL * Baseline/Post) and ANCOVA (controlled for absolute or relative weight change) were used to analyze the relative effect of the interventions on PeakTor, RTD parameters of interest (6 total; RTD200, Time2Peak, RTDPeak; Extension/Flexion) and LEPF outcomes (WALK, UPGO, CHAIR). Change scores were calculated (post – baseline values) for all outcomes, and subsequently the influence of weight change was assessed using correlation analysis. Linear regression models (18 = 6 RTD parameters * 3 LEPF tasks) were performed to examine if change in RTD parameter predicted change in LEPF task performance. Regression models were calculated in the following order: Step 1 (Force Entered), group code, and weight change as deemed appropriate (absolute or relative); Step 2 (Stepwise), RTD parameter and interaction term (RTD parameter * group code). An additional analysis evaluating the association of change in RTD parameters and change in LEPF task performance was conducted in the EX+WL group alone using bivariate correlation. Statistical significance was set at $P<0.05$. Data are presented as mean±SD unless otherwise stated.

3.4 Results

3.4.1 Participant Characteristics and Intervention Adherence

All-inclusive participant and intervention characteristics, including retention and adherence details, can be found elsewhere (Berg et al., 2018; Evans et al., 2021). No significant group differences in age, body mass, height, or BMI, were observed at baseline (all $p < 0.05$). Participants mean age was 69.1±3.6yrs, and collectively, on average, the sample was categorized as obese according to BMI (30.6±4.3 kg/m^2). Per protocol design, participants lost -7.1±4.1kg or 9.8±4.2% of initial body weight (p < 0.001), with 45.6% of individuals meeting the initial weight loss goal of ±10%. Weight loss, expressed as absolute or relative to baseline, did not differ between groups (p = 0.998 and 0.958, respectively).

Within group, no change in PeakTor in the EX+WL group was observed (Extensors: Baseline 81.4±21.6 Nm; Post 85.8±23.1 Nm; p = 0.147; Flexors: Baseline 48.4±14.4 Nm; Post 46.7±14.5 Nm; p = 0.587) whereas a reduction in the WL group was evident for both muscle actions (Extensors: Baseline 86.4±25.5 Nm; Post 72.3±24.5 Nm; $p = 0.033$; Flexors: Baseline 56.9±15.5 Nm; Post 49.2±15.1 Nm; $p = 0.015$) (Figure 1). Thus, a Group by Time interaction was apparent for Flexors ($p = 0.032$) whereby the WL group decreased PeakTor in response to the interventions when compared to the EX+WL group. PeakTor results were similar when controlling for absolute or relative weight loss.

3.4.2 Rate of Torque Development (RTD) Parameters

Results for RTD parameters of interest are presented in Table 1. Significant or strong trends were observed in all RTD parameters, irrespective of joint action (Extension/Flexion), in the EX+WL group (all $p < 0.05$ except RTD200-Flexion and T2P-Extension; $p = 0.059$) indicating improvements in response to the intervention. The WL group experienced significant improvements in RTDPeak-Flexion and T2P, for both actions (all $p < 0.05$). With weight change as a covariate, expressed as absolute, a significant Group by Time interaction was observed for RTD200-Flexion ($p = 0.031$) indicating that the EX+WL group experienced a greater improvement in this RTD parameter compared to the WL group. When the covariate of weight change, expressed as absolute weight change, was removed, a trend remained for the Group by Time interaction for RTD200-Flexion ($p = 0.089$). No further significant interactions were observed for any other RTD outcomes, regardless of the control for weight change, relative or absolute (all $p > 0.10$).

3.4.3 Lower Extremity Physical Function [LEPF]

Results for LEPF outcomes are presented in Table 2. Both EX+WL and WL groups experienced significant improvements for the three LEPF tasks (WALK, UPGO, and CHAIR; all $p < 0.05$). Furthermore, whilst controlling for absolute or relative change in body weight, a Group by Time interaction was observed for WALK and CHAIR (both $p < 0.001$) indicating that the EX+WL group experienced greater improvements in these

LEPF tasks compared to the WL group. When removing the covariate of weight change, the significant Group by Time interaction remained for both WALK and CHAIR (both $p < 0.001$). For the UPGO task a trend was evident for the Group by Time interaction indicating a greater improvement in the EX+WL compared to the WL group ($p = 0.064$), which remained when the weight change covariate was removed ($p = 0.090$).

3.4.4 Relationship Between Change in RTD and LEPF Performance

Multivariate linear regression analyses were performed to examine if change in RTD parameter predicted change in LEPF task performance following the interventions controlling for group as described above. Change in weight (absolute or relative) was not related to change in RTD parameters or change in LEPF task performance; therefore, it was not entered into the model. No models were significant (all $p > 0.05$) indicating that changes in the RTD parameter of interest did not influence change in the LEPF task performance (data not shown), for the complete sample. Bivariate correlation analysis between change in RTD parameters and LEPF task performance for the EX+WL group resulted in a significant positive correlation between RTD200-Flexion and WALK ($r = 0.39$; $p < 0.05$) and between T2P-Flexion and CHAIR ($r = 0.42$; $p < 0.05$).

3.5. Discussion

The purpose of this study was primarily to examine the relative effect of weight loss, with or without exercise training on RTD parameters, and subsequently explore if changes in RTD parameters were associated with changes in clinically relevant LEPF tasks in inactive overweight/obese older women. Partially supporting our hypothesis, our findings suggest that weight loss with or without exercise training improves some RTD parameters; however, exercise and weight loss significantly enhanced RTD200 for the Knee Flexors compared to the weight loss alone intervention. Conversely, no RTD parameters were significant predictors of improvement in LEPF task performance.

A novel aspect of the present study is the inclusion of clinically relevant interventions in the investigation of RTD parameters, specifically in overweight and obese older adults. It is well established that obesity exacerbates the age-related decline in physical function (Villareal et al., 2005). Moreover, current literature indicates that a combination of exercise and weight loss provides greater improvements in muscle strength (Englund et al., 2018; van den Helder et al., 2020), lower-extremity power (Straight et al., 2012) and physical function (Villareal et al., 2011), than either intervention alone in older adults. Nevertheless, the influence of acceptable protocols on mechanisms associated with physical function are limited in scope. Previous research has demonstrated that improvements in both muscle quality (Cunha et al., 2018), and muscle quantity (Welch et al., 2020) following similar protocols to the present study, positively impact physical function in older adults. However, considering the importance of producing muscle force rapidly in relation to LEPF and falls (Lanza et al., 2003), understanding the influence and trainability of RTD parameters is warranted.

Given the research design, interventions, outcomes, and population of interest in our study, it is difficult to directly compare our results to existing literature. To our knowledge, most research to date investigating RTD parameters addressed athletic adaptations (Mclean et al., 2012; Palmer et al., 2014), age related changes (Cogliati et al., 2020; Olmos et al., 2020; Thompson et al., 2014; Van Driessche et al., 2019), gender differences (Osawa et al., 2018), or the association with clinical measures and falls (Bento et al., 2010; LaRoche et al., 2017; Morcelli et al., 2016; Ochi et al., 2020), with all studies using cross-sectional designs. Expanding on these, our present findings, which suggest that exercise, independent of weight loss, positively improves multiple RTD parameters in both the Knee Flexor and Knee Extensor muscles in older, overweight/obese physically inactive women are salient given the urgent public health and clinical interest in physical disability and fall prevention with advancing age. Further research is warranted to understand the mechanisms associated with these adaptations.

Strength adaptations following multi-modal exercise training across the lifespan are well established. With specific reference to RTD parameters, several cross-sectional studies have reported an association between maximal strength and RTD parameters (Holtermann et al., 2007; Thelen et al., 1997). Thompson et al (2013) denoted their results implied that sarcopenia or loss in muscle mass may be the common mechanism responsible for loss of muscular strength and reductions in RTD. It is common for dietary alone weight loss programs to result in loss of muscle mass, which may further amplify the effect of sarcopenia on muscular strength and RTD parameters. Although, no significant increase in strength (PeakTor) was reported for the exercising group in the present findings, an attenuation of the decline compared to the weight loss group was reported, reinforcing the importance of incorporating exercise as a component of weight loss programs to preserve strength in older adults. Other mechanisms that could explain alterations in RTD specifically include both a reduction in age-related changes in muscle activation rate (Lockhart & Kim, 2006) and a compromised muscle action in response to high accelerations in older adults compared to younger individuals (Van Driessche et al., 2019), especially in obese individuals (Duan et al., 2018). Yet there’s reason to believe that exercise has the potential to attenuate reductions in neuromuscular properties with advancing age (Vila-Chã et al., 2010). Although neuromuscular and motor unit activation rate was not assessed in the present study, considering the previously reported associations between RTD and motor unit responses, there is reason to believe that enhanced motor unit, subsequent to exercise training, contributed, in part, to the results observed in the present study; however, it is recognized more research is needed, especially under weight loss conditions.

In discord with available literature reporting associations of RTD and physical function, our results suggest that RTD parameters do not play a role in LEPF task performance under conditions of weight loss interventions without concurrent exercise training. Significant correlations between change in RTD parameters and LEPF performance in EX+WL suggests the adaptations in the Knee Flexors have a greater influence on physical function than the Knee Extensors. The hamstrings have been previously identified in older adults as important contributors to maintaining standing balance (Palmer et al., 2017, 2020) and physical function performance, specifically stair ascent and descent (Orssatto et al., 2020). Furthermore, there is evidence to suggest that greater knee flexor peak torque is associated with reduced fall risk in ambulatory relatively healthy older adults (Bento et al., 2010; Perry et al., 2007). Our observations expand on this body of research by suggesting that enhancing hamstring contraction speed, or perhaps incorporating exercise to attenuate the decline in hamstring muscle function, after a weight loss regimen, may influence LEPF in overweight/obese physically inactive older women. Postulation of the reasons for this interaction primarily revolve around maintenance and capability to sustain balance and stability through rapid dynamic movements. Specifically, the CHAIR task requires the participant to promptly change direction, involving a shift in the body's center of mass around the base of support, requiring the individual to control the moment of inertia. Thelen et al (1997) corroborate this concept, reporting that age-related decline in balance recovery largely depended on lower extremity muscle rate of contraction. Thus, although decreasing body weight is an important element of physical function in overweight and obese individuals, the incorporation of exercise in any weight loss intervention appears imperative.

