

SKELETAL MUSCLE ADAPTATIONS TO RESISTANCE TRAINING WITH ISCHEMIA

by

CHRISTOPHER PAUL ELDER

(Under the direction of Kevin K. McCully)

ABSTRACT

Resistance training has been shown to produce increases in muscle size, strength, and whole body function in a wide array of patient populations. There is a need to develop new training approaches that either use lower training intensities or which maximize the adaptation to resistance training. Moderate resistance training with ischemia has been shown to enhance strength and size development relative to moderate resistance exercise without occlusion, and similar to an equal volume of heavy training without ischemia. The limitation of these studies has been an incomplete understanding of the mechanisms behind ischemic resistance training. The present experiment was designed to test the hypothesis that ischemia added to heavy resistance training results in enhanced strength and muscle size development relative to an equal volume of heavy resistance training without ischemia. Thirty (14 men, 16 women) untrained but recreationally active subjects volunteered to participate. Elbow flexor muscle volume was assessed via magnetic resonance imaging (MRI) and strength was assessed via one-repetition maximum before and after 12 weeks of resistance training 3 days per week. Increased muscle volume was observed only after heavy resistance training. There was no effect of ischemia in either moderate or heavy resistance conditions. Further studies were designed to determine if adaptations to training were related to muscle electrical activity measured with surface electromyography (EMG) during exercise, and to verify ischemic conditions during exercise via near infrared spectroscopy (NIRS). In 22 subjects, there was a significant effect of resistance, and a significant effect of ischemia (speed) on EMG. EMG during exercise was related to muscle hypertrophy following training and ischemia resulted in a decrease and not an increase in EMG activity. Oxygen saturation measured with NIRS was minimal during ischemic conditions and significantly higher during control conditions. It is concluded that ischemic resistance training did not have an independent effect on muscle size and strength, contrary to previous ischemic training studies. Slow continuous exercise appeared to be a valid method for producing ischemia, compared to rapid, discontinuous exercise. The absence of ischemic effects is important to understand how ischemia may enhance muscle hypertrophy in response to resistance training.

INDEX WORDS: Exercise, Skeletal muscle, Resistance training, KAATSU, Ischemia, Magnetic resonance imaging, EMG, Oxygen saturation, NIRS

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by

Christopher Paul Elder

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by

CHRISTOPHER PAUL ELDER

Major Professor:

Kevin K. McCully

Committee:

Ted Baumgartner
Kirk J. Cureton

Electronic Version Approved

Maureen Grasso
Dean of the Graduate School
The University of Georgia
December 2007

DEDICATION

This work is dedicated to my dad, Hal Elder, who always encouraged and supported me in whatever I put my mind to. You have been there in good times and bad to show me how incredibly strong the bond between father and son can be. You gave a lot of blood, sweat, and tears to this. Completing my degree is one of the ways I can say thank you. This work is also dedicated to my mother, Susan Elder, the heroine who works tirelessly behind the scenes. I will never know all the ways you sacrificed so that I could make it to this day, but I hope you will always know how much I love you.

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CHAPTER 1

INTRODUCTION

Performance of heavy resistance training is associated with increasing muscle size, strength, power, speed, local muscular endurance, motor performance, balance, and coordination (27). The health benefits of resistance training are becoming more widely studied and recognized. Resistance training is recommended by the American College of Sports Medicine (2) and the American Heart Association (50) for a wide range of populations including adolescents, healthy adults, the elderly, and clinical populations.

Exercise researchers are interested in maximizing the adaptations to resistance training while minimizing the amount and intensity of exercise that must be performed. This is particularly true when designing resistance training programs for frail or impaired populations. Traditional resistance training to maximize muscle size and strength is performed with heavy resistances $\geq 75\%$ of one repetition maximum. Ischemic resistance training is an alternative to traditional resistance training performed with light to moderate resistance (20 to 50% of one-repetition maximum) resistance coupled with vascular occlusion induced by inflation of pressure cuff proximal to the exercising muscle group. Significant increases in muscle size and strength have been observed with KAATSU (Japanese, 'with restriction') training in untrained middle-aged women (44), as well as in male athletes (43). Another study (46) reproduced the KAATSU effects on muscle size and strength without cuff occlusion by using slow tonic force repetitions to decrease muscle oxygenation. These studies have included groups training with 80% of one repetition maximum resistance without cuff occlusion (44) or without slow tonic force (46). In

each case, the adaptations to moderate resistance KAATSU training are comparable to adaptations in heavy resistance groups. The limitations to these studies are that KAATSU training has not been performed with heavy resistance training in order to determine if the effect of KAATSU training is additive with the effects of heavy resistance. In addition, the role of muscle activation and muscle ischemia has not been carefully addressed. Further research is necessary to determine the potential interaction between muscle ischemia and resistance on the adaptations resulting from resistance training.

Specific aims

1. To determine changes in muscle volume and strength in response to heavy and moderate intensity resistance training performed under ischemic and non-ischemic conditions.
2. To determine if slow, continuous muscle contractions can be classified as ischemic, and if fast, discontinuous muscle contractions can be classified as non-ischemic or normal using near infrared spectroscopy (NIRS).
3. To determine if changes in muscle activation measured with EMG could explain differences in adaptation to resistance training performed under ischemic and non-ischemic conditions

Hypotheses

1. Resistance training under ischemic conditions results in greater changes in muscle volume and one-repetition maximum strength of the elbow flexors than resistance training with matching resistance under non-ischemic conditions.
2. Slow continuous contractions result in oxygen desaturation during both heavy and moderate resistance exercise while rapid, discontinuous contractions will not result significant oxygen desaturation.
3. Muscle EMG magnitude will be greater under ischemic than non-ischemic exercise conditions.

Significance

This study may lead to further application of moderate intensity ischemic training in clinical populations such as in individuals with spinal cord injury and multiple sclerosis. It may also help to narrow the focus of future studies to elucidate the precise systemic and molecular mechanisms of the adaptations to resistance training.

Limitations

1. Participants are relatively young and healthy, and their results may not reflect what could be expected in older, more frail, or diseased populations.
2. The protocol used is a form of ischemic resistance training, but it may not truly reflect the ischemic resistance training protocols used in previous studies.
3. Training is confined to the elbow flexors, limiting the ability to generalize to larger, muscles of the thighs and trunk.

Assumptions

1. The genetic predisposition for muscle hypertrophy is normally distributed among the population under study.
2. Participants will give honest feedback concerning maximal efforts during repetition maximum tests

CHAPTER 2

REVIEW OF LITERATURE

Increasing physical activity is associated with adaptations to physiological systems that have functional and health consequences. Adaptations appear to be specific to the characteristics of the exercise. An important question answered by exercise researchers concerns the characteristics of the exercise needed to maximize important adaptations. Muscle size and capacity to produce force are two such important adaptations.

Muscle cross sectional area has been shown to be proportional to maximal isometric force in animals (see (13) and humans (24). The loss of muscle mass and strength with age or injury is associated with functional and lifestyle limitations. In addition, the mass of muscle an individual possesses may be important for regulating blood glucose levels (18, 29). Muscle mass is also important for success in sports such as bodybuilding, powerlifting, and weightlifting.

The purpose of this chapter is to review research concerning the characteristics of exercise necessary to maximize muscle hypertrophy and the capacity to produce force. The review will include discussions of potential mechanisms linking exercise characteristics to molecular and cellular signals resulting in muscle cell growth. The review will include observations of adaptations to training with vascular occlusion and evaluation of the consistency of these results with current models of training for hypertrophy. For the purposes of comparison between studies, effect sizes (ES) expressing the effects of training have been calculated using the following formula employed by Rhea et al. (39).

$$ES = \frac{\bar{x}_{post} - \bar{x}_{pre}}{SD_{pre}}$$

where

\bar{x}_{post} = mean of post training measurement

\bar{x}_{pre} = mean of pre training measurement

SD_{pre} = standard deviation of measurement pre training

Resistance exercise

The primary function of skeletal muscle is force (or torque) production. This torque results in motion of skeletal bones around joints. Resistance exercise involves using skeletal muscle actions to create torque sufficient to change the position of a mass (or resistance) supported by the bones. The degree of change in position of the resistance (range of motion) is limited by the anatomical features of the bones and joints involved. Torque produced by muscle actions is responsible for controlling the acceleration of the resistance in any direction throughout the range of motion. The resistance may vary throughout the range of motion. In isotonic resistance exercise, the mass of the resistance remains constant through the range of motion, but the resistance on the muscle changes with joint position as muscle lever arms change. During isotonic resistance exercise, a resistance of constant mass is moved through the range of motion and back to its original position (one repetition) anywhere from one to 100 times or more in a single set. A set is any collection of repetitions performed while supporting the resistance with the bones. During a set, repetitions may be performed with the resistance in continuous motion or interspersed with periods where the resistance remains at rest in its original position. Sets are separated by defined continuous rest periods during which the resistance is not

supported by any part of the body. These inter-set rest periods can vary in length from less than one second to 5 minutes or more. Resistance exercise may thus be defined as any movements or attempted movements of a resistance through a range of motion and back to its original position with a specific or nonspecific velocity using skeletal muscle actions for a limited number of repetitions in collections of any number of sets separated by inter-set rest periods.

There are many sources of variation in the performance of resistance exercise that could influence the acute physiological responses and the subsequent adaptations when resistance exercise is repeated over time.

Skeletal muscle hypertrophy. Roux (41) is credited as the first to scientifically generalize that skeletal muscle adapts to increased use with hypertrophy and decreased use with atrophy. The question remained concerning what characteristics of activity led to hypertrophy. DeLorme (14) prescribed programs of resistance exercise to soldiers experiencing the consequences of knee injury. The resistance exercise was performed for 10 sets of 10 knee extensions using a progressively increasing weight until 10 repetitions could just be completed in the final set. DeLorme observed that compared to the many low force contractions used to build endurance, a relatively small number of contractions performed with heavy resistance was more effective for restoring muscle size to its pre-injury level. Many of the characteristics of DeLorme's exercise programs still form the basis of current programs designed to build muscle mass and strength.

