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To the University Council:

The Thesis Committee for Kelley G. Hammond certifies that this is the approved version of the following thesis:

CENTRAL VS. PERIPHERAL MANIFESTATIONS OF NEUROMUSCULAR
FORCE IN PERSONS WITH PARKINSON'S DISEASE

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CENTRAL VERSUS PERIPHERAL MANIFESTATIONS OF
NEUROMUSCULAR FORCE PRODUCTION IN PERSONS WITH PARKINSON'S DISEASE

by

Kelley G. Hammond, BS, CSCS

A Thesis

Submitted in Partial Fulfillment of the

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Abstract

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Bradykinesia and reduced neuromuscular force exist in Parkinson's disease (PD). Percutaneous electrical stimulation (PES) has been used to evaluate central versus peripheral manifestations of neuromuscular strength in healthy, aging, and athletic populations, but this method has not previously been used in PD. This pilot study used PES of the quadriceps femoris to identify central and peripheral activation in persons with PD ($n = 7$) and neurologically healthy controls ($n = 6$). Maximal voluntary rate of force development (PD = $2544\text{N/s} \pm 1183$, control = $4599\text{N/s} \pm 1077$; $P = 0.008$) and the rate of force development ratio (RFDR; PD = 0.45 ± 0.15 , control = 0.80 ± 0.20 ; $P = 0.004$) were significantly ($P < 0.05$) lower in the PD group compared to controls. No other significant differences were found between groups. This study was the first to quantify the central deficits caused by PD which bring about reduced neuromuscular rate of force development.

Key words: neuromuscular disease; strength deficits; percutaneous electrical stimulation; central activation ratio

PREFACE

This thesis was written in article format for submission to the journal *Movement Disorders* following defense. The content and organization of this thesis represent and fulfill the requirements for submission to this journal.

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INTRODUCTION

Parkinson's disease (PD) is a central nervous system disorder that results in several debilitating symptoms. Among these symptoms are reduced neuromuscular strength and bradykinesia (slowness of movement)¹. These difficulties with motor control evolve deep within the brain in the substantia nigra, where dopaminergic neurons are killed by the disease. Because dopamine is a neurotransmitter that regulates movement, persons with PD are unable to control movement via signaling from the brain to the body's periphery in the same manner as healthy persons do. Symptoms include, but are not limited to, tremor of the hands, arms, legs, jaw, and face, rigidity (stiffness) of the limbs and trunk, bradykinesia, and postural instability (impaired balance and coordination)². Parkinson's disease is chronic and progressive. More Americans (~1 million) suffer from PD than Amyotrophic Lateral Sclerosis (Lou Gehrig's disease), multiple sclerosis, and muscular dystrophy combined, and the yearly cost of treatment and loss of ability to work is estimated at 25 billion dollars in the United States alone³.

Most studies comparing persons with PD to neurologically healthy, age-matched individuals have reported reduced strength in PD⁴⁻¹³. This supports the presumption that decreased strength is caused by the disease⁶. Corcos et al.⁷ and Nallegowda et al.⁴ reported reduced voluntary strength and rate of force development (RFD) following withdrawal from antiparkinson medication, which suggests that this weakness and reduction in RFD is a direct result of the disease, and that at least part of the weakness is central in nature. While neurologically healthy persons typically take less than one second to achieve peak force, PD patients with moderate bradykinesia can take 3-4 seconds^{4,7}. Further, Corcos et al.⁷ concluded that changes in strength correlate significantly with changes in contraction rate.

Central and peripheral effects of the disease include decreases and irregularities in motoneuron firing rates and deficits in muscular strength^{5,14}. Superimposed electrical stimulation is an effective method of evaluating and quantifying voluntary versus involuntary muscle activity¹⁵⁻¹⁷, but has not been used in PD. By stimulating a relaxed muscle, the maximal involuntary rate of force development (MIRFD) can be identified and used to estimate the aptitude of the muscle's contractility without central input. If this evoked twitch is added to a maximal voluntary contraction (MVC), the difference in force output can provide a quantitative value of central activation. One method of calculating this deficit is the central activation ratio (CAR = MVC/(MVC + stimulated force))¹⁸. The purpose of this study was to collect pilot data that

quantified the neurological deficiencies in persons with PD and observe the sources of reduced strength in this population and establish a protocol for future studies.

METHODS

Subjects

Thirteen men (n = 10) and women (n = 3) were recruited to participate in the study. The seven persons in the PD group (M=6, F=7) were diagnosed with idiopathic PD. Individuals with orthostatic hypotension, dementia (Mini-Mental State Examination Scores <24), or other significant co-morbidities (i.e., stroke, severe degenerative osteoarthritis) were not recruited into the study. Further, great care was taken to exclude individuals with other causes of Parkinsonism such as progressive supranuclear palsy, vascular PD, and multiple system atrophy. A board-certified neurologist rated each PD subject according to the Unified Parkinson's Disease Rating Scale (UPDRS) close to the time of testing.

Six neurologically healthy, age-similar individuals (M=4, F=2) were recruited from the local university faculty and staff for the control group. These subjects were of good general health based on self report and had no abnormal neurological diagnoses. All subjects completed a health history, drug usage, and fitness activity questionnaire, and provided written informed consent prior to data collection (see Table 1). All testing was approved by the university institutional review board for human subjects research.

Table 1. Descriptive Statistics

	PD (n = 7)	CONTROL (n = 6)
Gender	M = 6, W = 1	M = 4, W = 2
Age (yr)	65.4±7.3	60.5±4.9
Height (cm)	177.7±8.7	174.6±6.8
Weight (kg)	84.9±6.5	81.1±14.2
Thigh Circumference (cm)	52.6±5.4	52.9±5.1
Thigh Skin Fold (mm)	22.6±11.1	25.5±15.8
Thigh Cross-sectional Area (cm ²)	56.3±19.7	59.3±7.8
Maximum Voltage (mV)	283.3±25.8	271.4±56.7
UPDRS	15.7±5.0	N/A
Hoehn and Yahr Staging	HY1.5, n=1; HY2, n=6	N/A
Disease Duration	7.9±5.01	N/A

Procedures

Upon arrival to the laboratory, subjects filled out a health history, medication, and fitness activity questionnaire after providing written informed consent. Additionally, investigators verbally obtained informed consent and answered any questions subjects had pertaining to the study. Subjects' height and weight as well as thigh skinfold and circumference were measured (right leg). Skinfold and circumference were used to calculate quadriceps femoris cross-sectional area (CSA) according to the equation by Housh et al.¹⁹ ($[2.52 \times \text{mid-thigh circumference in cm}] - [1.25 \times \text{anterior thigh skinfold in mm}] - 45.13$). Pairs of round Ag-AgCl surface electrodes (Ambu Blue Sensor SP, 20 mm interelectrode distance) were affixed on the biceps femoris, vastus lateralis, and rectus femoris according to SENIAM guidelines²⁰, with a ground electrode placed on the patella. Vastus medialis electrodes were placed just proximal to the anode of the stimulating electrode pair. Electrodes were placed parallel to the relaxed pennation angle of each muscle and had an inter electrode distance of 30 mm. Prior to electrode placement, skin was shaved, vigorously abraded, and cleaned with alcohol. EMG was recorded during every trial using Myopac Jr (RUN Technologies; Mission Viejo, CA) with four dual-lead channels. This system has a common mode rejection of 90 dB, a band-pass filter (10-1000 Hz), and input impedance of 10 M Ω . Data were collected at 1 kHz and synchronized with the force signal. The EMG electrode leads were connected to a channel amplifier/encoder/fiber optic transmitter (Myopac Jr, Run Technologies) to obtain EMG signals, which were acquired via analog/digital conversion (Measurement Computing) at a sampling rate of 1000Hz utilizing Datapac5 software for processing and analysis.

