

**ECCENTRIC AND CONCENTRIC RESISTANCE EXERCISE  
INDUCED CHANGES ON  
INSULIN SENSITIVITY AND INFLAMMATION**

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the Faculty of the Graduate School  
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**Master of Arts**

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**By**

**TOM ELDER**

**Dr. Tom R. Thomas, Thesis Supervisor**

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The undersigned, appointed by the Dean of Graduate School, have examined the thesis  
entitled

ECCENTRIC AND CONCENTRIC RESISTANCE EXERCISE  
INDUCED CHANGES ON  
INSULIN SENSITIVITY AND INFLAMMATION

Presented by Thomas C. Elder

a candidate for the degree of Master of Arts

and hereby certify in their opinion is worthy of acceptance.

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Tom R. Thomas

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John P. Thyfault

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Stephen P. Sayers

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The path that I have taken to complete my research project has seemed like an uphill struggle the entire way. The schooling was difficult and the research was challenging. I have learned the hard way that the road to success is paved with many failures. In order to overcome these obstacles I had to rely heavily on experience, advice, and hard work from everyone around me.

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## TABLE OF CONTENTS

ACKNOWLEDGEMENTS.....	ii
TABLE OF CONTENTS.....	iii
LIST OF FIGURES.....	iv
LIST OF TABLES.....	v
ABSTRACT.....	vi
INTRODUCTION.....	1
METHODS.....	10
RESULTS.....	24
DISCUSSION.....	35
REFERENCES.....	47
APPENDIX A: EXTENDED LITERATURE REVIEW.....	56
APPENDIX B: INFORMED CONSENT.....	79
APPENDIX C: SUBJECT DATA FORMS.....	87
APPENDIX D: ANOVA TABLES.....	123
APPENDIX E: RAW DATA.....	126

## LIST OF FIGURES

Figure 1. Mechanism of increased insulin sensitivity after resistance exercise.....	9
Figure 2. Experimental design.....	13
Figure 3. Insulin AUCi during OGTT.....	27
Figure 4. Glucose AUCi during OGTT.....	28
Figure 5. Matsuda index during OGTT.....	29
Figure 6. IL-6 measures over time.....	30
Figure 7. TNF $\alpha$ measures over time.....	31
Figure 8. DOMS walking right thigh test.....	33
Figure 9. DOMS walking left thigh test.....	34
Figure 10. DOMS lengthening quadriceps test.....	35
Figure 11. List previous studies analyzing effects of an acute bout of resistance exercise on insulin sensitivity.....	36
Figure 12. Signaling cascade of ROS increasing cell proliferation.....	62
Figure 13. Generation of ROS via reduction of molecular oxygen.....	64
Figure 14. Pathways involved in exercise training adaptation.....	68

## LIST OF TABLES

Table 1. Power analysis for the calculation of sample size.....	24
Table 2. Subject characteristics.....	25
Table 3. Glucose tolerance and insulin sensitivity measures.....	26
Table 4. ANOVA table for insulin AUCi.....	28
Table 5. IL-6 and TNF $\alpha$ measures.....	30
Table 6. DOMS ratings.....	32

## ABSTRACT

**Purpose:** The aim of this study was to compare the effects of an acute bout of eccentric-only (ECC) resistance exercise to an acute bout of concentric-only (CON) resistance exercise on glucose tolerance. A secondary aim of this study was to investigate the role of inflammation in any observed differences in glucose tolerance after the acute exercise bouts. **Methods:** Fourteen overweight, untrained participants ( $BMI = 33.6 \pm 1.2$ ) completed a baseline oral glucose tolerance test, and then returned to the lab to perform either an ECC ( $N = 7$ ) or CON ( $N = 7$ ) resistance exercise session. Another oral glucose tolerance test was administered 24-hours post-exercise with blood sampled at baseline, 15-, 30-, 60-, and 120-minutes after glucose consumption. Blood samples were analyzed for glucose and insulin concentrations. The exercise session consisted of a contraction specific ECC or CON 1-repetition maximum (1RM) testing followed by three sets of ten repetitions at 75% of their contraction specific 1RM on a knee extension machine and leg curl machine. Blood samples taken before exercise (0h), one-hour post-exercise (1h), and 24-hours post-exercise (24h) were analyzed for interleukin-6 (IL-6) and tumor necrosis factor alpha ( $TNF\alpha$ ). Delayed onset muscle soreness (DOMS) was assessed at 0h, 1h, 24h, 48h, and 72h. **Results:** ANOVA calculations indicated a trend on glucose tolerance between the groups' pre- and post-exercise sessions ( $p = 0.098$ ); the ECC group decreased glucose tolerance and the CON group increased glucose tolerance. There was also a trend observed in IL-6 between the 1h and 24h measurements ( $p = 0.097$ ), but no differences between the groups. No changes in  $TNF\alpha$  were observed. Using ANOVA between groups analysis there were differences ( $p < 0.05$ ) in DOMS assessments for all but one ( $p = 0.062$ ) of the soreness tests of the quadriceps and hamstrings. ECC exercise

increased soreness that peaked at 48h and CON exercise induced no soreness changes.

**Conclusions:** These data suggest that in an overweight, untrained population, an acute bout of ECC-only or CON-only resistance exercise may cause opposite effects on glucose tolerance; ECC exercise decreasing glucose tolerance, CON exercise increasing glucose tolerance. Opposing effects on glucose tolerance from the exercise occurred in lieu of a similar response in IL-6 and TNF $\alpha$  to the exercise.



## INTRODUCTION

Physical activity levels across America have been steadily decreasing for decades while health care costs have been continually rising. Many Americans must plan and schedule physical activity sessions daily because the advances in technology have removed recreational or unintentional exercise from their everyday lives. With the lack of physical activity comes an increase in disease risk and mortality rates. When planned physical activity occurs, some individuals are unable to perform or do not enjoy aerobic-type exercise such as running or bike riding. A safe and healthy alternative to aerobic exercise is resistance training (42). Resistance training has become one of the most popular forms of exercise for developing musculoskeletal fitness and overall health (29). Less injuries (73) and better adherence (39, 40) occur during resistance training programs compared to aerobic walk/jog programs. When a resistance training program is combined with an aerobic exercise program, the health benefits can be compounding (58).

The health benefits of resistance training have been clearly shown in previous studies (42). Chronic resistance exercise contributes to the prevention and management of atherosclerotic coronary heart disease (61), hypertension (42), diabetes (1), and overweight and mild obesity (4). Chronic resistance exercise also increases muscular strength, which is directly correlated to a decreased risk in all-cause mortality in both men and women (26). Resistance exercise improves muscular strength by causing muscle damage, which in turn causes supercompensation of muscle fiber numbers and size during repair of the muscle damage (27). The greatest amount of muscle damage

occurs during the eccentric phase of contraction compared to the concentric phase of contraction (15, 27, 56, 74).

**Eccentric exercise.** Eccentric exercise refers to a resistance force that is greater than a muscular force, resulting in a lengthening of the muscle. This type of muscle action occurs in many daily activities, such as walking down a flight of stairs, which requires the muscles of the thigh to support weight while lengthening. In terms of resistance exercise, when the weight is being lifted, the muscle shortens and performs a concentric contraction. When the weight is being lowered, the muscle is lengthening in an eccentric contraction to prevent gravity from pulling the weight to the floor.

Eccentric exercise produces structural damage to the sarcomeres causing the greatest damage through streaming and smearing of the Z-disk. The streaming and smearing is caused by a tearing in the desmin and titin structural fibers between the actin and myosin filaments (29). Damage has also been shown to occur in the sarcolemma, T-tubules, myofibrils, and the cytoskeleton (29). Muscle hypertrophy is attributed to the body supercompensating the number of actin and myosin filaments and the addition of sarcomeres within existing muscle fibers during the repair of the muscle damage done from eccentrics (27). It has been shown that eccentric training is important for hypertrophy as well as increases in strength from resistance exercise, especially in leg exercises (32). Hakkinen et al. (32) found that performing 50% or 75% of the repetitions with an eccentric phase over 12 weeks of training resulted in greater increases in squat, but not bench press, ability when compared to the same training program in a concentric-only manner (27).

**Concentric exercise.** Concentric exercise refers to a muscle force that is greater than a resistance force. Sarcomeres change during concentric contraction by the distance between the Z-lines, I-bands, and H-zones decreasing, while A-band and filament lengths remaining constant. Concentric exercise has not evoked the same amounts of muscle protein synthesis as eccentric exercise (92, 93) most likely due to the shortening of the muscle fibers not causing damage to the structural fibers (27, 29, 92). There is no structural damage after concentric exercise because the overlap between myosin and actin filaments is not being stretched, thereby preventing the tearing of desmin and titin (29). Concentric exercise also has been shown to be less metabolically efficient, during contraction more ATP was utilized and produced compared to eccentric or isometric contractions (76). The decrease in metabolic efficiency may be attributed to eccentric exercise generating passive-force tension, which does not require much ATP, versus concentric exercise hydrolyzing more ATP to create shorter, more frequent power-strokes.

Concentric resistance exercise may have beneficial effects on metabolic health without the consequences observed from eccentric contraction induced inflammation. The increased energy expended during concentric exercise as compared to eccentric exercise (76) utilized muscle stores of glycogen and triglycerides (23, 58). The increased use of these substrates led to increased storage after exercise (21). The cycling of muscular glycogen after concentric endurance exercise has led to increased insulin sensitivity (IS), but not after eccentric endurance exercise (48). Increases in metabolic health may similarly (48) be observed after concentric resistance exercise compared to

eccentric resistance exercise because there is an increase in energy expenditure (76) but no muscle damage (27, 29, 92).

**Delayed onset muscle soreness.** The amount of damage caused by strenuous resistance exercise is most commonly measured by a rating of pain during the delayed onset of muscle soreness (DOMS). It has been shown that the highest levels of muscle tenderness and damage occur after intense, prolonged eccentric contractions in untrained individuals beginning at about 8 hours and lasting 2-3 days after an acute bout of resistance exercise (27, 56, 74). The DOMS associated with eccentric contractions has been well studied and attributed to many contributing factors such as connective tissue damage, muscle damage, inflammation, and enzyme efflux (14). A brief explanation of the mechanisms leading to DOMS can be summarized by eccentric exercise causing overstretched, disrupted sarcomeres, leading to membrane damage that allows uncontrolled release of calcium (Ca), which triggers proteolysis associated with fiber breakdown and repair (74). The efflux of Ca following the sarcolemmal damage is thought to activate proteases and phospholipases, causing further damage to the sarcolemma with the production of leukotrienes and prostaglandins (14).

The inflammatory response to eccentric exercise is thought to be initiated by the proteolytic enzymes contained in muscle fibers that degrade lipid and protein structures of cells following injury (14). The rapid breakdown of damaged muscle fibers and connective tissue in addition to bradykinin, histamine, and prostaglandins, attract monocytes and neutrophils to the injury site (35). Prostaglandin E<sub>2</sub> increases muscle protein degradation (20, 45) in response to eccentric exercise (34, 88) and is thought to be the primary cause of increased sensations of pain (71, 88). The time course of

inflammatory cell infiltration does not coincide directly with peak muscle soreness, even though it may be a contributing factor (14).

**Inflammation.** Inflammation has been observed as a major contributor to several unhealthy conditions such as sepsis, rheumatoid arthritis, insulin resistance, and atherosclerosis (38, 40, 53, 54, 72). Several stages of these diseases are mediated through inflammation, making the body's response to inflammation critical in the process of disease development (38, 40, 53, 54, 72). Clinical studies have shown that elevations in biomarkers of inflammation predict the outcome of patients with acute coronary syndromes, independently of myocardial damage (53). Circulating acute-phase reactants caused by inflammation increase the risk for cardiovascular events and contribute to the pathogenesis of an event. Chronic elevation of inflammation biomarkers indicate elevated risk of atherosclerosis as well as other chronic illnesses. Attenuation of circulating cytokines has shown to decrease the risk of a vascular event and inhibit the progression of many illnesses (38, 40, 53, 54, 72). An acute bout of resistance exercise may temporarily increase inflammation, but then inflammation returns to normal shortly after cessation of the resistance exercise (38, 66, 74).

There are many biomarkers of inflammation; interleukin-1 $\beta$  (IL-1 $\beta$ ), interleukin-6 (IL-6), and C-reactive protein (CRP) will be the focus of this paper due to their association with a variety of diseases (38, 40, 53, 54, 72). IL-1 $\beta$  stimulates the production of IL-6 from a variety of cells, but is difficult to detect in the plasma of healthy individuals because it acts mainly at the autocrine/paracrine levels without signaling peptides (10). IL-6 is an endocrine molecule that uses signaling peptides and can more easily be detected in the blood (10). IL-6 is also the major initiator of

hepatocytes in an acute phase response to produce CRP (53, 54). Elevated circulating CRP levels have been shown to be an independent cardiovascular risk factor and are indicative of coronary heart disease (49, 53, 54).

Paulsen et al. (66) found that 300 maximal eccentric contractions of the quadriceps increased circulating leukocyte, neutrophil, and monocyte counts, as well as IL-6 and CRP. CRP was significantly elevated at maximum systemic levels 23 hours post-exercise. Other studies also have documented significant increases in leukocyte, neutrophil, and monocyte counts after three sets of 10 repetitions of three leg, one trunk, and four upper body resistance exercises at 75% of their one-repetition maximum (78). Elevated levels of leukocytes, neutrophils, monocytes, IL-6, and CRP are directly correlated to atherosclerosis and cardiovascular events (51, 53). The cause of increased cytokines after intense exercise sessions has not been well studied. Bruunsgaard et al. (9) found that eccentric exercise induced significant increases ( $p < 0.05$ ) in IL-6 when compared to an equivalent concentric exercise bout. Through acute resistance exercise protocol modification of concentric-only versus eccentric-only, it may be possible to decrease circulating cytokines through a reduction in muscle damage. Measurements taken that compare contraction-type induced changes in cytokines will give a better understanding of the causality of differing physiological responses to differing exercise sessions.

**Insulin Sensitivity.** There have been conflicting views on whether a single bout of resistance exercise will increase whole-body insulin sensitivity (IS) (25, 28, 50, 51) or decrease whole-body IS (5, 40). Howlett et al. (40) found that an acute bout of resistance exercise involving a combination of eccentric and concentric contractions decreased

whole body insulin action immediately afterwards by measuring insulin using a hyperinsulinemic-euglycemic clamp and using an exercise prescription of three sets of 10-12 repetitions to failure of the leg extension, inclined leg press, and leg curls. The increase in insulin resistance was attributed to a different signaling pathway compared to endurance-type training and increased expression of  $\text{TNF}\alpha$  (40). Increased  $\text{TNF}\alpha$  levels have previously been associated with insulin resistance and impaired IRS-1 signaling (18) after an intense bout of eccentric-only resistance exercise (5, 47).

The conflicting studies that have been performed have attributed an increase in IS to the use of intramuscular stores and uptake of glucose after eccentric-concentric combination resistance exercise (25, 28, 50, 51). Fenicchia et al. (25) found an increase in IS after three sets of eight repetitions on eight different muscle groups using an oral glucose tolerance test in a type-2 diabetic population. Koopman et al. (51) found an increase in IS after eight sets of ten repetitions of leg extension and leg press, measuring muscle glycogen via muscle biopsy and plasma glucose levels. A possible explanation of increased IS after muscle-damaging exercise has been attributed by multiple authors to the observed increased IL-6 concentrations (68, 69). IL-6 produced by exercised muscle has been shown to increase GLUT4 translocation and AMP-activated protein kinase (AMPK), stimulating glucose uptake (68, 69). IL-6 has also been shown to have inhibitory effects on the production  $\text{TNF}\alpha$  (68, 69), which may offer potential protection from the  $\text{TNF}\alpha$ -induced insulin resistance. A direct comparison of concentric to eccentric resistance exercise on IS has not been well studied, but is warranted for the understanding of the mechanism by which IS changes after resistance exercise. Measurements of contraction-type induced changes on IS with measurements of IL-6 and

TNF $\alpha$  may provide evidence of the direct mechanism for the effects of resistance exercise on IS.

The two distinct mechanisms that can affect IS after resistance exercise are shown in figure 1. The first mechanism is through concentric exercise. Concentric exercise increases energy expenditure (EE) and increases glycogen breakdown at a high rate (21, 58, 76), resulting in an increased storage of glucose after exercise (21). The increased storage of glucose is facilitated by GLUT-4 translocation, leading to increased IS after resistance exercise (25, 28, 50, 51). Inflammation caused by eccentric exercise can increase IS as well. Eccentric exercise has been shown to increase circulating levels of IL-6 (9, 66). IL-6 has been shown to increase IS via increases in AMPK and GLUT4 translocation (12, 44, 68, 69).



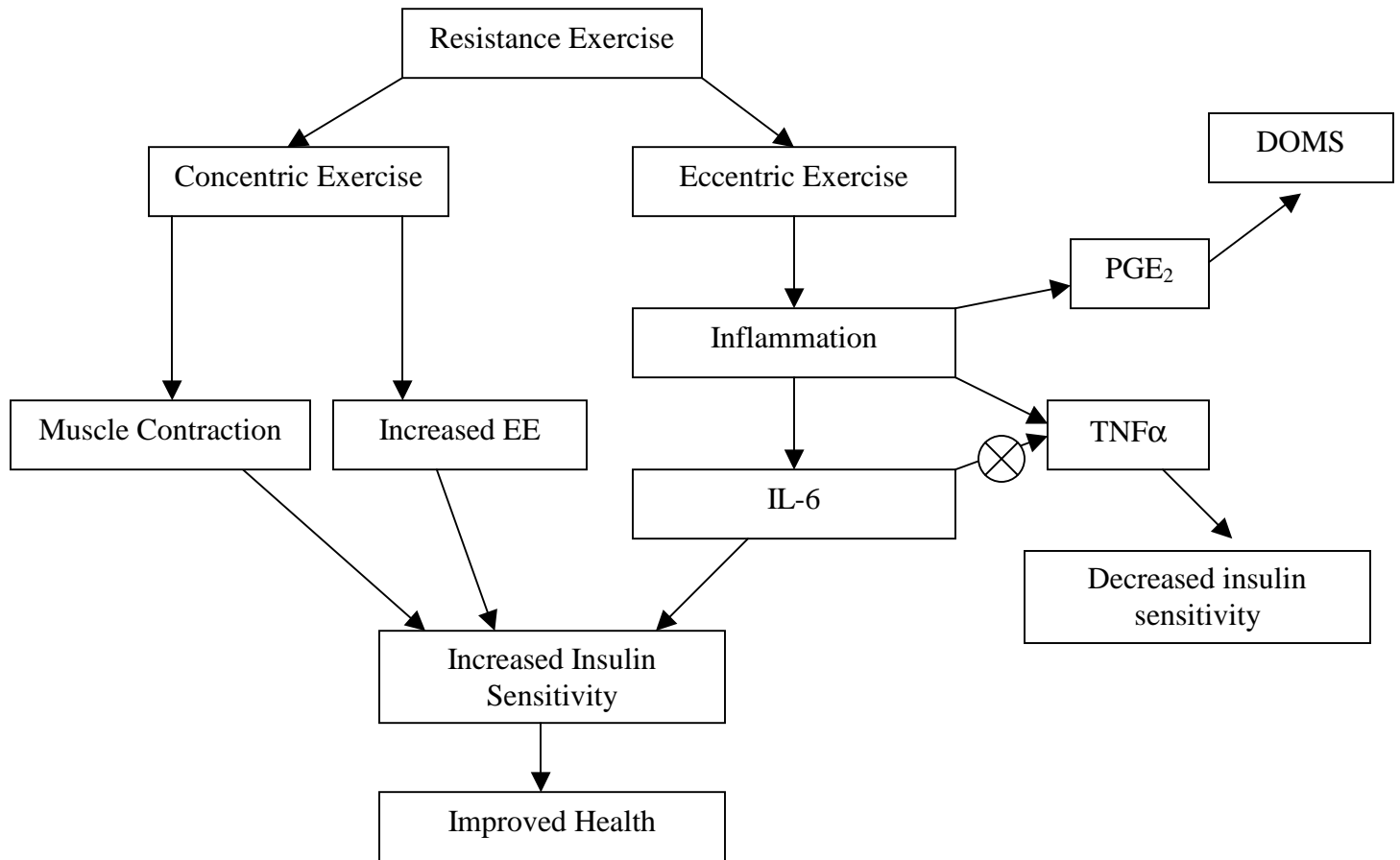



FIGURE 1 – Mechanism of increased insulin sensitivity after resistance exercise.  IL-6 has inhibitory effects on TNF $\alpha$  (67, 68).

**Purpose and Hypothesis.** The primary purpose of the study was to compare the effects of an acute bout of eccentric-only and concentric-only resistance exercise on glucose tolerance. The secondary purpose of the study was to determine the role of inflammation on the observed effects on glucose tolerance after an acute bout of eccentric-only and concentric-only resistance exercise.

It was hypothesized that an acute bout of eccentric-only and an acute bout of concentric-only resistance exercise would both increase glucose tolerance. The mechanism by which glucose tolerance increased would differ: eccentric-only resistance

exercise would increase IL-6 causing increased glucose tolerance; concentric-only resistance exercise would increase glucose tolerance through a mechanism not associated with inflammation.

## **METHODS**

**Subject Population.** Sedentary men and women with a BMI of 25-39.9 kg/m<sup>2</sup> were recruited for the present study (N = 14). Potential subjects were prescreened and excluded from the study if they were not weight stable (>5% body weight change in the previous three months), smokers, had a history of coronary heart disease, diabetes, or renal disease, or were taking oral contraceptives, anti-hypertensive, blood lipid lowering, or insulin sensitizing medications. Other exclusion criteria included regular intake of anti-inflammatory medication (including over-the-counter), and factors that increase the risk of rhabdomyolysis (asthma, acute infection, recreational drug use). Subjects were not participating in 30 or more minutes per week of planned physical activity. Subjects were not enrolled in other diet or exercise programs while participating in the current study. Qualifying volunteers were given informed consent and signed the consent form. Institutional approval was obtained from the University of Missouri – Columbia Health Sciences Institutional Research Board.

**Experimental Design.** The experimental design is shown in figure 2. A randomized cross-over design in which subjects were to complete both acute eccentric (ECC) and concentric (CON) exercise sessions would have been advantageous to the study, but was not used due to the amount of time that would have been required for ECC resistance exercise recovery. Previous studies have shown that eccentric exercise

recovery can last more than two weeks (62), so a randomly assigned, two-group model was used to avoid the necessity of prolonged recovery between trials.

Oral glucose tolerance tests have previously been described as an accurate measure of IS (83) and were used as the primary measure of IS in the current study. Female subjects completed all testing within the luteal phase of their menstrual cycle to decrease variability of the health parameters measured due to hormonal changes.

A visit description outline was included Appendix A. The timeline for the visits were as follows: visit one was accomplished 2-10 days prior to visit two, visit two was accomplished 1-8 days prior to visit three, visits three and four were accomplished 2-8 days prior to visit five, and visits six, seven and eight were accomplished on consecutive days after visit five. Subjects reported to the Exercise Physiology Laboratory during visit one of the study to complete a medical history and physical activity questionnaire. During this visit height and weight measurements were taken and a blood sample was collected for pre-screening analysis of exclusion criteria. Subjects also completed a familiarization session in which five repetitions of each exercise were performed using very light weight.