DeLorme (15) originated the concept of a repetition maximum (RM) to measure the maximum amount of resistance that can be lifted for a specific number of repetitions. The repetition maximum is an effective and consistent tool for quantifying resistance demands that

can be employed for different exercises. Current resistance exercise prescriptions are based on the concept of a repetition maximum continuum (20) in which different ranges of reps correspond to maximizing different adaptations. It has been suggested that muscular power is best developed with resistance equal to 1-3 RM, maximal strength 3-8 RM, muscle hypertrophy 8-15 RM, and muscle endurance > 20 RM. These ranges also correspond to specific resistance that can also be expressed relative to the maximal resistance that can be lifted for only one repetition of a given exercise (1RM).

The foregoing recommendations are based primarily on the work of Anderson and Kearney (3) who compared different strength and endurance adaptations in groups training with 6-8 RM, 30-40 RM, and 100-150 RM and another study in women (42) comparing 6-8 RM, 15-20 RM, and 30-40 RM. Campos et al. (12) designed a resistance training study to examine the muscular adaptations corresponding to different subdivisions of the RM continuum. Measurements were made of the muscle fiber type distribution and fiber cross sectional area from muscle biopsy samples before and after eight weeks of training in three groups training with 3-5, 9-11, or 20-28 RM. All groups showed increases in the average area of all three fiber types (Type 1, 2a, and 2x), but Type 2x > 2a > 1. The largest overall increases in fiber size were observed in the group training with 3-5 RM (4 sets of 4 and 90% of 1RM (ES 1.32, 1.24, and 0.68 for 2x, 2a, 1 respectively). However, the 9-11 RM group (3 sets of 10 at 75% of 1RM) showed comparable changes in fiber area (ES 1.42, 1.08, and 0.61 for 2x, 2a, 1 respectively). Kraemer et al. (26) examined the effect of different training load and repetitions on muscle size of the elbow flexors assessed via magnetic resonance imaging. Changes in muscle size were greater in participants training with 80-93% of one repetition maximum than those training with 67-80% of 1RM (ES 1.37, 0.90 vs. 0.77, 0.73). Thus, empirical research results suggest that

training resistance in the range of 3 to 11 RM (75-90 % of 1RM) result in the greatest increases in muscle size.

Mechanisms of hypertrophy. Increases in muscle size as a result of resistance training appear to have three necessary components (10). The first component is initiation of the anabolic processes leading to the accretion of protein in skeletal muscle. The second component is the proliferation of satellite cells to provide nuclei to enlarging fibers, and the third component is a suppression of protein degradation. Many nervous, paracrine and endocrine signals appear to control these three components. These signals could be initiated by mechanoreceptors sensitive to resistance and stretch (23), metabolic sensors sensitive to metabolite concentrations (16), or oxygen sensors sensitive to intracellular or extracellular partial pressure of oxygen (47). There are many factors in skeletal muscle signaling that are just recently becoming better understood and more research, particularly in humans is necessary before definitive conclusions can be drawn concerning signaling and mechanisms of hypertrophy.

Skeletal muscle strength. Strength of skeletal muscle may be defined as its capacity to produce force. It became known very early that the increase in capacity was specific to the type of activity. The primary concern in most traditional isotonic resistance training is dynamic force production through both concentric and eccentric ranges of motion with no time limits. As with muscle hypertrophy, resistance appears to have a primary role in strength development. In addition to the resistance range for hypertrophy, the repetition maximum continuum also describes the resistance range for strength development. Muscular power (rate of force development) is best developed with resistance equal to 1-3 RM, maximal strength 3-8 RM,

muscle hypertrophy 8-15 RM, and muscle endurance > 20 RM. The works of Berger and colleagues (4-8) in the early 1960s formed the basis of classic recommendations concerning training to develop maximal dynamic strength. Resistance training of untrained physical education students with different loads, sets, and repetitions revealed that three sets of 6 repetitions led to the greatest increases in 1RM (30.6%, ES 1.76). The repetition continuum investigation by Campos et al. (12) also supports the results of Berger. However, a meta-analysis by Rhea et al. (39) found the greatest increases in strength of untrained participants at 60% of 1 RM or >15 RM resistances (ES 2.8). Training at 80% or 8 RM still had a large effect (ES 2.0). Rhea et al. also found 4 sets superior to 3 sets for strength development (ES 2.28 vs. 1.94). Because of these inconsistencies, more research is necessary to determine the optimal values for exercise variables if maximal strength development is the goal.

Mechanisms of increased skeletal muscle strength. There are two general adaptations that lead to increases in strength. The first is changes in excitation patterns of trained muscle; the second is an increase in muscle size. There is much evidence that the development of strength is dependent on changes in the nervous system to a greater degree than changes in muscle size. The greatest increases in strength occur early in a training program before any measurable increase in muscle size (1). In addition, unilateral training induces increases in strength of the untrained contralateral muscle group without measurable increases in muscle size. Meta-analysis of contralateral strength effects suggests that the untrained side increases in strength by one third of the increase in the trained side (34).

Resistance training with ischemia

Resistance training with ischemia, labeled KAATSU or ‘with restriction’, is an alternative to traditional resistance training (43, 44). Ischemic resistance training has been performed with light to moderate resistance (20 to 50% of one-repetition maximum) coupled with vascular occlusion and ischemia induced by inflation of pressure cuff proximal to the exercising muscle group. Early studies by Maisson (30, 31) established that muscle ischemia could also be induced by contraction force alone with a lower threshold of 20% of maximal voluntary contraction. A later study by Tanimoto et al. (46) utilized slow tonic force contractions to induce low muscle oxygen saturation and mimic the effects of pressure cuffs. Resistance training with ischemia results in unique adaptations in skeletal muscle size and strength which will be reviewed next.

Ischemia and skeletal muscle hypertrophy. Dons et al. (17) compared skeletal muscle adaptations between groups training for seven weeks with either 20 repetitions at 50% or 12 repetitions at 80% of one repetition maximum. Training with moderate resistance resulted in greater increases in muscle cross sectional area (ES 1.46) than heavy resistance training (ES 0.45) assessed via ultrasound scanning. These results suggest that the heaviest resistance may not necessary to maximize muscle hypertrophy. More recently, Takarada and colleagues (43, 44) have also studied adaptations resulting from training with moderate resistance. In a study involving untrained middle aged females (44), moderate resistance alone showed a small percent increase (6.9%, ES 1.09) in average biceps cross sectional area measured with MRI. However, moderate resistance coupled with vascular occlusion resulted in a large increase in average area (18.4%, ES 0.94) and was comparable to the increase observed after heavy resistance training

performed without controlled vascular occlusion (17.4%, ES 0.60). Takarada et al. (43) also found a large effect on average muscle area (12.3%, ES 2.29) of resistance training at 50% of one repetition maximum in elite rugby athletes. A separate group trained with moderate resistance and no occlusion, but comparisons could not be made because muscle area was not reported. It appears from these limited data that vascular occlusion does have an effect on muscle size that complements the effect of moderate resistance.

Ischemia and mechanisms of skeletal muscle hypertrophy. The mechanism of the adaptations to low intensity occlusive training remains unknown. Blood lactate concentrations and reactive hyperemia were greater after low intensity occlusive exercise than after high intensity at the same cuff pressure (44); suggesting that the metabolic demand was greater after low intensity exercise. It is possible that the metabolite accumulation resulting from occlusive training stimulates an as yet undiscovered metabolic sensor (16). Normal heavy resistance training with shorter inter-set rest periods and thus a greater anaerobic demand may stimulate the same receptor. This type of training results in greater GH secretion than training with longer rest periods and the same mechanical resistance (25). However, the effects of GH on muscle mass are not clear (38). Vascular occlusion alone does not result in significant muscle hypertrophy, suggesting that either some level of metabolite accumulation and mechanical load are both necessary; and occlusion alone does not exceed the threshold metabolic stimulus (45).

Muscle electrical activity is increased with moderate resistance and occlusion to a greater extent than with occlusion alone, and the increased activity is comparable to heavy resistance training without ischemia. The EMG signal has been suggested to represent the sum of motor unit activity; and this activity is increased toward maximal in the presence of fatigue (49).

Therefore, it is possible that resistance training with ischemia leads to muscle hypertrophy through the fatiguing effects of ischemia and subsequent recruitment of more type 2 motor units. The concept of an activation threshold for hypertrophy has been reviewed recently by Toigo et al. (47) and is consistent with other ischemic training results that are similar to resistance training with heavy resistance. Further research examining the effects of heavy resistance and ischemia could help to elucidate the interaction among resistance, ischemia, EMG and muscle hypertrophy.

Ischemia and Skeletal muscle strength. Takarada and colleagues showed similar increases in overall isokinetic strength in participants training for 16 weeks with moderate resistance and occlusion (18.4%, ES 3.70) in one arm and heavy resistance with no occlusion (22.6%, ES 3.41) in the contralateral arm. These effects were much larger compared to a group training with moderate resistance and no occlusion (1.0%, ES 0.25). Isokinetic strength was increased at all velocities of shortening and lengthening. Smaller increases in strength are normally observed in highly trained athletes than the untrained. However, Takarada (43) found similar effects of moderate resistance training in rugby athletes. The occluded group showed a greater increase in isokinetic strength (14.3%, ES 2.92) compared to moderate resistance only (3.2%, ES 0.57), and increases in strength were similar across all lengthening and shortening velocities. In contrast to the previous results, Burgomaster et al. (11) and Moore et al. (33) showed no effect of occlusion on strength with similar increases in isotonic strength (22, 23%, ES 1.60, 1.64) between arms trained for 8 weeks at 50% of 1RM with or without ischemia respectively. However, in a companion study, isometric force increased 10 % (ES 1.18) in the ischemic group only. More research is necessary to determine, the effects of ischemic resistance

training on strength, including measuring the effects of heavy versus moderate resistance with ischemia.

