THE EFFECTS OF AN ACUTE BOUT OF ECCENTRIC, CONCENTRIC, AND TRADITIONAL RESISTANCE EXERCISE ON ADIPONECTIN CONCENTRATIONS

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By

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

THE EFFECTS OF AN ACUTE BOUT OF ECCENTRIC, CONCENTRIC, AND TRADITIONAL RESISTANCE EXERCISE ON ADIPONECTIN CONCENTRATIONS

Presented by Ryan W. Puck

a candidate for the degree of Master of Science

and hereby certify that in their opinion is worthy of acceptance.

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"Very few men are wise by their own counsel, or learned by their own teachings. For he that was only taught by himself had a fool for a master." -Ben Johnson

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"Keep away from people who try to belittle your ambitions. Small people always do that, but the really great make you feel that you, too, can become great" – Mark Twain

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THE EFFECTS OF AN ACUTE BOUT OF CONCENTRIC, ECCENTRIC, AND TRADITIONAL RESISTANCE EXERCISE ON ADIPONECTIN CONCENTRATIONS

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ABSTRACT

Introduction: Adiponectin is a protein secreted from adipose tissue which displays both anti-diabetic and anti-atherogenic properties. Studies have found that with resistance exercise, adiponectin concentrations can be increased. **Purpose:** The primary aim of the study was to examine the effects of a single session of eccentric, concentric, and traditional resistance exercise on total adiponectin and high molecular weight adiponectin (HMWA) concentrations. **Methods:** Forty-three overweight (BMI 32.3 $\pm$ 0.6 kg/m^2), untrained participants (15 males and 28 females) were randomly assigned to either eccentric (ECC), concentric (CON), or traditional resistance exercise (TRE). Subjects in the study participated in a one repetition maximum (1RM) session which was immediately followed up by an acute exercise session. Subjects initially performed a 1RM using the non dominant leg for CON, ECC, or TRE. Immediately following the 1RM testing, subjects performed three sets of 10 repetitions of bilateral leg extensions and leg curls, with both legs together, at 75% of the respective two legged-1RM (2L-1RM). The 2L-1RM was calculated by doubling the weight of the 1RM and then 75% 2L-1RM was used for the exercise session. Baseline characteristics were taken prior to exercise testing and included height, weight, dual energy X-Ray absorptiometry (DEXA) body composition, heart rate, and blood pressure. Outcome measurements were assessed at baseline, and 1 h, 24 h, and 48 h post exercise and include blood collection and muscle soreness assessments. Blood samples were analyzed for total adiponectin, high

molecular weight adiponectin (HMWA), glucose, and insulin. **Results:** There was no significant difference among groups at baseline for total adiponectin (CON- 10.9 ± 0.6 ng/mL; ECC- 11.8 ± 1.3 ng/mL; TRE- 12.6 ± 1.3 ng/mL) or HMWA (CON- 13.9 ± 2.1 ng/mL; ECC- 20.1 ± 3.0 ng/mL; TRE- 20.1 ± 3.0 ng/mL). A single session of CON exercise elicited a significant increase in total adiponectin concentrations by ~15% from baseline to 1 h post exercise (10.9 ± 0.6 ng/mL to 12.5 ± 0.8 ng/mL) while no changes were observed with ECC or TRE exercise 1 h post resistance exercise. ECC and TRE groups had significant decreases in total adiponectin concentration from baseline at 24 h and 48 h post exercise. ECC, CON, and TRE had no influence on HMWA or insulin sensitivity following an acute bout of resistance exercise. C**onclusion:** The results of the current investigation suggest that the concentric phase of resistance exercise can stimulate an increase in total adiponectin concentrations 1 h post exercise while ECC and TRE had no significant influence on total adiponectin concentrations 1 h post exercise period. However, since total adiponectin levels significantly decreased from baseline 24 h and 48 h post exercise, this may suggest that the eccentric component of resistance exercise could inhibit changes in adiponectin concentrations. The results from the study also indicate that an acute bout of resistance exercise, regardless of the mode, does not elicit a significant change in HMWA or in insulin sensitivity in these specific populations.

INTRODUCTION

Obesity, which currently affects approximately 53 million (27%) U.S. adults (14, 94), is a serious public health concern due to the increased risk for metabolic diseases including insulin resistance, hypertension, dyslipoproteinemia, inflammation, and vascular diseases (10, 58, 89, 114). Obesity is characterized by an accumulation of excess adipose tissue which was once thought to primarily serve as a depot for triglycerides. Over the past 10 years, emerging evidence suggests that adipose tissue is actually a highly active endocrine organ, sensing metabolic signals, and responding through hormonal secretions that affects whole body energy homeostasis (5, 74, 82).

Adipokines are a group of soluble proteins secreted from adipose tissue that modulate a variety of biological functions (2, 39). Several of these bioactive mediators and adipokines include tumor necrosis factor-α (TNF- α), interleukin (IL)-6, IL-1, leptin, and adiponectin which have been shown to directly or indirectly affect insulin sensitivity through modulation of insulin signaling and the molecules involved in glucose and lipid metabolism (54, 69, 89, 105). Adiponectin is unique in that it displays both anti-diabetic and anti-atherogenic properties and thus has a potential future as a novel therapeutic instrument for treating diabetes, coronary heart disease, and the metabolic syndrome (21, 41, 54, 69, 111).

Adiponectin. Adiponectin, produced exclusively by the adipocytes, is influenced by changes in adipose tissue mass (41, 103). Many studies have indicated that an inverse correlation exists between adiponectin and body fat (21, 82). Bruun et al. (10) assessed changes in adiponectin concentrations following diet-induced weight loss in obese adults. The 20 wk diet intervention led to an average weight loss of 20 lbs and a 51% increase in

circulating adiponectin (10). Bruun et al. (10) also examined the effects of obesity status on these outcomes. Compared to the obese subjects, the lean participants exhibited reduced insulin resistance along with a 45% increase in adiponectin mRNA expression and a 53% increase in serum adiponectin concentrations (10). Further, adiponectin mRNA expression and serum concentrations of adiponectin were significantly reduced with obesity, type 2 diabetes (T2D), and cardiovascular disease (CVD) indicating a possible metabolic role in insulin resistance (5, 112). To investigate the effects of adiponectin on insulin resistance, Berg et al. (5) infused varying quantities of total adiponectin into ob/ob mice that displayed hyperglycemia and severe hyperinsulinemia. The two- to three-fold increases in total adiponectin concentrations reduced glucose concentrations to near normal levels, demonstrating the positive and significant impact of total adiponectin on insulin resistance. Schulze et al. (97) showed that a two-fold increase in circulating total adiponectin was associated with a 30% risk reduction of a cardiovascular event in men with T2D.

Adiponectin is distinct from other adipokines in that it not only improves insulin sensitivity but also inhibits vascular inflammation (69). Low levels of adiponectin, hypoadiponectinemia, are significantly correlated with endothelial dysfunction and insulin resistance (16, 24, 41, 69, 89). Endothelial dysfunction is characterized by impaired nitric oxide (NO) release from the endothelium and decreased blood flow to insulin targeted tissues (41, 78, 89).

Researchers have identified that production of NO, through the subsequent activation of phosphatidylinositol 3(PI3) - kinase, in response to insulin action can improve glucose disposal due the increased vasodilation and blood flow to muscle in the

vasculature (16, 41, 77). Chen et al. (16) identified adiponectin stimulated NO production in a PI3- kinase dependent manner through phosphorylation eNOS at serine-1179 by 5'-AMP-activated protein kinase (AMPK) within endothelium. The ability of adiponectin to stimulate production of NO in the vasculature may lead to vasodilation and increased blood flow that contributes to enhanced glucose disposal rate (16).

Adiponectin vs. HMW Adiponectin. The majority of past studies have focused on assessing changes in total adiponectin concentrations and health. Recent technology has led to the identification of three main oligomeric isoforms: a low molecular weight adiponectin (LMWA), medium molecular weight adiponectin (MMWA), and high molecular weight adiponectin (HMWA) (63, 103).

Similar to that observed with total adiponectin, an inverse correlation exists between HMWA and body fat percentage/BMI. Kobayashi et al. (59) investigated HMWA concentrations in patients with coronary artery disease (CAD) and weight reduction in obese patients. Reduced HMWA was positively associated with patients with CAD. Additionally, significant weight reductions in overweight adults were associated with increases in HMWA. MMWA and LMWA remained unchanged in both groups, indicating that HMWA has a greater role in CVD associated with obesity (59). A study by Hara et al. (42) found, in patients being treated for insulin resistance or metabolic syndrome, that low levels of HMWA or a low HMWA-to-total adiponectin ratio were better predictors of insulin resistance or metabolic syndrome than total adiponectin alone. The HMWA ratio value for predicting the presence of metabolic syndrome reached 80% (42).

HMWA has been identified as the more biologically active form of adiponectin and may be more suited as a predictor of metabolic parameters vs. total adiponectin (6, 68, 98). HMWA has been found to bind more intensely to the adiponectin receptors causing greater AMPK activation (42) suggesting a more relevant role in increasing insulin sensitivity and diabetes prevention, through the stimulation of beta-oxidation and glucose uptake in myocytes (16), along with improving endothelial dysfunction by the phosphorylation of eNOS (16). Although HMWA appears to be a more superior biomarker for metabolic abnormalities, no studies to date have assessed whether exercise alters the circulating concentrations of HMWA vs. total adiponectin.

Exercise and Adiponectin

Exercise has been recognized as an effective nonpharmacological tool for maintaining or improving an individuals' overall health (2, 9, 67). It has been reported that regular physical exercise is an efficient preventative method in combating the development of T2D and atherosclerosis (8, 18, 58, 62). It has been recommended that individuals take part in a minimum of 30 min of aerobic exercise five times a week at moderate intensity or resistance exercise twice a week (43, 50, 76). A combination of both endurance and resistance exercise above the minimum recommendation can provide additional health benefits and result in higher levels of physical fitness (18, 43).

Endurance Exercise. Chronic endurance exercise can increase vascularization and mitochondrial density within the muscle improving oxidative capacity making the muscle more fatigue resistant (73, 108). Endurance training has traditionally been prescribed as a form of treatment or management to those with or at risk of developing T2D or CVD due to its ability to improve insulin sensitivity and glucose tolerance, and

reduce the circulation of pro-inflammatory adipokines (2, 9, 58, 92, 106). A reduction in body fat has been associated with a reduction in inflammatory markers associated with metabolic diseases. Chronic endurance exercise has been found to be an effective tool in reducing body weight and adipose tissue mass (2, 58, 92) and research has reported that a 10% reduction in body weight might be necessary to elicit an increase in circulating adiponectin concentrations (6, 83). Christiansen et al. (17) conducted a 12 wk intervention study comparing the effects of diet induced weight loss and exercise induced weight loss on inflammatory markers. Both groups reported an 11% reduction in body weight which was accompanied with reductions in the inflammatory markers TNF-α and IL-6 and a significant increase in adiponectin (17). In a similar study by O'Leary et al. (83), subjects participated in a 12 wk diet and aerobic exercise intervention to examine the combined effects of diet and improvements in aerobic capacity on adiponectin concentrations. After 12 wks, aerobic capacity was improved, body weight was modestly reduced by 8.1%, but adiponectin concentrations were unchanged. Based on these reports it can be speculated that an eight percent or greater reduction in body weight may be necessary to cause an increase in adiponectin concentrations.

An acute bout of endurance exercise has been shown to increase insulin sensitivity along with enhancing glucose transport to active muscle (33, 45). Though it has been reported that adiponectin can enhance insulin sensitivity (15, 88), increases in adiponectin concentrations following endurance exercise were a result of weight loss or reductions in total body water (29, 53, 83). According to Ferguson et al (29), a 60 min bout of cycling (intensity level: 65% of maximal oxygen consumption (VO_2Max) led to improvement in insulin sensitivity; however, circulating adiponectin concentrations were

unaltered (29). Jamurtas et al. (51), conducted a similar study using healthy overweight male subjects and found that after a 45 min bout of sub-maximal exercise (65% of VO2max) there was no significant change in immediate or prolonged alteration in adiponectin concentrations. These data suggest that an acute bout of endurance exercise, regardless of intensity, may not be an adequate stimulus to increase adiponectin concentrations.

Stimulation of adiponectin with resistance exercise. Resistance exercise has been viewed as the best approach to improve muscular strength, muscular power, muscular endurance, and muscle mass. Previous studies have identified that resistance exercise can influence vascular function, whole body insulin sensitivity, and increase plasma concentrations of adiponectin (9, 28, 71, 86, 106). One repetition maximum (1RM) testing is the preferred method for assessing muscular strength of an individual. Muscular strength is related to the amount of force that can be generated by a muscle or muscle group in one maximal effort. Muscular strength is quantified by the maximum weight a subject can lift for one repetition (23).

Studies have reported that chronic resistance exercise of moderate (~60-75% 1RM) to high (~75-90% 1RM) intensity can stimulate an increase in circulating adiponectin concentrations which has been correlated with an increase in insulin sensitivity and a reduced risk of CVD (9, 28, 86, 106). Oberbach et al. (84) found after 4 weeks of chronic resistance exercise in T2D, total adiponectin and CRP plasma concentrations normalized and insulin sensitivity increased. The improvement in insulin sensitivity was associated with increases in total adiponectin concentrations. Fatouros et al. (28) had 50 overweight sedentary men resistance train for six months at different

levels of intensity. Without any significant changes in body weight or body mass index (BMI), total adiponectin concentrations significantly increased (~30%) in groups that trained at moderate (60-65% 1RM) and high (80-85% 1RM) intensities, with a greater increase in the latter. These data suggest that resistance exercise by itself (without changes in body weight) was sufficient to induce changes in total adiponectin concentrations.

Recently, it has been shown that resistance exercise regulates the concentration of IL-15, which is highly expressed at the mRNA level in skeletal muscle acting as a myokine (80, 93). IL-15 functions in a muscle-to-fat endocrine axis that modulates insulin sensitivity by preventing hypertrophy of adipose tissue through the activation of peroxisome proliferator-activated receptor alpha (PPARα) which suppresses obesity linked cytokines like TNFα (1, 3, 19, 104). Quinn et al. (93) identified that administration of IL-15 inhibited the accumulation of the 3T3-L1 preadipocyte in lipid , stimulating secretion of adiponectin by adipocytes differentiation.

Along with the activation of PPARα, exercise has been found to increase activation of PPARγ which is involved in adipocyte differentiation through the coactivation PPARγ coactivator (PGC)-1α. PGC-1α will up regulate adiponectin through adipocyte cell differentiation which will in turn activate 5'-AMP-activated protein kinase (AMPK) essential to the metabolic effects of adiponectin for increasing insulin sensitivity (6) and for the phosphorylation and activation of eNOS (44). The evidence presented suggests that, exercise can lead to the activation IL-15 in skeletal muscle which will in turn signal PPARγ and PPARα in adipose tissue potentially suppressing the inflammatory effects of TNFα. PPARγ in adipocytes will enhance circulating levels of adiponectin,

which will in turn dampen TNFα production commonly associated with decreased insulin sensitivity and increased atherogenesis, (Figure 1). Furthermore, increasing levels of adiponectin stimulates the activation of AMPK which leads to an improvement in insulin sensitivity via beta oxidation and increased insulin independent glucose uptake (109, 111). Activation of AMPK also results in improved endothelial function via increased phosphorylation and activation of eNOS consequently leading increased circulation of NO (16, 36).

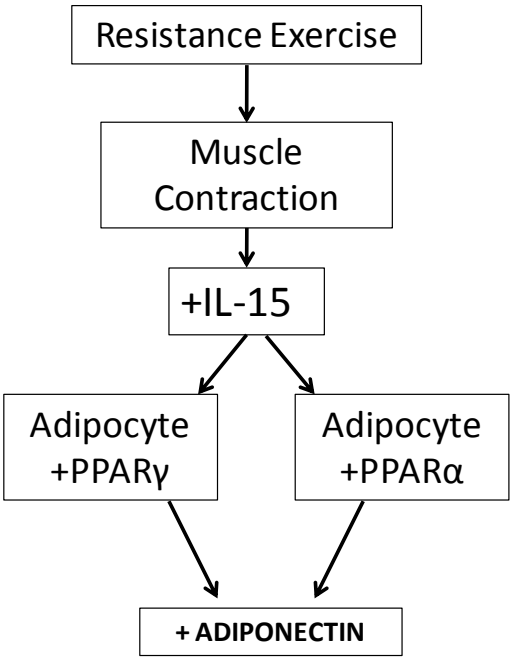

FIGURE 1. Activation of adiponectin with resistance exercise in skeletal muscle which will stimulate adiponectin production in adipose tissue (+ = improve/ promote production; ⊗ = inhibit action).

Along with enhancing insulin sensitivity, adiponectin has a significant impact on endothelial function (24, 87, 106). A study by Varady et al. (106) demonstrated that individuals who incorporated weight training into their training regimen had significant increases in plasma adiponectin concentrations post exercise and improvements in flow mediated dilation (FMD). Other studies have indicated that due to the increase in blood

flow and sheer stress on the endothelium with resistance training, FMD in blood vessels is largely dependent on endothelial release of NO (30, 71-72). In addition, improvements in FMD were associated with increases in adiponectin concentrations through the ability of adiponectin to stimulate an endothelial release of NO (35, 77). The shear stress and mechanical stretch of the endothelium with muscle contractions and the pulsation of blood pressure and flow may mediate the effects of exercise training on endothelial function (27, 106). Maeda et al. (71) identified increases in NO concentrations after 12 weeks of resistance training was linked with improvements in endothelial function. Previous studies have provided evidence that resistance training associated improvements in endothelial function are correlated with increased plasma concentrations of adiponectin and NO, however, there has yet to be a study where both adiponectin and NO concentrations are measure simultaneously.

Eccentric vs. Concentric. Activities of daily living and exercise are achieved through the repetitive actions of three types of muscle contractions: eccentric contractions, concentric contractions, and isometric contractions, containing a static action (85, 100).

Eccentric Exercise. An eccentric contraction is one in which a muscle lengthens as it exerts a force performing negative work (4, 22). An eccentric muscle action can be broken down into two phases: the generation of muscle tension and the passive stretch of the muscle by an external force while generating additional tension (32). Eccentric muscle contractions generate greater amounts of tension per cross sectional area of active muscle and greater degrees of muscle damage in comparison to concentric contractions (4, 22) with majority of mechanical damage through the streaming and smearing of the Z-

disks (4, 22, 52). In addition, eccentric actions involve less motor unit activation per specific level of tension and require less energy per level of force compared to a concentric muscle contraction (64). With sustained or intense strain placed on the muscle itself, inflammatory proteins (TNF-α and IL-6) are released into circulation as result of damage to the active skeletal muscle (20, 49, 81). Researchers have found that an exercised muscle can initiate protective adaptations to an exercise which can prevent further damage to skeletal muscle if exercise is performed within a 24 h period (95). Therefore, if the same eccentric exercise was repeated after recovery the inflammatory response, which is correlated with muscle damage, would be significantly less compared to the initial bout of exercise (26, 66, 95). An increase in inflammatory proteins such as TNF-α and IL-6 can reduce circulating levels of adiponectin as a result of damage to skeletal muscle tissue, so with a reduction in circulating inflammatory markers the beneficial effects of adiponectin are less likely to be dampened days following a bout of eccentric exercise (Figure 2A).

Concentric Exercise. Concentric muscle contractions produce tension while shortening; the action is attributed to the alignment of actin and myosin, optimizing cross-bridge formation (32). Concentric contraction produces significantly less muscle damage compared to an eccentric contraction while the energy demands are greater due to the amount of active muscle (94). Following a bout of concentric exercise, insulin sensitivity is improved increasing the uptake of glucose into muscle which is typically not observed with eccentric exercise (57, 91). With an increase in active muscle IL-15 is activated allowing there to be a cross talk between adipocytes and skeletal stimulating the production of adiponectin by the adipocyte (Figure 2B) (80, 93).

Isometric Exercise. An isometric muscle contraction is when the muscle length does not change due to the contractile force equaling the resistive force (23, 94). Isometric muscle actions are the basis of posture maintenance (94). When isometric muscle contractions are incorporated into dynamic resistance exercise, strength gains are enhanced (37). Studies have reported that isometric exercise was effective increasing cross sectional area of muscle along with increases in isometric strength (38, 55). However, with isometric training strength gains are joint angle specific which makes it even more important to perform isometric exercises at a variety of angles (12, 23). In addition, isometric contractions can induce damage to skeletal muscle tissue, which has been proven through measuring increases in markers of skeletal muscle damage like creatine kinase (CK) and z-line disruption (70). However, the degree of skeletal muscle damage is still significantly less compared to the damage induced with an eccentric muscle contraction (4, 12).

Impact of muscle contraction on vasculature and adiponectin concentrations. It has been proven that a relationship exists between blood pressure response during exercise and active muscle mass (11, 85). Increases in arterial stiffness, due to endothelial dysfunction, and blood pressure are significantly less if not unchanged with eccentric training compared to concentric training at both maximal and sub maximal intensities (85, 90). It is for this reason eccentric exercise is utilized more frequently in rehabilitation type practices in those with diminished work capacities (90). On the other hand, concentric exercise has been identified as contributing to the increases in cardiovascular stress (47, 90). Overend et al. (90) found that greater active muscle mass may explain the increase in heart rate (HR), mean arterial pressure (MAP), and rate

pressure product (RPP) due to the increases in motor unit recruitment. It is the mode of muscle contraction that can impact the vasculature; concentric exercise induces a vasopressor response increasing the load on the blood vessels potentially reducing elasticity of the artery causing arterial stiffness. (Figure 2B)

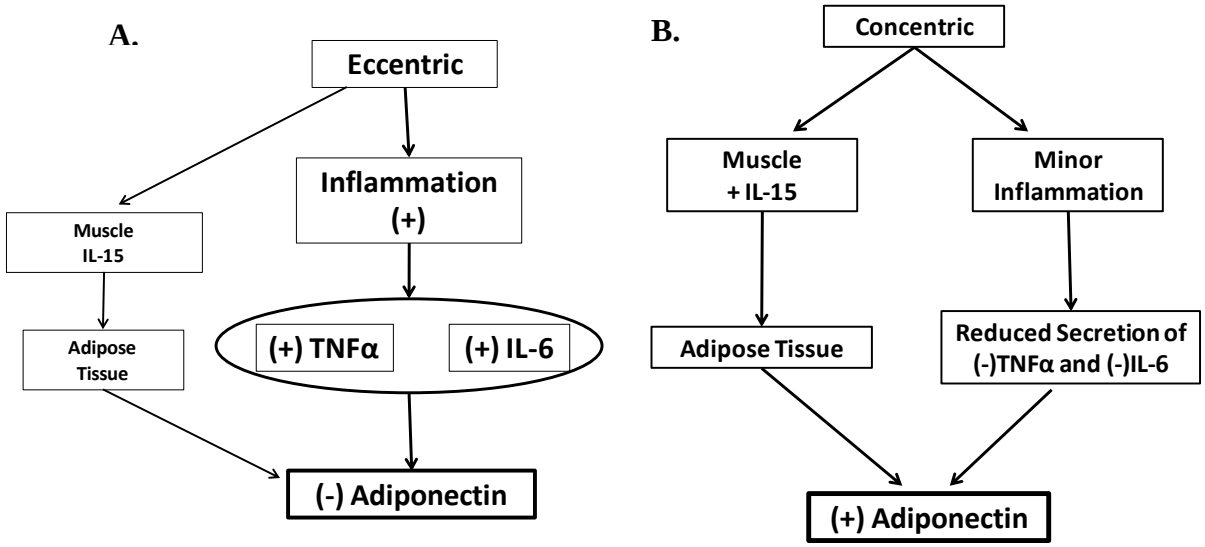

FIGURE 2. A. Proposed dampening of adiponectin with eccentric muscle contractions (+ = enhanced expression/ maintained concentrations; (-- = dampening/reduced activation). B. Effects of concentric resistance exercise on concentrations of adiponectin (+ = enhance beneficial effects).

Although it is evident that an acute bout of resistance exercise will increase concentrations of adiponectin (24, 28, 106), it is currently unclear as to whether the type of muscle contraction (i.e., eccentric vs. concentric) will influence adiponectin secretion. We suggest that an increase in inflammatory markers that accompanies eccentric exercise will dampen the beneficial effects of adiponectin on the endothelium through a reduction in circulating adiponectin (Figure 2A). Alternately, with concentric exercise (Figure 2B), inflammation is significantly less in comparison to eccentric exercise thus influential effects of adiponectin on the endothelium are less likely to be impeded. However, with

concentric muscle contractions there is a greater strain placed on the cardiovasculature system potentially leading to the disruption of the endothelium, which could again inhibit the beneficial effects of adiponectin.

Purpose and Hypothesis. The primary aim of the study was to examine the effects of a single session of eccentric, concentric, and traditional resistance exercise on total adiponectin and HMWA concentrations. It was hypothesized that due to the increased magnitude of damage to the skeletal muscle and secretion of inflammatory cytokines that occurs with eccentric exercise, an acute bout of concentric exercise will lead to greater increases in total adiponectin and HMWA concentrations. It was also hypothesized that the TRE group would have greater increases in total adiponectin concentration because the eccentric load would essentially be determined based off of what can be lifted concentrically. Therefore the degree of muscle damage accompanying the TRE group will be much less compared to the ECC group.

METHODS

Subjects. Forty-three sedentary male and premenopausal female individuals, age 18 to 50 y with a BMI between 25-39.9 kg/m^2, were recruited for this study. Potential participants were prescreened and included in the study based on inclusion and exclusion criteria. Subjects were non-smokers, that maintained a stable body weight (no more than $\pm$ 5% body weight change) over a three month period prior to beginning the study, had no history of coronary heart disease, diabetes, or renal disease, not on any form of hormone therapy, lipid lowering drugs, blood pressure medication, or anti-inflammatory medication (over the counter included). Gender and oral contraceptive use can influence circulating levels of pro- and anti-inflammatory cytokines (34). Therefore, female

subjects taking an oral contraceptive were excluded from the study and blood samples were obtained during the follicular phase of the menstrual cycle to reduce the influence of hormonal variations on variables. Subjects were classified as sedentary if participation of exercise was less than 30 min per week. Subjects were excluded from the study if they were following a formal diet for three months prior to the study or had any orthopedic problems that would limit ability to perform the required exercises. Approval for the study was obtained from the University of Missouri-Columbia Health Sciences Institutional Review Board.

Experimental Design. Subjects for the study reported to the University of Missouri Exercise Physiology Lab for screening and testing. Prior to initial visit, subjects participated in a phone or email screening process. Subjects were asked to keep a three day food log which was brought to the first visit to the lab. Each food log was analyzed using the Food Processor SQL Edition (EHSA Research, Salem, OR) to calculate daily caloric intake of the subject. Subjects were assigned a control diet at the conclusion of the initial visit that matched the average daily caloric intake of the food log submitted. Subjects returned to the lab on three subsequent visits for testing and data collection.

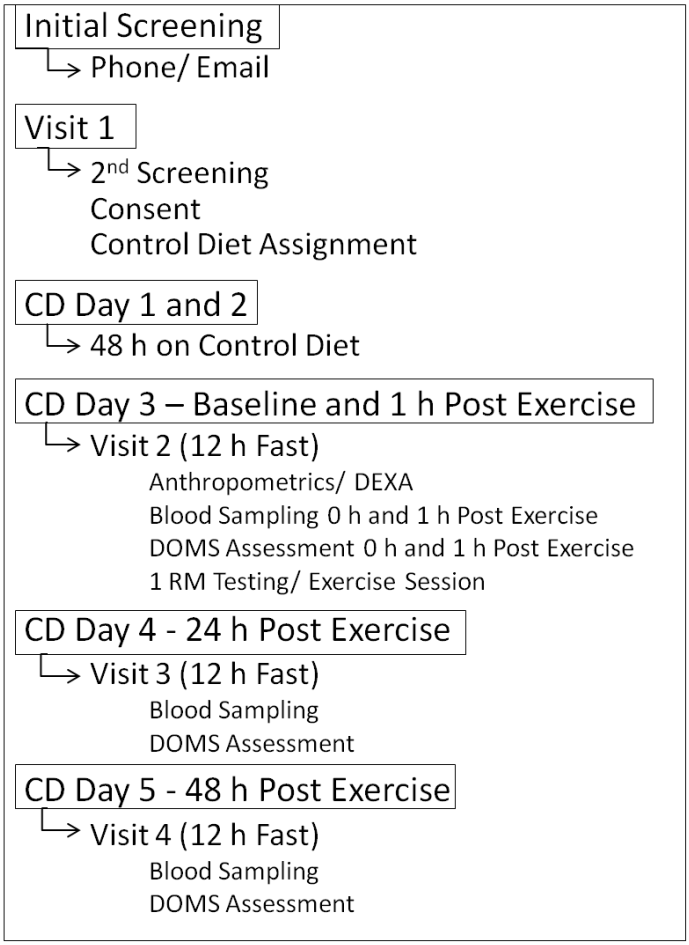

FIGURE 3. Experimental Design. Subjects participated in an initial screening prior to initial visit. Upon starting assigned control diet (CD) subjects would complete the entire study over a five day period.