Subjects reported to the laboratory during visit two of the study to perform a baseline oral glucose tolerance test (BOGT). The oral glucose tolerance test procedure can be reviewed on page 18. Subjects had been consuming their individual control diet beginning 48-hours prior to their visit and had fasted 12-hours prior to the BOGT test. Subjects had been given a water bottle and were instructed to consume 20 ounces (oz) of water in the morning before the BOGT. The baseline BOGT blood sample was used to assess baseline IL-6, TNF $\alpha$ , fasting glucose, and fasting insulin levels.

During visit three, subjects returned to the lab after a 12-hour fast for their scheduled exercise session. DOMS was assessed immediately before the exercise session (0h). Randomization of groups (Conc group or Ecc group) was performed using a coin flip. One-repetition maximum (1RM) testing was performed first, followed by the acute exercise session. After the exercise session, subjects remained fasted and recovered in the laboratory for one-hour until blood was drawn to measure IL-6 and DOMS was assessed again (1h). Subjects consumed 10 oz of water during the exercise session and 20 oz during the recovery period after the exercise session.

Visit four consisted of the subjects returning to the lab 24-hours after their exercise session for a post-exercise oral glucose tolerance test (EOGT). Subjects had been on their individual control diet for 48-hours and had fasted for 12-hours prior to the test. Subjects were again instructed to consume 20 oz of water the morning of the test. Upon arrival to the lab DOMS was assessed in the subjects, and then the EOGT was performed. The first EOGT blood sample was used to assess baseline IL-6, TNF $\alpha$ , fasting glucose, and fasting insulin levels. After the EOGT was accomplished, subjects were no longer required to maintain the control diet because no additional blood samples were needed.

Subjects returned to the lab 48-hours and 72-hours after the exercise session for DOMS assessments because previous studies had shown that 24-hours was not ample time for peak soreness to occur after resistance exercise (27, 56, 74).

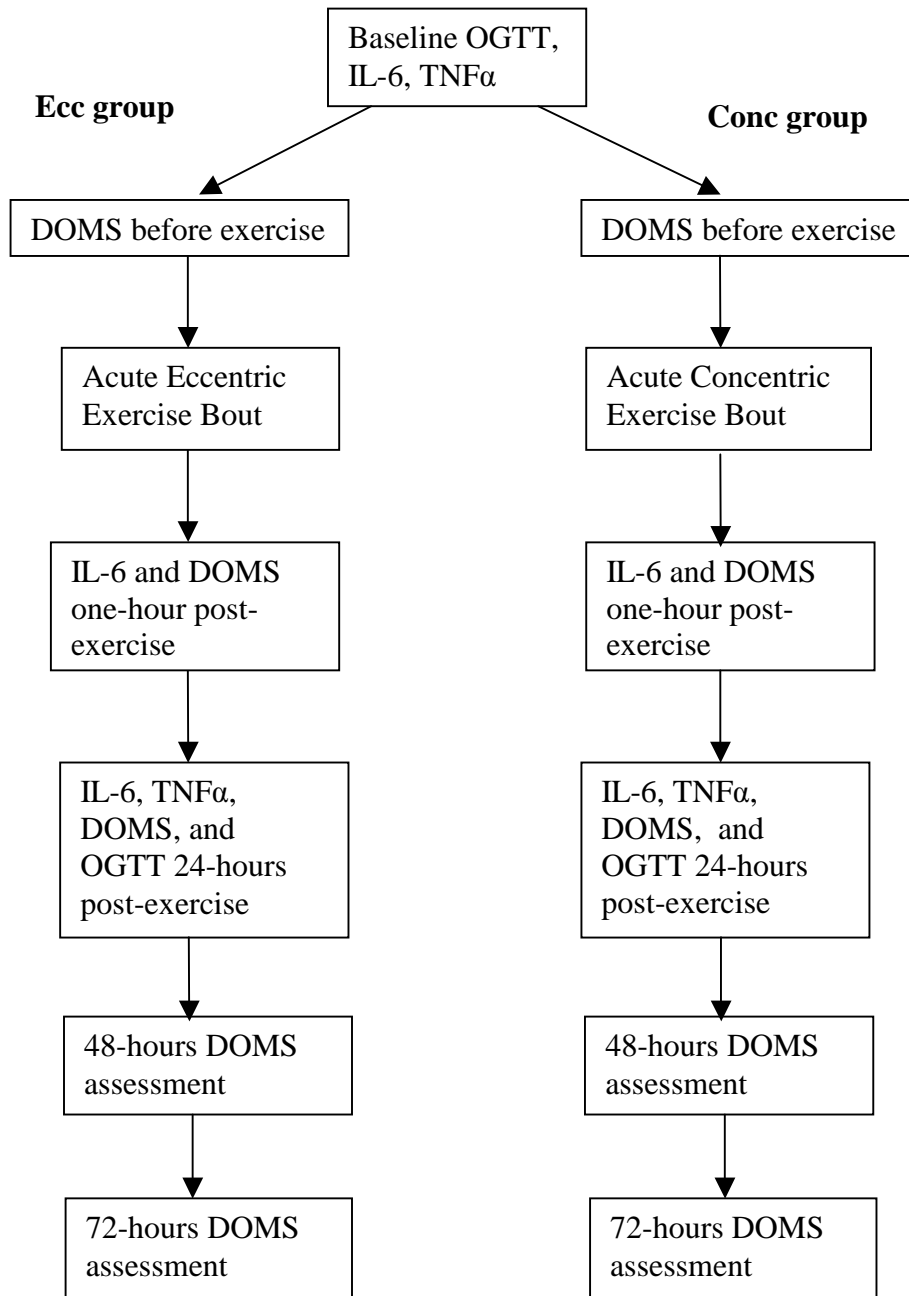


FIGURE 2 - Experimental Design.

**Exercise Protocol.** Subjects began the exercise session with a warm-up by walking at a slow pace (~2.5 mph and 0% grade) on a treadmill for 3 minutes. To perform the 1RM test, leg dominance was first assessed (if the subject was right-handed, then that subject was left leg dominant, or vice-versa). Subjects then performed a 1RM

trial using their dominant leg on a knee extension machine (Body Masters, Rayne, LA) at a predicted 1RM weight utilizing their quadriceps and using only the phase of contraction for their assigned group (Con group or Ecc group). Subjects were then asked to rate their perceived exertion on a scale of 1-10, and the weight was adjusted accordingly for the next attempt. The weight was increased ~30% if the subject rated their exertion <6, ~20% if the subject rated their exertion 6-7, and 5-10% if the subject rated their exertion 8-10. CON contractions were performed in a controlled manner (~2 seconds (sec)) in which the subject extended the knee and the investigator caught the weight after full extension, removing all weight from the ECC phase of the movement. ECC contractions were performed to a 5 sec cadence by the investigator. During the ECC contractions the investigator lifted the weight, the subject then positioned his/her feet under the weight, and with warning, the investigator released the weight causing the subject to eccentrically contract his/her muscle in a controlled manner to lower the weight during the entire 5 sec. Subjects rested for two minutes in between each attempt. During the rest period, the subject walked to the adjacent leg curl machine (Body Masters, Rayne, LA) and performed a 1RM test on the hamstrings of the dominant leg. The same testing protocol was used for the leg curl exercise as was used for the knee extension exercise. Attempts were continued until the subject could not perform the specified contraction in a controlled manner; the maximum weight lifted was then considered the 1RM. All subjects performed a total of 3-5 attempts before the 1RM was achieved.

The exercise protocol for both groups was performed on the knee extension and leg curl machines bilaterally. The amount of weight used was determined by multiplying the 1RM of the dominant leg by two, and then prescribing 75% of that total for the

exercise session. Ten repetitions were prescribed for each set because 75% of the 1RM is equivalent to the 10-repetition maximum for concentric leg resistance exercise (27). In order to equivocate the intensity of work by each group, 10 repetitions at 75% of the ECC 1RM were prescribed for the Ecc group and 10 repetitions at 75% of the CON 1RM were prescribed for the Conc group. Subjects performed three sets of 10 repetitions with a one-minute rest in between each set (protocol recommended for novice resistance training in Fleck et al. (27)). Concentric exercise was performed by the subjects lifting the weight by concentric-only contractions lasting 2 sec, then the investigator held the weight as the subject returned their leg to the starting position, and the investigator then lowered the weight to the starting position. Eccentric contractions were performed by the investigator lifting and holding the weight while the subject lengthened the muscle. As soon as the investigator released the weight, the subject began lowering the weight in a controlled manner with an audible 5 sec-cadence count by the investigator. If the subject lowered the weight before the 5 sec-count was finished, the repetition was accepted, but subject was instructed to try and keep the timing correct. All subjects performed the exercises in order of knee extension and then leg curl.

To perform ECC- and CON-only contractions on the leg curl machine, a pulley system was used that allowed the investigator to either lift and hold the weight at a position in which unresisted full knee flexion by the subject could occur (for the Ecc group), or the weight could be caught after being lifted and the investigator could slowly lower it back to the starting position (for the Conc group). For the Ecc group, a compound pulley was used that attached to the moving arm and the other end of the pulley attached to the top of the weight stack to give the proper angle at which full knee

flexion could occur. For the Conc group, a single swiveling pulley was used that was attached at the top of the weight stack and had a steel cable that was attached to the moving arm, then ran through the pulley, and the other end of the steel cable had a T-bar attached to it, allowing the investigator to control the weight.

**Dietary Control.** Subjects were asked to consume a control diet beginning 48-hours before both the BOGT and EOGT, and lasting until the completion of the each test. Subjects completed a seven-day diet log and average daily caloric intake was assessed using Food Processor SQL Edition (EHSA Research, Salem, OR). Based on each subject's average daily caloric intake, an individual control diet of either 1500-2000, 2000-2500, 2500-3000, or 3000-3500 calories was prescribed to maintain the same intake levels. The control diets, which are listed in Appendix C, consisted of 55% carbohydrate, 30% fat, and 15% protein.

## **Measures**

All blood collections and measurements occurred at the University of Missouri Exercise Physiology Laboratory. Subject characteristics and body composition measurements were accomplished during the subject screening process. A BOGT, EOGT, one post-exercise blood draw, and five DOMS assessments were performed (fig. 2). Blood analyses were performed to measure TNF $\alpha$ , IL-6, insulin, and glucose. Baseline blood sampling was performed at least 48-hours prior to the exercise session, and exercise blood sampling was 24-hours after the exercise session. To reduce the variability of measures in the blood samples, subjects were instructed to consume only the control diet and water 48-hours prior to testing. As part of the control diet, subjects had fasted 12-hours prior to all blood sampling.



**Blood pressure.** During visit two subjects sat quietly in a padded chair for 10 min prior to blood pressure and heart rate analysis. Systolic and diastolic blood pressure was obtained by the same investigator using a standard aneroid sphygmomanometer.

**Body composition.** Body composition was assessed using waist-to-hip ratio (WHR), BMI, and skin fold measurements during visit two. WHR was calculated as the waist circumference, measured at the narrowest point superior to the hip to the nearest 0.1 cm, divided by hip circumference, measured at its greatest gluteal protuberance to the nearest 0.1 cm. Weight was measured to the nearest 0.05 kg and height was measured to the nearest 0.1 cm. BMI was calculated as subject weight in kg divided by subject height in m<sup>2</sup>. Skin fold measurements were assessed using the three-site method and Jackson-Pollock equations (3). For males, the mean of three measurements at the chest, abdomen, and thigh were used to calculate body fat percent. For females, the mean of three measurements at the triceps, suprailiac, and thigh were used to calculate body fat percent.

**Delayed onset muscle soreness.** During visits five, six, seven, and eight DOMS was assessed using a numbering scale of 0-100 (shown in Appendix A) during slow treadmill walking and quadriceps lengthening immediately before the exercise session (0h), one-hour after the exercise session (1h), 24-hours after the exercise session (24h), 48-hours after the exercise session (48h), and 72-hours after the exercise session (72h). Subjects were first instructed to walk on a treadmill at 2.0 mph and 0% grade while a lab technician read aloud a scripted questionnaire to assess soreness. A copy of this script is located in Appendix A. Subjects first rated soreness in the front of their right leg while walking (walking right quadricep), then the front of their left leg (walking left quadricep), then back of their right leg (walking right hamstring), and then the back of their left leg

(walking left hamstring). Subjects were instructed not to touch their legs while rating the soreness. After walking on the treadmill, subjects then laid in the supine position as the script was read instructing the subjects to bend their right leg and rate the pain in the front of the right leg while lengthening (lengthening right quadricep). The subjects then performed the same task for the left leg (lengthening left quadriceps). MacIntyre et al. (36) reviewed studies related to DOMS, finding tenderness beginning medially, laterally, and distally, and then becoming more diffuse throughout the quadriceps muscles by 24 and 48 hours after exercise. The findings indicated the musculotendinous attachment of the quadriceps was the main site of pain and tenderness. Perceived DOMS ratings return to normal 168 hours (7days) after ECC exercise (36).

**Blood collection and preparation.** Whole blood was collected via a butterfly needle inserted into an antecubital vein. If the antecubital vein could not be located, blood was drawn from a vein in the hand. Blood samples were collected into 10mL ethylenediaminetetraacetic acid (EDTA) and serum separator (SST) vacuum sealed tubes. The SST tubes contained a gel that separated blood cells from the serum and the EDTA tubes contained an anticoagulant and chelating agent. All SST samples were allowed to clot at room temperature (24°C) for 30 min, and EDTA samples were placed in an ice water bath for 30 minutes. All samples were then separated by centrifugation at 4°C for 15 minutes in a Marathon 21000R centrifuge (Fisher Scientific, Pittsburgh, PA). Both the SST and EDTA were then transferred into cryogenic vials and stored at -80°C until analyzed. All of the samples from one subject were analyzed on the same day, at the same time to reduce unnecessary variability. All subject samples were analyzed in duplicate or triplicate.

**Glucose tolerance, insulin sensitivity, and insulin resistance.** It was of particular importance of this study to measure the effects of ECC and CON exercise on glucose tolerance (GT) and IS. To measure the GT, oral glucose tolerance tests were performed at prior to (BOGT) and 24-hours after exercise (EOGT). Insulin and glucose measures that were obtained during the 0h blood draw from each oral glucose tolerance test were used to calculate Homeostatic Model Assessment (HOMA) and Quantitative Insulin Sensitivity Check Index (QUICKI), estimates of IS and IR.

*Oral Glucose Tolerance Test.* Subjects had a baseline blood sample collection (0h) and then were asked to consume a sugary drink (Ever Scientific, Exton, PA) consisting of 75g of glucose. For the next two hours the participants were asked to lie still on a reclined, padded chair (reading, watching TV/movies, listening to music was allowed). During these two hours, blood samples were collected at 15, 30, 60, and 120 minutes after consuming the drink. Blood samples collected during the glucose tolerance tests were measured for insulin and glucose levels, and the means were plotted as the total area under the curve (AUC<sub>t</sub>) and incremental area under the curve (AUC<sub>i</sub>) (82). AUC<sub>t</sub> and AUC<sub>i</sub> was determined using the trapezoidal method:

$$\text{AUC}_t = (((0\text{min}+15\text{min})/2) \times 15) + (((15\text{min}+30\text{min})/2) \times 15) + (((30\text{min}+60\text{min})/2) \times 30) \\ + (((60\text{min}+120\text{min})/2) \times 60)$$

$$\text{AUC}_i = (\text{AUC}_t) - (0\text{min} \times 120)$$

*Matsuda Index.* GT was assessed using the Matsuda index as well (59). The Matsuda index (MI) provided a simple method to compare hepatic and whole-body IS

from the glucose and insulin concentrations during the OGTT. The formula to determine the MI calculation was:

$$MI = \frac{10,000}{(\sqrt{\text{fasting plasma glucose} \times \text{fasting plasma insulin}}) \times (\text{mean OGTT glucose concentration} \times \text{mean OGTT insulin concentration})}$$

*HOMA.* Insulin resistance was assessed by the use of HOMA to compare insulin and glucose concentrations. The calculation of insulin resistance was based on the modeling of fasting insulin and glucose concentrations using the formula derived by Matthews et al. (60):

$$HOMA = \text{fasting plasma insulin } (\mu\text{U/mL}) \times \text{fasting glucose (mmol/L)} / 22.5$$

*QUICKI.* IS was assessed by the use of QUICKI to compare basal insulin and glucose concentrations. The calculation of IS was based on the modeling of fasting insulin and glucose concentrations using the formula derived by Katz et al. (43):

$$QUICKI = 1 / \{ \log [\text{fasting plasma insulin } (\mu\text{U/mL})] + \log [\text{fasting plasma glucose (mg/dL)}] \}$$

*Glucose.* Glucose was measured via the glucose oxidase method using an enzymatic glucose reagent (Fisher Scientific, Pittsburg, PA). This assay utilized a liquid stable Infinity<sup>TM</sup> reagent for the glucose oxidase reaction in conjunction with an auxiliary reaction that has been widely used for the determination of glucose in biological fluids.

The method is based on a hydrogen peroxide indicator reaction that couples with 4-aminoantipyrine to a phenolic compound. The phenolic compound forms a red quinoneimine of an intensity that can be measured photometrically at 500nm.

The methodology of the assay required separating the samples into numerous cuvettes and mixing them with reagent at a 1:150 ratio. Then the cuvettes were placed in a warm water bath at 37°C for 10 minutes. Timers were used to ensure precise incubation times. The samples were then removed from the warm water bath and set at room temperature (24°C) for 10 minutes, again using timers to ensure proper timing. A spectrophotometer capable of reading a primary wavelength of 500nm (460nm-560nm) was then used to measure the amount of glucose in the samples. The actual glucose concentrations were determined using the following formula:

$$= (\text{Absorbance of Unknown Sample} / \text{Absorbance of Calibrator}) \times \text{Calibrator Value}$$

The calibrator value used was 100 mg/dL. The coefficient of variation measured on triplicate samples of glucose was 2.3%.

*Insulin.* An Immulite 1000 (LKCR1, Siemens Healthcare Diagnostics Inc., Deerfield, IL) was used to determine plasma EDTA concentrations of insulin. All samples were analyzed at the same time. The Immulite 1000 used a proprietary wash technique in which insulin-specific coated beads served as a reaction vessel for all sample processing. The test units were spun at a high speed allowing all serum insulin to bind to the bead and excess fluids were pumped into an integral sump chamber. Multiple washes were done to ensure separation of unbound material. Enzyme-amplified

chemiluminescence was sustained allowing multiple light signal attenuation readings to ensure precise measurements. The coefficient of variation measured on triplicate samples of insulin was 1.3%.

**Interleukin-6 and TNF $\alpha$ .** Two separate commercially available enzyme-linked immunosorbent assay (ELISA) kits were used to determine serum concentrations of TNF $\alpha$  and IL-6 (RayBiotech Inc., Norcross, GA). The ELISA kits were based on the sandwich principle. First, antibodies specific for TNF $\alpha$  or IL-6 were pre-coated in the bottoms of 96 wells on a microtitre plate. Serum samples were then thawed, diluted and pipetted into 94 wells and 2 wells were filled with standards. The pre-coated antibodies bound to and completely immobilized TNF $\alpha$  or IL-6. Then the wells were rinsed with a specific solution to remove any unbound substances. Another antibody was then added to the wells that had specific binding to only TNF $\alpha$  or IL-6. Another wash was then performed to remove any non-bound antibody in the wells. The third addition to the wells was an acidic substrate solution that developed a specific depth of color in proportion to the amount of TNF $\alpha$  or IL-6 bound to the antibodies in each well. A stop solution was then added and the depth of color was measured at a wavelength of 450 nm. The coefficient of variation measured on triplicate samples of TNF $\alpha$  and IL-6 were 2.1% and 6.7% respectively.

**Statistical Analysis.** There were two independent variables associated with the current study; group (Ecc group, Conc group) remained constant for all variables and time measures differed among the variables. Values were reported as means  $\pm$  standard error of the mean (SE) with the significance set at  $P \leq 0.05$ . The OGTTs were analyzed using a two-way ANOVA, comparing the changes in the AUC measurements with

repeated measures at the glucose tolerance test performed at baseline (BOGT) and the glucose tolerance test performed 24h post-exercise (EGOT). The analysis of HOMA, QUICKI, and TNF $\alpha$  were compared using a two-way analysis of variance (ANOVA) with repeated measures on 0h and 24h time measurements. The analysis of IL-6 was compared using a two-way analysis of variance with repeated measures on 0h, 1h, and 24h. DOMS was compared using a two-way ANOVA with repeated measures at 0h, 24h, 48h, and 72h. When a post-hoc analysis was necessary, a Bonferroni correction was used.

**Sample Size and Power Calculations.** Sample size was determined based on the data reported by several investigators for each variable on an individual basis. The number of subjects required for many of the outcome measures in the current study are reported in Table 1. The calculated N's in the table are at a power = 0.80 and  $p < 0.05$  significance level. An N of 14 should be sufficient for the main effect of CON and ECC exercise to be observed in the proposed measures.

TABLE 1. Power analysis table for the calculation of sample size.

Exercise	Measure	Reference	Sample Size	SE or SD	Difference btn Means	1-	2-
						sided	sided
						N	N
Ecc vs Base Aero	IL-6	Del Aguila	8	0.3	2.9	4	
Conc vs Base Aero	IL-6	Bruunsgard	9	0.514	0.918	10	
Ecc vs Conc Aero	IL-6	Bruunsgard	9	0.183	1.105	4	
Ecc vs Base Aero	IL-6	Bruunsgard	9	0.183	2.805	4	
Ecc vs Base Resist	IL-6	Paulsen	11	102	299	6	
Ecc vs Base Aero	TNF $\alpha$	Del Aguila	8	0.3	1.5	4	
Resist vs Base in young males	Insulin AUC	Fluckey	7	0.65	1.55		8
Ecc vs Conc Aero	GDR	Kirwan	6	0.51	2.08		6
Resist vs Base in NIDDM	Insulin AUC	Fluckey	7	1.5	2.06		20
Ecc vs Base Aero	GDR	Kirwan	6	0.51	2.01		6
Ecc vs Base Aero	GDR	Del Aguila	8	0.7	0.9		22
Conc vs Base Aero	GDR	Kirwan	6	0.94	0.07		5660

Ecc = eccentric, Conc = concentric, Resist = resistance exercise, Aero = aerobic exercise, NIDDM = non-insulin dependent diabetes mellitus, GDR = insulin-mediated glucose disposal rate.

## RESULTS

Fourteen subjects successfully participated in the current investigation (7 in Ecc group and 7 in Conc group). No significant differences were found between the groups for anthropometric data (table 2). During the oral glucose tolerance tests for 3 subjects investigators were unable to obtain 15 minute blood samples due to difficulty with venipuncture. For these measurements the value was estimated using the equation:  $(0\text{min subject value} + 30\text{min subject value})/X$ . X was the group average of the equation:  $(0\text{min} + 30\text{min})/15\text{min}$  (X for Ecc group = 1.783, X for Conc group was 1.784). The measured value of TNF $\alpha$  for one time point for one subject was below detectable levels



for the kit used, so the lowest measured value was substituted for that time point. No subjects withdrew from the study. ANOVA table can be found in appendix D.

TABLE 2. Subject characteristics.

