NEUROENDOCRINE AND PERFORMANCE RESPONSES TO ECCENTRIC-ENHANCED RESISTANCE EXERCISE

By

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This work is dedicated to my mother, Julie Yarrow. Thanks for being incredibly supportive and always believing in me. I love you very much.

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Cochair: Paul A. Borsa
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Reduced skeletal muscle strength and/or mass are associated reduced mobility, increased injury risk, a loss of functional independence, and an increased risk for hypokinetic diseases. Resistance training may improve both muscle strength and mass, by modulating neuroendocrine factors known to increase protein synthesis. The purpose of this study was to evaluate the neuroendocrine, metabolic, and muscle performance responses to traditional and eccentric-*enhanced* progressive resistance training, in previously untrained, college-age men. Participants completed a five-week traditional or eccentric-*enhanced* resistance training intervention. Chest and leg muscular strength and endurance were assessed before and after the training intervention. Blood samples acquired at rest and following an acute exercise session, both before (untrained) and after (trained) the training intervention, were assessed for growth hormone, total testosterone, bioavailable testosterone, and lactate concentrations. Blood lactate accumulation was greater following eccentric-*enhanced*, compared to traditional resistance training, in the untrained state, but not the trained state. Resting total testosterone concentrations did not change in either group, whereas resting bioavailable testosterone concentrations were lower in the trained state, compared to the untrained state in both groups. Post-exercise serum testosterone concentrations remained unchanged in the untrained state, but increased in the trained state in both groups. Post-exercise bioavailable testosterone concentrations increased similarly between groups, both before and after the training intervention. Post-exercise serum growth hormone concentrations increased in both the trained and untrained state in both groups. Absolute muscular strength (1RM) increased similarly between groups; however, relative strength (1RM x body mass-1 and 1RM x lean body mass-1) improvements were greater in the traditional resistance training group for the squat exercise, but not the chest press. Muscular endurance (total work) increased similarly between groups. This study suggests that both traditional and eccentric-*enhanced* resistance training result in similar neuroendocrine and performance responses during the early phase of resistance exercise, in previously untrained, college-age men.

CHAPTER 1
INTRODUCTION

Significance

Skeletal muscle atrophy, reduced strength, and increased muscular fatigue are associated with the aging process. Interventions involving resistance exercise have been shown to promote muscle hypertrophy, increase strength, and decrease fatigue in both young and elderly populations.[65, 104] Traditional resistance exercise is performed with an identical load during both the concentric (shortening) muscle contraction and eccentric (lengthening) muscle action. Eccentric-*enhanced* weight training is an alternative form of resistance exercise performed by increasing the load during the eccentric muscle action. In healthy populations, the majority of studies report that eccentric-*enhanced* training is superior for developing muscular strength and skeletal muscle mass, compared to traditional resistance exercise.[25, 51, 86, 87, 95, 118] However, the mechanism(s) underlying the accentuated skeletal muscle adaptations following eccentric-*enhanced* resistance exercise remain unclear, but are likely related to enhanced anabolic processes.

Increased anabolic hormone concentrations (growth hormone, total testosterone, and bioavailable testosterone), at rest and acutely following resistance exercise, are associated with the skeletal muscle adaptation process.[113] It is possible that the anabolic hormone responses following eccentric-*enhanced* resistance training may be relatively higher compared to traditional resistance training, thus indicating a possible mechanism for the accentuated muscular strength and skeletal muscle mass results accompanying eccentric-*enhanced* resistance training. Therefore, the objective of this study was to compare specific neuroendocrine, metabolic, and muscle performance responses to traditional and eccentric-*enhanced* resistance training.

Specific Aims and Hypotheses

Specific Aim #1

The first specific aim is to compare the post-exercise concentrations of whole-blood lactate and serum total testosterone, bioavailable testosterone, and growth hormone concentrations following a single bout of eccentric-*enhanced* resistance exercise to the post-exercise concentrations following a single bout of traditional resistance exercise.

Hypothesis #1

The post-exercise concentrations of serum total testosterone, bioavailable testosterone, and growth hormone will be greater following the eccentric-*enhanced* resistance exercise bout compared to the concentrations following the traditional resistance exercise bout, whereas the whole-blood concentration of lactate will be lower following the eccentric-*enhanced* resistance exercise bout compared to the concentrations following the traditional resistance exercise bout. To accomplish this aim, blood was sampled immediately prior to exercise, immediately post exercise, and every 15 minutes for 60 minutes post exercise. Blood was analyzed for lactate, total testosterone, bioavailable testosterone, and growth hormone.