3.6. Practical Application

The practical implications of RTD are extensive for both the athletic and clinical populations; thus, understanding trainability of these parameters is salient. Our results suggest that exercise can improve RTD parameters in older adults, specifically those considered overweight or obese who are undergoing a weight loss and/or exercise intervention. These results support the benefit of multimodal exercise interventions as an important element to consider when proposing interventions, including weight loss, to maintain or enhance LEPF in older overweight/obese women, known to be at higher risk of physical disability compared to their male counterparts.

3.7. Limitations

Whilst our results provide novel evidence regarding the relative utility of weight loss with or without exercise training to positively impact RTD parameters and physical function in inactive overweight/obese physically older women, there are several primary limitations to this study. Firstly, certainly constraints, for example unequal sample sizes, exist considering the secondary analysis nature of our study. Yet, the results observed support the importance of our findings and definitively informs future work in this area of public health concern. Secondly, although RTD currently lacks a standardized testing and analysis protocol, and subsequently absolute values vary significantly across the literature, our design lacked the sample frequency recommended (Maffiuletti et al., 2016b). Despite this, the frequency selected has been utilized by previous studies (Osawa et al., 2018) and thus the results still warrant consideration. These limitations are arguably tempered by a number of study strengths including, a) high degree of instruction and supervision of the exercise treatment, b) length of intervention, and c) most importantly, the novelty of investigating RTD parameters using a randomized clinical trial design in a population of high clinical and public health interest due to increased risk for physical disability.

3.8. Conclusion

In summary, the results of our study indicate that a weight loss regimen that incorporates exercise training can improve RTD parameters in overweight/obese physically inactive older women. Moreover, our results reinforce the importance of exercise during weight loss to prevent both reductions in strength and attenuations in improvements in LEPF and RTD. An unanticipated additional finding of our data was the observation that the Knee Flexor muscle group may play a more important role in functional task performance than Knee Extensor muscle group. Additional research is needed to confirm the mechanistic adaptations; however, our data supports the importance of exercise in the management of obesity and physical functional decline in older women, which remains a public health concern.

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Table 3.1. Rate of Torque Development (M±SD) at Baseline and in Response to the Intervention at 6 Months (Post-Test).

	EX+WL (n = 30)			WL (n = 14)			
	Baseline	Post-Test	*p-Value*	Baseline	Post-Test	*p-Value*	Group*Time
RTD200 (Nm/s)							
Extension	180.6±90.6	261.2±188.5	0.013	185.4±131.4	230.3±172.4	0.468	0.305
Flexion	125.5±65.4	170.7±124.3	0.059	172.7±95.3	144.9±91.1	0.462	0.031
RTDPeak (Nm/s)							
Extension	429.0±236.1	616.6±273.4	0.003	462.0±279.2	517.7±245.8	0.508	0.232
Flexion	215.9±80.7	304.6±148.4	0.002	251.0±101.2	385.7±223.7	0.038	0.455
T2P (ms)							
Extension	576.7±250.4	460.0±221.4	0.059	557.1±200.8	403.6±171.5	0.035	0.638
Flexion	571.7±282.1	426.7±163.9	0.003	542.9±167.4	367.9±118.7	0.010	0.883

Note: RTD200 = Rate of Torque Development at 200ms; RTDPeak = Peak Rate of Torque Development; T2P = time (ms) from onset to first peak.

p-value = within group comparison

Group*Time = *p-value* for the interaction effect

Table 3.2. Physical Function Performance (M±SD) at Baseline and in Response to the Intervention at 6 Months (Post-Test).

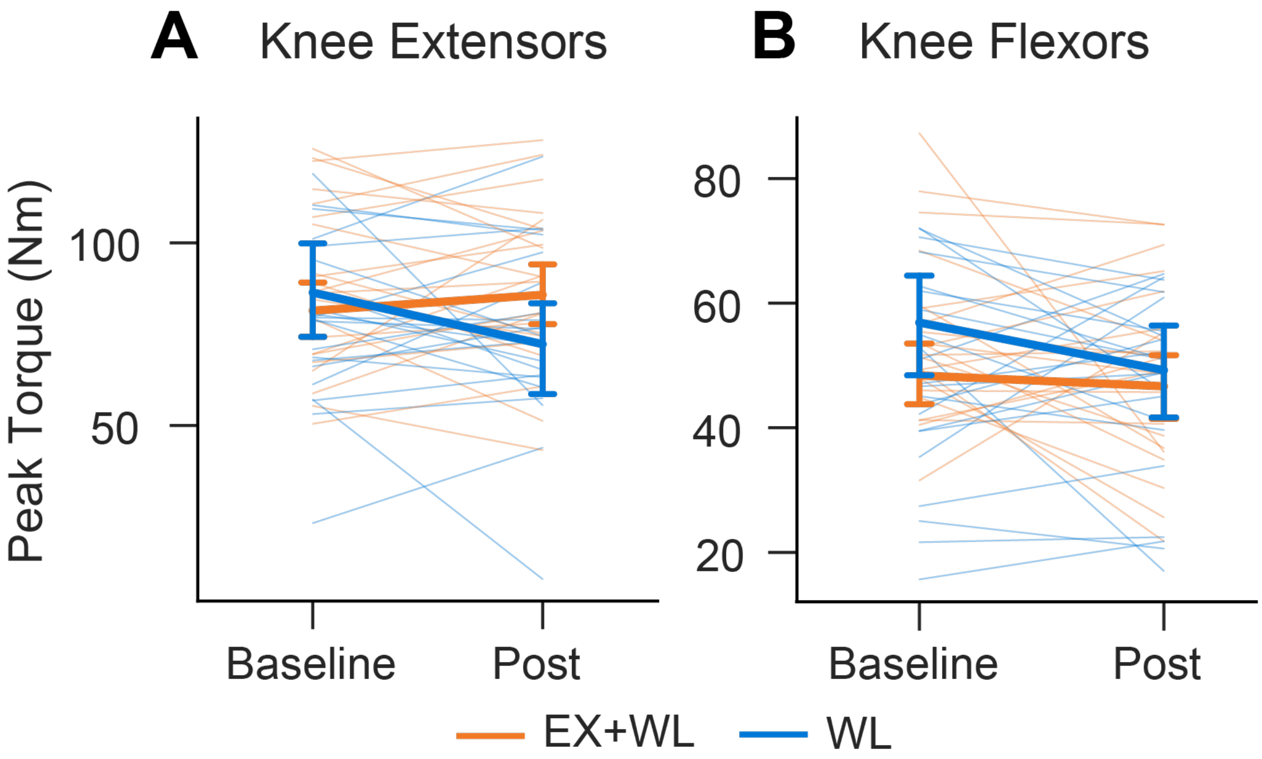
	EX+WL (n = 30)			WL (n = 14)			
	Baseline	Post-Test	*p-Value*	Baseline	Post-Test	*p-Value*	Group*Time
WALK (m)	526.2±59.9	585.2±55.9	0.000	516.4±66.2	533.1±63.7	0.030	0.000
UPGO (s)	6.2±1.0	5.5±0.6	0.000	6.3±1.0	5.9±0.9	0.018	0.064
CHAIR (rep)	13.6±2.2	21.4±5.8	0.017	14.7±2.7	16.2±2.8	0.004	0.000

Note: WALK = 6-minute Walk Test; UPGO = Up and Go Test; CHAIR = 30 sec Chair Stand Test

p-value = within group comparison

Group*Time = *p-value* for the interaction effect

Figure 3.1. Individual and Mean (M±SD) Peak Torque value at Baseline and in Response to the Intervention at 6 Months (Post-Test).



Note: Individual thin lines represent individual participants, conversely single thick bold line depicts the group mean for each group.

Chapter 4

Effects of Weight Loss and Exercise on Leg Muscle Capacity Asymmetry and Physical Function in Overweight Older Women

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4.1 Abstract

Purpose: Asymmetry [ASYM] of >10% in leg muscle capacity parameters may be clinically meaningful, adversely impacting lower extremity physical function [LEPF] in older adults. Obesity negatively impacts LEPF whereas exercise, especially strength training, is known to improve LEPF in older adults. The potential interactive effects of weight loss and exercise on ASYM and relatedly LEPF is unknown. Thus, the aim of this study was to determine the relative effect of weight loss with or without exercise on intra- and between-limb power ASYM in inactive overweight/obese older women and the subsequent influence on clinically relevant LEPF tasks. **Methods:** As a secondary data analysis, overweight inactive postmenopausal women (68.8±36 yrs; 30.7±4.3 kg/m^2; n=38) who completed the 6-month intervention within two groups: 1) exercise and weight loss [EX+WL; (N=26)] and weight loss alone [WL; (N=12)] were evaluated. Single- and multi-joint muscle power was assessed via isokinetic dynamometry and a Nottingham power rig, respectively. Relative degree of muscle power asymmetry [%ASYM] between limbs and intra-limb (Hamstrings vs. Quadriceps) were subsequently calculated. LEPF was assessed via 6-minute walk [WALK], 8-foot up and go [UPGO], and 30-second chair stand tests [CHAIR]. **Results:** Changes in absolute or relative weight loss were similar (-7.1±4.1kg; -9.8±4.2%; $p > 0.05$). At baseline, average %ASYM ranged from 10.1-16.1% and Leg Flexor %ASYM was associated with all three LEPF tasks (r range = 0.46-0.60; all $p < 0.05$); no other associations were observed. All power outcomes improved in EX+WL ($p < 0.05$); however; no significant changes in %ASYM were observed, irrespective of group. Reductions in Leg Flexors %ASYM, alone, were associated with improvements in UPGO ($r = 0.55$; $p < 0.05$). **Conclusions:** Weight loss which includes exercise may be a factor for improving LEPF through Leg Flexor %ASYM in overweight/obese inactive older women. Further research is warranted to explore the effect of improving leg power ASYM on LEPF in older adults.