	<b>All Subjects</b>	<b>Conc group</b>	<b>Ecc group</b>	<b>p-value</b>
Age (years)	35.4 ± 2.5	31.1 ± 3.5	39.6 ± 2.9	0.089
% Body Fat Skinfolds	32.3 ± 2.9	32.2 ± 3.5	32.4 ± 4.9	0.981
Waist (cm)	106.7 ± 2.8	110.5 ± 3.7	103.0 ± 3.9	0.183
Hip (cm)	118.7 ± 2.5	118.7 ± 3.1	118.8 ± 4.2	0.989
Waist/Hip	0.90 ± 0.02	0.93 ± 0.03	0.87 ± 0.03	0.180
Bodyweight (kg)	96.9 ± 3.5	100.6 ± 5.3	93.3 ± 4.5	0.317
Height (cm)	170.1 ± 2.0	171.4 ± 3.5	168.8 ± 2.1	0.542
BMI	33.6 ± 1.2	34.3 ± 1.7	32.9 ± 1.9	0.582

Values reported as means ± SE. p-value = significance level of 2-tailed t-test .

**Glucose tolerance.** Calculations of insulin AUC<sub>i</sub>, glucose AUC<sub>i</sub>, MI, HOMA, and QUICKI are presented in table 3 with no significant differences. Figures 3-4 represent AUC<sub>i</sub> levels of insulin and glucose. Table 4 is the ANOVA calculations for insulin AUC<sub>i</sub>, demonstrating a trend in the group x time interaction (p = 0.098). The trend indicates the observed decrease of insulin needed for glucose clearance in the Conc group versus the observed increase of insulin needed for glucose clearance in the Ecc group shown in figure 3. No significant differences were found in glucose tolerance using the MI (figure 5).

TABLE 3. Glucose tolerance, insulin sensitivity and insulin resistance measures.

<b>Variable</b>	<b>Group</b>	<b>Baseline</b>	<b>24-Hours</b>
Insulin AUCi	Conc	9439.3 ± 1908.9	8324.6 ± 2250.9
	Ecc	8413.1 ± 1220.2	9499.8 ± 1499.8
Glucose AUCi	Conc	5055.6 ± 1086.3	4944.5 ± 769.5
	Ecc	5549.0 ± 886.4	4985.0 ± 1503.3
Matsuda index	Conc	3.2 ± 0.5	3.6 ± 0.6
	Ecc	3.7 ± 0.6	3.5 ± 0.5
HOMA	Conc	2.7 ± 0.5	2.9 ± 0.6
	Ecc	2.3 ± 0.4	2.4 ± 0.0
QUICKI	Conc	0.3 ± 0.0	0.3 ± 0.0
	Ecc	0.3 ± 0.0	0.3 ± 0.0
INSULIN (uIU/mL)	Conc	12.1 ± 2.0	12.2 ± 2.7
	Ecc	9.2 ± 1.2	8.7 ± 1.5
INSULIN (pmol/L)	Conc	84.2 ± 14.0	84.5 ± 18.6
	Ecc	63.8 ± 8.6	60.3 ± 10.2
GLUCOSE (mg/dl)	Conc	90.6 ± 4.6	96.0 ± 1.8
	Ecc	98.6 ± 3.7	106.0 ± 6.8
GLUCOSE (mmol/L)	Conc	5.0 ± 0.3	5.3 ± 0.1
	Ecc	5.5 ± 0.2	5.9 ± 0.4

Values reported as means ± SE. Insulin AUCi reported in mmol/L. Glucose AUCi reported in mg/dL. There were no significant differences by group or time.

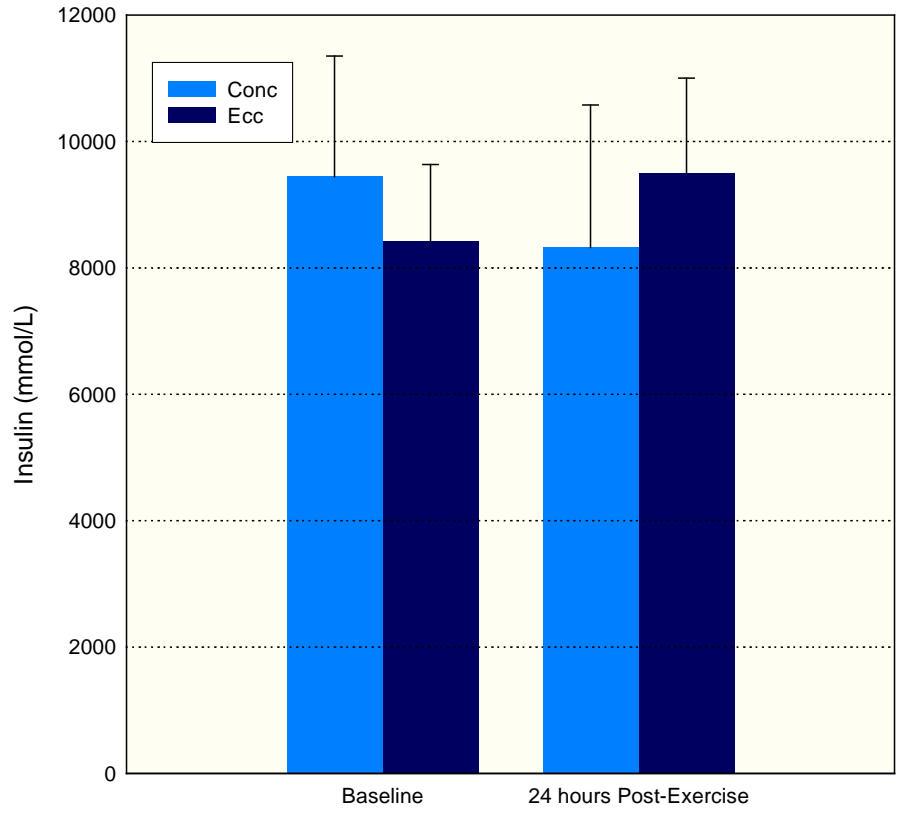


FIGURE 3 – Insulin AUCi during OGTT. Values reported as means  $\pm$  SE. A trend was observed for the group x time interaction ( $p = 0.098$ ). There were no significant differences by group or time.

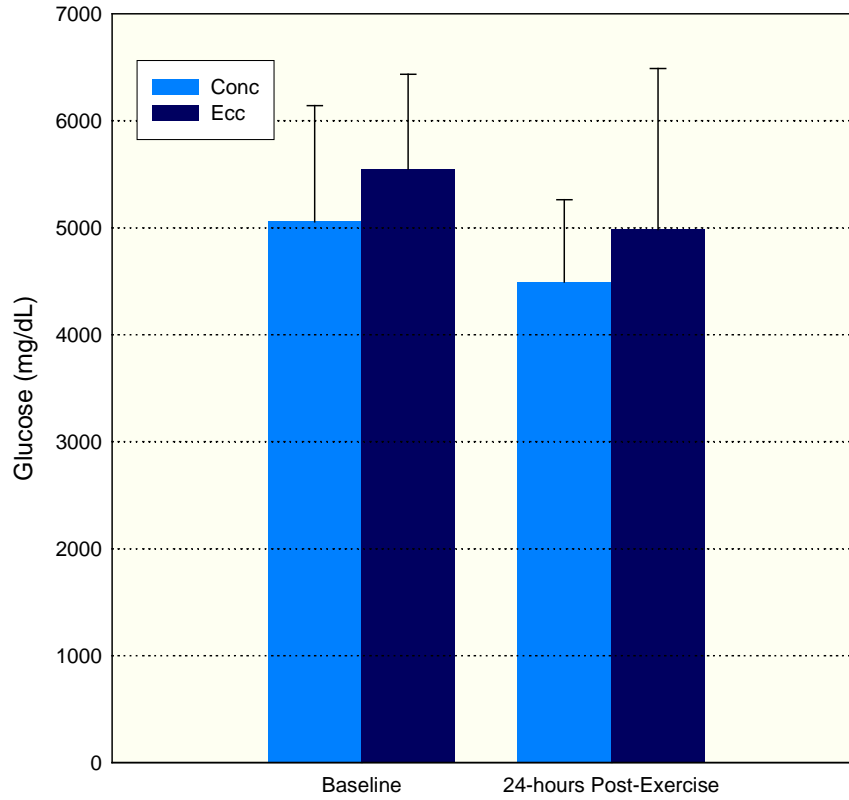


FIGURE 4 – Glucose AUCi during OGTT. Values reported as means  $\pm$  SE. There were no significant differences by group or time.

TABLE 4. ANOVA table for insulin AUCi (mmol/L).

Source	df	F	P-value
Time	1	0.001	0.982
Group	1	0.001	0.976
Time x Group	1	3.221	0.098

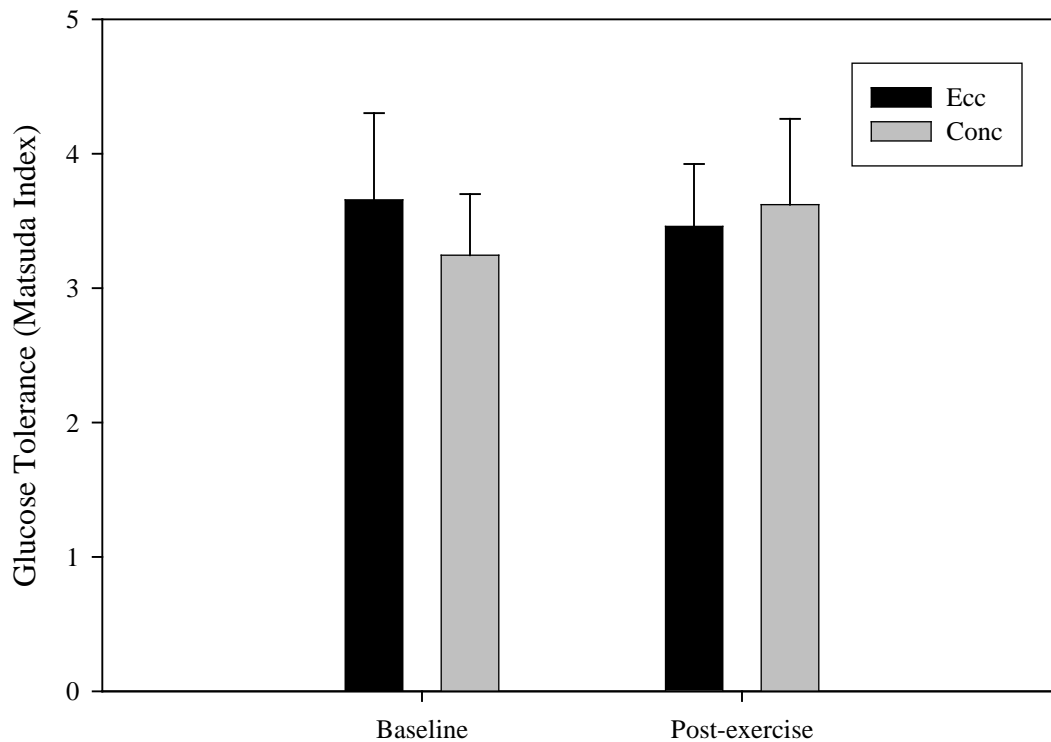


FIGURE 5 – Matsuda index scores during OGTT. Values reported as means  $\pm$  SE. There were no significant differences by group or time.

**Interleukin-6 and tumor necrosis factor alpha.** Results for IL-6 and TNF $\alpha$  are shown in table 5 and figures 6-7. IL-6 did not have significant changes between the 0h and 1h measurements, but a trend was observed between 1h and 24h measurements ( $p = 0.097$ ). There were no significant differences found between Ecc group and Conc group for IL-6. No significant differences were observed pre- and post-exercise or between groups for TNF $\alpha$ .

TABLE 5. IL-6 and TNF $\alpha$  measures.

Variable	Group	Baseline	1-Hours	24-Hours
IL-6	Conc	1.8 $\pm$ 0.4	2.1 $\pm$ 0.5	1.6 $\pm$ 0.2*
	Ecc	1.9 $\pm$ 0.5	2.2 $\pm$ 0.5	1.7 $\pm$ 0.4
TNF $\alpha$	Conc	1.2 $\pm$ 0.4		1.0 $\pm$ 0.1
	Ecc	1.5 $\pm$ 0.3		1.1 $\pm$ 0.3

Values reported as means  $\pm$  SE. IL-6 reported in pg/mL. TNF $\alpha$  reported in pg/mL.  
 \*Difference between 1h and 24h measures ( $p = 0.097$ ).

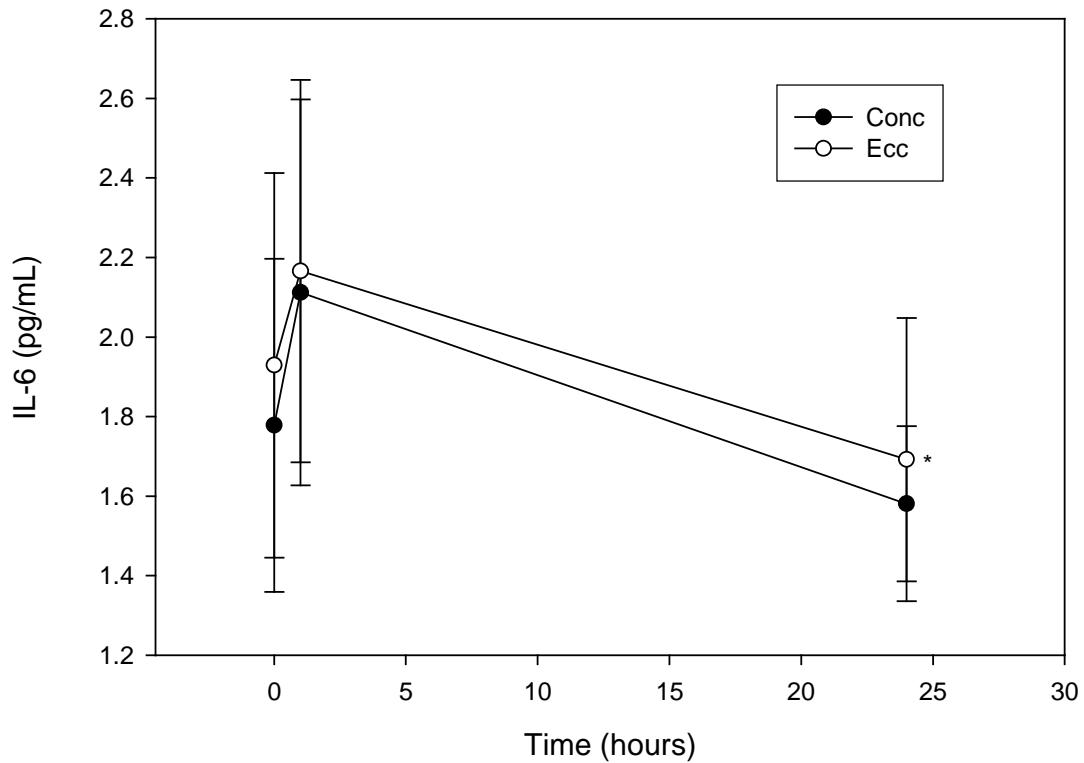


FIGURE 6 – IL-6 measures over time. Values reported as means  $\pm$  SE. IL-6 reported in pg/mL. \*Difference between 1h and 24h measures ( $p = 0.097$ ).

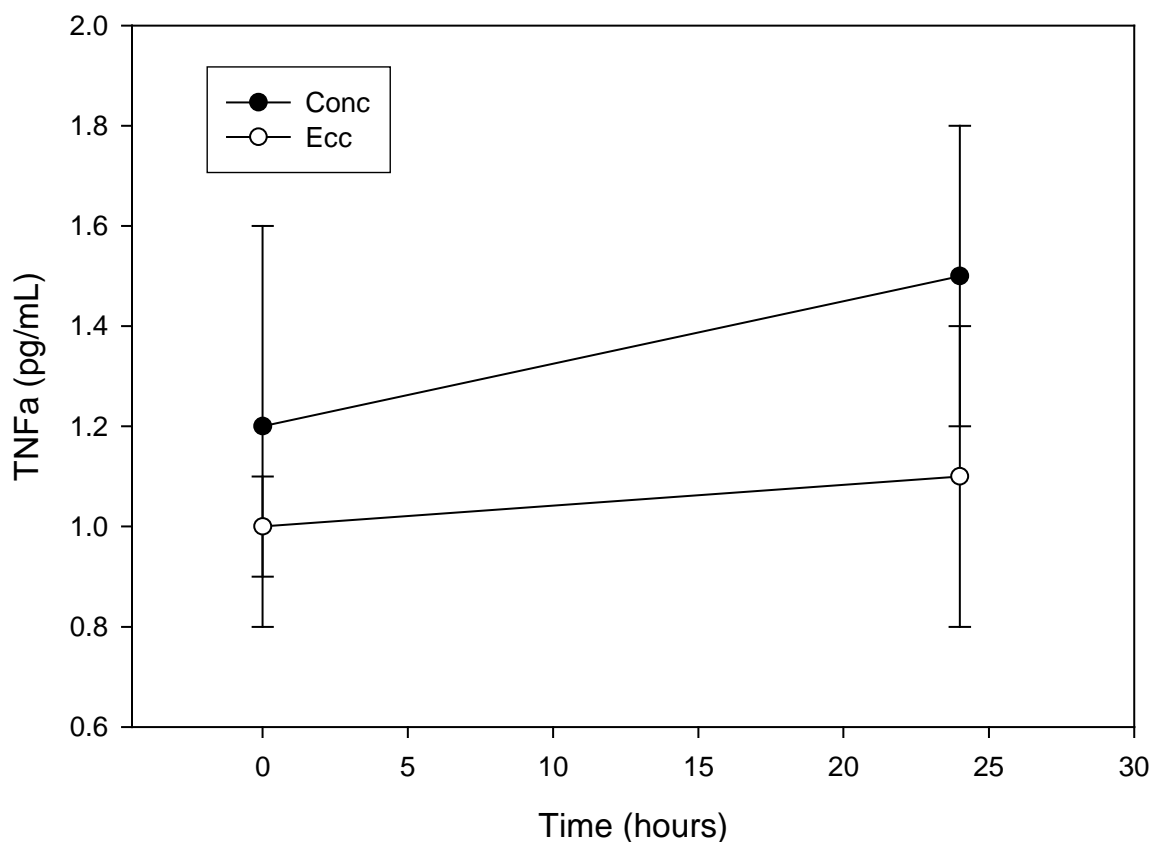


FIGURE 7 - TNF $\alpha$  measures pre- and post-exercise. Values reported as means  $\pm$  SE. TNF $\alpha$  reported in pg/mL. No significant differences observed.

**Delayed Onset Muscle Soreness.** DOMS ratings by the subjects for baseline through 72-hours post-exercise are presented in table 6 and figures 8-10. The Ecc group was significantly different from the Conc group for the right quadriceps walking test ( $p = 0.04$ ), left quadriceps walking test ( $p = 0.032$ ), left hamstrings walking test ( $p = 0.025$ ), left quadriceps lengthening test ( $p = 0.001$ ), and right quadriceps lengthening test ( $p = 0.008$ ). The Ecc group presented an almost significant difference from the Conc group for the right hamstrings walking test ( $p = 0.062$ ).

TABLE 6. DOMS ratings

Variable	Group	Baseline	1-Hour	24-Hours	48-Hours	72-Hours
Walking Right Quad	Conc	0.0 ± 0.0	1.0 ± 0.8	0.4 ± 0.4	0.1 ± 0.1	0.0 ± 0.0
	Ecc <sup>a</sup>	0.3 ± 0.3	5.0 ± 2.7*	7.6 ± 3.4*	12.7 ± 5.1*	5.6 ± 3.3*
Walking Right Ham	Conc	0.1 ± 0.1	2.1 ± 1.1	2.4 ± 1.5	1.0 ± 0.7	0.6 ± 0.4
	Ecc <sup>b</sup>	0.3 ± 0.3	3.9 ± 1.4*	4.9 ± 2.6*	10.7 ± 2.1*	4.0 ± 2.8*
Walking Left Quad	Conc	0.0 ± 0.0	0.9 ± 0.9	1.0 ± 0.7	0.1 ± 0.1	0.0 ± 0.0
	Ecc <sup>a</sup>	0.3 ± 0.3	4.4 ± 2.7*	7.6 ± 3.4*	10.3 ± 3.1*	4.1 ± 2.7*
Walking Left Ham	Conc	0.3 ± 0.2	1.7 ± 0.9	2.7 ± 1.5	0.7 ± 0.4	0.6 ± 0.3
	Ecc <sup>a</sup>	1.0 ± 0.7	3.0 ± 1.4*	5.4 ± 3.3*	10.4 ± 1.9*	3.9 ± 1.8*
Lengthening Right Quad	Conc	0.4 ± 0.4	1.6 ± 1.2	0.4 ± 0.4	0.7 ± 0.4	0.4 ± 0.3
	Ecc <sup>a</sup>	1.6 ± 0.9	5.4 ± 2.6*	15.3 ± 4.3*	21.3 ± 6.0*	11.9 ± 5.8*
Lengthening Left Quad	Conc	0.4 ± 0.4	1.0 ± 1.0	0.6 ± 0.4	0.4 ± 0.2	0.6 ± 0.4
	Ecc <sup>a</sup>	1.6 ± 0.9	4.3 ± 2.1*	14.6 ± 3.4*	19.9 ± 4.3*	8.4 ± 2.6*

Values reported as means ± SE. \*Significantly different from baseline (p<0.05). <sup>a</sup> Group significantly different from Conc group (p<0.05). <sup>b</sup> Group difference (p = 0.062) from Conc group.