At the initial visit, subjects reported to lab after a 2 h fast to have height and weight measured to ensure that each subject fell within the BMI requirement of 25-39.9 kg/m^2. Next subjects sat quietly in the lab for 10 min and had heart rate and blood pressure measurements recorded. Subjects that qualified for the study completed an informed consent and HIPPA Privacy Authorization Form along with a health history questionnaire, dietary habit questionnaire covering both past and current health and nutrition status (Appendices B-D). Subjects participated in an orientation session regarding the testing protocol to further ensure understanding of study (Appendix E for

study protocol). Subjects were assigned a control diet at the initial visit which was to be followed 48 h prior to the scheduled exercise session or the second visit to lab. Refer to Appendix E to view examples of control diets.

During the second visit, subjects were randomly assigned via coin flip to either the concentric resistance exercise (CON) group or the eccentric resistance exercise (ECC) group. The final 13 subjects recruited were assigned to the traditional resistance exercise (TRE) group. In addition, the second visit consisted of anthropometric measurements, delayed onset muscle soreness (DOMS) assessment, blood draw, and exercise session. Subjects followed their control diet for 48 h prior to this session and reported to the lab having fasted for 12 h. Upon arrival, weight, waist circumference, and hip circumference measurements which were recorded using a Toledo Scale (Toledo, OH) and spring loaded tape measure. A baseline DOMS assessment was performed after collection of anthropometric measurements. Next subjects had a blood sample taken; subjects were required to sit in a semi-supine position for 20 min before blood draw. Body composition was assessed by dual energy X-ray absorptiometry (DEXA) scanning. Following the DEXA scan, subjects reported to the laboratory training facility to complete a 1RM testing session followed immediately by an acute exercise session; more detail will be given on 1RM testing and acute exercise in the Exercise Protocol section. Subjects consumed 10 oz of water during the 1RM testing and acute exercise session. At the conclusion of the exercise session, subjects remained in the gym for 35 min, and as part of the recovery period subjects consumed 20 oz of water. After 35 min subjects performed a second DOMS assessment which was followed by the 1 h post exercise blood draw. Subjects were instructed to sit in a semi supine position for 20 min prior to

blood draw. Refer to Appendix F for data collection forms of anthropometric and testing data.

Subjects returned to the lab 24 h and 48 h following the conclusion of the exercise session. The subjects followed the control diet until the last day of scheduled visit (48 h post exercise visit). Subjects were reminded to report the lab having fasted for 12 h. At these two subsequent visits subjects performed a DOMS assessment followed by a blood draw. After the final visit, subjects returned to eating a normal diet. Refer to Appendix F for forms used for data collection.

Dietary Control. Subjects that passed the phone/email screening were asked to keep a three day diet log which would be analyzed upon first visit to lab. Each diet log was analyzed using the Food Processor SQL Edition (EHSA Research, Salem, OR) and an appropriate control diet that matched each subjects' caloric intake was assigned. Based upon analysis subjects were assigned a control diet of either 1500-2000, 2000-2500, 2500-3000, or 3000-3500 calories. The macronutrient composition of the control diet was 55% carbohydrates, 30% fat, and 15% protein while still maintaining the daily caloric intake range prior to study. Refer to Appendix E to view examples of control diets and diet log recording sheets. For this study, subjects chose one of the three control diets within the assigned caloric range and consumed this diet for five consecutive days. Subjects consumed a control diet 48 h prior to the scheduled acute exercise session and for 48 h following the acute exercise session.

Blood Pressure. Subjects sat in quiet environment in a comfortable chair for at least 10 min to allow blood pressure levels to normalize. Measurements of systolic and

diastolic pressures were conducted using a standard aneroid sphygmomanometer and stethoscope.

Body Composition. Height was measured in cm using a basic stadiometer and rounded to the nearest 0.1 cm. Weight was measured in pounds using a Toledo Scale (Toledo, OH) and was converted into kilograms, rounded to the nearest 0.1 kg. BMI was calculated as weight in kg divided by height in m^2. Body composition was assessed using waist to hip ratio (WHR) and DEXA scanning. WHR was determined by measuring the waist circumference at the narrowest area between the costal region and iliac crest, divided by the hip circumference measured at the point of greatest gluteal protrusion.

Delayed Onset Muscle Soreness. During visits two, three, and four DOMS assessments were conducted using a soreness scale from 0-100. Subjects walked on a treadmill at a speed of 2.0 mph at a 0% grade before the exercise session (baseline), and 1 h, 24 h, and 48 h post acute exercise session. Investigators read aloud a scripted questionnaire to subjects to assess soreness. Subjects first rated soreness in the front of the right leg while walking, then the front of the left leg, then the back of the right leg, and then the back of the left leg. Subjects were instructed not to touch their legs while rating degree of soreness. Following the walking assessment, subjects were instructed to lay face down on a table for the DOMS assessment muscle lengthening. Researchers used another scripted questionnaire instructing subjects to bend at the right knee driving the foot to the buttocks and rate the degree of soreness using the same 0-100 scale. The same procedure was repeated for the left leg.

Exercise Protocol. Forty-three subjects were recruited for the study, 15 were assigned to the CON group, 15 were assigned to the ECC group, and 13 were assigned to

the TRE group. On the second visit to the lab subjects participated in a battery of tests and data collection (Figure 4). Subjects began the exercise session with a warm-up on a treadmill for three to five minutes at a slow speed (2.0-2.5 mph) while the investigator gave instruction on the exercise protocol. For the 1RM testing and acute resistance exercise session subjects performed either the concentric phase of the lift (CON), the eccentric phase of the lift (ECC), or both phases (TRE). In order to equivocate training intensities among the three training groups during the acute exercise session, all three groups performed three sets of 10 repetitions at 75% of a two legged predicted 1RM (64). The two legged 1RM (2L-1RM) weight was determined by doubling the weight for the single leg 1RM and then based the exercise intensity off of the new 1RM value.

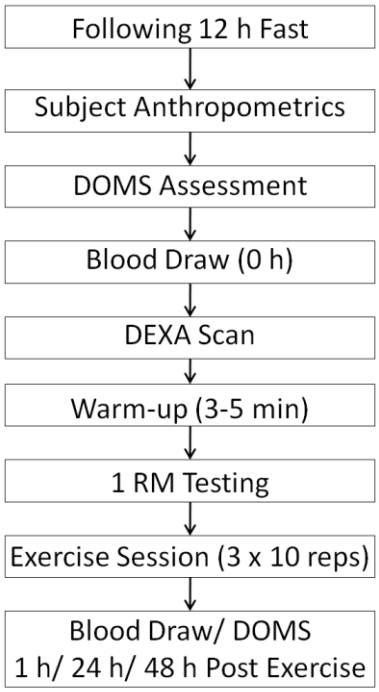

FIGURE 4. Visit 2: Testing Protocol. Depicts the order and battery of tests endured by each subject for the exercise component of the study.

Concentric Resistance Exercise Group. The CON group performed the concentric component of the exercise for both the 1RM and acute exercise sessions. During the 1RM session, subjects used the non-dominant leg to lift the weight to a three second cadence through the full range of motion of the knee. Subjects were not required to perform the eccentric component of the lift, so researchers would catch the weight at the top of the concentric movement and return the weight back down to the starting position using either a hook bar or pulley system (Appendix G). An attempt was ruled a failure during 1RM testing if the subject was unable to lift the weight at a three second cadence through the full range of motion of the knee on the leg extension and leg curl machine. Subjects were given five attempts to reach a 1RM with weight being adjusted based off of degree of difficulty rated by the subject on a scale from one (easy) to 10 (hard). Subjects performed the leg extension and leg curl exercises as a super set/push-pull set with a 2 min rest following the leg curl during the 1RM testing session.

Immediately following the 1RM session subjects in the CON group participated in an acute exercise session that required the use of both legs in unison. Subjects performed three sets of 10 repetitions on the leg extension and leg curl machine at an intensity of 75% of predicted 2L-1RM. Since subjects had to use two legs during the acute exercise session the single legged 1RM was doubled giving a predicted 2L-1RM. The acute exercise intensity level was set at 75% of the 2L-1RM. Subjects performed the concentric phase of the lift to a three second cadence with a minute rest between each set. It is recommended to allot one minute rest for novice lifters that are performing three sets of 10 repetitions (31). After subjects completed three sets of leg extensions subjects then

performed the three sets of leg curls; the acute exercise session was not performed as a super set as with the 1RM portion of the session.

Eccentric Resistance Exercise Group. Subjects in the ECC group performed the second phase or eccentric portion of the lift for both the 1RM and acute exercise sessions. During the 1RM session, subjects used the non-dominant leg to lower the weight to a five second cadence through the full range of motion of the knee. Subjects were not required to perform the concentric phase of the lift, so researchers lifted the weight to the top of the first phase of the lift or the end of the concentric component of the exercise using a hook bar or the pulley system (Appendix G). The subject positioned his/her feet under the pad of the movement arm of the leg extension or leg curl machine and then with a verbal cue from the researcher the weight was released. An attempt was ruled a failure during 1RM session if the subject was unable eccentrically lower the weight through the full range of motion of the knee at a rate of five seconds on the leg extension and leg curl machine. Subjects were given five attempts to reach a 1RM with weight being adjusted based off of degree of difficulty rated by the subject on a scale from one (easy) to 10 (hard). Subjects performed the leg extension and leg curl exercises as a super set/push-pull set with a 2 min rest following the leg curl during the 1RM testing session.

Immediately following the 1RM session subjects in the ECC group participated in an acute exercise session which required both legs to be used in unison. Subjects performed three sets of 10 repetitions on the leg extension and leg curl machine at an intensity 75% of the respective 2L-1RM. Subjects performed the eccentric phase of the lift to a five second cadence with a minute rest between each set. After subjects

completed three sets of leg extensions subjects performed three sets of leg curls; the acute exercise session was not performed as a super set as with the 1RM portion of the session.

Traditional Resistance Exercise Group. Subjects in the TRE group performed both the concentric and eccentric components of the lift concurrently for both the 1RM and acute exercise sessions. During the 1RM session, subjects used the non-dominant leg to concentrically lift the weight to a three second cadence through the full range of motion of the knee and then eccentrically lower the weight to a three second cadence. Essentially the 1RM value for the TRE was based off the weight that could be lifted concentrically. When comparing isokinetic strength capabilities between concentric and eccentric muscle contractions, research has established eccentric strength as being 20 to 60% greater than concentric strength (46, 48). Subjects were instructed to briefly pause (~0.5 seconds) at the conclusion of the concentric portion of the lift to signify completion of the first phase of the lift prior to transitioning to second phase of the lift or eccentric component. Subjects were given five attempts to reach a 1RM with weight being adjusted based off of degree of difficulty rated by the subject on a scale from one (easy) to 10 (hard). A set would be ruled a failure if a subject was unable to successfully lift the weight through the first phase of the lift or lowered the weight faster than the three second cadence during the second phase of the lift. Subjects performed the leg extensions and leg curl exercises as a super set/push-pull set with a 2 min rest following the leg curl.

Immediately following the 1RM session subjects in the TRE group used both legs in unison during the acute exercise session. Subjects performed three sets of 10 repetitions on the leg extension and leg curl machine at an intensity 75% of the respective

2L-1RM. Subjects performed the first phase of the lift (concentric) to a two second cadence and the second phase (eccentric) of the lift to a two second cadence. Subjects completed three sets of leg extensions first followed by three sets of leg curls. A minute rest was given between each set.

Blood Collection and Analysis. During visits two, three, and four subjects sat in a semi-supine position for 20 min before blood samples were be taken. Blood was taken from the antecubital vein using a 23 gauge x ¾ inch Angle Wing butterfly needle at 0 h and 1 h, 24 h, and 48 h post exercise. Using two 10 ml blood draw syringes, 20 ml of blood was collected and evenly distributed between one 10 ml serum separator (SST) vacuum sealed tube and one 10 ml ethylenediaminetetraacetic acid (EDTA) vacuum sealed tube. The SST tubes contained a barrier gel that separated blood cells from the serum when centrifuged. The EDTA tubes contained an anticoagulant and stabilizing agent to slow blood clotting. Each tube of blood was inverted 10 times and placed at room temperature (SST) or on ice (EDTA) for 30 min.

Two capillary tubes were used to collect the remaining 0.5 ml of blood in the syringe for hematocrit measurements. The capillary tubes were filled three quarters of the way, plugged at one end with putty, and were then centrifuged using an IEC MB centrifuge (International Equipment Co., Needham Heights, MA) for three minutes at 14,000 rpms. Hematocrit was measured using a Micro Hematocrit Tube Reader.

At the conclusion of 30 min, blood samples were taken into the chemistry laboratory to be spun and aliquoted. The test tubes were centrifuged using a Fischer Scientific-Marathon 21000R centrifuge (International Equipment Co., Needham Heights, MA) for 15 min at -4°C at 2000g. At the conclusion of the 15 min, plasma from the

EDTA tubes and serum from the SST tubes was extracted and aliquoted into 0.5 ml cryogenic vials. Serum and plasma was stored in a subzero Legaci freezer at -80°C until analysis.

Adiponectin. Adiponectin was analyzed using two different types of Human adiponectin enzyme-linked immunosorbent assay (ELISA) kits (Linco Research Inc., St. Charles, Missouri) designed for the quantitative determination of HMWA and total adiponectin. Serum samples were thawed, diluted, and pipetted into appropriate wells. Antibodies specific for total adiponectin or HMWA were pre-coated at the bottoms of all 96 wells on a micro titier plate. The pre-coated anti-bodies, from the respective kits, immobilized total adiponectin or HMWA allowing for the rest of unbound material to be washed away using specific wash buffer solution. An enzyme solution was added to allow for immobilization of antibodies necessary for quantification. Another wash was performed to remove any remaining un-bound antibodies from the wells. A substrate solution was added to each well to develop a blue color proportional to concentrations of total or HMWA adiponectin. A stop solution was added and the depth of color was measured at a wavelength of 450 nm and 590 nm within 5 min of the stop solution administration.

The coefficient of variation (CV) was calculated and samples that were above the 15% CV were re-analyzed. Results for the samples were calculated at a four to five parameter logistic function along a sigmoidal curve. The appropriate range of the total adiponectin assay was 1.56 ng/mL to 100 ng/mL while the appropriate range for the HMWA assay was be 1.56 ng/mL to 200 ng/mL.

Insulin. Chemiluminiscence technique (Immulite 1000 LKCR1, Siemens Healthcare Diagnostics Inc., Deerfield, IL) was used to determine fasting plasma levels of insulin from the EDTA tube. The Immulite 1000 used a proprietary wash technique; insulin-specific coated beads were used as reaction container for sample processing. Multiple washes were performed to ensure separation of unbound material.

Glucose. Glucose was measured using the glucose oxidase method utilizing an enzymatic glucose reagent (Fisher Scientific, Pittsburg, PA). The assay utilized a liquid stable Infinity^{TM} reagent for the glucose oxidase reaction in conjunction with an auxiliary sp reaction that determined serum glucose concentrations in the biological fluids. Glucose was oxidized by glucose oxidase into gluconic acid and hydrogen peroxide (H_2O_2); H_2O_2 was coupled with 4-aminoantipyrin to a phenolic compound forming a red quinoneimine dye of intensity which was measured at 500 nm photometrically.

Statistical Analysis. Standard descriptive statistics were calculated for each independent measurement using means and standard errors (SE). The analyses of total adiponectin, HMWA, glucose, and insulin concentrations were compared using a two way analysis of variance (ANOVA) with repeated measures for time (0 h, 1 h, 24 h, and 48 h) and to determine a group effect (CON, ECC, and TRE). A mixed factor analysis was used to determine a group x time interaction. When necessary, a post hoc analysis was performed using an independent sample t-test to detect specific group difference (i.e., between-subject comparisons, CON, ECC, vs. TRE). A paired t-test was run to determine significance between time points within each group. All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS; version 16.0; Chicago, IL). An alpha level of $p < 0.05$ was considered statistically significance.

Preliminary Data. The data presented in Table 1 were previously reported by Warner et al. (107), where they compared a single session of eccentric or concentric resistance exercise on metabolic health. Following an acute bout of eccentric and concentric resistance exercise, there were no significant differences between groups with regard to the accumulation of inflammatory markers. The eccentric exercise group had a significantly ($p<0.05$) greater accumulation of CK indicating a significant degree of skeletal muscle damage.

Table 1. Preliminary results. Inflammatory markers, insulin, and glucose responses following a single session of eccentric vs. concentric exercise.

Variable	Group	Baseline	1h Post	24h Post	48h Post
IL-6 pg/mL	CONC (n=15)	13.94 ± 3.80	19.58 ± 3.98	12.96 ± 3.71	14.80 ± 4.15
	ECC (n=15)	17.39 ± 3.80	18.25 ± 3.98	18.24 ± 4.15	18.07 ± 3.63
	Combined (n=30)	15.67 ± 2.69	18.91 ± 2.81	13.61 ± 2.62	16.52 ± 2.94
TNFα pg/mL	CONC (n=15)	4.44 ± 0.48	5.05 ± 0.54	4.30 ± 0.29	4.40 ± 0.98
	ECC (n=15)	4.95 ± 0.48	4.20 ± 0.54	4.35 ± 0.29	5.52 ± 0.98
	Combined (n=30)	4.70 ± 0.34	4.63 ± 0.38	4.32 ± 0.20	4.96 ± 0.69
CRP mg/L	CONC (n=15)	4.00 ± 1.10	4.01 ± 1.09	4.54 ± 1.15	4.08 ± 1.17
	ECC (n=15)	2.64 ± 1.10	2.82 ± 1.09	3.54 ± 1.15	3.31 ± 1.17
	Combined (n=30)	3.32 ± 0.77	3.42 ± 0.77	4.04 ± 0.81	3.70 ± 0.82
CK U/L	CONC (n=15)	98.9 ± 8.9	113.1 ± 11.0*	295.5 ± 64.8*	228.7 ± 730.7
	ECC (n=15)	93.6 ± 8.9	111.5 ± 11.0*	392.5 ± 64.8*	4596.2 ± 730.7*†
	Combined (n=30)	96.3 ± 6.3	112.3 ± 7.8*	344.0 ± 45.8*	2412.5 ± 516.7*
INSULIN uIU/mL	CONC (n=15)	12.5 ± 1.5	11.4±1.4	11.2 ±1.3	12.8 ± 1.8
	ECC (n=15)	9.5 ± 1.5	10.1 ± 1.4	8.8 ± 1.3	9.2 ± 1.8
	Combined (n=30)	11.0 ± 1.1	10.7 ± 1.0	10.0 ± 0.9	11.0 ± 1.3
GLUCOSE mg/dL	CONC (n=15)	92.6 ± 3.6	89.5 ± 3.4	91.9 ± 3.8	91.2 ± 3.8
	ECC (n=15)	94.8 ± 3.6	94.5 ± 3.4	93.2 ± 3.8	91.8 ± 3.8
	Combined (n=30)	93.7 ± 2.5	92.0 ± 2.4	92.6 ± 2.7	91.5 ± 2.7

Values reported as means ± SE. *Difference from baseline value ($p < 0.05$). † Significantly different from concentric.

RESULTS

Forty-three subjects were recruited to participate in the exercise study (15 CON, 15 ECC, and 13 TRE group). Subject demographics are presented in Table 2. When comparing subject demographics among groups, the waist to hip ratio of the TRE group was significantly less compared to both the CON and ECC groups. Body fat percentage and waist circumference were significantly different among groups with the ECC group being significantly less than the CON group and significantly greater than the TRE group. Waist circumference measurements were significantly lower in the TRE group compared to the CON and ECC groups. There was no significant difference among the groups for BMI.

Table 2. Baseline subject characteristics for single bout of resistance exercise.

Subject Characteristics	CON (n = 15)	ECC (n = 15)	TRE (n = 13)
Gender (% male)	40	33.3	26.7
Age (years)	31 ± 2.3	35 ± 2.5	28 ± 2.3
Weight (kg)	98.7 ± 7.3	91.8 ± 3.0	91.7 ± 4.3
Height (cm)	171.7 ± 2.2	168.4 ± 1.7	172.5 ± 2.8
Body Fat %	37.7 ± 1.6[a]	36.0 ± 2.4[b]	30.9 ± 1.7[c]
Waist Circumference (cm)	110.1 ± 2.5[a]	102.9 ± 2.7[b]	90.5 ± 2.5[c]
Hip Circumference (cm)	119.4 ± 1.9	116.2 ± 2.4	117.8 ± 6.9
Waist: Hip ratio	0.92 ± 0.02[a]	0.89 ± 0.02[a]	0.79 ± 0.03[b]
Body Mass Index (kg/m²)	33.4 ± 0.9	32.4 ± 1.1	30.7 ± 1.0

Values are means ± SE. Different letters indicate significant difference ($p < 0.05$) between groups.

Total Adiponectin

Between group differences. No significant differences in total adiponectin concentrations were present among groups at baseline, 1 h, 24 h, and 48 h time points (Table 3). A significant main effect of time was evident following an acute bout of resistance exercise. Specifically, resistance exercise led to initial increases in total adiponectin at 1 h post exercise followed by a decrease in total adiponectin throughout

the remaining 24 h and 48 h periods (Table 3). Although there was no main effect of group, a time x group interaction was observed.

Within group. Post-hoc t-tests showed that CON exercise significantly influenced the post-exercise total adiponectin concentrations compared to ECC or TRE at the 1 h time point. Specifically, while the CON group exhibited significant increases in total adiponectin 1 h post exercise; the TRE and ECC had no significant change in total adiponectin 1 h post exercise. ECC and TRE displayed significant decreases in total adiponectin 24 h and 48 h from baseline and 1 h post exercise. Refer to Appendix J for Post Hoc analysis data.

Additionally, the TRE and ECC groups had significant decreases in total adiponectin at 24 h and 48 h from baseline, while the CON group had no significant change from baseline at 24 h and 48 h time points (Table 3 and Figure 5). No significant differences were present among groups at any of the time points (Table 3 and Figure 5). Additional analysis identified that there was no significant difference in total adiponectin average or AUC change from baseline among groups (Figure 5B).

Table 3. Serum concentrations of total adiponectin pre- and post exercise.

	Baseline	**1 h**	**24 h**	**48 h**
CON (n =15)	10.9 ± 0.6	12.5 ± 0.8*	10.5 ± 0.8	10.5 ± 0.7
ECC (n =15)	11.8 ± 1.3	11.8 ± 1.3	11.1 ± 1.1*	10.7 ± 1.1*
TRE (n =13	12.6 ± 0.8	12.6 ± 1.3	11.5 ± 1.0*	11.5 ± 1.1*
Average	11.7 ± 0.5	12.3 ± 0.6*	10.9 ± 0.6*	10.9 ± 0.5*

Units are ng/mL. Values are means ± SE. *Significant difference from baseline ($p < 0.05$). There were no significant differences among groups in each column.

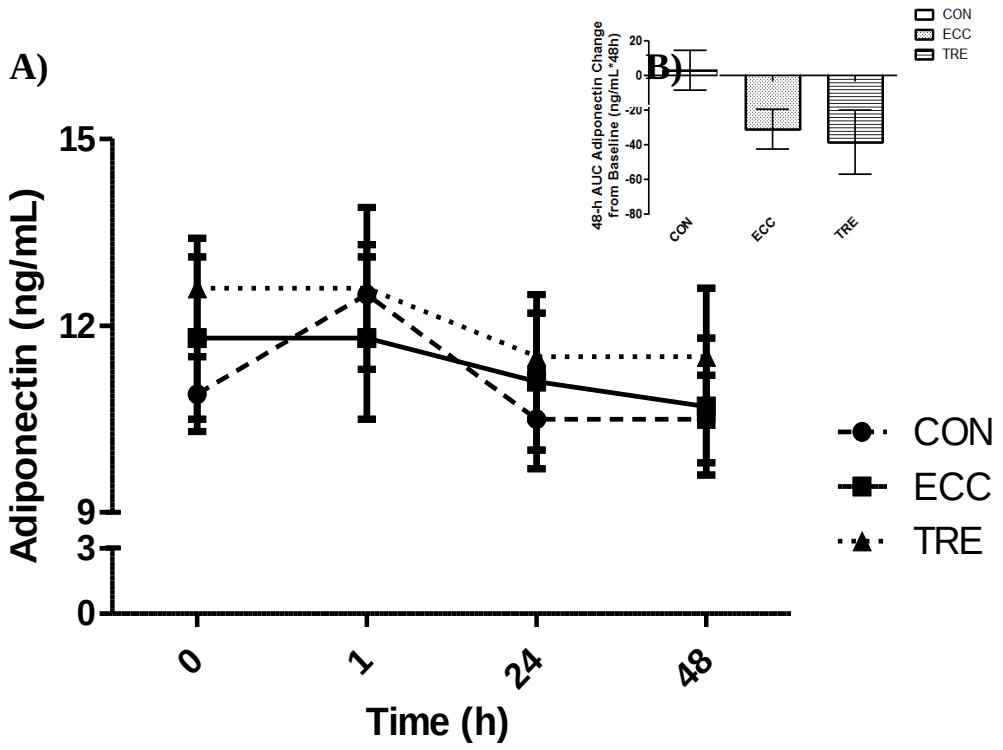

FIGURE 5 –A) Total adiponectin concentration over 48 h periods. B) Total adiponectin 48 h AUC changes from baseline for CON, ECC, and TRE groups. *Significant difference from baseline ($p < 0.05$) for CON group. † Significant difference from baseline for ECC and TRE groups.

High molecular weight adiponectin

Results for HMWA are shown in Table 4 and Figure 7. There was no main effect of time or a group effect for HMWA. There was no significant difference in HMWA concentrations between groups over the four time periods (Table 4). A significant difference in HMWA AUC change from baseline was found between the TRE and CON groups (Figure 6B).

Table 4. Serum concentrations of high molecular weight adiponectin pre- and post exercise.

	Baseline	1 h	24 h	48 h
CON (n =15)	13.9 ± 2.1	15.3 ± 1.9	15.2 ± 2.1	14.8 ± 2.2
ECC (n =15)	20.1 ± 3.0	20.1 ± 2.9	18.9 ± 2.8	19.3 ± 2.7
TRE (n =13	19.2 ± 5.0	16.9 ± 3.9	18.9 ± 4.6	17.7 ± 4.2
Average	17.7 ± 1.9	17.5 ± 1.7	17.6 ± 1.8	17.3 ± 1.7

Units are ng/mL. Values are means ± SE. There were no significant differences from baseline values for any group across the four time points. There were no significant differences among groups in each column.