Key Words: Asymmetry, Older Adults, Physical Function, Strength, Weight Loss

4.2. Introduction

Lower extremity physical function [LEPF], is considered a multidimensional construct that is key to the maintenance of independence and quality of life with advancing age. Numerous variables, all impacted by the aging process, influence LEPF, however it appears a salient factor is sex/gender with prevalence of physical disability being higher in older women compared to their male counterparts. The resultant cycle of increased limitations and restrictions in LEPF has a multitude of adverse effects including reduced independence and an augmented risk of fractures and falls (Feskanich et al., 2002; Matthews et al., 2012; Patel et al., 2010). Delineating directly associated antagonistic variables that fluctuate with aging to account for a decline in LEPF is challenging. However, it is widely accepted that muscle power is a primary factor that may affect mobility (Frontera et al., 2000; Lindle et al., 1997). Additional contributing causes are related to injury, pain or progressive changes (Leveille et al., 2001; Thakral et al., 2019), all of which can be exaggerated in a single leg, ultimately leading to distinctive leg asymmetries (Byrne et al., 2016; Valtonen et al., 2009) which may in turn further exacerbate LEPF difficulties as the vast majority require bilateral activation.

Whilst some degree of muscle capacity asymmetry [ASYM] is common in individuals, reports suggest lower limb strength ASYM >10% may be clinically meaningful in older adults and may represent an early detectable risk factor for future impaired functional capacity (Carabello et al., 2010). Previous studies have reported an increase in strength ASYM of the leg extensors to be associated with impaired postural balance (Portegijs et al., 2005), increased incidence of falls (Laroche et al., 2012; Skelton et al., 2002), and a reduction in LEPF (Straight et al., 2016). However, a consensus in the literature is lacking regarding change in ASYM via various interventions and the relative importance for LEPF. For example, it has been reported that a reduction in strength ASYM might be less important than improving global generalized strength for functional performance (LaRoche et al., 2017; Mertz et al., 2019). Discrepancies in methodologies, included single- vs. multi-joint assessment, power vs. strength measurement, muscle actions (e.g., antagonist vs. agonist), and/or a lack statistical of controls (e.g., cross-sectional area) may be contributing to these observational differences.

Performance of LEPF requires both muscle strength and power, however, reports directly comparing the two have indicated power training to be more effective than strength training for improving lower extremity physical function in community-dwelling older adults (Marsh et al., 2009). Yet, power modulation outcome measures, specifically bi-lateral outcomes have not been assessed. Furthermore, a cross-sectional study by Straight et al (2016) observed that a greater magnitude in leg power asymmetry was associated with poorer LEPF in older women, yet the effect of training to potentially reduce ASYM and subsequently improve LEPF is unknown. In addition to this, the contribution of bi-lateral vs. intra-lateral ASYM in power is unestablished, yet the influence of leg flexors in functional movements has recently been recognized.

It is well-established that obesity negatively impacts LEPF and is associated with loss of independent living in part due to reduced muscle quality and capacity (Villareal et al., 2005; Vincent et al., 2010). The impact of excess body weight on joint load bearing is clinically substantial and a reduction in body weight is advocated to enhance physical function in older adults (Villareal et al., 2011) through numerous mechanisms (e.g., lipid infiltration into muscle, reductions in joint inflammation, reduced load to move with greater muscle capacity to move the load, etc.) (Maden-Wilkinson et al., 2015; Mazzali et al., 2006) However, the potential influence of reductions in muscle power ASYM in response to weight loss with or without exercise, and the associated effect on LEPF in older overweight/obese inactive older adults has not been explored.

The primary objective of this study is to determine the relative effect of weight loss, with or without exercise training on between and intra- leg power ASYM in overweight/obese inactive older women. Subsequent to this, a secondary aim was to explore the association between changes in ASYM and changes in clinically relevant LEPF performance tasks. It was hypothesized that a) exercise training would reduce all indices of ASYM and b) reductions in ASYM would be associated with improvements in LEPF.

4.3. Methods

4.3.1 Parent Project

4.3.1a Research Design

The parent project which allowed for this secondary data analysis involved a randomized controlled trial investigating the effect of two different 6-month dietary treatments with or without exercise on body composition, strength, and physical function in older women (Evans et al., 2021). Participants were randomized into three groups: Higher protein (PRO) or conventional carbohydrate (CON) weight loss diet combined with exercise [PRO+EX and CON+EX which combined; EX+WL] or a (2) higher protein weight loss diet without exercise for 6 months [WL], with the underlying purpose of the parent project for each participant to lose ~10% of initial body weight. For the purpose of this analysis the two dietary and exercise groups were combined to investigate the impact of EX+WL (N=26) compared to WL (N=12).

4.3.1b Participants

A total of 38 community-dwelling healthy but overweight/obese inactive older women (N = 38, 68.8 ± 3.6 yrs) were included based on the following criteria: aged 65 to 80 yrs, body mass index [BMI] ≥25.0 kg/m^2, and physically inactive (<1 hour per week of physical activity or less than 2 exercise sessions per week) over the past 6 months, non-smoking or tobacco using, independently ambulating, and free from any chronic disease/condition that would preclude safe participation in exercise training or dietary restriction procedures. All participants provided written informed consent to participate in the study, of which all procedures were approved by the universities Institutional Review Board. This study was a registered protocol (NCT01893684; clinicaltrials.gov).

4.3.1c Exercise

Participants randomized to exercise interventions, completed a multicomponent exercise session 3 d/wk for 6 months, in accordance with the ACSM guidelines (Chodzko-Zajko et al., 2009). Each session consisted of 1) cardiorespiratory training performed at 70-80% of age-predicted maximal heart rate for 30 minutes during each session, 2) Upper- (chest press, shoulder press, and back row) and lower-body (leg press, knee extension, and knee curl) resistance training exercises, and 3) balance and flexibility exercises. Two sets of 8-10 repetitions at 65% of one-repetition maximum (1-RM) were performed for each resistance training exercise, with muscle strength reassessed every 6 weeks to ensure a progressive overload.

4.3.1d Weight Loss

As detailed elsewhere (Evans et al., 2021) all participants were prescribed a hypocaloric diet that reduced estimated energy needs by ~500 kcal/d to facilitate ~10% weight loss at 6 months. Participants randomized to the EX+WL group received one of two dietary treatments: 1) a higher protein diet [30% protein (1.6 g/kg/d) and 40% carbohydrate], or 2) a conventional protein diet [18% protein (0.8 g/kg/d) and 52% carbohydrate]; dietary fat was matched at 30% of calories. Participants in the WL group received the same higher protein diet as previously described. During the initial phase of the intervention, participants attended at least 2 individual sessions with a registered dietitian nutritionist or supervised nutrition graduate student for instruction.

4.3.2 Outcomes Measures

4.3.2a Weight Status

As with all outcome measures, anthropometric measures were obtained at both baseline and immediately post intervention with standing height (Seca, Model 242) and weight (Tanita, Model WB-110A) being measured using conventional clinical methods.

4.3.2b Muscle Power

Unilateral single-joint leg power was measured using a calibrated Biodex dynamometer (System 4 Pro, Biodex Medical Systems Inc, Shirley, NY). All participants were seated with the axis of rotation at the knee aligned with the dynamometer arm and back support at 90°. All positional measurements were recorded for replication throughout the study. Following familiarization, participants performed two isokinetic trials with an angular speed of 180°/s trials for each direction [i.e., Flexion, Extension], separated by 30s of rest. Participants were asked to push or pull, with maximal effort against the mechanism through the complete range of motion. Raw signal was sampled at 100Hz and exported as raw data files for subsequent data analysis. Absolute power was considered the highest point on the torque-time trajectory. Verbal encouragements and visual feedback were provided throughout for additional motivation.

To assess unilateral multi-joint leg power participants completed 10 maximum trials on the Nottingham Power Rig (University of Nottingham Medical School, Model NG72UG, Nottingham, UK), on each leg. Trials 4 SD or greater away from the means were removed and the average of the remaining trials was calculated for the assessment of this outcome.

To determine the relative degree of asymmetry in muscle power between limbs, the percentage difference (%ASYM) was calculated as ([(Power of dominant leg – Power of nondominant leg]/ Power of the dominant leg x 100)). Thus, a larger %ASYM represents a greater degree of asymmetry. Intra-limb asymmetry was calculated as the ratio between quadricep [Leg Extensor] and hamstring [Leg Flexor] power on the participant's dominant leg via the Hamstring: Quadricep Ratio [H:Q], whereby the closer the ratio to 0.0, the greater risk for muscular imbalance.

4.3.2c Lower-Extremity Physical Function [LEPF]

A battery of physical functional tasks was performed at the same time-points, to assess LEPF. Participants performed 1) a 6-minute walk [WALK], 2) the 8-foot up-and-go [UPGO], and 3) a 30-s chair stand [CHAIR], in a randomized order and could rest between tasks as desired. All tasks were selected based upon being clinically well-established, with very good to excellent within-session reliability (Northgraves et al., 2016; Rikli & Jones, 2013).

4.3.3 Statistical Analysis

All statistical analyses were conducted using SPSS for Windows version 26.0 (SPSS Inc., Chicago, IL). Normality and assumptions were verified using Kolmogorov-Smirnov and Levene tests, respectively. Independent sample *T*-tests were used to test between group differences at baseline on outcomes of interest. Bivariate correlational analyses determined the associations between primary %ASYM outcomes (%ASYM Power Rig, Leg Extensor, Leg Flexors, H:Q Dominant and H:Q Nondominant) and LEPF outcomes (WALK, UPGO, and CHAIR) at baseline. To assess the within-group effect of the interventions, paired sample *T*-tests were used for weight status, power and %ASYM outcomes of interest. Between group comparison of both relative and absolute weight change was assessed by independent *T*-test. Four separate mixed model repeated measure ANCOVAs (group [WL versus EXWL] x time-point [baseline verse post-intervention]), controlling for absolute weight change, were used to analyze the relative effect of the interventions on %ASYM outcomes. Change scores were calculated (post – baseline values) for all outcomes, and linear regression models (9 = 3 %ASYM * 3 LEPF tasks) were performed to examine the contribution of change in %ASYM parameter on the change in LEPF task performance. Regression models were calculated in the following order: Step 1 (Force Entered), group code; Step 2 (Stepwise), %ASYM and interaction term (%ASYM parameter * group code). Statistical significance was set at $p < 0.05$. Data are presented as mean (SD) unless otherwise stated.

