THE INFLUENCE OF CHRONIC STRETCH ON THE GASTROCNEMIUS MUSCLES OF ABLE BODIED ADULTS

by

EMMA LEIGH WALKER

(Under the Direction of KEVIN K. MCCULLY)

ABSTRACT

To improve strength, numerous methods have been suggested as alternatives to resistance training. One method of interest is passive chronic stretching. The hypothesis was that chronic stretching will result in increase in muscle mass as compared to strength training and that chronic stretch will increase ankle dorsiflexion angle. Two groups either stretch or strength trained for eight weeks. MRI analysis was used to evaluate gastrocnemius muscle mass before and after training. There were no differences in muscle mass pre and post training in the two groups. Chronic stretch did increase ankle passive dorsiflexion ROM. It can be concluded that chronic stretch did not provide enough stimuli to induce muscle hypertrophy.

INDEX WORDS: chronic stretch, dorsiflexion

THE INFLUENCE OF CHRONIC STRETCH ON THE GASTROCNEMIUS MUSCLES OF ABLE BODIED ADULTS

by

EMMA LEIGH WALKER

B.S. Albany State University, 2003

A Thesis Submitted to the Graduate Faculty of The University of Georgia in Partial Fulfillment

of the Requirements for the Degree

MASTER OF SCIENCE

ATHENS, GEORGIA

© 2007

EMMA LEIGH WALKER

All Rights Reserved

THE INFLUENCE OF CHRONIC STRETCH ON THE GASTROCNEMIUS MUSCLES OF ABLE BODIED ADULTS

by

EMMA LEIGH WALKER

Major Professor:

Kevin K. McCully

Committee:

Kathy Simpson Mike Ferrara

Electronic Version Approved:

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

DEDICATION

In memory of Fred Walker, Jr. (2/15/32-8/10/07)

Without your love, guidance, and strong will, this work would have not come into

fruition. You will always be loved and cherished throughout the coming years.

This degree is for you, Dad.

ACKNOWLEDGEMENTS

In no particular order, I would like to thank the following people.

I would first like to give thanks to our Savior All Mighty for his guidance and strength throughout this process. I thank my mom, brother, niece, and the rest of my family for giving unconditional love, support, encouragement, and motivation to complete my degree. Also, I would like to thank my "brothers and sisters": Kaleena, Kenya, Brandon, and Nick for providing support, a "listening ear", and keeping my sanity throughout my studies. I thank all my participants that volunteered for the study. I had some of the best participants in the WORLD and your assistance was greatly appreciated.

I would like to thank Dr. McCully for all his encouragement, guidance, patience, and support throughout this process. I am extremely grateful that he stepped up to become my major professor due to the unfortunate passing of my first major professor, Dr. Gary Dudley. Dr. Ferrara and Dr. Simpson also deserve gratitude for their support and expertise that assisted in this project.

A big thank-you goes to Christopher Black for taking the time to answer ALL my questions and concerns throughout my studies and project. Other thanks of gratitude go out to Tracee Kendall (thanks for calming me down as I wrote my thesis), Christopher Elders, Cherie Rooks, Brian Williams, Keturah Armstrong, Jennifer Trilik and Akilah R. Carter for all their support.

v

Finally, I would like to thank my other graduate family in the Department of Microbiology: former major professor, Dr. Stabb, former lab mates: Jeff Bose, Dawn Buchner, and Ann Dunn for their support and guidance. Last but not least, I thank my friends Adrienne Cottrell, Danielle Webster, Dana Waller-Simmons, Andrea Ewings for all their patience and unconditional love and support.

Thanks to everyone for all your assistance throughout my endeavors. I am extremely blessed to have found countless people to help make this project possible. Without your support, this degree would not be possible. Thanks again and God Bless.

TABLE OF CONTENTS

Page			
ACKNOWLEDGEMENTSv			
LIST OF TABLES			
LIST OF FIGURES			
CHAPTER			
1 INTRODUCTION			
Specific Aims4			
Hypotheses4			
Significance of Study			
2 REVIEW OF LITERATURE			
Resistance Training6			
Stretching and Muscle Adaptation7			
Stretching and Muscle Gene Expression			
Stretching and Flexibility			
MRI Analysis11			
3 THE INFLUENCE OF CHRONIC STRETCH ON THE GASTROCNEMIUS			
MUSCLES OF ABLE BODIED ADULTS14			
Abstract15			
Introduction16			
Methods17			

	Results	21
	Discussion	22
	Conclusion	25
	References	
4	CLOSING REMARKS	42
5	REFERENCES	44

LIST OF TABLES

	Page
Table 1: Physical Characteristics	26
Table 2: Volume Analysis	27
Table 3: Statistical Analysis of Stretch Training Group	28
Table 4: Statistical Analysis of Strength Training Group	29
Table 5: Statistical Analysis of Maximum Dorsiflexion Angle	30
Table 6: Dorsiflexion Angle Analysis	31

LIST OF FIGURES

Page

Figure 1: MRI Scans of Gastrocnemius Muscles	32
Figure 2: Histogram of Gastrocnemius Volume Analysis	33
Figure 3: Correlation Analysis of MRI Analysis of Control Leg Pre & Post Training	34
Figure 4: Correlation Analysis of MRI Analysis of Experimental Leg Pre & Post Training	35
Figure 5: Muscle Volume Analysis of Stretch and Strength Training Pre & Post Training	36
Figure 6: Flexibility Analysis of Stretch Training Pre & Post Training	37

CHAPTER ONE

Introduction

An estimated 250,000 persons are living with some type of spinal cord injury and/or disorder in the United States (13). The 2000 Census Bureau estimated that there are 35 million people 65 years old or older, with 12% people of that population greater than 85 years old (32). The common link between these two populations is that both groups suffer from muscle atrophy. The muscular system is one of the most important systems in the human body. Inadequate muscle mass, leads to decrease in movements of body parts, reduce communication via body movements, speech, writing, and perhaps most importantly, reduction in postural stability and balance (58).

Three problems are associated with muscle atrophy. Two problems are disuse and aging. Studies have shown that muscle mass reduction begins to decline starting at the age of 50, with an average of 1.9/1.1kg/decade for men and women, respectively (35, 49). Decline in muscle mass strength leads to postural instability and increases in fall and injury incidents. Narici et al.., also suggested that not only a decrease in muscle mass among the elderly, there is also a decrease in single fiber specific tension, an increase in co-activation of antagonist muscles, and a decrease in motor unit activation capacity (49). All of these factors serve to further limit function and stability in the elderly. Gladys et al. experiment showed a correlation with postural imbalance with that of decrease muscle strength, activation, and tendon mechanical properties with age (51).

The third condition associated with muscle atrophy is unloading, commonly found in the spinal cord injury population. Studies analyzing quadriceps muscle biopsies showed within six months of injury, cross sectional area is reduced by one-third (9).

Castro et al., examined muscle biopsies of spinal cord injury patients within six months of injury and concluded there was a 16% reduced in quadriceps cross sectional area (9).

One of the best ways to reverse muscle atrophy is through resistance training. Resistance training stimulates muscle fiber proliferation that will result in an increase in strength, muscle mass, and endurance. Over recent years, numerous findings supported that the three modes of resistance training – eccentric, concentric, isometric training are effective in increasing muscle mass (1, 20, 36). Adams et al. (1), compared muscle DNA and RNA synthesis in response to isometric, concentric, and eccentric contraction using electrical stimulation rat training model. The result indicated that there was equal increase in muscle DNA and RNA across all three modes of resistance training mode and overall similar increases in muscle hypertrophy (1). Garma et al. compared three modes of resistance training in acute rat model training program using electrical stimulation to simulate resistance training and found that all three bouts showed similar increases in similar molecular responses (20). Jones and Rutherford compared the three modes of resistance training during 12 weeks of training in able bodied college students. It was also concluded that all three modes showed 11-15% increase in strength and 5% increase muscle cross sectional area (36). In 2007, Wernborn et al. perform an intensive review of literature of muscle adaptation responses to three modes of resistance training and concluded that equating frequency, weight, and intensity, all three modes of resistance training can effectively induced muscle hypertrophy (69).

Though resistance training is the preferred choice to increase and maintain muscle mass and strength, some population, e.g., sedentary, elderly, and spinal cord injured, lack

the capability to perform such actions. There have been numerous suggestions in overcoming this problem, including chronic stretch.

The American Academy of Orthopedic Manual Physical Therapy (AAOMPT) and American Physical Therapy Association (APTA) define chronic stretching as " a clinical approach utilizing skilled, specific hands-on techniques, including but not limited to manipulation/mobilization, used by the physical therapist to diagnose and treat soft tissues and joint structures for the purposes of modulation of pain, increasing range of motion (ROM), inducing relaxation, improving contractile and non-contractile tissue repair, extensibility and/or stability, facilitating movement; and improving function" (65). As simply stated, using a mechanical stimulus, stretch, to increase muscle adaptation responses.