The subjects were seated in a customized chair which provided back support and placed the subject in an upright position²¹. Seatbelt restraints were placed across the subject's trunk and lap to minimize movement of the torso^{17,21-24}. Rubber stimulating electrodes (7.5 x 13 cm) were secured with tape over the femoral triangle (cathode) and just above the superior border of the patella (anode)^{14,17,21,22,25-28}. The subject's right ankle (all subjects were right-leg dominant) was inserted into a padded sleeve and cuff, and attached to the load cell (Transducer Techniques® MLP-1K load cell) with enough tension to eliminate slack^{22,23,25}. This fixed the knee at 90°, and the hips at 100° (see Fig.1).

Subjects were instructed to cross their arms over their chest during testing. For the first trial, subjects were asked to relax prior to being given a $200\mu\text{s}^{16}$ triplet pulse of 50mA at 400v^{29} (Digitmer® DS7AH) to the quadriceps¹⁴. The amperage was then increased in 50mA increments for subsequent trials¹⁶ until the peak force reached a plateau (less than 5% change¹⁵), which was expected to occur between 200-400mA^{23,30,31}. An octet pulse was administered at the parameters that caused plateau in force to identify MIRFD³⁰. Subjects were given as much time as they needed between twitches, which was less than one minute^{14,15}.

The subject was then instructed to maximally contract the quadriceps of their restrained leg to familiarize the feeling of performing MVCs. Two MVCs were performed with one minute rest between trials or when subject was ready to continue (see Fig. 2). The investigators then repeated the instructions for the MVC, and the subject was asked to perform a MVC where the predetermined triplet pulse (same maximal parameters) was applied during the plateau phase^{14,16,30,32}. The MVC with stimulation trial was repeated twice²⁵, with a minute break between each repetition, or until the subject was ready to continue. The better of two trials was used for analysis. Reliability of this protocol has been previously established in the literature^{17,33,34}.

Force signals were acquired via analog/digital conversion (Measurement Computing) utilizing Datapac5 software for both acquisition and processing. The force signal was filtered through a fourth-order Butterworth low-pass filter with a cutoff frequency of 30Hz. The maximal RFD during electrically stimulated (MIRFD) and MVC (MVRFD) were calculated as the maximum velocity of the signal (N/s) during the rise phase. Start of the action was defined as the point at which the first derivative of the filtered force signal crossed zero for the last time. The rate of force development ratio (RFDR) was calculated as the quotient of MVRFD divided by MIRFD.

Statistics

Because of the pilot nature of this study, simple independent t-tests were used to compare MVF, seated isometric twitch force (SITF), MVRFD, MIRFD, CAR, RFDR, and rmsEMG between the groups. Effect sizes were calculated to determine the magnitude of differences between groups. Bivariate correlations were not run because there was no spread in the UPDRS data. Data were analyzed using SPSS 16.0 software.

RESULTS

Eighteen subjects were brought in for testing, however, two did not finish the protocol due to discomfort and three of the subject's data were not useable due to impact artifact in the force channel. We found significant differences between groups in MVRFD (PD = $2544.7\text{N/s} \pm 1183.6$, CTRL = 4598.9 ± 1076.8 ; $P = 0.008$; see Fig. 3) and RFDR (PD = 0.45 ± 0.15 , CTRL = 0.80 ± 0.20 ; $P = 0.004$; see Fig. 4), with the PD group having reduced scores compared to controls. No significant differences were found between groups for all other notable variables, including MIRFD (PD = $6145.2\text{N/s} \pm 2641.3$, CTRL = $5836.8\text{N/s} \pm 959.7$; $P = 0.79$; see Fig. 5), SITF (PD = $697.6\text{N} \pm 86.4$, CTRL = $679.2\text{N} \pm 108.2$; $P = 0.74$; see Fig. 6), MVF (PD = $690.7\text{N} \pm 85.2$, CTRL = $665.9\text{N} \pm 98.1$; $P = 0.64$; see Fig. 7), and CAR (PD = 0.99 ± 0.03 , CTRL = $0.98 \pm .03$; $P = 0.63$; see Fig. 8). There was no difference in voluntary activation (rmsEMG; Fig. 9) of the biceps femoris (PD = $209.97\text{mV} \pm 50.6$, CTRL = $275.59\text{mV} \pm 128.3$; $P = 0.24$), vastus lateralis (PD = $238.52\text{mV} \pm 90.4$, CTRL = $259.66\text{mV} \pm 142.0$; $P = 0.75$), rectus femoris (PD = $147.51\text{mV} \pm 95.0$, CTRL = $178.0\text{mV} \pm 78.1$; $P = 0.95$), and vastus medialis (PD = $187.27\text{mV} \pm 70.8$, CTRL = $213.74\text{mV} \pm 95.9$; $P = 0.60$). Large effect sizes were found for RFDR ($d = 2.03$), biceps femoris rmsEMG ($d = 1.84$), and MVRFD ($d = 1.82$).

DISCUSSION

This is the first investigation using PES to determine involuntary neuromuscular activation in PD. We have employed a PES protocol that has been established in other populations, but is novel in PD. We observed significant deficits in the PD group's MVRFD and RFDR of the quadriceps femoris (QF) compared to healthy, similar age controls. Because the intent of this study was to collect pilot data, the sample size was small, and may be a limitation to our findings. This, paired with the high level of functioning of the subjects could have affected the overall results of the study—in particular the strength (MVF) measures. It should be noted that small effect sizes were noted in cases of no significant difference between groups.

As PD progresses, bradykinesia is commonly a troublesome symptom which adds to the difficulty of activities of daily living (ADL). Because MIRFD was similar for PD and controls, the mechanisms responsible for this deficit early in the disease appear to be purely central in nature. The PES-induced activation of the QF demonstrates the peripheral ability of the muscles to function, but the individuals with

PD were unable to actively replicate the voluntary RFD of healthy controls. Other investigations of strength measures reported similar findings of reduced voluntary RFD in persons with PD^{4,7,10}, but this is the first to examine MIRFD in evoked contractions. Corcos et al.⁷ found a correlation between maximal strength and RFD and Allen et al.³⁵ found similar deficits, reporting decreased leg strength and power (force x velocity) in PD compared to controls, whereas our results only suggest a difference in RFD. Allen et al.³⁶ also investigated the relationship between reduced muscle power, slower walking velocity, and falling in PD, reporting that muscle power, compared to muscle strength, greatly affected walking velocity, and had stronger associations to falling than muscle strength alone. This indicates that the rate (velocity) at which force can be produced is as important as the force of muscle contraction³⁶, and both should be considered when designing training protocols.