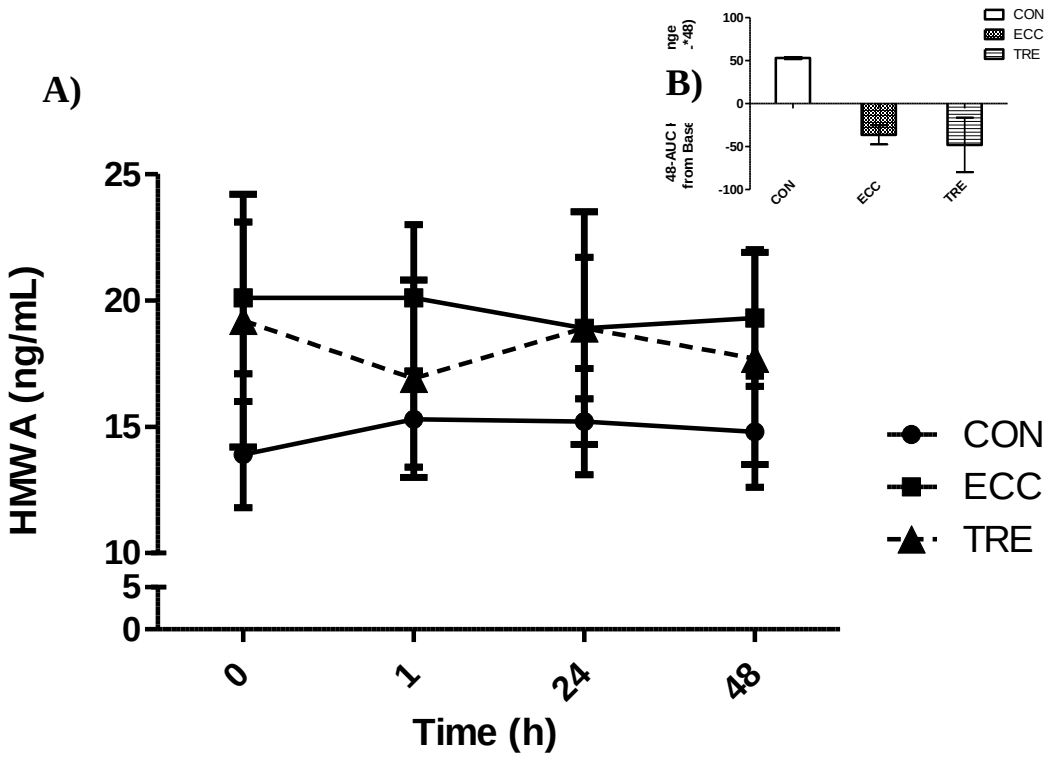

FIGURE 6- A) HMWA concentrations over full 48 h period. No significant change from baseline was observed in any group. B) HMWA 48 h AUC changes from baseline for CON, ECC, and TRE groups. Groups with different letters are significantly different from each other ($p < 0.05$).

*Quicki (*logInsulin + logGlucose)

Between groups. There was no significant main effect of time or a time x group interaction for insulin sensitivity across all time points. A significant group effect was found between the TRE and CON group (Table 5). There was a significant difference in insulin sensitivity values between the TRE and CON groups at 48 h (Table 5).

Within groups. There was no significant difference in insulin sensitivity among groups at 0 h, 1 h or 24 h post exercise time. There was a significant difference in insulin sensitivity among groups at the 48 h time point. At the 48 h time point the TRE group had significantly higher QUICKI value levels compared to the ECC group.

Table 5. QUICKI analysis pre- and post exercise.

	Baseline	**1 h**	**24 h**	**48 h**
CON (n =15)	0.34 ± 0.01	0.35 ± 0.01	0.34 ± 0.01	0.34 ± 0.01[a]
ECC (n =15)	0.34 ± 0.01	0.34 ± 0.01	0.35 ± 0.01	0.35 ± 0.01[a,b]
TRE (n =13	0.37 ± 0.01	0.37 ± 0.02	0.37 ± 0.01	0.38 ± 0.01[b]
Average	0.35 ± 0.01	0.35 ± 0.01	0.35 ± 0.01	0.35 ± 0.01

Units are (1/logI + logG). Values are means + SE. There were no significant differences from baseline values for any group across the four time points. Different letters indicate a significant difference among groups ($p < 0.05$).

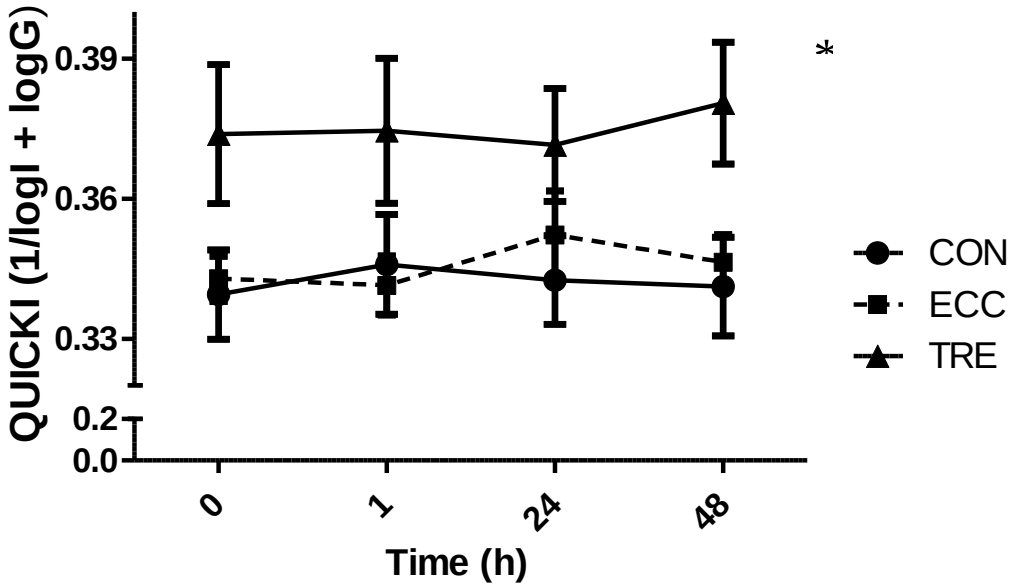

FIGURE 7- QUICKI levels over full 48 h period. *Significant difference between CON and TRE.

Correlation

A correlation analysis was performed to determine whether there was an association between indices of subject demographics, 1RM, and baseline levels of total adiponectin, HMWA, and QUICKI. Waist circumference showed a significant inverse correlation with total adiponectin, and QUICKI at baseline. Body weight was significantly correlated with baseline levels of total adiponectin and QUICKI. An unexpected result was found indicating that body fat percentage had no impact on baseline levels of total adiponectin or HMWA while a significant correlation was found between body fat percentage and QUICKI. A significant correlation was found between baseline levels of adiponectin and 1RM. (Table 6)

Table 6. Correlation matrix of subject characteristics and baseline sample values.

	Total Adiponectin	HMWA	QUICKI	Waist Circ.	Body Weight	BF%
Total Adiponectin	1					
HMWA	0.632*	1				
QUICKI	0.065	-0.002	1			
Waist Circ.	-0.382*	-0.285	-0.450*	1		
Body Weight	-0.382*	-0.231	0.358*	0.730*	1	
BF%	0.223	0.221	0.372*	0.265	-0.001	1
1RM	-0.454*	-0.360*	-0.166	0.633*	0.516*	-0.351*

r-values from Pearson product bivariate correlation.
*Correlation is significance at $p < 0.05$.

DISCUSSION

To our knowledge this is the first study comparing different modes of resistance exercise on adiponectin concentrations in a healthy group of sedentary overweight individuals. It has become apparent that adipose tissue houses various adipokines that are actively involved with the regulation of skeletal muscle metabolism. Adiponectin has received much attention due the observation of its impact on health. Adiponectin is the only adipokine released into circulation that has been shown to have both insulin sensitizing and antiatherogenic effects (16, 24, 41, 69, 89). There is evidence supporting the fact that an inverse relationship exists between body fat and adiponectin (21, 39, 42) and thus it is logical that with weight loss, adiponectin concentrations can increase (6, 83).

Resistance training is becoming a new method in the prevention and management of diabetes, hypertension, vascular disease, and obesity (2, 85, 90, 107). An acute bout of resistance exercise has the potential to influence insulin sensitivity and other biomarkers that can impact overall health (16, 24, 41, 69, 89). Studies have reported that resistance exercise can elicit an increase in adiponectin concentrations (9, 28, 86, 106), however, it

has yet to be determined whether it is the concentric or eccentric component of resistance exercise alone that can influence changes in adiponectin concentrations or if the two need to work collectively.

Total adiponectin. Following a single session of resistance exercise, the CON group was the only group that had a significant increase in total adiponectin concentrations. The CON group had a 14.3% increase in total adiponectin concentrations 1 h post exercise while both the ECC and TRE groups displaying no increases 1 h post exercise. These results contradict and support findings from other investigations.

Varady et al. (106) have shown that following an acute bout of TRE, plasma concentrations of total adiponectin were significantly increased by nearly 37%. There were two major differences between the study by Varady et al. (106) and the current investigation. In the other investigation, subjects performed TRE only with leg press, a multi-joint movement exercise, where as in the current investigation TRE, CON, and ECC exercise was performed through single joint exercises, leg extensions and leg curls. With multi-joint exercises, a much greater load can be tolerated in comparison to a single joint exercise, allowing for a greater recruitment of muscle fibers at one time. Subjects from the Varady et al. (106) study displayed significant increases in total adiponectin concentrations through an intense training session that included four working sets of eight to 12 repetitions (~75-85% 1RM), with weight being subsequently added to each set. Though the intensity level was relatively similar between the studies, the workloads subjects were using were significantly different because of the number of muscle fibers needing to be recruited.

The second major difference was subject population. Subjects from the Varady et al. (106) study were classified as an active population, with subjects having six months of TRE training, running, or a combination of both running and TRE prior to participation in the study. The adaptations to resistance exercise can lead to a reduction in the accumulation of inflammatory markers known to inhibit adiponectin expression (101). In addition, subjects from the Varady et al. (106) study would have more efficient recruitment and increased neural activation which would allow significantly greater force production maximizing performance (99).

There are limited studies examining the effects of resistance exercise on adiponectin acutely, however, there are studies that have examining the chronic effects of resistance exercise on adiponectin. Fatorous et al. (28) trained 65-78 yr male subjects, much older population compared to the current investigation of 18-50 yr males and females, at different intensities for a period of 24 wks and found that total adiponectin plasma concentrations significantly increased (21-61%) in groups that exercised at intensities of 60-85% of 1RM up until the final exercise session. Groups that exercised at an intensity of 45-60% of 1RM had no significant changes in total adiponectin concentrations immediately after exercise. Though the time was not specified, subjects in the Fatorous et al. (28) study collected blood samples immediately following the final bout of exercise while the current investigation collected blood samples 1 h post exercise. Subjects from the Fatorous et al. (28) study (60-85% of 1RM)and the current investigation exercised at similar intensities, however, subjects from the other investigation exercised muscles of both the upper and lower body, increasing the amount of active muscle, while the current investigation was strictly lower body.

The current investigation measured total adiponectin concentrations at baseline and 1 h, 24 h, and 48 h post exercise and found that the CON group was the only group with significant increases in total adiponectin 1 h post exercise. At 24 h and 48 h total adiponectin concentrations were significantly decreased from 1 h post exercise in CON group. The ECC and TRE group from the current investigation exhibited no significant changes from baseline to the 1 h time point in total adiponectin levels but showed significant decreases in total adiponectin at 24 h and 48 h from baseline. However, based off of the increase in total adiponectin concentrations in the CON group at 1 h, we are confident that the exercise intensity level chosen was sufficient to elicit an adiponectin response.

When comparing the three exercise groups from the current investigation, it was the CON group alone that expressed significant increases in total adiponectin concentrations post exercise. All three exercise groups displayed significant decreases in total adiponectin from 1 h post exercise at 24 h and 48 h time points. However it was the ECC and TRE groups that displayed significant decreases in total adiponectin from baseline at 24 h and 48 h. Both the TRE and ECC groups had an eccentric component and it is possible that an eccentric muscle contraction can dampen the stimulating effects of a concentric muscle contraction since there was no change 1 h post exercise in total adiponectin followed by significant decreases in both the ECC and TRE groups.

Studies by Klimcakova et al. (58), that measured changes in total adiponectin in plasma at 48 h and 72 post final exercise bout, and Ahmadizad et al. (2), that measured changes in total adiponectin in serum at 96 h post final exercise bout, reported no changes or slight decreases in total adiponectin concentrations at those time points. This was in

response to resistance exercise programs performed at an intensity of 60-70% of 1RM, within the exercise stimulus range known to modulate adiponectin levels, and 50-60% which is below the minimum exercise threshold to stimulate changes in total adiponectin. Both studies were 12 week training studies that reported no change in body weight or body composition eliminating the possibly that the decreases in total adiponectin concentration were due increased body fat accumulation.

The eccentric component of a muscle contraction is responsible for the majority of mechanical damage through streaming and smearing of the Z-disks (4, 22, 25, 32). c-Jun N-terminal kinase (JNK) is regarded as a critical stress kinase involved in the progression of insulin resistance, chronic inflammation, and T2D and responds to sheer stress, pro-inflammatory cytokines, and stretch (7, 56). Activation of the JNK is related to the degree of injury sustained to the muscle and the greatest effects on JNK are noted after eccentric exercise as opposed to concentric exercise (7). With an increase in active skeletal muscle with concentric exercise, IL-15 is activated allowing for cross talk between skeletal muscle and adipose tissue (3, 80, 93). This increase in active muscle with potentially minor skeletal muscle damage could potentially allow for the increased production of adiponectin through assistance of particular PPARs. JNK has been reported to negatively regulate adiponectin through inhibiting transcriptional activation of PPAR-γ, which is one of the mechanisms that can play a role in stimulating adiponectin production (13, 60). With the degree of skeletal muscle damage being significantly less with concentric exercise, compared to eccentric exercise, the amount of JNK activation could potentially be less with a concentric contractions allowing for a greater accumulation of adiponectin. In addition, the fact that adiponectin concentration

decreased from baseline at 24 h and 48 h post exercise suggests that the eccentric component of dynamic exercise could impair the beneficial health effects along with the possible production of adiponectin that was found with concentric exercise. It can also be speculated, that through chronic resistance training adiponectin concentrations and beneficial effects could be further enhanced due protective adaptations of the muscle (75). With training the contractile stresses placed on the skeletal muscle are distributed among a greater number of muscle fibers due to the improved muscle fiber recruitment through training (20, 75, 99). With an increase in the number of skeletal muscle fibers lead to an increase in IL-15 expression and activation augmenting adiponectin release from adipose tissue (80).

Based off of the finding of the previous investigations, exercise intensity was an essential component in designing a program that could stimulate an increase in total adiponectin concentrations following resistance exercise. Unlike the two studies by Fatorous et al. (28) and Varady et al. (106) that reported significant increases in total adiponectin concentrations with TRE, the current investigation reported no significant change in total adiponectin concentrations 1 h post exercise but reported a significant decrease in total adiponectin from baseline at 24 h and 48 h post exercise. One possibility for this lack of change 1 h post exercise could be due to the time points when total adiponectin was measured. It is probable that the window to measure changes in total adiponectin concentrations following an acute bout of resistance exercise falls within a 24 h window and incorporating an ECC component to exercise might further narrow the time frame to measure changes in total adiponectin. The current investigation exhibited no change in total adiponectin with TRE 1 h post exercise while the studies that

collected samples within the 1 h post exercise time period found significant increases in total adiponectin. In the study by Varady et al. (106) subjects that had a incorporated weight training into their daily workout regimen had significant increases in total adiponectin concentrations from baseline immediately post exercise bout while the sedentary and running only group showed modest increases in total adiponectin concentrations following an acute bout of resistance exercise. This further supports the notion that resistance exercise can induce a stimulus necessary to elicit an increase in total adiponectin concentrations.

High Molecular Weight Adiponectin and Insulin Sensitivity. Exercise is known to increase insulin sensitivity and previous studies have indicated a strong association between total adiponectin and insulin sensitivity (5, 110-111). The current investigation resulted in no significant changes in insulin sensitivity, measured by QUICKI, following an acute bout of ECC, CON, or TRE. Studies have identified HMWA as being a major contributor to improving insulin sensitivity and glucose uptake. HMWA binds more intensely to the adiponectin receptors stimulating the activation of AMPK (42, 59), suggesting a role in increasing insulin sensitivity and preventing T2D through the stimulation of beta oxidation and inhibition of gluconeogenesis (16, 113). The current investigation did not demonstrate a significant correlation between adiponectin and HMWA with QUICKI. This is in contrast to other studies which identified an association of insulin sensitivity to both total adiponectin and HMWA using the hyperinsulinemic-euglycemic clamp technique (61, 65).

Koopman et al. (61) also found that a single bout of whole body resistance exercise improved insulin sensitivity for 24 h. Koopman et al. (61) attributed the increase

in insulin sensitivity to an increase in Glut-4 expression and translocation because of increased AMPK activation. Subjects for the study performed 16 sets (eight sets of leg press and eight sets of leg extension) of 10 repetitions of lower body exercise and nine sets for 10 repetitions of upper body exercise both at intensities 75% of 1RM. The current investigation had subjects perform three sets of 10 repetitions of leg extensions and leg curls at 75% of 1RM. Though the intensity of the Koopman et al. (61) study matched the intensity of the current investigation, the current investigation did not incorporate upper body resistance exercises into the exercise program, or match the Koopman et al. study for total exercise volume. The current investigation failed to demonstrate any significant change in estimated insulin sensitivity. This may be due to the fact that subjects had healthy fasting insulin and glucose levels, suggesting that there was little room for improvement. A more accurate means of assessing insulin sensitivity is through the hyperinsulinemic-euglycemic clamp technique. This may have been more effective in identifying a relationship between adiponectin and HMWA with insulin sensitivity. The euglycemic clamp technique is a much more sensitive measure of change in insulin sensitivity and is now considered to be the gold standard for determining insulin sensitivity (79, 102).

Future Direction. One of the major limitations to the study was that subjects recruited were sedentary with limited experience in resistance exercise. When it comes to strength training, particularly beginners, any strength gains made within the first six to eight weeks have been attributed to neural adaptations (40, 64, 96, 99). Early in training there is not only an improvement in neural activation of motor units but a more efficient synchronization recruitment resulting in increased force production capability (99). It is

likely that due to the lack of resistance exercise experience, subjects could have been exercising below the threshold, in ECC and TRE groups, necessary to elicit a response in adiponectin concentrations because they did not reach a true 1RM.

In the future, a sedentary population should still be recruited but should go through a resistance training regimen for four to six weeks to allow for allowing for neural adaptation to improve performance. Also, since some studies (28, 106) had reported changes in total adiponectin concentration immediately following exercise, it is possible that blood collection 1 h post exercise, particularly following TRE, missed the opportunity to measure changes in total adiponectin concentrations. If this study was to be repeated, blood sampling would occur immediately post exercise (within 15 min) and 1 h post exercise followed by a 24 h and 48 h blood draw. In addition, the same subjects would participate in a four to six week training study to determine if baseline levels of adiponectin can be increased with chronic resistance training. At this point subject would have already achieved neural adaptation and the next phases of training would be increasing muscle hypertrophy and endurance, followed by improving basic strength and power, and followed by another 1RM test session (23).

Conclusion. The current investigation found that the concentric phase of resistance exercise can stimulate an increase in total adiponectin concentrations 1 h post exercise while ECC and TRE had no significant influence on total adiponectin concentrations 1 h post exercise period. However, since total adiponectin levels significantly decreased from baseline 24 h and 48 h post exercise, this may suggest that the eccentric component of resistance exercise could inhibit changes in adiponectin concentrations. The results from the study also indicate that an acute bout of resistance

exercise, regardless of the mode, does not elicit a significant change in HMWA or in insulin sensitivity in these specific populations.

REFERENCE

1. **Adamo KB, Sigal RJ, Williams K, Kenny G, Prud'homme D, and Tesson F**. Influence of Pro12Ala peroxisome proliferator-activated receptor gamma2 polymorphism on glucose response to exercise training in type 2 diabetes. *Diabetologia* 48: 1503-1509, 2005.
2. **Ahmadizad S, Haghighi AH, and Hamedinia MR**. Effects of resistance versus endurance training on serum adiponectin and insulin resistance index. *Eur J Endocrinol* 157: 625-631, 2007.
3. **Almendro V, Fuster G, Busquets S, Ametller E, Figueras M, Argiles JM, and Lopez-Soriano FJ**. Effects of IL-15 on rat brown adipose tissue: uncoupling proteins and PPARs. *Obesity (Silver Spring)* 16: 285-289, 2008.
4. **Balnave CD, and Thompson MW**. Effect of training on eccentric exercise-induced muscle damage. *J Appl Physiol* 75: 1545-1551, 1993.
5. **Berg AH, Combs TP, Du X, Brownlee M, and Scherer PE**. The adipocyte-secreted protein Acrp30 enhances hepatic insulin action. *Nat Med* 7: 947-953, 2001.
6. **Bluher M, Bullen JW, Jr., Lee JH, Kralisch S, Fasshauer M, Kloting N, Niebauer J, Schon MR, Williams CJ, and Mantzoros CS**. Circulating adiponectin and expression of adiponectin receptors in human skeletal muscle: associations with metabolic parameters and insulin resistance and regulation by physical training. *J Clin Endocrinol Metab* 91: 2310-2316, 2006.
7. **Boppart MD, Aronson D, Gibson L, Roubenoff R, Abad LW, Bean J, Goodyear LJ, and Fielding RA**. Eccentric exercise markedly increases c-Jun NH(2)-terminal kinase activity in human skeletal muscle. *J Appl Physiol* 87: 1668-1673, 1999.
8. **Bouassida A, Chamari K, Zaouali M, Feki Y, Zbidi A, and Tabka Z**. Review on leptin and adiponectin responses and adaptations to acute and chronic exercise. *Br J Sports Med* 44: 620-630, 2010.
9. **Brooks N, Layne JE, Gordon PL, Roubenoff R, Nelson ME, and Castaneda-Sceppa C**. Strength training improves muscle quality and insulin sensitivity in Hispanic older adults with type 2 diabetes. *Int J Med Sci* 4: 19-27, 2007.
10. **Bruun JM, Lihn AS, Verdich C, Pedersen SB, Toubro S, Astrup A, and Richelsen B**. Regulation of adiponectin by adipose tissue-derived cytokines: in vivo and in vitro investigations in humans. *Am J Physiol Endocrinol Metab* 285: E527-533, 2003.
11. **Buck JA, Amundsen LR, and Nielsen DH**. Systolic blood pressure responses during isometric contractions of large and small muscle groups. *Med Sci Sports Exerc* 12: 145-147, 1980.
12. **Byrne C, Twist C, and Eston R**. Neuromuscular function after exercise-induced muscle damage: theoretical and applied implications. *Sports Med* 34: 49-69, 2004.
13. **Camp HS, Tafuri SR, and Leff T**. c-Jun N-terminal kinase phosphorylates peroxisome proliferator-activated receptor-gamma1 and negatively regulates its transcriptional activity. *Endocrinology* 140: 392-397, 1999.
14. **CDC**. Fast Stats; Overweight and Obesity http://www.cdc.gov/nchs/fastats/overwt.htm.
15. **Ceddia RB, Somwar R, Maida A, Fang X, Bikopoulos G, and Sweeney G**. Globular adiponectin increases GLUT4 translocation and glucose uptake but reduces glycogen synthesis in rat skeletal muscle cells. *Diabetologia* 48: 132-139, 2005.

16. **Chen H, Montagnani M, Funahashi T, Shimomura I, and Quon MJ**. Adiponectin stimulates production of nitric oxide in vascular endothelial cells. *J Biol Chem* 278: 45021-45026, 2003.
17. **Christiansen T, Paulsen SK, Bruun JM, Pedersen SB, and Richelsen B**. Exercise training versus diet-induced weight-loss on metabolic risk factors and inflammatory markers in obese subjects: a 12-week randomized intervention study. *Am J Physiol Endocrinol Metab* 298: E824-831, 2010.
18. **Church TS, Blair SN, Cocreham S, Johannsen N, Johnson W, Kramer K, Mikus CR, Myers V, Nauta M, Rodarte RQ, Sparks L, Thompson A, and Earnest CP**. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: a randomized controlled trial. *JAMA* 304: 2253-2262, 2010.
19. **Combs TP, Wagner JA, Berger J, Doebber T, Wang WJ, Zhang BB, Tanen M, Berg AH, O'Rahilly S, Savage DB, Chatterjee K, Weiss S, Larson PJ, Gottesdiener KM, Gertz BJ, Charron MJ, Scherer PE, and Moller DE**. Induction of adipocyte complement-related protein of 30 kilodaltons by PPARgamma agonists: a potential mechanism of insulin sensitization. *Endocrinology* 143: 998-1007, 2002.
20. **de Salles BF, Simao R, Fleck SJ, Dias I, Kraemer-Aguiar LG, and Bouskela E**. Effects of resistance training on cytokines. *Int J Sports Med* 31: 441-450, 2010.
21. **Degawa-Yamauchi M, Moss KA, Bovenkerk JE, Shankar SS, Morrison CL, Lelliott CJ, Vidal-Puig A, Jones R, and Considine RV**. Regulation of adiponectin expression in human adipocytes: effects of adiposity, glucocorticoids, and tumor necrosis factor alpha. *Obes Res* 13: 662-669, 2005.
22. **Dolezal BA, Potteiger JA, Jacobsen DJ, and Benedict SH**. Muscle damage and resting metabolic rate after acute resistance exercise with an eccentric overload. *Med Sci Sports Exerc* 32: 1202-1207, 2000.
23. **Earle TRBaRW**. *Essentials of Strength Training and Conditioning. National strength and conditioning association.* Champaign, IL: Human Kinetics, 2008.
24. **Elbatarny HS, Netherton SJ, Ovens JD, Ferguson AV, and Maurice DH**. Adiponectin, ghrelin, and leptin differentially influence human platelet and human vascular endothelial cell functions: implication in obesity-associated cardiovascular diseases. *Eur J Pharmacol* 558: 7-13, 2007.
25. **Evans RK, Knight KL, Draper DO, and Parcell AC**. Effects of warm-up before eccentric exercise on indirect markers of muscle damage. *Med Sci Sports Exerc* 34: 1892-1899, 2002.
26. **Evans WJ, Meredith CN, Cannon JG, Dinarello CA, Frontera WR, Hughes VA, Jones BH, and Knuttgen HG**. Metabolic changes following eccentric exercise in trained and untrained men. *J Appl Physiol* 61: 1864-1868, 1986.
27. **Fargnoli JL, Sun Q, Olenczuk D, Qi L, Zhu Y, Hu FB, and Mantzoros CS**. Resistin is associated with biomarkers of inflammation while total and high-molecular weight adiponectin are associated with biomarkers of inflammation, insulin resistance, and endothelial function. *Eur J Endocrinol* 162: 281-288, 2010.
28. **Fatouros IG, Tournis S, Leontsini D, Jamurtas AZ, Sxina M, Thomakos P, Manousaki M, Douroudos I, Taxildaris K, and Mitrakou A**. Leptin and adiponectin responses in overweight inactive elderly following resistance training and detraining are intensity related. *J Clin Endocrinol Metab* 90: 5970-5977, 2005.

29. **Ferguson MA, White LJ, McCoy S, Kim HW, Petty T, and Wilsey J**. Plasma adiponectin response to acute exercise in healthy subjects. *Eur J Appl Physiol* 91: 324-329, 2004.
30. **Figard H, Gaume V, Mougin F, Demougeot C, and Berthelot A**. Beneficial effects of isometric strength training on endothelial dysfunction in rats. *Appl Physiol Nutr Metab* 31: 621-630, 2006.
31. **Fleck SJ, and Kraemer WJ**. *Designing Resistance Training Programs*. Champagne, IL: Human Kinetics, 2004.
32. **Friden J, and Lieber RL**. Eccentric exercise-induced injuries to contractile and cytoskeletal muscle fibre components. *Acta Physiol Scand* 171: 321-326, 2001.
33. **Fujita S, Rasmussen BB, Cadenas JG, Drummond MJ, Glynn EL, Sattler FR, and Volpi E**. Aerobic exercise overcomes the age-related insulin resistance of muscle protein metabolism by improving endothelial function and Akt/mammalian target of rapamycin signaling. *Diabetes* 56: 1615-1622, 2007.
34. **Giraldo E, Hinchado MD, Garcia JJ, and Ortega E**. Influence of gender and oral contraceptives intake on innate and inflammatory response. Role of neuroendocrine factors. *Mol Cell Biochem* 313: 147-153, 2008.
35. **Gleissner CA, Galkina E, Nadler JL, and Ley K**. Mechanisms by which diabetes increases cardiovascular disease. *Drug Discov Today Dis Mech* 4: 131-140, 2007.
36. **Goldstein BJ, and Scalia R**. Adiponectin: A novel adipokine linking adipocytes and vascular function. *J Clin Endocrinol Metab* 89: 2563-2568, 2004.
37. **Gruber M, Gruber SB, Taube W, Schubert M, Beck SC, and Gollhofer A**. Differential effects of ballistic versus sensorimotor training on rate of force development and neural activation in humans. *J Strength Cond Res* 21: 274-282, 2007.
38. **Haddad F, Adams GR, Bodell PW, and Baldwin KM**. Isometric resistance exercise fails to counteract skeletal muscle atrophy processes during the initial stages of unloading. *J Appl Physiol* 100: 433-441, 2006.
39. **Hajer GR, van Haeften TW, and Visseren FL**. Adipose tissue dysfunction in obesity, diabetes, and vascular diseases. *Eur Heart J* 29: 2959-2971, 2008.
40. **Hakkinen K, Alen M, Kallinen M, Newton RU, and Kraemer WJ**. Neuromuscular adaptation during prolonged strength training, detraining and re-strength-training in middle-aged and elderly people. *Eur J Appl Physiol* 83: 51-62, 2000.
41. **Han SH, Quon MJ, Kim JA, and Koh KK**. Adiponectin and cardiovascular disease: response to therapeutic interventions. *J Am Coll Cardiol* 49: 531-538, 2007.
42. **Hara K, Horikoshi M, Yamauchi T, Yago H, Miyazaki O, Ebinuma H, Imai Y, Nagai R, and Kadowaki T**. Measurement of the high-molecular weight form of adiponectin in plasma is useful for the prediction of insulin resistance and metabolic syndrome. *Diabetes Care* 29: 1357-1362, 2006.
43. **Haskell WL, Lee IM, Pate RR, Powell KE, Blair SN, Franklin BA, Macera CA, Heath GW, Thompson PD, and Bauman A**. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Circulation* 116: 1081-1093, 2007.
44. **Hattori Y, Suzuki M, Hattori S, and Kasai K**. Globular adiponectin upregulates nitric oxide production in vascular endothelial cells. *Diabetologia* 46: 1543-1549, 2003.