4.4. Results

4.4.1 Participant Characteristics and Weight Loss

Complete participant and intervention characteristics, including retention and adherence details can be found elsewhere (Evans et al., 2021). For the current study, no significant differences were observed between groups for any demographics of interest (all $p > 0.05$). Participants mean age was 68.8±3.6yrs, and collectively were categorized as obese according to BMI (30.7±4.3 kg/m^2). Weight loss did not differ between the two groups. Changes in absolute or relative weight loss were similar (-7.1±4.1kg; -9.8±4.2%; both $p > 0.05$).

4.4.2 Muscle Power and Asymmetry

Table 1 presents muscle power and asymmetry characteristics by group, at both baseline and post intervention. Average between limb asymmetry ranged from 10.1% to 16.1%, depending on muscle group and single- vs multi-joint assessment technique at baseline. Despite significant changes in the six power outcomes (all $p < 0.05$) within the EX+WL group, no %ASYM changes were observed for either the single- or multi-joint variables (all $p > 0.05$). No changes in either power or %ASYM outcomes were observed in the WL group (all $p > 0.05$). Similarly, no significant Group*Time effects were reported for any of the %ASYM outcomes (all $p > 0.05$). An improvement in the H:Q ratio in the dominant leg for the EX+WL was observed ($p < 0.01$), but no other significant adaptations occurred.

4.4.3 Changes in Lower Extremity Physical Function

Significant improvements were observed for all three physical function tasks ($p < 0.05$) in the EX+WL (Table 2); with improvements in UPGO and CHAIR ($p < 0.05$) and a strong trend for improvements in WALK ($p = 0.06$) in the WL group. Analysis of covariance results indicated a Group*Time interaction for both CHAIR and WALK (both $p < 0.05$) and a strong trend for UPGO ($p = 0.06$), with EX+WL resulting in greater performance improvements than WL alone.

4.4.4 Associations between Asymmetry and Lower Extremity Physical Function (LEPF).

At baseline, for the entire sample, baseline multi-joint and Leg Extensor %ASYM was significantly correlated with UPGO performance (both r = 0.33; $p < 0.05$). Furthermore, Leg Flexor %ASYM was moderately to strongly associated with baseline WALK, UPGO and CHAIR in favorable directions (r range = -0.46 to 0.60; all $p < 0.05$; Figure 1). Multivariate linear regression models were created to examine the prediction of change in LEPF task performance from change in %ASYM as described above. The only significant model was the prediction of change in UPGO from Leg Flexor %ASYM (R^2 = 23.6%, $p < 0.05$) whereas Leg Flexor %ASYM accounted for 15.8% of the variance (standardized $\beta = 0.40$; $p = 0.011$) beyond Group (standardized $\beta = 0.26$; $p = 0.088$). No other models were significant indicating that neither changes in multi-joint nor Leg Extensor %ASYM, nor H:Q influenced change in the LEPF task performance (data not shown).

4.5. Discussion

The primary purpose of the present study was to determine the relative effect of weight loss with or without exercise training on intra- and between-limb muscle power asymmetries in overweight/obese inactive older women. Furthermore, we aimed to explore the association between any observed changes in asymmetry on changes in clinically relevant LEPF tasks. To our knowledge we are the first group to examine the relative effect of exercise and weight loss on parameters of muscle power asymmetry. Our results showed, that despite absolute changes in muscle power following EX+WL, no changes in %ASYM were observed in response to the intervention, irrespective of group. Furthermore, although correlations between all measures of %ASYM and LEPF performance at baseline, only associations between changes in Leg Flexor %ASYM and LEPF task performance were observed following the intervention.

Consistent with the literature, the data revealed the average between-limb leg muscle power ranged 10-13.5% at baseline (Mertz et al., 2019; Perry et al., 2007; Straight et al., 2016). Few investigations have examined lower limb asymmetry in this cohort, yet this marker may be an additional factor predisposing this population to future LEPF limitations. To our best knowledge, the inclusion of the H:Q ratio has not been reported previously, thus a normative value is lacking, however our results suggested no change or association with LEPF performance.

Muscle power has been determined a critical determinant of LEPF; however, the literature regarding lower limb asymmetry in muscle power is less conclusive. A plethora of studies have reported no association between knee extensor power asymmetry and physical function in healthy older adults (Carabello et al., 2010; Mertz et al., 2019; Saunders et al., 2008), However, Straight et al (2016) recently demonstrated that leg power asymmetry impacted LEPF in community-dwelling older adults. Our baseline results align with Straight et al, that suggests a positive but weak association between lower limb asymmetry, inter- and between-limb, and LEPF.

Despite a couple of controversial studies, it is well established that being overweight or obese exacerbates the age-related decline in physical function (Elkins et al., 2006; Larrieu et al., 2004), and that a combination of exercise and weight loss provides greater improvements in physiological components and physical function

(Villareal et al., 2011), than either intervention alone. Furthermore, it is relatively well established that risk of functional impairment is greater in women compared to men (Kuh et al., 2005; Valentine et al., 2009). Thus, understanding factors that negatively impact LEPF in overweight and obese older women is clinically important. To the authors knowledge only cross-sectional studies have examined the relationship between lower-limb ASYM and LEPF in older adults, thus integrating our findings with the extant literature is not possible. We found that, irrespective of treatment group, between and intra- limb %ASYM was not significantly changed, however improvements in Leg Flexor %ASYM was related to improvements in LEPF task performance. These latter results suggest that Leg Flexors may play an important role in LEPF performance and subsequently warrants further investigation.

Further to our findings regarding %ASYM, our data integrates well with the literature that recommends a combined intervention of exercise and weight loss for overweight and obese individuals, especially older adults (Villareal et al., 2011). Significant improvements in LEPF task performance were observed irrespective of group; however, the magnitude of these developments was significantly greater for both the WALK and CHAIR task, with a strong trend for greater improvements in UPGO in the EX+WL group, reinforcing the importance of exercise training during weight loss to realize full benefits of weight loss for LEPF improvements.

Tempering a number of design and clinical application strengths, this study is not without limitations. Firstly, as previously noted, task sensitivity and specificity of some measures of LEPF have been questioned, especially in the older population (Francis et al., 2019), underlying the importance of task selection in relation to the population. Despite selecting the most common clinically relevant LEPF tasks, arguably these challenges are less indicative of activities of daily living that require sufficient levels of bilateral activation. Future studies should deliberate utilize an assessment tool combining multiple challenging bilateral tasks which may alleviate potential ceiling effects and highlight contralateral limitations (Balasubramanian, 2015; Bergquist et al., 2020). Secondly, our study was not specifically designed to reduce either between- or intra-limb asymmetry. In addition, the multicomponent exercise recommendations for older adults utilized are best practice for the primary aim of the parent project (Chodzko-Zajko et al., 2009); however, exercises were not designed to enhance muscle power specifically. Thus, additional research focused on reducing %ASYM and enhancing muscle power are warranted.

4.6. Conclusion

In conclusion, the present observations showed that between-limb asymmetry, irrespective of single vs. multi-joint, ranged from 10-13.5% in overweight and obese older women. At baseline, %ASYM was significantly correlated to LEPF task performance. However, despite no meaningful reductions in asymmetry, following a 6-month exercise and weight loss intervention, change in Leg Flexor %ASYM was associated to change LEPF task performance in this population. Future studies should investigate muscle power training protocols specifically designed to reduce %ASYM of lower limb muscles and evaluate as outcome measures, lifestyle conducive functional tasks to account for the utilizations of bilateral movement in activities of daily living.

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Table 4.1. Lower Limb Muscle Power and Asymmetries (M±SD) at Baseline and in Response to the Intervention at 6 Months (Post-Test).

	EX+WL (n = 26)			WL (n = 12)			
	Baseline	Post-Test	*P-Value*	Baseline	Post-Test	*P-Value*	Group*Time
Power Rig %ASYM	12.1±9.9	11.1±12.2	0.860	12.4±11.0	15.1±7.1	0.259	0.563
Dominant Leg, PR (watts)	90.9±22.7	100.5±20.3	0.023	102.8±19.7	107.4±28.0	0.629	
Nondominant Leg, PR (watts)	79.8±21.1	94.6±19.5	0.000	90.0±21.2	100.1±24.8	0.130	
Leg Extensors %ASYM	10.1±6.3	11.0±9.2	0.642	12.5±10.4	14.7±10.8	0.527	0.719
Dominant Leg, LE (Nm)	55.6±9.6	59.5±10.8	0.019	61.9±12.3	59.7±10.1	0.371	
Nondominant Leg, LE (Nm)	52.1±9.2	58.2±11.3	0.000	57.1±11.3	57.1±10.1	0.997	
Leg Flexors %ASYM	16.1±18.1	14.2±10.3	0.521	10.9±10.0	12.2±5.9	0.671	0.257
Dominant Leg, LF (Nm)	30.9±6.7	37.8±8.1	0.000	33.7±10.9	32.9±9.7	0.516	
Nondominant Leg, LF (Nm)	31.0±5.3	36.1±5.7	0.001	35.6±5.7	35.9±4.7	0.230	
H:Q Ratio Dominant Leg	0.56±0.1	0.64±0.1	0.005	0.54±0.1	0.58±0.2	0.206	0.690
H:Q Ratio Nondominant Leg	0.61±0.1	0.64±0.1	0.253	0.60±0.1	0.65±0.1	0.430	0.579

Note: %ASYM = Percentage Asymmetry; LE = Leg Extensors; LF = Leg Flexors; H:Q = Hamstring:Quadricep Ratio

P-value = within group comparison

Group*Time = *p-value* for the interaction effect

Table 4.2. Physical Function Performance (M±SD) at Baseline and in Response to the Intervention at 6 Months (Post-Test).