Specific Aim #2

The second specific aim is to compare the post-exercise concentrations of blood lactate, serum total testosterone, bioavailable testosterone, and growth hormone after a single bout of eccentric-*enhanced* or traditional resistance exercise (Exercise Training Session #1) to the post-exercise concentrations obtained in individuals after participation in a five-week eccentric-*enhanced* or traditional resistance exercise intervention (Exercise Training Session #15).

Hypothesis #2

The post-exercise concentrations of whole blood lactate, serum total testosterone, bioavailable testosterone, and growth hormone will be higher following the resistance exercise intervention (Exercise Training Session #15) compared to the post-exercise concentrations obtained after the initial resistance training session (Exercise Training Session #1) in both groups. Further, the post-exercise concentrations of lactate will be lower in the eccentric-*enhanced* group compared to the traditional group at the end of the exercise intervention. Additionally, the total testosterone, bioavailable testosterone, and growth hormone concentrations will be higher in the eccentric-*enhanced* group compared to the traditional group at the end of the intervention. To accomplish this aim, blood was sampled immediately prior to exercise, immediately post exercise, and every 15 minutes for 60 minutes post exercise. Blood was analyzed for lactate, total testosterone, bioavailable testosterone, and growth hormone.

Specific Aim #3

The third specific aim is to compare the resting concentrations of serum total testosterone and bioavailable testosterone in untrained individuals to the resting concentrations in the same individuals following a five-week eccentric-*enhanced* or traditional resistance exercise intervention.

Hypothesis #3

The resting concentrations of serum total and bioavailable testosterone will be higher at the conclusion of a five-week exercise intervention in both groups. Additionally, the resting concentrations of serum total and bioavailable testosterone will be greater following the five-week eccentric-*enhanced* training protocol compared to the traditional resistance training protocol. To accomplish this aim, blood was sampled at rest and at the same time of day at the beginning and end of a five-week exercise intervention. Blood was analyzed for total and bioavailable testosterone.

Specific Aim #4

The fourth specific aim is to compare muscular strength and endurance following a five-week eccentric-*enhanced* resistance exercise intervention to that following a five-week traditional resistance exercise intervention.

Hypothesis #4

Eccentric-*enhanced* resistance training will result in greater muscular strength and muscular endurance than traditional resistance training. To accomplish this aim, subjects will perform a one-repetition maximum (1RM) test (muscular strength) and four sets at 52.5% 1RM (muscular endurance) on both the chest press and squat exercises prior to and after completion of the five-week exercise intervention.

CHAPTER 2
REVIEW OF LITERATURE

Significance

Skeletal muscle atrophy, reduced strength, and increased fatigue are associated with aging[175] and degenerative diseases such as multiple sclerosis[155] and muscular dystrophy.[11] Reduced strength and increased muscular fatigue may limit ambulatory movement and/or increase risk of musculoskeletal injury in frail and fatigued individuals. Participation in progressive resistance exercise increases muscular strength and lean muscle mass and is associated with reduced musculoskeletal injury risk and improved functional capacity in both healthy and at-risk populations.[65, 104]

Traditional, isotonic, resistance exercise involves a concentric (shortening) muscle action and an eccentric (lengthening) muscle action separated by a brief isometric (transition) action.[104] Resistance exercise combining both concentric and eccentric muscle actions has been demonstrated to result in greater strength outcomes than either phase performed separately.[35, 46, 76, 87, 94, 134] When movement velocity is held constant, eccentric muscle actions produce significantly greater force than concentric muscle actions,[97] suggesting that during traditional resistance exercise the eccentric muscle action is underloaded. Alternative forms of resistance exercise such as eccentric-*only*[35, 46, 49, 93, 119, 130, 146, 158, 163] or eccentric-*enhanced* weight training protocols[17, 25, 51, 59, 86, 87, 95, 118, 156] have been proposed as a means of supra-maximally loading skeletal muscle to optimize training adaptations during resistance exercise; however, the effectiveness of such protocols has not been substantiated.