Initial strength improvements consequent to resistance training appear to be largely accounted for by neural adaptations³⁷. Del Olmo et al.³⁸ specifically reported an adaptation in the central nervous system following resistance training, and confirmed the sustainability of this adaptation with chronic training. Carroll et al.³⁹ found similar results, and proposed that resistance training alters the organization of the central nervous system so that a given magnitude of corticospinal input activates fewer motoneurons during muscle contraction than were recruited prior to training, and the maximal voluntary force is greater³⁸.

To date no PD resistance training studies have specifically trained (and tested) subjects with the objective of increasing RFD. Schilling et al.⁸ did instruct the subjects to “lift the weight as fast as possible with good form”, which has not been emphasized in the other literature to date. The literature on the effects of resistance training on RFD in healthy populations proposes that RFD is trainable over time^{40,41}, but emphasizes the importance of the intent of moving the load quickly. Behm and Sale⁴⁰ indicated that RFD can be increased by trying to move rapidly when moving heavy loads, in which case the actual velocity of the movement would be slow. This seems to correspond well with training prescriptions for improving maximal strength as well (high weight, moderate repetition). Also, instruction for the desired movement should be highly specific, asking the subject to perform the exercise (concentric portion) as fast as possible⁴².

The PD group's CAR scores and peak force measures were similar to the control group, even when adjusted for QF CSA. Full activation of the QF has been reported by several studies^{30,43-45}, so the CARs being nearly 100% in the controls was not unfounded. As strength deficits were expected in this investigation, CAR scores for PD were also expected to be lower than controls, but the lack of differences in MVF may have translated to no differences in CAR. Also, our findings did not suggest reduced strength in the PD group, although several studies have reported decreased strength in persons with PD compared to controls⁴⁻¹³. Our hypothesis included similar strength deficits, but it is possible that our findings are a result of the PD group having only mild to moderate PD (UPDRS = 15.7 ± 5.0 ; H&Y = 1.9 ± 0.20) and minimal presence of symptoms when optimally medicated (as they were during testing). While our results did not agree with previous investigations for these strength variables, the literature has considerable agreement that reduced strength is a symptom of PD and this implies the value of resistance training interventions for this population^{1,46}.

Several resistance training studies have revealed increases in strength in persons with PD following 8-12 weeks of training^{8,47-51}. Despite considerable differences in mode, intensity, volume, and frequency of resistance training in this population, all studies have reported increases in strength indices, which is promising. Still, the optimal resistance prescription has yet to be identified, and none of the aforementioned studies used RFD as an outcome measure. This prescription should specify the aforementioned training variables for persons with PD and indicate appropriate progression of training to optimize benefits and minimize fatigue.

Percutaneous electrical stimulation could enable quantitative measures of involuntary activation for the manipulation of numerous variables ranging from medication dose to the effects of exercise and physical therapy training programs. This pilot study identifies the efficacy of the PES protocol as an evaluation method for quantifying central versus peripheral neuromuscular RFD deficits in persons with PD. Using PES for pre- and post-testing in training interventions would establish a quantitative assessment for evaluating training protocols for persons with PD. This is especially critical in a time when exercise is becoming a more commonly investigated supplemental therapy for managing the progression and symptoms of the disease, and the optimal exercise prescription has yet to be found. Our investigation used PES to quantify QF activation (CAR), maximal strength (MVF), RFD (MVRFD and MIRFD), and RFDR.

The PD subjects had decreased MVRFD and RFDR, as they were unable to voluntarily produce force at the same rate as age-similar, healthy controls. We did not find significant differences in MVF, despite reports of this deficit in the current literature, which we attribute to a combination of small sample size and high function of the PD subjects. As investigations of exercise interventions are being proposed more frequently, a quantitative evaluation protocol, compared to qualitative testing and questionnaires, such as PES would be most advantageous for providing consistent comparisons among individual subjects and intervention protocols and examining central adaptations.