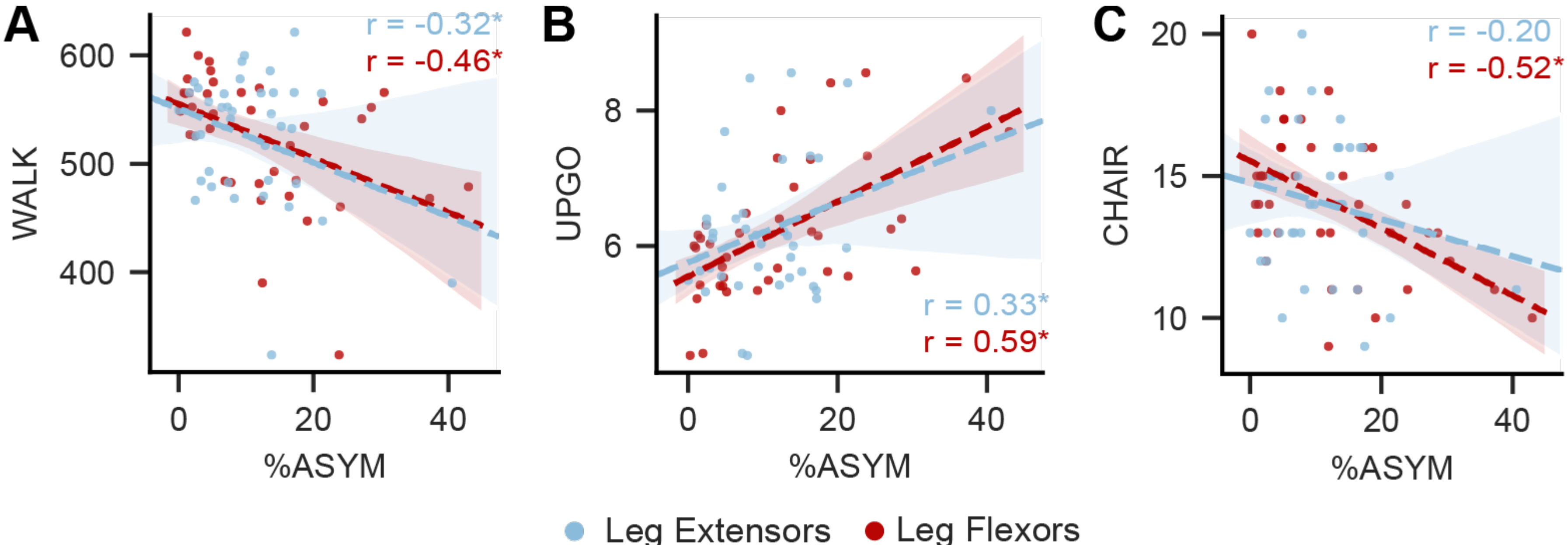
	EX+WL (n = 26)			WL (n = 12)			
	Baseline	Post-Test	*P-Value*	Baseline	Post-Test	*P-Value*	Group*Time
WALK (m)	525.2±61.3	582.8±53.9	0.000	523.0±60.5	539.9±57.8	0.060	0.002
UPGO (s)	6.3±1.1	5.5±0.6	0.000	6.1±1.0	5.8±0.7	0.038	0.063
CHAIR (rep)	13.7±2.3	21.9±5.9	0.000	15.0±2.7	16.3±2.6	0.013	0.000

Note:

p-value = within group comparison

Group*Time = *p-value* for the interaction effect

Figure 4.1. Association between % Asymmetry and WALK [Panel A], UPGO [Panel B] and CHAIR [Panel C] performance, for Leg Extensors and Leg Flexors, at Baseline.



CHAPTER 5

Effects of Power Training on Rate of Torque Development, Gait Characteristics and Walking Speed, in Chronic Stroke Patients

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5.1 Abstract

Purpose: Maximizing independence and ambulation ability post stroke are two common goals of therapy. Rate of torque development [RTD] in lower extremity muscles has recently been reported to influence walking speed, however the trainability and subsequent effect on gait characteristics, including walking speed, is unknown. Thus, the aim of this study was to determine the effect of muscle power training on RTD parameters of both the paretic and non-paretic limb and potential improvements in gait characteristics and walking speed in chronic stroke survivors. **Methods**: Individuals with chronic stroke (n=12; 59.8 ± 9.0 yrs; n = 3 female) completed 24 sessions of power training over 8 weeks. Knee extensor strength was assessed via dynamometry with RTD parameters [RTD200 = RTD at 200ms, RTDPeak = Peak RTD, T2P = Time to First Peak] subsequently measured from the maximal voluntary isometric contractions [MVIC]. Gait characteristics were assessed via an instrumented gait mat and a 6-minute walking endurance trial [WALK] was measured at the same timepoints. **Results**: RTDPeak improved 21.7% in the paretic limb ($p = 0.003$), whereas RTD200 improved 76.9% in the non-paretic limb ($p = 0.047$). On average, self-selected walking speed [SSWS], fastest-comfortable walking speed [FCWS] and WALK performance improved 17.7%, 18.2%, and 20.8% respectively (all $p < 0.05$). RTD200 of the non-paretic limb was positively associated with SSWS and FCWS (both $r = 0.66$, $p < 0.05$) and WALK distance ($r = 0.88$, $p < 0.001$). **Conclusions**: These findings suggest power training is an effective intervention for improving RTD and clinically relevant gait characteristics in individuals with chronic stroke. Further research to explore the utility and mechanistic aspects of power training for gait function in chronic stroke survivors is warranted.

Key Words: Gait, Stroke, Rehabilitation, Dynamometer, Power

5.2. Introduction

Muscular symmetry, function, and bilateral activation patterns are important components of ambulation, and all are commonly adversely affected post stroke (Bohannon & Andrews, 1988; Park et al., 2015; Signal, 2014). These impairments are in part due to the damage caused to the brain itself by the stroke but are also subsequent to typical lifestyle changes in stroke survivors (Sunnerhagen et al., 1999). Alterations in neural and muscular determinants vary with location of the stroke, the severity or degree of damage to the brain, and concurrent comorbidities. Unfortunately, ~60-85% of stroke survivors exhibit motor coordination deficits and ~40+% have total hemiparesis (Algurén et al., 2010; Perry et al., 1995). Despite this, it is suggested that ~90% of stroke survivors regain walking ability within 6 months post stroke; however, poor balance, limb weakness and asymmetrical motor control remain issues in the vast majority of ambulatory stroke survivors. Subsequently, regaining the ability to ambulate and maximizing independence are traditionally two primary goals of stroke rehabilitation (R. Bohannon & Andrews, 1988).

Stroke survivors frequently exhibit reductions in ambulatory speed; therefore, a variety of intervention approaches have been designed to attenuate/ameliorate these impairments (Laufer et al., 2001; Lee et al., 2008; McCrimmon et al., 2015); however, critical reviews in the field (Dickstein, 2008; Wonsetler & Bowden, 2017) have questioned the methodologies. We recently developed a high-intensity and high-velocity lower limb training program, Post-stroke Optimizing of Walking using Explosive Resistance (POWER training) and have shown it to stimulate positive improvements in self-selected walking speed (SSWS) (Morgan et al., 2015; Hunnicutt et al., 2016), and general locomotor function (Aaron et al., 2017). Our previous work has reported strength as the highest force value produced during a maximal voluntary isometric contraction [MVIC] of the knee extensors, however, recently, rate of torque development [RTD] has been recommended for the assessment of muscle contractility due to its sensitivity to assess acute and chronic changes in neuromuscular function (Maffiuletti et al., 2016).

RTD parameters in chronic stroke patients have rarely been studied. Horstman et al. (2010) reported a lower RTD, indicating slower contractility, in the quadriceps of the paretic limb compared to the non-paretic limb in patients who could ambulate independently. Moreover, normalized paretic and non-paretic limb RTD has been reported to influence walking speed (Horstman et al., 2010) and is lower in chronic stroke patients compared to healthy adults (Mentiplay et al., 2018; Pohl et al., 2002). Research in this area could benefit from a greater understanding of the impact of RTD on mobility, especially in chronic stroke patients. However, it is likely more important to determine the effect of novel interventions, especially exercise, on the plasticity of RTD and the subsequent impact on ambulation in chronic stroke patients.

To this end, the purpose of this study was to 1) determine the effect of POWER training on knee extensor RTD parameters, and 2) explore the association among changes in RTD parameters and gait characteristics and walking task performance, in chronic stroke patients. It was hypothesized that a) the intervention would improve bilateral RTD parameters and b) changes in RTD parameters would be positively associated with improvements in walking speed.

5.3. Methods

5.3.1. Participants

Twelve individuals with chronic stroke (>6 months post-stroke) who completed the POWER training intervention were included in this secondary data analysis. Inclusion criteria were as follows: 1) age 50-70 yrs, 2) residual paresis in the lower extremity with a Fugl-Meyer LE motor score <34 [FMA-LE], and 3) ability to walk at a SSWS > 200 cm/s without assistance and without Ankle Foot Orthotics [AFO]. Additionally, exclusion criteria included: 1) unable to ambulate at least 150 feet prior to stroke, or intermittent claudication while walking; 2) history of congestive heart failure, unstable cardiac arrhythmias, hypertrophic cardiomyopathy, severe aortic stenosis, angina or dyspnea at rest or during activities of daily living [ADL]; 3) severe arthritis or impairments at the knee or hip that limited range of motion; 4) preexisting neurological disorders or dementia; 5) history of major head trauma; 6) legal blindness or severe visual impairment; 7) life expectancy <1 yr; 8) history of deep vein thrombosis [DVT] or pulmonary embolism within 6 months; 9) uncontrolled diabetes with recent weight loss, diabetic coma, or frequent insulin reactions; 10) severe hypertension with systolic >200 mmHg and diastolic >110 mmHg at rest (Billinger et al., 2014); and, 11) current enrollment in a clinical trial to enhance motor recovery. All subjects who met criteria for exercise training completed an exercise tolerance test and were cleared for participation by the study cardiologist. Furthermore, any screening and clinical assessments for inclusion were performed by a staff physical therapist within the Center for Rehabilitation Research in Neurological Conditions. This study was approved by the Institutional Review Board of the Medical University of South Carolina and all participants completed and signed an informed consent document prior to participation. This study was a registered protocol (NCT01970592; clinicaltrials.gov).