A host of factors may affect skeletal muscle adaptations following resistance exercise including load or intensity, repetition selection, repetition speed, total volume, and rest periods;[104] each of these factors may also affect hormonal[6, 8, 64, 106, 109, 111, 128, 143, 171] and/or metabolic responses[36, 112] following exercise. Acute elevations in serum anabolic hormone concentrations (i.e., total testosterone, bioavailable testosterone, and growth hormone) and metabolic factors (i.e., lactate) during resistance exercise have been shown to, directly or indirectly, influence muscle hypertrophy and performance.[113] Thus, determining serum anabolic hormone concentrations, at rest and following exercise, may provide a theoretical framework to further understand the skeletal muscle adaptation process following eccentric-*enhanced* exercise. The following review discusses eccentric exercise and the anabolic hormone responses underlying the muscular adaptation process.

Eccentric Exercise

Eccentric-*only* resistance exercise is an alternative form of weight training that is typically performed on an isokinetic dynamometer and entails coupled eccentric actions involving antagonist muscle groups (e.g. knee flexors and extensors). Eccentric-*only* resistance training protocols (6-11 weeks) have been shown to result in greater increases in muscular strength compared to concentric-*only* training.[35, 49, 119, 130] The accentuated strength improvements following eccentric-*only* resistance exercise may be due, in part, to a ~40-50% greater maximal workload typically performed during the eccentric phase of exercise.[46] However, some research reports that concentric-*only* training (4-20 weeks) results in similar[93, 158, 163] or greater strength improvements[146] compared to eccentric-*only* training. Additionally, some research demonstrates that the strength adaptations following concentric-*only* and eccentric-*only* resistance training are mode and/or speed specific,[79, 88, 157] suggesting that a variety of factor(s) may affect the skeletal muscle adaptation process.

The energy requirements and metabolic fatigue associated with resistance exercise are of concern when prescribing weight training programs for both healthy and at-risk populations. Metabolic acidosis may contribute to skeletal muscle fatigue during anaerobic exercise,[16] while reduced energy requirements and/or metabolic fatigue during exercise may diminish perceived exertion and result in reductions in overall fatigue. Therefore, evaluating the metabolic responses to eccentric-*only* resistance exercise may provide a possible mechanistic understanding of the underlying factors associated with skeletal muscle fatigue.

A variety of studies have evaluated the energy cost of concentric and eccentric training including cycling and traditional weight training.[2, 3, 20, 30, 31, 45, 119, 129, 159] During resisted eccentric-*only* cycling at similar submaximal loads, the metabolic cost of exercise is 1/6th -1/7th lower than concentric-*only* cycling.[20] The energy requirements during maximal eccentric-*only* cycling (~0.9-1.0 L O_2/min) are reportedly equal to or lower than the energy requirements during concentric-*only* cycling (~1.0-1.5 L O_2/min) despite a 300-700% greater workload performance during eccentric-*only* cycling.[119] Further, Dudley et al.[45] (1991) reported that during traditional resistance training the eccentric action of exercise was responsible for ~14% of the total energy cost, suggesting that the concentric phase of traditional resistance exercise has a higher energy demand. Similarly, the caloric cost of isoinertial (traditional/concentric-eccentric) resistance exercise (3 sets, 8 repetitions leg press) was comparable to the caloric cost of concentric-*only* resistance exercise (86.10 ± 4.83 kcal vs. 87.21 ± 4.60 kcal, $p>0.05$), although significantly greater work was performed during the traditional exercise trial (9955.23 ± 643.10 vs. 6318.15 ± 363.45 J, $p<0.05$).[30] Collectively, these results suggest that the eccentric phase of exercise is less metabolically demanding than the concentric phase.

Metabolic acidosis is associated with skeletal muscle fatigue.[149] A few studies have reported that the lactate responses following maximal eccentric-*only* exercise are lower than the responses following maximal concentric-*only* exercise.[22, 47, 83, 101] Conversely, at least one study has demonstrated no difference in lactate accumulation between concentric and eccentric muscle actions, when loads were held constant.[102] At similar exercise volumes, the lactate and ammonia responses were 3-4 fold lower following an eccentric-*only* (60°· sec^{-1}) muscular endurance test compared to a concentric-*only* (180°· sec^{-1}) one-minute muscular endurance test.[85] Similarly, Hollander et al.[83] (2003) reported an ~5-7 fold greater lactate response following concentric-*only* resistance training compared to eccentric-*only* resistance training (4 sets of 12 reps performed at 60-65% 1RM on 4 exercises). These results suggest that eccentric-*only* exercise produces lower concentrations of lactate and ammonia than an equal volume of concentric exercise.