Ischemia and mechanisms of increased skeletal muscle strength. Little is known about the mechanisms of increased strength following resistance training with ischemia. Moore et al. (33) found differences in isometric force but not dynamic torque between groups training dynamically with or without ischemia. Differences in strength as a result of ischemia were observed in an unpracticed test but not a practiced test, suggesting that increases in strength were due to muscle hypertrophy rather than neural adaptations. Similar effects of ischemic training have been observed between trained (ES 2.92) (43) and untrained (ES 3.70) (44) participants suggesting only a small effect of training status on strength gains. This is in contrast to strength training results reviewed by Rhea et al. (39) suggesting that trained participants show less increase in strength than the untrained.

Moore et al. (33) examined neuromuscular changes in ischemic and non-ischemic groups training with moderate resistance. They found decreased evoked twitch torque, decreased twitch: MVC ratio and increased post-activation potentiation in the ischemic group only. The authors were unable to make clear the implications of these changes for maximal strength development. Metabolic measures by Burgomaster (11) showed greater increases in glycogen concentrations and decreases in ATP concentrations after ischemic training than control, but the implications of these differences are not clear given that there were no effects of ischemia on changes in strength. More studies are needed to determine the precise mechanisms associated with strength gains resulting from resistance training with ischemia.

Measuring muscle size

DeLorme (14) assessed changes in muscle size using measures of thigh circumference. These measures were subject to errors due to the presence of subcutaneous fat and other non-muscle tissue included in the measurement. Thigh circumference is also not a direct measure of an increase in skeletal muscle cell size. With the advent of the muscle biopsy procedure by Bergstrom (9) it became possible to assess muscle fiber changes in humans in response to resistance training. The availability of technologies such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI) allowed non-invasive assessment of muscle size changes, but at the expense of the more direct measures of muscle fibers. MRI and CT offer the advantage of direct visualization of whole muscle and muscle group areas (19). Some resistance training studies rely on a single axial anatomical cross-sectional area (ACSA) measurement as the measure of muscle size (36, 37). Fewer investigations describe the measurement of multiple axial sections along the whole muscle length (35). Single slice area measurement minimizes investigator time required to digitize many muscle cross-sections on large numbers of subjects, radiation exposure during CT, and the expense of longer MRI scan times. Muscle volume can be determined by measuring muscle ACSA in multiple axial sections along the entire length of the muscle (21, 40, 48). As a measure of muscle size, muscle volume is preferable to ACSA because it is a closer approximation of a physiological cross-sectional area (PCSA). PCSA is the cross-sectional area of all muscle fibers oriented perpendicular to the longitudinal axis of the muscle and thus is more closely associated with maximal muscle force (21, 28). Tracy et al. also found measures of muscle volume to be more sensitive to changes in muscle size after resistance training than single slice cross-sectional areas. Therefore, it appears that muscle volume

measured by MRI is the best non-invasive method for determining muscle size changes resulting from resistance training.

In studies that have demonstrated significant increases in muscle size after ischemic resistance training, muscle size was assessed from magnetic resonance images of the elbow flexors (44) and knee extensors (43, 46). The investigators based the cross sectional area of the muscle on an average of two slices taken from the midpoint of the humerus or femur in images acquired at low magnetic field strength. Resistance training studies designed to evaluate the effectiveness of ischemic resistance training could benefit from more accurate and sensitive measures of muscle volume from MRI.

Measuring muscle electrical activity and oxygen saturation

Changes in muscle electrical activity have been suggested to mediate the adaptations to resistance training with ischemia. In studies designed to determine the effectiveness of ischemic resistance training, measuring electrical activity and the level of ischemia may be crucial to understanding both similarities and differences in the adaptations observed.

Muscle electrical activity. Muscle electrical activity may be assessed non-invasively by surface electromyography. The surface electromyogram (EMG) comprises the sum of the electrical contributions made by the active motor units detected by electrodes placed on the skin overlying the muscle. The information extracted from the surface EMG is often considered a global measure of motor unit activity, because of the inability of the traditional (2 electrode) recording configuration to detect activity at the level of single motor units. The global characteristics of the surface EMG, such as its amplitude and power spectrum, depend on the

membrane properties of the muscle fibers as well as on the timing of the motor unit action potentials. Therefore, the surface EMG reflects both peripheral and central properties of the neuromuscular system. This measure is ideal for global measurement of muscle electrical activity during ischemic and non-ischemic exercise.

Muscle oxygen saturation. Muscle oxygen saturation may be measured non-invasively using near infrared spectroscopy (NIRS). Near infrared light passes through biological tissues, and specific wavelengths are absorbed by the iron porphyrin complexes contained within oxygenated and deoxygenated hemoglobin traveling through blood vessels (22). Full spectrum light is emitted into the tissue while detectors filter all but 760 and 850 nm. These values correspond to the peak absorbance of oxy and deoxy-hemoglobin. Continuous wave devices measuring muscle oxygen saturation rely on light reflected in a shallow arc through peripheral muscle for the oxygenation signal (32). The best contrast between emitted and absorbed signals comes from muscle capillary beds as large vessels absorb too much of the signal. Thus, NIRS is ideal for measuring muscle oxygen saturation in peripheral muscle groups during resistance exercise.

CHAPTER 3

SKELETAL MUSCLE ADAPTATIONS TO HEAVY RESISTANCE TRAINING WITH ISCHEMIA

Abstract

New resistance training approaches are being developed that either use lower training intensities or maximize the response to a given intensity of resistance training. This study tested the hypothesis that ischemia added to heavy or moderate resistance training enhances strength and muscle size compared to resistance training without ischemia. Thirty males ($n = 13$) and females ($n=17$) volunteered to participate. Elbow flexor muscle volume was assessed via MRI and strength assessed via one-repetition maximum (1RM) before and after 12 weeks of resistance training 3 days per week in groups training with heavy (80% 1RM) or moderate (50% 1RM) resistance and ischemia (slow continuous) or normal (fast discontinuous) determined by repetition speed and duration. There was a significant resistance \times time interaction ($p < 0.001$) but no differences were found between slow and fast groups at each level of resistance. Training resulted in a 7.4 (5.2)%, 6.0 (4.0)%, 1.4 (3.0)%, and 0.3 (1.1)% increase in muscle volume in the heavy slow and fast, and moderate slow and fast groups respectively. There was no effect of ischemia in moderate or heavy load conditions. For strength, there was a significant resistance \times time interaction ($p = 0.010$) but no differences between ischemic and normal groups at each level of resistance. Training resulted in a 16.8 (8.9)%, 34.5 (15.4)%, 9.8 (4.0)%, 21.0 (18.4)% increase in strength in the heavy slow and fast, and moderate slow and fast groups respectively. The results of this study do not support the hypothesis that ischemic training enhances muscle hypertrophy or strength. Further studies are needed to address why this study is in contrast to previous studies.

Introduction

Resistance exercise programs have been shown to be important in optimizing and restoring function in weak and frail individuals (4). The need to optimize function in weak and frail populations has led to a number of experimental approaches designed to optimize muscle hypertrophy. One of these approaches involves has been training and uses partial ischemia to enhance muscle strength and muscle mass.

Ischemic training is resistance training performed with moderate to light resistance and vascular occlusion induced by inflation of pressure cuff proximal to the exercising muscle group. Significant increases in muscle size and strength have been observed with ischemic training in untrained middle-aged women (12), as well as in male athletes (11). Another study (13) reproduced the ischemic effects on muscle size and strength without cuff occlusion by using slow movement tonic force contractions to decrease muscle oxygenation. Each of these studies has included a heavy resistance group training either without cuff occlusion or without slow tonic force. In each case, the adaptations to moderate resistance ischemic training are comparable to adaptations in heavy resistance groups. The results of these studies suggest that heavy resistance is not necessary to increase muscle size, and introduce the idea that low muscle oxygenation may mediate increases in muscle size. However, previous studies have not tested whether ischemia combined with heavy resistance produces an additive effect.

The purpose of this study was measure muscle volume and strength after ischemic training using a balanced design of heavy and moderate resistance, coupled with ischemic and non-ischemic movements. This will be accomplished by comparing the adaptations of groups training with either heavy or moderate resistance and slow continuous contractions or fast contractions. We hypothesize that both heavy resistance and muscle ischemia will affect muscle

volume and strength such that training with heavy resistance and muscle ischemia will result in the greatest increases in muscle volume and strength.

Methods

Participants

The procedures were approved by the Institutional Review Board at the University of Georgia and all participants provided informed written consent prior to their participation. Thirty healthy men and women participated in the study. Participants were recreationally active and had some previous resistance training experience but were currently performing ≤ 1 day of resistance exercise with the biceps. Self report questionnaires were administered and the data used to exclude those with cardiovascular or metabolic disorders and also those with injuries to the upper extremities. Physical characteristics of the participants before and after training are presented in Table 1. There were no differences in age, height, and weight between groups before or after training. In an F test of training effects, a total sample size of $N = 20$ was necessary to detect a small effect of training of 0.15 SD with a power of 0.8 and an alpha level of 0.05.

General Design

Participants were randomly assigned to one of four experimental groups. Two groups trained with heavy resistance equal to 80% of one-repetition maximum and two groups trained with 50% of one repetition maximum. Within each resistance condition, one group trained with continuous 10 second duration repetitions (slow) and the other with discontinuous 2 second duration repetitions (fast) including 8 seconds of rest between repetitions. In a companion study (3), the longer duration continuous repetitions resulted in lower muscle oxygen saturation than the shorter duration intermittent repetitions. Each group trained the elbow flexors of their non-

dominant arm 3 days per week for 12 weeks. Muscle volume and maximal dynamic strength and were assessed before and after training.