Stretching has been used mainly for increasing range of motion (30, 31) and flexibility, particularly prior to an athletic event (18), however, more recently, researchers have observed that stretching can perhaps increase muscle mass (10, 11, 23, 25, 47, 66). Gomes et al., found that passively stretching the soleus of rat for one bout of thirty minutes of stretching increased myoD mRNA concentration, which is part myogenic regulator family that controls myogenesis, indicating upregulation of muscle synthesis (27). Tatsumi et al. reported increases in satellite cells, muscle stem cells, in rats after twelve hours of chronic stretching (63). Another study, using a rat model, demonstrated that either fast or slow chronic stretching bouts produced a 10% and 13% increase in muscle size, respectively (62).

However, the efficacy of a chronic stretch regimen to increase muscle mass has not been demonstrated conclusively for humans. The major aim of this study was to

determine if the use of a chronic stretching regimen by typical humans will induce similar muscle hypertrophy responses found in rats. Another aim is to determine the efficacy of chronic stretch to increase muscle mass in compromised adults, by determining whether this program benefits able bodied adults.

Specific Aims

1. To examine muscle mass increase of the medial gastrocnemius to chronic stretch training.

2. To determine muscle mass increase of the medial gastrocnemius due to chronic stretch is as effective as traditional resistance training.

Hypotheses

Compared to pre-training, after eight weeks of training,

1. Chronic stretching will result in an increase in gastrocnemius cross sectional area.

2. Plantar flexion resistance exercise will result in an increase in gastrocnemius cross sectional area.

3. Chronic stretching will result in an increase in ankle dorsiflexion range of motion (ROM).

Significance of Study

Most of chronic stretching studies have been tested using rat model and it is unknown whether the same effects can been seen in human population. This study will attempt to answer whether chronic stretch can be another training mode to cause muscle hypertrophy. These findings will aid those populations who cannot perform traditional resistance exercises.

CHAPTER TWO

REVIEW OF LITERATURE

Resistance Training

Numerous studies have shown that an increase in strength and muscle size is due to functional overload to muscle groups (21, 46). Over the years, many studies have concluded that eccentric, concentric, or isometric resistance training will increase muscle size and strength.

In 1987, Jones and Rutherford showed similar gains in strength and muscle size among the three modes of training. In the study, twelve healthy subjects were randomized into two groups: 1) isometric exercise only and 2) concentric exercise on one leg and eccentric exercise on the other and performed knee extensor exercises to compare muscle adaptation to either training mode. The training sessions were performed 3days/week for twelve weeks at 80% of 1RM. All weight was equated to ensure each group was training at similar weight. Quadriceps muscle cross sectional area (CSA) was scanned using computerized tomography (CT) pre and post training. It was concluded that after twelve weeks of training, there was a 4-5% increase in CSA among each of the three bouts but no significant differences across the training bouts, indicating each mode had similar increases in muscle size (36).

In 2004, Adams et al. tested the hypothesis that each of the three modes of resistance training produced similar muscle hypertrophy responses with the use of a rat model. The rats were given electrical stimulation to simulate muscle activation. Muscle DNA and RNA concentrations along with medial gastrocnemius muscle mass were analyzed. The rats were divided into three groups: isometric, concentric, and eccentric

contraction with one leg serving as the experimental limb and the other serving as the control limb. Each of the rats was electrically stimulated every other day for four weeks. Electrical stimulation parameters were equated across all groups to ensure each group received similar doses. Results indicated that there were relatively similar increases in muscle mass among three groups – 11% eccentric only, 12% concentric only, and 14% isometric only. Also, each of the groups showed similar increases in muscle DNA and RNA concentrations. It was therefore suggested that given similar activation parameters, there were no differences in three modes of resistance training and that all three modes are sufficient in increasing muscle size (1).

In 2007, Wernbom et al. performed a systematic review of literature comparing the three resistance training modes to studies that measure changes to quadriceps cross sectional area with resistance training. The research indicated that on average, training 3 days/ week for 12 weeks, performing 5-6 sets of 10 repetitions of exercises on the quadriceps, resulting in an average of 5.8% and 6.1% increase in CSA in eccentric only and concentric only exercises, respectively(5-7, 33, 34, 50, 52, 60, 61, 64, 69). It was also demonstrated that performing isometric only exercises, training 3days/week for 21 weeks, CSA increased on average of 8.9% (19, 36, 38-40, 59, 69). The overall evidences indicated that either type of resistance training, given adequate intensity, frequency, and volume, is sufficient enough to increase muscle size.

Stretching and Muscle Adaptation

Vandenburg and Kaufman was one of the first research teams showing that static stretch induces hypertrophic responses by mechanically stretching cultured chicken

skeletal muscle cells (68). Stretching is a mechanical stimulus that causes fiber lengthening, which stimulates contractile protein myofibril synthesis at the myotendinous junction (4). It has been first suggested that the increase of fiber lengthening was due to the addition of serial sacromeres at myotendinous junction. Adding new sacromeres to existing myofibrils resulted in an adjustment of length tension curve (26). Several studies have shown that stretch is an important factor for the increase in new serial sacromeres (22, 29, 47, 70). In 1964, Goldspink showed that stretching post-natal skeletal fibers led to the addition of sacromeres to existing ends of myofibrils (24). Dix and Eisenberg analyzed passive stretching and muscle adaptation of tibialis anterior (TA) muscle using rabbit model. The hind limb was placed in a cast to induce full plantar flexion stretch and muscle analysis was assessed on day 4 and day 6. Overall, there was an in 130% and 129% increase in TA muscle mass from day 4 and day 6 of stretching, respectively. Also, TA length was increased 111% and 118% in day 4 and day 6 stretching bouts (12). Dix and Eisenberg further indicated that there was in increase in the protein, vinculin -amajor component of myofibril attachment to myotendinous junction, indicating the attachment of new fibrils. They also observed greater concentration of T-tubules, sacroplasmic reticulum, Golgi apparatus, and sacromeres, all key components needed for muscle formation (12). Another study concluded that by stretching an adult rat soleus for 40mins/days, 3 sessions/wk, led to increases in serial sarcomere and CSA (23).

Stretching and Muscle Gene Expression

Since it has been demonstrated that the stretch causes fiber lengthening, it also has been demonstrated that stretch induces protein synthesis. In order to provide constant and

consistent force due to stretch, new muscle fibers must be synthesized. Goldspink et al. were one of the first to suggest that stretch increases protein synthesis and upregulated muscle gene transcription (25, 41). Several pathways have been implicated that are responsible for myogenesis due to stretch. One is myogenic regulatory factors (MRFs), which are a family of skeletal muscle specific transcription factors that control several muscle gene expression (28). It is composed of four members: myogenic differentiation (MyoD), myogenic factor 5, myogenin, and myogenic regulatory factor 4 (MRF4). MRFs assists in the establishment of myoblasts and myofibers (44, 57). Several studies correlated upregulation of MRFs in stretch induced hypertrophy (8, 28, 42, 43). Gomes et al. found by passively stretching rat soleus one day for 30 minutes, there was an overall 300% increase in MyoD mRNA expression (28).

Another pathway is mechano-growth factor (MGF). MGF is an isoform of IGF-1 found in the liver, and this isoform is only expressed in skeletal muscle in response to exercise or stretch (48, 71). MGF is responsible for local tissue repair, maintenance and remodeling of muscle. Mckoy et al. compared MGF upregulation responses to three stimuli using rabbit model: stretch only, electrical stimulation only, and stretch + electrical stimulation. The results implied that the stretch only group provided greater expression of MGF, and stretch + electrical stimulation group had greater expression of MGF compared to stretch only, while electrical stimulation only had no effect (47), further indicating that stretch is the stimulus for the upregulation of MGF. Goldspink et al. compared MGF biological activity and local action on the TA muscle two weeks after injecting MGF cDNA directly into the muscle. Results indicated that mRNA of MGF

was detected after mechanical stimulation of the muscle and mRNA of MGF was still detected at resting levels (25).

Not only does stretch induce muscle gene expression, but it also has the capability to activate satellite cells. Satellite cells are myogenic stems cells located between basement membrane and sarcolemma. Tatsumi et al. (63) suggested that stretch caused activation of satellite cells through activation hepatic growth factor (HGF). HGF increases activation of satellite cells and causes them to enter the muscle and stimulates new muscle fiber formation. It is believed that HGF is activated by a mechanical stimulus. Tatsumi used 9 mo. - old rat satellite cell cultures, stretched them in 12s intervals and analyzed them at 12, 24, and 36 hr. points. They found HGF activated satellite cells and laso found HGF in abundance in extracellular matrices of muscle fibers (63).