45. **Henriksen EJ**. Invited review: Effects of acute exercise and exercise training on insulin resistance. *J Appl Physiol* 93: 788-796, 2002.
46. **Hollander DB, Kraemer RR, Kilpatrick MW, Ramadan ZG, Reeves GV, Francois M, Hebert EP, and Tryniecki JL**. Maximal eccentric and concentric strength discrepancies between young men and women for dynamic resistance exercise. *J Strength Cond Res* 21: 34-40, 2007.
47. **Hortobagyi T, and DeVita P**. Favorable neuromuscular and cardiovascular responses to 7 days of exercise with an eccentric overload in elderly women. *J Gerontol A Biol Sci Med Sci* 55: B401-410, 2000.
48. **Hortobagyi T, and Katch FI**. Role of concentric force in limiting improvement in muscular strength. *J Appl Physiol* 68: 650-658, 1990.
49. **Howlett KF, Sakamoto K, Garnham A, Cameron-Smith D, and Hargreaves M**. Resistance exercise and insulin regulate AS160 and interaction with 14-3-3 in human skeletal muscle. *Diabetes* 56: 1608-1614, 2007.
50. **Hu FB, Stampfer MJ, Solomon C, Liu S, Colditz GA, Speizer FE, Willett WC, and Manson JE**. Physical activity and risk for cardiovascular events in diabetic women. *Ann Intern Med* 134: 96-105, 2001.
51. **Jamurtas AZ, Theocharis V, Koukoulis G, Stakias N, Fatouros IG, Kouretas D, and Koutedakis Y**. The effects of acute exercise on serum adiponectin and resistin levels and their relation to insulin sensitivity in overweight males. *Eur J Appl Physiol* 97: 122-126, 2006.
52. **Jimenez-Jimenez R, Cuevas MJ, Almar M, Lima E, Garcia-Lopez D, De Paz JA, and Gonzalez-Gallego J**. Eccentric training impairs NF-kappaB activation and over-expression of inflammation-related genes induced by acute eccentric exercise in the elderly. *Mech Ageing Dev* 129: 313-321, 2008.
53. **Jurimae J, Purge P, and Jurimae T**. Adiponectin is altered after maximal exercise in highly trained male rowers. *Eur J Appl Physiol* 93: 502-505, 2005.
54. **Kadowaki T, Yamauchi T, Kubota N, Hara K, Ueki K, and Tobe K**. Adiponectin and adiponectin receptors in insulin resistance, diabetes, and the metabolic syndrome. *J Clin Invest* 116: 1784-1792, 2006.
55. **Kanehisa H, Nagareda H, Kawakami Y, Akima H, Masani K, Kouzaki M, and Fukunaga T**. Effects of equivolume isometric training programs comprising medium or high resistance on muscle size and strength. *Eur J Appl Physiol* 87: 112-119, 2002.
56. **Kim KY, Kim JK, Jeon JH, Yoon SR, Choi I, and Yang Y**. c-Jun N-terminal kinase is involved in the suppression of adiponectin expression by TNF-alpha in 3T3-L1 adipocytes. *Biochem Biophys Res Commun* 327: 460-467, 2005.
57. **Kirwan JP, and Jing M**. Modulation of insulin signaling in human skeletal muscle in response to exercise. *Exerc Sport Sci Rev* 30: 85-90, 2002.
58. **Klimcakova E, Polak J, Moro C, Hejnova J, Majercik M, Viguerie N, Berlan M, Langin D, and Stich V**. Dynamic strength training improves insulin sensitivity without altering plasma levels and gene expression of adipokines in subcutaneous adipose tissue in obese men. *J Clin Endocrinol Metab* 91: 5107-5112, 2006.
59. **Kobayashi H, Ouchi N, Kihara S, Walsh K, Kumada M, Abe Y, Funahashi T, and Matsuzawa Y**. Selective suppression of endothelial cell apoptosis by the high molecular weight form of adiponectin. *Circ Res* 94: e27-31, 2004.

60. **Koh EH, Park JY, Park HS, Jeon MJ, Ryu JW, Kim M, Kim SY, Kim MS, Kim SW, Park IS, Youn JH, and Lee KU**. Essential role of mitochondrial function in adiponectin synthesis in adipocytes. *Diabetes* 56: 2973-2981, 2007.
61. **Koopman R, Manders RJ, Zorenc AH, Hul GB, Kuipers H, Keizer HA, and van Loon LJ**. A single session of resistance exercise enhances insulin sensitivity for at least 24 h in healthy men. *Eur J Appl Physiol* 94: 180-187, 2005.
62. **Kraemer RR, Aboudehen KS, Carruth AK, Durand RT, Acevedo EO, Hebert EP, Johnson LG, and Castracane VD**. Adiponectin responses to continuous and progressively intense intermittent exercise. *Med Sci Sports Exerc* 35: 1320-1325, 2003.
63. **Kraemer RR, and Castracane VD**. Exercise and humoral mediators of peripheral energy balance: ghrelin and adiponectin. *Exp Biol Med (Maywood)* 232: 184-194, 2007.
64. **Kraemer WJ, and Ratamess NA**. Fundamentals of resistance training: progression and exercise prescription. *Med Sci Sports Exerc* 36: 674-688, 2004.
65. **Lara-Castro C, Luo N, Wallace P, Klein RL, and Garvey WT**. Adiponectin multimeric complexes and the metabolic syndrome trait cluster. *Diabetes* 55: 249-259, 2006.
66. **Lavender AP, and Nosaka K**. A light load eccentric exercise confers protection against a subsequent bout of more demanding eccentric exercise. *J Sci Med Sport* 11: 291-298, 2008.
67. **Lee CD, Blair SN, and Jackson AS**. Cardiorespiratory fitness, body composition, and all-cause and cardiovascular disease mortality in men. *Am J Clin Nutr* 69: 373-380, 1999.
68. **Ligibel JA, Giobbie-Hurder A, Olenczuk D, Campbell N, Salinardi T, Winer EP, and Mantzoros CS**. Impact of a mixed strength and endurance exercise intervention on levels of adiponectin, high molecular weight adiponectin and leptin in breast cancer survivors. *Cancer Causes Control* 20: 1523-1528, 2009.
69. **Lyon CJ, Law RE, and Hsueh WA**. Minireview: adiposity, inflammation, and atherogenesis. *Endocrinology* 144: 2195-2200, 2003.
70. **Mackey AL, Bojsen-Moller J, Qvortrup K, Langberg H, Suetta C, Kalliokoski KK, Kjaer M, and Magnusson SP**. Evidence of skeletal muscle damage following electrically stimulated isometric muscle contractions in humans. *J Appl Physiol* 105: 1620-1627, 2008.
71. **Maeda S, Tanabe T, Otsuki T, Sugawara J, Ajisaka R, and Matsuda M**. Acute exercise increases systemic arterial compliance after 6-month exercise training in older women. *Hypertens Res* 31: 377-381, 2008.
72. **Maiorana A, O'Driscoll G, Cheetham C, Dembo L, Stanton K, Goodman C, Taylor R, and Green D**. The effect of combined aerobic and resistance exercise training on vascular function in type 2 diabetes. *J Am Coll Cardiol* 38: 860-866, 2001.
73. **Maltais F, LeBlanc P, Simard C, Jobin J, Berube C, Bruneau J, Carrier L, and Belleau R**. Skeletal muscle adaptation to endurance training in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 154: 442-447, 1996.
74. **Mangge H, Almer G, Haj-Yahya S, Grandits N, Gasser R, Pilz S, Moller R, and Horejsi R**. Nuchal thickness of subcutaneous adipose tissue is tightly associated

with an increased LMW/total adiponectin ratio in obese juveniles. *Atherosclerosis* 203: 277-283, 2009.
75. **McHugh MP**. Recent advances in the understanding of the repeated bout effect: the protective effect against muscle damage from a single bout of eccentric exercise. *Scand J Med Sci Sports* 13: 88-97, 2003.
76. **Medicine ACoS**. *ACSM's Guidelines for Exercise Testing and Prescription*. Philidelphia Wolter Kluwer/ Lippincott Williams and WIlkins, 2009.
77. **Montagnani M, Chen H, Barr VA, and Quon MJ**. Insulin-stimulated activation of eNOS is independent of Ca2+ but requires phosphorylation by Akt at Ser(1179). *J Biol Chem* 276: 30392-30398, 2001.
78. **Motoshima H, Wu X, Mahadev K, and Goldstein BJ**. Adiponectin suppresses proliferation and superoxide generation and enhances eNOS activity in endothelial cells treated with oxidized LDL. *Biochem Biophys Res Commun* 315: 264-271, 2004.
79. **Nerpin E, Riserus U, Ingelsson E, Sundstrom J, Jobs M, Larsson A, Basu S, and Arnlov J**. Insulin sensitivity measured with euglycemic clamp is independently associated with glomerular filtration rate in a community-based cohort. *Diabetes Care* 31: 1550-1555, 2008.
80. **Nielsen AR, Mounier R, Plomgaard P, Mortensen OH, Penkowa M, Speerschneider T, Pilegaard H, and Pedersen BK**. Expression of interleukin-15 in human skeletal muscle effect of exercise and muscle fibre type composition. *J Physiol* 584: 305-312, 2007.
81. **Nieman DC, Dumke CL, Henson DA, McAnulty SR, Gross SJ, and Lind RH**. Muscle damage is linked to cytokine changes following a 160-km race. *Brain Behav Immun* 19: 398-403, 2005.
82. **Nishida M, Funahashi T, and Shimomura I**. Pathophysiological significance of adiponectin. *Med Mol Morphol* 40: 55-67, 2007.
83. **O'Leary VB, Jorett AE, Marchetti CM, Gonzalez F, Phillips SA, Ciaraldi TP, and Kirwan JP**. Enhanced adiponectin multimer ratio and skeletal muscle adiponectin receptor expression following exercise training and diet in older insulin-resistant adults. *Am J Physiol Endocrinol Metab* 293: E421-427, 2007.
84. **Oberbach A, Tonjes A, Kloting N, Fasshauer M, Kratzsch J, Busse MW, Paschke R, Stumvoll M, and Bluher M**. Effect of a 4 week physical training program on plasma concentrations of inflammatory markers in patients with abnormal glucose tolerance. *Eur J Endocrinol* 154: 577-585, 2006.
85. **Okamoto T, Masuhara M, and Ikuta K**. Cardiovascular responses induced during high-intensity eccentric and concentric isokinetic muscle contraction in healthy young adults. *Clin Physiol Funct Imaging* 26: 39-44, 2006.
86. **Olson TP, Dengel DR, Leon AS, and Schmitz KH**. Changes in inflammatory biomarkers following one-year of moderate resistance training in overweight women. *Int J Obes (Lond)* 31: 996-1003, 2007.
87. **Ouchi N, Kihara S, Arita Y, Maeda K, Kuriyama H, Okamoto Y, Hotta K, Nishida M, Takahashi M, Nakamura T, Yamashita S, Funahashi T, and Matsuzawa Y**. Novel modulator for endothelial adhesion molecules: adipocyte-derived plasma protein adiponectin. *Circulation* 100: 2473-2476, 1999.
88. **Ouchi N, Kihara S, Arita Y, Okamoto Y, Maeda K, Kuriyama H, Hotta K, Nishida M, Takahashi M, Muraguchi M, Ohmoto Y, Nakamura T, Yamashita S,**

Funahashi T, and Matsuzawa Y. Adiponectin, an adipocyte-derived plasma protein, inhibits endothelial NF-kappaB signaling through a cAMP-dependent pathway. *Circulation* 102: 1296-1301, 2000.
89. **Ouchi N, and Walsh K**. Adiponectin as an anti-inflammatory factor. *Clin Chim Acta* 380: 24-30, 2007.
90. **Overend TJ, Versteegh TH, Thompson E, Birmingham TB, and Vandervoort AA**. Cardiovascular stress associated with concentric and eccentric isokinetic exercise in young and older adults. *J Gerontol A Biol Sci Med Sci* 55: B177-182, 2000.
91. **Pedersen BK, Akerstrom TC, Nielsen AR, and Fischer CP**. Role of myokines in exercise and metabolism. *J Appl Physiol* 103: 1093-1098, 2007.
92. **Pollock ML, Franklin BA, Balady GJ, Chaitman BL, Fleg JL, Fletcher B, Limacher M, Pina IL, Stein RA, Williams M, and Bazzarre T**. AHA Science Advisory. Resistance exercise in individuals with and without cardiovascular disease: benefits, rationale, safety, and prescription: An advisory from the Committee on Exercise, Rehabilitation, and Prevention, Council on Clinical Cardiology, American Heart Association; Position paper endorsed by the American College of Sports Medicine. *Circulation* 101: 828-833, 2000.
93. **Quinn LS, Strait-Bodey L, Anderson BG, Argiles JM, and Havel PJ**. Interleukin-15 stimulates adiponectin secretion by 3T3-L1 adipocytes: evidence for a skeletal muscle-to-fat signaling pathway. *Cell Biol Int* 29: 449-457, 2005.
94. **Ryschon TW, Fowler MD, Wysong RE, Anthony A, and Balaban RS**. Efficiency of human skeletal muscle in vivo: comparison of isometric, concentric, and eccentric muscle action. *J Appl Physiol* 83: 867-874, 1997.
95. **Sakamoto A, Maruyama T, Naito H, and Sinclair PJ**. Effects of exhaustive dumbbell exercise after isokinetic eccentric damage: recovery of static and dynamic muscle performance. *J Strength Cond Res* 23: 2467-2476, 2009.
96. **Sale DG**. Neural adaptation to resistance training. *Med Sci Sports Exerc* 20: S135-145, 1988.
97. **Schulze MB, Shai I, Rimm EB, Li T, Rifai N, and Hu FB**. Adiponectin and future coronary heart disease events among men with type 2 diabetes. *Diabetes* 54: 534-539, 2005.
98. **Shetty S, Kusminski CM, and Scherer PE**. Adiponectin in health and disease: evaluation of adiponectin-targeted drug development strategies. *Trends Pharmacol Sci* 30: 234-239, 2009.
99. **Staron RS, Karapondo DL, Kraemer WJ, Fry AC, Gordon SE, Falkel JE, Hagerman FC, and Hikida RS**. Skeletal muscle adaptations during early phase of heavy-resistance training in men and women. *J Appl Physiol* 76: 1247-1255, 1994.
100. **Stupka N, Lowther S, Chorneyko K, Bourgeois JM, Hogben C, and Tarnopolsky MA**. Gender differences in muscle inflammation after eccentric exercise. *J Appl Physiol* 89: 2325-2332, 2000.
101. **Stupka N, Tarnopolsky MA, Yardley NJ, and Phillips SM**. Cellular adaptation to repeated eccentric exercise-induced muscle damage. *J Appl Physiol* 91: 1669-1678, 2001.
102. **Suraamornkul S, Kwancharoen R, Ovartlarnporn M, Rawdaree P, and Bajaj M**. Insulin clamp-derived measurements of insulin sensitivity and insulin secretion

in lean and obese asian type 2 diabetic patients. *Metab Syndr Relat Disord* 8: 113-118, 2010.
103. **Trujillo ME, and Scherer PE**. Adiponectin--journey from an adipocyte secretory protein to biomarker of the metabolic syndrome. *J Intern Med* 257: 167-175, 2005.
104. **Tsuchida A, Yamauchi T, Takekawa S, Hada Y, Ito Y, Maki T, and Kadowaki T**. Peroxisome proliferator-activated receptor (PPAR)alpha activation increases adiponectin receptors and reduces obesity-related inflammation in adipose tissue: comparison of activation of PPARalpha, PPARgamma, and their combination. *Diabetes* 54: 3358-3370, 2005.
105. **Van Gaal LF, Mertens IL, and De Block CE**. Mechanisms linking obesity with cardiovascular disease. *Nature* 444: 875-880, 2006.
106. **Varady KA, Bhutani S, Church EC, and Phillips SA**. Adipokine responses to acute resistance exercise in trained and untrained men. *Med Sci Sports Exerc* 42: 456-462, 2010.
107. **Warner SO**. The effects of concentric and eccentric resistance exercise on metabolic health. In: *Exercise Physiology*. Columbia University of Missouri, 2010.
108. **Wilkinson SB, Phillips SM, Atherton PJ, Patel R, Yarasheski KE, Tarnopolsky MA, and Rennie MJ**. Differential effects of resistance and endurance exercise in the fed state on signalling molecule phosphorylation and protein synthesis in human muscle. *J Physiol* 586: 3701-3717, 2008.
109. **Winder WW, and Hardie DG**. AMP-activated protein kinase, a metabolic master switch: possible roles in type 2 diabetes. *Am J Physiol* 277: E1-10, 1999.
110. **Wu X, Motoshima H, Mahadev K, Stalker TJ, Scalia R, and Goldstein BJ**. Involvement of AMP-activated protein kinase in glucose uptake stimulated by the globular domain of adiponectin in primary rat adipocytes. *Diabetes* 52: 1355-1363, 2003.
111. **Yamauchi T, Kamon J, Minokoshi Y, Ito Y, Waki H, Uchida S, Yamashita S, Noda M, Kita S, Ueki K, Eto K, Akanuma Y, Froguel P, Foufelle F, Ferre P, Carling D, Kimura S, Nagai R, Kahn BB, and Kadowaki T**. Adiponectin stimulates glucose utilization and fatty-acid oxidation by activating AMP-activated protein kinase. *Nat Med* 8: 1288-1295, 2002.
112. **Yamauchi T, Kamon J, Waki H, Terauchi Y, Kubota N, Hara K, Mori Y, Ide T, Murakami K, Tsuboyama-Kasaoka N, Ezaki O, Akanuma Y, Gavrilova O, Vinson C, Reitman ML, Kagechika H, Shudo K, Yoda M, Nakano Y, Tobe K, Nagai R, Kimura S, Tomita M, Froguel P, and Kadowaki T**. The fat-derived hormone adiponectin reverses insulin resistance associated with both lipoatrophy and obesity. *Nat Med* 7: 941-946, 2001.
113. **Yamauchi T, Nio Y, Maki T, Kobayashi M, Takazawa T, Iwabu M, Okada-Iwabu M, Kawamoto S, Kubota N, Kubota T, Ito Y, Kamon J, Tsuchida A, Kumagai K, Kozono H, Hada Y, Ogata H, Tokuyama K, Tsunoda M, Ide T, Murakami K, Awazawa M, Takamoto I, Froguel P, Hara K, Tobe K, Nagai R, Ueki K, and Kadowaki T**. Targeted disruption of AdipoR1 and AdipoR2 causes abrogation of adiponectin binding and metabolic actions. *Nat Med* 13: 332-339, 2007.
114. **You T, and Nicklas BJ**. Effects of exercise on adipokines and the metabolic syndrome. *Curr Diab Rep* 8: 7-11, 2008.

Appendix A:
Extended Literature Review

Adiponectin and Cardiovascular Disease

CARDIOVASCULAR DISEASE PREVELANCE

Cardiovascular disease (CVD) is the leading cause of death and disability among men and women in nearly all nations (52). There are an estimated 17 million people worldwide at risk for CVD (28, 34) and in the U.S. alone over 700,000 people have died as a result of some form cardiovascular event (34, 64). Individuals that are overweight are at increased risk of developing CVD due to the increased prevalence of diabetes (24). Nearly three quarters of the diabetic population develop CVD and die from cardiovascular complications (32). The American Heart Association (AHA) has determined that obesity is a major risk factor for CVD (18) and more than 1 billion of those at risk for CVD are already overweight or obese. By the year 2015, it is predicted that the number of overweight and obese individuals in the world will increase to ~2.3 billion which means the CVD mortality rate will also increase (15).

The increased prevalence of obesity is a direct result of a less active lifestyle along with a diet high in fat, sugar, and foods that are more energy dense (58). Based on reports from the AHA, more than 2,220 Americans died of CVD each day in 2007 and over the course of a year 150,000 Americans that died as a result of CVD were under the age of 65 yr. Atherosclerosis accounts for more than 600,000 deaths in the United States due to myocardial infarction and stroke (65). Unfortunately this unhealthy lifestyle is becoming more prevalent in younger generations, especially in the United States. It has been found that children who are obese are more likely to become obese as adults thus enhancing the rate of health related morbidities and mortality in the future. In the past three decades, the prevalence of obesity has nearly tripled for children 2 to 5 yr and youth 12 to 19 yr, and has nearly quadrupled for children six to 11 yr (16). During the 1980's

and 1990's the prevalence of obesity among U.S. adults increased by nearly 50%; now nearly 70% of adults are classified as either overweight or obese (40). From 1997 to 2007 the number of cardiovascular operations and procedures increased by 27% with an estimated cost of $286 billion (64).

An excess of adipose tissue has been found to disrupt homeostasis in the human body by altering hormones and adipokines circulating throughout the vasculature. There is no one mechanism that is responsible for the development of CVD, however, it has been theorized that a disruption in the circulating adipokine, adiponectin, can exacerbate the development of diabetes eventually leading to the development of CVD.

ADIPONECTIN

At one time adipose tissue was identified as only a major energy storage site, but recently it has been classified as a large endocrine gland that takes part in regulating a multitude of biological functions (10, 17, 47). Adipose tissue releases a large number of bioactive mediators that influence not only body weight homeostasis but also insulin resistance as well as alterations in lipids, blood pressure, and inflammation, leading to endothelial dysfunction and atherosclerosis (3, 14, 19). These factors include secretion of free fatty acids (FFAs), tumor necrosis factor-α (TNF- α), plasminogen activator inhibitor type 1 (PAI-1), interleukins (ILs), resistin, and leptin and have implications in the development of CVD (33, 58, 61). However from adipose tissue comes a protein that has been found to enhance insulin sensitivity and protect against CVD when adiposity is maintained at healthy levels (17, 27, 45).

Adiponectin, recognized as a adipocyte-derived cytokine, is the most abundant gene product in adipose tissue (8). Structurally, adiponectin is related to the complement

1q family and contains a carboxyl-terminal globular domain and an amino-terminal collagenous domain which a member of a soluble collagen super-family (23). The 244-amino-acid protein (adiponectin) shows structural similarities with collagen VIII and X, known to form characteristic multimers and TNF-α suggesting an evolutionary link between the TNF-α family and adiponectin (23, 74).

Adiponectin exists in a range of multimer complexes in plasma and combines through the collagen domain to create 3 different oligomeric forms of adiponectin: a low molecular weight (LMWA) trimmer, a middle molecular weight (MMA) hexamer, and a high molecular weight (HMWA) dodecamer (33, 74). Many studies have demonstrated that adiponectin is abundant in circulation (9, 21, 79); a study by Arita et al. (5) demonstrated that adiponectin accounts for approximately 0.01% of total plasma when measuring plasma levels in the microgram per ml range. In contrast to other adipokines, adiponectin concentrations were found to be decreased in obese individuals along with a strong association with an increased risk of CVD in those same individuals (2, 6, 79).

Influence of high molecular weight adiponectin. Research has been studying the metabolic significance of total adiponectin, but the focus has started to shift towards one of the other multimeric forms of adiponectin. HMWA has been identified as the more biologically active form of the three adiponectin isoforms and is a preferred predictor for the metabolic syndrome (9, 41, 67). HMWA binds more intensely to the adiponectin receptors stimulating the activation of AMPK (29, 37), suggesting a more relevant role in increasing insulin sensitivity and diabetes prevention through the stimulation of beta-oxidation and inhibition of gluconeogenesis (12, 84).

A study by Lara-Castro et al. (39) identified HMWA concentrations, along with total adiponectin concentrations, were highly correlated with multiple traits within the metabolic syndrome and found reduced levels of HMWA were strongly associated with a high body fat percentage and insulin resistance similar to that of total adiponectin. Pajvani et al. (63) showed that injection of HMW adiponectin reduced plasma glucose levels and that an increase in the proportion of HMW adiponectin correlated with improved hepatic insulin sensitivity (79). This inverse relation that exists between HMWA and insulin could potentially be one of the many mechanism linked to the development of CVD (51). However, some studies revealed that the HMW isoforms alone might not be a strong enough indicator for CVD. Tsutamoto et al. (77) studied the prognostic role of HMWA along with total adiponectin and identified that total adiponectin was a more useful tool for assessing mortality risk. There is still a great deal of research that is needed to better understand the mechanistic effects of HMWA on factors that influence CVD such as inflammatory markers and receptor interaction.

Correlation between adiposity and adiponectin. Secretion of adiponectin, produced exclusively from mature adipocytes, is influenced by changes in adipose tissue mass (27, 74). Adiponectin contributes to the homeostatic control of glucose, lipid, energy metabolism, and anti-inflammatory activity (13, 22, 39). To demonstrate the importance of adiponectin, Yamauchi et al. (83) treated mice with an inhibitor of peroxisome proliferator-activated (PPAR)-γ/retinoide-X receptor (RWR) to deplete mice of white adipose tissue (WAT). Over four weeks WAT disappeared and adiponectin levels were completely absent from sera of these lipoatrophic mice. A loss of adiponectin was associated with an increase in free fatty-acids (FFA) in serum, increased

triglyceride content in skeletal muscle and liver, along with hyperinsulinemia and hyperglycemia (83). A study by Berg et al. (7) found that after injecting purified adiponectin into *ob/ob* mice and non-obese diabetic mice, adiponectin levels rose over a period of two to four hours followed by a drop in serum glucose to near normal levels. The insulin-sensitizing effects appeared to be mediated by the inhibition of gluconeogenesis and the stimulation of fatty acid oxidation (7, 81, 84) via the activation of AMP-activated protein kinase (AMPK) (81) and PPAR-α (82). Adiponectin has not only been shown to enhance insulin sensitivity in muscle and liver through the stimulation of fatty acid oxidation but also exerts various anti-inflammatory and antiatherogenic effects suggesting adiponectin to be a key metabolic regulator of factors linked to CVD development (33, 39, 45).

AMPK is a critical metabolic regulator that promotes glucose uptake and fatty acid oxidation and is activated through muscle contraction or stresses, such as hypoxia and starvation (53). Studies have shown that activation of AMPK is integral to the signaling effects of adiponectin on insulin sensitivity (80-81). With AMPK activation in the liver there is a down regulation of G6P and PEPCK inhibiting the gluconeogenic pathway preventing further release of glucose into circulation (53). Yamauchi et al. (81) found that when administering adiponectin to liver and to skeletal muscle in vivo and in vitro there was an increase in glucose uptake due to the increased activation of AMPK. This suggests that replenishment of adiponectin can be used as a form of therapeutic treatment for patients with metabolic syndrome or that are diagnosed as hypertensive, pre-diabetic, T2D, or CVD.