Elbow flexor volume

Muscle volume was assessed from magnetic resonance images of the arm collected perpendicular to the long axis of the humerus from the distal border of the acromion process to the distal epicondyles. Images were acquired at 3.0 T using GE superconducting magnet, Signa HDx imaging system (General Electric, Milwaukee, WI), and a standard phased array torso coil. Fast spin echo images were 5 mm thick with 5 mm spacing acquired in a 512×512 matrix and 20 cm field of view with a repetition time of 3000 ms, an echo time of 87.5 ms and 4 excitations. Scan time was 7:28. Participants were supine with the torso coil placed across the chest and over both arms. Each arm was scanned independently. The post measure was recorded at least 48 hours after the final training session.

Images were analyzed in a blinded fashion by assigning a random number to each set of images corresponding to each arm. The investigator was unaware of the group or the time point for any image set. Muscle volume was calculated from manually traced regions of the biceps and brachialis muscles of the arm. Images were analyzed using WinVessel 2.033 (Ron Meyer, Michigan State). Each manually traced region was automatically segmented into pixels containing muscle, fat, bone, and connective tissue to allow expression of only the volume of skeletal muscle as described previously (8). To calculate total muscle volume, pixel numbers were converted to cross-sectional areas corresponding to each muscle, multiplied by the slice thickness and spacing, then summed from each slice acquired along the length of the humerus. A representative image is presented in Figure 1

Elbow flexor strength

Muscular strength was assessed in each arm before and after training by determining the one-repetition maximum (1RM) elbow flexion. Tests were performed for both 10s and 5s repetitions. The 1RM was assessed using a standard set of free-weight dumbbells with the participants standing with the back and hips braced against a wall. The dumbbells were also used for all training bouts. Participants were instructed that their 1RM is the maximum weight they can lift with good form for 1 repetition of elbow flexion. Good form was defined as moving the dumbbell with constant velocity, completing the concentric phase of the flexion in about 1s or 5s, and returning the dumbbell to the rest position with constant velocity in 1s or 5s. Pacing was kept by using a metronome. Weight was increased in successive trials until a weight was found that could not be lifted for 1 repetition with good form. Tests were completed within 5 trials. Each maximal attempt was separated by 2 minutes of rest to avoid fatigue.

Resistance Training

Resistance training of the elbow flexors was performed by each of the four groups three times per week for 12 weeks. The non-dominant arm was trained while the dominant arm served as a control. Resistance exercise consisted of unilateral dumbbell curls performed standing with the back and hips braced against a wall. All groups performed 3 sets with 1 minute of rest separating each set. The heavy slow group trained with 80% of the fast 1RM and performed continuous repetitions with 10 second duration, 5s concentric, and 5s eccentric. Repetitions were performed either to volitional failure, defined as the inability to continue repetitions in good form and at the correct pace or to a maximum of 12 repetitions per set. If the participant was able to complete 3 sets of 12 repetitions for two consecutive sessions, weight was increased by approximately 0.5 kg. Only 1 participant required increases in weight due to competing the

required repetitions. The moderate resistance slow continuous group trained with 50% of the fast 1RM and performed continuous repetitions with 10 second duration, 5s concentric, and 5s eccentric. Repetitions were matched to the average number of repetitions performed by the heavy resistance ischemic group. The heavy fast group trained with 80% of the fast 1RM and performed intermittent repetitions with 2s duration, 1s concentric, 1s eccentric followed by 8s of rest. Repetitions were matched to the average number of repetitions performed by the heavy resistance ischemic group. The moderate fast group trained with 50% of the fast 1RM and performed intermittent repetitions with 2s duration, 1s concentric, 1s eccentric followed by 8s of rest. Repetitions were matched to the average number of repetitions performed by the heavy slow group. 1RM strength was reassessed for each group after 6 weeks of training and training weights adjusted accordingly.

Statistics

Statistics were calculated using SPSS version 15 (SPSS Chicago, IL). Descriptive statistics were used to derive means and standard deviations for each variable. All results are expressed as mean (standard deviation). Training loads, repetitions and training compliance were evaluated with a 2 x 2 (resistance x ischemia) ANOVA. Participant characteristics were evaluated with a 2 x 2 x 2 (resistance x ischemia x time) analysis of variance (ANOVA) with time as a within subjects factor. Muscle volume, and one repetition maximum strength were evaluated with a 2 x 2 x 2 x 2 (resistance x ischemia x condition x time) ANOVA with time as a within subjects factor. The condition factor refers to the trained or untrained arms as the two conditions. Significant interactions were followed by tests of simple effects. Significance level was set at $\alpha = 0.05$. All data are presented as mean (standard deviation).

Results

Resistance training

No differences were detected in relative training resistance between continuous and intermittent groups within either resistance condition. Total reps performed, and training compliance were similar among all groups indicating that the treatment was administered equally among groups. Selected training variables are presented in Table 2. In addition, no differences were detected in age, height, or body mass either between groups or before or after training (Table 1).

Elbow flexor volume

Volume of the biceps and brachialis were combined into elbow flexor volume for analysis. Training with heavy slow contractions resulted in a 7.4 (5.2) % increase in elbow flexor muscle volume. The heavy fast contraction group showed a 6.0 (4.0) % increase in muscle volume. Training with moderate and slow contractions resulted in a 1.4 (3.0) % increase in muscle volume. The moderate fast contraction group showed a 0.3 (1.1) % increase in muscle volume. The untrained arm showed a -0.7 (3.2) and 3.0 (5.4) % changes in muscle volume in the heavy slow and fast groups respectively. There was a -2.2 (4.6) and 1.4 (6.5) % change in muscle volume in the moderate slow and fast groups respectively. The four way interaction of resistance, ischemia, condition and time was not significant ($F(1, 52) < 0.001$, $p = 0.987$). Examination of the three way interactions revealed non-significant interactions of ischemia, condition, and time ($F(1, 26) = 2.96$, $p = 0.091$) and also a non-significant interaction of ischemia, resistance and time ($F(1, 26) = 0.26$, $p = 0.612$). There was a significant interaction of resistance, condition and time ($F(1, 26) = 5.86$, $p = 0.019$). The interaction of resistance and time was not significant in

the control condition ($F(1, 26) = 0.004$, $p = 0.950$), but there was a significant resistance \times time interaction in the trained condition ($F(1, 26) = 19.46$, $p < 0.001$). No differences were found between slow and fast groups at each level of resistance. These data suggest that the effects of training were limited to heavy resistance only and that ischemia did not enhance muscle volume with either moderate or heavy resistance training.

Elbow flexor strength

For clarity, changes in one-repetition maximum are presented at the trained speed only. Training with heavy resistance and slow contractions resulted in a 16.8 (8.9) % increase in strength. The heavy fast group showed a 34.5 (15.4) % increase in strength. The moderate slow condition resulted in a 9.8 (4.0) % increase in muscle strength. The moderate fast group demonstrated a 21.0 (18.4) % increase in muscle strength. The untrained arm showed a 6.5 (5.3) and 12.6 (9.6) % changes in muscle volume in the heavy slow and fast groups respectively. There was a 3.2 (6.3) and 14.4 (10.0) % change in muscle volume in the moderate slow and fast groups. The four way interaction of resistance, ischemia, condition and time was not significant ($F(1, 52) = 0.667$, $p = 0.418$). Examination of the three way interactions revealed non-significant interactions of ischemia, condition, and time ($F(1, 26) = 0.004$, $p = 0.950$) and also a non-significant interaction of ischemia, resistance and time ($F(1, 26) = 0.291$, $p = 0.592$). There was a significant interaction of resistance, condition and time ($F(1, 26) = 5.86$, $p = 0.019$). The interaction of resistance and time was not significant in the control condition ($F(1, 26) = 0.004$, $p = 0.950$), but the effect of time in the control condition was significant ($F(1, 28) = 23.713$, $p < 0.001$). This indicated that there was a significant increase in strength in the control group over the training period, but there were no differences in the effect of time between groups. There was a significant resistance \times time interaction in the trained condition ($F(1, 26) = 7.77$, $p = 0.01$). No

differences were found between slow and fast groups at each level of resistance. These data suggest that the effects of training on strength were limited to heavy resistance protocols only and there was no effect of ischemia with either moderate or heavy resistance training. The magnitude of the gains in strength were greater than increases in muscle volume, including a significant increase in strength in the control arm over time for all protocols.

Discussion

The key finding of this study was that ischemic resistance training did not show enhanced muscle volume relative to the non-ischemic training groups. This was true for both the moderate slow group, which was designed to produce an ischemic training effect, as well as the heavy slow group, designed to test whether heavy resistance plus ischemia produced enhanced responses. These results are in contrast to previous resistance training studies in which ischemia was controlled by proximal cuff occlusion (12). The use of a different methodology to control ischemia could explain the discrepancy or results between studies. However, the current results are also in contrast to other studies that have shown an ischemic effect using alternative methods to increase metabolic demand such as slow tonic force contractions (13) or metabolically intense continuous isometric actions (10). The differences in results could be explained by different methods of measurement of muscle size. Schott (10) used a single slice computed tomography scan and Tanimoto (13) averaged 3 slices from the midpoint of the thigh. In the present study, muscle volume was calculated from 33 cross sections along the length of the muscle. It has been shown by Tracy et al. (14) that muscle volume is a more sensitive measure of changes with training than a single or a few cross

sections. Thus, more sensitive muscle size measures may explain the difference between our study and previous studies.