Stretching and Flexibility

The increase in range of motion of muscle is due to viscoelastic behavior of muscle. One study suggests that passive stretching brings adaptive responses to the connective tissue around the myotendinous junction , allowing the junction to become more compliant and more resistant to higher stress loads brought on by daily movement of life (17). As previously stated, Dix and Eisenberg demonstrated that there were increases in contractile proteins, vinculin, talin, and α actin (attaches myofibrils to myotendinous junction) (12). Several studies have indicated that passive stretching increases dorsiflexion range of motion. Guissard et al. trained twelve women using the following exercises: standing calf stretch only, standing calf stretch with foot on the

wall, sitting calf stretch, and standing calf stretch on steps. Each training group performed a total of 30 stretch sessions at 10 minutes/stretch. The results showed that compared to the first and last session, dorsiflexion increased 30% in all training groups (30). Another study compared static passive stretching to ballistic stretching. In this study subjects were randomized into three groups: static stretch, ballistic stretch, and control group. The training study lasted 6 weeks, with stretch sessions lasting 20s. The results indicated that both types of stretching increase dorsiflexion range of motion, with no differences between stretching groups, implying that both types of stretching techniques are capable of reducing muscle-tendon stiffness and increasing range of motion (45). A systematic review of literature focusing on stretching to dorsiflexion range of motion was performed by Radford et al. in 2006. The conclusion of this review was that on average, after performing static stretching for 15 minutes or less, resulted in 2.07° increase in dorsiflexion ROM, 15-30 minutes = 3.03° increase, and >30 minutes = 2.49° increase in ROM (56). This suggests that an half an hour of stretching at the most, produced the most increase in dorsiflexion ROM.

MRI Analysis

Magnetic resonance imaging (MRI) provides anatomic details of soft tissues such as muscle, tendon, cartilage, and organs (2). MRI signals are generated using a powerful static magnetic field combined with varying magnetic fields and excitation of proton's nuclei with radio frequency energy. The radio frequency increases the energy state of the proton's nuclei, which gives off a detectable signal once the radio frequency excitation is turned off and the proton nuclei relaxes back to its original energy state. (2). There are

two forms of signal relaxation: T_1 and T_2 relaxation. Adams et al., defined T_1 relaxation as the loss of energy to surrounding nuclei with similar frequencies and defines T_2 relaxation as the interaction between excited nuclei and any other magnetic field with no transfer of energy (2). In today's imaging world, T_1 relaxation imaging is used to highlight fat in a tissue, and T_2 relaxation is used to highlight water (muscle) (2).

Over the years, MRI has been used to analyze muscle adaptation responses to exercise. Fisher et al. (14) and Adams et al. (2) demonstrated the use of MRI analysis when performing a graded exercise assessment. It showed that with increased intensity there was increased in skeletal muscle contrast. This increase in skeletal intensity in MRI was due to changes in water distribution in the skeletal muscle (3, 37). MRI, more importantly, showed which muscle groups were activated during the graded exercise assessment(2, 14). In 1992, Adams et al. (2) compared electromyography (EMG) of muscle activation to T₂ weighted imaging. Seven participants performed five sets of 10 repetitions of eccentric and concentric dumbbell curls at 40%, 60%, and 50% 1RM. EMG and MRI scans of triceps and biceps of arm were analyzed. The results indicated that there was a relationship between EMG muscle activation and increase intensity of MRI scans in triceps and biceps of participants. In 1995, Ploutz-Snyder et al. (54) tested the effect of skeletal muscle unloading use during resistance training. Seven participants had their lower leg suspended to produce the effect of unloading for five weeks. After five weeks of unloading, each participants of 5 sets of 10 repetitions of concentric knee extension at 25, 40, 55, and 70% 1RM. MRI scans quadriceps femoris muscle groups were taken pre and post training. MR imaging showed greater contrast intensity in

trained quadriceps femoris muscle groups compared to pre training quadriceps. This indicates that more of the muscle group was activated after five weeks of unloading.

Another use of MRI is the calculation of muscle volume. In prior years of muscle scanning, muscle size was calculated using CSA only and this was done on a specific part of the muscle, not the entire length of the muscle (67). Recently, muscle volume calculation has become the standard for calculation muscle size. Tracey et al. (67) have indicated that muscle volume is more accurate than CSA for it: 1) measures the whole length of the muscle and 2) is a close estimation of physiological cross sectional area, which more closely association with maximal muscle force (15, 16, 55, 67). In 1995, Ploutz-Snyder et al. (53) compared the effect of muscle volume to resistance training. Eight participants performed 6 sets of 10 repetitions of barbell squats until fatigue. MR images of vastus lateralis, adductor, hamstring, rectus femoris muscles were collected pre and post training. The results showed that there was a 9% and 5% increase in rectus femoris and hamstring muscle groups immediately after training, but no change in adductor, vastus lateralis muscle size (53). In summary, MRI has become a valuable and precise measurement tool to measure changes in muscle volume due to training, whether through resistance or aerobic exercise.

CHAPTER THREE

THE INFLUENCE OF CHRONIC STRETCH ON THE GASTROCNEMIUS MUSCLES OF ABLE BODIED ADULTS¹

¹Emma Walker and Kevin K. McCully. To be submitted to Dynamic Medicine

Abstract

To improve strength, numerous methods have been suggested as alternatives to resistance training. One method of interest is passive chronic stretching. The hypothesis was that chronic stretching will result in increase in muscle mass as compared to strength training and that chronic stretch will increase ankle dorsiflexion angle. Two groups either stretch or strength trained for eight weeks. MRI analysis was used to evaluate gastrocnemius muscle mass before and after training. There were no differences in muscle mass pre and post training in the two groups. Chronic stretch did increase ankle passive dorsiflexion ROM. It can be concluded that chronic stretch did not provide enough stimuli to induce muscle hypertrophy.

INDEX WORDS: chronic stretch, gastrocnemius

Introduction

One of the best ways to reverse muscle atrophy is through resistance training. Over recent years, numerous findings supported the efficacy in increasing muscle mass of three modes of resistance training – eccentric, concentric, isometric training (30). Muscle hypertrophy through resistance training has been associated with increased physical function and reduced risk of health problems in a number of populations, including spinal cord injuries and the elderly. Mahoney et al. (19) showed that after twelve weeks of neuromuscular electric stimulation – induced resistance training in spinal cord injured patients, there was a 35 and 39% increase in left and right quadriceps CSA and a decline in plasma glucose level, a strong indicator of diabetes mellitus. Hunter et al. (14) meta analysis of the effects of resistance training concluded that resistance training increased muscle hypertrophy, thereby increasing the ability to perform daily living activities.

Resistance training however, can be difficult to perform by some people with muscle atrophy, whether due to limited motor control through age, disease, or injury. There have been numerous alternatives to resistance training suggested, including chronic stretch. In this study, chronic stretch is defined as using a mechanical stimulus to increase muscle adaptation responses. Stretching has been used mainly for increasing range of motion (12, 13). More recently, researchers have observed that stretching can perhaps increase muscle mass in animal studies. (5, 6, 9, 10, 20, 29). Gomes et al., found that passively stretching the soleus of rats for one thirty-minute bout, increased myoD mRNA concentration, which is part of the myogenic regulator family that controls myogenesis, indicating upregulation of muscle synthesis (11). Tatsumi et al. (28) reported increases in satellite cells, muscle stem cells, in rats after twelve hours of chronic stretching. Another study, using rat model, demonstrated

that either fast or slow chronic stretching bouts produced a 10% and 13% increase in muscle size, respectively (27).

To our knowledge, there has been limited research into muscle adaptation responses to chronic stretch for humans. The majority of stretching studies in the human population focused mainly on increasing flexibility. The overall evidence demonstrated that chronic stretch induced muscle hypertrophy utilized invasive animal models; therefore, the purpose of this study was to determine if chronic stretching would induce similar muscle hypertrophy responses in humans as previously reported for animals.

Methods

Participants

Table 1 contains the physical characteristics of participants in each of the group. Fourteen healthy males and females aged 18-22 years were recruited and randomized into two training groups: stretch training and strength training. The study was conducted with the approval of the Institutional Review Board at the University of Georgia. All subjects filled out health questionnaires and provided written consent to participate in the study. All participants reported the absence of the following exclusion criteria for the study: 1) highly endurance trained or resistance trained, 2) orthopedic injury below the knee, 3) other musculoskeletal disorders, 4) psychological disorders including claustrophobia and 5), metal implants.

Study Design

Study design was an experimental pre-post design. Participants were randomized into two training groups – stretch training or strength training. Within each group, each of the

participants' dominant and non-dominant legs was randomized into either control or experimental leg.

Training Session

The training period lasted eight weeks. All participants had MRI before and after training period. Each participant trained three days/week on nonconsecutive days.