In summary, it appears that eccentric-*only* resistance training results in similar or greater strength gains than concentric-*only* training. Further, the energy cost and metabolic fatigue associated with eccentric-*only* exercise appear to be less than that during concentric-*only* and traditional resistance training, suggesting that eccentric-*only* exercise may be more metabolically efficient than concentric-*only* and traditional resistance exercise. Therefore, eccentric-*only* exercise may be beneficial to at-risk populations with limited cardiovascular capabilities or those prone to fatigue.

Eccentric-*Enhanced* Exercise

Eccentric-*enhanced* resistance exercise involves a concentric contraction coupled with a supramaximally loaded eccentric action. A variety of methods (e.g. manual resistance) and machines (i.e. isokinetic dynamometers, isoload inertial strength training ergometers, and eccentric-*enhanced* selectorized machines) are capable of providing a supramaximal eccentric overload during resistance exercise.[21, 30, 42, 81, 95] Traditionally, isokinetic dynamometers are used to perform eccentric-*enhanced* resistance exercise; however, limitations exist in isokinetic dynamometry including the inability to perform bilateral exercises and lack of exercise selection. A weight training machine called the Maxout (Myonics Corporation, Metairie, LA) is also capable of providing a supramaximal overload during the eccentric phase of resistance exercise.[17, 95] Additionally, the Maxout can be used with a variety of bilateral multiple-joint exercises, such as the chest press or squat.

Theoretically, supramaximally overloading the eccentric phase of exercise may enhance the muscular strength and hypertrophic responses associated with resistance training. However, it remains unclear whether eccentric-*enhanced* training accentuates the strength outcomes following resistance exercise. Several studies have reported greater increases in muscular strength [51, 86, 87, 95, 118] and skeletal muscle mass [51, 118] following (7 days-11 weeks) eccentric-*enhanced* training compared to traditional resistance training. One study reported significantly greater strength gains for the elbow extensors (+25% eccentric-*enhanced* vs. +10% traditional; $p<0.05$), but not the elbow flexors (+10% eccentric-*enhanced* vs. +10% traditional) following nine weeks of eccentric-*enhanced* training, suggesting that the accentuated muscular adaptations following eccentric-*enhanced* resistance training may be muscle specific.[25] Conversely, two studies reported similar strength gains following (10-12 weeks) eccentric-*enhanced* and traditional resistance training.[17, 59] No studies have reported the effects of eccentric-*enhanced* multiple-joint resistance training (chest press and/or squat) compared to traditional multiple-joint resistance training. Table 1 summarizes the muscular strength results form the published reports on eccentric-*enhanced* resistance training.

The metabolic demand and production of fatiguing metabolites associated with eccentric-*enhanced* resistance training has not been reported. However, when training volume is held constant the eccentric-*enhanced* exercising heart rate response (90 bpm vs. 102 bpm, $p<0.05$), mean arterial pressure (117 mm Hg vs. 132 mm Hg, $p<0.05$), rate pressure product (151 vs. 191, $p<0.05$), and rating of perceived exertion (10 vs. 13, $p<0.05$) are reportedly lower than traditional training, respectively.[86] These results suggest that during eccentric-*enhanced* resistance training the metabolic demand and presence of fatiguing metabolites may be lower than during traditional resistance training; however, this remains to be fully substantiated.

In summary, eccentric-*enhanced* resistance training appears to result in similar or greater strength gains, lower cardiovascular responses, and lower levels of perceived exertion than traditional resistance training. Determining the neuroendocrine and metabolic responses to eccentric-*enhanced* resistance exercise would improve knowledge related to the effects of this form of exercise on muscle metabolism compared to more traditional forms, as well as help explain the greater muscular adaptations associated with eccentric-*enhanced* resistance training

Anabolic Hormone Responses to Resistance Training

Anabolic hormones, including testosterone and growth hormone (GH), have been shown to favorably affect muscle hypertrophy and exercise performance due to their impact on protein synthesis.[38, 92, 113, 161] Traditional resistance training protocols have been shown to acutely stimulate the release of both GH and testosterone in a load[109, 111, 128, 143, 156] and volume[64, 106, 109, 111, 144, 171] dependent manner. It has been suggested that the acute post-exercise elevations of serum anabolic hormone concentrations (i.e. total testosterone, bioavailable testosterone, and growth hormone) enhances the skeletal muscle hypertrophic response to resistance training.[113] Thus, determining the serum anabolic hormone concentrations, following resistance exercise, may provide a basic mechanistic understanding of the skeletal muscle adaptation process, particularly as related to eccentric-*enhanced* training. Further information regarding the neuroendocrine responses to traditional resistance training is presented in several review articles.[38, 113] The following sections will provide a brief overview of the specific metabolic responses of testosterone and GH to resistance exercise.