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Appendix A – Figures

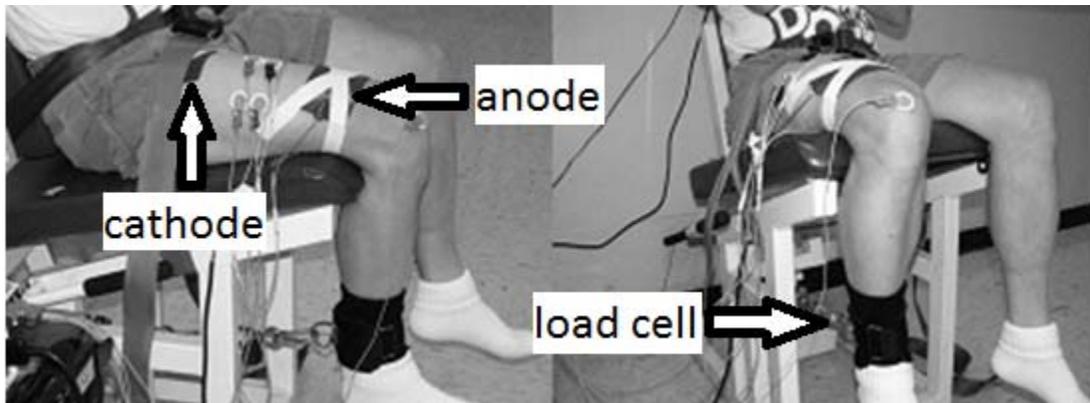


Fig. 1. Testing set-up for percutaneous electrical stimulation

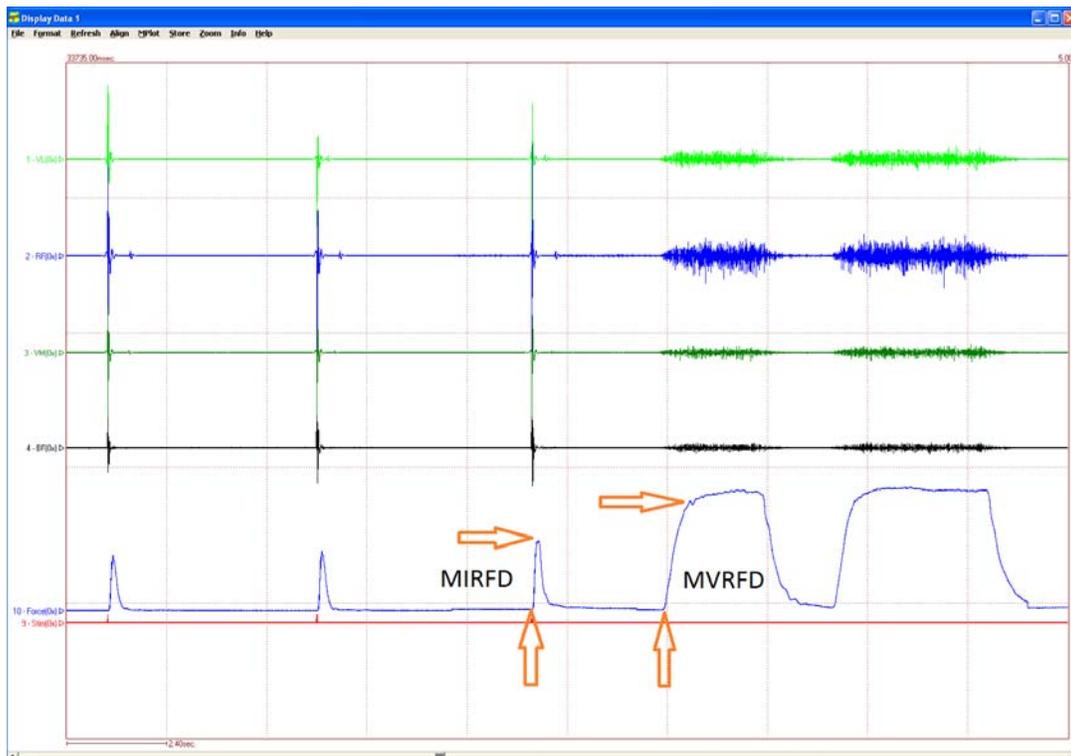


Fig. 2. Voluntary and involuntary rate of force development

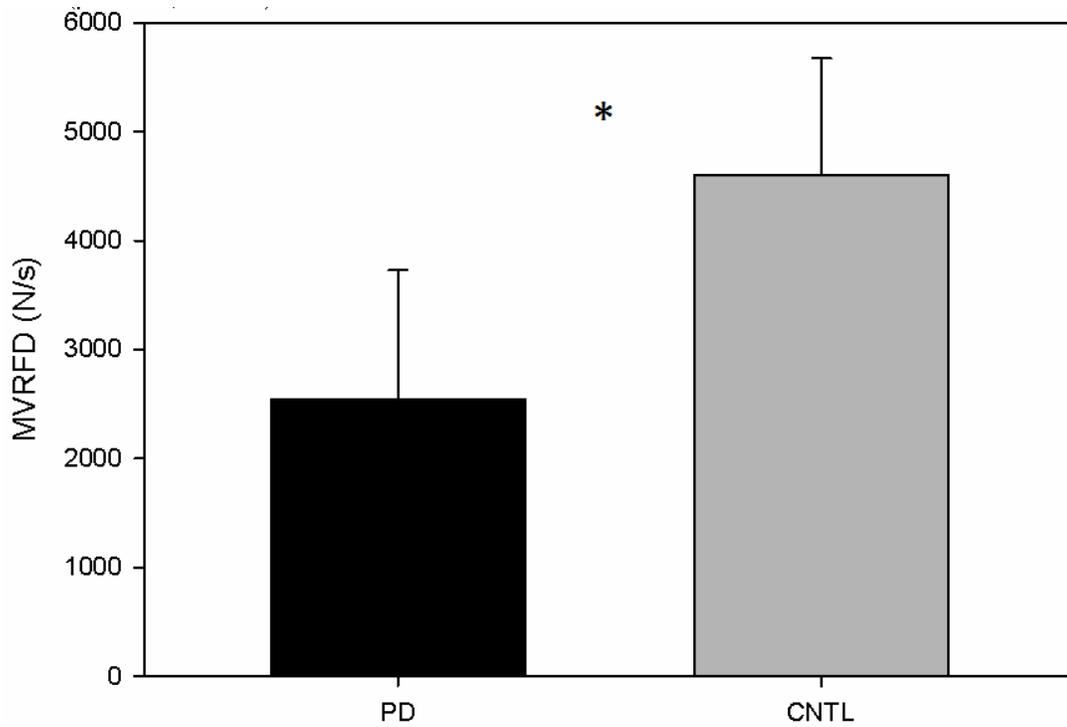


Fig. 3. Maximal voluntary rate of force development (Mean \pm SD) for PD (2544.7N/s \pm 1183.6) and CNTL (4598.9N/s \pm 1076.8). Significant differences were noted between groups ($P = 0.008$, $d = 1.82$)

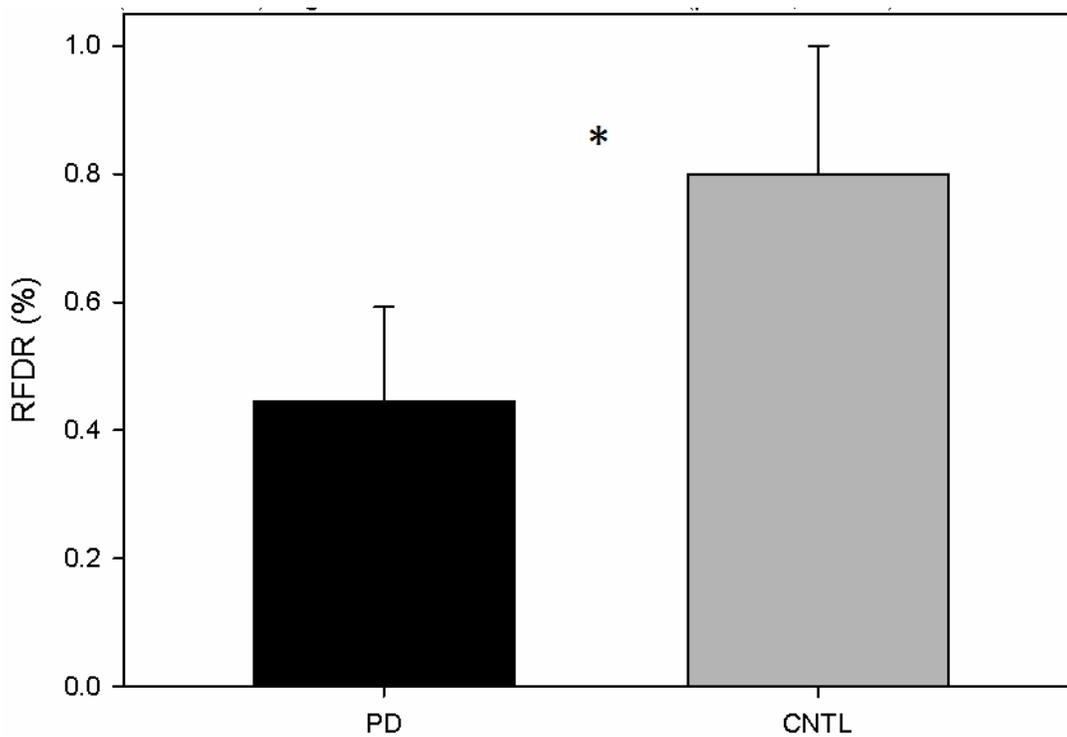


Fig. 4. Rate of force development ratio (Mean \pm SD) for PD (0.45 \pm 0.15) and CNTL (0.80 \pm 0.20). Significant differences were noted between groups ($P = 0.004$, $d = 2.07$)