<u>Stretch Training Group</u>: Each participant was placed in an upright position on a comfortable stretching mattress (*Stretching Mattress* ®, Orangeburg, NY). Both legs were extended to 180° (full extension). A researcher placed the *Night Splint*® on the experimental leg and the device was secured properly. Once the device was secured and the participant was comfortable, the *Night Splint*® was adjusted to the maximal stretch dorsiflexion position that the participant could tolerate. Once maximal dorsiflexion position was attained, the participants remained in the stretched position for thirty minutes. The dorsiflexion position was increased in some subjects during the thirty minute session to insure maximal stretch position.

<u>Strength Group:</u> Each participant performed plantar flexion calf exercises using *Life Fitness* Horizontal Calf Machine®. One-repetition maximum (1RM) was measured prior to start of training study. Participants sat in an upright position with both legs extended 180° to ensure full knee extension. The machine was adjusted to ensure full knee extension. Once the adjustment was made, 1RM was determined on the experimental leg by the maximum amount of weight that the participant can lift while performing a 2s plantar flexion contraction of the experimental leg. Once the weight has been set, the participant performed

three sets of 10 repetitions with one minute rest between each set using experimental leg only.

MRI Analysis

The volume of the calf muscles was determined using MRI collected with a 3T GE Scanner®. The general approach was based on that of previous studies (1, 2, 16, 19, 23-25). MRI scans were done a day before training sessions and a day after the training session. The participant laid in supine position inside the magnet and a torso coil (40cm in diameter) placed over both legs with both legs extended 180°. Both feet were secured with tape to ensure no movements took place while imaging was performed. A dielectric pad was placed over the legs to minimize distortion produced by the magnet. To ensure the entire calf muscle was imaged, MRI scans started from the patella and ended at the talocrural joint (ankle). The pulse sequence consisted of a T2-weighted fast spin echo sequence (30cm field of view; 20 slices; 1mm slice thickness; 10mm slice spacing; 3 NEX; 512 x 512 matrix; total scan time 8mins 10 seconds). MR images were transferred to a computer for calculations of muscle CSA using modified version WinVessel (2.01) written by Ronald A. Meyer of Michigan State University. A region of interest (ROI) was established for gastrocnemius by tracing around the image of the muscle. The CSA was calculated after spatial calibration. Muscle volume was calculated based upon the sum of CSA of 20 images multiplied by image slice thickness (0.1) and spacing between each image (1.0cm). MRI analysis technique is a very tedious process that required excellent hand and eye coordination and the ability to recognized different muscle group of interest. To ensure that MRI analysis was consistent, only one researcher performed all analysis of participant pre and post training images. Each

image was analyzed three times to ensure consistently between measures. A representative MRI image of gastrocnemius muscles is shown in Figure 1. Figure 2 shows a histogram of muscle cross sectional area from all the images collected on both legs.

Flexibility Measurement

Stretch Group participants' flexibility was assessed using goniometry measurement (21, 22). Briefly, participants were seated knee extended 180°. The talocrural joint was allowed to hang over freely to ensure accurate measurements. The middle of talocrural joint was used bony landmark for goniometry measurement. The center of the joint was marked, to ensure consistent measurements throughout training sessions, and used to place the goniometer with the field arm aligned with fibula and the movable arm aligned with the fifth metatarsal of the foot. Once alignment was completed, researchers flexed the talocrural joint to the maximal amount of dorsiflexion tolerated by the participants. Three measurements were taken and averaged. Flexibility measurements were taken before and after each of the stretch training sessions. Flexibility was measured as the difference between neutral (90°) and the maximum tolerated dorsiflexion angle.

Statistical Analysis

All analysis was conducted using SPSS v. 15.0 for Windows (SPSS, Inc. Chicago, IL). Muscle volume was assessed using a 2x2 ANOVA to compare leg (experimental and control) time (pre and post training) for each stretch and strength groups. Flexibility measurements were evaluated using a 2x2 ANOVA to compare session (before and after a stretch session) and time (pre and post training). Interpretation of the analysis used statistical significance level of $\alpha < 0.05$. All values were reported as means and (standard deviations).

Results

Compliance of training study for stretch and strength groups were 82% and 77%, respectively (see Table 1). Correlation of MRI analysis technique was performed to show consistent and precise analysis of images across groups, subjects, control and experimental legs and pre and post training and the results of the MRI correlation analysis are shown in figures 3-4. Across the control leg, the reliability coefficient (R^2) was 0.957 and experimental leg, R^2 was 0.872.

Pre and post medial gastrocnemius volume of control and experimental data are presented in Table 2 and Figure 5. A 2x2 ANOVA compared stretch and strength training to muscle volume, with statistical analysis of stretch and strength groups are represented in Tables 3 and 4. In stretching group, there were no main effect of stretch training for muscle volume as a result of training, with a statistical value of F(1,8) 2.53; p = 0.34. With a statistical value of F(1,8) 0.57; p = 0.47, there were no main effect of pre and post measurement due to stretch training. In comparing an interaction effect between pre and post measurements and control and experimental leg, the results indicated that there were no interaction between time and limb with a statistical value of F(1,8) 0.94; p = 0.36.

In strength training, there was no main effect of resistance training to muscle volume with a statistical value of F(1,4) 1.09; p = 0.34. Statistical analysis of pre and post training due to strength training was F(1,4) 0.04; p= 0.86, indicating no main effect of pre and post training due to strength training. In comparing an interaction effect between pre and post

measurements and control and experimental leg, the results indicated that there were no interaction between time and limb with a statistical value of F(1,4) 0.29; p = 0.62 due strength training.

The statistical analysis and results for the flexibility tests are presented in Table 5 and 6; respectively, and in Figure 6. Maximum doriflexion angle was not different before and after a bout of stretching, but was different pre and post training for the stretch group. The 2x2 ANOVA were F(1,8) = 3.57 p = 0.10, for an effect of acute stretch, and was F(1,8) 107.1; p= 0.0001 for stretch training. There was also no interaction effect between the acute effect of stretch and the training effect of stretch F(1,8) = 0.35.

Discussion

The primary finding of this study is that there was no main effect of chronic stretch training to muscle mass in able bodied adults. This was not anticipated as previous studies, mostly in animal models, concluded that chronic stretch increases muscle mass (4, 11, 17, 18). It is not clear why we did not see a hypertrophy response to chronic stretch. Several possibilities exist: length of training programs, magnitude of stretch, length of stretch training session, and inclusion of moderate active populations. One possibility is that the program was not long enough. The length of the study was 8 weeks, which is relatively short compared to other training studies, which last on average 12 weeks for resistance training (15, 30). Another possibility is that we did not stretch the subjects enough. The magnitude of the stretch was as much as the subjects said they could tolerate. It is possible that greater stretch is necessary. It was difficult to measure the approximate degree of stretch in the *Night Splint* due to the configuration of the device, so magnitude of the stretch in the boot

is unknown. It is possible that we did not have the subjects stretch for long enough or often enough. However, previous resistance training programs have been successful with equal or even fewer training sessions per week, and our 30 minute stretch should have been comparable to a calf resistance training program in terms of duration of stimulus. It maybe that able bodied subjects show less responsiveness to stretch that previously atrophied individuals or muscles. We did not monitor normal daily activity and therefore it may be possible that their normal activity program could have interacted in the ability to induce a hypertrophy response due to chronic stretching. Further studies will be needed to clarify different findings.

There was no main effect of resistance training to muscle volume. This was not expected as the purpose of the strength group was to produce expected increases in muscle mass due to resistance training (30). However, a potential reason for this negative finding was the level of resistance training. The resistance training protocol had subjects train using 50% of 1RM throughout the study. Previous studies have reported training intensities from 70% to 90% of 1RM (3, 15). The subjects in this study were moderately active and the level of resistance training may not have been sufficient to induce hypertrophy.

While we did not find pre and post training differences in muscle mass, we did find a good agreement between our pre and post measurements within subjects. This indicates that we were able to reproduce muscle volume measurements.

Majority of the strength trained participants were moderately active it may be suggested that training at 50% 1RM would not have brought about adaptive muscle responses normally seen in resistance training, suggesting that they were training below their

normal intensity. Even through we had a strict screening process, it was difficult to get sedentary to light physical active participants on a college campus.

It is of interest to know that we found that the stretching program caused an increase in the maximum dorsiflexion angle This increase in angle was consistent with an increase in joint and/ or muscle flexibility Previous studies have shown that chronic stretching (7, 8, 26), although not performed as continuous as this study, can increase flexibility in a similar manner (26). We did not see an effect of stretching on dorsiflexion angle pre and post session, although previous studies have suggested that this occurs (26). While we did not see changes in muscle mass with stretching, the increase in flexibility suggests that our stretching program was influencing the muscle to some degree. So while the muscles show plasticity to chronic stretch, it was not in terms of muscle hypertrophy.