In the present study, there was a clear effect of the level of resistance during training on skeletal muscle volume after resistance training. Both heavy resistance groups showed increases in muscle volume that were consistent with similar intensity non ischemic training programs including a mix of males and females in their sample (6, 7). More interestingly, the 5-7% increase in muscle volume in the heavy slow and fast groups is comparable to the 4% increase in average cross sectional area observed by Tanimoto et al. (13) in a heavy resistance non-ischemic group using a similar protocol to that employed in the current study. The moderate fast group did not show increases in muscle volume, also consistent with previous studies (13). This suggests that the protocol and experimental design used in this study was capable of producing and measuring changes in muscle volume after resistance training.

The design of the exercise program in the current study may have important implications for the results. In the previous studies (12, 13), groups training with moderate resistance and occlusion and heavy resistance without occlusion performed repetitions to volitional failure. In the present study, only the group training with heavy resistance and ischemia trained to volitional failure; all other groups performed a similar number of repetitions that did not result in volitional failure. These results suggest that volitional failure might be important for the ischemic effect on hypertrophy with moderate resistance.

Muscle strength changes also showed a clear effect of resistance and no effect of ischemia in the present study. This result is consistent with our muscle volume measurements, and consistent with studies showing that heavy resistance produces greater

strength improvements than lower resistance (1, 2). However, they are in contrast to previous studies showing increases in strength when resistance training was performed with ischemia (12, 13). In addition, there is evidence of a neural component of strength development in the current study. Muscle force has been observed to be proportional to muscle area (5), and muscle volume has been suggested to be a superior to area as an indicator of muscle force capacity (14). Relative gains in one-repetition maximum strength in the present study are at least double the relative gains in muscle volume. In addition, the control arm in each group showed increases in strength that were proportionally smaller than the gains in the trained arm. These results are consistent with the magnitude of the cross-over effect found in the meta-analysis by Munn et al. (9). Strength was measured in all groups at both slow and fast speed, and significant increases in strength only occurred at the trained speed (data not shown). Though changes in strength are related to changes in muscle volume, strength effects require a more complex interpretation than effects on muscle volume. Measures of muscle volume were analyzed in a non-biased manner by using a system of blinding. It was not possible to blind the investigator to the time point or the group of the participants during strength testing. For this reason, greater emphasis should be placed on changes in muscle volume as a measure of the adaptations to training in the current study and strength results should be interpreted carefully.

In conclusion, the results of the present study do not support the hypothesis that resistance training with ischemia enhances muscle hypertrophy when coupled with moderate resistance. The results also fail to support the hypothesis that heavy resistance and ischemia would lead to enhanced muscle hypertrophy compared to heavy resistance alone. Negative outcomes such as these results are important to understand how ischemic training may

enhance hypertrophy in response to resistance training. More research into ischemic resistance training is needed, in particular to address the question of whether ischemic resistance training might enhance muscle hypertrophy through changes in muscle activation.

Table 3.1 – Participant characteristics before and after training. No differences were detected between groups on any measure before or after training.

Group	n	Age (years)	Height (cm)	Body Mass (kg)
HEAVY SLOW				
Pre	8	23 (3)	170 (5)	67.5 (10.3)
Post		23 (3)	170 (5)	66.8 (11.1)
HEAVY FAST				
Pre	8	23 (4)	167 (8)	71.0 (21.8)
Post		23 (4)	168 (8)	69.8 (18.9)
MODERATE SLOW				
Pre	8	24 (4)	169.7 (13.1)	73.5 (13.9)
Post		24 (4)	169.7 (13.1)	73.0 (15.1)
MODERATE FAST				
Pre	6	22 (4)	167.4 (10.7)	78.9 (11.4)
Post		22 (3)	167.7 (10.6)	78.0 (10.8)

Table 3.2 – Selected resistance exercise variables.

Group	Intensity (% Fast 1RM)	Repetition Duration (seconds)	Total Reps/session	Compliance (%)
HEAVY SLOW	80.5 (0.5)	10	20 (1)	86 (8)
HEAVY FAST	79.5 (1.4)	2	20 (1)	86 (5)
MODERATE SLOW	50.4 (1.2)	10	20 (1)	87 (8)
MODERATE FAST	51.2 (1.7)	2	20 (1)	85 (5)

Table 3.3 – Absolute muscle volume and strength

Group	n	Elbow Flexor Volume (cm ³)	Elbow Flexor Strength (kg)		
		Trained	Control	Trained	Control
HEAVY SLOW					
Pre	8	279 (124)	293 (124)	14 (6)	15 (6)
Post		297 (128)	291 (124)	17 (6)	15 (6)
HEAVY FAST					
Pre	8	236 (90)	253 (107)	9 (4)	9 (5)
Post		250 (94)	258 (98)	12 (6)	11 (5)
MODERATE SLOW					
Pre	8	258 (108)	252 (113)	13 (6)	14 (6)
Post		260 (111)	249 (120)	14 (6)	14 (7)
MODERATE FAST					
Pre	6	230 (136)	241 (132)	8 (6)	9 (6)
Post		237 (148)	249 (155)	9 (5)	10 (6)

Figure Legends

Figure 3.1 – Representative MR image. Shown is an image from the upper middle control arm of a female participant prior to training. T₁ weighted fast spin echo image, field of view 20 cm TR = 3000 ms, TE = 87.5 ms

Figure 3.2 – Elbow flexor volume. The striped bars represent the moderate slow continuous condition * Heavy resistance is greater than moderate resistance (p =0.001) Values are mean + SD.

Figure 3.3 – Elbow flexor strength. Red bars represent the trained arm blue bars represent the control arm. The striped bars represent the moderate ischemic condition * Significant effect of resistance (p =0.010) Values are mean + SD.



Figure 3.1

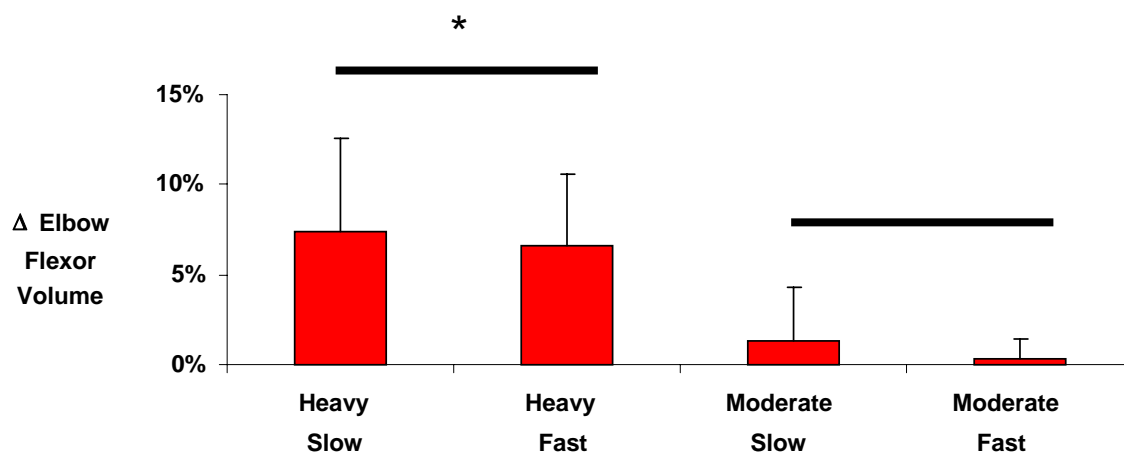


Figure 3.2

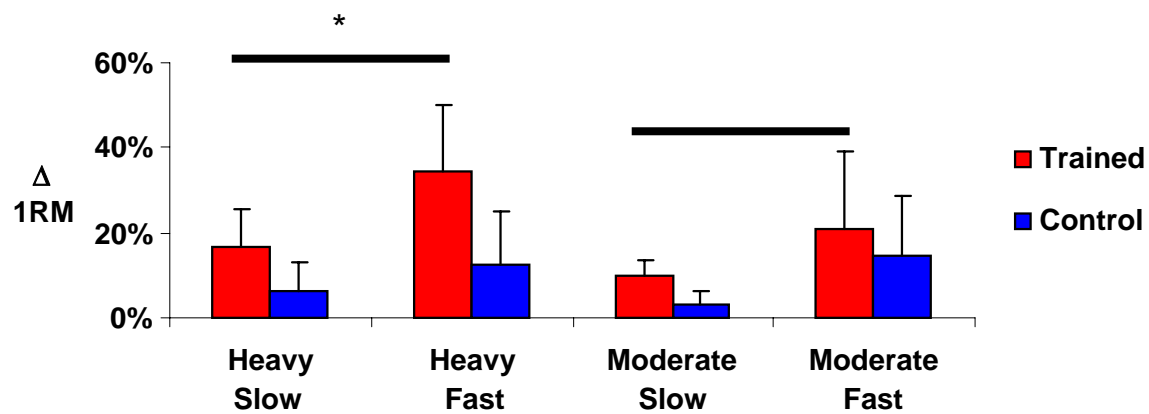


Figure 3.3

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CHAPTER 4

OXYGEN SATURATION AND EMG DURING RESISTANCE EXERCISE WITH ISCHEMIA

Abstract

Moderate intensity resistance exercise has been shown to produce greater muscle hypertrophy under ischemic compared to non-ischemic conditions. The present study was designed to determine slow continuous contractions produced greater ischemia and greater muscle activation compared to fast, discontinuous contractions. Non-resistance trained men ($n = 11$) and women ($n = 11$) volunteered to participate. Surface electromyography (EMG) was collected from the biceps muscle during a single exercise session consisting of 3 sets of resistance exercise at high (75% of maximal) or moderate (50% of maximal) intensities. Continuous contractions produced ischemia measured with infrared spectroscopy (NIRS) during both high and moderate intensities, while non-continuous contractions did not. The average RMS EMG over three sets of resistance exercise was 73.0 (15.5) % and 75.3 (6.1) % of a maximum contraction for heavy resistance ischemic and normal respectively. Moderate resistance RMS EMG was 36.4 (9.0) % and 55.3 (11.9) %. There was a significant main effect for resistance ($F(1, 18) = 35.54, p < 0.001$) with heavy greater than moderate, and a significant main effect for ischemia ($F(1, 18) = 4.98, p = 0.039$) with ischemia less than normal. The lack of rise in EMG during exercise was associated with the lack of hypertrophy and strength development in moderate resistance ischemic and normal conditions while hypertrophy and strength development was associated with greater relative magnitudes of EMG in heavy resistance ischemic and normal conditions. It is concluded that three sets of continuous contractions of the biceps muscle produced ischemia without an increase in muscle activation. Thus, resistance exercise with slow continuous contractions can provide ischemic conditions, but more repetitions would be needed to produce elevated muscle activation during moderate intensity exercise.