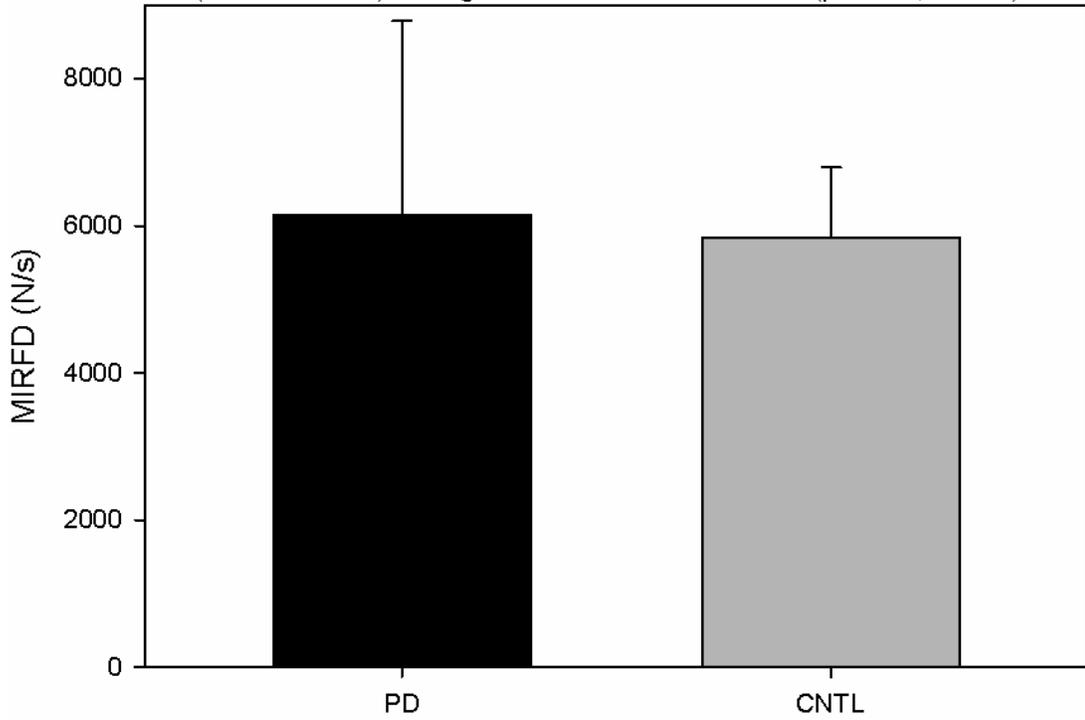


Fig. 5. Maximal involuntary rate of force development (Mean \pm SD) for PD (6145.2N/s \pm 2641.3) and CNTL (5836.8N/s \pm 959.7). No significant difference was noted between groups ($P = 0.792$, $d = 0.17$)

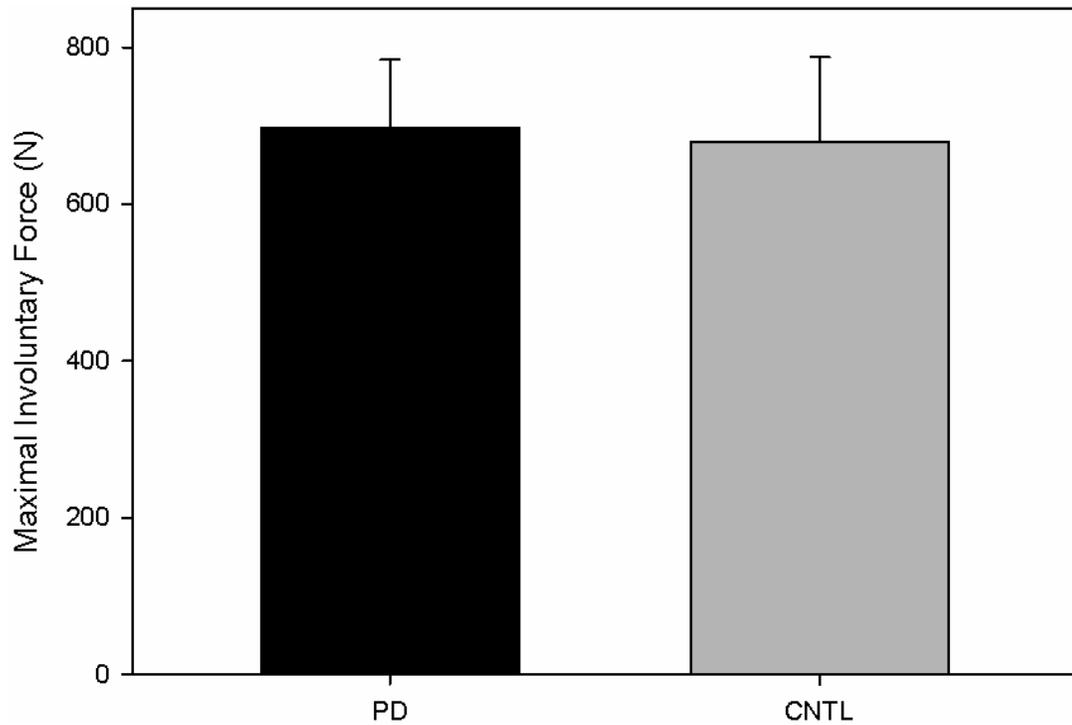


Fig. 6. Maximal involuntary force (Mean \pm SD) for PD (697.57N \pm 86.4) and CNTL (679.2N \pm 108.2). No significant difference was noted between groups ($P = 0.739$, $d = 0.19$)

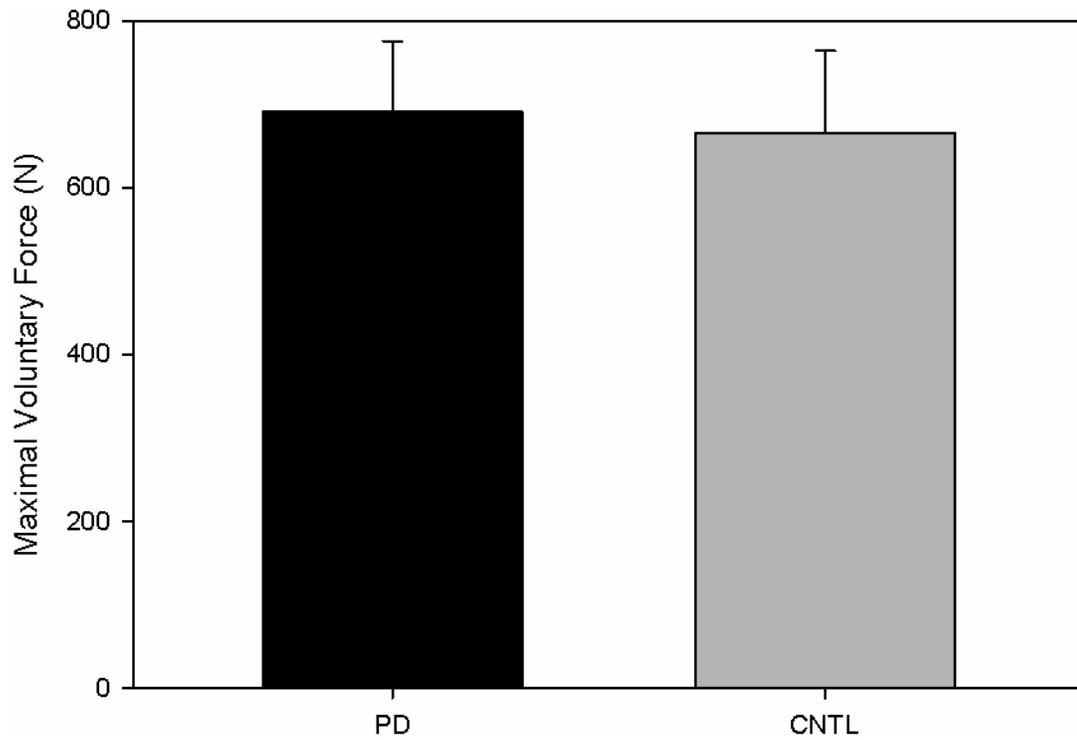


Fig. 7. Maximal voluntary force (Mean \pm SD) for PD (690N \pm 58.2) and CNTL (655.9N \pm 98.1). No significant difference was noted between groups ($P = 0.636$, $d = 0.27$)