The original number of participants prior to MRI scans, was 24, 10 dropped out due to scheduling conflicts, one with pregnancy, several non-related injuries prior to the start of the study, and one noncompliant participant. Based upon statistical analysis program, the statistical number needed to detect a difference was 14 - 18 participants at effect size = 0.8, $\alpha = 0.05$, power 0.7, so enough participants were tested. Majority of the dropout occurred in the strength training group, which could have played a role in seeing no main effect in muscle volume for resistance training. Compliance for the study was extremely high, shown in Table 1, 82% and 77% in stretch and strength train group, respectively, which ruled out the notion that perhaps not enough training session were completed to see a change in muscle mass. Another theory is that animals show greater muscle adaptation to a particular stimulus whether resistant training or chronic stretching, this is the reason why chronic stretching seems to work so well in the rat model experimentation.

Based upon figures 4-5, reliability of each leg were extremely high, R^2 of 0.96 and 0.87 among control pre /post and experimental pre/post measurements. The correlation of experimental leg was lower, but this was due to some training effect, though not significantly found, among the two groups.

Conclusions

Our results showed that chronic stretch did not increase muscle mass over the eight weeks of training, nor did strength training. These results did not support our hypothesis that chronic stretch might be used in place of resistance exercise to induce muscle hypertrophy. While a long duration study might be necessary, it is also possible that inactive subjects might be more sensitive to chronic stretch. Future studies may include using active stretching to provide a greater adaptive response to muscle mass.

Group	Height (cm)	Mass (kg)	Age (yr)	Training Session
			•	Compliance (%)
Stretch	168.7 (7.1)	143.3 (15.6)	22.6 (2.7)	81.9 (20.8)
Strength	168.1 (15.0)	145.0 (37.3)	22.2 (2.8)	77.3 (19.2)

Table 1: Physical characteristics of N=9 stretch participants and N=5 of strength participants. Values are mean and (standard deviations).

Gastrocnemius (volume cm ³)						
Control			Experimental			
Group	Pre	post	%∆ Volume	Pre	Post	%∆ Volume
Stretch	144.2	140.0	-2.9	129.7	129.5	1.1
	(44.7)	(41.9)		(32.5)	(29.0)	
Strength	146.5	146.1	-1.7	136.9	139.7	1.6
	(48.6)	(53.6)		(50.1)	(58.5)	

 Table 2: Volume analysis of gastrocnemius of stretch participants and strength participants. Volumes are mean and (standard deviations).

Stretch Group			
	Leg (Control vs. Experimental)	Time (Pre Training vs. Post	Leg x Time
		Training)	
F- value (1,8)	2.53	0.57	0.94
p-value	0.15	0.47	0.36
Effect size (η^2)	0.24	0.06	0.11

 Table 3: Statistical analysis of stretch training group.

Strength Group				
	Leg (Control vs. Experimental)	Time (Pre Training vs. Post Training)	Leg x Time	
F- value (1,4)	1.09	0.04	0.29	
p-value	0.34	0.86	0.62	
Effect size (η^2)	0.21	0.01	0.07	

Table 4. Statistical analysis of stength training group.

Maximum Dorsiflexion Angle (Stretch Group Only)			
	Session (pre- stretch vs. post- stretch)	Time (Pre training vs. Post training)	Session x Time
F- value (1,8)	107.0	3.57	1.00
p-value	< 0.001	0.10	0.35

 Table 5: Statistical analysis of maximum dorsiflexion angle of stretch training group only.

Maximal Dorsiflexion Angle (Degree)

	Pre	Post
First Training Session	8.4 (7.3)	9.3 (8.9)
Last Training Session	34.5 (5.8)	37.0 (6.3)

Table 6: Dorsiflexion Flexibility Analysis of stretch participants.Degree measurements are means and (standard deviations).

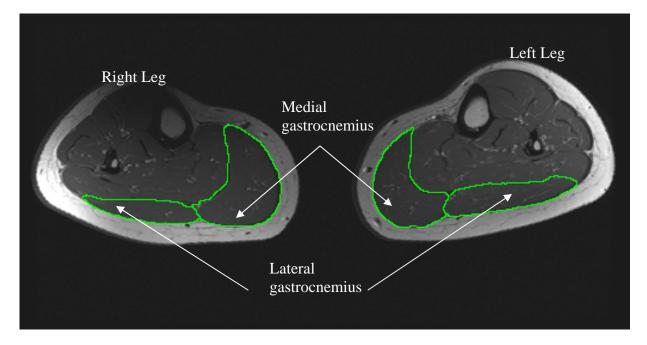


Figure 1: MRI scans of gastrocnemius muscle images of a right and left leg. The total volume of the medial gastrocnemius was calculated from medial gastrocnemius cross sectional area across 20 images.

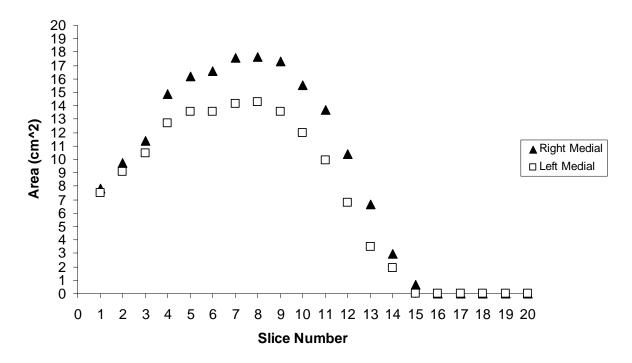


Figure 2: This figure shows representative cross sectional area (CSA) from the medial gastrocnemius muscles of one subject. The total CSA was 226.0 cm² the right gastrocnemius and 237.4 cm³ for the left gastrocnemius.

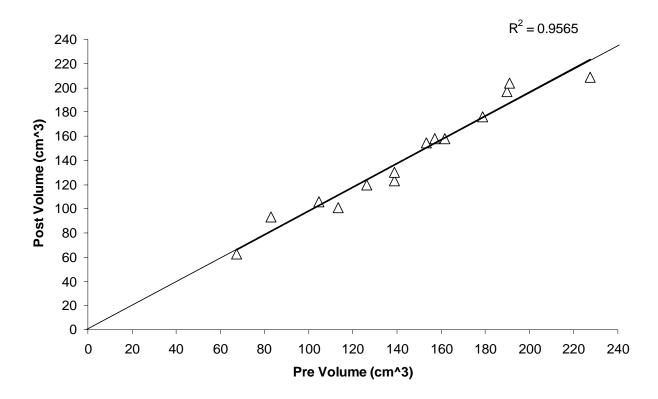


Figure 3: Correlation analysis of MRI analysis of control leg measured before and after the training period.

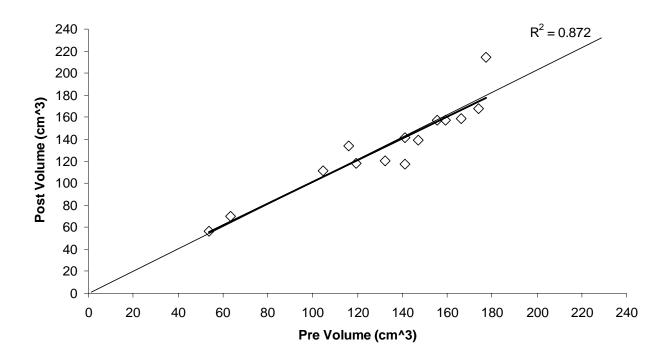


Figure 4 Correlation analysis of muscle volumes of experimental leg before and after the training period.

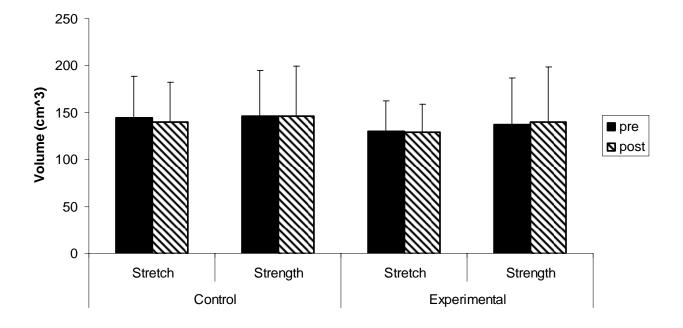


Figure 5. Muscle volumes in the stretch group and strength groups before and after the training period. No statistically significant differences were observed between groups, legs, and before and after the training period. Values are means plus standard deviations.