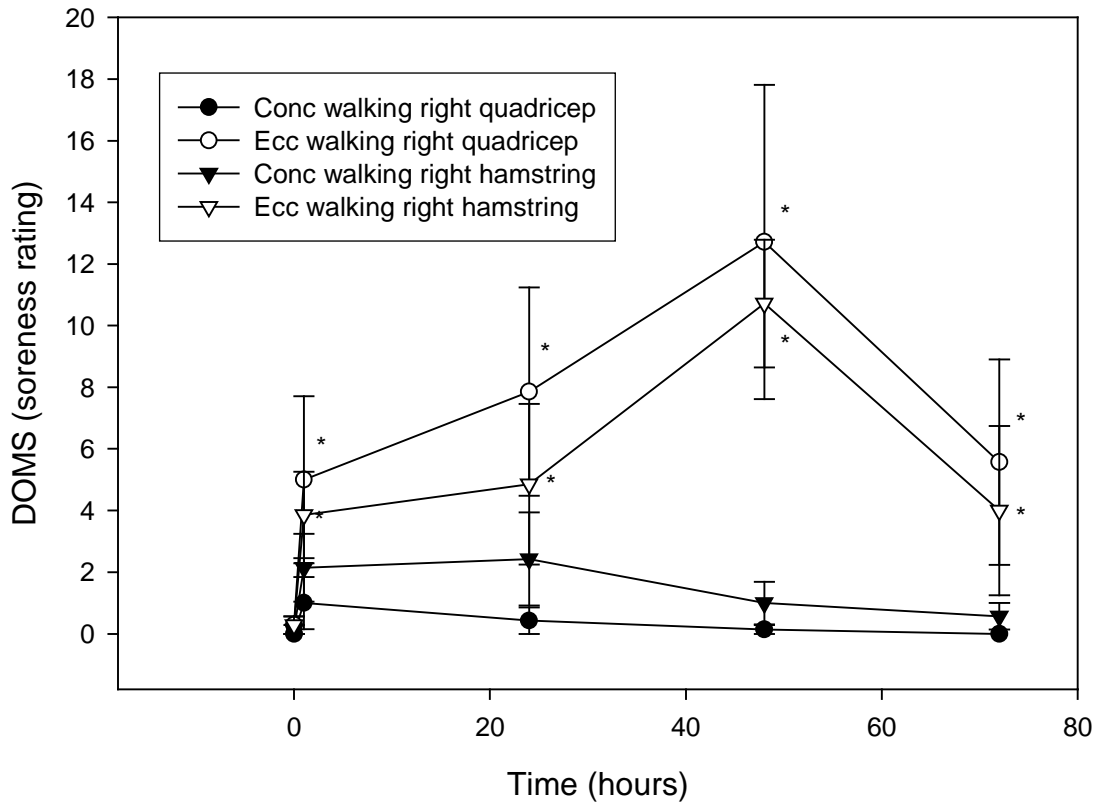


FIGURE 8 – DOMS walking right thigh test. Values reported as means  $\pm$  SE.  
 \*Significantly different from baseline ( $p = 0.05$ )

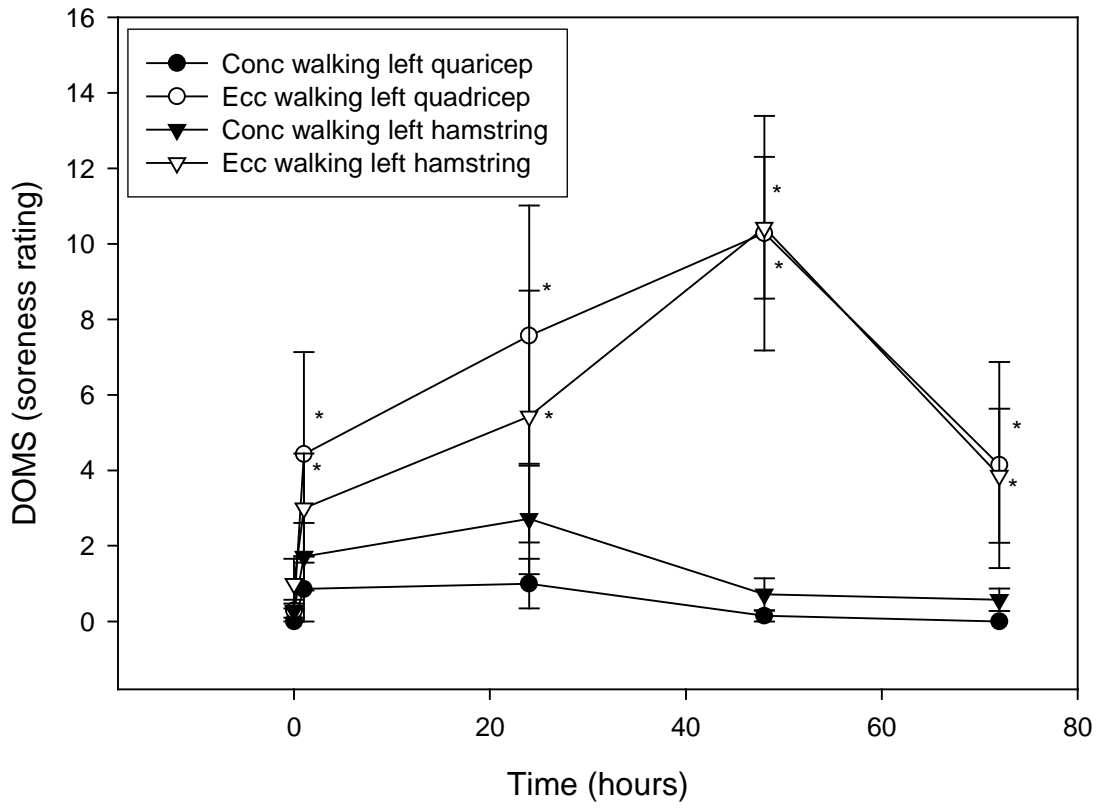


FIGURE 9 – DOMS walking left thigh test. Values reported as means  $\pm$  SE.  
 \*Significantly different from baseline ( $p = 0.05$ )

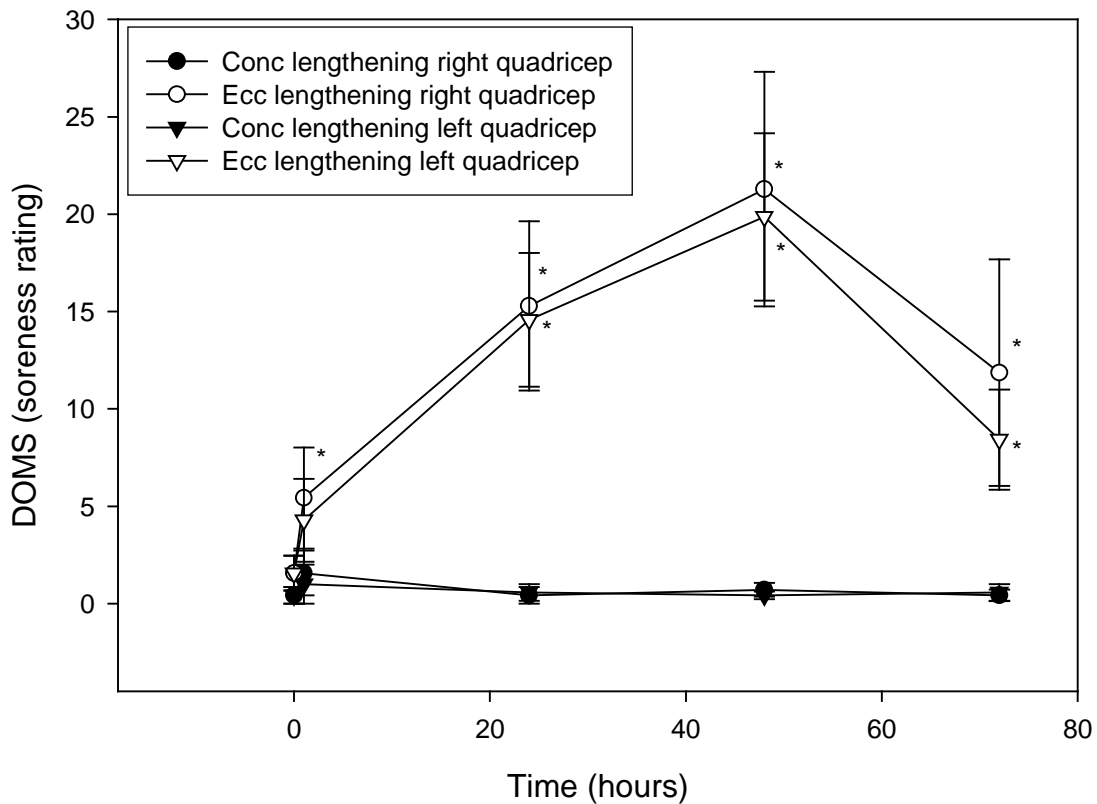


FIGURE 10 – DOMS lengthening quadriceps test. Values reported as means  $\pm$  SE. \*Significantly different from baseline ( $p = 0.05$ )

## DISCUSSION

It is known that an acute bout of resistance exercise has the potential to affect IS and biomarkers of inflammation (9, 25, 40, 66, 70). The unknown interactions between ECC and CON phases of contraction on IS, multiple markers of inflammation, and different subject populations make the current study unique. The almost statistically significant ( $p = 0.098$ ) result of the two different types of contraction causing opposite GT responses in an overweight, sedentary population is a key finding of the study. Another key finding of the study is the non-significant difference in IL-6 and TNF $\alpha$  responses between the two groups. The resulting increase in DOMS after the exercise

session is not a unique finding of the study but does reinforce the relationship between DOMS and ECC exercise.

**Glucose tolerance, insulin sensitivity and insulin resistance.** The results suggest a potential difference in the pre- and post-exercise GT response between the two groups in the current study. The mean insulin concentration required to maintain glucose levels in the Ecc group appear to slightly increase after exercise, versus the mean insulin concentration of the Conc group appear to slightly decrease after exercise. The individual findings from each group yielded no significant change, but when insulin concentrations pre- and post-exercise in the groups were compared, the contradictory changes on GT showed a trend ( $p = 0.098$ ). These results both contradict and coincide with findings from other investigators. In order to explain the results of the current study, previous studies measuring the affect of an acute bout of resistance exercise on GT must

Source	IS Assessment	Muscle Groups	# of Contractions	BMI	Result in IS
Fennichia (Control) (25)	OGTT	total body	3 x 8-12	25.8 ± 1.3	no change
Fennichia (NIDDM) (25)	OGTT	total body	3 x 8-12	37.9 ± 1.9	increase
Chapman (13)	IVGTT	total body	3 x 10	27.0 ± 1.7	no change
Koopman (50)	ITT	legs-only	8 x 10	23.1 ± 0.7	increase
Fluckey (NIDDM) (28)	OGTT	total body	3 x 10	No data	increase
Fluckey (Control) (28)	OGTT	total body	3 x 10	No data	increase
Howlett (40)	Euglycemic clamp	total body	3 x 10	22.8 ± 0.9	decrease

FIGURE 11 – List previous studies analyzing effects of an acute bout of resistance exercise on insulin sensitivity. # of Contractions is sets x reps.

Koopman et al. (50) has previously shown that a single session of whole-body resistance exercise can increase IS 24-hours post-exercise. One of the major differences between that study and the current study was exercise prescription. The group obtained

the increased IS through a training session that included three sets of ten repetitions of three upper body exercise and 16 sets of ten repetitions of two lower body exercises at the same relative intensity of the current study. Another major difference in exercise prescription was the exercise included both ECC and CON phases of resistance exercise. A major difference outside of exercise prescription was that the subject population was of healthy weight ( $BMI 23.1 \pm 0.7$ )(50).

Fluckey et al. (28) has also shown that the IS response in subjects increased 18-hours after a three-set, total body resistance exercise session. The group measured IS using an OGTT and found that the IS increase was due to an increased glucose clearance, not a decrease in insulin secretion. The subject population included young (mean body fat percent  $18.9 \pm 0.9$ ) and elderly (mean body fat percent  $22.6 \pm 2.3$ ) groups, all having had previously diagnosed NIDDM and were untrained. The total-body resistance exercise protocol included both CON and ECC phases of exercise.

The primary differences observed between the lack of change of each group in the current study and previous studies that had increased IS through an acute resistance exercise session were exercise prescription and subject population. The difference in exercise prescription could have led to less glucose utilization and turnover through three major causes. First, an exercise prescription in which more muscle groups of both the upper- and lower-body are used recruits more muscle fibers, causing more glucose to be utilized by the muscles during total-body exercise versus lower-body only exercise (22, 36, 50). Second, an increased amount of sets or repetitions can have a similar effect of GLUT-4 translocation when compared to lesser volume because of the greater number of muscle contractions. Third, Ryschon et al. (75) concluded that ECC exercise had lesser

amounts of ATP turnover than CON exercise. From the Ryschon group conclusion, we can draw the assumption that performing either ECC-only or CON-only resistance exercise will use less ATP than performing both phases of resistance exercise together. This would again lead to less GLUT-4 translocation and AMPK activation.

Previous studies that attempted to isolate ECC and CON muscle action have also yielded conflicting results with the current study. Del Aguila et al. (19) found that an acute bout of downhill running decreased insulin-mediated glucose uptake due to the inflammation caused by muscle damage associated with ECC exercise. The subject population consisted of young healthy males that were of normal weight. The same group had conducted a similar study in a similar population but the exercise was primarily CON (48, 52). The results from the CON exercise session had no effect on insulin action, similar to the current study, but again the exercise mode differed. The difference between the two studies by Del Aguila et al. (19, 48, 52) provide combined results that are similar to the current study showing that the human body has a different IS response to severe muscle damaging exercise versus non-damaging exercise.

The differences in subject population may have also accounted for the difference in the group IS results between the current study and previous studies. Overweight and obese populations have shown increased levels of insulin resistance (IR) when compared to leaner populations (17, 31). The increase in IR is attributed to decreased intracellular signaling. With decreased intracellular signaling, less GLUT-4 may translocate to the cell surface, thereby decreasing the amount of glucose absorbed by the muscle from the blood, causing a decrease in IS. A combination of all of the differences between the studies may have had compounding influence that led to no IR or IS change due to ECC-

only or CON-only resistance exercise. Further studies isolating ECC and CON phases of resistance exercise as well as the effects of resistance exercise in varying populations are needed.

The previous studies that have resulted in similar IS findings to the group findings of the current study have had a similar subject population. Chapman et al. (13) had subjects (mean BMI  $27.0 \pm 1.7$ ) perform an exercise session modeled after Fluckey et al. (28) in which the subjects performed both phases of exercise for three sets of 10 repetitions on seven machines that made for a total-body workout. Chapman et al. (13) found no change in IS after the resistance exercise session. Fennichia et al. (25) found no change in IS of the healthy group after a resistance exercise session that involved 8 exercise encompassing upper and lower body exercises for 3 sets of 8-12 repetitions. The subject population for Fennichia et al. (25) was comprised of two different groups; one with diagnosed type 2 diabetes (mean BMI  $37.9 \pm 1.9$ ) and a control group without type 2 diabetes (mean BMI  $25.8 \pm 1.3$ ). The commonality of an overweight subject population combined with the differing exercise prescription leads to the assumption that body weight is more important than resistance exercise prescription when measuring the effects on IS.

**Interleukin-6.** Exercise stimulated increases in IL-6 have been caused by many contributing factors yielding varied degrees of change. Muscle mass has been a primary factor; larger muscle groups such as the quadriceps had the most impact on IL-6 as compared to smaller upper-body muscle groups (71). Exercise duration has also been another key factor to IL-6 production. Six minutes of exercise has shown to double IL-6 levels (63) but no studies have shown even a 10-fold increase in exercise lasting less than

1-hour. Long exercise sessions such as a marathon in Ostrowski et al. (64) have shown 128-fold increases in IL-6. Exercise intensity has been the third, main contributing factor to the IL-6 response. A direct relationship has been observed in the sensitivity of response of IL-6 to increased exercise intensity (37, 65).

The trend observed in the current study between the measured time points of one-hour post exercise and 24-hours post-exercise showed a decline in IL-6 ( $p = 0.097$ ). This suggests that muscle contraction, regardless of whether it is an ECC or CON muscle contraction, will elevate circulating IL-6 for only a brief period. This finding confirms work done by Starkie et al. (79) that demonstrated that the IL-6 gene was expressed in human skeletal muscle and muscle contraction had a marked increase on the gene expression. Through measurements using PCR techniques, the group was able to determine a significant increase in muscle IL-6 following moderate intensity exercise. Muscle contraction was the primary cause of the IL-6 increase, not glycogen content, because the group measured and replenished glycogen stores during the exercise session. Similar IL-6 findings in the Nielsen et al. (63), Steensberg et al. (81) and Peake et al. (67) groups confirm that IL-6 concentration can be effected by exercise. The primary difference between the current study and the previous studies was exercise modality; the exercise mode was running. The second major difference was subject population; the subjects were recreationally trained or well trained.

The primary differences of exercise modality and subject population could cause potentially contradictory findings as observed with the current study when comparing the baseline IL-6 levels to the one-hour post-exercise due to the principals by which exercise increases circulating IL-6. The exercise mode of running produced constant, extended



muscle contractions during previous studies, generally running 45-180 minutes continuously. The absolute number of muscle contractions in the previous running studies was far greater than the 60 total contractions of the current study. This point can be further proven by the MacIntyre et al. (57) and Paulsen et al. (66) groups in which subjects performed 300 maximal eccentric quadriceps contractions and significant IL-6 changes were found. The training status of the subjects may have played a more important role than expected in the current study. Even though the subjects were told and then encouraged during the exercise to give their full effort, with the intention of the exercise being at maximum intensity; untrained subjects do not have the neurological adaptations to activate enough muscle fibers to lift their true repetition maximums. The neurological adaptations come with training, which the previous studies used well-trained or recreationally trained subjects.

The anticipated differences of IL-6 between the Ecc and Conc groups were based on muscle damage. Previous studies have shown that muscle contraction produced increased circulating IL-6 regardless of whether it was ECC or CON contractions (41, 55, 68, 69, 70). Those findings contradicted other research that had found that only ECC contractions produced elevations in IL-6 due to the high amount of muscle damage (9, 66, 85, 87). Boppart et al. (7) isolated ECC and CON muscle contractions with an exercise prescription of 20 sets of 10 repetitions of either ECC or CON isokinetic knee extensions at maximum intensity. The subject population consisted of healthy, sedentary, normal weight individuals and measured JNK activity. The results showed that both CON and ECC exercise increased JNK activity, with ECC exercise having a much larger

effect on JNK (7). These results contradict the current study because JNK is an upstream activator of IL-6.

The current findings suggest that the type of contraction, even at a high intensity is not the primary cause of elevated IL-6 levels in the blood. Other factors appear to be of greater importance, which may include health, weight, and exercise duration. These findings also suggest that when IL-6 is elevated due to exercise, circulating levels will drop to or below baseline measures by 24-hours post-exercise, but the exact amount of time required for IL-6 levels to drop was not shown by the current study because measurements between 1-24 hours were not taken.

**Tumor necrosis factor alpha.** The current study found no change in TNF $\alpha$  over time and no difference in TNF $\alpha$  levels between the Ecc and Conc groups. These results coincide with previous studies that had also found TNF $\alpha$  levels unaltered due to ECC exercise (80, 81, 85). The physiological explanation for why exercise of any modality does not raise TNF $\alpha$  levels may be due to the inhibition of glucose transport into the cell caused by the cytokine (8, 46, 75). Because TNF $\alpha$  inhibits the glucose transport, elevations in TNF $\alpha$  during or after exercise would block the primary fuel source of contracting muscle, lessening the longevity and intensity of the muscle contractions.

Previous studies have also shown that after intense exercise with a large ECC component TNF $\alpha$  levels have increased in response to muscle damage and elevated creatine kinase levels (19, 91, 94). The cause of elevation in TNF $\alpha$  after muscle damage was the role of the cytokine as part of an acute phase immunological response (11, 19). It is possible that the current study did not cause enough damage to sarcomeres to trigger this response in the Ecc group.

### **Glucose tolerance, interleukin-6, and tumor necrosis factor alpha**

**relationships.** The current study resulted in no significant difference between Ecc and Conc groups on TNF $\alpha$  or IL-6 and suggested a difference in IS response to the different types of contraction. This result was unexpected, but the combined lack of change of TNF $\alpha$  and IL-6 warrants a more detailed review of the possible interactions.

Previous research has shown that TNF $\alpha$  plays a significant role in insulin action. Muscle TNF $\alpha$  expression has been shown to be elevated in diabetic and previously diagnosed insulin resistant subjects (8, 77), and in previously eccentrically exercised muscle that experienced insulin resistance post-exercise (19, 33, 94). The mechanism by which TNF $\alpha$  decreased insulin action was through the serine phosphorylation of IRS-1, which impairs the association to the insulin receptor, thereby inhibiting downstream signaling (8, 75). Previous studies involving CON-only exercise have been shown to produce no change in TNF $\alpha$  (48, 81), but exercise of a highly ECC-contraction nature has shown to increase expression of TNF $\alpha$  (19, 33, 94). These findings have led to previous conclusions that TNF $\alpha$  has been the cause of decreased insulin responsiveness in muscle after ECC exercise (19, 33, 94). In the current study, the lack of change in TNF $\alpha$  indicates that it is not the main mechanism of any changes observed in IS after the ECC exercise.

The link between the suggested increase in IL-6 of both groups and the opposing change in IS post-exercise is unclear. Febbraio et al. (24) has shown that IL-6 levels were the primary regulator of increased glucose disposal due to exercise. The group exogenously elevated circulating IL-6 during low-intensity exercise to match levels found during high intensity exercise, and then compared glucose disposal rate during that

exercise to low-exercise intensity alone, finding that at the same level of exercise intensity, elevated IL-6 levels significantly increased GDR. It was also shown that IL-6 was not the sole factor for the increase because during low-intensity exercise, no elevation in IL-6 was seen, but increased GDR was observed. Carey et al. (12) has shown that the mechanism by which IL-6 enhanced insulin-stimulated glucose disposal was the AMPK. The effect of circulating IL-6 increased whole-body glucose disposal through an increased activation of AMPK, a known regulator of insulin signaling transduction. The result that both exercise groups had the same IL-6 response to exercise and opposing IS response indicates that IL-6 is not the primary indicator of the exercise induced changes in IS.

The combined lack of differences between groups of both IL-6 and TNF $\alpha$  resulting in opposing IS response indicates that neither of the markers measured in the current study were the source of IS change. It has previously been thought that when no change in TNF $\alpha$  is observed, there will not be a phosphorylation of IRS-1, and normal glucose homeostasis will occur. When no change in IL-6 is observed, AMPK activity will remain constant and no increase in GLUT4 translocation will occur. It is of note that a previously determined indirect relationship exists between TNF $\alpha$  and IL-6. Starkie et al. (80) found that when subjects were either injected with recombinant human IL-6 or exercised until IL-6 levels rose, circulating TNF $\alpha$  levels dropped. It was within the scope of the current study to determine which marker of inflammation would have elevated and affected IS after the exercise session, but the lack of difference between groups yielded inconclusive results.

**Delayed onset muscle soreness.** The clinical manifestation of DOMS is due to exercise induced muscle damage most often associated with unfamiliar, high-force exercise that contains a heavy eccentric component (14, 16, 27, 62). The significant finding of DOMS peaking at 48 hours for the Ecc group in all measured muscle groups was further evidence of the cause of DOMS (56). The sedentary population performing intense ECC contractions in the current study was expected to experience DOMS.

The significant difference between the Ecc and Conc groups provided further evidence for previous research that found CON exercise to not cause DOMS in most cases (14, 56, 57). Most CON exercise does not cause significant muscle damage, thereby not causing the inflammation associated with sarcomere disruption or free radicals. The inflammation that may be the cause of DOMS cannot be measured using IL-6 and TNF $\alpha$  because the between group differences of DOMS did not show a similar interaction in IL-6 or TNF $\alpha$  (table 3 and table 6). The exercise prescription in the current study, even in the Ecc group, did not cause severe enough DOMS to cause subjects to withdraw from the study due to pain.

**Study limitations.** The largest limitation of our study was the variety of effort given by the subjects. The primary researcher provided uniform verbal motivation for the subjects, but varying intrinsic motivation may have caused a varying degree of effort during 1-RM testing. Whether the subject did not try enough or tried too much, the 1-RM measurement would be slightly different than the true 1-RM, but the variability would not have been great enough to significantly affect the exercise intensity or data following the exercise session.

**Conclusions.** In an untrained, overweight population eccentric-only resistance exercise and concentric-only resistance exercise may have an opposite affect on glucose tolerance. The different contraction types bear no difference of response in IL-6 or TNF $\alpha$ . The current study does not indicate IL-6 or TNF $\alpha$  to be the primary mechanism by which glucose tolerance is affected by resistance exercise in this specific population.