5.3.2. Intervention

Training included 24 sessions (3 times/week) occurring over an 8-week period and included both muscle resistance and task-specific elements. Inclusive of rest intervals, sessions lasted ~60 minutes. The POWER study intervention protocol included resistance activities aimed at improving muscle power distinctly contributing to improved walking performance. Resistance activities included: sit to stand, leg press exercises, repeated step-up training, and calf raises (i.e., plantar flexion). In addition, jump training was performed during each exercise training session (Jump Trainer, Shuttle MVP Pro, Shuttle System Inc: Glacier, Washington), focusing on lower extremity muscle power generation. Task-specific elements took the form of progressive loaded overground walking during each session. Performing 10 trials of fast walking (10 meters per trial), subjects were asked to complete the distance at speeds ≥ 125% of self-selected overground velocity. Progressive training was attained by average calculations following each session. When the average speed exceeded 125% of self-selected speed, a weighted vest was worn, and a 5% increase in mass was systematically added to allow progression.

Exercise Safety Considerations: Blood pressure (BP) and heart rate (HR) were monitored prior to, during, and at completion of each session. Subjects' resting BP was required to be <100 mmHg diastolic, < 200 mmHg systolic, with a heart rate <110 beats/min to begin testing or training. Criteria for session termination included subject complaints of shortness of breath, light-headedness, confusion, severe headache, or dyspnea; onset of angina; excessive blood pressure (systolic BP > 200 mm Hg, diastolic BP >110 mm Hg), or drop in systolic BP >10 mm Hg and inappropriate bradycardia (drop-in heart rate >15 bpm).

5.3.3. Outcomes

5.3.3a Muscle Strength and Power

Isometric assessments were performed for knee extension prior to and immediately following POWER training using a Biodex isokinetic dynamometer (Biodex Corp., Shirley, NY). Prior to testing, each subject progressed through a standardized period of familiarization and warm-up consisting of 5 minutes of cycling and 3 sub-maximal contractions. Five maximum voluntary isometric contractions [MVIC] were subsequently completed (~3 sec contractions separated by a minimum of 60 seconds rest). If MVIC peak torque values during the trials differed by more than 5%, additional contractions were performed. During all dynamometric testing, subjects were instructed to 1) develop torque as fast as possible and 2) produce a maximal contraction. Subjects were given an auditory cue and received continuous visual feedback. All contractions were performed with subjects seated upright in the dynamometer and the axis of the dynamometer aligned with the knee joint axis of rotation. Proximal stabilization was achieved with straps at the chest, hips, and knee as appropriate. All signals were sampled at 100Hz and exported as raw data files for subsequent data analysis.

5.3.3b Rate of Torque Development [RTD]

The three trials presenting highest torque values were averaged and the torque time trajectories smoothed with a 5-point moving grade (50 ms EPOCH). Onset of force production was defined as the first time point greater than 7.5 Nm (Aagaard et al., 2002). RTD was calculated as the slope of the torque-time relationship (Δtorque/0.05) within each epoch up to 200 ms (Suchomel et al., 2018). Furthermore, the first derivative after onset where percentage change from the previous time point was <3% change was considered the first peak, with time to peak considered the time frame between onset and this point. Finally, peak RTD was defined as the highest value across all epochs. Thus, the three RTD parameters of interest were designated as: RTD200, T2P, and RTDPeak. Finally, absolute peak torque was also calculated from the raw torque-time curve [PeakTor].

5.3.3c Walk Task Performance and Gait Characteristics

Subjects walked on a 20 ft-long gait mat (GAITRite, CIR Systems Inc; Sparta, New Jersey) for assessment of SSWS and the fastest comfortable walking speed [FCWS]. Analyzed data were the average of the three trials at both SSWS and FCWS. In addition to velocity, standardized gait characteristics, including stride length (ipsilateral heel contact to subsequent contact), cycle time (time between two ipsilateral heel strikes), step length (contralateral heel strikes) and gait cadence were assessed. Furthermore, participants performed a 6-minute walk [WALK] at both time points for assessment of walking endurance and locomotion (Poole & Whitney, 2001).

5.3.4 Statistical Analysis

Statistical analyses were conducted using SPSS for Windows version 26.0 (SPSS Inc., Chicago, IL). Normality and assumptions were verified using Kolmogorov-Smirnov and Levene tests, respectively. Bivariate correlations were conducted to assess the association between RTD parameters and gait characteristics and walk task performance at baseline. Paired sample *T-tests* were subsequently used to examine significance of change from baseline to post-intervention. Further, correlations were conducted to explore the effect of changes in RTD parameters on changes in gait characteristics and walking task performance. Statistical significance was set at $p < 0.05$. Data are presented as mean±SD unless otherwise stated.

5.4. Results

5.4.1. Participant Characteristics

Twelve individuals (59.8 ± 9.0 yrs; n = 3 female) with chronic stroke (23.1 ± 18.3 mos post; FMA-LE: 21.5 ± 5.7) completed the POWER training intervention and provided outcome measures of interest. The majority, 64%, suffered a left hemisphere stroke. Although not an exclusion criterion, none of the patients demonstrated any profound neglect or apraxia that would limit testing or intervention completion.

5.4.2. RTD Parameters and Strength

Table 1 presents the strength and RTD parameter outcomes for the paretic and non-paretic legs in response to the intervention. Significant improvements in RTDPeak ($p < 0.01$) were reported for the paretic limb only. Despite a strong trend for T2P ($p < 0.056$), RTD200 was the only significant change for the non-paretic limb ($p < 0.05$). No significant improvements were reported for peak torque, irrespective of limb. Figure 1 depicts the average torque at baseline and post intervention for both limbs.

5.4.3. Walk Task Performance and Gait Characteristics

Gait characteristics are presented in Table 2. Although step count did not change, gait velocity improved for SSWS and FCWS (18.2% and 17.7%, respectively, both $p < .05$) (Fig 2). A strong trend was also apparent for improvement in gait cadence in the SSWS condition (8.6%, $p = 0.053$). Stride length significantly increased for both walking conditions (both $p < 0.05$); however, step length and cycle time was unchanged when evaluated by paretic and non-paretic limbs (all $p > 0.05$). In addition, a significant improvement was observed for participant WALK performance (Baseline: 200.0 ± 112.3 m; Post: 241.7 ± 123.3 m; $p < 0.01$).

5.4.4. Association of Change in RTD Parameters and Gait Characteristics

No significant correlations were reported at baseline between any RTD parameters or walk task performance and gait characteristics (all $p > 0.05$; data not shown). Raw change score correlations are presented in Table 3. Change in RTD200 for the non-paretic limb was associated with change in velocity and stride length for both SSWS and FCWS (r range = 0.60 to 0.70, all $p < 0.05$). Similarly, in the non-paretic limb, RTDPeak was associated with step length in the SSWS and FCWS conditions (r = 0.68 and 0.78, respectively, both $p < 0.05$) and PeakTor was associated with step length (r = 0.63, $p < 0.05$). Alternatively expressed with relative change, Figure 3 illustrates the significant association between %change in RTDPeak and %change in velocity in the SSWS (Panel A) and FCWS (Panel B) conditions for the non-paretic limb only (r = 0.50 and 0.52, respectively, both $p < 0.05$); whereas the association in the paretic limb was attenuated and unexpectedly negative yet nonsignificant (r = -0.32 and -0.27, $p > 0.05$). Finally, change in RTD200 for the non-paretic limb was associated with change in improvement in WALK (r = 0.88, $p < 0.001$). Change in T2P was not associated with any adaptations in gait characteristics in either limb ($p > 0.05$)

5.5. Discussion

The purpose of this study was twofold, initially, to examine the relative effect of POWER training on RTD parameters of paretic and non-paretic limbs, and secondly to explore the association among the changes in RTD parameters and changes in gait characteristics and walking task performance in response to POWER training in chronic stroke survivors. Partly in agreement with our hypothesis, the data revealed that POWER training can significantly improve muscle contractile function (as reflected by RTD parameters). Similarly, despite a relatively short intervention, significant improvements in SSWS, FCWS and WALK were observed, with moderate-strong associations between RTD200 and/or RTDPeak, and these clinically relevant walk performance and gait measures.

There is a body of evolving evidence that supports the beneficial role of physical activity and exercise in addressing a number of patient and caregiver priorities after stroke (Saunders et al., 2014). These priorities include cognition (Cumming et al., 2013), upper limb function (Harris & Eng, 2010), fatigue (Zedlitz et al., 2012), and mobility and physical function (Saunders et al., 2020); however, despite these established benefits, distinct exercise program recommendations for this cohort are lacking. Often times, muscle strength, power and contraction velocity are used interchangeably to denote muscle function. Yet, the individual influence of each parameter on gait and walking performance may vary. Muscle strength is commonly investigated in the stroke literature; yet, studies suggest muscle power, and muscle contractility may be more important factors to consider, especially regarding walking performance and functional status (Bean et al., 2003; Kostka et al., 2019). It is well established that muscle power in the paretic limb for stroke survivors is markedly reduced (Hunnicutt & Gregory, 2017; Kostka et al., 2019; Stavric & McNair, 2012) compared to healthy age-matched counterparts. Reductions in RTD parameters have also recently been reported in stroke survivors

(Maffiuletti et al., 2016; Shimose et al., 2019). It has been suggested that RTD may be a useful assessment tool for muscle contractility due to the sensitivity to detect acute and chronic changes in neuromuscular function.

Often misinterpreted as strength training, power training is designed to distinctly improve muscle function by enhancing its ability to produce maximum force in minimal time. Miszko et al (2003), proposed power training as a promising stimulus for improving physical functionality as a way of improving motor-unit firing rate, muscle activation levels and individual muscular response time in older adults. Investigating balance recovery with a focus on ankle strategy, Robinovitch et al (2002) demonstrated that an individual's ability to recover from a loss in balance is dependent on the ability to produce torque with minimal time delay. Loss of balance whilst walking is a common challenge following stroke, thus improving RTD in stroke survivors is theoretically beneficial. To our knowledge, the present study is the first to investigate the plasticity of RTD parameters in stroke patients. Albeit not all parameters, our data shows that power training can enhance torque development, in both the paretic and non-paretic limbs although effects were observed in differing RTD parameters (RTD 200 vs. RTD Peak, respectively). Fimland et al (2011), utilized electromyography and twitch interpolation to assess and compare neuromuscular function between limbs in chronic stroke patients. They reported, when compared to the non-paretic limb, the paretic limb showed deteriorations in voluntary activation and fast neural activation. The lack of change in peak torque along with improvements in RTD in our data set suggests a neural component to the adaptation to POWER training. Further research is warranted as to the mechanisms; however, these results suggest there may be the potential to partially attenuate impaired paretic limb muscle function.