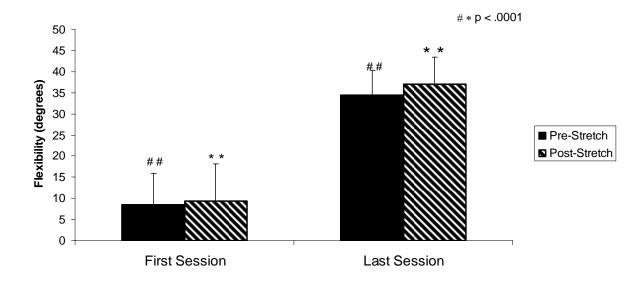


Figure 6. Flexibility measurements of stretch group only comparing acute effect and training effect of stretching. Flexibility measured as the difference between neutral (90°) and the maximum tolerated joint angle was not different before and after a bout of stretching, but was different pre and post stretch training with a statistical value of F(1,8) 107.0; p < .0001.

REFERENCES

1. Adams GR, Duvoisin MR, and Dudley GA. Magnetic resonance imaging and electromyography as indexes of muscle function. *J Appl Physiol* 73: 1578-1583, 1992.

2. **Bickel CS, Slade JM, Haddad F, Adams GR, and Dudley GA**. Acute molecular responses of skeletal muscle to resistance exercise in able-bodied and spinal cord-injured subjects. *J Appl Physiol* 94: 2255-2262, 2003.

3. Blazevich AJ, Cannavan D, Coleman DR, and Horne S. Influence of concentric and eccentric resistance training on architectural adaptation in human quadriceps muscles. *J Appl Physiol* 103: 1565-1575, 2007.

4. **Carson JA, and Booth FW**. Myogenin mRNA is elevated during rapid, slow, and maintenance phases of stretch-induced hypertrophy in chicken slow-tonic muscle. *Pflugers Arch* 435: 850-858, 1998.

5. **De Deyne PG**. Application of passive stretch and its implications for muscle fibers. *Phys Ther* 81: 819-827, 2001.

6. **De Deyne PG**. Formation of sarcomeres in developing myotubes: role of mechanical stretch and contractile activation. *Am J Physiol Cell Physiol* 279: C1801-1811, 2000.

7. **Dix DJ, and Eisenberg BR**. Myosin mRNA accumulation and myofibrillogenesis at the myotendinous junction of stretched muscle fibers. *J Cell Biol* 111: 1885-1894, 1990.

8. **Gajdosik RL, Allred JD, Gabbert HL, and Sonsteng BA**. A stretching program increases the dynamic passive length and passive resistive properties of the calf muscle-tendon unit of unconditioned younger women. *Eur J Appl Physiol* 99: 449-454, 2007.

9. **Goldspink G**. Changes in muscle mass and phenotype and the expression of autocrine and systemic growth factors by muscle in response to stretch and overload. *J Anat* 194 (Pt 3): 323-334, 1999.

Goldspink G, Scutt A, Loughna PT, Wells DJ, Jaenicke T, and Gerlach GF.
 Gene expression in skeletal muscle in response to stretch and force generation. *Am J Physiol* 262: R356-363, 1992.

11. **Gomes AR, Coutinho EL, Franca CN, Polonio J, and Salvini TF**. Effect of one stretch a week applied to the immobilized soleus muscle on rat muscle fiber morphology. *Braz J Med Biol Res* 37: 1473-1480, 2004.

12. **Guissard N, and Duchateau J**. Effect of static stretch training on neural and mechanical properties of the human plantar-flexor muscles. *Muscle Nerve* 29: 248-255, 2004.

13. **Harvey LA, Batty J, Crosbie J, Poulter S, and Herbert RD**. A randomized trial assessing the effects of 4 weeks of daily stretching on ankle mobility in patients with spinal cord injuries. *Arch Phys Med Rehabil* 81: 1340-1347, 2000.

14. **Hunter GR, McCarthy JP, and Bamman MM**. Effects of resistance training on older adults. *Sports medicine (Auckland, NZ* 34: 329-348, 2004.

15. **Jones DA, and Rutherford OM**. Human muscle strength training: the effects of three different regimens and the nature of the resultant changes. *J Physiol* 391: 1-11, 1987.

16. **Kendall TL, Black CD, Elder CP, Gorgey A, and Dudley GA**. Determining the extent of neural activation during maximal effort. *Medicine and science in sports and exercise* 38: 1470-1475, 2006.

17. **Lowe DA, and Alway SE**. Stretch-induced myogenin, MyoD, and MRF4 expression and acute hypertrophy in quail slow-tonic muscle are not dependent upon satellite cell proliferation. *Cell Tissue Res* 296: 531-539, 1999.

 Lowe DA, Lund T, and Alway SE. Hypertrophy-stimulated myogenic regulatory factor mRNA increases are attenuated in fast muscle of aged quails. *Am J Physiol* 275: C155-162, 1998.

Mahoney ET, Bickel CS, Elder C, Black C, Slade JM, Apple D, Jr., and Dudley
 GA. Changes in skeletal muscle size and glucose tolerance with electrically stimulated
 resistance training in subjects with chronic spinal cord injury. *Arch Phys Med Rehabil* 86:
 1502-1504, 2005.

20. McKoy G, Ashley W, Mander J, Yang SY, Williams N, Russell B, and Goldspink G. Expression of insulin growth factor-1 splice variants and structural genes in rabbit skeletal muscle induced by stretch and stimulation. *J Physiol* 516 (Pt 2): 583-592, 1999.

21. **Menadue C, Raymond J, Kilbreath SL, Refshauge KM, and Adams R**. Reliability of two goniometric methods of measuring active inversion and eversion range of motion at the ankle. *BMC musculoskeletal disorders* 7: 60, 2006.

22. Norkin CCDJW editor. *Measurement of joint: A guide to goniometry*. PhiladelphiaF.A. Davis, 1995.

Ploutz-Snyder LL, Convertino VA, and Dudley GA. Resistance exercise-induced fluid shifts: change in active muscle size and plasma volume. *Am J Physiol* 269: R536-543, 1995.

24. **Ploutz-Snyder LL, Tesch PA, Crittenden DJ, and Dudley GA**. Effect of unweighting on skeletal muscle use during exercise. *J Appl Physiol* 79: 168-175, 1995.

25. **Ploutz LL, Tesch PA, Biro RL, and Dudley GA**. Effect of resistance training on muscle use during exercise. *J Appl Physiol* 76: 1675-1681, 1994.

26. **Radford JA, Burns J, Buchbinder R, Landorf KB, and Cook C**. Does stretching increase ankle dorsiflexion range of motion? A systematic review. *British journal of sports medicine* 40: 870-875; discussion 875, 2006.

27. **Stauber WT, Miller GR, Grimmett JG, and Knack KK**. Adaptation of rat soleus muscles to 4 wk of intermittent strain. *J Appl Physiol* 77: 58-62, 1994.

28. **Tatsumi R, Sheehan SM, Iwasaki H, Hattori A, and Allen RE**. Mechanical stretch induces activation of skeletal muscle satellite cells in vitro. *Exp Cell Res* 267: 107-114, 2001.

29. **Tidball JG**. Mechanical signal transduction in skeletal muscle growth and adaptation. *J Appl Physiol* 98: 1900-1908, 2005.

30. Wernbom M, Augustsson J, and Thomee R. The influence of frequency, intensity, volume and mode of strength training on whole muscle cross-sectional area in humans. *Sports medicine (Auckland, NZ* 37: 225-264, 2007.

CHAPTER FOUR

CLOSING REMARKS

Muscle mass plays an important role in everyday living- from assisting with transport, i.e. walking, biking, running, etc., to communication- speech, writing, body language. Maintaining and/or increase muscle mass is an important factor for increasing quality of life. One way to maintain or increase muscle mass is by resistance training. As people become older and/or those become severely injured, i.e. spinal cord injury, resistance training may not be an option. We attempted to address this need by through the technique of passive stretch. Tentatively, our results indicate that there was no main effect of passive chronic stretching to increase muscle volume. It is possible that able bodied individuals are less tolerant to passive stretch than injured bodied but could have been more receptive to active stretching. Another possibility is the stretching session was not long enough to induce a hypertrophy response. It could be that passive stretching may not be a sufficient mechanism to overcome muscle atrophy.

Though we did not see induced hypertrophy response in the study, we did see an increase in dorsiflexion flexibility. These results could have relevant implications in that in some populations increasing flexibility might be useful even if muscle did not increase in size.

Overall, I believe the study went well. Recruitment of participants went extremely well, by using listservs. of various departments across campus, a total of 24 people were initially screen and approved for the study. The study started after spring break and lasted to the first part of the first session of summer school, many of those could not commit to the study. Most of the dropout occurred in the strength group because many of the people

wanted to be in the stretch group. Since my stretch group was my primary focus, strength group trained on their own. It would have been greatly appreciated that an assistant was assigned to monitor the strength training group, but given participants schedule, this would have been difficult on both parties. Overall, all of my participants were extremely nice and honorable when it came to the study and compliance was high.

I was very pleased with MRI scans of the gastrocnemius given that new MRI scanner was bought by the university within eight months of the study and also given the initial problems occurring with a new device, the scanner provided me with great images of the gastrocnemius. I had no difficulty in analyzing my images.