Testosterone

Testosterone is synthesized from cholesterol and secreted primarily by testicular Leydig cells, in response to a hormonal cascade beginning with the release of gonadotropin-releasing hormone (GnRH) from the hypothalamus.[168] Gonadotropin-releasing hormone stimulates both follicle-stimulating hormone (FSH) and leutenizing hormone (LH) from the anterior pituitary, which exert separate effects on testosterone secretion. Leutenizing hormone directly stimulates testosterone secretion from Leydig cells, whereas FSH upregulates LH receptors in the testis, ultimately leading to increased testosterone release.[168] *In vivo*, testosterone is present in three forms, 1) free (unbound), 2) sex-hormone-binding-globulin (SHBG)-bound, and 3) albumin-bound.[172] Both albumin-bound and free testosterone readily traverse tissue membranes and thus are referred to collectively as bioavailable testosterone.[139] Bioavailable testosterone is

Table 1. Overview of strength outcomes from eccentric-*enhanced* studies

Author Year	Length	Subjects	Training	Test	% Δ Traditional	% Δ ECC-E*nhanced*
Hortobagyi et al (2001)	1 week 7 sessions	SED F n=30	CON 60%, ECC 100-110% 1RM	3RM	+11% ECC* +27% CON*	+27% ECC*† +26% CON *
Hortobagyi et al (2000)	1 week 7 sessions	UNT F n=30	CON 60%, ECC 110% 1RM 5-6 sets, 9-12 reps	3RM	+18% ECC* +43% CON*	+33% ECC*† +43% CON
Friedmann et al (2004)	4 weeks 12 sessions	UNT M n=18	CON 30%, ECC 70% 1RM 3 sets, 25 reps	ISO	Value Not Reported	+5%*
Kaminski et al (1998)	6 weeks 12 sessions	Healthy M n=27	CON 40%, ECC 100% 1RM 2 sets, 8 reps	ECC ISO	Value Not Reported	+37.7%(60º/sec)* † +22%(180º/sec)* †
Brandenburg et al (2002)	9 weeks 25 sessions	TRN M,F n=23	CON 75%, ECC 100-110% 1RM	1RM	+10% EF* +10% EE*	+8% EF* +25% EE*†
Barstow et al (2003)	10 weeks 20 sessions	UNT M n=28	CON 80%, ECC 120% 1RM 1 set, 8-12 reps	1RM CON	95%*	+93%*
Godard et al (1998)	12 weeks 24 sessions	TRN M,F n=39	CON 66%, ECC 100% 1RM 3 sets 6-10 reps	1RM CON	+13.8%	+15.5%

Mean strength differences were calculated or estimated. * Results significantly greater than baseline ($p<0.05$). † Results significantly greater than traditional resistance training ($p<0.05$). Abbreviations: % Δ (percent change in strength), UNT (Untrained), TRN (trained), SED (Sedentary), M (Males), F (Females), ECC (Ecentric), CON (Concentric), ISO (Isokinetic), KE (Knee Extension), KF (Knee Flexion), EE (Elbow Extension), EF (Elbow Flexion).

capable of binding to androgen receptors located in heart, brain, liver, kidney, prostate, bone, and skeletal muscle tissues.[160] Upon binding in skeletal muscle, the androgen-receptor complex 1) is directed to the cell nucleus, 2) attaches to nuclear chromatin, 3) stimulates mRNA transcription, and 4) upregulates protein synthesis; therefore, contributing to skeletal muscle hypertrophy.[160] Conversely, SHBG-bound testosterone cannot cross tissue membranes and therefore, is unable to interact with androgen receptors.[139] Detailed information regarding the effects of testosterone on muscle metabolism has been previously reported.[38, 151, 160, 161]