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APPENDIX A:  
EXTENDED LITERATURE  
REVIEW



## **THE OBESITY EPIDEMIC**

There are 1.1 billion overweight adults in the world, 312 million of them are considered obese (82). Obesity is directly associated with an increased incidence of cardiovascular disease, which causes more than 18 million deaths per year (27). Obesity can also increase the risk of cancer, in which there are over 1.4 million predicted new cancer cases per year (31). Because of the adoption of a lifestyle that consists of low levels of physical activity and increased consumption of high fat, high sugar foods, the obesity rates have tripled in the past 20 years in developing countries. This unhealthy lifestyle is not limited to only adults, there are over 155 million overweight or obese children worldwide (27). The actual cost of the obesity epidemic was \$123 billion in America alone in 2001 for healthcare costs that were directly and indirectly related to obesity (82).

Obesity leads to an increased risk of atherosclerosis and cancer through the compounding effects of multiple mechanisms. One of the main sources of increased risk is from secretion of cytokines from adipocytes (adipokines). Most adipokines have adverse effects on health, such as plasminogen activator inhibitor-1 (PAI-1) and TNF $\alpha$ , which have been directly implicated in the progression of atherosclerosis and insulin resistance with obesity (28, 69, 78). Adipocytes also secrete adiponectin into circulation. Adiponectin has insulin-sensitizing (4, 5, 20, 88) and anti-thrombotic properties (46, 56, 87), but decreased plasma adiponectin levels have been associated with obesity (21). The exact mechanisms by which adipokines are dysregulated in obesity have not yet been conclusively found, but it has been theorized that oxidative stress precludes and contributes to dysregulated adipokines.

## **OXIDATIVE STRESS**

Oxidative stress plays a critical role in the pathogenesis of many diseases, may induce the dysregulation of adipokines, and increases with obesity (6, 21, 76). It has been reported that oxidative stress precedes disease states including insulin resistance and obesity when induced by a high-fat diet (47). Free fatty acids and adipose tissue alone have been shown to stimulate increases in oxidative stress (24, 29, 78). When a high-fat diet has led to increased adiposity, both oxidative adipokines increased and the protective adiponectin secretions decreased because of the adipose tissue (21, 47, 76, 80, 88). Oxidative stress can be defined as an imbalance between oxidants and antioxidants in favor of the oxidants, potentially leading to damage. Oxidants are most commonly referred to as reactive oxygen species (ROS), which encompasses a wide range of oxidizing molecules including superoxide anion radical, hydrogen peroxide, and hydroxyl radical (85). ROS molecules are constantly produced during metabolic reactions but are often counteracted and balanced by physiologic antioxidants. Some of the most common sites of ROS production include mitochondria during oxidative phosphorylation, leukocytes during oxidative burst, peroxisomes during the degradation of fatty acids, and the cytochrome P450 system which serves as a mixed function oxidation system (25, 79).

There have been many markers that have been measured in previous studies to determine the level of oxidative stress on the body. Some of the more established markers have been malondialdehyde (MDA), oxidized low-density lipoprotein (ox-LDL), MDA-modified LDL, auto-antibodies against ox-LDL and MDA-modified LDL, F2-isoprostane, and conjugated diene (25, 84, 85). Recently the 8-hydroxy-2'-

deoxyguanosine (8-OHdG) has become a primary measure of oxidative stress in humans due to the non-invasive measurement of urinary 8-OHdG (11, 12, 13, 42, 60, 61, 62, 63, 79).

The main source of oxidative stress in obese individuals has been shown to be caused by chronic poor diet. Elevated glucose intake during a meal has been shown to induce acute oxidative stress at a molecular level for a period of three hours (14, 18, 50). Mixed fast-food meals have been shown to induce similar oxidative stress for a period of four hours postprandially (15). When obese subjects had a restricted diet of 1000 calories per day for four weeks, the ROS generation dropped more than 50% and a significant decline in the ratios of indexes for lipid oxidation occurred (15). Elevated blood glucose and free fatty acid levels observed in obese populations can also increase systemic oxidative stress (14, 29). Inoguchi et al. (29) documented elevated ROS in cultured vascular smooth muscle cells and endothelial cells through protein kinase C (PKC)-dependent activation of NADPH oxidase in both elevated glucose and palmitate environments, which are commonly seen in obese populations (14). The elevation of ROS in smooth muscle and endothelial cells may provide a mechanistic link between obesity and cancer or atherosclerosis.

**The role of oxidative stress in cancer.** Oxidative damage has most commonly been seen on the nuclear and mitochondrial DNA in tissues and blood lymphocytes (10, 79). Guanine has been the most common target for DNA-modification through an addition of a hydroxyl group to the 8<sup>th</sup> position (84, 85). The mutation of the guanine base leads to misreading of the modified base and a loss of base-pairing specificity. Repair enzymes that mediate transcription generally remove or repair oxidatively

damaged DNA, but sometimes the oxidized DNA gets transcribed, increasing the risk of cancer (58). The highest levels of oxidatively modified DNA found in humans have been found in tumors, measured through increased levels of 8-OHdG (35, 44).

There is further evidence of the link between oxidized-DNA and cancer in studies conducted with malignant tumor and cancer patients. Tumors have been shown to generate large amounts of hydrogen peroxide (74), which has led to higher levels of oxidized DNA lesions in malignant cells (75). Mussarat et al. (53) showed that elevated accumulations of 8-OHdG in nuclear DNA could significantly predict increased risk of breast cancer during patient assessment and was a significant contributor to breast neoplasia. The same group found a 9.76-fold increase in 8-OHdG in malignant breast tissue cells compared to normal cells. Previous groups have also found significant increases in 8-OHdG and analogs of 8-OHdG in patients with bladder and prostate cancers compared with healthy individuals (9).

After DNA lesions occur, ROS can further contribute increased cancer risk through regulation of gene expression, increasing cell proliferation as shown in figure 10 (35). Hydrogen peroxide ( $H_2O_2$ ) is a common oxidant that can physiologically signal downstream to increase transcription and decrease apoptosis through two distinct pathways. The first signaling pathway occurs through the activation of mitogen-activated protein kinase (MAPK) (52). After activation of MAPK, the signaling cascade will eventually up-regulate extracellular-signal regulated kinases (ERK), which increase cell proliferation, and down-regulate c-Jun N-terminal kinases (JNK), which increase apoptosis (45, 86, 68). The second signaling pathway occurs through the nuclear localization of NFkB. Wu et al. (84) found that ROS oxidized p53 to a disulphide that

caused NFκB to translocate from the nucleus. When NFκB exits the nucleus, an observed increase in cell proliferation occurs (64).

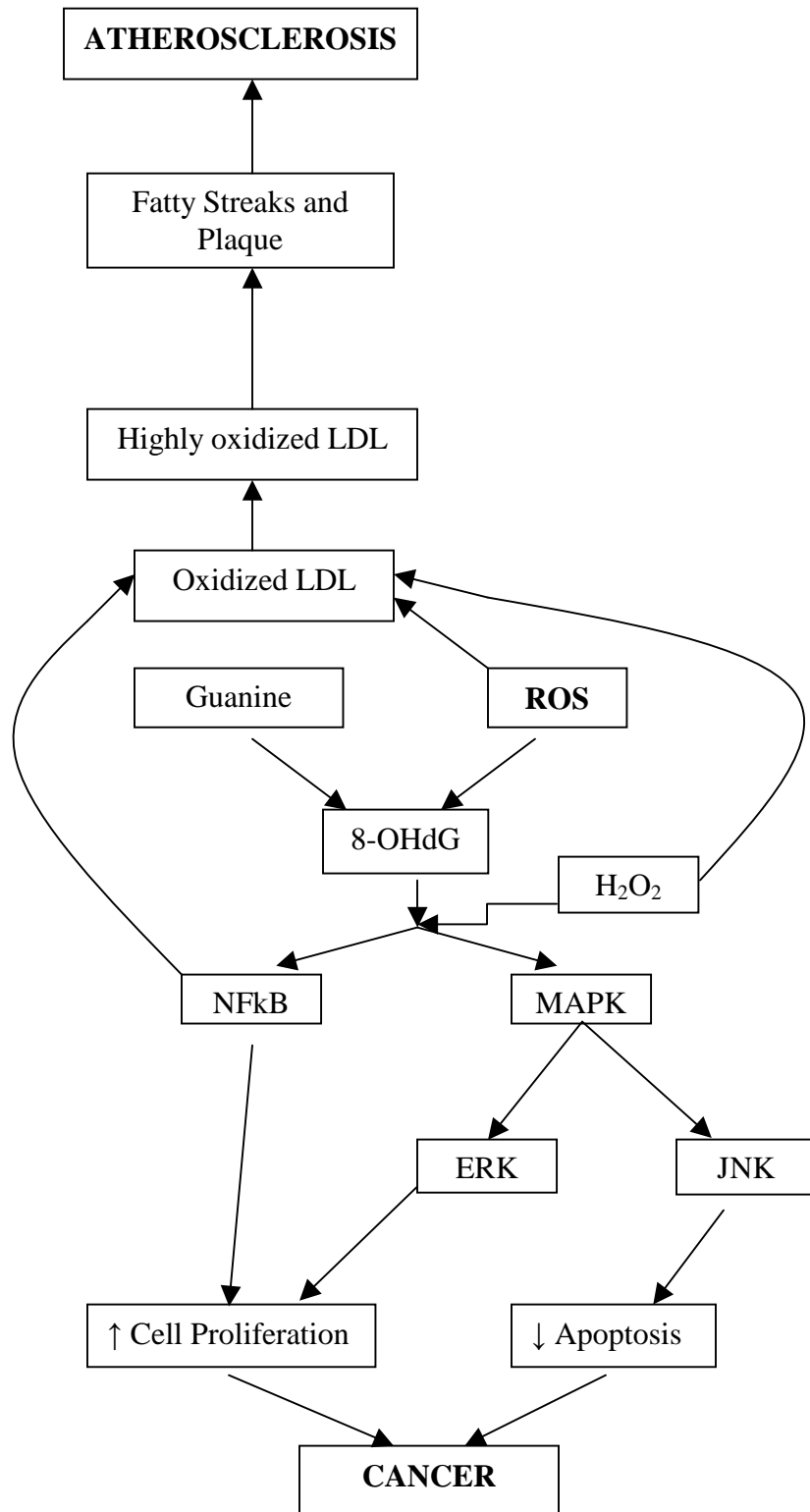


FIGURE 12 - Signaling cascade of ROS increasing cell proliferation.

**The role of oxidative stress in atherosclerosis.** An important initiating event in atherosclerosis is that transport of ox-LDL across the endothelium into the artery wall (54). The transport often occurs at sites that have been previously damaged by circulating ox-LDL, have had physical or chemical damage to the endothelial wall, or have been a site of infection (65). LDL oxidation takes place due to phospholipid modification from the oxidants of endothelial cells, smooth muscle cells, and macrophages (26). The endothelial damage induces the expression of adhesion molecules that attract monocytes and T-lymphocytes (49). The monocytes then ingest lipoproteins, causing them to morph into ROS secreting macrophages. The macrophages form highly oxidized LDL from ox-LDL, which is then reabsorbed by the macrophages to form foam cells. The foam cells then combine with leukocytes to form fatty streaks in the intima, indicative of atherosclerosis.

Evidence suggests that nicotinamide adenine dinucleotide phosphate (NADPH) oxidase and xanthine oxidase (XO) are the major sources of superoxide generation in the vasculature through univalent reduction of oxygen (24, 26, 51). Vascular NADPH oxidase has been shown to increase with numerous atherogenic markers including angiotensin II, thrombin, platelet derived growth factor, and TNF $\alpha$  (17, 26, 57, 73, 77). Warnholtz et al. (81) has shown in hypercholesterolemic rabbits prone to atherosclerosis, elevated levels of NADPH oxidase were associated with greater endothelial dysfunction. In human studies high levels of NADPH oxidase and XO agonists have been observed in atherosclerotic plaques (2, 8, 55, 67).

**Atherosclerosis and cancer.** Both atherosclerosis and cancer share a similar molecular pathway that involve inflammation and oxidation during the progression of the

disease states. Elevations of ROS lead to a significant increases in inflammatory markers, thereby increasing the risk of both disease states, providing a possible link between the diseases. NFkB is an upstream indicator of many biomarkers of inflammation including TNF $\alpha$ , which has been shown to play a primary role in the pathogenesis of atherosclerosis (41). TNF $\alpha$  was among the first reported cytokines to generate ROS, along with ROS being a secondary messenger during the activation of TNF $\alpha$  (78). TNF $\alpha$  can be directly secreted by adipose tissue (41) or can be elevated through a signaling cascade in association with NFkB (fig. 12). The inflammatory biomarker TNF $\alpha$  has been implicated in the progression and pathogenesis of both atherosclerosis and cancer.

Another common source of oxidation linking the two diseases is H<sub>2</sub>O<sub>2</sub>. H<sub>2</sub>O<sub>2</sub> is a by-product of many enzymatic reactions (fig. 13) that will commonly change the redox milieu extracellularly or can cross the plasma membrane and change the intracellular redox environment. H<sub>2</sub>O<sub>2</sub> is the less reactive, more readily diffusible precursor to the hydroxyl radical (34). The hydroxyl radical is a highly reactive oxidative molecule that quickly oxidizes adjacent molecules. The hydroxyl radical is a primary source of base modification causing DNA damage, as well as a source of lipid oxidation (26, 34).

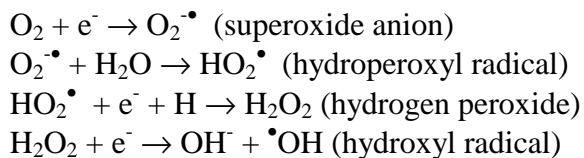


FIGURE 13 – Generation of ROS via reduction of molecular oxygen.



**Exercise as protection from Oxidative Stress.** Regular physical exercise has been shown to have beneficial health effects through reducing the risk of cardiovascular disease, cancer, osteoporosis, and diabetes (32, 37, 38). These health benefits occur through many different mechanism including decreased adipose tissue, altered lipid and hormonal profiles, improved mitochondrial uncoupling, and up-regulated antioxidant defenses (39, 61). In order for these health benefits to occur, the body must up-regulate these defenses to combat stress-induced damage during exercise from ROS (39). The ROS produced during acute exercise are byproducts of aerobic metabolism that occur during normal respiration and inflammation. The oxidative stress caused by acute exercise in trained and untrained individuals has been shown to cause DNA, enzymatic, protein receptor, and lipid membrane damage (1, 36, 59). The beneficial adaptations that occur from regular physical exercise as they pertain to ROS can best be explained through the hormesis theory.

The hormesis theory has been applied and discussed in various fields for many years because the theory principle is that low doses of toxins and/or radiation can exert beneficial effects in lower organisms (60, 61, 71). The theory has recently been found to apply to higher organisms as well (7, 33, 72). The theory is based on the findings that low doses of chronic stressors cause the body to supercompensate during recovery, thereby preparing itself for future stressors. The theory can be applied to exercise training adaptations in many ways; the most common is through the glycogen storage response to endurance exercise training. During long bouts of endurance exercise glycogen stores become depleted, but after numerous bouts of endurance exercise sessions with adequate recovery between sessions, resting glycogen stores are elevated

beyond the levels before training commenced due to supercompensation. Physiological antioxidants respond to exercise in a similar manner through ROS eliciting a response in the body that follows a bell-shaped curve; low doses of ROS have stimulatory effects and high doses have enzyme inhibition and apoptotic effects.

Low levels of ROS are necessary for exercise training adaptations to occur. Without the production of ROS, some of the major protective effects of exercise training are lost. In an animal model, Sun et al. (72) pre-conditioned the heart with low doses of ROS repeatedly, which then protected it from abnormal functioning during a future high-oxidative stress challenge. This study was relevant to exercise physiology because the low levels of ROS produced during exercise can protect the heart from future ROS-induced atherosclerosis. Further evidence has found that blocking ROS production during and after exercise inhibited exercise training adaptations that would normally occur (22). Gomez-Cabrera et al. (22) used allopurinol to block ROS through decreased XO production in rats. They then observed a lack of up-regulation of superoxide dismutase (SOD) and nitric oxide synthase that prevented any protection from the NFkB and MAPK signaling pathways (22).

The three major mechanisms by which exercise provides protective effects involves many pathways that enhance the antioxidant systems as shown in figure 14 (30, 60). First, Exercise primarily increases  $H_2O_2$  during calcium release in muscle contraction (30, 40, 60). Because of the oxidative damage potential of  $H_2O_2$ , regular exercise stimulates an increase in the activity of the proteasome complex and an increase in the DNA damage repair system (60, 62, 63, 66, 83). The proteasome complex is responsible for the degradation of oxidized proteins, which upon degradation, leads to

more efficient cell function and decreased amounts of mutagen DNA (23, 70). Increased proteasome efficiency also leads to a decrease in oxidative potential of ROS due to a decrease in the amount of time to oxidize (3). In human studies, regular exercisers exhibit lower levels of 8-OHdG in leukocytes when compared with sedentary controls (66, 83). Regular exercisers also display increased mRNA for the DNA repair enzyme 8-oxoG DNA glycosylase, which provides greater protection due to stimulation and stabilization of the transcriptional mRNA (66, 83).

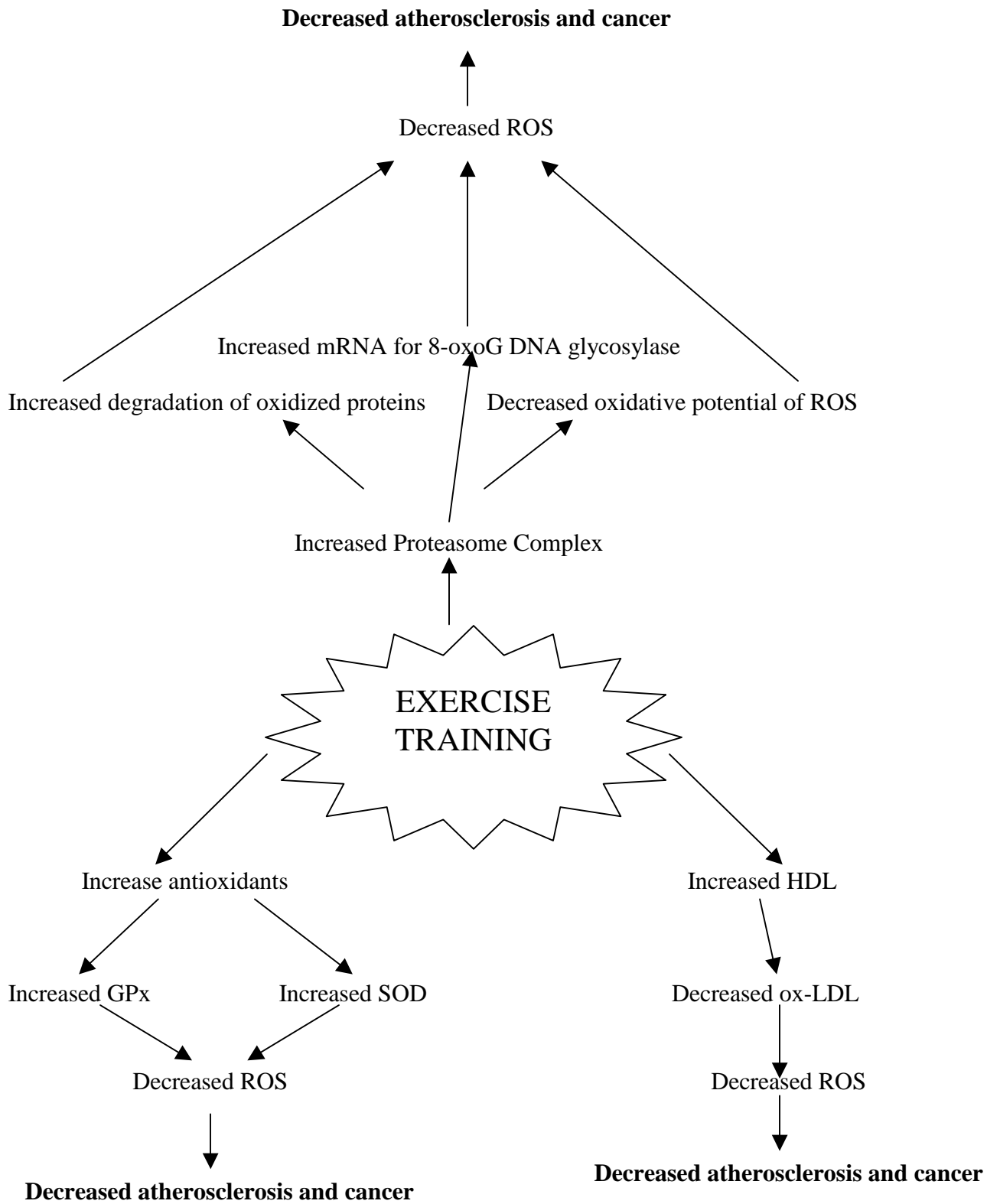


FIGURE 14 - Pathways involved in exercise training adaptation.

The second major antioxidant system is the removal of free radicals from ROS via catalase, glutathione peroxidase (GPx) and SOD. Regular exercise had been shown to increase production of antioxidant enzymes cytosolic GPx and mitochondrial SOD (30, 39, 40, 61), but catalase has shown to be unaffected (40). Both GPx and SOD are potent enzymatic antioxidants that directly reduce ROS, removing the harmful oxidation potential (79). In animal models, endurance training has been shown to increase glutathione production 33%, GPx activity 62%, and SOD activity 27% when compared to untrained rats, indicating the protective effects of endurance training (39).

The third major antioxidant system involved in the regulation of oxidative stress that can be enhanced by exercise training is the elevation of high-density lipoprotein (HDL) subfractions. Plasma HDL has been well established as an effective combatant of atherosclerotic progression due to antioxidant and anti-inflammatory properties (80). HDL reduces and prevents formation of ox-LDL through the actions of paraoxonase-1, platelet-activating factor acetylhydrolase, lecithin-cholesterol acetyltransferase, glutathione selenoperoxidase, and apolipoprotein A-1. Plasma HDL has been shown to significantly increase with endurance training (19), thereby reducing the effects of oxidative stress.

**Summary.** The worldwide obesity epidemic has brought about increases in lifestyle related diseases including atherosclerosis and cancer. Both atherosclerosis and cancer can be caused by oxidative stress, which is related to obesity through high-fat diets and large amounts of adipose tissue. Exercise training can serve as preventative protection from oxidative stress through mechanisms related to the hormesis theory;

small exercise-induced elevations in oxidative stress cause up-regulation of the physiological antioxidant defenses protecting the body from future damage.

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APPENDIX B:  
INFORMED CONSENT

CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

Project # 1133997

Date of Project Approval: April 22, 2009

<b>FOR HS IRB USE ONLY</b>	
<b>APPROVED</b>	
<i>Dan Villan</i>	<i>4/12/10</i>
HS IRB Authorized Representative	Date
<b>EXPIRATION DATE:</b>	
<i>4.22.2010</i>	

**STUDY TITLE: THE EFFECTS OF ECCENTRIC AND CONCENTRIC RESISTANCE EXERCISE ON METABOLIC HEALTH.**

INTRODUCTION

**This consent may contain words that you do not understand. Please ask the investigator or the study staff to explain any words or information that you do not clearly understand.**

This is a research study. Research studies include only people who choose to participate. As a study participant you have the right to know about the procedures that will be used in this research study so that you can make the decision whether or not to participate. The information presented here is simply an effort to make you better informed so that you may give or withhold your consent to participate in this research study.