Adiponectin receptors. Adiponectin multimers mediate both in unison and independently signal transduction pathways through two integral membrane proteins. Adiponectin receptors, AdipoR1 and AdipoR2, act as receptors for both globular and full length adiponectin and are expressed in pancreatic β-cells, macrophages, and atherosclerotic lesions (27). AdipoR1 is abundantly expressed in skeletal muscle whereas the majority of AdipoR2 is expressed in the liver (3, 84) with some present in skeletal muscle (54). Just like adiponectin, adiponectin receptors are inversely correlated with adiposity (84). A reduced expression of adiponectin receptors within skeletal muscle can lead to a reduction in adiponectin sensitivity and increased insulin resistance (54, 76) suggesting that insulin levels influence not only changes in adiponectin concentration but also adiponectin receptor expressions. Tsuchida et al. (76) tested the hypothesis that insulin can negatively regulate expression levels of AdipoR1 and AdipoR2. Mice given streptozotocin (STZ), which induces insulin deficiencies through the destruction of pancreatic β-cells (24), had reduced levels of insulin while simultaneously increasing AdipoR1 and AdipoR2 mRNA expression. When insulin was replenished and administration of STZ had stopped, AdipoR1 and AdipoR2 mRNA expression decreased indicating an inverse relationship between insulin and adiponectin receptors.

The binding of adiponectin to specific adiponectin receptors gives adiponectin its insulin sensitizing effects. When adiponectin binds to AdipoR1 and AdipoR2 this will stimulate AMPK and PPAR–α in addition to fatty acid oxidation and glucose uptake (34). Yamauchi et al. (84) used AdipoR1 -/- and AdipoR2 -/- mice for administration of an adenovirus that would restore AdipoR1 or AdipoR2 to mice. Disruption of either AdipoR1 or AdipoR2 resulted in insulin resistance and glucose intolerance. Upon

administration of adenovirus AdipoR1 to AdipoR1 -/- mice showed improved activation of AMPK pathway regulating the inhibition of gluconeogenesis by reducing expression of glucose-6-phosphatase (G6P) and phosphoenolpyruvate carboxykinase (PEPCK)-1 improving diabetes in the mice (84). Adenovirus-mediated over expression of AdipoR2 in AdipoR2 -/- significantly increased glucose uptake via increased expression of PPAR-α pathway leading not only to an improvement in insulin resistance but a reduction in oxidative stress, associated with the development of CVD (11, 84). The activation of both AMPK and PPAR-α can lead to increased fatty acid oxidation and a reduction in tissue triglyceride content indicating that both receptors have an integral role in improving insulin resistance and reducing CVD risk (35, 42, 70).

CORRELATION BETWEEN ADIPONECTIN AND TYPE 2 DIABETES

Both total adiponectin and HMWA can be manipulated by conditions of metabolic stress and by hormones involved in the regulation of metabolic functions (26, 29, 76, 79). Elevated levels of insulin have been found to have a major impact on HMWA and total adiponectin concentrations. A study by Weyer et al. (79) not only identified low levels of adiponectin concentration were associated with obesity and T2D but total adiponectin concentration were associated more with insulin sensitivity rather than glycemia.

Hyperglycemia is the common end stage form of diabetes, which may account for macrovascular complications (atherosclerosis) (24, 71). A strong association has been identified with the onset of cardiovascular risk factors and a reduction in insulin sensitivity in metabolically responsive tissue. A meta-analysis revealed that a treatment

designed to improve glycemic control reduced the incidence of macrovascular events in diabetic patients (73).

In addition, hyperglycemia induces monocyte adhesion to the endothelium through the activation of protein kinase C (PKC) which leads to the activation of advanced glycation end products (AGE) known to stimulate macrophage activity and increase cytokine expression (24, 32). Binding of extra/intra cellular proteins to AGE receptors leads to the translocation of nuclear factor kappa-β (NF-κβ) to the nucleus and increased transcription of adhesion molecules and pro-inflammatory factors, such as IL-6 and TNF-α (24). Since adiponectin has been found to enhance insulin sensitivity, maintaining normal levels (~5-30 ng/ml) of adiponectin should sustain a constant homeostatic removal of glucose as a result of insulin function, dramatically reducing atherosclerotic lesion development

ATHEROSCLEROSIS AND ADIPONECTIN

Atherosclerotic lesions are influenced by the interplay between metabolic abnormalities, hemodynamic factors and local inflammation and are the result of chronic inflammatory conditions of the large arteries suffering from endothelial dysfunction (26). An excess in adipose tissue, accompanied with obesity and T2D, plays a pivotal role in the development of atherosclerosis. At the early stages of atherosclerosis, endothelial cell activation by various inflammatory stimuli results in the synthesis of adhesion molecules and increases the adherence of monocytes crucial for the development of vascular disease (58).

Atherosclerosis, stemming from a collection of inter-related pro-atherogenic mechanisms (43, 47), is a symmetric focal thickening of the innermost layer of the artery resulting from an accumulation of fatty material such as cholesterols (28). Circulating monoyctes attach to injured endothelial cells through adhesion molecules and invade the sub-intimal space; these same cytokines secrete various other cytokines that promote proliferation of the smooth muscle cells (34). The inflammatory response occurring in the arterial walls is due to the accumulation of macrophages or monocytes, promoted by low density lipoproteins (LDL) (44). An over accumulation of macrophages can lead to the development of more complex lesions promoting an exorbitant accumulation of inflammatory cells (44).

Adiponectin has been shown to have inhibitory effects on all molecular mechanism linked to the development of atherosclerosis. Adiponectin has the ability to inhibit monocyte adhesion molecules and oxidized-LDL (Ox-LDL) uptake by macrophage through the down-regulation of scavenger receptor-A (SR-A), acetyl-coenzyme A (acetyl-CoA) and acytl-transferase-1 (ACT-1) expression (59). With a reduction in circulating adiponectin levels the atherogenic risk is increased. Cytokines, like TNF- α, mediate the formation and accumulation of adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1) and vascular adhesion molecule-1 (VCAM-1) essential in the development of atherosclerosis (19, 78). Adiponectin acts as an endogenous regulator of endothelial cells in response to inflammation (58, 62). Studies have reported that adiponectin treatments can reduce TNF-α stimulated expression of adhesion molecules along with suppressing TNF- α secretion from macrophages and

foam cells thereby reducing the risk of adhesion molecules invading the subintimal space (36, 58).

SR-A plays a pivotal role in foam cell formation from macrophages by mediating the uptake of modified LDL (56). By treating macrophages with physiological concentrations of adiponectin (30 μg/mL), lipid content within macrophages can be suppressed along with a reduction in SR-A proteins (59) signifying that adiponectin can prevent the macrophage-foam cell transformation thereby reducing the uptake of cholesterol (LDL) into the endothelium reducing lesion formation. By reducing circulating cholesterol adiponectin may prove to be a beneficial form of treatment or prevention of atherosclerosis.

Suppression of cholesterol and triglycerides. In the early stages of atherosclerosis, circulating monocytes bind to the injured endothelial wall and differentiate into macrophages. The monocyte transforms into a macrophage through the uptake of oxidized-LDL (Ox-LDL) via SR-A (43, 56, 78). Research has shown that with obesity, macrophage cells can constitute roughly 40% of the cell population within an adipose tissue depot (43). These same macrophages are capable of secreting a variety of inflammatory cytokines associated with atherogenesis (53). A study by Hulthe et al. (31) found that Ox-LDLs along with circulating LDLs were associated with increased levels of CRP and TNF-α, which was associated with the development of atherosclerotic lesions.

Correlation between HDL and adiponectin. An adverse lipid profile is just one of many factors that can contribute to the development of atherosclerosis. HDL is essential in the removal of excess cholesterol from the atheroma/endothelium by

transporting cholesterol back to the liver through the reverse cholesterol transport (RCT) system (48, 75). A study by Tsubakio-Yamamoto et al. (75) found that adiponectin not only impacted RCT system but may have the ability to accelerate the RCT system and protect against atherosclerosis (48, 56). Adiponectin was able to influence the expression of ATP-binding cassette transporter (ABC) -A1, ABC-G1, and the SR-BI known to be the rate limiting factors in HDL generation (48, 75). With a positive shift in the lipid profile as a result of adiponectin treatment further supports literature about the anti-atherogenic effects of adiponectin (39).

Studies have revealed that patients with hypoadiponectinemia had an increased prevalence of coronary artery disease (CAD) due to a reduction in circulating HDL (13, 38, 79). A study by Oku et al. (57) found that in adiponectin-KO mice ABCA1 expression was reduced along with apoA-I suggesting that low levels of adiponectin may suppress HDL assembly. Adiponectin is able to reduce hepatic lipase activity increasing HDL assembly; however, with low concentrations of circulating adiponectin hepatic lipase activity can increase allowing for an abundance of LDL cholesterol to accumulate and be taken up by the macrophage into the endothelium (48, 66). Lara-Castro et al.(39) and Cnop et al. (14) both found that higher levels of total adiponectin and HMWA were strongly correlated with higher levels of large HDL particles and particle size along with a reduction in very low density lipoprotein (VLDL) particle and small dense LDL particle number. Though studies have revealed a positive correlation between adiponectin and HDL does exist, adiponectin's anti-atherogenic properties might stem from its influence on the rate of cholesterol clearance (28, 48, 85).

TNF- α and adiponectin. Research has also concluded that adiponectin plays an important role in maintaining endothelial homeostasis through the inhibition of specific inflammatory cytokines (25, 69). A key inflammatory marker linked to atherosclerotic plaque development is TNF-α. Through the activation of nuclear factor kappa-β (NF-κβ), TNF-α has the potential to induce a series of inflammatory changes in vascular tissue, such as increased expression of adhesion molecules, on the endothelial surface (45). Ouchi et al. (58) demonstrated that adiponectin concentrations had inhibitory effects on TNF-α-induced monocyte adhesion molecule expression in endothelial cells. In patients suffering from CAD, adiponectin concentrations were significantly lower in comparison to the healthy control subjects. This suggests that adiponectin levels may be related to the development of CAD.

It has been shown that adiponectin and TNF-α inhibit one another's expression and production in adipocytes and actions in target organs (68). Hypoadiponectimia has been associated with an increased risk of monocyte adhesion to the endothelium as a result of increased expression of TNF- α (13, 33, 62). NF- κβ is known to play a critical role in regulating inflammatory action occurring in various types of cells (3, 58, 60). Through the activation of TNF-α, NF- κβ is involved in the transcriptional regulation of VCAM-1, endothelial leukocyte adhesion molecule-1 (E-selectin) and ICAM-1 which are essential in formation of atherosclerotic lesions (33). With administration of adiponectin, studies have shown there to be a decrease in adhesion molecules through the suppression of TNF-α activation. Ouchi et al. (60) found that adiponectin treatment decreased the amount of DNA-binding complex induced by TNF-α stimulation indicating that adiponectin suppressed TNF-α induced NF-κβ activation. This decreased NF-κβ

activation was the result of the inhibitory effects of adiponectin mediated through the activation of cAMP-protein kinase A pathway (PKA) (46, 60). This indicates that adiponectin acts as an endogenous modulator by acting as an anti-inflammatory factor for atherosclerosis (60).

ENDOTHELIAL DYSFUNCTION

The AHA has determined that obesity is a major risk factor for CAD (18). Vascular dysfunction plays a vital role in the pathogenesis of atherosclerosis. In obese and diabetic populations the risk of endothelial dysfunction is significant (72). Excess adiposity is associated with a reduction in adiponectin concentrations and this excess in adiposity disrupts the hormone and cytokine balance necessary to maintain normal endothelial function. It is evident that with obesity comes a significant reduction in the adiponectin concentration and this has been shown be negatively associated with T2D and obesity which, as a result, leads to endothelial dysfunction (20, 27, 45, 62).

Endothelial dysfunction is characterized by impaired nitric oxide (NO) release from the endothelium and decreased blood flow to insulin targeted tissue (27, 50, 62). It has been shown that adiponectin mimics the vascular and metabolic actions of insulin which stimulates endothelial production of nitric oxide, causing vasodilation, increased blood flow (12) and angiogenesis (62). Studies have shown that adiponectin will activate AMPK (60) within the endothelial cell which will in turn stimulate NO production through the activation of eNOS (49). Morrow et al. (49) found that stressors that stimulate AMPK activation lead to the production of NO improving endothelial function.

An impairment in NO production contributes to the development of hypertension, increased expression of adhesion molecules, and other inflammatory markers (25) essential in the development of atherosclerosis. The ability of adiponectin to stimulate AMPK activation suggests that adiponectin plays a crucial role in the regulation of endothelial function.

Impact of adiponectin on hypertension. Plasma levels of adiponectin have been consistently reported to be negatively correlated with BMI, waist circumference, body fat, plasma glucose, insulin, and triglycerides. It is possible that adiponectin may be involved with the progression of hypertension (30). A study by Ohashi et al. (55) reported that adiponectin deficient mice displayed significantly higher systolic blood pressures compared to wild type mice consuming a high salt diet. The adiponectin deficient mice had reduced levels of mRNA eNOS but upon re-administration of adiponectin to adiponectin deficient mice, blood pressures returned to normal resting values. This was attributed to the ability of adiponectin to reverse the reduced mRNA levels of eNOS.

In clinical studies, the association between adiponectin and hypertension is also evident with hypoadiponectimia being a major risk factor for hypertension, independent of insulin resistance and diabetes. A study by Adamczak et al. (1) evaluated the role of adiponectin in 33 overweight essential hypertensive patients (EHP) and 33 overweight normotensive healthy patients (NHP). Adiponectin concentrations were significantly lower in EHP compare to NHP along with mean arterial pressure being significantly higher in EHP. Adamczak et al. (1) suggest that the low adiponectin concentration in the

EHP allowed there to be an increased deposition of triglycerides in the injured arterial wall elevating blood pressure.

A study by Araki et al. (4) investigated pharmaceutical effects insulin sensitizers on arterial stiffness. The study reported that after six months of treatment arterial stiffness in T2D improved and was significantly associated with changes in plasma adiponectin levels. Subjects took either pioglitazone or metformin with both drugs increasing circulating levels of adiponectin. Araki et al. (4) hypothesized that the two mechanisms responsible for the improvement in arterial stiffness were through the ability of adiponectin to decrease insulin resistance and the ability to inhibit expression of endothelial adhesion molecules in endothelial cells. These studies (1, 4, 55) further support the notion of the anti-atherogenic effects of adiponectin occurring through its ability to regulate normal physiological functions within the vasculature.

Summary. An accumulation of excess adipose tissue has been linked to increased morbidity and mortality rates in the human populations. Adiponectin has been found to be inversely correlated with adipose tissue mass and appears that low levels of adiponectin can play a causal role in the development of insulin resistance, T2D, and CVD, all of which are associated with obesity. The maintenance or reduction of body fat and incorporation of exercise into lifestyle can dramatically reduce the risk of disease by reversing low levels of circulating adiponectin further contributing to the maintenance of normal biological functions.

References

1. **Adamczak M, Wiecek A, Funahashi T, Chudek J, Kokot F, and Matsuzawa Y**. Decreased plasma adiponectin concentration in patients with essential hypertension. *Am J Hypertens* 16: 72-75, 2003.
2. **Almeda-Valdes P, Cuevas-Ramos D, Mehta R, Gomez-Perez FJ, Cruz-Bautista I, Arellano-Campos O, Navarrete-Lopez M, and Aguilar-Salinas CA**. Total and high molecular weight adiponectin have similar utility for the identification of insulin resistance. *Cardiovasc Diabetol* 9: 26, 2010.
3. **Antoniades C, Antonopoulos AS, Tousoulis D, and Stefanadis C**. Adiponectin: from obesity to cardiovascular disease. *Obes Rev* 10: 269-279, 2009.
4. **Araki T, Emoto M, Teramura M, Yokoyama H, Mori K, Hatsuda S, Maeno T, Shinohara K, Koyama H, Shoji T, Inaba M, and Nishizawa Y**. Effect of adiponectin on carotid arterial stiffness in type 2 diabetic patients treated with pioglitazone and metformin. *Metabolism* 55: 996-1001, 2006.
5. **Arita Y, Kihara S, Ouchi N, Takahashi M, Maeda K, Miyagawa J, Hotta K, Shimomura I, Nakamura T, Miyaoka K, Kuriyama H, Nishida M, Yamashita S, Okubo K, Matsubara K, Muraguchi M, Ohmoto Y, Funahashi T, and Matsuzawa Y**. Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. *Biochem Biophys Res Commun* 257: 79-83, 1999.
6. **Aso Y, Yamamoto R, Wakabayashi S, Uchida T, Takayanagi K, Takebayashi K, Okuno T, Inoue T, Node K, Tobe T, Inukai T, and Nakano Y**. Comparison of serum high-molecular weight (HMW) adiponectin with total adiponectin concentrations in type 2 diabetic patients with coronary artery disease using a novel enzyme-linked immunosorbent assay to detect HMW adiponectin. *Diabetes* 55: 1954-1960, 2006.
7. **Berg AH, Combs TP, Du X, Brownlee M, and Scherer PE**. The adipocyte-secreted protein Acrp30 enhances hepatic insulin action. *Nat Med* 7: 947-953, 2001.
8. **Bernstein EL, Koutkia P, Ljungquist K, Breu J, Canavan B, and Grinspoon S**. Acute regulation of adiponectin by free fatty acids. *Metabolism* 53: 790-793, 2004.
9. **Bluher M, Bullen JW, Jr., Lee JH, Kralisch S, Fasshauer M, Kloting N, Niebauer J, Schon MR, Williams CJ, and Mantzoros CS**. Circulating adiponectin and expression of adiponectin receptors in human skeletal muscle: associations with metabolic parameters and insulin resistance and regulation by physical training. *J Clin Endocrinol Metab* 91: 2310-2316, 2006.
10. **Bobbert T, Wegewitz U, Brechtel L, Freudenberg M, Mai K, Mohlig M, Diederich S, Ristow M, Rochlitz H, Pfeiffer AF, and Spranger J**. Adiponectin oligomers in human serum during acute and chronic exercise: relation to lipid metabolism and insulin sensitivity. *Int J Sports Med* 28: 1-8, 2007.
11. **Cai H, and Harrison DG**. Endothelial dysfunction in cardiovascular diseases: the role of oxidant stress. *Circ Res* 87: 840-844, 2000.
12. **Chen H, Montagnani M, Funahashi T, Shimomura I, and Quon MJ**. Adiponectin stimulates production of nitric oxide in vascular endothelial cells. *J Biol Chem* 278: 45021-45026, 2003.
13. **Chen MP, Tsai JC, Chung FM, Yang SS, Hsing LL, Shin SJ, and Lee YJ**. Hypoadiponectinemia is associated with ischemic cerebrovascular disease. *Arterioscler Thromb Vasc Biol* 25: 821-826, 2005.

14. **Cnop M, Havel PJ, Utzschneider KM, Carr DB, Sinha MK, Boyko EJ, Retzlaff BM, Knopp RH, Brunzell JD, and Kahn SE**. Relationship of adiponectin to body fat distribution, insulin sensitivity and plasma lipoproteins: evidence for independent roles of age and sex. *Diabetologia* 46: 459-469, 2003.
15. **Czernichow S, Kengne AP, Huxley RR, Batty GD, de Galan B, Grobbee D, Pillai A, Zoungas S, Marre M, Woodward M, Neal B, and Chalmers J**. Comparison of waist-to-hip ratio and other obesity indices as predictors of cardiovascular disease risk in people with type-2 diabetes: a prospective cohort study from ADVANCE. *Eur J Cardiovasc Prev Rehabil* 2010.
16. **Daniels SR, Jacobson MS, McCrindle BW, Eckel RH, and Sanner BM**. American Heart Association Childhood Obesity Research Summit Report. *Circulation* 119: e489-517, 2009.
17. **Degawa-Yamauchi M, Moss KA, Bovenkerk JE, Shankar SS, Morrison CL, Lelliott CJ, Vidal-Puig A, Jones R, and Considine RV**. Regulation of adiponectin expression in human adipocytes: effects of adiposity, glucocorticoids, and tumor necrosis factor alpha. *Obes Res* 13: 662-669, 2005.
18. **Eckel RH, and Krauss RM**. American Heart Association call to action: obesity as a major risk factor for coronary heart disease. AHA Nutrition Committee. *Circulation* 97: 2099-2100, 1998.
19. **Ekmekci H, and Ekmekci OB**. The role of adiponectin in atherosclerosis and thrombosis. *Clin Appl Thromb Hemost* 12: 163-168, 2006.
20. **Elbatarny HS, Netherton SJ, Ovens JD, Ferguson AV, and Maurice DH**. Adiponectin, ghrelin, and leptin differentially influence human platelet and human vascular endothelial cell functions: implication in obesity-associated cardiovascular diseases. *Eur J Pharmacol* 558: 7-13, 2007.
21. **Ferguson MA, White LJ, McCoy S, Kim HW, Petty T, and Wilsey J**. Plasma adiponectin response to acute exercise in healthy subjects. *Eur J Appl Physiol* 91: 324-329, 2004.
22. **Fisher FF, Trujillo ME, Hanif W, Barnett AH, McTernan PG, Scherer PE, and Kumar S**. Serum high molecular weight complex of adiponectin correlates better with glucose tolerance than total serum adiponectin in Indo-Asian males. *Diabetologia* 48: 1084-1087, 2005.
23. **Galic S, Oakhill JS, and Steinberg GR**. Adipose tissue as an endocrine organ. *Mol Cell Endocrinol* 316: 129-139, 2010.
24. **Gleissner CA, Galkina E, Nadler JL, and Ley K**. Mechanisms by which diabetes increases cardiovascular disease. *Drug Discov Today Dis Mech* 4: 131-140, 2007.
25. **Goldstein BJ, and Scalia R**. Adiponectin: A novel adipokine linking adipocytes and vascular function. *J Clin Endocrinol Metab* 89: 2563-2568, 2004.
26. **Goodfellow J, Bellamy MF, Ramsey MW, Jones CJ, and Lewis MJ**. Dietary supplementation with marine omega-3 fatty acids improve systemic large artery endothelial function in subjects with hypercholesterolemia. *J Am Coll Cardiol* 35: 265-270, 2000.
27. **Han SH, Quon MJ, Kim JA, and Koh KK**. Adiponectin and cardiovascular disease: response to therapeutic interventions. *J Am Coll Cardiol* 49: 531-538, 2007.

28. **Hansson GK**. Inflammation, atherosclerosis, and coronary artery disease. *N Engl J Med* 352: 1685-1695, 2005.
29. **Hara K, Horikoshi M, Yamauchi T, Yago H, Miyazaki O, Ebinuma H, Imai Y, Nagai R, and Kadowaki T**. Measurement of the high-molecular weight form of adiponectin in plasma is useful for the prediction of insulin resistance and metabolic syndrome. *Diabetes Care* 29: 1357-1362, 2006.
30. **Huang KC, Chen CL, Chuang LM, Ho SR, Tai TY, and Yang WS**. Plasma adiponectin levels and blood pressures in nondiabetic adolescent females. *J Clin Endocrinol Metab* 88: 4130-4134, 2003.
31. **Hulthe J, and Fagerberg B**. Circulating oxidized LDL is associated with subclinical atherosclerosis development and inflammatory cytokines (AIR Study). *Arterioscler Thromb Vasc Biol* 22: 1162-1167, 2002.
32. **Janket SJ, Jones JA, Meurman JH, Baird AE, and Van Dyke TE**. Oral infection, hyperglycemia, and endothelial dysfunction. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 105: 173-179, 2008.
33. **Kadowaki T, Yamauchi T, Kubota N, Hara K, Ueki K, and Tobe K**. Adiponectin and adiponectin receptors in insulin resistance, diabetes, and the metabolic syndrome. *J Clin Invest* 116: 1784-1792, 2006.
34. **Kawano J, and Arora R**. The role of adiponectin in obesity, diabetes, and cardiovascular disease. *J Cardiometab Syndr* 4: 44-49, 2009.
35. **Kersten S, Desvergne B, and Wahli W**. Roles of PPARs in health and disease. *Nature* 405: 421-424, 2000.
36. **Kobashi C, Urakaze M, Kishida M, Kibayashi E, Kobayashi H, Kihara S, Funahashi T, Takata M, Temaru R, Sato A, Yamazaki K, Nakamura N, and Kobayashi M**. Adiponectin inhibits endothelial synthesis of interleukin-8. *Circ Res* 97: 1245-1252, 2005.
37. **Kobayashi H, Ouchi N, Kihara S, Walsh K, Kumada M, Abe Y, Funahashi T, and Matsuzawa Y**. Selective suppression of endothelial cell apoptosis by the high molecular weight form of adiponectin. *Circ Res* 94: e27-31, 2004.
38. **Kumada M, Kihara S, Sumitsuji S, Kawamoto T, Matsumoto S, Ouchi N, Arita Y, Okamoto Y, Shimomura I, Hiraoka H, Nakamura T, Funahashi T, and Matsuzawa Y**. Association of hypoadiponectinemia with coronary artery disease in men. *Arterioscler Thromb Vasc Biol* 23: 85-89, 2003.
39. **Lara-Castro C, Luo N, Wallace P, Klein RL, and Garvey WT**. Adiponectin multimeric complexes and the metabolic syndrome trait cluster. *Diabetes* 55: 249-259, 2006.
40. **Lavie CJ, Milani RV, and Ventura HO**. Obesity and cardiovascular disease: risk factor, paradox, and impact of weight loss. *J Am Coll Cardiol* 53: 1925-1932, 2009.
41. **Ligibel JA, Giobbie-Hurder A, Olenczuk D, Campbell N, Salinardi T, Winer EP, and Mantzoros CS**. Impact of a mixed strength and endurance exercise intervention on levels of adiponectin, high molecular weight adiponectin and leptin in breast cancer survivors. *Cancer Causes Control* 20: 1523-1528, 2009.
42. **Long YC, and Zierath JR**. AMP-activated protein kinase signaling in metabolic regulation. *J Clin Invest* 116: 1776-1783, 2006.

43. **Luo N, Liu J, Chung BH, Yang Q, Klein RL, Garvey WT, and Fu Y**. Macrophage adiponectin expression improves insulin sensitivity and protects against inflammation and atherosclerosis. *Diabetes* 59: 791-799, 2010.
44. **Luu NT, Madden J, Calder PC, Grimble RF, Shearman CP, Chan T, Dastur N, Howell WM, Rainger GE, and Nash GB**. Dietary supplementation with fish oil modifies the ability of human monocytes to induce an inflammatory response. *J Nutr* 137: 2769-2774, 2007.
45. **Lyon CJ, Law RE, and Hsueh WA**. Minireview: adiposity, inflammation, and atherogenesis. *Endocrinology* 144: 2195-2200, 2003.
46. **Manna SK, and Aggarwal BB**. Alpha-melanocyte-stimulating hormone inhibits the nuclear transcription factor NF-kappa B activation induced by various inflammatory agents. *J Immunol* 161: 2873-2880, 1998.
47. **Marinou K, Tousoulis D, Antonopoulos AS, Stefanadi E, and Stefanadis C**. Obesity and cardiovascular disease: from pathophysiology to risk stratification. *Int J Cardiol* 138: 3-8, 2010.
48. **Matsuura F, Oku H, Koseki M, Sandoval JC, Yuasa-Kawase M, Tsubakio-Yamamoto K, Masuda D, Maeda N, Tsujii K, Ishigami M, Nishida M, Hirano K, Kihara S, Hori M, Shimomura I, and Yamashita S**. Adiponectin accelerates reverse cholesterol transport by increasing high density lipoprotein assembly in the liver. *Biochem Biophys Res Commun* 358: 1091-1095, 2007.
49. **Morrow VA, Foufelle F, Connell JM, Petrie JR, Gould GW, and Salt IP**. Direct activation of AMP-activated protein kinase stimulates nitric-oxide synthesis in human aortic endothelial cells. *J Biol Chem* 278: 31629-31639, 2003.
50. **Motoshima H, Wu X, Mahadev K, and Goldstein BJ**. Adiponectin suppresses proliferation and superoxide generation and enhances eNOS activity in endothelial cells treated with oxidized LDL. *Biochem Biophys Res Commun* 315: 264-271, 2004.
51. **Motoshima H, Wu X, Sinha MK, Hardy VE, Rosato EL, Barbot DJ, Rosato FE, and Goldstein BJ**. Differential regulation of adiponectin secretion from cultured human omental and subcutaneous adipocytes: effects of insulin and rosiglitazone. *J Clin Endocrinol Metab* 87: 5662-5667, 2002.
52. **Mozaffarian D, Wilson PW, and Kannel WB**. Beyond established and novel risk factors: lifestyle risk factors for cardiovascular disease. *Circulation* 117: 3031-3038, 2008.
53. **Nawrocki AR, Rajala MW, Tomas E, Pajvani UB, Saha AK, Trumbauer ME, Pang Z, Chen AS, Ruderman NB, Chen H, Rossetti L, and Scherer PE**. Mice lacking adiponectin show decreased hepatic insulin sensitivity and reduced responsiveness to peroxisome proliferator-activated receptor gamma agonists. *J Biol Chem* 281: 2654-2660, 2006.
54. **O'Leary VB, Jorett AE, Marchetti CM, Gonzalez F, Phillips SA, Ciaraldi TP, and Kirwan JP**. Enhanced adiponectin multimer ratio and skeletal muscle adiponectin receptor expression following exercise training and diet in older insulin-resistant adults. *Am J Physiol Endocrinol Metab* 293: E421-427, 2007.
55. **Ohashi K, Kihara S, Ouchi N, Kumada M, Fujita K, Hiuge A, Hibuse T, Ryo M, Nishizawa H, Maeda N, Maeda K, Shibata R, Walsh K, Funahashi T, and Shimomura I**. Adiponectin replenishment ameliorates obesity-related hypertension. *Hypertension* 47: 1108-1116, 2006.