Introduction

Resistance training has been shown to produce increases in muscle size, strength, and whole body function in a wide array of patient populations (2, 5, 9, 15, 18). However, there are difficulties associated with training frail or impaired populations. Given these difficulties, there is a need to develop new training approaches that either use lower training intensities or which maximize the response to resistance training. For example, electrical stimulation induced resistance training has been used successfully in people with complete paralysis due to spinal cord injury (7). However, the use of electrical stimulation is complicated and requires expert supervision.

Ischemic resistance training is an alternative to traditional resistance training performed with light to moderate resistance (20 to 50% of one-repetition maximum) coupled with vascular occlusion induced by inflation of pressure cuff proximal to the exercising muscle group. Traditional resistance training to maximize muscle size and strength is performed with heavy resistance $\geq 75\%$ of one repetition maximum. Significant increases in muscle size and strength have been observed with ischemic training in untrained middle-aged women (13), as well as in male athletes (12). Another study (14) reproduced the ischemic effects on muscle size and strength without cuff occlusion by using slow tonic force repetitions to decrease muscle oxygenation. These studies have included groups exercising with 80% of one repetition maximum resistance without cuff occlusion (13) or without slow tonic force (14) and the adaptations to moderate resistance ischemic training are comparable to adaptations in heavy resistance groups.

In a companion to the present study, resistance training was performed with different levels of resistance and either slow continuous repetitions or fast intermittent repetitions.

Differences in repetition speed and duration were intended to control oxygen saturation in a manner similar to the design of Tanimoto et al. (14). The results of the companion study (3) suggest that low muscle oxygen saturation does not have an effect on muscle hypertrophy or strength in response to resistance training. In previous ischemic resistance training studies (11-14), examinations of the responses to acute exercise have shown that the muscle electrical activity measured by EMG is increased with moderate resistance and vascular occlusion compared to moderate resistance alone. The electrical activity with moderate resistance and occlusion is comparable to exercise with heavy resistance.

The purpose of the present study is to measure muscle EMG activity and oxygen saturation during heavy and moderate intensity exercise performed either slowly and continuously (ischemic) or rapidly and discontinuously (normal). Because all exercises involved the same number of contractions, it was hypothesized that emg activity would vary with resistance and not with ischemia. It was also hypothesized that near infrared spectroscopy measurements of oxygen saturation would show a significant effect of speed (ischemic versus normal) and not resistance. These measurements would help in the interpretation of the changes in muscle volume and strength reported in the previous training study.

Methods

Participants

The procedures were approved by the Institutional Review Board at the University of Georgia and all participants provided informed written consent prior to their participation. Twenty two healthy men ($n = 11$) and women ($n = 11$) participated in the study. Participants were recreationally active and had some previous resistance training experience but were

currently performing ≤ 1 day of resistance exercise with the biceps. Self report questionnaires were administered and the data used to exclude those with cardiovascular or metabolic disorders and also those with injuries to the upper extremities. Physical characteristics of the participants are presented in Table 1. There were no differences in age, height, and weight between groups.

General design

This study was designed to compare skeletal muscle electrical activity during resistance exercise performed with either 80% or 50% of one-repetition maximum and either 10s continuous repetitions or 2s intermittent repetitions followed by 8s of rest. The longer duration continuous repetitions were intended to result in low muscle oxygen saturation (ischemia) while the shorter duration intermittent repetitions were intended to maintain high muscle oxygen saturation (normal). Muscle oxygen saturation was verified by near infrared spectroscopy (NIRS) in a separate exercise session. This study was performed on the same subjects who also performed a training study to evaluate changes in muscle volume and strength (3).

Elbow flexor strength

Muscular strength was assessed in each arm before testing by determining the one-repetition maximum (1RM) elbow flexion. Tests were performed for both 10s and 5s repetitions. The 1RM was assessed using a standard set of free-weight dumbbells with the participants standing with the back and hips braced against a wall. The dumbbells were also used for all exercise bouts. Participants were instructed that their 1RM is the maximum weight they can lift with good form for 1 repetition of elbow flexion. Good form was defined

as moving the dumbbell with constant velocity, completing the concentric phase of the flexion in about 1s or 5s, and returning the dumbbell to the rest position with constant velocity in 1s or 5s. Pacing was kept by using a metronome. Weight was increased in successive trials until a weight was found that could not be lifted for 1 repetition with good form. Tests were completed within 5 trials. Each maximal attempt was separated by 2 minutes of rest to avoid fatigue.

Resistance exercise

Resistance exercise consisted of unilateral dumbbell curls performed standing with the back and hips braced against a wall. All groups performed 3 sets with 1 minute of rest separating each set. The heavy resistance ischemic group exercised with 80% of the fast 1RM and performed continuous repetitions with 10 second duration, 5s concentric, and 5s eccentric. Repetitions were performed to volitional failure, defined as the inability to continue repetitions in good form and at the correct pace. The maximum number of repetitions allowed in each set was 12. The moderate resistance ischemic group exercised with 50% of the fast 1RM and performed continuous repetitions with 10 second duration, 5s concentric, and 5s eccentric. Repetitions were matched to the average number of repetitions performed by the heavy resistance slow continuous group. The heavy resistance fast discontinuous group exercised with 80% of the fast 1RM and performed discontinuous repetitions with 2s duration, 1s concentric, 1s eccentric followed by 8s of rest.

Muscle electrical activity

Electromyography (EMG) signals were recorded from the non-dominant biceps brachii muscle. Bipolar surface electrodes (BioPac Systems, Goleta, CA) were placed over

the belly of the muscle with a constant inter-electrode distance of 20 mm. Electrode position was standardized by centering the electrodes one-third of the distance along a line from the middle of the cubital fossa to the acromion process of the scapula. Data were collected at 2000 Hz and processed using AcqKnowledge software version 3.7.2 (BioPac Systems, Goleta, CA). The average root mean square (RMS) EMG of the signal was calculated along concentric and eccentric portions of the repetitions separately. In the slow continuous groups a 5s portion of the signal was averaged while a 1s portion was averaged in the fast discontinuous groups. Data during exercise sets were then normalized to the 1RM data at the corresponding speed and are reported as a percentage of maximum. Eccentric and concentric data from each set were averaged into an overall score for analysis.

Muscle oxygen saturation

Muscle oxygen saturation was assessed by near infrared spectroscopy (NIRS) using a continuous light source, dual-wavelength spectrophotometer (Cogniscope; NIM, Inc.). Two light sources and six photodetectors were arranged to produce 8 different signals. The separation distance between the light sources and detector pairs were 3 cm. The source detector pairs were located in two rows covering a distance of 9.5 cm and 5 cm wide. The source detector pairs were positioned horizontally over the elbow flexors, perpendicular to the direction of the muscle fibers. Light photons migrating through the tissue were collected by the detectors with optical filters set at 760, 805, and 850 nm. Oxygen-heme groups have a greater absorbance at 850 nm compared with 760 nm, with deoxy-heme groups absorbing more at 760 nm than at 850 nm. The difference signal between 760 and 850 nm was used to indicate changes in oxygen saturation. Voltage signals were converted to optical density using the Beer-Lambert Law, and used to calculate oxygen saturation (ratio of HbO_2/Hb

signal). Total blood volume measured as the Hb + HbO₂ signal was also recorded but not presented. Oxygen saturation values were calibrated as a percentage of the physiological range using 0% as the lowest value at the end of cuff ischemia, and 100% as the peak value after releasing the cuff. The average response of each muscle included 2 channels corresponding to the muscle belly.

Statistics

Statistics were calculated using SPSS version 15 (SPSS Chicago, IL). Descriptive statistics were used to derive means and standard deviations for each variable. All results are expressed as mean (standard deviation). Relative root mean square EMG signals, participant characteristics, and resistance exercise variables were each evaluated with a separate 2 x 2 (resistance x ischemia) analysis of variance (ANOVA) Significant interactions were followed by tests of simple effects. Significance level was set at $\alpha = 0.05$

Results

Resistance exercise

Selected resistance exercise variables are presented in Table 2. The relative resistance was not different between slow continuous and fast discontinuous groups when comparing within resistance conditions. The number of repetitions completed during exercise was similar among all groups.

Muscle electrical activity

Muscle electrical activity measured via EMG in each exercise group is presented in Figure 2. The average RMS EMG over three sets of resistance exercise was 73.0 (15.5) %

and 75.3 (6.1) % for heavy resistance slow continuous and fast discontinuous groups respectively. Moderate resistance RMS EMG was 36.4 (9.0) % and 55.3 (11.9) % slow continuous and fast discontinuous groups respectively. There was a significant main effect for resistance ($F(1, 18) = 35.54, p < 0.001$) with heavy having greater EMG levels than moderate, and a significant main effect for ischemia ($F(1, 18) = 4.98, p = 0.039$) with ischemia having lower EMG levels than normal. The interaction between resistance and ischemia on EMG was not significant, and the moderate resistance slow continuous group demonstrated the lowest average RMS EMG. Therefore, the hypothesis that slow continuous training at moderate intensity enhanced muscle activation was not supported by these data.