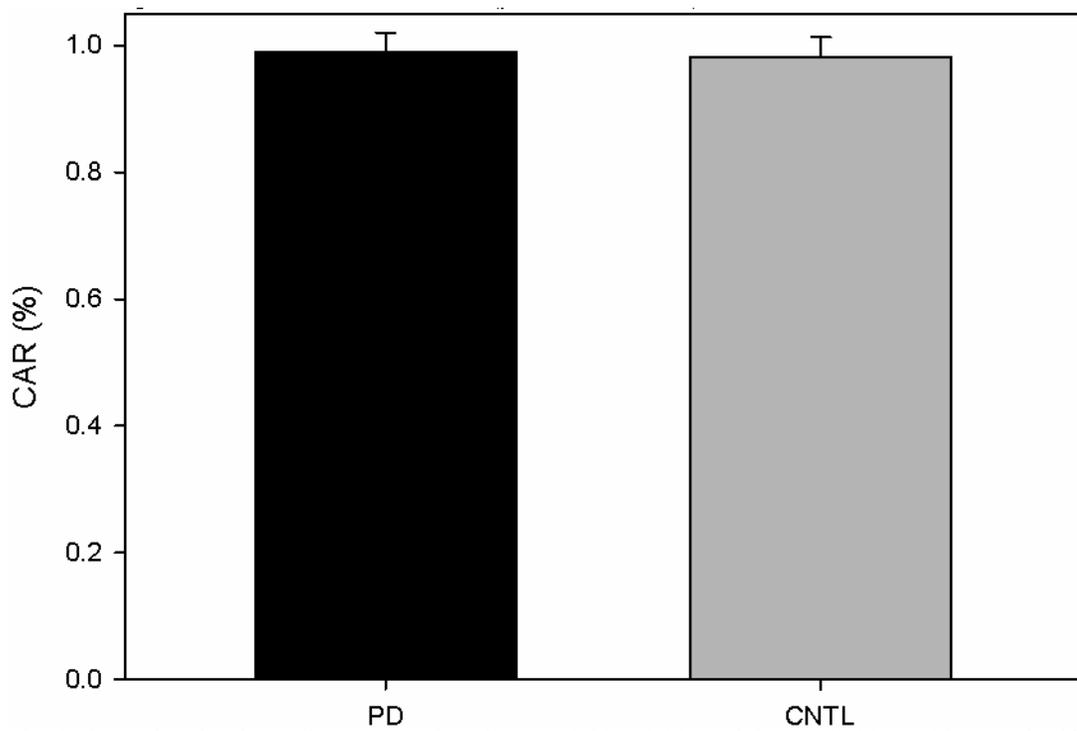


Fig. 8. Central activation ratio (Mean \pm SD) for PD (0.99 \pm 0.03) and CNTL (0.98 \pm 0.03). No significant difference was noted between groups ($P = 0.634$, $d = 0.27$)

Appendix A – Extended Literature Review

Resistance training places significant amounts of stress on the muscles involved in the training program. As a result, many physiological adaptations occur within the body in response to the new demands placed on the muscles. The initial changes in strength are due to neurological adaptations that occur both at the muscle and peripheral nervous system as well as in the brain and spinal cord (central nervous system). The most effective evaluation method of the activity within the muscle is through superimposed electrical stimulation. When the muscle is relaxed, an electrically evoked, involuntary contraction can be used to estimate the capacity of the muscle's contractility. If the subject voluntarily maximally contracts the muscle and an electrical stimulus is added to that, central activation deficiencies can be measured. If no additional recruitment is noted, the subject is able to maximally recruit that musculature.

Although an abundance of studies have evaluated the methods of evoked contractions, only a small number of those have investigated neurological changes that occur as a result of resistance training. Consistent baseline measures have become available through testing healthy subjects, and new research can now be conducted to examine specific aspects of the neurological maladaptations taking place due to disease. With sufficient review, this may become an innovative tool for evaluating special populations such as those with neuromuscular disorders.

ELECTRIC STIMULATION AS TECHNIQUE FOR MEASUREMENT

Interpolated Twitch

When determining levels of activation within the muscles, one of the most common techniques is superimposing electrical stimulation (ES) on the target muscle or the nerve that innervates the targeted muscle. The goal of the interpolated twitch technique (ITT) is to stimulate the nerve innervating the targeted muscle to determine the percentage of the muscle that can be recruited involuntarily. ITT identifies the difference between activation of the muscle with superimposed twitch at rest and activation of the muscle during maximal voluntary contraction (MVC) with the same superimposed twitch^{1,2}. Motor unit (MU) activation has been evaluated in many studies using two methods which include ITT torque and the central activation ratio (CAR). ITT torque is reported as the amplitude in the force from the supramaximal twitch, whereas CAR is the ratio of ITT torque to the maximal voluntary torque level that immediately

preceded the delivery of the supramaximal stimulus³. When compared to the CAR method, ITT torque resulted in higher sensitivity to joint-angle changes and decreased sensitivity to changes in number of stimuli².

Effect on different muscles

Each muscle within the human body has its own specific make-up of MU and filaments in order to most efficiently carry out specialized movements. Also, despite systematic activation of MUs according to Henneman's size principle, the areas of the muscle are recruited at random due to the distribution of the MU fibers in the cross-section of the muscle. Thus, several muscles and muscle groups have produced different responses to ITT. The most commonly studied have been the adductor pollicis, biceps brachii, triceps surae (gastrocnemius and soleus), and quadriceps femoris, in addition to the tibialis anterior. According to some studies^{4,5} not all of these muscles are able to be fully activated voluntarily, while others have consistently reported that the quadriceps femoris are typically capable of achieving maximal activation^{1,6}. The differences in these findings are dependent on several variables including stimulation technique, location of stimulation, and intensity of stimulation. Specifically, converse outcomes have been reported when describing results using the percutaneous superimposed electrical stimulation technique (stimulating the muscle belly) versus the interpolated twitch technique (stimulating the muscle nerve). Also, the discrepancies in the maximal performance of the muscles could be due to differing distributions of fiber types within each individual muscle⁵.