Please take your time to make your decision and discuss it with your family and friends.

You are being asked to take part in this study because you are an untrained, overweight person who may benefit from initiating a resistance-exercise program.

This study is being sponsored by the Department of Nutrition and Exercise Physiology and the Exercise Physiology Laboratory.

In order to participate in this study, it will be necessary to give your written consent.

WHY IS THIS STUDY BEING DONE?

Americans are getting heavier and more prone to lifestyle related diseases such as coronary heart disease and type 2 (formerly called adult onset) diabetes. Impaired insulin sensitivity, chronic inflammation, and elevated blood fats increase the risk of diabetes, heart disease, and cancer. Exercise training can reduce the risk for these diseases. Resistance exercise training (weight lifting) has become a popular form of exercise and has been shown to improve strength, body composition, and insulin sensitivity. Its effects on many other factors related

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VERSION 1.4  
NOVEMBER, 2004

1 of 7



to health have not been studied however. It is also unclear if different types of muscle contractions have different affects on health risks. The purpose of this study is to compare two different types of muscle contractions to see if they differ in their metabolic health benefits. We will test the effects of concentric contractions (lifting a weight) and eccentric contractions (lowering a weight). We will measure the effects that each contraction type has on specific indicators of health after a single session of exercise. The specific indicators of health risk that will be studied include: blood fats, blood sugar, and inflammation.

#### HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 40-45 people will take part in this study at this institution.

#### WHAT IS INVOLVED IN THE STUDY?

If you volunteer, your participation will consist of the following:

1. You will complete an initial screening consisting of:
  - a. Questionnaires on the following: medical, diet, activity, and menstrual cycle and pregnancy test (females only).
  - b. You will undergo a screening to assess kidney function. This screening consists of a blood draw to determine measures in the blood that indicate impaired kidney function.
2. You will undergo measurements of resting blood pressure and heart rate at the beginning of the study.
3. You will have your height and weight and waist and hip circumference measured. You will have your body composition assessed by DEXA. This machine uses a mild radiation (X-ray) dose to measure bone and muscle density. These measurements will be taken at the beginning of the study. The radiation from this exposure is less than one airplane ride.
4. You will undergo an orientation session which will consist of a light exercise session to familiarize yourself with the weight training equipment that will be used in the study.
5. You will record your food intake for two days during the baseline testing period of the study, including a 12-hour fast prior to the testing period. You will be asked to repeat this diet later prior to subsequent testing procedures.
6. You will be randomly assigned (like a coin flip) to one of two resistance exercise groups: 1. Concentric-only resistance exercise or 2. Eccentric-only resistance exercise.
7. Complete a one-repetition maximum (1-RM) test on both a leg extension and leg curl machine to determine the maximal amount of weight you are able to lift.
8. You will participate in a single session of resistance exercise. This session will consist of either concentric-only or eccentric-only exercise. This sessions will require you to:
  - a. Record your diet for 2 days prior to the single session of exercise.
  - b. Eat a diet (control diet) containing recommended values of fat, carbohydrate, and protein the day of the exercise session and for three days following the exercise session. You will

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need to record what you eat during this time period. You will be provided with some food and guidelines and recommendations on what to eat during this time.

- c. Report to the lab the morning of the exercise session after a 12-hour fast.
  - d. Assess muscle soreness, complete a test on the Biodex to measure your muscular strength, and have a lab technician draw your blood [approximately 10-15 ml (~ 1 tablespoon)].
  - e. Complete a five-minute warm-up on either a treadmill or stationary bicycle.
  - f. Complete three sets of ten repetitions at 80% of your maximum on the leg extension and leg curl machines.
  - g. Wait in the lab for one-hour and then assess soreness, complete a muscular strength test, and have your blood drawn again [10-15 ml (~ 1 tablespoon)] by a trained technician.
  - h. Report to the lab 24-hours after the exercise session and a 12-hour fast for another OGTT.
  - i. You will also be asked to return to the lab 48-hours and 72-hours following the resistance exercise session. During these visits, soreness will be assessed, a maximal strength test will be done, and blood samples [10-15 ml each (~ 1 tablespoon)] will be taken from a vein in your arm.
9. You will not receive any placebos.
10. You will not change your exercise or activity other than what the research requires.
11. You will maintain your normal dietary habits during the study other than changes required by consuming the control diet.
12. Blood will be kept in storage until all tests have been run in case of errors in the lab testing process. Once tests are completed, blood will be discarded.

19. Optional:

Since new markers of metabolic health risk are discovered frequently, we would like to save a small amount of your blood to be used in case of the discovery of unique variable(s) which would add to our information. We ask that you give approval for these tests to be performed using these samples. Your samples would be stored a maximum of 5 years. If you change your mind in the future and do not want us to keep your blood contact Dr. Thomas and the blood will be discarded.

Accept \_\_\_\_\_ Decline \_\_\_\_\_ Initials \_\_\_\_\_

HOW LONG WILL I BE IN THE STUDY?

If you volunteer, your participation will last approximately two-three weeks, but it will be ended at any time at your request, and Dr. Thomas or Dr. Whaley Connell (study physician) may end it at any time that, in their judgment, it is in your best interest to do so. Your time commitment for testing and treatment will be a maximum of 10 hours. Most of this is the exercise program.

**You can stop participating at any time. Your decision to withdraw from the study will not affect in any way your medical care and/or benefits.**

WHAT ARE THE RISKS OF THE STUDY?

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VERSION 1.4  
NOVEMBER, 2004

3 of 7

While in the study, you are at risk for the side effects described below. You should discuss these with the investigators and/or your doctor. There may be other side effects that we cannot predict.

1. Potential lightheadedness and tiredness during or at the end of the exercise session.
2. Heart problems may occur during the exercise training session. These potential problems include irregular heart beats, chest, back or jaw pain and/or nausea. In the event you experience any heart problems, we will stop the exercise session immediately and evaluate you to determine if you need medical attention.
3. It is likely that you will experience muscle soreness from the exercise. This soreness should subside within a few days. There is the potential for developing muscle damage (a condition called rhabdomyolysis) from the eccentric exercise (1-10% of the study participants) and this has the potential to affect your kidneys. For this reason we will perform an initial screening to check for impaired kidney function and will exclude you from participating in the study if you have any conditions that would increase your risk of developing rhabdomyolysis (muscle damage) from the eccentric exercise. Also, you will be asked to consume adequate amounts of water during and after the exercise sessions as well as have your urine tested for the presence of hemoglobin (protein) following the exercise sessions. Additionally, you will be asked to look for symptoms of muscle damage, including dark urine, painful muscle soreness and swelling and will be asked to report any symptom to a member of the study staff immediately. If your urine tests positive for hemoglobin you will be withdrawn from the study.
4. You may experience temporary discomfort and bruising where a needle is inserted to collect blood.
5. You will be exposed to X-rays during the DEXA scan.
6. Since the effects of purely eccentric or concentric resistance training on pregnant women have not been previously studied, this study will not include pregnant women. Females will be given a pregnancy test before beginning the study. If you start the study and then become pregnant, you will need to inform an investigator so that you may be safely withdrawn from the study.
8. As is true of all medications and medical treatment, there is always the possibility of a new or unexpected risk.

For reasons stated above we will observe you closely while giving you the treatment described. If you have any worrisome symptoms or symptoms that my associates and I have described to you, notify Dr. Thomas or Dr. Whaley Connell (study physician) immediately. **Dr. Thomas' telephone number is (573) 882-0062 or 882-8191 and Dr. Whaley Connell may be reached at (573) 882-7992.**

#### ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you. You may expect to benefit from taking part in this research to the extent that you are contributing to the medical knowledge. Other benefits include: general health and fitness information, blood lipid profile (cholesterol, etc), and body fat percentage assessment. You also will have access to parking during all study related visits.

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WHAT OTHER OPTIONS ARE THERE?

An alternative would be to not participate in this research.

WHAT ABOUT CONFIDENTIALITY?

Information produced by this study will be stored in the investigator's file and identified by a code number only. The code key connecting your name to specific information about you will be kept in a separate, secure location. Information contained in your records may not be given to anyone unaffiliated with the study in a form that could identify you without your written consent, except as required by law. If the investigator conducting this study is not your primary, or regular doctor, (s)he must obtain your permission before contacting your regular doctor for information about your past medical history or to inform them that you are in this trial.

Results of this research may be published and reports may be made to government agencies, funding agencies, manufacturers or scientific bodies, but you will not be identified in any such publication or report. In addition, the Federal Food and Drug Administration, other government agencies, and the manufacturer of the drug(s) used in this study may inspect and copy your medical records that apply to this research. In all cases, information about you will be treated confidentially.

WHAT ARE THE COSTS?

Examinations and tests for this research will be paid for by the Exercise Physiology Laboratory.

WILL I BE PAID FOR PARTICIPATING IN THE STUDY?

You will be paid \$50 for completion of the study.

WHAT IF I AM INJURED?

It is not the policy of the University of Missouri to compensate human subjects in the event the research results in injury. The University of Missouri, in fulfilling its public responsibility, has provided medical, professional and general liability insurance coverage for any injury in the event such injury is caused by the negligence of the University of Missouri, its faculty and staff. The University of Missouri also will provide, within the limitations of the laws of the State of Missouri, facilities and medical attention to subjects who suffer injuries while participating in the research projects of the University of Missouri. In the event you have suffered injury as the result of participation in this research program, you are to contact the Risk Management Officer, telephone number (573) 882-1181, at the Health Sciences Center, who can review the matter and provide further information. This statement is not to be construed as an admission of liability.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

**Participation in this study is voluntary. If you do not volunteer or if your participation is ended for any reason, this will not affect any care or consideration to which you are entitled.** In addition, the investigator of this study may decide to end your participation in this study at any time after Dr. Thomas or his representative has explained the reasons for doing so.

You will be informed of any significant new findings discovered during the course of this study that might influence your health, welfare, or willingness to continue participation in this study.

**WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?**

Please ask any questions you have about this research or how it will affect you, and I will answer them. In addition, if you have any questions during your participation Dr. Thomas, Shana Warner or one of their associates, will be glad to discuss them with you. You may call Dr. Thomas at (573) 882-8191 or 882-0062, Shana Warner at (573) 882-8191 or the study physician, Dr. Whaley Connell at (573) 882-7992.

If you have any questions regarding your rights as a participant in this research and/or concerns about the study, or if you feel under any pressure to enroll or to continue to participate in this study, you may contact the University of Missouri Health Sciences Institutional Review Board (which is a group of people who review the research studies to protect participants' rights) at (573) 882-3181.

A copy of this consent form will be given to you to keep.

**Signature**

I confirm that the purpose of the research, the study procedures, the possible risks and discomforts as well as potential benefits that I may experience have been explained to me. Alternatives to my participation in the study also have been discussed. I have read this consent form and my questions have been answered. My signature below indicates my willingness to participate in this study.

\_\_\_\_\_  
Subject/Patient\* \_\_\_\_\_  
Date

\_\_\_\_\_  
Legal Guardian/Advocate/Witness (if required)\*\* \_\_\_\_\_  
Date

\_\_\_\_\_  
Additional Signature (if required) (identify relationship to subject)\*\*\* \_\_\_\_\_  
Date

\*A minor's signature on this line indicates his/her assent to participate in this study. A minor's signature is not required if he/she is under 7 years old. Use the "Legal Guardian/Advocate/Witness" line for the parent's signature, and you may use the "Additional Signature" line for the second parent's signature, if required.

\*\*The presence and signature of an impartial witness is required during the entire informed consent discussion if the patient or patient's legally authorized representative is unable to read.

\*\*\*The "Additional Signature" line may be used for the second parent's signature, if required. This line may also be used for any other signature which is required as per federal, state, local, sponsor and/or any other entity requirements.

"If required" means that the signature line is signed only if it is required as per federal, state, local, sponsor and/or any other entity requirements.

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SIGNATURE OF STUDY REPRESENTATIVE

I have explained the purpose of the research, the study procedures, identifying those that are investigational, the possible risks and discomforts as well as potential benefits and have answered questions regarding the study to the best of my ability.

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Study Representative\*\*\*\*

Date

\*\*\*\*Study Representative is a person authorized to obtain consent. Per the policies of the University of Missouri Health Care, for any 'significant risk/treatment' study, the Study Representative must be a physician who is either the Principal or Co-Investigator. If the study is deemed either 'significant risk/non-treatment' or 'minimal risk,' the Study Representative may be a non-physician study investigator.

APPENDIX C:  
SUBJECT DATA FORMS

Date:

Day of Week:

Time	Food/Drink	Brand	Amount (tsp, cup, oz)	Condiments Food Prep	Location/Place Restaurant
<b>BREAKFAST</b>					
<b>MORNING SNACK</b>					
<b>LUNCH</b>					

Time	Food/Drink	Brand	Amount (tsp, cup, oz)	Condiments Food Prep	Location/Place Restaurant
<b>AFTERNOON SNACK</b>					
<b>DINNER</b>					
<b>EVENING SNACK</b>					



Visit Type <i>Duration</i>	<b>Special Instructions</b>	<b>What to expect</b>	<b>Where to go</b>
<b>Study Description</b> <i>45 minutes</i>  <b>Date:</b> ___/___/___ <b>Time:</b> ___:___		1) A detailed description of the study procedures and the risks and benefits associated with participating in the ECC/CON Study will be described to you. You will be given the opportunity to ask any questions that you may have. If you choose to participate in the study, you will be asked to sign an informed consent document. 2) If you choose to participate you will be given a food diary.	Room 10 McKee Gymnasium (3 buildings south of Memorial Union on Hitt Street)
<b>Visit 1 Screening Measures</b> <i>60-90 minutes</i>  <b>Date:</b> ___/___/___ <b>Time:</b> ___:___	1) Do not eat or drink anything, other than water, for at least 12 hours before this visit. 2) Wear or bring comfortable clothes. Locker rooms are available for you to change clothes in. 3) Bring your planner.	1) You will complete a short medical history questionnaire as well as a questionnaire asking about your current and past physical activity levels and basic dietary habits. 2) We will record all of the medications and supplements that you are taking. 3) Your height and weight will be measured. 4) We will collect a small sample of blood. 5) During this visit you will ‘walk through’ the strength testing procedures in order to familiarize yourself with the equipment prior to testing.	Room 10 McKee Gymnasium

<p><b>Visit 2</b>  <b>HR, BP &amp; Body composition</b>  <i>45-60 minutes</i></p> <p><b>Date:</b> ___/___/___  <b>Time:</b> ___:___</p>	<p>1) Avoid caffeine for 4 hours prior 2) Do not perform rigorous physical activity for 12 hours prior to the test 3) Wear or bring along a short sleeve shirt and clothes that do not contain metal (e.g., zippers, underwire bras, metal snaps). 4) Avoid wearing body lotion. 5) Bring your planner.</p>	<p>1) Your heart rate and blood pressure will be measured after resting quietly for 10 minutes (seated). 2) Your waist and hip circumference will be measured using a tape measure. 3) Your body composition will be assessed by measuring the thickness of skinfolds and by a DXA scan.</p>	<p>Room 10  McKee  Gymnasium</p>
<p><b>Visit 3</b>  <b>OGTT</b>  <i>~2 1/2 hours</i></p> <p><b>Date:</b> ___/___/___  <b>Time:</b> ___:___</p>	<p>1) Eat control diet for 2 days prior to the trial. 2) Do not eat or drink anything, other than water, for at least 12 hours before this visit. 3) Refrain from alcohol for 24 hours prior to the test. 4) Do not exercise for 48 hours prior to the test.</p>	<p>1) You will complete a test to assess your response to the consumption of a high-glucose meal. We will draw a small blood sample upon your arrival to the lab. 2) You will then drink a sugary drink. Subsequent blood samples will be collected at 15, 30, 60, and 120 minutes. You will need to remain seated in the lab during this 2 hour period. You may bring movies, music, or reading material if you wish.</p>	<p>Room 10  McKee  Gymnasium</p>

Visit Type <i>Duration</i>	<b>Special Instructions</b>	<b>What to expect</b>	<b>Where to go</b>
<b>Visit 4</b> <b>CT scan</b> <i>~20 minutes</i>  <b>Date:</b> ___/___/___ <b>Time:</b> ___:___	1) Do not perform rigorous physical activity for 12 hours prior to the scan.	1) After checking in at the Registration desk you will be directed to the Radiology department. You will lie down on a table on your back and the technician will perform two quick scans: one at the level of your umbilicus and one at mid-thigh.	Ellis Fischel Cancer Center on the corner of Business Loop 70 and Garth. Park in front of Ellis Fischel. Enter the main doors and check-in at the Registration desk in the main lobby.
<b>Visit 5</b> <b>Single Session of Exercise Trial</b> <i>~3 hours</i>  <b>Date:</b> ___/___/___ <b>Time:</b> ___:___	1) Eat control diet for 2 days prior to the trial. 2) Do not eat or drink anything, other than water, for at least 12 hours before this visit. 3) Refrain from alcohol for 24 hours prior to the test. 4) Do not exercise for 48 hours prior to the test. 5) Wear or bring comfortable clothes and gym shoes.	1) Muscle strength and soreness will be assessed and blood will be collected upon your arrival to the lab. 2) You will then undergo a strength test to determine the maximal amount of weight you can lift with your legs. 3) You will perform the exercise session (leg exercises only) 4) You will rest in the lab for 1 hour after the exercise session. 5) Muscle strength and soreness will be assessed and blood will be collected again. 6) You should expect to feel muscular fatigue.	Room 10 McKee Gymnasium
<b>Visit 6</b> <b>Follow-up measurements &amp; OGTT</b> <i>~3 hours</i>  <b>Date:</b> ___/___/___	1) Continue to eat control diet. 2) Do not eat or drink anything, other than water, for at least 12 hours before this visit. 3) Refrain from	1) Muscle strength and soreness will be assessed and blood will be collected upon your arrival to the lab. 2) You will then drink a sugary drink. Subsequent blood	Room 10 McKee Gymnasium

<b>Time:</b> ___ : ___	alcohol for 24 hours prior to the test. 4) Do not perform any rigorous physical activity.	samples will be collected at 15, 30, 60, and 120 minutes. You will need to remain seated in the lab during this 2 hour period. You may bring movies, music, or reading material if you wish.	
<b>Visit 7</b> <b>Follow-up measurements</b> <i>20-30 minutes</i>  <b>Date:</b> ___/___/___ <b>Time:</b> ___ : ___	1) Continue to eat control diet. 2) Do not eat or drink anything, other than water, for at least 12 hours before this visit. 3) Refrain from alcohol for 24 hours prior to the test. 4) Do not perform any rigorous physical activity.	1) Muscle strength and soreness will be assessed and blood will be collected upon your arrival to the lab.	Room 10 McKee Gymnasium
<b>Visit Type</b> <i>Duration</i>	<b>Special Instructions</b>	<b>What to expect</b>	<b>Where to go</b>
<b>Visit 8</b> <b>Follow-up measurements</b> <i>20-30 minutes</i>  <b>Date:</b> ___/___/___ <b>Time:</b> ___ : ___	1) Continue to eat control diet. 2) Do not eat or drink anything, other than water, for at least 12 hours before this visit. 3) Refrain from alcohol for 24 hours prior to the test. 4) Do not perform any rigorous physical activity.	1) Muscle strength and soreness will be assessed and blood will be collected upon your arrival to the lab.	Room 10 McKee Gymnasium

**Parking Instructions for McKee Gymnasium:**

-You may park on Hitt Street before 8:00 AM or after 6:00 PM. If you choose to park there any other time, you must pay the meters.

-You may park in the 'Volunteer Only' parking spaces behind McKee at any time. To park there, you must display a parking hang-tag given to you by one of the study staff members.

-You may park in the parking lot behind McKee without a hang tag on Weekends or before 7:00 AM or after 5:00 PM on Weekdays.

# Testing Procedure for 1 RM Test

1. Subjects will be given a familiarization session on the exercises being used for 1-RM tests. Subjects will be instructed on form and be allowed to practice the movements with **VERY** submaximal loads and repetitions. 1-RM testing will occur at least 48 h after this session.
2. The subject should warm-up by completing 5 submaximal repetitions of the selected exercise.
3. Determine the 1 RM within four trials with rest periods of 3 minutes between trials.
4. Select an initial weight that is within the subject's perceived capacity (~50-70% of capacity). This should be based off of the form and weight of the subject's initial warm-up with the exercise.
5. Resistance is progressively increased by 5 to 50 pounds until the subject cannot complete the selected repetition. All repetitions shall be performed at the same speed of movement and range of motion to ensure consistency between trials.
6. The final weight lifted successfully is recorded as the absolute 1 RM.
7. 1-RM will be determined for two lifts on the day of each acute trial: Leg Extension, and Leg Curl. A rest period of 3 minutes should be utilized between lifts to allow subjects to recover and prepare for the next lift.

University of Missouri-Columbia  
**Exercise Physiology Lab**  
**Female anthropometric data sheet**

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Subject #: \_\_\_\_\_ Group: \_\_\_\_\_ Tester: \_\_\_\_\_ Age: \_\_\_\_\_ Height  
 (cm): \_\_\_\_\_

**Baseline**

\*\*Use mean of two closest values within 1mm\*\*

Date: _____
Weight (kg/lb): _____
BMI _____

Site	Trial 1 (mm)	Trial 2 (mm)	Trial 3 (mm)	Mean
Triceps				
Suprailliac				
Thigh				

(cm)

Waist circumference				
Hip circumference				

Waist/Hip Ratio \_\_\_\_\_  
 Blood Pressure \_\_\_\_\_  
 Heart rate \_\_\_\_\_

Sum of SF \_\_\_\_\_  
 % Body Fat \_\_\_\_\_

University of Missouri-Columbia  
**Exercise Physiology Lab**  
**Male anthropometric data sheet**

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Subject #: \_\_\_\_\_ Group: \_\_\_\_\_ Tester: \_\_\_\_\_ Age: \_\_\_\_\_ Height  
 (cm): \_\_\_\_\_

**Baseline**

\*\*Use mean of two closest values within 1mm\*\*

Date: _____
Weight (kg/lb): _____
BMI _____

Site	Trial 1 (mm)	Trial 2 (mm)	Trial 3 (mm)	Mean
Chest				
Abdomen				
Thigh				

(cm)

Waist circumference				
Hip circumference				

Waist/Hip Ratio \_\_\_\_\_  
 Blood Pressure \_\_\_\_\_  
 Heart rate \_\_\_\_\_

Sum of SF \_\_\_\_\_  
 % Body Fat \_\_\_\_\_

**University of Missouri-Columbia  
Exercise Physiology Lab**

**Activity Questionnaire**

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(Please circle appropriate response and elaborate when necessary)

Name: \_\_\_\_\_ Date: \_\_\_\_\_ Weight: \_\_\_\_\_

Gender: Male Female Age: \_\_\_\_\_

1. Do you usually engage in some form of planned regular or semi-regular exercise?

Yes No (If no, please go to the last question)

2. Are you currently exercising?

Yes No (If Yes, please answer Question #3 in detail)

3. Please complete the following table. Please give your best estimate!

Mode of exercise (jog, bike, swim, etc.)	Days per week	Duration (minutes)	Pace (mph)	Intensity (mild/mod/vigor)	History (# of months)
_____	_____	_____	_____	_____	_____
_____	_____	_____	_____	_____	_____
_____	_____	_____	_____	_____	_____
_____	_____	_____	_____	_____	_____

4. Are you presently, or have you recently trained for a competitive event?

Yes No (If yes, what event \_\_\_\_\_ and duration of training \_\_\_\_\_)

5. Do you have any comments about your exercise program that you feel we should know about?

Yes No (If yes, Please explain in space provided below)

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6. Does your occupation or daily routine involve a considerable amount of activity? For example, walking, stair climbing, lifting, etc.?