Growth Hormone

Growth hormone is secreted by the anterior pituitary gland in response to elevated levels of growth hormone releasing hormone (GHRH).[92] Since GH receptors are present in numerous tissues (bone, immune cells, skeletal muscle, fat cells, and liver cells), it has various effects, including: decreasing glucose utilization and glycogen synthesis, increasing protein synthesis, fatty acid utilization, collagen synthesis, nitrogen retention, and amino acid transport into cells, and stimulating cartilage growth.[92, 164] Growth hormone directly affects cellular amino acid uptake and enhances protein synthesis and thus contributes to skeletal muscle hypertrophy.[92] Many of the anabolic effects of GH may also be due to its stimulatory effects on IGF-1 production.[92, 133, 164] Detailed information regarding the effects of GH on muscle metabolism has been previously reported.[92, 133, 164]

Growth Hormone and Testosterone Responses to Resistance Exercise

The GH and testosterone responses to traditional resistance exercise are well characterized. In general, it appears that higher volumes of exercise (i.e. greater number of reps/sets),[64, 82] short rest periods (~1-minute),[109, 111] moderate intensities (8RM-

12RM),[109, 111, 142, 171] and large muscle group exercises (e.g. squats, deadlifts, etc)[75, 108] result in the largest serum GH concentrations. Similarly, higher volumes of exercise,[24, 64, 144] short rest periods,[109, 111] higher intensities (~5RM),[109, 111] and large muscle group exercises[75, 174] result in the largest serum free and/or total testosterone concentrations. Conversely, Ahtiainen et al. have reported that differing rest times (between sets)[6] and exercise intensities[8] do not alter the free and total testosterone responses following resistance exercise; however, the rest times (2-minutes vs. 5-minutes) and exercise intensities (8RM vs. 12RM) reported in these studies were outside the ideal ranges for testosterone release suggested in previous studies,[109, 111] possibly confounding the results.

The use of forced repetitions (i.e. repetitions performed beyond concentric muscle failure with the assistance of a spotter) has been reported to result in a larger GH response than traditional resistance exercise,[7, 8] suggesting that work performed beyond concentric muscular fatigue may enhance the anabolic response to exercise. Eccentric-*enhanced* resistance exercise is an alternative method of performing work beyond concentric muscle fatigue. It is possible that the anabolic hormone responses to eccentric-*enhanced* resistance exercise may be accentuated due to the stimulus of this form of exercise. One study has reported that, at identical workloads, eccentric-*only* resistance exercise results in significantly lower lactate, GH, total testosterone, and free testosterone responses than concentric-*only* resistance exercise; suggesting that the neuroendocrine and metabolic responses to resistance training are less responsive to submaximal eccentric-*only* exercise.[47] However, Kraemer et al. (2001) reported that the GH response following resistance exercise is dependent upon the mode of training and testing. Specifically, subjects were divided into four groups, a 1) concentric-*only* exercise, 2) double volume concentric-*only* exercise, 3) concentric-eccentric exercise, or 4) no exercise (control) group. Following 19-weeks of training subjects performed separate eccentric-*only* and concentric-*only* exercise tests to evaluate the neuroendocrine responses following differing muscle actions. The results of this study demonstrate that the GH responses for the 1) concentric-*only* and 2) double volume concentric groups were ~2-2.5 fold greater following the concentric-*only* exercise test compared to the eccentric-*only* test, whereas the GH response for the 3) concentric-eccentric exercise group was ~70% greater following the eccentric-*only* exercise test, compared to the concentric-*only* test. These results suggest that the GH response following exercise is specific to the mode of training and that the eccentric phase of traditional (concentric-eccentric) resistance training results in the largest GH release.[105] The neuroendocrine and metabolic responses to eccentric-*enhanced* resistance exercise remain to be determined.

Conclusion

Eccentric-*only* resistance exercise results in similar, or greater, strength gains with a lower metabolic demand compared to concentric-*only* exercise. Similarly, eccentric-*enhanced* resistance exercise results in greater muscular strength and skeletal muscle hypertrophy than traditional resistance exercise.[25, 51, 86, 87, 95] While there are no published reports on the neuroendocrine or metabolic responses to eccentric-*enhanced* resistance training, it is possible that eccentric-*enhanced* resistance training may result in accentuated neuroendocrine and/or blunted metabolic responses. Research designed to elucidate the neuroendocrine and metabolic responses to eccentric-*enhanced* resistance exercise would contribute to an improved understanding of the mechanism(s) underlying the muscular strength and hypertrophic responses to resistance exercise.