Variables measured

When assessing data from the ITT, several variables are available to measure and report. Among these are resting twitch torque, which can be measured using an isokinetic/isometric dynamometer or a force transducer³. Maximal voluntary torque is reported using the same protocol as previously described, but is measured during MVC versus at rest with an involuntary contraction. Either measure of maximal evoked torque (resting or voluntary) involves percutaneous stimulation of the muscle which is particularly uncomfortable for the instant the stimulus is applied. Maximal rate of torque development is the change in force over the change in time. CAR is the ratio of MVC to total torque. Also, maximal firing rate was reported in several studies, referring to assessment of maximal motor unit action potentials which were measured using a needle electrode placed within the muscle belly³. The torque time integral is typically

measured at 40ms (TTI40). The TTI40 is the area under the curve on the torque-time graph from 0-40 seconds. The results of this variable are noteworthy. Lastly, force has often been reported as absolute and relative rate of force development and maximal voluntary force (MVF).

Variables concerning special populations

Presently, all known studies using the ITT have used healthy subjects for their research. Although there have been studies that have evaluated fatigued muscles and musculoskeletal injuries, none to date have reported the use of ITT on special populations. Bampouras et al.² and Kendall et al.⁷ suggested that when neural activation is accurately assessed during maximal efforts, new studies could evaluate the extent of neurological damage causing inactivation of skeletal muscles due to neuromuscular diseases^{2,7}.

Variance between men and women

Although many studies have included both men and women in their investigations involving interpolated twitch and related stimulation techniques, there are few reports on gender differences. A study by Kramer⁸ included findings of trends which suggested differences in the results of men and women. His explanations for variation included different proportions of large muscle fibers and distinction in sensitivity via cutaneous impedance⁸. Additionally, Maffiuletti et al.⁹ reported that women had a lower sensory threshold than men and required lower amplitude of stimuli to achieve supramotor threshold. The data collected in this study suggested that women have a higher sensory and supramotor excitability to cutaneous electrical stimulation⁹.

Muscles stimulated

As protocols and technology for electrical stimulation have evolved over the last two decades, four muscles have been studied extensively, including the adductor pollicis, biceps brachii, triceps surae, and quadriceps femoris. Because the adductor pollicis is a small muscle with limited surface area to stimulate, investigators have primarily used the ulnar nerve as opposed to the muscle belly. Cannon and Cafarelli¹⁰, Herbert and Gandevia¹¹, and Bigland-Ritchie et al.¹² followed similar methods by restraining the arm with the palm facing medially and placed the electrode directly over the ulnar nerve on the distal anterior side of the forearm.

The biceps brachii is near optimal length for force production when the elbow is flexed at 90°. As a result, most investigators^{1,4,13} use an apparatus to fix the arm in this position. The electrodes are then

placed over the motor point of the biceps brachii midway between the bicipital groove and the elbow crease and the distal biceps tendon^{1,13}. Behm et al.⁴ used slightly different placement of the distal electrode, securing it to the proximal, anterior portion of the forearm flexors.

The triceps surae have been evaluated using two, slightly different placements of the electrodes, depending on which particular muscles the investigators were trying to stimulate. When exciting the triceps surae as a group, the tibial nerve is typically the target for stimulation. The electrodes are therefore placed in the popliteal fossa and at the distal triceps surae where it intersects the tendon^{4,6,14}. Aagaard et al.¹⁵ and Bigland-Ritchie et al.¹² focused specifically on activation of the soleus, and placed one of the electrodes just distal to the gastrocnemius. The other electrode was placed either ~13cm proximal to the calcaneus¹⁵ or over the Achilles' tendon at the malleolus¹².

The quadriceps femoris have been extensively investigated using electrical stimulation. Since this muscle group is involved in activities such as rising from a chair and locomotion, activation is of prime importance. Many studies have used the percutaneous superimposed electrical stimulation technique (PES) to activate the quadriceps by stimulating the muscle bellies of the anterior thigh. Electrode placement for this technique has been reported without specific detail, or at similar, but slightly varying positions of the proximal and distal anterior thigh^{2-4,6,7,9,16-20}. Dudley et al¹⁷ and Kendall et al⁷ placed 4.1 x 8.8-cm and 8 x 10-cm electrodes (respectively) distally over the vastus medialis and the proximally over the vastus lateralis. Additionally, studies have been investigated using the ITT to stimulate the quadriceps. In this case, the femoral nerve was stimulated with the cathode over the femoral triangle above the femoral nerve and the anode placed transversely over the gluteal fold^{21,22}.

Interpolated Twitch Technique v. Percutaneous Superimposed Electrical Stimulation Technique

Over many years of critical analysis of superimposed electrical stimulation methods, two techniques have become generally accepted for producing reliable results. While both techniques are able to activate the muscle, variation occurs in the location of stimulation. The ITT activates the muscle by stimulating the motor units with a twitch applied to the muscle nerve, whereas with the PES, the muscle is stimulated by electrodes placed directly on the muscle belly. Paillard et al⁵ noted the greatest drawback of the superimposed technique is the high level of pain that is inflicted with the electrical stimulation; if the stimulation of the muscle is too great, this could result in activation of the antagonist muscles. Paillard

concluded through analysis of the available literature that ITT was used most often for evaluation purposes while the PES was typically applied in training programs ⁵.

Muscle action

There seems to be little or no influence of each muscles said actions (flexion or extension) affecting the results of activation when measured using interpolated twitch. The biceps brachii are flexors of the arm, the quadriceps femoris are extensors of the knee, and the adductor pollicis muscle in the hand adducts the thumb; all three muscles (muscle groups) have been described as capable of full activation^{1,12}. In contrast, Behm et al.⁶ suggested that when comparing the dorsiflexors of the foot with the plantar flexors, the dorsiflexors had a greater capacity to achieve full activation. It can be inferred that while there are a number of muscles that reportedly cannot voluntarily reach full activation, there is no apparent correlation between the action of the muscle and its ability to do so.

ITT parameters: intensity, frequency, timing, and number of stimulation

The variables of percutaneous electrical stimulation delivered during ITT have been greatly varied between studies. The intensity of the stimuli is measured in volts (v), and milliamps (mA). Reports of these measures have ranged from 100-400v at 10mA-1A. The frequencies of stimulation vary between 10-100Hz. Generally, 200-300 μ s pulses are administered 10-2000 μ s apart. The number of stimuli has ranged from single tetanus to octets.

PHYSIOLOGY

Different muscles

The proportion of fiber types within each muscle and the elastic characteristics of its tendons seem to have a great impact on the muscle's ability to reach full activation with voluntary contractions ⁵. According to Henneman's size principle, MU will be recruited from smallest to largest in relationship to the intensity of stimulation applied. Fast twitch fibers are able to produce more force at a faster rate than slow oxidative fibers. As a result, if the muscle is maximally stimulated, whether voluntarily or involuntarily, muscles that have a greater percentage of fast twitch fibers (more fast twitch MU), have an increased opportunity for maximal activation. Behm et al.⁴ concluded that dorsiflexors of the foot have a greater capacity for complete activation than the plantar flexors due to the faster twitch of the MU in the muscles.