Research suggests that walking speed is challenging to improve in chronic stroke patients (Jonkers et al., 2009), implying that survivors are often walking at capacity. Furthermore, walking is often a vulnerable activity for stroke survivors as the majority of falls occur whilst ambulating (Belgen et al., 2006; Middleton et al., 2017). Our findings show that an 8-week POWER training intervention can increase self-selected and fast comfortable walking speeds and walking task performance. Associations between improvements in muscle power generation and walking speeds have been reported in acute stroke survivors (Brincks & Nielsen, 2012). However, in contrast to this and prior literature (Davies et al., 1996; Nakamura et al., 1985), our data suggests that focusing on paretic knee extensor muscle power generation may be less important and improving muscle power generation in both limbs is salient to improve gait characteristics. This could reflect the adaptation of compensatory walking patterns following training to allow for increased speeds. Nonetheless, despite significant improvements in RTDPeak in the paretic limb in response to POWER training, there was no association between change in these parameters and change in walking speed.

Traditionally, gait retraining is designed to facilitate paretic limb neuromotor recovery, reducing the reliance on the nonparetic limb's generation of propulsive forces to increase walking speed (Bowden et al., 2006). Our findings suggest that an improvement in RTD in the non-paretic leg may reflect greater propulsive forces or expand on the individuals' ability to compensate for deficits in paretic limb to accomplish increased walking speeds. Although future research is required to understand the mechanisms, our data implies that the paretic limb may be less a limiting factor than previously considered. However, investigating these adaptations with a ratio of asymmetry and during alternative lower extremity physical function tasks may present a different conclusion.

5.6. Limitations

To our knowledge this is the first study to investigate the trainability of RTD in chronic stroke patients, specifically utilizing POWER training, however a number of limitations must be considered. Results of this study are limited by sample size. Furthermore, the training methods utilized in this study focused on power development during uni- and bilateral lower extremity ballistic movements but did not distinctly focus on gait training (e.g., weight assisted stepping practice). Although conceptually, one logically influences the other, direct inference may be a limiting factor to the results presented. Furthermore, the high functionality of the participants enrolled in this small clinical study may limit the generalization of this findings and may also diminish the potential improvements consequent to the intervention (i.e., impacted statistical power). Finally, RTD parameters were assessed during a leg extension MVIC trial, focused on a single joint. Gait involves a complex interaction among multiple joints and muscle groups; thus, extrapolation of results should be done with precaution and future agonist and antagonist RTD studies should be conducted.

5.7. Conclusion

To our knowledge, this is the first study to investigate the trainability of RTD parameters in chronic stroke survivors, and subsequently the association of these adaptations to improvements in gait characteristics and walking task performance. Further research is required to examine the underlying mechanisms contributing to increases in walking speed, however, overarching, these findings suggest POWER training to be an effective treatment intervention for improving RTD parameters and clinically relevant walk task performance and gait characteristics.

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Table 5.1. Knee extensor Rate of Torque Development and Peak Torque (M±SD) at Baseline and in Response to the POWER Intervention for the Paretic and Non-Paretic Limbs.

	Paretic Limb (n = 12)			Non-Paretic Limb (n = 12)		
	Baseline	Post-Test	*p-Value*	Baseline	Post-Test	*p-Value*
RTD Parameters						
RTD 200 (Nm/s)	71.1±77.0	73.0±74.8	0.911	85.4±61.6	151.1±115.9	**0.047***
RTD Peak (Nm/s)	108.9±76.0	132.5±83.5	**0.003***	212.8±91.5	291.7±240.3	0.264
T2P (ms)	508.3±329.5	725.0±448.5	0.240	787.5±453.8	458.3±338.3	0.056

RTD200 = Rate of Torque Development at 200ms; RTDPeak = Peak Rate of Torque Development; T2P = time (ms) from onset to first peak.

p-value = within limb comparison

Table 5.2. Gait Characteristics (M±SD) at Baseline and in Response to the POWER Intervention for the Paretic and Non-Paretic Limbs.

	SSWS (n = 12)			FCWS (n = 12)		
	Baseline	Post-Test	*p-Value*	Baseline	Post-Test	*p-Value*
Gait Characteristics						
Velocity (cm/s)	55.4±31.4	65.5±34.9	**0.010***	76.8±45.5	90.4±49.8	**0.009***
Step Count	35.2±16.5	36.1±14.1	0.852	31.9±14.7	31.0±12.3	0.817
Cadence (Steps/min)	72.1±21.7	78.3±22.5	0.053	85.3±27.5	92.8±28.4	0.117
Stride Length (cm)	85.8±30.9	98.5±31.9	**0.028***	100.7±34.4	110.2±32.4	**0.021***
Paretic Limb						
Step Length (cm)	39.8±24.1	43.3±19.5	0.483	50.2±19.5	53.4±22.9	0.128
Cycle Time (s)	1.9±0.8	1.9±1.2	0.912	1.6±0.7	1.6±0.7	0.635
Non-Paretic Limb						
Step Length (cm)	45.9±15.6	45.7±18.3	0.938	49.2±18.5	51.0±20.1	0.419
Cycle Time (s)	1.9±0.7	2.0±1.6	0.685	1.7±0.9	1.6±0.8	0.610

Notes: SSWS – self-selected walking speed; FCWS – fasted-comfortable waking speed.

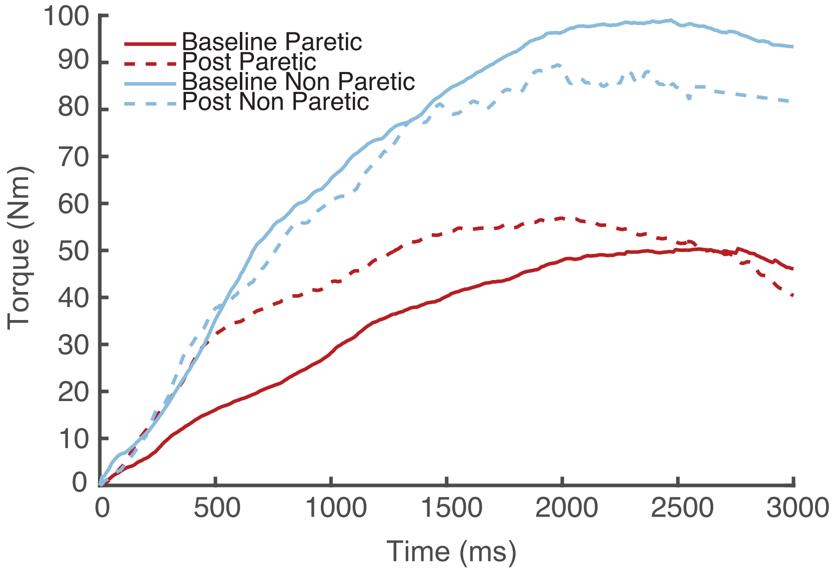
Table 5.3. Associations Between Raw Change Score for RTD Parameters and Gait Characteristics for Paretic and Non-Paretic Limbs.

	SSWS (n = 12)				FCWS (n = 12)			
RTD Parameters	RTD200	RTDPeak	T2P	*PeakTor*	RTD200	RTDPeak	T2P	*PeakTor*
Paretic Limb								
Velocity	-0.124	-0.316	-0.130	-0.219	-0.129	-0.270	-0.088	-0.349
Step Count	0.274	0.280	-0.060	-0.084	0.215	0.191	0.051	0.069
Step Length	-0.231	0.188	-0.084	-0.207	-0.159	0.034	-0.269	-0.227
Cycle Time (s)	0.143	-0.272	-0.200	0.201	0.002	-0.024	0.082	0.176
Stride Length	-0.067	-0.560	-0.285	-0.088	-0.164	-0.318	0.008	-0.249
Non-Paretic Limb								
Velocity	**0.701***	0.499	0.314	0.238	**0.679***	0.520	0.210	0.178
Step Count	-0.020	-0.375	0.095	-0.429	0.086	-0.412	0.251	-0.310
Step Length	0.235	**0.678***	-0.158	**0.628***	0.167	**0.780***	-0.100	0.373
Cycle Time (s)	-0.220	-0.244	0.177	-0.479	0.052	-0.528	0.066	-0.230
Stride Length	**0.601***	0.416	0.455	-0.012	**0.645***	0.207	0.177	0.080

Notes: SSWS – self-selected walking speed; FCWS – fasted-comfortable waking speed.

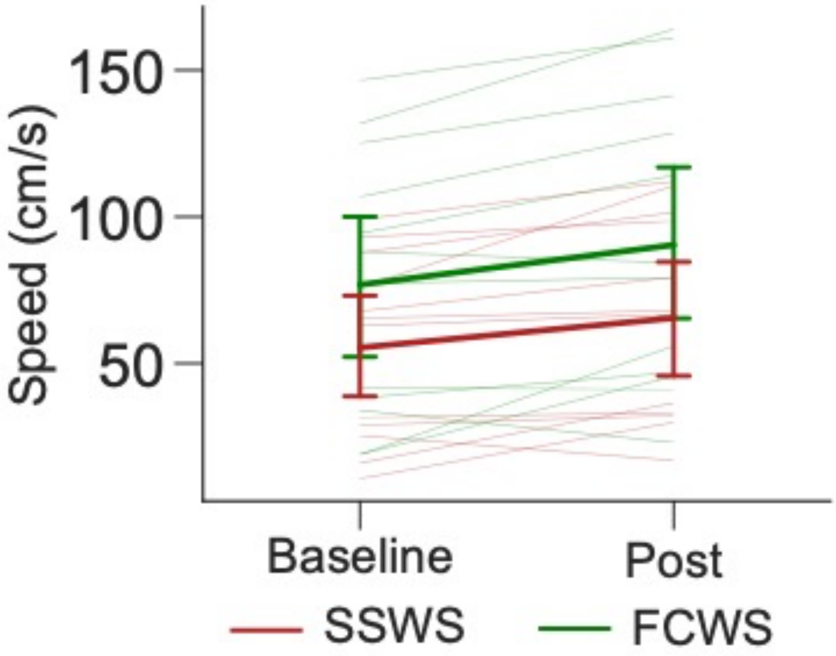
(*) – Denotes significant correlation

Figure 5.1. Torque Development at Baseline and in Response to the Intervention for Paretic and Non-Paretic Legs.