Muscle oxygen saturation

The pattern of muscle oxygen saturation in each of the exercise protocols is shown in the examples presented in Figure 1. Due to experimental limitations to placing cuff for the ischemic calibration on the arm above the NIRS probe, only two subjects were tested for each protocol. Despite these small sample sizes, the data were consistent within groups. Maximal desaturation expressed relative to the maximal saturation recorded after the release of cuff ischemia was 91.2 (2.7) % in the heavy slow continuous group and 85.6 (1.9) % in the moderate slow continuous group. Heavy resistance fast discontinuous exercise was 60.9 (5.1) % desaturated and moderate resistance fast discontinuous exercise was 36.3 (1.7) % desaturated. Exploratory data analysis indicated a significant resistance \times ischemia interaction. While this result is difficult to interpret with small sample size, it seems clear that ischemia was achieved with slow continuous contractions and that normal saturation was higher.

Discussion

The primary finding of this study was that with our protocol, slow continuous contractions did not result in increased RMS EMG levels. This is in contrast to previous ischemic training studies that reported greater EMG activity during resistance exercise with moderate resistance and ischemia than with moderate resistance alone, comparable to heavy resistance exercise (13, 14). The differences in EMG between this and other studies may be due to the absence of significant fatigue with moderate ischemic exercise as performed in the current study. Matching repetitions between moderate and heavy resistance groups (\approx 20/session) in the present study prevented fatigue the moderate intensity group. In the study by Takarada et al. (13), participants performed approximately 54 repetitions per session in a moderate intensity ischemic condition and each of four sets were continued to fatigue. Muscle activation is increased with the onset of fatigue (17) and may be enhanced by ischemia (8).

Increasing the extent of muscle activation indicates recruitment of a greater muscle mass to produce force, increasing frequency of activation, and increased synchronization of motor unit activity. Following the size principle (4), increasing activated muscle mass indicates the recruitment of a greater proportion of type 2 muscle fibers. The recruitment of Type 2 fibers has long been associated with adaptations to resistance training in athletes (6, 16), and type 2 fibers show the greatest hypertrophy in response to varied resistance training programs (1). The present results are consistent with the idea that increasing the extent of muscle activation including type 2 fiber recruitment may be the essential component of resistance exercise design that leads to increases in muscle size.

A second finding in our study was that NIRS measured oxygen saturation indicated, although in a small sample size, that slow continuous contractions produced significantly more ischemia than the faster discontinuous contractions. This supports the use of the term ‘ischemia’ when describing the exercise protocols. Previous studies have suggested that resistance training with vascular occlusion produces muscle hypertrophy by inducing muscle ischemia. While our study may not have employed a cuff occlusion exercise protocol, it was similar in producing ischemia. The magnitude of oxygen desaturation observed in the present study is consistent with oxygen saturation data of Tanimoto (14) who used a similar slow tonic force protocol to induce ischemia. The present results also agree with the magnitude of changes in high energy phosphate achieved by Schott et al. (10) in response to a continuous and discontinuous isometric contraction protocols. The continuous contraction protocols resulted in significant changes in muscle high energy phosphates, consistent with exercise in ischemic conditions.

There are a limited number of previous studies that have attempted to quantify ischemia during ischemic resistance exercise. The practice of ischemic exercise also varies widely with differences in cuff pressures and durations. It is possible that the lack of hypertrophy observed in the moderate ischemic group and the lack of additional hypertrophy in the heavy ischemic group of the companion study could be explained by insufficient ischemic duration. In the present study, we present an attempt to quantify ischemia by taking into account both the relative magnitude of desaturation and the duration of ischemia. Multiplying the average desaturation by the duration of each set gives an “ischemic intensity” that can be expressed as desaturation seconds or minutes. In the present study, heavy and moderate ischemic groups had an ischemic intensity of 3 % minutes per exercise

session. That is equivalent to 3 minutes of physiological minimum oxygen saturation during exercise. The exercise session including inter-set rest periods was approximately 5:20. This measure of ischemic intensity could be used in future studies to determine if an ischemic threshold exists for increases in muscle size and strength.

Plots of the NIRS data presented in Figure 1 provide evidence that resistance exercise using slow continuous repetitions was effective at inducing ischemia in both heavy and moderate resistance groups. The plots also provide evidence that fast intermittent repetitions led to much less of an ischemic effect than their slow continuous counterparts. It was not possible to measure oxygen saturation on all participants. This was due primarily to limitations in penetration depth of the light emitters. We were interested in training participants who were not highly physically active, however many in this population have significant subcutaneous fat covering the elbow flexor muscles, requiring a greater light penetration distance to reach muscle tissue for absorption. The levels of oxygen saturation measured in our small sample are consistent with the study by Tanimoto et al. (14) that utilized slow tonic force contractions. We are confident that these plots are representative of the conditions during exercise in all participants in resistance training.

In conclusion, the present results suggest first that slow continuous repetitions were effective for inducing skeletal muscle ischemia during resistance exercise that was greater than ischemia in normal conditions. Second, the results suggest that muscle electrical activity has a greater dependence on the magnitude of the resistance and the repetition velocity than on the presence of ischemia in skeletal muscle when compared among groups performing the same volume of exercise with either heavy or moderate load and ischemia or normal. Third, when taken together with the companion study in which resistance training was performed

using these exercise parameters, the results suggest indirectly that adaptations to moderate resistance training with ischemia are dependent on increasing EMG to mimic heavy resistance exercise. Further research needs to be done to establish a more direct link between muscle electrical activity, ischemia, and adaptations to resistance training with both moderate and heavy resistance.

Table 4.1 – Participant characteristics. Values are means (SD).

Group	Age (years)	Height (cm)	Body Mass (kg)
HEAVY ISCHEMIC	24 (3)	168.0 (4.9)	63.0 (10.6)
HEAVY NORMAL	24 (4)	171.7 (6.3)	77.7 (23.7)
MODERATE ISCHEMIC	25 (4)	168.3 (13.8)	75.1 (15.8)
MODERATE NORMAL	22 (4)	167.4 (10.7)	78.9 (11.4)

Table 4.2 – Selected resistance exercise variables. Values are means (SD).

Group	Intensity (% 2s 1RM)	Repetition Duration (seconds)	Total Reps/session
HEAVY ISCHEMIC	80.3 (0.5)	10	22 (8)
HEAVY NORMAL	79.8 (1.2)	2	22 (3)
MODERATE ISCHEMIC	50.6 (1.4)	10	22 (2)
MODERATE NORMAL	50.7 (1.3)	2	20 (2)

Figure Legends

Figure 4.1 – Relative RMS EMG. Muscle electrical activity expressed as the root mean square signal relative to the signal during one-repetition maximum. The striped bar represent the moderate resistance ischemic condition * Heavy resistance is greater than moderate resistance ($p < 0.001$). # fast discontinuous is greater than slow continuous ($p = 0.039$) Values are mean (SD)

Figure 4.2 – Representative NIRS plots. Representative tracings of muscle oxygen saturation during resistance exercise followed by cuff occlusion in each of the four groups. The y-axis is arbitrary units.