CHAPTER 3
METHODS

Subjects

Twenty-nine, healthy, college-aged males volunteered for this study. Each participant completed a health history questionnaire (Appendix A), physical activity and dietary questionnaire (Appendix B), and signed an informed consent document approved by the University of Florida Institutional Review Board prior to participating in the study. Prior to data collection, a total of five subjects were removed from this study; four subjects were removed for failure to abide by study protocol and one subject was removed due to an injury unrelated to this study. During the study, two subjects completed the baseline testing/blood acquisition sessions and subsequently asked to be removed from the study due to time constraints. Additionally, blood could not be acquired from two subjects; therefore, a total of twenty subjects completed all portions of this study.

Inclusionary/Exclusionary Criteria

To be included in the study, subjects had to be untrained (no resistance exercise during the previous six months). Subjects were excluded if they 1) had an orthopedic injury that would limit participation, 2) had a metabolic disease, 3) had a dietary intake low in calories, fat, carbohydrates, or protein that could affect hormonal levels,[154] 4) were a competitive athlete or competed in powerlifting or bodybuilding during the previous year, 5) had used any ergogenic aid within the past month, 6) had used nutritional supplements within the past month that may affect hormonal levels (Appendix C), or 7) were taking pharmacological agents that could alter test results such as anabolic steroids or sympathoadrenal drugs. Additionally, during the study subjects were excluded if they missed more than four total exercise training sessions (75% attendance rate) or if they were absent for more three consecutive exercise training sessions.

Experimental Design

For this randomized study, subjects participated in a total of 20 experimental sessions, including three (3) baseline testing, fifteen (15) exercise training, and two (2) follow-up testing sessions (see Figure 1). Prior to the exercise training sessions, subjects were randomly assigned to either the traditional progressive resistance exercise group or an eccentric-*enhanced* progressive exercise group. During each session, subjects performed a 5-minute warm-up at moderate intensity on a stationary bicycle (Monark, Vansbro, Sweden). Following the warm-up, subjects performed both a chest press and squat exercise on the MaxOut exercise machine (Myonics Corporation, Metairie, LA), at pre-determined loads (see section entitled Exercise Training). Three sessions were performed per week, with a minimum of 48 hours separating each session. Dietary recalls were monitored throughout the testing period to ensure all subjects consumed a similar diet on testing days.[154] During the study intervention, subjects were instructed to continue their normal activities and nutrient intakes. Additionally, subjects were asked to abstain from weight lifting not associated with this study.