Two problems I would like to address in future studies. I would like to have the resistance trained group exercising at a higher intensity of their 1RM. The group in the study was training at 50% of 1RM, which is a low training rate. The purpose of them training higher was to insure an increase in muscle mass between the two groups.

Second problem about the study was the use of a *Night Splint*® to provide passive stretch to the participants. Though, I personally tested the apparatus, along with several of my colleagues, I questioned whether it provided an enough stimulus to induce muscle hypertrophy. All participants in the stretch group commented that they did indeed felt that the apparatus was stretching them, I still have doubts. In the future, if possible, I would to investigate whether there was upregulation of muscle gene transcription in response to stretch in human population.

REFERENCES

1. Adams GR, Cheng DC, Haddad F, and Baldwin KM. Skeletal muscle hypertrophy in response to isometric, lengthening, and shortening training bouts of equivalent duration. *J Appl Physiol* 96: 1613-1618, 2004.

2. Adams GR, Duvoisin MR, and Dudley GA. Magnetic resonance imaging and electromyography as indexes of muscle function. *J Appl Physiol* 73: 1578-1583, 1992.

3. Akima H, Ushiyama J, Kubo J, Tonosaki S, Itoh M, Kawakami Y, Fukuoka H, Kanehisa H, and Fukunaga T. Resistance training during unweighting maintains muscle size and function in human calf. *Med Sci Sports Exerc* 35: 655-662, 2003.

4. **Antin PB, Tokunaka S, Nachmias VT, and Holtzer H**. Role of stress fiber-like structures in assembling nascent myofibrils in myosheets recovering from exposure to ethyl methanesulfonate. *J Cell Biol* 102: 1464-1479, 1986.

5. Bell GJ, Petersen SR, MacLean I, Reid DC, and Quinney HA. Effect of high velocity resistance training on peak torque, cross sectional area and myofibrillar ATPase activity. *The Journal of sports medicine and physical fitness* 32: 10-18, 1992.

6. Bell GJ, Petersen SR, Wessel J, Bagnall K, and Quinney HA. Adaptations to endurance and low velocity resistance training performed in a sequence. *Canadian journal of sport sciences = Journal canadien des sciences du sport* 16: 186-192, 1991.

7. Bell GJ, Petersen SR, Wessel J, Bagnall K, and Quinney HA. Physiological adaptations to concurrent endurance training and low velocity resistance training. *Int J Sports Med* 12: 384-390, 1991.

8. **Bickel CS, Slade JM, Haddad F, Adams GR, and Dudley GA**. Acute molecular responses of skeletal muscle to resistance exercise in able-bodied and spinal cord-injured subjects. *J Appl Physiol* 94: 2255-2262, 2003.

9. Blazevich AJ, Cannavan D, Coleman DR, and Horne S. Influence of concentric and eccentric resistance training on architectural adaptation in human quadriceps muscles. *J Appl Physiol* 103: 1565-1575, 2007.

10. **Carson JA, and Booth FW**. Myogenin mRNA is elevated during rapid, slow, and maintenance phases of stretch-induced hypertrophy in chicken slow-tonic muscle. *Pflugers Arch* 435: 850-858, 1998.

 Castro MJ, Apple DF, Jr., Staron RS, Campos GE, and Dudley GA. Influence of complete spinal cord injury on skeletal muscle within 6 mo of injury. *J Appl Physiol* 86: 350-358, 1999.

12. **De Deyne PG**. Application of passive stretch and its implications for muscle fibers. *Phys Ther* 81: 819-827, 2001.

13. **De Deyne PG**. Formation of sarcomeres in developing myotubes: role of mechanical stretch and contractile activation. *Am J Physiol Cell Physiol* 279: C1801-1811, 2000.

14. **Dix DJ, and Eisenberg BR**. Myosin mRNA accumulation and myofibrillogenesis at the myotendinous junction of stretched muscle fibers. *J Cell Biol* 111: 1885-1894, 1990.

15. **Evans C**. Spinal Cord Injury VA Office of Research and Development, Health Services Research and Development Services. http://www.hsrd.research.va.gov/queri.

16. **Fisher MJ, Meyer RA, Adams GR, Foley JM, and Potchen EJ**. Direct relationship between proton T2 and exercise intensity in skeletal muscle MR images. *Investigative radiology* 25: 480-485, 1990.

17. Fukunaga T, Roy RR, Shellock FG, Hodgson JA, Day MK, Lee PL, Kwong-Fu H, and Edgerton VR. Physiological cross-sectional area of human leg muscles based on magnetic resonance imaging. *J Orthop Res* 10: 928-934, 1992.

18. **Fukunaga T, Roy RR, Shellock FG, Hodgson JA, and Edgerton VR**. Specific tension of human plantar flexors and dorsiflexors. *J Appl Physiol* 80: 158-165, 1996.

19. **Gajdosik RL, Allred JD, Gabbert HL, and Sonsteng BA**. A stretching program increases the dynamic passive length and passive resistive properties of the calf muscle-tendon unit of unconditioned younger women. *Eur J Appl Physiol* 99: 449-454, 2007.

20. **Gajdosik RL, Vander Linden DW, McNair PJ, Williams AK, and Riggin TJ**. Effects of an eight-week stretching program on the passive-elastic properties and function of the calf muscles of older women. *Clinical biomechanics (Bristol, Avon)* 20: 973-983, 2005.

21. **Garfinkel S, and Cafarelli E**. Relative changes in maximal force, EMG, and muscle cross-sectional area after isometric training. *Med Sci Sports Exerc* 24: 1220-1227, 1992.

22. Garma T, Kobayashi C, Haddad F, Adams GR, Bodell PW, and Baldwin KM. Similar acute molecular responses to equivalent volumes of isometric, lengthening, or shortening mode resistance exercise. *J Appl Physiol* 102: 135-143, 2007.

23. Goldberg AL, Etlinger JD, Goldspink DF, and Jablecki C. Mechanism of work-induced hypertrophy of skeletal muscle. *Medicine and science in sports* 7: 185-198, 1975.

24. **Goldspink G**. Alterations in myofibril size and structure during growth, exercise and changes in environmental tempperature. Bethesda, MD: The American Physiological Society, 1984.

25. **Goldspink G**. Changes in muscle mass and phenotype and the expression of autocrine and systemic growth factors by muscle in response to stretch and overload. *J Anat* 194 (Pt 3): 323-334, 1999.

26. **Goldspink G**. Increase in Length of Skeletal Muscle During Normal Growth. *Nature* 204: 1095-1096, 1964.

27. Goldspink G, Scutt A, Loughna PT, Wells DJ, Jaenicke T, and Gerlach GF. Gene expression in skeletal muscle in response to stretch and force generation. *Am J Physiol* 262: R356-363, 1992.

28. Goldspink G, Williams P, and Simpson H. Gene expression in response to muscle stretch. *Clin Orthop Relat Res* S146-152, 2002.

29. Gomes AR, Coutinho EL, Franca CN, Polonio J, and Salvini TF. Effect of one stretch a week applied to the immobilized soleus muscle on rat muscle fiber morphology. *Braz J Med Biol Res* 37: 1473-1480, 2004.

30. Gomes AR, Soares AG, Peviani S, Nascimento RB, Moriscot AS, and Salvini TF. The effect of 30 minutes of passive stretch of the rat soleus muscle on the myogenic differentiation, myostatin, and atrogin-1 gene expressions. *Archives of physical medicine and rehabilitation* 87: 241-246, 2006.

31. **Griffin GE, Williams PE, and Goldspink G**. Region of longitudinal growth in striated muscle fibres. *Nature: New biology* 232: 28-29, 1971.

32. **Guissard N, and Duchateau J**. Effect of static stretch training on neural and mechanical properties of the human plantar-flexor muscles. *Muscle Nerve* 29: 248-255, 2004.

33. Harvey LA, Batty J, Crosbie J, Poulter S, and Herbert RD. A randomized trial assessing the effects of 4 weeks of daily stretching on ankle mobility in patients with spinal cord injuries. *Arch Phys Med Rehabil* 81: 1340-1347, 2000.

34. **Hetzel A**. The 65 Years and Over Population 2000.

35. **Higbie EJ, Cureton KJ, Warren GL, 3rd, and Prior BM**. Effects of concentric and eccentric training on muscle strength, cross-sectional area, and neural activation. *J Appl Physiol* 81: 2173-2181, 1996.

36. **Housh DJ, Housh TJ, Johnson GO, and Chu WK**. Hypertrophic response to unilateral concentric isokinetic resistance training. *J Appl Physiol* 73: 65-70, 1992.

37. Hunter GR, McCarthy JP, and Bamman MM. Effects of resistance training on older adults. *Sports medicine (Auckland, NZ* 34: 329-348, 2004.