Support for ability to increase MVC

The amplitude of MVC depends on several factors that together affect the performance of the muscle. MVCs are directly related to α -motoneuron excitability, neural drive, MU recruitment, and motoneuron firing frequencies, among other things. Without optimal levels of all these elements, the muscle can still establish a contraction, however, when these variables increase, it directly results in an increase in MVC. While hypertrophy (increase in cross-sectional area of the muscle) typically has a positive relationship with strength, hypertrophy doesn't correlate with increases in MVC, as these increases typically occur as a result of central and peripheral neural adaptations¹⁵.

Different muscle actions

Several muscles have been studied with various types of electrical stimulation attempting to find the most accurate and reliable way to measure the contractility of the muscles. One of the variables in these investigations is the action being completed by the muscle while measurements are collected. According to Paillard et al⁵, activation levels of each muscle are strongly influenced by the muscle action performed during testing. Overall, studies with healthy subjects who performed isometric contractions generally reported similar peak torque scores during voluntary and evoked contractions. PES trials requiring concentric muscle contractions during evaluation produced comparable or lesser peak torque values than voluntary contractions. In comparison, few studies have examined torque with eccentric muscle actions. However, some studies have suggested that voluntary actions will either be limited or improved due to neural protection of the muscles through mechanisms such as the golgi tendon organs (GTO), muscle spindles, and coactivation. Nonetheless, superimposed electrical stimulation creates physiological effects which are directly related to the mode of muscle action⁵.

Healthy subjects

The results of many prior studies using superimposed electrical stimulation have been collected from healthy subjects^{1,2,7,9,12-16,18-25}. These findings, while some are still inconclusive, are estimates of the musculoskeletal system's maximal physiological capacity. Because the subjects were reportedly healthy during participation, inferences can be made about trends and could provide critical baseline measures for future investigations with special populations.

Special populations

To date, few studies have explored PES or ITT methods to evaluate special populations. Specifically, physiological changes evolve with the onset and progression of neurological disorders which could be assessed and monitored using healthy subjects' measures to establish a baseline. Because of reliability deficiencies in methods used in the past, electrical stimulation has not yet been used for this purpose^{2,7}. There are several movement disorders that degenerate or alter central activation of motor control. Parkinson's Disease, Progressive Supranuclear Palsy, and Huntington's Disease, just to name a few, could all use the superimposed technique to monitor progression of the disease or progress in counteracting the disease as well as to measure degeneration of muscle activation capabilities.

ADAPTATIONS TO RESISTANCE TRAINING

Increased maximal voluntary activation

As it has been well established in the literature, resistance training triggers an increase in strength of the involved muscles. In fact, the initial onset of the increase has been determined to be the result of neural adaptations, not physiological adaptations (hypertrophy) of the muscle itself. Some studies have assessed muscle activation in terms of this adaptive response and have found that resistance training increases levels of activation as well as maximal motor unit firing rate, although there was a weak correlation between the two variables³.

Aagaard et al.¹⁵ investigated amplitudes of the V-wave in pre- and post-14 wk resistance training regimens. When supramaximal nerve stimulation is applied during MVC, the efferent motor impulses generated because of activation of motoneurons via central descending pathways will collide with the antidromic potentials, thus allowing a part of the evoked reflex response to pass to the muscle, called the V-wave. It's been termed the V-wave to indicate its presence during voluntary efforts, but not at rest¹⁵.

The subjects were put through a progressive heavy-resistance strength training program which resulted in elevated V-wave amplitudes, indicating neurological adaptations at spinal and supraspinal levels. The study identifies the possibility that these neural changes could implicate transformations in α -motoneuron excitability and descending motor drive. The increased amplitude of the V-wave in response to resistance training is indicative of amplified neural drive in descending corticospinal pathways which is paralleled by an increase in motor neuron excitability. The study reports as much as 49% increases in V-

wave amplitude in response to 9-21 wk of heavy-resistance strength training. The investigators suggest that this increase is the consequence of increases in motoneuron firing frequency and/or motoneuron recruitment. The conclusion that heavy-resistance strength training initiates a considerable increase in efferent motor output during MVC suggests that further studies should be done to investigate the this positive outcome¹⁵.

Dynamic versus isometric testing

Typically, to measure activation within a muscle through isometric contraction the evoked response is calculated by finding the difference between the peak force (PF) following MVC plus superimposed twitch and the PF of MVC. This approach is fairly straightforward and reliable when testing multiple sessions and has been frequently used. When testing with dynamic actions such as concentric contractions, force trace preceding stimulation is inferred to suggest an approximation of what the voluntary force would have been when evoked force reaches its peak²⁶. These numbers are somewhat arbitrary and this method has produced a negligible effect on estimations of voluntary activation when applied to isometric contractions¹. Although isometric testing is less specific to dynamic training, the method of estimating voluntary activation of the muscle isometrically is far more accurate than testing with dynamic exercises.

Increased maximal rate of force development (MRFD)

When rationalizing an increase in MRFD, several factors seem to play a role in decreasing the amount of time required to reach maximal force. Aagaard et al.¹⁵ reported that following 14 wk of resistance training, the results suggested increases in efferent motor output, enhanced neural drive, and increased motoneuron excitability which produce increases in MVC. When more signals are sent with greater intensity to motoneurons which are increasingly accepting of the signals to stimulate the muscle, it seems logical that the muscle would respond by producing force at a faster rate. Although there will be an expected plateau at some point as the MRFD increases with resistance training, no longitudinal studies have been conducted to measure at what point this occurs. Further studies could investigate what specifically increases each factor to reach optimal MRFD for individuals.

Using PES in special populations: A case example of Parkinson's Disease

Parkinson's Disease (PD) is a central nervous system (CNS) disorder that results in reduced strength²⁷ among other disabling symptoms. Miscommunication within the nervous system of persons with PD first occurs deep within the brain, where the production of chemicals, called neurotransmitters, is altered by the disease. From there motor-control messages are encrypted with problems along the way, which result in either the message never reaching the muscle or the message being misrepresented by the time it gets there. Nallegowda et al²⁸ has demonstrated that strength deficits are at least partially central in nature, but techniques such as ITT and PES have not yet been used on this population.

As a result of the impairment of neurological efficiency when a message relaying motor-control is sent from the brain to initiate a voluntary movement, an individual with PD would be expected to have decreased MVC. However, if the muscle were directly stimulated using ITT or PES, the involuntary activation should still be maximal because the PD has not been found to damage the peripheral nervous system. Thus, persons with PD should have a reduced CAR, but this has yet to be determined. Also, PES may be able to give us more information about the adaptations in the CNS with strength training in persons with CNS disorders.

CONCLUSIONS

Due to the neuromuscular stress when an individual engages in resistance training, the body reacts quickly by adapting the neurological pathways for communication between the muscle and the central nervous system (spinal cord and brain), causing changes to occur both at the periphery and centrally. The neurological adaptations that take place can be identified and evaluated by methods including ITT and PES. Following decades of critical analysis of the techniques used to interpret muscle contractility and its relationship to the nervous system, general conclusions can be made regarding the ability to stimulate different muscles and the most reliable methods can be elucidated from the many methodologies that have already been explored. Studies have been conducted to measure these effects on healthy populations, but there remain endless possibilities for further investigation involving neurological impairment.

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