56. **Okamoto Y**. Adiponectin provides cardiovascular protection in metabolic syndrome. *Cardiol Res Pract* 2011: 313179, 2011.
57. **Oku H, Matsuura F, Koseki M, Sandoval JC, Yuasa-Kawase M, Tsubakio-Yamamoto K, Masuda D, Maeda N, Ohama T, Ishigami M, Nishida M, Hirano K, Kihara S, Hori M, Shimomura I, and Yamashita S**. Adiponectin deficiency suppresses ABCA1 expression and ApoA-I synthesis in the liver. *FEBS Lett* 581: 5029-5033, 2007.
58. **Ouchi N, Kihara S, Arita Y, Maeda K, Kuriyama H, Okamoto Y, Hotta K, Nishida M, Takahashi M, Nakamura T, Yamashita S, Funahashi T, and Matsuzawa Y**. Novel modulator for endothelial adhesion molecules: adipocyte-derived plasma protein adiponectin. *Circulation* 100: 2473-2476, 1999.
59. **Ouchi N, Kihara S, Arita Y, Nishida M, Matsuyama A, Okamoto Y, Ishigami M, Kuriyama H, Kishida K, Nishizawa H, Hotta K, Muraguchi M, Ohmoto Y, Yamashita S, Funahashi T, and Matsuzawa Y**. Adipocyte-derived plasma protein, adiponectin, suppresses lipid accumulation and class A scavenger receptor expression in human monocyte-derived macrophages. *Circulation* 103: 1057-1063, 2001.
60. **Ouchi N, Kihara S, Arita Y, Okamoto Y, Maeda K, Kuriyama H, Hotta K, Nishida M, Takahashi M, Muraguchi M, Ohmoto Y, Nakamura T, Yamashita S, Funahashi T, and Matsuzawa Y**. Adiponectin, an adipocyte-derived plasma protein, inhibits endothelial NF-kappaB signaling through a cAMP-dependent pathway. *Circulation* 102: 1296-1301, 2000.
61. **Ouchi N, Kihara S, Funahashi T, Matsuzawa Y, and Walsh K**. Obesity, adiponectin and vascular inflammatory disease. *Curr Opin Lipidol* 14: 561-566, 2003.
62. **Ouchi N, and Walsh K**. Adiponectin as an anti-inflammatory factor. *Clin Chim Acta* 380: 24-30, 2007.
63. **Pajvani UB, Hawkins M, Combs TP, Rajala MW, Doebber T, Berger JP, Wagner JA, Wu M, Knopps A, Xiang AH, Utzschneider KM, Kahn SE, Olefsky JM, Buchanan TA, and Scherer PE**. Complex distribution, not absolute amount of adiponectin, correlates with thiazolidinedione-mediated improvement in insulin sensitivity. *J Biol Chem* 279: 12152-12162, 2004.
64. **Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, Carnethon MR, Dai S, de Simone G, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Greenlund KJ, Hailpern SM, Heit JA, Michael Ho P, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, McDermott MM, Meigs JB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Rosamond WD, Sorlie PD, Stafford RS, Turan TN, Turner MB, Wong ND, and Wylie-Rosett J**. Executive Summary: Heart Disease and Stroke Statistics--2011 Update: A Report From the American Heart Association. *Circulation* 123: 459-463, 2011.
65. **Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N, Hailpern SM, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell C, Roger V, Sorlie P, Steinberger J, Thom T, Wilson M, and Hong Y**. Heart disease and stroke statistics--2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 117: e25-146, 2008.

66. **Ryo M, Nakamura T, Kihara S, Kumada M, Shibazaki S, Takahashi M, Nagai M, Matsuzawa Y, and Funahashi T**. Adiponectin as a biomarker of the metabolic syndrome. *Circ J* 68: 975-981, 2004.
67. **Shetty S, Kusminski CM, and Scherer PE**. Adiponectin in health and disease: evaluation of adiponectin-targeted drug development strategies. *Trends Pharmacol Sci* 30: 234-239, 2009.
68. **Shimada K, Miyazaki T, and Daida H**. Adiponectin and atherosclerotic disease. *Clin Chim Acta* 344: 1-12, 2004.
69. **Shimomura I, Maeda K, Nakamura T, and Funabashi T**. [Metabolic syndrome and adiponectin]. *Masui* 55 Suppl: S11-17, 2006.
70. **Shulman GI**. Cellular mechanisms of insulin resistance. *J Clin Invest* 106: 171-176, 2000.
71. **Sobel BE**. Optimizing cardiovascular outcomes in diabetes mellitus. *Am J Med* 120: S3-11, 2007.
72. **Steinberg HO, Chaker H, Leaming R, Johnson A, Brechtel G, and Baron AD**. Obesity/insulin resistance is associated with endothelial dysfunction. Implications for the syndrome of insulin resistance. *J Clin Invest* 97: 2601-2610, 1996.
73. **Stettler C, Allemann S, Juni P, Cull CA, Holman RR, Egger M, Krahenbuhl S, and Diem P**. Glycemic control and macrovascular disease in types 1 and 2 diabetes mellitus: Meta-analysis of randomized trials. *Am Heart J* 152: 27-38, 2006.
74. **Trujillo ME, and Scherer PE**. Adiponectin--journey from an adipocyte secretory protein to biomarker of the metabolic syndrome. *J Intern Med* 257: 167-175, 2005.
75. **Tsubakio-Yamamoto K, Matsuura F, Koseki M, Oku H, Sandoval JC, Inagaki M, Nakatani K, Nakaoka H, Kawase R, Yuasa-Kawase M, Masuda D, Ohama T, Maeda N, Nakagawa-Toyama Y, Ishigami M, Nishida M, Kihara S, Shimomura I, and Yamashita S**. Adiponectin prevents atherosclerosis by increasing cholesterol efflux from macrophages. *Biochem Biophys Res Commun* 375: 390-394, 2008.
76. **Tsuchida A, Yamauchi T, Ito Y, Hada Y, Maki T, Takekawa S, Kamon J, Kobayashi M, Suzuki R, Hara K, Kubota N, Terauchi Y, Froguel P, Nakae J, Kasuga M, Accili D, Tobe K, Ueki K, Nagai R, and Kadowaki T**. Insulin/Foxo1 pathway regulates expression levels of adiponectin receptors and adiponectin sensitivity. *J Biol Chem* 279: 30817-30822, 2004.
77. **Tsutamoto T, Tanaka T, Sakai H, Ishikawa C, Fujii M, Yamamoto T, and Horie M**. Total and high molecular weight adiponectin, haemodynamics, and mortality in patients with chronic heart failure. *Eur Heart J* 28: 1723-1730, 2007.
78. **Wajchenberg BL, Nery M, Cunha MR, and Silva ME**. Adipose tissue at the crossroads in the development of the metabolic syndrome, inflammation and atherosclerosis. *Arq Bras Endocrinol Metabol* 53: 145-150, 2009.
79. **Weyer C, Funahashi T, Tanaka S, Hotta K, Matsuzawa Y, Pratley RE, and Tataranni PA**. Hypoadiponectinemia in obesity and type 2 diabetes: close association with insulin resistance and hyperinsulinemia. *J Clin Endocrinol Metab* 86: 1930-1935, 2001.

80. **Wu X, Motoshima H, Mahadev K, Stalker TJ, Scalia R, and Goldstein BJ**. Involvement of AMP-activated protein kinase in glucose uptake stimulated by the globular domain of adiponectin in primary rat adipocytes. *Diabetes* 52: 1355-1363, 2003.
81. **Yamauchi T, Kamon J, Minokoshi Y, Ito Y, Waki H, Uchida S, Yamashita S, Noda M, Kita S, Ueki K, Eto K, Akanuma Y, Froguel P, Foufelle F, Ferre P, Carling D, Kimura S, Nagai R, Kahn BB, and Kadowaki T**. Adiponectin stimulates glucose utilization and fatty-acid oxidation by activating AMP-activated protein kinase. *Nat Med* 8: 1288-1295, 2002.
82. **Yamauchi T, Kamon J, Waki H, Imai Y, Shimozawa N, Hioki K, Uchida S, Ito Y, Takakuwa K, Matsui J, Takata M, Eto K, Terauchi Y, Komeda K, Tsunoda M, Murakami K, Ohnishi Y, Naitoh T, Yamamura K, Ueyama Y, Froguel P, Kimura S, Nagai R, and Kadowaki T**. Globular adiponectin protected ob/ob mice from diabetes and ApoE-deficient mice from atherosclerosis. *J Biol Chem* 278: 2461-2468, 2003.
83. **Yamauchi T, Kamon J, Waki H, Terauchi Y, Kubota N, Hara K, Mori Y, Ide T, Murakami K, Tsuboyama-Kasaoka N, Ezaki O, Akanuma Y, Gavrilova O, Vinson C, Reitman ML, Kagechika H, Shudo K, Yoda M, Nakano Y, Tobe K, Nagai R, Kimura S, Tomita M, Froguel P, and Kadowaki T**. The fat-derived hormone adiponectin reverses insulin resistance associated with both lipoatrophy and obesity. *Nat Med* 7: 941-946, 2001.
84. **Yamauchi T, Nio Y, Maki T, Kobayashi M, Takazawa T, Iwabu M, Okada-Iwabu M, Kawamoto S, Kubota N, Kubota T, Ito Y, Kamon J, Tsuchida A, Kumagai K, Kozono H, Hada Y, Ogata H, Tokuyama K, Tsunoda M, Ide T, Murakami K, Awazawa M, Takamoto I, Froguel P, Hara K, Tobe K, Nagai R, Ueki K, and Kadowaki T**. Targeted disruption of AdipoR1 and AdipoR2 causes abrogation of adiponectin binding and metabolic actions. *Nat Med* 13: 332-339, 2007.
85. **Yuhanna IS, Zhu Y, Cox BE, Hahner LD, Osborne-Lawrence S, Lu P, Marcel YL, Anderson RG, Mendelsohn ME, Hobbs HH, and Shaul PW**. High-density lipoprotein binding to scavenger receptor-BI activates endothelial nitric oxide synthase. *Nat Med* 7: 853-857, 2001.

APPENDIX B:

INFORMED CONSENT FORMS

Principle Investigator's name: Ryan Puck
Project # 1133997
Date of Project Approval: April 22, 2009

FOR HS IRB USE ONLY
APPROVED
4/12/10
HS IRB Authorized Representative
Date
EXPIRATION DATE: 4.22.2011

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 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 pressure, blood fats, blood sugar, inflammation, and abdominal fat.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 60 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).

2. On one occasion, you will undergo a measurement of resting blood pressure and heart rate.

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 and end 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.

6. You will be assigned to a traditional resistance exercise group. This group will perform both the concentric and eccentric muscle contractions during the resistance exercise.

7. You will 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 an exercise session of concurrent concentric and eccentric 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 containing recommended values of fat, carbohydrate, and protein the day of the exercise session and for three days following the exercise session. You will 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 and have a lab technician draw your blood (approximately 20 ml).
e. Complete a five-minute warm-up on either a treadmill or stationary bicycle.
f. Complete three sets of ten repetitions at 75% of your maximum on the leg extension and leg curl machines.
g. Wait in the lab for one-hour and then assess soreness and have your blood drawn again (20 ml) by a trained technician.
h. Report to the lab 24-hours after the exercise session and a 12-hour fast. . During this visit, soreness will be assessed and blood samples (10 ml each) will be taken from a vein in your arm.
i. You will also be asked to return to the lab 48-hours following the resistance exercise session following another 12 hour fast. During this visit, soreness will be assessed and blood samples (20 ml each) will be taken from a vein in your arm.

9. At the end of the study you will have had 80 ml of blood drawn. All blood draws for the entire study amount to less than the 450 ml of blood collected at one time when you donate blood.

10. You will not receive any placebos.

11. You will not change your exercise or activity other than what the research requires.

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.

13. 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 2 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, if in their judgment, it is in your best interest to do so. Your time commitment for testing and treatment will be a maximum of 8 hours.

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?

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 sessions.

2. Heart problems may occur during the exercise training sessions. 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. You will be asked to look for symptoms of muscle damage, painful muscle soreness and swelling and will be asked to report any symptoms to a member of the study staff immediately.

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, but the dose is much lower than a regular CT scan.

6. 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: insulin sensitivity assessment, general health and fitness information, blood lipid profile (cholesterol, etc), body fat percentage assessment, and improved fitness. You also will have access to a fully equipped fitness center with free parking.

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. Payment is for your time and inconvenience.

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, Ryan Puck 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,** Ryan Puck 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.

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.

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:

HIPPA AUTHORIZATION FORM

UNIVERSITY OF MISSOURI-COLUMBIA
Institutional Review Board

HIPAA AUTHORIZATION FORM

Authorization for the Use and Disclosure of Personal Health Information Resulting from Participation in a Research Study

FOR IRB USE ONLY
Acknowledged
IRB Authorized Representative — Date: 11/12/10

Principal Investigator's Name: Ryan W. Puck
Project # 1133997
Project Title: The effects of eccentric and concentric exercise on metabolic health.

You have agreed to participate in the study mentioned above. This authorization form gives more detailed information about how your health information will be protected.

1. Description of the information
My authorization applies to the information described below. Only this information may be used and/or disclosed in accordance with this authorization:

- Medical and Health History Questionnaires
- DEXA scan results
- Blood analysis: 4 blood draws will be taken (0hr, and 1hr, 24hr, 48hr post exercise bout) and analyzed
- Social Security Number (for accounting purposes only)

2. Who may use and/or disclose the information
I authorize the following persons (or class of persons) to make the authorized use and disclosure of my PHI: Tom Thomas, Ryan W. Puck (Principal Investigator) and study staff.

3. Who may receive the information
I authorize the following persons (or class of persons) to receive my personal health information

- Health Sciences Institutional Review Board
- Governmental regulatory bodies for auditing purposes

4. Purpose of the use or disclosure
My PHI will be used and/or disclosed upon request for the following purposes:
Publications and presentation that will not identify me, auditing, study outcomes including safety and efficacy, and submission to the government agencies that may monitor the study

5. Expiration date or event
This authorization expires upon:
☐ The following date: _____
☐ End of research study
☒ No expiration date
☐ Other: _____

6. Right to revoke authorization
I understand that I have a right to revoke this authorization at any time. My revocation must be in writing in a letter sent to the Principal Investigator at the University of Missouri, 113 McKee Gym, Columbia, MO, 65211. I am aware that my revocation is not effective to the extent that the persons I have authorized to use and/or disclose my PHI have already acted in reliance upon this authorization.

7. Statement that re-disclosures are no longer protected by the HIPAA Privacy Rule
I understand that my personal health information will only be used as described in this authorization in relation to the research study. I am also aware that if I choose to share the information defined in this authorization to anyone not directly related to this research project, the law would no longer protect this information. In addition, I understand that if my personal health information is disclosed to someone who is not required to comply with privacy protections under the law, then such information may be re-disclosed and would no longer be protected.

8. Right to refuse to sign authorization and ability to condition treatment, payment, enrollment or eligibility for benefits for research related treatment
I understand that I have a right not to authorize the use and/or disclosure of my personal health information. In such a case I would choose not to sign this authorization document I understand I will not be able to participate in a research study if I do not do so. I also understand that treatment that is part of the research project will be conditioned upon my authorization for the use and/or disclosure of my personal health information to and for use by the research team.

9. Suspension of right to access personal health information
I agree that I will not have a right to access my personal health information obtained or created in the course of the research project until the end of the study.

10. If I have not already received a copy of the University of Missouri Healthcare Privacy Notice, I may request one. If I have any questions or concerns about my privacy rights I should contact, the HS Privacy Officer at 573-882-9054 or the Campus Privacy Officer at 573-882-7254.

11. Individuals' signature and date
I certify that I have received a copy of the authorization.

_____ _____
Signature of Research Participant Date

_____ _____
Research Participant's Legally Authorized Representative Date

_____
Describe Representative Authority to Act for the Participant

APPENDIX D:

BACKGROUND QUESTIONNAIRES

Table of Contents:

University of Missouri-Columbia

Exercise Physiology Lab

Initial Screening Interview – Resistance Training

Name: _____

Phone: _____

E-mail: _____

Age _____

Do you smoke: Yes No

How much time and how often do you exercise per week? Describe

Have you participated in a formal diet program within the last 3 months? If yes, describe

Has your body weight changed (± 5%) during the past 3 months? If yes, how much

BMI $\frac{\text{Weight } \_\_\_\_\_ \text{ lbs}/2.2}{(\text{Height } \_\_\_\_\_ \text{ in.} * .0254)^2} = \_\_\_\_\_ = \_\_\_\_\_ \text{ kg/m}^2$

Are you currently taking any lipid lowering drugs?

What medications are you taking?

Do you have known diabetes or cardiovascular problems?

Do you have any orthopedic problems that would limit your ability to participate in resistance training?

University of Missouri-Columbia
Exercise Physiology Lab
Health History and Medical Questionnaire

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?
_____

Medical Questionnaire:

Have you ever been advised by a physician to avoid exercise? **Y / N**
Do you ever have shortness of breath during or after exercise? **Y / N**
Have you ever experienced fainting or dizzy spells? **Y / N**
Have you ever experienced pain or discomfort in the chest? **Y / N**
Have you ever experienced back, jaw or left arm pain or recurrent indigestion? **Y / N**
Have you ever experienced swollen ankles (excluding sprains)? **Y / N**
Have you recently experienced heart palpitations (rapid heartbeat) at rest? **Y / N**
Have you ever experienced claudication (pain in the calf, thigh, or buttocks with walking)? **Y/N**
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

---

1. Have you had any surgeries? Please List

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

3. Do you take any vitamins or dietary supplements? Please list.

University of Missouri-Columbia
Exercise Physiology Lab
Additional Medical Questionnaire
(For Women only)

1. Do you have a menstrual cycle? Yes No
   If Yes, go to question #2
   If No, go to question #5

What is the frequency of your menstrual cycle? _____ times/year

How many days does each cycle last? _____ days.

When was your last menstrual period?

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

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

Name	Frequency (i.e. 1 per day)
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

Additional comments:

University of Missouri-Columbia
Exercise Physiology Lab

Activity Questionnaire

(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)

_____
_____
_____
_____
_____
_____

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)

University of Missouri-Columbia
Exercise Physiology Lab

Dietary Questionnaire

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:

_____

_____

_____

APPENDIX E:

SUBJECT STUDY FORMS

Table of Contents:

Acute Resistance Training Study Visit Descriptions

Visit Type *Duration*	Special Instructions	What to expect	Where to go
Study Description *45 minutes* **Date:**___/___/____ **Time:**___:____		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)
Visit 1 **Screening Measures** *60-90 minutes* **Date:**___/___/____ **Time:**___:____	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) 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
Visit 2 **HR, BP & Body composition** *45-60 minutes* **Date:**___/___/____ **Time:**___:____	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.	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.	Room 10 McKee Gymnasium

Visit Type *Duration*	Special Instructions	What to expect	Where to go
Visit 3 **Single Session of Exercise Trial** *~3 hours* **Date:**___/___/____ **Time:**___:____	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 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
Visit 4 **Follow-up measurements** *20-30 minutes* **Date:**___/___/____ **Time:**___:____	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 soreness will be assessed and blood will be collected upon your arrival to the lab.	Room 10 McKee Gymnasium
Visit 5 **Follow-up measurements** *20-30 minutes* **Date:**___/___/____ **Time:**___:____	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 soreness will be assessed and blood will be collected upon your arrival to the lab.	Room 10 McKee Gymnasium

Parking Instruction 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 space behind McKee at anytime. 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 with a hang tag on Weekends or before 7:00AM or after 5:00PM on Weekdays.

Date: **EXAMPLE DIET LOG** **Day of Week:** **12/31**

Time	Food/Drink	Brand	Amount	Condiments Food Prep	Location/Place Restaurant
BREAKFAST					
7:15	**Coffee**	Folgers	8 oz	Teaspoon sugar (equal)	
	Medium sized eggs		2	Pinch salt	
	Whole Wheat toast	Sara Lee	2 slice		
	Butter	Land O Lakes	Tablespoon		
MORNING SNACK					
9:30	Red Apple		1		
LUNCH					
12:30	Big Mac w/cheese		1		**McDonalds**
	Large Fry		1		
	Large Coke		16oz		
	Ketchup	Hunts	2 Tbl		
	Apple Pie	McDonalds	1		
AFTERNOON SNACK					
3:00	Peanut Butter Chocolate Granola Bar	Quakers	2		
DINNER					
7:30	Steak		10 oz		
	A1 Steak Sauce		2 Tbs		
	Sweet Potatoe (baked)		1 large	Salt/pepper/butter/ cinnamon	
	Butter	Land O Lakes	1 Tbs		
	Green Beans		1 cup/8 oz		
	Milk 1%	Hyvee	16 oz		
EVENING SNACK					
9:00	Ice Cream chocolate	Breyers	8 oz		
	Whipped Cream	Cool Whip	Tbs		

Date: **Day of Week:**

Time	Food/Drink	Brand	Amount	Condiments Food Prep	Location/Place Restaurant
BREAKFAST					
MORNING SNACK					
LUNCH					
AFTERNOON SNACK					
DINNER					
EVENING SNACK					

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With LEAN CUISINE® Dinnertime Selects™, you get larger portions you can feel good about. Our brown-label entrées have 30% more food than the average Café Classic entrée with no more than 400 calories. Try our Jumbo Rigatoni with Meatballs in a fire-roasted tomato sauce.

Page **1** of **2** | **12** products

next>

Balsamic Glazed Chicken

Chicken Fettuccini

Chicken Florentine

Chicken Tuscan

Grilled Chicken & Penne Pasta

Orange Peel Chicken

Roasted Turkey Breast

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)	6 in
	*no regular mayonnaise, ranch dressing or chipotle southwest sauce	single serve
	chips, baked	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
	[**OR** 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)	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	1.5 cup
	(ie: broccoli, snap peas, carrots, onions, peppers, etc)	
	orange	medium
	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

*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
		single serve
	chips, baked	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
	[**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 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
	[**OR** 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
	[**OR** 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
	[**OR** 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
	[**OR** 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
	hamburger bun, white	1 bun (43 gm)
	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
	hamburger bun, white	1 bun (43 gm)
	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	single serve
	chips, baked	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
	hamburger bun, white	1 bun (43 gm)
	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
	hamburger bun, white	1 bun (43 gm)
	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
	chips, baked	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

APPENDIX F:

TESTING AND DATA COLLECTION FORMS

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University of Missouri-Columbia Exercise Physiology Lab

Acute Resistance Exercise

Subject #: _____ Date: _____ Group: _____

Age: _____

Height (in): _____

Weight (lbs): _____

BMI =

Weight lbs/2.2 = _____ = kg/m^2

(Height _____in * 0.0254)^2

Waist Circumference (cm): _____

Hip Circumference (cm): _____

Waist: Hip Ratio: _____

Heart Rate: _____

Blood Pressure: _____

DEXA Scan BF%: _____

Delay Onset of Muscle Soreness Assessment

Assessment 1.

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 rating of pain. We will begin with the muscles in the **front** of your **right leg**.

- While you are walking and without touching your leg, 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.**

Assessment 2

Now I want to know the pain intensity while lengthening your muscle. I would like for you to lie face down on the table. Now, starting with your **right leg,** I would like for you to bend your leg at the knee bringing the heel of your foot towards your buttocks and hold. While holding this position, using the same pain rating scale as before, how would rate the intensity of any pain you're feeling in the muscle in the **front** your **right leg**?

- Repeat for the **front** of **left leg.**

Muscular pain/soreness ratings

Subject: _____ **Group:** **TRE** **Date:** _____

	Walking		**Walking**		**Lengthening**	
	right quad	left quad	right ham	left ham	right quad	left quad
Baseline						
1 h post						
24 h post						
48 h post						

Blood Hematocrit Levels

Blood will be collected in 2 Capillary Tubes per subject at 0h, 1h, 24h, and 48h. Tubes will be filled ¾ and spun for 3 min with Hematocrit Centrifuge. (Be sure to plug the ends of each tube with puddy without passing red marker line.)

The two hematocrit reading will be averaged.

Hematocrit Readings

0h		**Average**
_____	_____	_____
1h Post		
_____	_____	_____
24h Post		
_____	_____	_____
48 Post		
_____	_____	_____

1-RM Attempt Recording Sheet

Subject #: Test: LB Date:

Group:

1 RM TEST	1st Attempt	2nd Attempt	3rd Attempt	4th Attempt	5th Attempt
LIFT					
Leg Extension	_____	_____	_____	_____	_____
Leg Curl	_____	_____	_____	_____	_____

ACUTE EXERCISE SESSION

Subject # _____

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

Date _____
Group_____
1-RM LE _____
75% 1-RM_____
1-RM LC _____

75% 1-RM_____

All subjects will attempt to complete three sets of ten repetitions of each exercise. Each concentric repetition will be in a controlled manner. Each eccentric repetition will be lowered using an audible 5-second cadence by the laboratory technician. Each traditional resistance exercise will raised and lowered in a controlled manner by subjects at a 2-3 second cadence (1:1 ratio). 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 DEXA _____

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 _____

APPENDIX G:

PULLEY SYSTEM

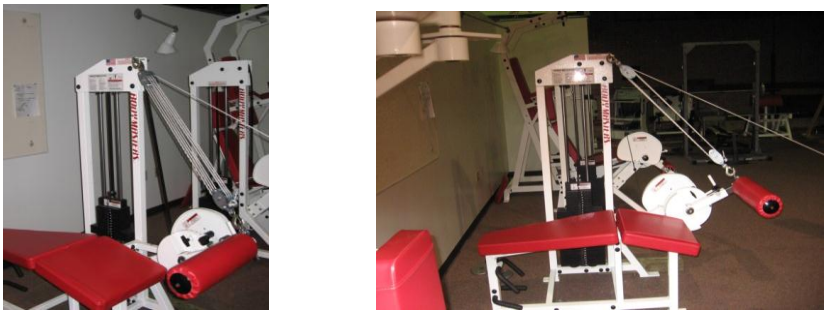

Figure 1. Pulley set-up for CON and ECC group. Attachment of compound pulley system to the leg curl machine. Pulley system was anchored to the top of the weight tower. Pulley system was used to assist researchers in lifting weight for ECC and lowering weight for CON group.

Figure 2. Compound pulley system for the leg extension was anchored to a support frame, constructed by researchers, and the class 2 pulley was attached to the lever arm of the leg extension by a U-bolt attached to an eye bolt. Pulley system was used to raise weight for ECC and lower weight for CON group.

A.

B.

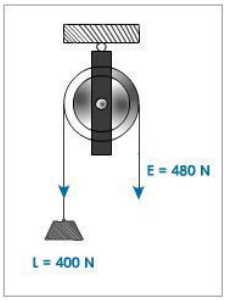

Figure 3. Compound and fixed pulley system designs. A. The movable pulley (class 2 pulley) was attached to lever arm of the leg curl machine by a U-bolt attached to an eye bolt. A hook bar could also be used by researchers that attached to same U-bolt to allow researchers to raise and lower weight. B. Depicts a fixed pulley system; the pulley itself was fixed to the top of the weight tower and the looped end of the cable was attached to the lever arm of the leg curl machine by a U-bolt attached to an eye bolt.

APPENDIX H:
RAW DATA

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Subject characteristics.