38. Janssen I, Heymsfield, SB., Wang, ZM., and Ross, R. Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr. *J Appl Physiol* 89: 81-88, 2000.

39. Jones DA, and Rutherford OM. Human muscle strength training: the effects of three different regimens and the nature of the resultant changes. *J Physiol* 391: 1-11, 1987.

40. Kendall TL, Black CD, Elder CP, Gorgey A, and Dudley GA. Determining the extent of neural activation during maximal effort. *Medicine and science in sports and exercise* 38: 1470-1475, 2006.

41. **Kinugasa R, Kawakami Y, and Fukunaga T**. Quantitative assessment of skeletal muscle activation using muscle functional MRI. *Magnetic resonance imaging* 24: 639-644, 2006.

42. **Kubo K, Kanehisa H, and Fukunaga T**. Effects of different duration isometric contractions on tendon elasticity in human quadriceps muscles. *J Physiol* 536: 649-655, 2001.

43. Kubo K, Ohgo K, Takeishi R, Yoshinaga K, Tsunoda N, Kanehisa H, and Fukunaga T. Effects of isometric training at different knee angles on the muscle-tendon complex in vivo. *Scandinavian journal of medicine & science in sports* 16: 159-167, 2006.

44. **Kubo K, Yata H, Kanehisa H, and Fukunaga T**. Effects of isometric squat training on the tendon stiffness and jump performance. *Eur J Appl Physiol* 96: 305-314, 2006.

45. Loughna PT, Izumo S, Goldspink G, and Nadal-Ginard B. Disuse and passive stretch cause rapid alterations in expression of developmental and adult contractile protein genes in skeletal muscle. *Development (Cambridge, England)* 109: 217-223, 1990.

46. **Lowe DA, and Alway SE**. Stretch-induced myogenin, MyoD, and MRF4 expression and acute hypertrophy in quail slow-tonic muscle are not dependent upon satellite cell proliferation. *Cell Tissue Res* 296: 531-539, 1999.

47. **Lowe DA, Lund T, and Alway SE**. Hypertrophy-stimulated myogenic regulatory factor mRNA increases are attenuated in fast muscle of aged quails. *Am J Physiol* 275: C155-162, 1998.

48. **Ludolph DC, and Konieczny SF**. Transcription factor families: muscling in on the myogenic program. *Faseb J* 9: 1595-1604, 1995.

49. Mahieu NN, McNair P, De Muynck M, Stevens V, Blanckaert I, Smits N, and Witvrouw E. Effect of static and ballistic stretching on the muscle-tendon tissue properties. *Med Sci Sports Exerc* 39: 494-501, 2007.

50. Mahoney ET, Bickel CS, Elder C, Black C, Slade JM, Apple D, Jr., and Dudley GA. Changes in skeletal muscle size and glucose tolerance with electrically stimulated resistance training in subjects with chronic spinal cord injury. *Arch Phys Med Rehabil* 86: 1502-1504, 2005.

51. **McDonagh MJ, and Davies CT**. Adaptive response of mammalian skeletal muscle to exercise with high loads. *Eur J Appl Physiol Occup Physiol* 52: 139-155, 1984.

52. McKoy G, Ashley W, Mander J, Yang SY, Williams N, Russell B, and Goldspink G. Expression of insulin growth factor-1 splice variants and structural genes in rabbit skeletal muscle induced by stretch and stimulation. *J Physiol* 516 (Pt 2): 583-592, 1999.

53. McKoy G, Hou Y, Yang SY, Vega Avelaira D, Degens H, Goldspink G, and Coulton GR. Expression of Ankrd2 in fast and slow muscles and its response to stretch are consistent with a role in slow muscle function. *J Appl Physiol* 98: 2337-2343; discussion 2320, 2005.

54. **Menadue C, Raymond J, Kilbreath SL, Refshauge KM, and Adams R**. Reliability of two goniometric methods of measuring active inversion and eversion range of motion at the ankle. *BMC musculoskeletal disorders* 7: 60, 2006.

55. **Narici MV, Maganaris CN, Reeves ND, and Capodaglio P**. Effect of aging on human muscle architecture. *J Appl Physiol* 95: 2229-2234, 2003.

56. **Narici MV, Roi GS, Landoni L, Minetti AE, and Cerretelli P**. Changes in force, cross-sectional area and neural activation during strength training and detraining of the human quadriceps. *Eur J Appl Physiol Occup Physiol* 59: 310-319, 1989.

57. **Onambele GL, Narici MV, and Maganaris CN**. Calf muscle-tendon properties and postural balance in old age. *J Appl Physiol* 100: 2048-2056, 2006.

58. **Petersen S, Wessel J, Bagnall K, Wilkins H, Quinney A, and Wenger H**. Influence of concentric resistance training on concentric and eccentric strength. *Arch Phys Med Rehabil* 71: 101-105, 1990.

59. **Ploutz-Snyder LL, Convertino VA, and Dudley GA**. Resistance exerciseinduced fluid shifts: change in active muscle size and plasma volume. *Am J Physiol* 269: R536-543, 1995.

60. **Ploutz-Snyder LL, Tesch PA, Crittenden DJ, and Dudley GA**. Effect of unweighting on skeletal muscle use during exercise. *J Appl Physiol* 79: 168-175, 1995.

61. **Ploutz LL, Tesch PA, Biro RL, and Dudley GA**. Effect of resistance training on muscle use during exercise. *J Appl Physiol* 76: 1675-1681, 1994.

62. **Powell PL, Roy RR, Kanim P, Bello MA, and Edgerton VR**. Predictability of skeletal muscle tension from architectural determinations in guinea pig hindlimbs. *J Appl Physiol* 57: 1715-1721, 1984.

63. **Radford JA, Burns J, Buchbinder R, Landorf KB, and Cook C**. Does stretching increase ankle dorsiflexion range of motion? A systematic review. *British journal of sports medicine* 40: 870-875; discussion 875, 2006.

64. Saborin LaR, MA. The molecular regulation of myogenesis. *Clin Genet* 57: 16-25, 2000.

65. Saladin KS. Anatomy and Physiology: The Unity of Form and Function. New York: McGraw-Hill, 2004.

66. Schott J, McCully K, and Rutherford OM. The role of metabolites in strength training. II. Short versus long isometric contractions. *Eur J Appl Physiol Occup Physiol* 71: 337-341, 1995.

67. Seger JY, Arvidsson B, and Thorstensson A. Specific effects of eccentric and concentric training on muscle strength and morphology in humans. *Eur J Appl Physiol Occup Physiol* 79: 49-57, 1998.

68. Seynnes OR, de Boer M, and Narici MV. Early skeletal muscle hypertrophy and architectural changes in response to high-intensity resistance training. *J Appl Physiol* 102: 368-373, 2007.

69. **Stauber WT, Miller GR, Grimmett JG, and Knack KK**. Adaptation of rat soleus muscles to 4 wk of intermittent strain. *J Appl Physiol* 77: 58-62, 1994.

70. **Tatsumi R, Sheehan SM, Iwasaki H, Hattori A, and Allen RE**. Mechanical stretch induces activation of skeletal muscle satellite cells in vitro. *Exp Cell Res* 267: 107-114, 2001.

71. **Tesch PA, Ekberg A, Lindquist DM, and Trieschmann JT**. Muscle hypertrophy following 5-week resistance training using a non-gravity-dependent exercise system. *Acta Physiol Scand* 180: 89-98, 2004.

72. **Therapists AAoOMP**. Orthopaedic Manual Therapy: Description of Advanced Clinical Practice. 1999, p. 29.

73. **Tidball JG**. Mechanical signal transduction in skeletal muscle growth and adaptation. *J Appl Physiol* 98: 1900-1908, 2005.

74. **Tracy BL, Ivey FM, Jeffrey Metter E, Fleg JL, Siegel EL, and Hurley BF**. A more efficient magnetic resonance imaging-based strategy for measuring quadriceps muscle volume. *Med Sci Sports Exerc* 35: 425-433, 2003.

75. Vandenburgh H, and Kaufman S. In vitro model for stretch-induced hypertrophy of skeletal muscle. *Science* 203: 265-268, 1979.

76. Wernbom M, Augustsson J, and Thomee R. The influence of frequency, intensity, volume and mode of strength training on whole muscle cross-sectional area in humans. *Sports medicine (Auckland, NZ* 37: 225-264, 2007.

77. Williams PE, and Goldspink G. Longitudinal growth of striated muscle fibres. *Journal of cell science* 9: 751-767, 1971.

78. **Yang H, Alnaqeeb M, Simpson H, and Goldspink G**. Changes in muscle fibre type, muscle mass and IGF-I gene expression in rabbit skeletal muscle subjected to stretch. *J Anat* 190 (Pt 4): 613-622, 1997.