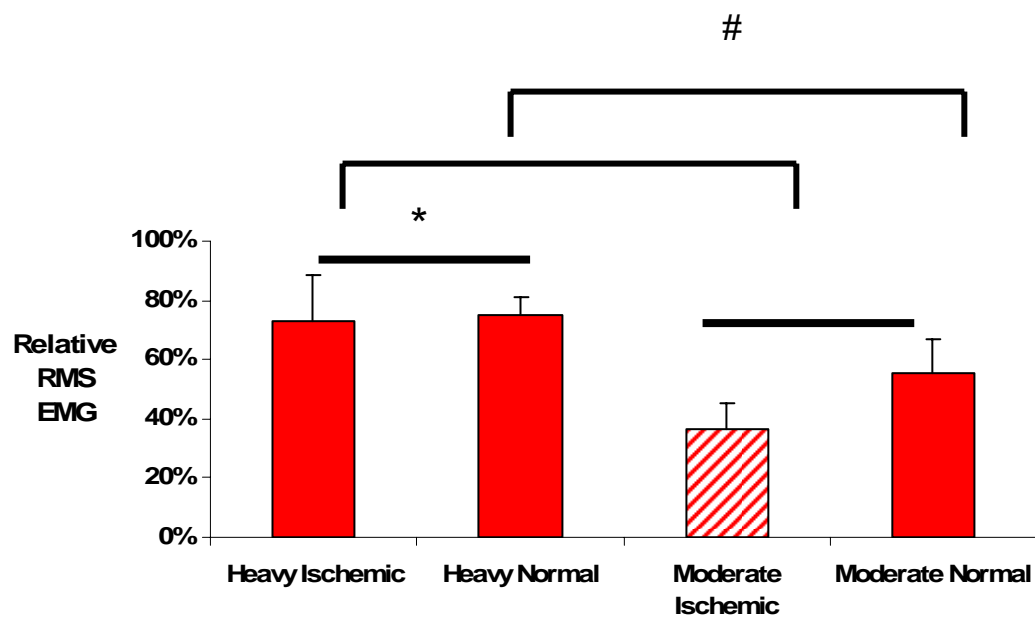


Figure 4.1

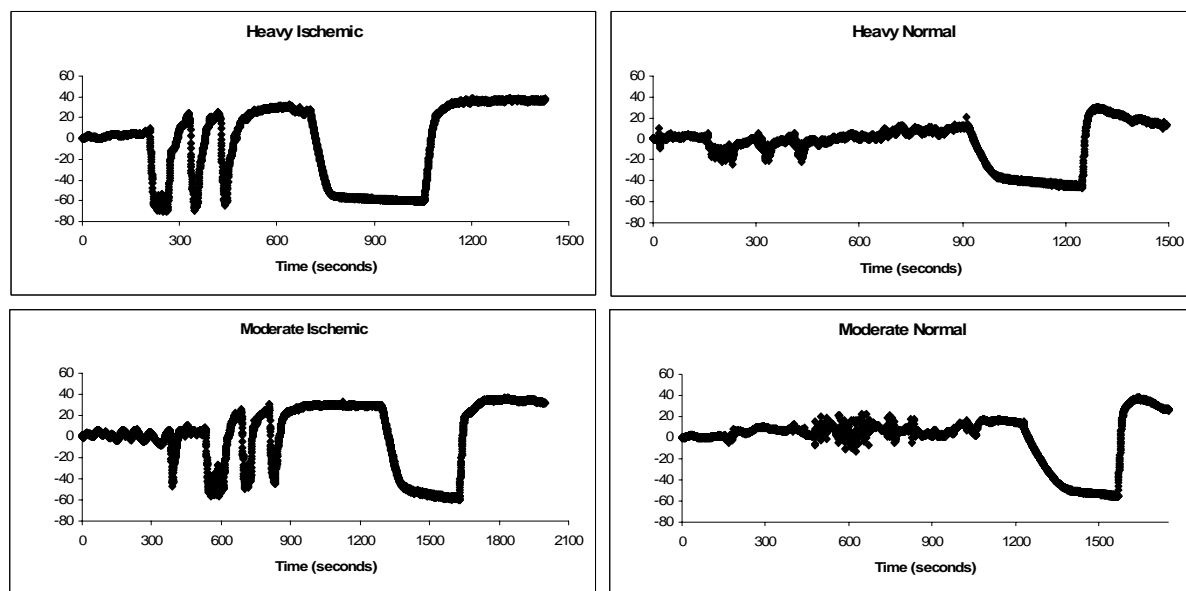


Figure 4.2

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CHAPTER 5

SUMMARY

Activities of daily living such as lifting groceries, opening doors, rising from a chair and climbing stairs require generally fixed levels of force production across all populations. Frail and diseased individuals have diminished force capacity, limiting their ability to complete these everyday tasks. The loss of muscle mass in the frail and diseased may affect glucose handling and other metabolic processes in addition to force capacity. Resistance training is effective for increasing both muscle size and force capacity; however, as long as rates of adaptation to resistance remain fixed, frail, and diseased individuals require longer periods of training to reach the necessary functional force capacity or muscle size. Exercise researchers are tasked with discovering methods to enhance adaptations to training with the goal of achieving health, independence, and greater quality of life more quickly in the frail and diseased.

Takarada et al. (44) hypothesized that moderate resistance training with ischemia could potentially enhance recovery of strength and muscle size in patients and the elderly. Their results in healthy older women indicate enhanced strength and size development when ischemia is added to moderate resistance exercise. While they were able to enhance adaptations to moderate resistance training, it remained important to know if it was possible to produce even greater adaptations with heavy resistance and ischemia. The present experiment was designed to test the hypothesis that ischemia added to heavy

resistance training would result in enhanced strength and muscle size development relative to heavy resistance training alone.

The results of the present study indicate that the addition of ischemia to heavy resistance does not enhance muscle hypertrophy and strength development compared to an equal volume of heavy resistance without ischemia. The results also indicate that moderate resistance training with ischemia does not enhance muscle hypertrophy and strength development relative to an equal volume of moderate resistance training without ischemia. There was no effect of ischemia on either strength or muscle size adaptations to resistance training, contrary to previous studies of resistance training with ischemia.

The explanation for these contrary results may lie in the interaction of ischemia and muscle activation and the limitations imposed by the design of the resistance exercise employed in the current study. Previous work with ischemic exercise has suggested that maximal motor unit recruitment occurs more quickly in the presence of ischemia than when oxygen and blood supply are intact. Thus it was important to determine the magnitude of ischemia as well as the extent of muscle activation during exercise performed during resistance training in the first study. An additional study was designed first to determine if the slow continuous movement resulted in greater ischemia than fast discontinuous movement and second to determine if muscle activation was greater in ischemic than non-ischemic exercise conditions.

We found that our exercise bout of slow continuous repetitions resulted in approximately 3 minutes of full desaturation while the bout with fast discontinuous repetitions resulted in only 1.5 minutes of desaturation. These data support the hypothesis that slow continuous repetitions result in greater ischemia than fast discontinuous repetitions. Muscle activation measured by EMG showed no effect of ischemia in either heavy or moderate resistance conditions. The

hypothesis that ischemic exercise conditions would lead to greater activation than non-ischemic conditions was not supported. Equal numbers of repetitions were performed in slow continuous and fast discontinuous exercise conditions. The heavy, more ischemic exercise was performed to volitional failure while other groups matched repetitions and their exercise did not lead to failure. Considering the interaction of, muscle activation and resistance exercise design and ischemia in the second study, a general theory may be put forth regarding the lack of ischemic effect on muscle volume observed in study 1.

The pattern of increases in muscle volume with training was related to the extent of muscle activation during exercise. Greater activation during exercise suggested a greater increase in muscle volume with training. The resulting hypothesis is that the extent of muscle activation during exercise controls the magnitude of adaptation of muscle volume to training and that maximizing the extent of activation will maximize the adaptation. Further, the specific exercise design may influence the extent of muscle activation. With moderate resistance exercise, the initial extent of activation is less than with heavy resistance exercise. If the extent of activation increases over time at a similar rate with both heavy and moderate resistance, more repetitions have to be performed with moderate resistance to reach maximal recruitment. A similar number of repetitions were performed in both heavy and moderate resistance exercise in the present study, and the extent of activation during moderate resistance exercise was not maximal while activation during heavy resistance exercise did approach maximal. This supports the idea that a greater number of repetitions need to be performed with moderate resistance exercise to reach maximal recruitment, and that maximizing recruitment maximizes the adaptation of muscle volume to training.

The presence of different ischemic conditions allows for a more complex interpretation of the results of the two studies. The extent of activation increases at a faster rate with ischemia than without ischemia during moderate resistance exercise (44). Ischemia has little effect on the extent of activation during heavy resistance exercise because recruitment is already close to maximal. The extent of activation during moderate resistance exercise was neither close to maximal nor increased compared to a similar number of repetitions of less ischemic exercise in the present study. There are two possible explanations for these observations. As stated above, the number of repetitions was likely not sufficient to allow enough time for the extent of activation to increase, in addition, the magnitude of ischemia was not sufficient to increase the rate at which the extent of activation reached maximal. The magnitude of adaptation to moderate resistance training could be increased in two different ways, both leading to maximal recruitment. Either increase the number of repetitions performed until failure is reached, or increase the ischemic stimulus enough to increase the rate of fatigue such that volitional failure and maximal recruitment occurs in fewer repetitions.

Taken together, the results of the two present studies, while not establishing a causal relationship, support the hypothesis that the extent of muscle activation is the key to the magnitude of increase in muscle volume with resistance training. In addition, the metabolic events consequent to ischemia may not have a direct link to increases in muscle volume, but may act secondarily to increase the extent of muscle activation. These hypotheses could be tested with several additional experiments.

Additional experiments

Additional experiments could be designed to determine if training with moderate resistance exercise leading to volitional failure in the absence of ischemia resulted in similar adaptations to training with moderate resistance exercise with ischemia leading to volitional failure. Based on the current study, the hypothesis would be that these two training programs would lead to similar increases in muscle volume. It is possible that including different magnitudes of ischemia in different groups would lead to similar adaptations but would require different numbers of repetitions to reach volitional failure. It is also possible that the adaptations would be similar compared to heavy resistance training to failure with or without ischemia.

The idea that maximal recruitment is necessary to maximize increases in muscle size with resistance training suggests that some characteristic of maximal recruitment holds the key signal for muscle growth. The most likely candidates are the Type 2 fibers which are only recruited during maximal or near maximal force development or during prolonged continuous contractions to maintain force output in the presence of fatigue. These fibers could generate a greater signal to a limited number of contractions than type 1 fibers. Further experiments should focus on the specific characteristics of Type 2 fibers and possible differences in intracellular and extracellular signaling events consequent to their recruitment compared to the signaling resulting from recruitment of Type 1 fibers. Such experiments could first be carried out in single fiber preparations and subsequently in more complex preparations to determine which components of the muscle structure and system are necessary to create the optimal signaling environment leading to hypertrophy.

The current results may mean that any alternative form of resistance training that ultimately leads to maximal activation could result in a similar magnitude of adaptations when

compared to other methods. This idea has important implications for exercise prescription in both health and disease. Interventions that target type 2 fibers directly such as nerve stimulation and eccentric only training could lead to the greatest adaptations in muscle size. The differences in adaptation between activation of Type 2 fibers along with the whole muscle versus selective type 2 recruitment would then have to be determined.

Applications to clinical populations

There are many different possible methods of resistance training to increase strength and muscle size. The question concerning which individual method or combination of methods results in the greatest adaptations remains unanswered. The current results suggest that any resistance training leading to maximal activation results in the greatest adaptations. Maximal activation could potentially be achieved using a variety of methods including ischemia, heavy resistance, pre heating, electrical stimulation, stretch and others. However, any method leading to maximal activation may prove difficult, uncomfortable or unsafe for those unaccustomed to exercise. The results also suggest that there is no natural shortcut to gains in strength and muscle mass. For populations with neuromuscular disease, achieving activation of all available motor units may be a necessary step before significant gains in muscle size can be achieved. In populations that are simply unable to activate maximally, other pharmacological interventions may be necessary.

In addition to training for functional strength leading to simple everyday task completion, further investigation into the advantages and disadvantages of high levels of muscle mass in maintaining a healthy lifestyle are warranted. Skeletal muscle is incredibly adaptable to diverse stimuli, and we have only begun to learn how muscle mass participates in the regulation of other body systems in both health and disease. Laying a strong foundation for how muscle responds

and adapts to diverse exercise and training stimuli will lead to the most efficient application of new therapies for current and emerging conditions.

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