Subject	Group	Gender	Age	BF% DXA	Waist Circ. (cm)	Hip Circ. (cm)	Waist:Hip Ratio	Body Wt. (lbs)	Body Wt. (kg)	HT. (in)	HT. (cm)	BMI
402	CON	M	30	30.6	111.0	116.5	0.95	216.0	98.18	69.21	175.8	31.8
403	CON	F	38	46.2	117.0	136.0	0.86	227.0	103.18	63.15	160.4	40.1
405	ECC	F	47	40.9	104.5	119.0	0.88	194.5	88.41	63.50	161.3	34.0
406	ECC	F	21	44.6	120.8	124.5	0.97	228.3	103.77	65.16	165.5	37.9
407	CON	F	40	46.3	116.0	132.0	0.88	242.2	110.09	69.21	175.8	35.6
408	ECC	M	39	23.9	106.5	115.0	0.93	221.9	100.86	68.70	174.5	33.1
409	ECC	F	29	43.7	116.3	123.8	0.94	213.6	97.09	65.12	165.4	35.5
411	CON	M	31	34.3	127.0	118.8	1.07	283.2	128.73	71.06	180.5	39.5
413	ECC	M	21	22.8	96.0	110.0	0.87	203.0	92.27	70.12	178.1	29.1
414	CON	F	44	39.6	97.5	119.0	0.82	188.5	85.68	62.48	158.7	34.0
415	ECC	M	30	22.0	94.5	103.5	0.91	175.2	79.64	67.99	172.7	26.7
418	CON	M	48	28.7	111.0	113.0	0.98	219.0	99.55	71.02	180.4	30.6
419	ECC	M	48	28.2	105.0	112.0	0.94	210.4	95.64	69.13	175.6	31.0
420	CON	F	23	44.6	106.0	119.5	0.89	218.0	99.09	64.76	164.5	36.6
421	CON	F	27	41.3	105.5	117.0	0.90	182.7	83.05	62.95	159.9	32.5
423	ECC	F	44	51.6	109.0	139.0	0.78	247.2	112.36	64.57	164.0	41.8
424	ECC	F	40	42.7	85.0	119.0	0.71	174.1	79.14	66.14	168.0	28.0
428	ECC	F	26	29.6	85.0	101.0	0.84	150.4	68.36	64.37	163.5	25.4
432	CON	M	29	36.3	120.0	118.5	1.01	226.5	102.95	68.07	172.9	34.4
436	ECC	F	42	36.5	107.0	110.5	0.97	210.8	95.82	69.61	176.8	30.7
438	CON	F	22	40.3	100.0	115.5	0.87	183.2	83.27	67.60	171.7	28.2
439	CON	F	21	35.5	94.5	107.5	0.88	164.2	74.64	65.31	165.9	27.1
440	ECC	M	28	31.5	111.0	118.0	0.94	235.9	107.23	69.41	176.3	34.5
443	CON	M	28	32.4	113.5	118.5	0.96	246.5	112.05	69.09	175.5	36.4
444	ECC	F	38	38.6	99.1	110.5	0.90	175.5	79.77	63.35	160.9	30.8
445	CON	F	40	41.3	108.5	116.3	0.93	197.8	89.91	66.54	169.0	31.5
446	CON	F	25	41.3	116.3	129.0	0.90	235.5	107.05	71.50	181.6	32.5
448	ECC	F	46	37.7	108.6	116.5	0.93	195.2	88.73	64.45	163.7	33.1
449	ECC	F	22	46.2	96.5	120.8	0.80	196.1	89.14	63.11	160.3	34.7
452	CON	M	22	27.3	108.0	113.5	0.95	228.2	103.73	72.20	183.4	30.8
475	TRE	M	28	29.5	95.0	103.5	0.92	195.5	88.86	67.25	170.8	68.0
519	TRE	M	42	27.5	91.5	107.0	0.86	197.0	89.55	67.50	171.5	68.4
520	TRE	F	22	37.8	87.50	109.3	0.80	176.0	80.00	64.50	163.8	62.5
522	TRE	M	46	30.3	103.5	114.0	0.91	228.0	103.64	71.00	180.3	77.2
529	TRE	F	19	37.0	77.5	114.5	0.68	181.0	82.27	65.14	165.5	64.0
530	TRE	F	22	38.0	80.3	105.0	0.76	152.0	69.09	62.25	158.1	54.9
540	TRE	M	27	17.8	90.0	104.0	0.87	232.0	105.45	77.00	195.6	75.4
545	TRE	F	23	37.2	87.0	114.0	0.76	194.0	88.18	64.00	162.6	69.2
569	TRE	F	28	34.4	74.5	110.0	0.68	158.2	71.91	64.50	163.8	56.2
570	TRE	M	32	24.3	92.5	108.0	0.86	198.0	90.00	70.00	177.8	67.5
571	TRE	M	29	25.5	95.5	197.0	0.48	197.0	89.55	69.00	175.3	67.6
590	TRE	M	26	31.8	101.5	129.5	0.78	273.0	124.09	68.50	174.0	94.1
591	TRE	M	19	30.1	100.5	116.0	0.87	241.0	109.55	72.25	183.5	80.9

Gender Difference in Total Adiponectin and High Molecular Weight Adiponectin

Concentrations of total adiponectin pre- and post exercise between males and females.

	0hr	1hr	24hr	48hr	Avg.
Female	12.7 ± 0.7[a]	13.6 ± 0.8[a*]	12.1 ± 0.7[a]	11.9 ± 0.7[a]	12.6 ± 0.8[a]
Male	10.4 ± 0.8	10.5 ± 0.9	9.7 ± 0.8*	9.7 ± 0.8*	10.1 ± 0.8

Units are in ng/mL. Values are means ± SE. *Significant difference from 0 h ($p < 0.05$). [a]Significant difference from males in columns.

Concentrations of high molecular weight adiponectin pre- and post exercise between males and females.

	0hr	1hr	24hr	48hr	Avg.
Female	21.1 ± 2.6[a]	20.1 ± 2.1[a]	21.2 ± 2.3[a]	20.5 ± 2.2[a]	20.7 ± 2.8[a]
Male	13.4 ± 2.9	14.1 ± 2.4	13.1 ± 2.6	13.1 ± 2.5	13.4 ± 1.6

Units are in ng/mL. Values are means ± SE. *Significant difference from 0 h ($p < 0.05$). [a]Significant difference from males in columns.

Plasma concentrations of total adiponectin (ng/ml) in subjects.

Subject	Group	0 hr	1 hr	24hr	48 hr	Average	Average Post Exercise	AUC Change from Base Line
402	CON	10.2	11.29	9.98	11.27	10.69	10.85	20.21
403	CON	11.13	12	12.01	11.84	11.75	11.95	39.21
405	ECC	8.01	9.65	7.91	7.28	8.21	8.28	7.75
406	ECC	11.53	13	12.5	13.33	12.59	12.94	61.3
407	CON	14.45	15.4	15.07	14.77	14.92	15.08	29.34
408	ECC	6.76	6.01	6.04	6.09	6.23	6.05	-33.59
409	ECC	12.43	11.2	11.11	11.08	11.46	11.13	-61.37
411	CON	7.99	8.41	8.61	8.32	8.33	8.45	23.36
413	ECC	13.43	12.45	13.53	13.14	13.14	13.04	-12.4
414	CON	13.64	19.37	14.19	14.68	15.47	16.08	91.3
415	ECC	13.01	12.12	12.38	11.12	12.16	11.87	-47.72
418	CON	6.27	7.35	5.97	5.53	6.28	6.28	-3.51
419	ECC	6.94	7.23	7.1	6.42	6.92	6.92	0.86
420	CON	11.78	12.38	10.84	10.36	11.34	11.19	-32.23
421	CON	12.2	12.11	13.57	13.11	12.75	12.93	42.08
423	ECC	13.95	12.32	12.86	12.09	12.81	12.42	-66.68
424	ECC	26.52	25.7	23.33	23.01	24.64	24.01	-126.52
428	ECC	12.97	12.47	10.72	11.23	11.85	11.47	-79.51
432	CON	9.58	9.33	8.88	8.76	9.14	8.99	-29.17
436	ECC	7.23	7.26	7.4	6.67	7.14	7.11	-2.38
438	CON	9.37	11.98	6.91	8.68	9.24	9.19	-36.08
439	CON	14.68	16.74	11.74	11.13	13.57	13.2	-88
440	ECC	7.55	6.95	7.75	7.04	7.32	7.25	-8.32
443	CON	10.15	12.21	8.86	7.94	9.79	9.67	-33.15
444	ECC	7.89	8.27	7.2	7.95	7.83	7.81	-11.13
445	CON	8.23	11.13	7.65	8.16	8.79	8.98	18.88
446	CON	13.98	16.01	14.78	13.43	14.55	14.74	35.55
448	ECC	17.05	19.7	16.17	10.84	15.94	15.57	-64.73
449	ECC	11.93	12.46	10.13	13.23	11.94	11.94	-20.61
452	CON	10.02	11.22	8.2	9.77	9.8	9.73	-31.97
475	TRE	11.99	11.39	9.81	9.29	10.62	10.16	-90.53
519	TRE	17.16	23.07	17.87	19.86	19.49	20.27	117.05
520	TRE	18	20.06	18.19	17.05	18.33	18.43	16.76
522	TRE	14.15	14.41	14.71	15.03	14.58	14.72	26.71
529	TRE	11.92	12.6	10.84	11.14	11.63	11.53	-26.92
530	TRE	13.56	12.27	10.9	12.16	12.22	11.78	-94.15
540	TRE	8.99	8.75	6.85	7.21	7.95	7.6	-74.41
545	TRE	11.93	9.09	9.31	8.82	9.79	9.07	-131.55
569	TRE	12.29	13.86	14.42	12.55	13.28	13.61	71.23
570	TRE	12.66	10.41	11.07	11.72	11.47	11.07	-74.52
571	TRE	14.54	14.59	11.09	11.75	12.99	12.48	-113.98
590	TRE	9.52	7.44	7.95	6.73	7.91	7.37	-94.3
591	TRE	7.16	5.81	6.58	6.81	6.59	6.4	-33.36

Plasma concentrations of high molecular weight adiponectin (ng/ml) in subjects.

Subject	Group	0 hr	1 hr	24 hr	48 hr	Average	Average Post Exercise	AUC Change from Base Line
402	CON	16.73	14.27	16.43	22.53	17.49	17.74	34.26
403	CON	14.33	16.12	15.76	16.09	15.58	15.99	75.31
405	ECC	8.58	9.39	9.26	9.87	9.28	9.51	40.78
406	ECC	9.93	12.74	12.03	12.89	11.9	12.55	117.19
407	CON	30.64	26.14	29.29	28.12	28.55	27.85	-113.72
408	ECC	4.62	3.63	3.24	3.19	3.67	3.35	-60.98
409	ECC	8.8	8.94	8.52	5.93	8.05	7.8	-39.41
411	CON	4.81	4.78	6.18	5.48	5.31	5.48	39.89
413	ECC	30.68	29.87	28.41	29.53	29.62	29.27	-76.46
414	CON	17.01	21.14	23.32	23.54	21.25	22.67	274.14
415	ECC	12.35	12.72	12.68	13.91	12.92	13.1	30.73
418	CON	5.36	27.91	5.14	5	10.85	12.68	249.84
419	ECC	15.63	15.02	14.03	13.17	14.46	14.07	-74.14
420	CON	27.82	19.35	26.19	25.53	24.72	23.69	-163.19
421	CON	14.8	12.56	12.94	14.18	13.62	13.23	-76.91
423	ECC	41.71	39.42	39.59	36.74	39.37	38.58	-135.8
424	ECC	43.53	43.81	40.26	38.89	41.62	40.99	-129.31
428	ECC	30.49	30.31	26.31	30.3	29.35	28.97	-102.58
432	CON	9.31	8.76	8.07	8.91	8.76	8.58	-40.27
436	ECC	18.8	17.87	17.86	19.7	18.56	18.48	-21.99
438	CON	4.74	6.06	7.92	4.77	5.87	6.25	90.27
439	CON	20.13	13.95	21.23	18.38	18.42	17.85	-66.22
440	ECC	18.96	18.47	14.98	20.09	18.13	17.85	-85.61
443	CON	10.54	12.93	11.97	8.34	10.95	11.08	34.69
444	ECC	18	19.34	18.46	18.17	18.49	18.66	28.26
445	CON	9.43	12.75	10.59	11.58	11.09	11.64	91.24
446	CON	19.55	25.28	26.35	24.84	24.01	25.49	289.18
448	ECC	18.78	18.23	17.2	17.36	17.89	17.6	-60.5
449	ECC	20.54	21.09	21.61	19.89	20.78	20.86	24
452	CON	4.68	8.1	6.11	5.01	5.98	6.41	76.9
475	TRE	4.5	4.99	6.65	4.45	5.15	5.36	55.56
519	TRE	22.19	22.53	23.1	20.7	22.13	22.11	7.42
520	TRE	74.16	58.89	67.45	62.73	65.81	63.02	-470.45
522	TRE	21.19	20.92	21.68	20.2	21	20.93	-3.47
529	TRE	8.75	9.4	8.42	8.5	8.77	8.77	-3.28
530	TRE	6.05	6.51	5.94	5.89	6.1	6.11	0.79
540	TRE	9.92	9.24	10.24	9.69	9.77	9.72	-3.06
545	TRE	13.48	12.25	11.85	11.78	12.34	11.96	-72.85
569	TRE	25.74	21.79	31.23	27.47	26.56	26.83	104.35
570	TRE	22.1	17.25	20.14	20.25	19.94	19.21	-124.04
571	TRE	21.14	16.96	20.36	19.28	19.44	18.87	-88.72
590	TRE	10.67	10.24	9.55	9.18	9.91	9.66	-49.15
591	TRE	9.24	9.22	9.94	9.62	9.51	9.59	20.78

Plasma concentrations of QUICKI (1/logInsulin + logGlucose).

Subject	Group	0 hr	1 hr	24hr	48 hr	Average	Average Post Exercise	AUC Change from Base Line
402	CON	-1.43	0.38	0.35	0.34	0.36	0.35	-1.43
403	CON	0.93	0.3	0.33	0.33	0.31	0.32	0.93
405	ECC	-1.75	0.33	0.34	0.34	0.34	0.34	-1.75
406	ECC	3.09	0.35	0.36	0.38	0.36	0.36	3.09
407	CON	-0.06	0.28	0.29	0.29	0.28	0.28	-0.06
408	ECC	1.55	0.33	0.32	0.32	0.32	0.32	1.55
409	ECC	2.46	0.36	0.36	0.37	0.36	0.37	2.46
411	CON	0.14	0.32	0.32	0.32	0.32	0.32	0.14
413	ECC	1.59	0.35	0.34	0.35	0.35	0.35	1.59
414	CON	-0.08	0.32	0.31	0.32	0.32	0.32	-0.08
415	ECC	-0.89	0.33	0.34	0.35	0.34	0.34	-0.89
418	CON	0.34	0.36	0.37	0.37	0.37	0.37	0.34
419	ECC	2.54	0.36	0.36	0.38	0.37	0.37	2.54
420	CON	-0.47	0.31	0.31	0.3	0.31	0.31	-0.47
421	CON	-0.11	0.37	0.35	0.38	0.36	0.36	-0.11
423	ECC	-2.07	0.32	0.32	0.33	0.32	0.32	-2.07
424	ECC	2.1	0.36	0.36	0.36	0.36	0.37	2.1
428	ECC	3.04	0.38	0.4	0.46	0.41	0.42	3.04
432	CON	0.8	0.32	0.33	0.33	0.33	0.34	0.8
436	ECC	-1.09	0.34	0.32	0.32	0.33	0.32	-1.09
438	CON	-1.78	0.36	0.34	0.32	0.34	0.33	-1.78
439	CON	-0.01	0.35	0.35	0.34	0.35	0.35	-0.01
440	ECC	1.73	0.32	0.31	0.34	0.33	0.33	1.73
443	CON	1.91	0.3	0.31	0.35	0.32	0.33	1.91
444	ECC	-4.12	0.32	0.32	0.34	0.33	0.33	-4.12
445	CON	1.01	0.42	0.45	0.44	0.44	0.45	1.01
446	CON	0.14	0.36	0.38	0.34	0.36	0.37	0.14
448	ECC	-0.55	0.34	0.35	0.34	0.35	0.35	-0.55
449	ECC	-1.78	0.34	0.31	0.31	0.32	0.32	-1.78
452	CON	1	0.35	0.4	0.36	0.37	0.38	1
475	TRE	-2.5	0.33	0.29	0.34	0.32	0.32	-2.5
519	TRE	3.08	0.36	0.37	0.37	0.37	0.37	3.08
520	TRE	4.95	0.37	0.39	0.41	0.38	0.38	4.95
522	TRE	2.96	0.34	0.39	0.35	0.37	0.39	2.96
529	TRE	5.43	0.47	0.44	0.42	0.44	0.44	5.43
530	TRE	-0.11	0.36	0.38	0.35	0.36	0.36	-0.11
540	TRE	6.8	0.45	0.45	0.47	0.46	0.46	6.8
545	TRE	-0.53	0.3	0.32	0.36	0.34	0.36	-0.53
569	TRE	4.17	0.39	0.44	0.41	0.4	0.41	4.17
570	TRE	-0.75	0.38	0.35	0.35	0.36	0.35	-0.75
571	TRE	2.89	0.45	0.42	0.38	0.43	0.42	2.89
590	TRE	0.74	0.31	0.3	0.31	0.31	0.31	0.74
591	TRE	-4.47	0.35	0.32	0.33	0.33	0.33	-4.47

Plasma concentrations of insulin (uIU/mL) in subjects.

Subject	Group	0 hr	1 hr	24 hr	48 hr	Average	Average Post Exercise	AUC Change from Base Line
402	CON	4.67	5.76	8.77	6.67	6.47	7.07	132.89
403	CON	21.6	17.3	16.3	21.9	19.28	18.5	-170.4
405	ECC	8.99	7.16	7.3	9.33	8.2	7.93	-56.68
406	ECC	7.96	7.34	6.49	11.3	8.27	8.38	-1.59
407	CON	28.4	25.1	22.7	38.2	28.6	28.67	-54.3
408	ECC	9.61	10.2	13.6	12.3	11.43	12.03	132.83
409	ECC	5.98	6.46	6.46	6.54	6.36	6.49	23.52
411	CON	15.3	15.3	16.9	16.6	16.03	16.27	53.2
413	ECC	7.15	7.87	7.57	7.34	7.48	7.59	20.43
414	CON	15.8	14.9	15.2	16.4	15.58	15.5	-17.25
415	ECC	9.57	8.18	6.15	10	8.48	8.11	-91.2
418	CON	6.23	5.77	5.37	7.51	6.22	6.22	-10.14
419	ECC	6.86	6.27	5.41	7.91	6.61	6.53	-28.26
420	CON	16.8	18.4	22.3	25.5	20.75	22.07	252.05
421	CON	5.74	7.32	5.57	7.78	6.6	6.89	38.66
423	ECC	14.6	15.6	13.6	15	14.7	14.73	-7.2
424	ECC	6.97	7.85	6.8	7.6	7.31	7.42	13.69
428	ECC	5.11	4.34	2.99	2.99	3.86	3.44	-84.12
432	CON	13.1	12.4	12.6	9.65	11.94	11.55	-61.2
436	ECC	9.67	11.6	12.1	9.54	10.73	11.08	77.74
438	CON	6.73	8	10.8	10.3	8.96	9.7	153.09
439	CON	7.97	8.33	7.61	9.07	8.25	8.34	8.88
440	ECC	13.5	14.8	10.8	10.6	12.43	12.07	-83.3
443	CON	25.6	18.6	7.94	8.86	15.25	11.8	-696.39
444	ECC	9.85	12.8	8.66	11.3	10.65	10.92	23.36
445	CON	2.99	2.69	3.35	2.46	2.87	2.83	-1.35
446	CON	7.35	6.23	8.13	6.81	7.13	7.06	-1.03
448	ECC	10.3	11.5	11.8	10.2	10.95	11.17	47.85
449	ECC	15.7	16.8	17.2	12.3	15.5	15.43	7.1
452	CON	9.05	4.73	7.84	8.34	7.49	6.97	-86.64
475	TRE	10.4	29.3	11.2	11.8	15.68	17.43	252.95
519	TRE	5.89	5.63	7.24	6.28	6.26	6.38	33.42
520	TRE	6.88	5.3	4.82	8.78	6.45	6.3	-43.78
522	TRE	10.2	5.21	7.72	3.15	6.57	5.36	-200.27
529	TRE	2	2.32	2.84	2	2.29	2.39	23.42
530	TRE	8.02	6.36	10.4	8.94	8.43	8.57	47.88
540	TRE	2	2	2	2	2	2	0
545	TRE	25	14	8.79	6.72	13.63	9.84	-726.8
569	TRE	4.9	2.06	3.19	4.87	3.76	3.37	-73.21
570	TRE	4.86	7.53	9.52	9.01	7.73	8.69	190.02
571	TRE	2	3.11	4.47	2.21	2.95	3.26	73.33
590	TRE	17.4	20.9	18.9	16	18.3	18.6	58.7
591	TRE	8.02	15.8	14.4	13.7	12.98	14.63	307.56

Glucose (mg/dL) measurements in subjects.

Subject	Group	0 hr	1 hr	24 hr	48 hr	Average	Average Post Exercise	AUC Change from Base Line
402	CON	94.8	97.6	98.8	97.6	97.2	98	159.8
403	CON	98	88.7	102	104	98.18	98.23	59.05
405	ECC	109.2	102.8	111.2	108	107.8	107.33	-41
406	ECC	84	78.4	82.4	89.6	83.6	83.47	-34.8
407	CON	116.8	105.6	124	125.6	118	118.4	146
408	ECC	101.2	96.8	105.1	111.2	103.58	104.37	161.05
409	ECC	98.4	96.4	96	95.2	96.5	95.87	-117.8
411	CON	97.6	96.4	107.3	95.1	99.1	99.6	184.15
413	ECC	93.3	94	93.3	91.9	93.13	93.07	-8.75
414	CON	90.4	88	90.4	87.1	88.98	88.5	-67.2
415	ECC	123.1	112.5	121.2	123.1	119.98	118.93	-166.55
418	CON	94.4	84.5	89.7	95.6	91.05	89.93	-209.9
419	ECC	83.2	83.5	79.3	79.3	81.33	80.7	-135
420	CON	89.7	92.5	94.4	90.1	91.68	92.33	147.45
421	CON	89.5	88.3	88.7	98.4	91.23	91.8	74.2
423	ECC	99.6	91.6	103	100.4	98.65	98.33	-2.5
424	ECC	87.6	83.9	96	87.2	88.68	89.03	150.05
428	ECC	81.4	84.9	73.1	72.8	78.05	76.93	-258
432	CON	102.2	98.5	103.3	98.1	100.53	99.97	-65.9
436	ECC	93.2	97.5	108.6	105.8	101.28	103.97	562.55
438	CON	82	80.9	89.6	87.4	84.98	85.97	230.75
439	CON	96.4	86.1	88.6	87.9	89.75	87.53	-403.75
440	ECC	105.7	101.9	100.4	100.4	102.1	100.9	-231.85
443	CON	94.9	95.3	88.4	96.4	93.75	93.37	-130.15
444	ECC	121.9	113.3	105	105	111.3	107.77	-698.85
445	CON	78.6	76.9	74.7	82.2	78.1	77.93	-68
446	CON	86.4	90.6	86.4	83.9	86.83	86.97	18.3
448	ECC	82.5	76.3	88	74.6	80.35	79.63	-36.85
449	ECC	58.2	82.8	96.2	83.2	80.1	87.4	1475.9
452	CON	76.6	75.9	78.3	78.3	77.28	78	52
475	TRE	96.23	109.14	93.13	95.87	98.59	99.38	71.3
519	TRE	97.93	94.73	81.31	83.43	89.35	86.49	-601.37
520	TRE	70.62	70.93	64.58	74.39	70.13	69.97	-93.14
522	TRE	87.04	74.44	93.18	79.81	83.62	82.48	-87.37
529	TRE	69.23	74.49	74.8	71.24	72.44	73.51	215.51
530	TRE	79.66	75.16	80.22	76.82	77.97	77.4	-72.67
540	TRE	80.95	83.17	92.05	91.17	86.84	88.8	409.02
545	TRE	86.37	76.77	79.6	74.55	79.32	76.97	-411.34
569	TRE	80.22	78.47	85.28	83.32	81.82	82.36	135.99
570	TRE	88.12	86.06	86.01	89.83	87.51	87.3	-52.76
571	TRE	82.29	86.21	85.39	83.68	84.39	85.09	134.61
590	TRE	99.44	94.26	97.44	69.1	90.06	86.93	-470.65
591	TRE	86.77	97.12	95.93	93.62	93.36	95.56	416.49

AUC measurement of total adiponectin, HMWA, insulin, and glucose for each subject.

Subject	Group	Total Adiponectin (ng/dL)	HMW Adiponectin (ng/dL)	QUICKI	Insulin (ulU/mL)	Glucose (mg/dL)
402	CON	510.35	836.07	16.7	357.59	4711.6
403	CON	573.88	764.05	15.38	864.25	4758.4
405	ECC	393.05	453.02	16.35	373.93	5197.4
406	ECC	615.48	595.23	17.58	380.18	3994.4
407	CON	723.41	1354.76	13.58	1307.25	5746.8
408	ECC	290.52	160.29	15.23	594.41	5016.45
409	ECC	534.66	383.06	17.62	310.8	4604.4
411	CON	407.09	270.76	15.26	787.6	4868.35
413	ECC	631.75	1395.78	16.84	363.99	4470
414	CON	748.89	1092.69	15.14	740.7	4270.8
415	ECC	576.32	623.72	16.41	367.47	5736.95
418	CON	297.99	518.39	17.68	288.67	4316.35
419	ECC	334.12	675.8	17.69	300.73	3858.75
420	CON	533.51	1167.94	14.63	1059.25	4454.45
421	CON	627.64	632.37	17.59	314.97	4369.6
423	ECC	602.11	1865.14	15.59	694.1	4774.3
424	ECC	1146.04	1960.28	17.49	348.69	4353
428	ECC	542.81	1360.85	20.57	160.78	3650.95
432	CON	430.55	406.34	16.15	567.25	4837.85
436	ECC	344.68	879.95	15.53	542.87	5038.3
438	CON	414.99	318.45	15.71	476.77	4166.2
439	CON	617.67	896.93	16.63	391.62	4218.3
440	ECC	353.78	824.23	15.93	565.35	4839.85
443	CON	455.09	541.81	16.09	528.91	4425.25
444	ECC	367.79	892.93	16.02	497.64	5148.05
445	CON	415.37	545.54	21.27	142.02	3703.95
446	CON	707.6	1230.44	17.27	351.21	4167.6
448	ECC	755	840.67	16.56	542.85	3920.05
449	ECC	552.3	1010	15.09	761.25	4281.8
452	CON	449.59	303.25	17.92	345.61	3729
475	TRE	484.69	271.81	15.57	761.6	4696.79
519	TRE	943.69	1072.71	17.58	316.01	4097.67
520	TRE	881.79	3081.6	18.68	285.67	3296.78
522	TRE	706.04	1013.52	18.13	286.84	4084.25
529	TRE	545.58	417.05	20.78	119.58	3541.18
530	TRE	556.09	291.42	17.23	432.01	3748.76
540	TRE	356.99	472.76	22.04	96	4295.73
545	TRE	439.67	573.58	17.12	467.71	3729.63
569	TRE	661.94	1337.9	19.61	160.58	3985.67
570	TRE	532.04	934.34	16.76	424.63	4175.98
571	TRE	583.97	923.91	19.61	169.89	4086.49
590	TRE	361.63	462.8	14.93	895.65	4299.88
591	TRE	309.65	464.29	15.68	696.41	4586.62

Hematocrit measurements pre and post exercise with changes in plasma volume from baseline.