Yes                      No                      (If yes, Please explain in the space provided below)

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**University of Missouri-Columbia  
Exercise Physiology Lab**

**Dietary Questionnaire**

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1. Are you taking any single vitamin supplements?

Y / N

2. If Yes, what vitamin (s)?

Name	Amount	Times/day
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____
_____	_____	_____

3. Are you taking any multivitamin pills?

Y / N

4. If Yes, please record the brand name \_\_\_\_\_, the amount \_\_\_\_\_, and how many times per day \_\_\_\_\_.

5. Are you taking any "ANTIOXIDANT GROUP" supplements (e.g., vitamins E and/or A)? Y / N

6. If Yes, please record the brand name \_\_\_\_\_, the amount \_\_\_\_\_, and how many times per day \_\_\_\_\_.

7. Are you taking and fish oil or omega-3 fatty acid supplements?

Y / N

8. If Yes, please record the brand name \_\_\_\_\_, the amount \_\_\_\_\_, and how many times per day \_\_\_\_\_.

9. How often do you consume fish? Please record number of times per week \_\_\_\_\_  
and amount \_\_\_\_\_.
10. What kind of seafood do you usually consume?  
\_\_\_\_\_
11. How many whole eggs do you have every week? \_\_\_\_\_ per week.
12. What type (s) of cooking oil do you use?  
\_\_\_\_\_
13. How much cooking oil do you use on a daily basis? \_\_\_\_\_ tbsp. OR  
\_\_\_\_\_ cups
14. Do you use margarine or butter (circle one)?
15. How many times per week do you consume meat? \_\_\_\_\_ times per week
16. Please estimate how much meat you consume during a typical day. \_\_\_\_\_ oz.  
per day.

**Additional Comments:**

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**University of Missouri-Columbia  
Exercise Physiology Lab**

**Health History and Medical Questionnaire**

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Name: \_\_\_\_\_ Date: \_\_\_\_\_ Social Security #: \_\_\_\_\_  
Address: \_\_\_\_\_ Sex: Male Female  
Age: \_\_\_\_\_  
\_\_\_\_\_ Height: \_\_\_\_\_  
Weight: \_\_\_\_\_  
Telephone: \_\_\_\_\_ Email: \_\_\_\_\_ Date of Birth: \_\_\_\_\_  
\_\_\_\_\_

Personal Physician's Name: \_\_\_\_\_ Blood Pressure: \_\_\_\_\_ / \_\_\_\_\_  
Address & Telephone: \_\_\_\_\_  
\_\_\_\_\_

**Health History:**

**Have you ever had:** High Blood Pressure **Y / N** Low Blood Pressure **Y / N** Heart Disease **Y / N**  
Irregular Heart Beat **Y / N** Diabetes **Y / N** Heart Murmurs **Y / N** Chest Pain **Y / N**  
Thyroid Disease **Y / N** Lung Disease **Y / N** Arthritis **Y / N** High Blood Cholesterol **Y / N**  
Has a parent or sibling had any heart disorders prior to age 55? **Y / N**  
Has a sudden death ever occurred in a parent or sibling? **Y / N**  
Do you smoke? **Y / N** If Yes, how much? \_\_\_\_\_  
You are an/a African-American \_\_\_ Asian \_\_\_ Caucasian \_\_\_ Hispanic \_\_\_ Native American \_\_\_ Pacific Islander \_\_\_ Other \_\_\_

**Have you ever taken medication for?** Medication and Dosage  
Date  
**Y / N** High Blood Pressure: \_\_\_\_\_  
\_\_\_\_\_

**Y / N** Low Blood Pressure: \_\_\_\_\_  
\_\_\_\_\_

**Y / N** Heart Disease: \_\_\_\_\_  
\_\_\_\_\_

Y / N Diabetes: \_\_\_\_\_

Y / N Thyroid Disease: \_\_\_\_\_

Y / N Lung Disease: \_\_\_\_\_

Y / N Arthritis: \_\_\_\_\_

Do you participate in a regular exercise program? Y / N Times per week: \_\_\_\_\_

For how many years? \_\_\_\_\_ What activity? \_\_\_\_\_

If you are a woman, is there any chance you could be pregnant? \_\_\_\_\_

Do any members of your immediate family (mother, father, brother, sister) have Type II Diabetes? \_\_\_\_\_

### **Medical Questionnaire:**

1. Have you ever been advised by a physician to avoid exercise? Y / N
2. Do you ever have shortness of breath during or after exercise? Y / N
3. Have you ever experienced fainting or dizzy spells? Y / N
4. Have you ever experienced pain or discomfort in the chest? Y / N
5. Have you ever experienced back, jaw or left arm pain or recurrent indigestion? Y / N
6. Have you ever experienced swollen ankles (excluding sprains)? Y / N
7. Have you recently experienced heart palpitations (rapid heart beat) at rest? Y / N
8. Have you ever experienced claudication (pain in the calf, thigh, or buttocks with walking)? Y / N
9. Is there any other health condition that might limit your participation in exercise programs (e.g., bone or joint disorders, pregnancy, etc.)? Y / N If Yes, please explain: \_\_\_\_\_
10. Are you taking any medication not listed above? Y / N If Yes, please list: \_\_\_\_\_
11. Have you had a medical exam in the last 12 month? Y / N If Yes, please list date: \_\_\_\_\_

Signature: \_\_\_\_\_

Date: \_\_\_\_\_

## **University of Missouri-Columbia Exercise Physiology Lab**

## **Follow-up Medical History Questions**

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1. Have you had any surgeries? Please list

2. Did you have any medical conditions for which you received treatment during the past year?

Do you take any vitamins or dietary supplements? Please list

Additional Medical Questionnaire  
(For Women only)

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1. Do you have a menstrual cycle?      Yes      No

    If Yes, go to question #2

    If No, go to question #5

2. What is the frequency of your menstrual cycle? \_\_\_\_\_ times/year

3. How many days does each cycle last? \_\_\_\_\_ days.

4. When was your last menstrual period?

5. Are you taking birth control pills?    Yes    No

5a. If Yes, please record the brand name \_\_\_\_\_,  
    the amount \_\_\_\_\_.

6. Are you on estrogen therapy?    Yes    No

7. If Yes, please list the name (s), and frequency.

Name

Frequency (i.e. 1 per day)

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Additional comments:

Dear ,

Thank you for your interest in this study. In this email, I will give you a few brief details, and a few screening questions to determine if you qualify. If you do qualify and are interested, we would like to meet with you to give a complete explanation of procedures.

The study will begin after screening is completed and will last 4-5 months. You will undergo some initial testing including measurements of body fat and blood pressure, muscular strength and either an oral glucose tolerance or fat tolerance test. You will be randomly assigned to perform one of two types of resistance exercise and resistance training. During the first one-two weeks of the study you will participate in a single sessions of resistance exercise. Your blood will be drawn on the day of exercise and three days following the day of exercise. After the single session trial is completed you will begin the resistance training program during which time you will train 3-4 days per week for 12 weeks in our gym. Following the 12 week training program the initial testing will be repeated.

If you prefer to discuss the study before answering the following questions, please call us at 882-8191 or let us know a number and good time to call you.

Here are the questions to determine if you qualify : You may answer in email, or over the phone. Choose the option that you are most comfortable with.

1. Do you smoke ?
2. How much time and how often do you exercise per week ? Describe the activity and how long you have been engaged in the exercise (i.e. 3 mos, 1 wk, 3 yr).
3. Have you participated in a formal diet program within the last 3 mos ? If so, please describe.
4. Have you lost or gained weight in the last 3 months ? How much ? Describe fluctuations.
5. What medications do you take including vitamins, supplements, over the counter medications, and prescription drugs ?
6. Do you have diabetes, renal disease, or any know cardiovascular problems or family history of heart disease ?
7. What is your age ?
8. If female, have you experienced any symptoms of menopause?
9. What is your height and weight ? We need it to calculate your body mass index to determine if you qualify for the study.
10. Do you have any orthopedic problems that would limit your ability to walk/jog on a treadmill or participate in a weight lifting program?

You can contact the study administrators at 882-8191 from 8-5 M-F. Please leave a voicemail if the phone is not answered. We are in and out of the office all day. You may also give me a number and time when you can be reached, and one of us can try to contact you at that time. You are also welcome to stop by at anytime if you are in the area.

Thank you for your interest,  
Shana Warner  
Graduate Research Assistant  
Exercise Physiology Program  
106 McKee Gym  
University of Missouri-Columbia  
882-8191

## **PARTICIPANTS NEEDED FOR WEIGHT TRAINING STUDY**

**NEEDED: INACTIVE, OVERWEIGHT MEN & WOMEN, 18-50 YEARS**



*Do you exercise less than 1 hour per week?*

*Are you overweight?*

*Would you like to get individual exercise programs from professionals?*

**The Dept. of Nutrition and Exercise Physiology is seeking individuals for an exercise study. Find out if you are at risk for lifestyle related diseases. Do something about it!**

Study also includes: Personalized Exercise  
Free access to Fitness Center  
Blood Fat analysis  
Body Fat analysis  
Glucose analysis

Contact: Exercise Physiology Program  
Dept. of Nutrition and Exercise Physiology  
106 McKee Gym  
Email: [umchesexphys@missouri.edu](mailto:umchesexphys@missouri.edu)  
573-882-8191





**Research on weight training and health (Announcement sponsored by Department of Nutrition and Exercise Physiology)**

Seeking sedentary and overweight men and women (ages 18-50 years) to participate in an weight training program in a supervised, private setting in the Exercise Physiology Lab. Study includes a 3-4 month weight training program. Participants get blood lipid and glucose analysis, body composition, and muscular strength and fitness assessment. Participants will be compensated. If you are interested in participating, please contact the Exercise Physiology Program, 106 McKee Gym, via email [umchesexphys@missouri.edu](mailto:umchesexphys@missouri.edu).

# ACUTE EXERCISE SESSION

Subject # \_\_\_\_\_

Date \_\_\_\_\_

Group \_\_\_\_\_

1-RM LE \_\_\_\_\_

75% 1-RM \_\_\_\_\_

1-RM LC \_\_\_\_\_

75% 1-RM \_\_\_\_\_

eccentric repetition will be lowered using an audible 5-second cadence by the laboratory technician. Subjects will be given 60 seconds rest in between each set.

**Check list:**

0h pain ratings \_\_\_\_\_

0h blood (following 20 minutes supine rest) \_\_\_\_\_

Hematocrit and hemoglobin \_\_\_\_\_

0h Biodex \_\_\_\_\_

1RM

Acute trial \_\_\_\_\_

Acute trial water consumption (10 oz.) \_\_\_\_\_

Recovery water consumption (20 oz.) \_\_\_\_\_

1h pain ratings \_\_\_\_\_

1h blood (following 20 minutes supine rest) \_\_\_\_\_

Hematocrit and hemoglobin \_\_\_\_\_

1h Biodex \_\_\_\_\_

	Set 1	Set 2	Set 3
Leg Extension Wt/Reps			
Leg Curl Wt/Reps			

All subjects will attempt to complete three sets of ten repetitions of each exercise. Each concentric repetition will be in a controlled manner. Each

Throughout the study, we will ask you to rate the pain you feel in various muscle groups. We want you to rate the quantity or amount of any pain you feel and we will be using numeric rating scales from 0 -100 with 0 = no pain and 100 = most intense pain imaginable.

I need to know if you are currently feeling any pain in your legs so I will now get your ratings of pain. We will begin with the muscles in the front of your right leg.

- While you are walking, what number would you give for the intensity of any pain that you are currently feeling in the muscles in the **front** of your **right leg**?
- Repeat for **front** of **left leg**.
- Repeat for **back** of **right leg**.
- Repeat for **back** of **left leg**.

Now I want to know about the pain intensity during a different type of movement (while lengthening the muscles in the front of your legs). I would like for you to bend your knees and squat down as if you were going to sit in a chair. We'll start with your right leg. Please think about the intensity of any pain you feel in the muscles in the front of your right leg while you bend your knees and squat downward.

- What number would you give for the intensity of any pain that you are feeling in the muscles in the **front** of your **right leg** while squatting down?
- Repeat for **front** of **left leg**.

**100 - Most Unpleasant Pain Imaginable**



**0 - Not at all Unpleasant Pain**

**Lactaid**MENU A -2000-  
2499

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk, LACTAID	1 cup
	banana, medium OR orange juice (1 cup)	
	Toast, white bread	1 slice
	peanut butter	1 T
LUNCH	Subway sandwich (6 gm fat or less varieties) NO CHEESE	6 in
	*no regular mayonnaise, ranch dressing or chipotle southwest sauce	
	chips, baked	single serve bag
	apple	medium
	diet soft drink, unsweetened tea/coffee, water	
SNACK	baby carrots, medium	10
	Fat-free dip (ie Ranch dressing)	1 T
DINNER	fish (salmon), baked with favorite seasonings	4 oz
	prepared brown rice	1/2 cup
	sautéed vegetables with 1.5 T olive oil and favorite seasonings (ie: broccoli, snap peas, carrots, onions, peppers, etc)	1.5 cup
	orange	medium
	1 % milk, LACTAID	1 cup
DESSERT	cherry pie, 1/8 of a 9inch pie	1 slice

MENU A - 1500-1999

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk	1 cup
	banana, medium OR orange juice (1 cup)	
LUNCH	Subway sandwich with cheese (6 gm fat or less varieties) *no regular mayonnaise, ranch dressing or chipotle southwest sauce	6 in
	chips, baked	single serve bag
	apple	medium
	diet soft drink, unsweetened tea/coffee, water	
DINNER	fish (salmon)#, baked with favorite seasonings	3 oz
	prepared brown rice	1/2 cup
	sautéed vegetables with 1.5 T olive oil and favorite seasonings (ie: broccoli, snap peas, carrots, onions, peppers, etc)	1 cup
	orange	medium
	1 % milk	1 cup
DESSERT	ice cream, flavored without add-ins (ie: vanilla, chocolate, strawberry)	1 cup
	[ <b>OR</b> chip's ahoy cookies (chocolate chip)]	5 cookies

\*Veggie Delite and Sweet Onion Teriyaki not similar to Subway sandwich averages

\*\*If vegetarian, need to substitute meat products with non-meat substitute

#can substitute chicken, but must eliminate baked chips at lunch

MENU A -2000-  
2499

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk	1 cup
	banana, medium OR orange juice (1 cup)	
	Toast, white bread	1 slice
	peanut butter	1 T
LUNCH	Subway sandwich with cheese (6 gm fat or less varieties) *no regular mayonnaise, ranch dressing or chipotle southwest sauce	6 in
	chips, baked	single serve bag
	apple	medium
	diet soft drink, unsweetened tea/coffee, water	
SNACK	baby carrots, medium	10
	Fat-free dip (ie Ranch dressing)	1 T
DINNER	fish (salmon)#, baked with favorite seasonings	4 oz
	prepared brown rice	1/2 cup
	sautéed vegetables with 1.5 T olive oil and favorite seasonings (ie: broccoli, snap peas, carrots, onions, peppers, etc)	1.5 cup
	orange	medium
	1 % milk	1 cup
DESSERT	ice cream, flavored without add-ins (ie: vanilla, chocolate, strawberry)	1 cup
	[ <b>OR</b> chip's ahoy cookies (chocolate chip)]	5 cookies

\*Veggie Delite and Sweet Onion Teriyaki not similar to Subway sandwich averages

\*\*If vegetarian, need to substitute meat products with non-meat substitute

#can substitute chicken, but must eliminate baked chips at lunch

MENU A -2500-  
2999

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk	1 cup
	banana, medium OR orange juice (1 cup)	
	Toast, white bread	1 slice
	peanut butter	1 T
LUNCH	Subway sandwich with cheese (6 gm fat or less varieties) *no regular mayonnaise, ranch dressing or chipotle southwest sauce	foot long
	chips, baked	single serve bag
	apple	medium
	diet soft drink, unsweetened tea/coffee, water	
SNACK	baby carrots, medium	10
	Fat-free dip (ie Ranch dressing)	1 T
DINNER	fish (salmon)#, baked with favorite seasonings	4 oz
	prepared brown rice	1/2 cup
	sautéed vegetables with 1.5 T olive oil and favorite seasonings (ie: broccoli, snap peas, carrots, onions, peppers, etc)	1.5 cup
	orange	medium
	1 % milk	2 cup
DESSERT	ice cream, flavored without add-ins (ie: vanilla, chocolate, strawberry)	1.5 cup
	[OR chip's ahoy cookies (chocolate chip)]	7 cookies

\*Veggie Delite and Sweet Onion Teriyaki not similar to Subway sandwich averages

\*\*If vegetarian, need to substitute meat products with non-meat substitute

#can substitute chicken, but must eliminate baked chips at lunch



MENU A -3000-  
3499

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk	1 cup
	banana, medium OR orange juice (1 cup)	
	Toast, white bread	1 slice
	peanut butter	2 T
SNACK	yogurt, low-fat	6 oz
	pretzels, hard, salted	1.5 oz
LUNCH	Subway sandwich with cheese (6 gm fat or less varieties) *no regular mayonnaise, ranch dressing or chipotle southwest sauce	foot long
	chips, baked	single serve bag
	apple	medium
	diet soft drink, unsweetened tea/coffee, water	
SNACK	baby carrots, medium	10
	Fat-free dip (ie Ranch dressing)	1 T
DINNER	fish (salmon)#, baked with favorite seasonings	4 oz
	prepared brown rice	1/2 cup
	sautéed vegetables with 1.5 T olive oil and favorite seasonings (ie: broccoli, snap peas, carrots, onions, peppers, etc)	2 cup
	orange	medium
	1 % milk	2 cup
DESSERT	ice cream, flavored without add-ins (ie: vanilla, chocolate, strawberry)	1.5 cup
	[ <b>OR</b> chip's ahoy cookies (chocolate chip)]	7 cookies

\*Veggie Delite and Sweet Onion Teriyaki not similar to Subway sandwich averages

\*\*If vegetarian, need to substitute meat products with non-meat substitute

#can substitute chicken, but must eliminate baked chips at lunch

MENU B - 1500-  
1999

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk	1 cup
	banana, medium OR orange juice (1 cup)	
LUNCH	Lean Cuisine Dinnertime Selects	1 meal
	apple	medium
	diet soft drink, unsweetened tea/coffee, water	
DINNER	fish (salmon), baked with favorite seasonings	3 oz
	prepared brown rice	1/2 cup
	sautéed vegetables with 1.5 T olive oil and favorite seasonings (ie: broccoli, snap peas, carrots, onions, peppers, etc)	1 cup
	orange	medium
	1 % milk	1 cup
DESSERT	ice cream, flavored without add-ins (ie: vanilla, chocolate, strawberry)	1 cup
	[ <b>OR</b> chip's ahoy cookies (chocolate chip)]	5 cookies

MENU B -2000-  
2499

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk	1 cup
	banana, medium OR orange juice (1 cup)	
	Toast, white bread	1 slice
	peanut butter	1 T
LUNCH	Lean Cuisine Dinnertime Selects	1 meal
	apple	medium
	diet soft drink, unsweetened tea/coffee, water	
SNACK	baby carrots, medium	10
	Fat-free dip (ie Ranch dressing)	1 T
DINNER	fish (salmon), baked with favorite seasonings	4 oz
	prepared brown rice	1/2 cup
	sautéed vegetables with 1.5 T olive oil and favorite seasonings (ie: broccoli, snap peas, carrots, onions, peppers, etc)	1.5 cup
	orange	medium
	1 % milk	1 cup
DESSERT	ice cream, flavored without add-ins (ie: vanilla, chocolate, strawberry)	1 cup
	[ <b>OR</b> chip's ahoy cookies (chocolate chip)]	5 cookies

MENU B -2500-  
2999

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk	1 cup
	banana, medium OR orange juice (1 cup)	
	Toast, white bread	1 slice
	peanut butter	1 T
LUNCH	Lean Cuisine Dinnertime Selects	2 meals
	apple	medium
	diet soft drink, unsweetened tea/coffee, water	
SNACK	baby carrots, medium	10
	Fat-free dip (ie Ranch dressing)	1 T
DINNER	fish (salmon), baked with favorite seasonings	4 oz
	prepared brown rice	1/2 cup
	sautéed vegetables with 1.5 T olive oil and favorite seasonings (ie: broccoli, snap peas, carrots, onions, peppers, etc)	1.5 cup
	orange	medium
	1 % milk	2 cup
DESSERT	ice cream, flavored without add-ins (ie: vanilla, chocolate, strawberry)	1.5 cup
	[ <b>OR</b> chip's ahoy cookies (chocolate chip)]	7 cookies

MENU B -3000-  
3499

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk	1 cup
	banana, medium OR orange juice (1 cup)	
	Toast, white bread	1 slice
	peanut butter	2 T
SNACK	yogurt, low-fat	6 oz
	pretzels, hard, salted	1.5 oz
LUNCH	Lean Cuisine Dinnertime Selects	2 meals
	apple	medium
	diet soft drink, unsweetened tea/coffee, water	
SNACK	baby carrots, medium	10 carrots
	Fat-free dip (ie Ranch dressing)	1 T
DINNER	fish (salmon), baked with favorite seasonings	4 oz
	prepared brown rice	1/2 cup
	sautéed vegetables with 1.5 T olive oil and favorite seasonings (ie: broccoli, snap peas, carrots, onions, peppers, etc)	2 cup
	orange	medium
	1 % milk	2 cup
DESSERT	ice cream, flavored without add-ins (ie: vanilla, chocolate, strawberry)	1.5 cup
	[ <b>OR</b> chip's ahoy cookies (chocolate chip)]	7 cookies

MENU C - 1500-  
1999

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk	1 cup
	banana, medium OR orange juice (1 cup)	
LUNCH	cooked hamburger (80% lean, pan-boiled)	3 oz
	Cheese slice	1 slice
		1 bun (43 gm)
	hamburger bun, white	
	romaine lettuce, shredded	2 cups
	baby carrots	5 carrots
	cauliflower	0.5 cup
	Ranch dressing, light (not fat-free)	2 Tbsp
	diet soft drink, unsweetened tea/coffee, water	
DINNER	Lean Cuisine Dinnertime Selects	1 meal
	apple	medium
	peanut butter (with apple)	1 Tbsp
	diet soft drink, unsweetened tea/coffee, water	
DESSERT	ice cream, flavored without add-ins (ie: vanilla, chocolate, strawberry)	1 cup
	[OR chip's ahoy cookies (chocolate chip)]	5 cookies