Note: Each line is the average score across participants.

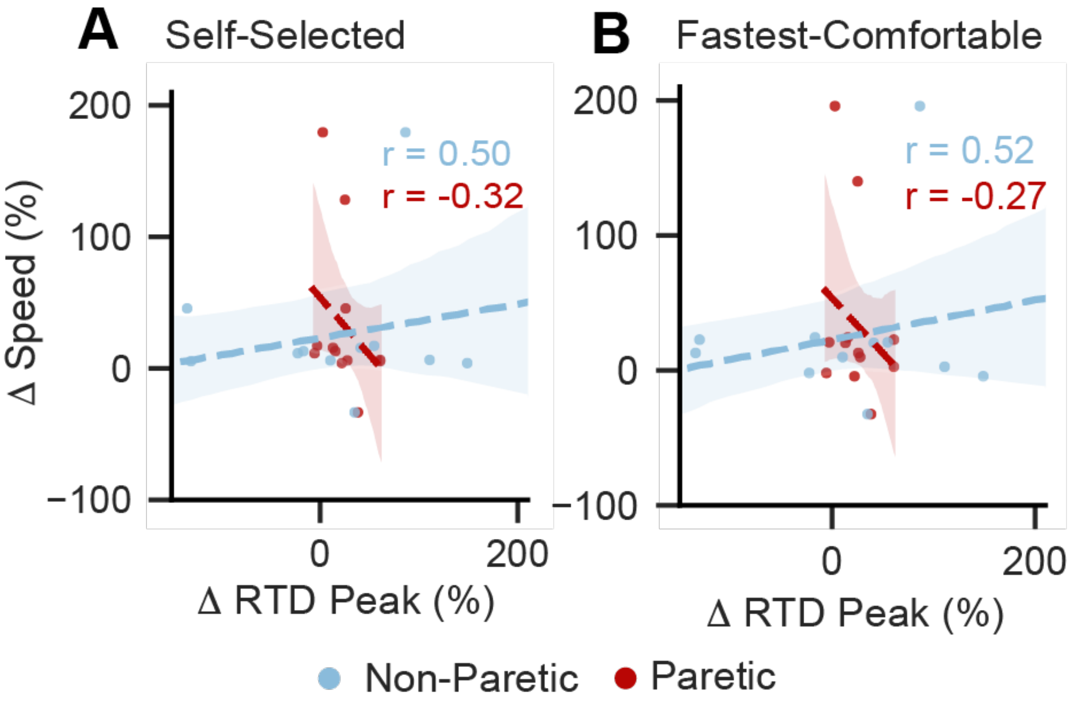
Figure 5.2. Group (M±SD) and Individual SSWS and FCWS velocity at Baseline and in Response to the POWER Intervention.



Note: Each thin line is a single subject, whereas the bold line corresponds to group mean.

SSWS – self-selected walking speed; FCWS – fasted-comfortable waking speed.

Figure 5.3. Association between percent change (Δ) in RTD and percent change in Self-Selected [Panel A] and Fastest-Comfortable walking speed [Panel B].



Note: Δ = (Post – Baseline values)

CHAPTER 6

SUMMARY AND CONCLUSIONS

In conclusion, the purpose of this dissertation was to determine and characterize the trainability of muscle power, characterized with RTD parameters, and contralateral limb activation pattern characteristics (i.e., %ASYM) and subsequently the implications for improvements in lower extremity physical function [LEPF] task performance, following an exercise intervention, in two clinical populations (overweight or obese older women; chronic stroke patients), using clinically available equipment and methodologies. Three independent secondary data analyses were completed on two separate datasets, to address the aforementioned aims. Summary of the two datasets is as follows.

Project DIVAS (Overweight/Obese Older Women; Dissertation Aims 1 and 2): A randomized controlled trial investigated the effect of two different 6-month dietary treatments with or without exercise on body composition, strength, and physical function in older women. Participants were randomized into three groups: 1) higher protein diet with exercise (PRO+EX), 2) higher protein diet without exercise (PRO), or 3) conventional protein control diet with exercise (CON+EX). The goal of the three treatments was to elicit a ~10% reduction in baseline body weight and all participants were prescribed a similar caloric restriction protocol. Notably, the exercise treatments were identical in the PRO+EX and CON+EX groups and were subsequently combined for the present dissertation projects [EX+WL, WL].

Project POWER (Chronic Stroke Survivors; Dissertation Aim 3): Ensuing a comprehensive inclusion and exclusion criteria, chronic (> 6months) stroke survivors were recruited to undertake 24 explosive resistance training sessions, 3 days/week for

8-weeks. Sessions involved uni- and bilateral resistance exercises, progressive loaded overground walking, and power generation activities aimed at improving muscle power distinctly contributing to improved walking performance. Clinical physical function, muscle strength and power, and walking locomotor were assessed at baseline and post-intervention.

The primary aims of this dissertation were three- fold: 1) To determine the relative effect of weight loss with or without concomitant exercise training on RTD parameters in overweight/obese inactive older women, and the association of these adaptations on LEPF task performance, 2) to investigate the relative effect of weight loss, with or without exercise training on between and intra- leg power ASYM in overweight/obese inactive older women. Subsequent to this, and to explore the association between any changes in ASYM and changes in clinically relevant LEPF performance tasks, and 3) to determine the effect of muscle power training on knee extensor RTD parameters of both the paretic and non-paretic limb and potential improvements in gait characteristics and walking speed in chronic stroke survivors, and explore the association among any adaptations in RTD parameters and gait characteristics and walking task performance, in chronic stroke patients.

Primary Aim 1: Obesity has been reported to negatively impact LEPF and is associated with loss of independent living, especially in older adults. Concurrent exercise/physical activity and weight loss interventions are known to be effective to enhance LEPF, however, the inclusion of power modulations, specifically Rate of Torque Development [RTD] parameters in response to these interventions has not been investigated. In the attempt to address primary aim 1, 44 overweight inactive postmenopausal women were divided into two groups: 1) exercise and weight loss [EX+WL; (N=30)] and weight loss alone [WL; (N=14)], completing a 6-moth intervention. Following the intervention, participants lost on average -7.1±4.1kg; -9.8±4.2%, irrespective of group as per study design. However, EX+WL alone reported greater improvements in most LEPF tasks. Rapid leg flexor contraction was improved in the EX+WL group and associated with a few LEPF task improvements. No other adaptations or associations between RTD parameters and LEPF performance were reported. These findings build on the previous work that suggests that concurrent exercise and weight loss are linked with positive LEPF improvements in older adults with a minimal contribution from changes in RTD. Additional research is needed to confirm the mechanistic adaptations; however, our data supports the importance of exercise in the management of obesity and physical functional decline in older women, which remains a public health concern.

Primary Aim 2: The second primary aim was addressed utilizing the same dataset as primary aim 1. The potential interactive effects of weight loss and exercise on degree of ASYM and relatedly, favorable improvements in LEPF are unknown. Thus, we aimed to determine the relative effect of weight loss with or without exercise on intra- and between-limb power %ASYM in inactive overweight/obese older women and the subsequent influence on clinically relevant LEPF tasks. At baseline Leg Flexor %ASYM was associated with all three LEPF tasks (WALK, UPGO, CHAIR). Consequent to the intervention all power outcomes improved in EX+WL, however, no significant changes in %ASYM were observed, irrespective of group. Emulating the baseline correlations, changes in Leg Flexor %ASYM, alone, was associated with improvements in LEPF performance, specifically UPGO performance, suggesting that reductions in between limb flexor asymmetry may be a beneficial focus for future interventions.

Primary Aim 3: Expanding on primary aim 1, we aimed to investigate the plasticity of RTD parameters in response to power training and the subsequent influence on gait characteristics in chronic stroke survivors (n = 12). RTD in lower extremity muscles has recently been reported to influence walking speed in this population, however the trainability and subsequent effect on gait characteristics, including walking speed is unknown. To our knowledge, this is the first study to investigate the trainability of these parameters, and the subsequent association of these adaptations to improvements in gait characteristics, physical function, and walking locomotion in chronic stroke survivors. Our results suggest power training is an effective exercise intervention for improving rapid muscle contraction and muscular power output in stroke survivors; however, variations in results existed based on paretic vs. nonparetic limb. Furthermore, these adaptations were observed to be positively associated to self-selected and fasted-comfortable walking speed and walking endurance locomotion. Future explorations into the mechanistic elements are required; however, our findings suggest that an improvement in RTD in the non-paretic leg may reflect greater propulsive forces or expand on the individual's ability to compensate for deficits in paretic limb to accomplish increase walking speeds. Thus, future work to explore exercise training and RTD related mechanisms as they relate to enhancing LEPF and gait ability in chronic stroke patients is warranted.

Due to the secondary analysis component of this dissertation, it is not without noteworthy constraints and limitations that should be discussed. 1) Ensuing data collection, mechanistic recommendations for the analysis of RTD have been proposed to ensure adequate and detailed data. Unfortunately, a number of these suggestions were unable to be followed. However, this limitation is arguably tempered by the novelty and high degree of instructional application provided in the parent study designs. 2) Unequal and low sample sizes are present within the datasets; therefore, statistical power is subsequently considered low; however, the results observed support the salient importance of our findings and definitively inform future work in areas of public health and clinical concern. Finally, 3) although conceptually, one logically influences the other, direct inference may be a limiting factor to the results presented. Furthermore, the high functionality of the participants enrolled in this small clinical study may limit the generalization of this findings and may also diminish the potential improvements consequent to the intervention (i.e., reduced statistical power).

In conclusion, we provide novel evidence that changes in lower limb muscle power modulation and bilateral asymmetry in response to exercising training are both significantly associated to improvements in physical function and mobility in two clinical populations, overweight and obese older women undergoing weight loss and chronic stroke survivors. Further research is warranted to explore intervention strategies to improve muscle power modulation in both populations and the subsequent impact on LEPF to ultimately reduce the risk of physical disability in two populations, obese inactive older women and chronic stroke survivors, that are increasing in prevalence.