Subject	Group	0 h Mean	1 h Mean	24 h Mean	48 h Mean	PV change 1h	PV change 24h	PV change 48h
402	CON	40.5	43.5	39.8	41.5	-11.59	3.17	-4.05
403	CON	39.0	36.3	35.3	37.8	12.44	17.44	5.43
405	ECC	37.3	38.3	37.3	37.8	-4.17	0.00	-2.11
406	ECC	37.8	37.8	35.5	35.3	0.00	10.18	11.39
407	CON	37.8	39.3	38.8	38.5	-6.14	-4.15	-3.13
408	ECC	43.8	47.5	44.0	45.0	-14.04	-1.01	-4.94
409	CON	39.8	40.3	37.5	37.0	-2.06	9.96	12.34
411	CON	43.5	42.8	41.0	41.5	3.11	10.79	8.53
413	ECC	44.3	45.8	44.2	43.3	-5.88	0.25	4.15
414	CON	40.3	42.3	41.0	40.8	-7.92	-3.06	-2.05
415	ECC	43.5	43.5	42.8	42.4	0.00	3.11	4.72
418	CON	46.3	46.0	46.0	45.8	1.01	1.01	2.03
419	ECC	45.3	47.0	46.0	44.3	-6.80	-2.98	4.13
420	CON	39.0	38.8	38.5	37.5	1.06	2.13	6.56
421	CON	38.5	39.0	36.8	37.8	-2.08	7.74	3.23
423	ECC	38.5	37.0	36.8	35.8	6.59	7.74	12.51
424	ECC	42.5	40.8	41.0	39.8	7.47	6.36	12.03
428	ECC	42.3	40.5	38.5	48.0	7.48	16.87	-20.74
432	CON	44.5	42.5	41.8	41.8	8.48	11.87	11.87
436	ECC	40.3	41.5	40.4	41.0	-5.04	-0.50	-3.06
438	CON	38.0	43.5	43.0	39.5	-20.39	-18.75	-6.12
439	CON	37.8	37.0	40.3	37.8	3.26	-9.98	0.00
440	ECC	41.8	42.0	39.5	40.5	-1.02	9.78	5.30
443	CON	44.8	45.5	45.0	45.8	-2.98	-1.01	-3.96
444	ECC	37.5	37.8	36.0	36.3	-1.06	6.67	5.52
445	CON	41.8	39.8	39.0	39.5	8.64	12.11	9.78
446	CON	38.0	35.5	39.9	36.0	11.36	-7.58	8.96
448	ECC	36.8	35.5	35.5	34.3	5.57	5.57	11.54
449	ECC	39.3	41.0	40.6	39.5	-7.03	-5.59	-1.04
452	CON	46.8	45.0	45.8	44.8	7.30	4.10	8.39
475	TRE	49.0	47.5	47.3	48.3	6.19	7.26	3.05
519	TRE	44.3	44.3	43.25	44.5	0.00	4.15	-1.01
520	TRE	37.5	36.5	36.5	39.0	4.38	4.38	-6.15
522	TRE	42.3	42.3	41.5	42.0	0.00	3.13	1.03
529	TRE	38.0	38.5	39.5	40.8	-2.09	-6.12	-10.88
530	TRE	39.3	37.3	38.3	38.3	8.84	4.30	4.30
540	TRE	47.5	47.4	44.6	45.8	0.52	12.52	7.29
545	TRE	39.0	42.0	38.0	35.0	-11.71	4.31	18.74
569	TRE	39.8	41.0	40.0	42.0	-5.06	-1.04	-8.89
570	TRE	46.0	46.3	44.5	46.8	-1.00	6.24	-2.97
571	TRE	43.5	42.5	44.5	42.5	4.16	-3.98	4.16
590	TRE	47.3	48.5	46.8	47.3	-4.89	2.03	0.00
591	TRE	43.3	42.5	41.3	40.0	3.11	8.54	14.32

DOMS walking right and left quadriceps test.

Subject	Group	Walking Rt. Quad 0 h	Walking Rt. Quad 1 h	Walking Rt. Quad 24 h	Walking Rt. Quad 48 h	Walking Lt. Quad 0 h	Walking Lt. Quad 1 h	Walking Lt. Quad 24 h	Walking Lt. Quad 48 h
402	CON	0	0	0	0	0	0	0	0
403	CON	0	0	0	1	0	0	0	1
405	ECC	0	5	3	5	0	5	3	6
406	ECC	0	5	20	20	0	6	18	25
407	CON	0	0	0	0	0	0	0	0
408	ECC	0	0	0	2	0	0	0	4
409	ECC	0	0	5	15	0	0	5	10
411	CON	0	0	0	0	0	0	0	0
413	ECC	0	6	3	0	0	6	4	0
414	CON	0	0	0	0	0	0	0	0
415	ECC	0	0	2	0	0	0	1	0
418	CON	0	0	0	0	0	0	0	0
419	ECC	0	20	15	15	0	20	15	15
420	CON	0	0	0	0	0	0	3	0
421	CON	0	1	0	0	0	0	0	0
423	ECC	2	3	5	12	2	4	4	12
424	ECC	0	7	25	40	0	2	25	25
428	ECC	0	5	20	5	0	10	25	10
432	CON	0	5	0	0	0	10	10	0
436	ECC	0	1	20	30	0	1	20	30
438	CON	0	0	0	0	0	0	0	0
439	CON	0	0	0	1	0	0	0	1
440	ECC	0	15	5	5	0	12	5	5
443	CON	0	0	0	0	0	5	5	0
444	ECC	0	5	40	40	0	5	30	30
445	CON	0	5	0	0	0	0	0	0
446	CON	0	0	0	0	0	0	2	1
448	ECC	0	0	0	0	0	0	0	0
449	ECC	0	1	0	5	0	0	1	7
452	CON	0	3	3	4	0	3	4	2
475	TRE	0	3	50	30	0	3	40	25
519	TRE	0	5	60	70	0	5	70	75
520	TRE	0	0	50	5	0	0	40	2
522	TRE	0	0	12	20	0	0	12	20
529	TRE	0	5	5	10	0	10	0	13
530	TRE	0	6	0	0	0	5	0	0
540	TRE	0	5	8	5	0	5	20	15
545	TRE	0	0	0	3	0	0	0	4
569	TRE	0	10	6	0	0	15	10	2
570	TRE	0	10	0	0	0	7	0	0
571	TRE	0	5	0	0	0	5	0	0
590	TRE	0	0	10	0	0	0	0	0
591	TRE	0	3	2	2	0	4	2	4

DOMS walking right and left hamstring test.

Subject	Group	Walking Rt. Ham 0 h	Walking Rt. Ham 1 h	Walking Rt. Ham 24 h	Walking Rt. Ham 48 h	Walking Lt. Ham 0 h	Walking Lt. Ham 1 h	Walking Lt. Ham 24 h	Walking Lt. Ham 48 h
402	CON	0	0	0	0	0	0	0	0
403	CON	1	3	1	1	1	3	1	1
405	ECC	0	5	2	3	0	5	2	3
406	ECC	3	6	25	35	0	6	20	30
407	CON	0	2	0	0	0	2	0	0
408	ECC	0	0	2	10	0	0	2	15
409	ECC	0	0	0	10	0	0	0	5
411	CON	0	0	10	0	0	0	10	0
413	ECC	0	7	6	5	0	6	6	3
414	CON	0	0	0	0	0	0	0	0
415	ECC	0	1	1	15	0	1	0	10
418	CON	0	0	0	1	0	0	0	1
419	ECC	0	5	5	10	0	5	5	15
420	CON	0	5	0	0	0	3	2	0
421	CON	0	0	0	0	1	0	0	0
423	ECC	2	6	4	7	4	10	4	10
424	ECC	0	10	20	20	3	0	25	15
428	ECC	0	5	15	20	0	10	20	27
432	CON	0	0	0	5	0	0	10	0
436	ECC	0	1	20	30	0	1	0	30
438	CON	0	0	0	0	0	0	1	2
439	CON	0	0	0	0	0	0	0	0
440	ECC	0	5	5	10	0	5	5	10
443	CON	0	0	0	0	0	0	0	0
444	ECC	0	10	20	30	0	10	20	30
445	CON	0	0	0	0	0	0	0	0
446	CON	0	0	0	0	0	0	1	0
448	ECC	0	0	0	0	0	0	0	0
449	ECC	0	0	0	6	0	0	0	8
452	CON	0	5	4	3	0	5	5	2
475	TRE	0	3	40	25	0	5	40	0
519	TRE	0	7	50	50	0	7	50	50
520	TRE	0	0	10	0	0	0	20	0
522	TRE	0	0	15	20	0	0	15	20
529	TRE	0	10	10	15	0	5	5	18
530	TRE	0	6	0	0	0	5	0	0
540	TRE	0	8	10	30	0	7	15	40
545	TRE	0	2	2	6	0	1	2	5
569	TRE	0	3	0	0	0	7	3	0
570	TRE	0	0	0	10	0	0	0	15
571	TRE	0	5	10	20	0	5	10	10
590	TRE	0	0	25	35	0	0	25	35
591	TRE	0	1	3	1	0	1	3	2

DOMS lengthening of the right and left quadriceps test.

Subject	Group	Length Rt. Quad 0 h	Length Rt. Quad 1 h	Length Rt. Quad 24 h	Length Rt. Quad 48 h	Length Lt. Quad 0 h	Length Lt. Quad 1 h	Length Lt. Quad 24 h	Length Lt. Quad 48 h
402	CON	0	0	0	0	0	0	0	0
403	CON	0	0	0	1	0	0	0	1
405	ECC	1	2	2	4	1	2	2	6
406	ECC	0	15	30	40	0	15	35	42
407	CON	0	0	2	0	0	0	2	0
408	ECC	5	5	15	25	5	5	20	25
409	ECC	0	0	25	30	0	0	25	30
411	CON	0	0	0	0	0	0	0	0
413	ECC	0	8	3	2	0	7	3	1
414	CON	0	2	0	0	0	1	0	0
415	ECC	0	0	5	5	0	0	3	5
418	CON	0	0	0	0	0	0	0	0
419	ECC	5	20	15	20	5	15	20	20
420	CON	3	3	0	2	3	0	0	1
421	CON	0	0	0	0	0	0	1	0
423	ECC	0	6	10	15	0	8	12	18
424	ECC	0	5	35	50	0	0	20	35
428	ECC	0	5	30	10	0	5	35	25
432	CON	5	10	10	5	10	15	20	5
436	ECC	0	1	10	30	0	1	10	35
438	CON	0	0	0	0	0	0	0	1
439	CON	0	0	0	1	0	0	0	2
440	ECC	0	5	5	7	0	5	5	5
443	CON	0	5	0	0	0	5	0	0
444	ECC	0	10	40	40	0	10	40	40
445	CON	0	5	0	0	0	0	0	0
446	CON	2	0	5	4	1	1	2	1
448	ECC	0	0	6	20	0	0	6	20
449	ECC	0	0	1	2	0	0	1	4
452	CON	5	3	6	6	5	3	8	4
475	TRE	0	3	70	85	0	4	80	60
519	TRE	1	8	80	85	1	7	70	80
520	TRE	0	1	65	14	1	2	50	4
522	TRE	0	0	12	20	0	0	12	20
529	TRE	0	0	0	7	0	5	5	10
530	TRE	0	6	2	2	0	5	3	3
540	TRE	2	10	20	20	2	10	30	20
545	TRE	0	1	5	8	0	1	5	6
569	TRE	3	5	0	0	0	10	3	5
570	TRE	1	5	0	8	1	0	0	12
571	TRE	0	5	10	5	0	3	10	5
590	TRE	2	0	10	40	2	0	0	40
591	TRE	0	0	1	0	0	1	2	2

Weight lifted by subjects in pounds during 1 RM testing and exercise session.

Weight lifted by subjects in pounds during 1 RM testing and exercise session.

Subject	Group	Leg Ext. 1 RM (one leg)	Calc. Two Legged Ext. 1 RM[1]	Leg Ext. Work Set[2]	Leg Curl 1 RM (one leg)	Calc. Two Legged Curl 1 RM[1]	Leg Curl Work Set[2]
402	CON	170	340	255	110	220	165
403	CON	90	180	135	45	90	67.5
405	ECC	110	220	165	90	180	135
406	ECC	150	300	225	100	200	150
407	CON	100	200	150	45	90	67.5
408	ECC	160	320	240	120	240	180
409	ECC	140	280	210	75	150	112.5
411	CON	160	320	240	110	220	165
413	ECC	140	280	210	135	270	202.5
414	CON	70	140	105	50	100	75
415	ECC	150	300	225	90	180	135
418	CON	130	260	195	110	220	165
419	ECC	160	320	240	100	200	150
420	CON	90	180	135	70	140	105
421	CON	90	180	135	60	120	90
423	ECC	110	220	165	70	140	105
424	ECC	80	160	120	60	120	90
428	ECC	90	180	135	70	140	105
432	CON	132.5	265	198.75	90	180	135
436	ECC	120	240	180	70	140	105
438	CON	105	210	157.5	60	120	90
439	CON	80	160	120	52.5	105	78.75
440	ECC	135	270	202.5	110	220	165
443	CON	150	300	225	105	210	157.5
444	ECC	110	220	165	75	150	112.5
445	CON	95	190	142.5	60	120	90
446	CON	110	220	165	80	160	120
448	ECC	95	190	142.5	55	110	82.5
449	ECC	85	170	127.5	60	120	90
452	CON	150	300	225	105	210	157.5
475	TRE	105	210	157.5	70	140.00	105
519	TRE	120	240	180	70	140	105
520	TRE	65	130	97.5	45	90	67.5
522	TRE	105	210	157.5	65	130	97.5
529	TRE	65	130	97.5	55	110	82.5
530	TRE	70	140	105	70	140	105
540	TRE	120	240	180	105	210	157.5
545	TRE	50	100	75	55	110	82.5
569	TRE	55	110	82.5	45	90	67.5
570	TRE	95	190	142.5	80	160	120
571	TRE	80	160	120	60	120	90
590	TRE	85	170	127.5	80	160	120
591	TRE	120	240	180	90	180	135

[1] Values for two legged 1 RM were calculated by doubling single leg 1 RM.
[2] Working set was calculated by multiplying calculated two legged 1 RM by 0.75.

Subject baseline heart rate (HR) and blood pressure readings.

Resting HR[1]				Resting SBP[2]				Resting DBP[3]		
Subject	**Group**	**Baseline**		**Subject**	**Group**	**Baseline**		**Subject**	**Group**	**Baseline**
402	CON	66		402	CON	128		402	CON	72
403	CON	74		403	CON	110		403	CON	84
405	ECC	76		405	ECC	126		405	ECC	80
406	ECC	64		406	ECC	118		406	ECC	68
407	CON	83		407	CON	120		407	CON	78
408	ECC	68		408	ECC	132		408	ECC	84
409	ECC	72		409	ECC	120		409	ECC	70
411	CON	110		411	CON	136		411	CON	100
413	ECC	68		413	ECC	124		413	ECC	80
414	CON	74		414	CON	148		414	CON	86
415	ECC	76		415	ECC	98		415	ECC	56
418	CON	78		418	CON	110		418	CON	74
419	ECC	76		419	ECC	126		419	ECC	80
420	CON	81		420	CON	124		420	CON	60
421	CON	56		421	CON	118		421	CON	70
423	ECC	78		423	ECC	138		423	ECC	76
424	ECC	74		424	ECC	96		424	ECC	60
428	ECC	71		428	ECC	100		428	ECC	74
432	CON	92		432	CON	110		432	CON	74
436	ECC	80		436	ECC	116		436	ECC	74
438	CON	86		438	CON	106		438	CON	72
439	CON	75		439	CON	98		439	CON	70
440	ECC	68		440	ECC	116		440	ECC	80
443	CON	64		443	CON	120		443	CON	70
444	ECC	74		444	ECC	102		444	ECC	76
445	CON	86		445	CON	120		445	CON	74
446	CON	81		446	CON	138		446	CON	80
448	ECC	75		448	ECC	132		448	ECC	78
449	ECC	64		449	ECC	130		449	ECC	78
452	CON	55		452	CON	118		452	CON	70
475	TRE	80		475	TRE	138		475	TRE	92
519	TRE	72		519	TRE	122		519	TRE	82
520	TRE	64		520	TRE	105		520	TRE	64
522	TRE	74		522	TRE	100		522	TRE	66
529	TRE	76		529	TRE	114		529	TRE	70
530	TRE	68		530	TRE	100		530	TRE	80
540	TRE	64		540	TRE	118		540	TRE	68
545	TRE	80		545	TRE	120		545	TRE	68
569	TRE	56		569	TRE	110		569	TRE	66
570	TRE	78		570	TRE	122		570	TRE	78
571	TRE	66		571	TRE	128		571	TRE	78
590	TRE	66		590	TRE	119		590	TRE	80
591	TRE	56		591	TRE	119		591	TRE	84

1) HR-Heart rate; 2) SBP- Systolic blood pressure; 3) DBP - Diastolic blood pressure

APPENDIX I:

STATISTICAL RESULTS
ANOVA

ANOVA table of total adiponectin (ng/mL).

Source	df	F	P-value
Group	2	0.398	0.674
Time	3	13.253	0.008
Group x Time	6	2.5	0.027

ANOVA table of HMWA (ng/mL).

Source	df	F	P-value
Group	2	0.693	0.506
Time	3	0.349	0.711
Group x Time	6	0.836	0.509

ANOVA table of QUICKI.

Source	df	F	P-value
Group	2	4.581	0.044
Time	3	0.209	0.747
Group x Time	6	1.221	0.556

ANOVA table of insulin (uIU/mL).

Source	df	F	P-value
Group	2	1.871	0.167
Time	3	0.351	0.788
Group x Time	6	0.901	0.496

ANOVA table of glucose (mg/dL).

Source	df	F	P-value
Group	2	3.914	0.028
Time	3	1.899	0.133
Group x Time	6	0.951	0.462

ANOVA table of total adiponectin based on gender.

Source	df	F	P-value
Group	1	5.221	0.028
Time	3	12.160	0.000
Group x Time	3	1.172	0.323

ANOVA table of HMWA based on gender.

Source	df	F	P-value
Group	1	4.581	0.038
Time	3	0.209	0.890
Group x Time	3	1.221	0.276

ANOVA table of HMWA based on gender.

Source	df	F	P-value
Group	2	4.581	0.038
Time	3	0.209	0.890
Group x Time	6	1.221	0.276

APPENDIX J:

STATISTICAL RESULTS
POST HOC

Dependent Variable	Group (I)	Group (J)	Mean difference (I-J)	Std. Error	Sig.
Total Adiponectin 0 h	TRE	CON	1.69405	1.43337	0.471
		ECC	0.79205	1.43337	0.846
	CON	TRE	-1.69405	1.43337	0.471
		ECC	-0.90200	1.38123	0.792
Total Adiponectin 1 h	TRE	CON	0.13415	1.69463	0.997
		ECC	0.81015	1.69463	0.882
	CON	TRE	-0.13415	1.69463	0.997
		ECC	0.67600	1.63299	0.910
Total Adiponectin 24 h	TRE	CON	1.02292	1.43595	0.758
		ECC	0.43159	1.43595	0.951
	CON	TRE	-1.02292	1.43595	0.758
		ECC	-0.59133	1.38372	0.904
Total Adiponectin 48 h	TRE	CON	1.03103	1.41048	0.747
		ECC	0.84636	1.41048	0.821
	CON	TRE	-1.03103	1.41048	0.747
		ECC	-0.18467	1.35917	0.990
Total Adiponectin Avg.	TRE	CON	0.9705	1.44898	0.782
		ECC	0.7200	1.44898	0.873
	CON	TRE	-0.9705	1.44898	0.782
		ECC	-0.2505	1.39627	0.982
There is no significant difference.					

Dependent Variable	Group (I)	Group (J)	Mean difference (I-J)	Std. Error	Sig.
HMWA 0 h	TRE	CON	5.17185	4.92110	0.063
		ECC	-0.2949	4.92110	0.804
	CON	TRE	-5.17185	4.92110	0550
		ECC	-6.10133	4.74209	0.411
HMWA 1 h	TRE	CON	1.59769	4.17596	0.923
		ECC	-3.11897	4.17596	0.737
	CON	TRE	-1.59769	4.17596	0.923
		ECC	-4.71667	4.02405	0.476
HMWA 24 h	TRE	CON	3.79938	4.57235	0.686
		ECC	0.00272	4.57235	1.000
	CON	TRE	-3.79938	4.57235	0.686
		ECC	0.00272	4.40603	0.667
HMWA 48 h	TRE	CON	2.85231	4.38209	0.793
		ECC	-1.63636	4.38209	0.926
	CON	TRE	-2.85231	4.38209	0.793
		ECC	-4.48867	4.22269	0.542
HMWA Avg.	TRE	CON	3.3553	4.43865	0.732
		ECC	-1.4205	4.43865	0.945
	CON	TRE	-3.3553	4.43865	0.732
		ECC	-4.7758	4.27719	0.510
There is no significant difference.					

Dependent Variable	Group (I)	Group (J)	Mean difference (I-J)	Std. Error	Sig.
Insulin 0 h	TRE	CON	-4.21405	2.34232	0.183
		ECC	-1.18005	2.34232	0.870
	CON	TRE	4.21405	2.34232	0.183
		ECC	3.03400	2.25712	0.380
Insulin 1 h	TRE	CON	-2.19482	2.43286	0.642
		ECC	-0.72415	2.43286	0.952
	CON	TRE	2.19482	2.43286	0.642
		ECC	1.47067	2.34436	0.806
Insulin 24 h	TRE	CON	-3.31072	1.90040	0.202
		ECC	-1.010405	1.83127	0.429
	CON	TRE	3.31072	1.90040	0.855
		ECC	2.29667	1.83127	0.429
Insulin 48 h	TRE	CON	-5.72692*	2.38308	0.050
		ECC	-2.27359	2.38308	0.610
	CON	TRE	5.72692	2.38308	0.054
		ECC	3.45333	2.29639	0.300
Insulin	TRE	CON	-3.8616	2.05152	0.157
		ECC	-1.2980	2.05152	0.803
	CON	TRE	3.8616	2.05152	0.157
		ECC	2.5637	1.97689	0.405

*The mean difference is at the 0.05 level.

Dependent Variable	Group (I)	Group (J)	Mean difference (I-J)	Std. Error	Sig.
Glucose 0 h	TRE	CON	-8.1790	4.00018	0.115
		ECC	-10.8324*	4.00018	0.026
	CON	TRE	8.1790	4.00018	0.115
		ECC	-2.6533	3.85467	0.772
Glucose 1 h	TRE	CON	-8.1790	4.00018	0.115
		ECC	-10.8324*	4.00018	0.026
	CON	TRE	8.1790	4.00018	0.115
		ECC	-2.6533	3.85467	0.772
Glucose 24 h	TRE	CON	-8.1790	4.00018	0.115
		ECC	-10.8324*	4.00018	0.026
	CON	TRE	8.1790	4.00018	0.115
		ECC	-2.6533	3.85467	0.772
Glucose 48 h	TRE	CON	-8.1790	4.00018	0.115
		ECC	-10.8324*	4.00018	0.026
	CON	TRE	8.1790	4.00018	0.115
		ECC	-2.6533	3.85467	0.772
Glucose	TRE	CON	-8.1790	4.00018	0.115
		ECC	-10.8324*	4.00018	0.026
	CON	TRE	8.1790	4.00018	0.115
		ECC	-2.6533	3.85467	0.772

*The mean difference is at the 0.05 level.

Dependent Variable	Group (I)	Group (J)	Mean difference (I-J)	Std. Error	Sig.
QUICKI 0 h	TRE	CON	0.03410	4.00018	0.115
		ECC	0.03101	4.00018	0.026
	CON	TRE	-0.03410	4.00018	0.115
		ECC	-0.00309	3.85467	0.772
QUICKI 1 h	TRE	CON	0.02866	4.00018	0.115
		ECC	0.03318	4.00018	0.026
	CON	TRE	-0.02866	4.00018	0.115
		ECC	0.00452	3.85467	0.772
QUICKI 24 h	TRE	CON	0.02901	4.00018	0.115
		ECC	0.01935	4.00018	0.026
	CON	TRE	-0.02901	4.00018	0.115
		ECC	-0.00965	3.85467	0.772
QUICKI 48 h	TRE	CON	0.03933*	4.00018	0.115
		ECC	0.03414	4.00018	0.026
	CON	TRE	-0.03933*	4.00018	0.115
		ECC	-0.00519	3.85467	0.772
*The mean difference is at the 0.05 level.					

Changes from baseline.					
Dependent Variable	**Group (I)**	**Group (J)**	**Mean difference (I-J)**	**Std. Error**	**Sig.**
Total adiponectin 1 h	TRE	CON	-1.55990*	0.64061	0.050
		ECC	-0.1810	0.64061	1.000
	CON	TRE	-1.55990*	0.64061	0.050
		ECC	-0.57800*	0.61731	0.038
Total Adiponectin 24 h	TRE	CON	-0.67113	0.50477	0.387
		ECC	-0.36046	0.50477	0.757
	CON	TRE	0.67113	0.50477	0.387
		ECC	0.31067	0.48641	0.800
Total Adiponectin 48 h	TRE	CON	-0.66303	0.62215	0.541
		ECC	0.05431	0.62215	0.996
	CON	TRE	0.66303	0.62215	0.541
		ECC	0.71733	0.59952	0.462
*The mean difference is at the 0.05 level.					

Changes from baseline					
Dependent Variable	**Group (I)**	**Group (J)**	**Mean difference (I-J)**	**Std. Error**	**Sig.**
HMWA 1 h	TRE	CON	-3.5742	1.85076	0.143
		ECC	-2.1895	1.85076	0.470
	CON	TRE	3.5748	1.85076	0.143
		ECC	1.3847	1.78344	0.720
HMWA 24 h	TRE	CON	-1.3725	0.91619	0.303
		ECC	0.9322	0.91619	0.570
	CON	TRE	1.3725	0.91619	0.303
		ECC	2.3047*	0.88286	0.033
HMWA 48 h	TRE	CON	-2.3195	1.06292	0.087
		ECC	-0.7069	1.06292	0.785
	CON	TRE	2.3195	1.06292	0.087
		ECC	1.6127	1.02425	0.268
*The mean difference is at the 0.05 level.					

Changes from baseline					
Dependent Variable	**Group (I)**	**Group (J)**	**Mean difference (I-J)**	**Std. Error**	**Sig.**
Insulin 1 h	TRE	CON	2.0087	1.58575	0.422
		ECC	0.4487	1.58575	0.957
	CON	TRE	-2.0087	1.58575	0.422
		ECC	-1.5600	1.52807	0.568
Insulin 24 h	TRE	CON	0.9128	1.73799	0.859
		ECC	0.1795	1.73799	0.994
	CON	TRE	-0.9128	1.73799	0.859
		ECC	-0.7333	1.67477	0.900
Insulin 48 h	TRE	CON	-1.5174	1.86044	0.696
		ECC	1.0974	1.86044	0.826
	CON	TRE	1.5174	1.86044	0.696
		ECC	0.4200	1.79276	0.970
There is no significant difference.					

Changes from baseline					
Dependent Variable	**Group (I)**	**Group (J)**	**Mean difference (I-J)**	**Std. Error**	**Sig.**
Glucose 1 h	TRE	CON	2.5179	2.67669	0.618
		ECC	1.4113	2.67669	0.858
	CON	TRE	-2.5179	2.67669	0.618
		ECC	-1.1067	2.57933	0.904
Glucose 24 h	TRE	CON	-0.7636	3.39281	0.972
		ECC	-2.0969	3.39281	0.811
	CON	TRE	0.7636	3.39281	0.972
		ECC	-1.3333	3.26940	0.913
Glucose 48 h	TRE	CON	-4.2231	3.35243	0.426
		ECC	-3.2697	3.35243	0.597
	CON	TRE	4.2231	3.35243	0.426
		ECC	0.9533	3.23048	0.953
There is no significant difference.					

APPENDIX K:

RECRUITMENT FORMS

Table of Contents

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 a weight training program in a supervised, private setting in the Exercise Physiology Lab. Study will consist of a single training session. Participants will receive blood analysis, body composition and muscular strength assessments. Participants will be compensated. If you are interested in participating, please contact the Exercise Physiology Program, 106 McKee Gym, via email umchesexphys@missouri.edu.

PARTICIPANTS NEEDED FOR WEIGHT TRAINING STUDY

<u>NEEDED:</u> 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 Session
- Strength Assessment
- Body Fat Analysis
- Blood Analysis

Contact: Exercise Physiology Program
Dept. of Nutrition & Exercise Physiology

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Are you overweight?

Would you like to get individual exercise programs from professionals?

Contact:
Exercise Physiology Program
Dept. of Nutrition & Exercise Physiology
106 McKee Gym
Email: umchesexphys@missouri.edu
573-882-8191

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umchesexphys@missouri.edu

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 2-3 weeks. You will undergo some initial testing including measurements of body fat and blood pressure. You will be assigned to a resistance training group and will then participate in a single sessions of resistance exercise. Your blood will be drawn and your muscular soreness and strength will be assessed on the day of exercise and two days following the day of exercise.

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 months, 1 wk, 3 yr).

3. Have you participated in a formal diet program within the last 3 months? 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 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,
Ryan Puck
Graduate Research Assistant
Exercise Physiology Program
106 McKee Gym
University of Missouri-Columbia
882-8191