MENU C - 2000-  
2499

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk	1 cup
	banana, medium OR orange juice (1 cup)	
	Toast, white bread	1 slice
	peanut butter	1 T
SNACK	orange	medium
LUNCH	cooked hamburger (80% lean, pan-boiled)	3 oz
	Cheese slice	1 slice
		1 bun (43 gm)
	hamburger bun, white	
	romaine lettuce, shredded	2 cups
	baby carrots	5 carrots
	cauliflower	0.5 cup
	Ranch dressing, light (not fat-free)	2 Tbsp
	diet soft drink, unsweetened tea/coffee, water	
	chips, baked	single serve bag
SNACK	baby carrots, medium	10
	Ranch dressing, light (not fat-free)	2 Tbsp
DINNER	Lean Cuisine Dinnertime Selects	1 meal
	apple	medium
	peanut butter (with apple)	1 Tbsp
	diet soft drink, unsweetened tea/coffee, water	
	1 % milk	1 cup
DESSERT	ice cream, flavored without add-ins (ie: vanilla, chocolate, strawberry)	1 cup
	[OR chip's ahoy cookies (chocolate chip)]	5 cookies

MENU C - 2500-  
2999

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk	1 cup
	banana, medium OR orange juice (1 cup)	
	Toast, white bread	1 slice
	peanut butter	1 T
SNACK	orange	medium
LUNCH	cooked hamburger (80% lean, pan-boiled)	3 oz
	Cheese slice	1 slice
		1 bun (43 gm)
	hamburger bun, white	
	romaine lettuce, shredded	2 cups
	baby carrots	5 carrots
	cauliflower	0.5 cup
	Ranch dressing, light (not fat-free)	2 Tbsp
	diet soft drink, unsweetened tea/coffee, water	
	chips, baked	single serve bag
SNACK	baby carrots, medium	10
	Ranch dressing, light (not fat-free)	2 Tbsp
DINNER	Lean Cuisine Dinnertime Selects	2 meals
	apple	medium
	peanut butter (with apple)	1 Tbsp
	1 % milk	2 cup
DESSERT	ice cream, flavored without add-ins (ie: vanilla, chocolate, strawberry)	1.5 cup
	[OR chip's ahoy cookies (chocolate chip)]	7 cookies



MENU C - 3000-3499

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	1 % milk	1 cup
	banana, medium OR orange juice (1 cup)	
	Toast, white bread	1 slice
	peanut butter	1 T
SNACK	orange	medium
	yogurt, low-fat	6 oz
	pretzels, hard, salted	1.5 oz
LUNCH	cooked hamburger (80% lean, pan-boiled)	3 oz
	Cheese slice	1 slice
		1 bun (43 gm)
	hamburger bun, white	
	romaine lettuce, shredded	2 cups
	baby carrots	5 carrots
	cauliflower	0.5 cup
	sunflower seeds, dry roasted with salt	1 oz (handful)
	Ranch dressing, light (not fat-free)	2 Tbsp
	diet soft drink, unsweetened tea/coffee, water	single serve bag
DINNER	Lean Cuisine Dinnertime Selects	2 meals
	apple	medium
	peanut butter (with apple)	2 Tbsp
	1 % milk	2 cup
DESSERT	ice cream, flavored without add-ins (ie: vanilla, chocolate, strawberry)	1.5 cup
	[OR chip's ahoy cookies (chocolate chip)]	7 cookies

## Soy milk

MENU A -2000-  
2499

	Item	AMT
BREAKFAST	Cereal (cornflakes, rice cereal, Cheerios, etc)	2 cups
	soy milk, SILK, vanilla	1 cup
	banana, medium OR orange juice (1 cup)	
	Toast, white bread	1 slice
	peanut butter	1 T
LUNCH	Subway sandwich (6 gm fat or less varieties) NO CHEESE *no regular mayonnaise, ranch dressing or chipotle southwest sauce	6 in
	chips, baked	single serve bag
	apple	medium
	diet soft drink, unsweetened tea/coffee, water	
SNACK	baby carrots, medium	10
	Fat-free dip (ie Ranch dressing)	1 T
DINNER	fish (salmon), baked with favorite seasonings	4 oz
	prepared brown rice	1/2 cup
	sautéed vegetables with 1.5 T olive oil and favorite seasonings (ie: broccoli, snap peas, carrots, onions, peppers, etc)	1.5 cup
	orange	medium
	soy milk, SILK, vanilla	1 cup
DESSERT	cherry pie, 1/8 of a 9inch pie	1 slice

\*Veggie Delite and Sweet Onion Teriyaki not similar to Subway sandwich averages

\*\*If vegetarian, need to substitute meat products with non-meat substitute

APPENDIX D:  
ANOVA TABLES

DOMS ratings for walking right quadriceps test ANOVA table

Source	df	F	P-value
Group	1	5.334	0.040
Time	4	3.554	0.013
Group x Time	4	3.502	0.014

DOMS ratings for walking right hamstrings test ANOVA table

Source	df	F	P-value
Group	1	4.234	0.062
Time	4	6.416	0.000
Group x Time	4	6.163	0.002

DOMS ratings for walking left quadriceps test ANOVA table

Source	df	F	P-value
Group	1	5.871	0.032
Time	4	3.724	0.010
Group x Time	4	3.211	0.020

DOMS ratings for walking left hamstrings test ANOVA table

Source	df	F	P-value
Group	1	6.578	0.025
Time	4	4.091	0.006
Group x Time	4	3.703	0.01

DOMS ratings for lengthening right quadriceps test ANOVA table

Source	df	F	P-value
Group	1	10.227	0.008
Time	4	5.214	0.001
Group x Time	4	5.524	0.001

DOMS ratings for lengthening left quadriceps test ANOVA table

Source	df	F	P-value
Group	1	21.317	0.001
Time	4	9.059	0.000
Group x Time	4	9.492	0.000

ANOVA table of insulin AUC<sub>i</sub> measures (mmol/L)

Source	df	F	P-value
Group	1	0.001	0.976
Time	1	0.001	0.982
Group x Time	1	3.221	0.098

ANOVA table of insulin AUC<sub>t</sub> measures (mmol/L)

Source	df	F	P-value
Group	1	0.015	0.906
Time	1	0.004	0.950
Group x Time	1	2.673	0.128

## ANOVA table of glucose AUCi measures (mg/dL)

Source	df	F	P-value
Group	1	0.124	0.731
Time	1	0.704	0.418
Group x Time	1	0.000	0.998

## ANOVA table of glucose AUCt measures (mg/dL)

Source	df	F	P-value
Group	1	0.995	0.338
Time	1	0.072	0.793
Group x Time	1	0.024	0.879

## ANOVA table of HOMA

Source	df	F	P-value
Group	1	0.562	0.468
Time	1	0.169	0.688
Group x Time	1	0.027	0.872

## ANOVA table of QUICKI

Source	df	F	P-value
Group	1	0.483	0.500
Time	1	0.082	0.779
Group x Time	1	0.000	1

## ANOVA table of IL-6 (pg/mL)

Source	df	F	P-value
Group	1	0.040	0.845
Time	2	2.485	0.105
Group x Time	2	0.023	0.977

ANOVA table of TNF $\alpha$  (pg/mL)

Source	df	F	P-value
Group	1	0.246	0.629
Time	1	1.596	0.23
Group x Time	1	0.207	0.657

## Matsuda

Source	df	F	P-value
Group	1	0.028	0.869
Time	1	0.128	0.727
Group x Time	1	1.279	0.280

APPENDIX E:  
RAW DATA

Anthropometric data.

Subj	Age	% Body Fat			
		Skinfolds	Waist	Hip	
					Waist/Hip
402	30	26.2	111.0	116.50	0.95
403	38	45.5	117.0	136.00	0.86
405	47	45.2	104.5	119.00	0.88
408	39	18.4	106.5	115.00	0.93
409	29	39.5	116.3	123.75	0.94
411	31	30.2	127.0	118.75	1.07
413	21	18.4	96.0	110.00	0.87
415	30	16.5	94.5	103.50	0.91
418	48	28.4	111.0	113.00	0.98
419	48	22.6	105.0	112.00	0.94
420	23	41.9	106.0	119.50	0.89
421	27	34.8	105.5	117.00	0.90
423	44	46.9	109.0	139.00	0.78
424	40	37.4	85.0	119.00	0.71

Anthropometric data continued.

Subj	Bodyweight	height	BMI	Fat Mass (Kg)	Fat-Free (Kg)
402	98.18	175.8	31.8	25.8	72.4
403	103.18	160.4	40.1	47.0	56.2
405	88.41	161.3	34.0	39.9	48.5
408	100.86	174.5	33.1	18.6	82.3
409	97.09	165.4	35.5	38.3	58.8
411	128.73	180.5	39.5	38.8	89.9
413	92.27	178.1	29.1	13.2	66.5
415	79.64	172.7	26.7	13.2	66.5
418	99.55	180.4	30.6	28.2	71.3
419	95.64	175.6	31.0	21.7	74.0
420	99.09	164.5	36.6	41.6	57.5
421	83.05	159.9	32.5	28.9	54.1
423	112.36	164	41.8	52.7	59.6
424	79.14	168	28.0	29.6	49.5

DOMS walking right quadriceps test.

Subject	Group	walking rt. quad 0h	walking rt. quad 1h	walking rt. quad 24h	walking rt. quad 48h	walking rt. quad 72h
402	CON	0	0	0	0	0
403	CON	0	0	0	1	0
405	ECC	0	5	3	5	2
408	ECC	0	0	0	2	0
409	ECC	0	0	5	15	5
411	CON	0	0	0	0	0
413	CON	0	6	3	0	0
415	ECC	0	0	2	0	0
418	CON	0	0	0	0	0
419	ECC	0	20	15	15	5
420	CON	0	0	0	0	0
421	CON	0	1	0	0	0
423	ECC	2	3	5	12	2
424	ECC	0	7	25	40	25

DOMS walking left quadriceps test.

Subject	Group	walking lft. quad 0h	walking lft. quad 1h	walking lft. quad 24h	walking lft. quad 48h	walking lft. quad 72h
402	CON	0	0	0	0	0
403	CON	0	0	0	1	0
405	ECC	0	5	3	6	2
408	ECC	0	0	0	4	0
409	ECC	0	0	5	10	0
411	CON	0	0	0	0	0
413	CON	0	6	4	0	0
415	ECC	0	0	1	0	0
418	CON	0	0	0	0	0
419	ECC	0	20	15	15	5
420	CON	0	0	3	0	0
421	CON	0	0	0	0	0
423	ECC	2	4	4	12	2
424	ECC	0	2	25	25	20



DOMS walking right hamstrings test.

<b>Subject</b>	<b>Group</b>	walking rt. ham 0h	walking rt. ham 1h	walking rt. ham 24h	walking rt. ham 48h	walking rt. ham 72h
402	CON	0	0	0	0	0
403	CON	1	3	1	1	0
405	ECC	0	5	2	3	1
408	ECC	0	0	2	10	0
409	ECC	0	0	0	10	0
411	CON	0	0	10	0	0
413	CON	0	7	6	5	3
415	ECC	0	1	1	15	0
418	CON	0	0	0	1	1
419	ECC	0	5	5	10	5
420	CON	0	5	0	0	0
421	CON	0	0	0	0	0
423	ECC	2	6	4	7	2
424	ECC	0	10	20	20	20

DOMS walking left hamstrings test.

<b>Subject</b>	<b>Group</b>	walking lft. ham 0h	walking lft. ham 1h	walking lft. ham 24h	walking lft. ham 48h	walking lft. ham 72h
402	CON	0	0	0	0	0
403	CON	1	3	1	1	0
405	ECC	0	5	2	3	1
408	ECC	0	0	2	15	0
409	ECC	0	0	0	5	0
411	CON	0	0	10	0	0
413	CON	0	6	6	3	1
415	ECC	0	1	0	10	0
418	CON	0	0	0	1	1
419	ECC	0	5	5	15	10
420	CON	0	3	2	0	2
421	CON	1	0	0	0	0
423	ECC	4	10	4	10	6
424	ECC	3	0	25	15	10

DOMS lengthening right quadriceps test.

<b>Subject</b>	<b>Group</b>	<b>length rt quad 0h</b>	<b>length rt quad 1h</b>	<b>length rt quad 24h</b>	<b>length rt quad 48h</b>	<b>length rt quad 72h</b>
402	CON	0	0	0	0	0
403	CON	0	0	0	1	0
405	ECC	1	2	2	4	5
408	ECC	5	5	15	25	2
409	ECC	0	0	25	30	15
411	CON	0	0	0	0	0
413	CON	0	8	3	2	1
415	ECC	0	0	5	5	1
418	CON	0	0	0	0	0
419	ECC	5	20	15	20	10
420	CON	3	3	0	2	2
421	CON	0	0	0	0	0
423	ECC	0	6	10	15	5
424	ECC	0	5	35	50	45

DOMS lengthening left quadriceps test.

<b>Subject</b>	<b>Group</b>	<b>length lft quad 0h</b>	<b>length lft quad 1h</b>	<b>length lft quad 24h</b>	<b>length lft quad 48h</b>	<b>length lft quad 72h</b>
402	CON	0	0	0	0	0
403	CON	0	0	0	1	0
405	ECC	1	2	2	6	6
408	ECC	5	5	20	25	2
409	ECC	0	0	25	30	15
411	CON	0	0	0	0	0
413	CON	0	7	3	1	1
415	ECC	0	0	3	5	2
418	CON	0	0	0	0	0
419	ECC	5	15	20	20	5
420	CON	3	0	0	1	3
421	CON	0	0	1	0	0
423	ECC	0	8	12	18	9
424	ECC	0	0	20	35	20

Glucose measures (mg/dL).

Subject #	Group	BOGT					Base AUCt	Base AUCi
		BOGT 0h	15min	30min	60min	120min		
402CON		99.6	135.2	174.4	120.0	82.4	14571.0	2619.0
403CON		101.9	136.8	154.1	197.7	188.3	20828.9	8595.5
405ECC		104.6	173.5	214.6	195.8	141.2	21259.6	8705.8
408ECC		104.0	148.4	189.5	159.3	150.0	18937.5	6453.7
409ECC		94.1	123.2	141.3	142.1	143.3	16429.1	5137.8
411CON		94.8	139.8	166.7	190.5	160.3	19938.8	8557.9
413CON		96.7	118.9	153.7	163.3	150.4	17827.8	6227.8
415ECC		114.8	150.7	195.2	172.2	104.8	18408.3	4630.6
418CON		66.4	120.1	127.6	122.8	78.7	13057.8	5087.7
419ECC		87.1	111.3	155.1	170.7	131.6	17443.4	6990.2
420CON		85.1	109.2	111.9	93.1	94.6	11821.8	1614.9
421CON		89.8	121.5	129.3	105.5	110.5	13467.8	2686.5
423ECC		96.7	152.0	188.1	150.4	111.5	17351.4	5744.9
424ECC		89.0	111.8	136.0	86.8	84.9	11856.6	1180.1

Glucose measures continued (mg/dL).

Subject #	Group	EOGT					Exerc AUCt	Exerc AUCi
		EOGT 0h	15min	30min	60min	120min		
402CON		102.0	144.0	150.0	116.0	96.0	14400.0	2160.0
403CON		100.0	140.2	150.2	182.5	198.4	20397.9	8397.9
405ECC		101.5	157.7	168.1	161.5	131.2	18112.5	5927.9
408ECC		137.9	199.9	218.5	235.5	151.6	24095.6	7547.3
409ECC		96.9	126.4	135.0	171.7	141.3	17625.0	6003.0
411CON		96.4	127.4	131.0	158.7	128.6	16581.0	5009.6
413CON		99.6	150.7	158.9	164.1	112.2	17333.3	5377.8
415ECC		122.2	145.2	153.3	116.7	102.2	14861.1	194.4
418CON		88.8	132.5	145.9	123.5	99.3	14471.1	3814.4
419ECC		85.5	137.9	142.2	212.1	211.7	21805.7	11540.0
420CON		92.3	110.7	115.3	141.8	109.2	14603.4	3523.0
421CON		93.0	134.0	144.9	125.0	91.4	14335.0	3178.7
423ECC		102.9	135.2	142.2	118.4	115.6	14797.1	2452.9
424ECC		95.2	126.8	132.0	101.5	83.5	12656.3	1229.8

Subjects 403, 408, and 411 did not have 15 minute samples. Detailed report on statistical calculation for included measured included in METHODS section of article.

Insulin measures (mmol/L).

Subject #	Group	BOGT		BOGT	BOGT	AUCt	AUCi	
		BOGT 0h	15min	30min	60min			120min
402	CON	7.4	52.5	94.5	82.4	58.2	8423.55	7530.75
403	CON	18.5	42.1	58.7	85.1	103.0	9010.24	6790.24
405	ECC	9.2	46.6	58.5	87.1	76.4	8295.6	7194
408	ECC	8.8	54.1	99.2	111.0	92.5	10879.07	9823.073
409	ECC	7.9	28.0	47.2	58.0	79.7	6542.55	5589.75
411	CON	13.9	89.9	151.0	287.0	120.0	21365.09	19697.09
413	CON	6.7	28.5	54.8	64.4	100.0	7608.375	6810.375
415	ECC	12.9	69.4	163.0	209.0	47.9	15647.25	14099.25
418	CON	9.6	75.6	133.0	159.0	34.7	12394.35	11244.75
419	ECC	6.0	22.3	45.2	95.3	67.2	7700.775	6984.375
420	CON	19.8	108.0	128.0	119.0	70.7	12124.5	9748.5
421	CON	9.0	29.9	45.4	52.2	48.3	5335.65	4253.25
423	ECC	14.1	67.7	111.0	135.0	79.1	12066.75	10374.75
424	ECC	5.4	28.8	48.9	60.1	39.9	5474.25	4826.25

Insulin measures continued (mmol/L).

Subject #	Group	EOGT		EOGT	AUCt	AUCi		
		EOGT 0h	15min	30min			EOGT60min120min	
402	CON	8.8	60.3	85.3	56.7	36.1	6524.025	5471.625
403	CON	16.3	45.2	58.8	79.3	118.0	9232.24	7276.24
405	ECC	7.3	33.3	60.5	55.1	38.8	5559	4683
408	ECC	14.0	63.9	106.0	193.0	90.1	14836.77	13156.77
409	ECC	6.4	37.6	47.4	103.0	124.0	10033.58	9264.375
411	CON	16.9	89.1	131.0	286.0	194.0	23100.45	21072.45
413	CON	7.2	23.4	31.7	32.3	63.7	4483.687	3616.087
415	ECC	6.2	40.3	109.0	283.0	29.7	16729.13	15991.13
418	CON	5.3	52.8	77.5	65.6	42.6	6805.2	6174
419	ECC	5.4	35.7	40.9	98.8	94.5	8777.25	8129.25
420	CON	24.2	83.7	113.0	164.0	45.1	12712.5	9808.5
421	CON	6.5	29.5	48.8	60.4	44.2	5633.25	4853.25
423	ECC	14.6	65.1	102.0	123.0	77.5	11241	9489
424	ECC	7.0	39.5	66.2	71.3	42.5	6619.125	5785.125

Subjects 403, 408, and 411 did not have 15 minute samples. Detailed report on statistical calculation for included measures in METHODS section of article.

Baseline QUICKI and HOMA measures.

Subject Group	insulin (uIU/mL)	insulin (pmol/L)	glucose (mg/dl)	glucose (mmol/L)	HOMA	log HOMA	1/HOMA	QUICKI
402CON	7.4	51.67	99.6	5.53	1.83	0.26	0.55	0.35
403CON	18.5	128.48	101.9	5.66	4.65	0.67	0.21	0.31
405ECC	9.2	63.76	104.6	5.81	2.37	0.37	0.42	0.34
408ECC	8.8	61.12	104.0	5.77	2.26	0.35	0.44	0.34
409ECC	7.9	55.14	94.1	5.22	1.84	0.27	0.54	0.35
411CON	13.9	96.54	94.8	5.26	3.25	0.51	0.31	0.32
413CON	6.7	46.18	96.7	5.37	1.59	0.20	0.63	0.36
415ECC	12.9	89.59	114.8	6.37	3.65	0.56	0.27	0.32
418CON	9.6	66.53	66.4	3.69	1.57	0.20	0.64	0.36
419ECC	6.0	41.46	87.1	4.83	1.28	0.11	0.78	0.37
420CON	19.8	137.51	85.1	4.72	4.15	0.62	0.24	0.31
421CON	9.0	62.64	89.8	4.99	2.00	0.30	0.50	0.34
423ECC	14.1	97.92	96.7	5.37	3.36	0.53	0.30	0.32
424ECC	5.4	37.50	89.0	4.94	1.19	0.07	0.84	0.37

Exercise QUICKI and HOMA measures.

Subject Group	insulin (uIU/mL)	insulin (pmol/L)	glucose (mg/dl)	glucose (mmol/L)	HOMA	log HOMA	1/HOMA	QUICKI
402CON	8.8	60.91	102.0	5.66	2.21	0.34	0.45	0.34
403CON	16.3	113.20	100.0	5.55	4.02	0.60	0.25	0.31
405ECC	7.3	50.70	101.5	5.64	1.83	0.26	0.55	0.35
408ECC	14.0	97.23	137.9	7.65	4.76	0.68	0.21	0.30
409ECC	6.4	44.52	96.9	5.38	1.53	0.19	0.65	0.36
411CON	16.9	117.37	96.4	5.35	4.02	0.60	0.25	0.31
413CON	7.2	50.21	99.6	5.53	1.78	0.25	0.56	0.35
415ECC	6.2	42.71	122.2	6.78	1.85	0.27	0.54	0.35
418CON	5.3	36.53	88.8	4.93	1.15	0.06	0.87	0.37
419ECC	5.4	37.50	85.5	4.75	1.14	0.06	0.88	0.38
420CON	24.2	168.07	92.3	5.12	5.51	0.74	0.18	0.30
421CON	6.5	45.14	93.0	5.16	1.49	0.17	0.67	0.36
423ECC	14.6	101.40	102.9	5.71	3.70	0.57	0.27	0.31
424ECC	7.0	48.27	95.2	5.28	1.63	0.21	0.61	0.35

IL-6 measures (pg/mL).

Subject	Group	0h (B0)	1h	24h (E0)
402	CON	1.042	1.117	1.164
403	CON	1.409	2.107	1.519
405	ECC	1.694	2.200	1.613
408	ECC	1.135	2.798	1.039
409	ECC	2.959	4.394	3.638
411	CON	1.087	1.722	1.205
413	CON	1.611	1.665	1.684
415	ECC	1.166	0.940	0.884
418	CON	1.334	1.668	1.521
419	ECC	0.708	1.665	1.292
420	CON	4.226	4.949	2.670
421	CON	1.737	1.556	1.302
423	ECC	4.339	2.558	2.066
424	ECC	1.500	0.607	1.313

TNF $\alpha$  measures (pg/mL).

Subject	Group	0h (Baseline)	24h (Post-exercise)
402	CON	0.043	0.666
403	CON	1.285	0.790
405	ECC	2.330	0.790
408	ECC	1.161	1.161
409	ECC	1.593	2.453
411	CON	1.038	1.161
413	CON	2.636	1.655
415	ECC	0.666	0.293
418	CON	0.168	1.161
419	ECC	2.575	1.326
420	CON	1.161	0.790
421	CON	2.024	0.852
423	ECC	0.955	1.408
424	ECC	0.914	0.043 (censored)

Subject 424 measured below the detectable limit for variable, so lowest value was substituted.