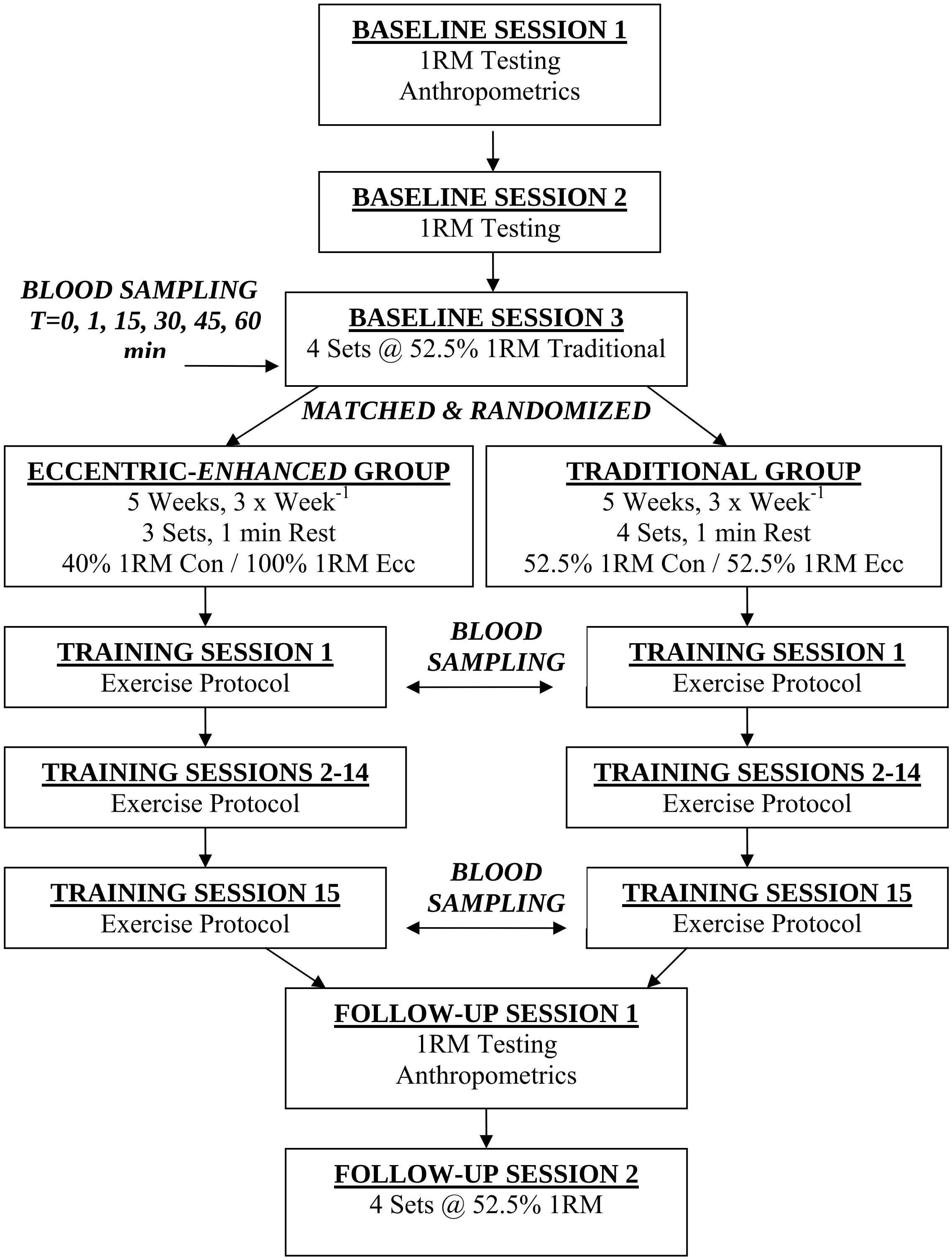

Figure 1. Experimental design. Abbreviations: Con (concentric), Ecc (eccentric).

Baseline Testing

During baseline session 1, subjects were familiarized with the exercise protocol. Familiarization included 1) instruction on proper use of the chest press and squat exercise and 2) practicing the chest press and squat exercises at a submaximal load. Subjects were subsequently asked to perform a 1RM on each exercise (chest press and squat), according to standard protocol.[27] Additionally, subject's height and weight were measured on a medical scale and body density was determined by a 3-site skinfold measure,[91] using Lange calipers (Beta Technology Incorporated, Cambridge, Maryland). Body density was used to estimate body composition.[28] During baseline session 2, subjects performed a 1RM on each exercise, according to standard protocol.[27] During baseline session 3, subjects entered the laboratory, following a 12-hour (overnight) fast, and rested for 10 minutes prior to 10ml (2 teaspoons) blood sample acquisition by a certified phlebotomist. Immediately following the initial blood acquisition, subjects performed four sets of each exercise at 52.5% 1RM; the speed of each repetition was standardized so that the concentric and eccentric actions were each performed for two seconds each. Each set was separated by one minute of rest. Additionally, 10ml blood was acquired at five additional time points, immediately post exercise (t=1), 15 minutes (min) post exercise (t=15), 30 min post exercise (t=30), 45 min post exercise (t=45), and 60 min post exercise (t=60). These time points were selected as both testosterone and GH concentrations peak within 30 min of exercise completion and remain elevated for ~60 min post-exercise.[113]

Exercise Training

During all exercise training sessions, the eccentric-*enhanced* group performed three sets (40% 1RM concentric, 100% 1RM eccentric) of six repetitions each and the traditional group performed four sets (52.5% 1RM concentric, 52.5% 1RM eccentric) of six repetitions each, for each exercise. Training load was increased 5-10 pounds for the subsequent training session when all repetitions were completed with proper form. During training, the traditional group performed an additional set in an attempt to equate exercise volumes between groups. Each repetition was performed at a cadence of two seconds concentric and two seconds eccentric, to account for possible differences in outcome measures due to the speed of movement.[90, 131, 136, 177] Each set was separated by one minute of rest. Additionally, during exercise training sessions 1 and 15, 10ml blood was acquired at six time points, corresponding to the previous protocol. No blood samples were acquired during exercise training sessions 2-14.

Follow-Up Testing

During follow-up session 1, subjects performed a 1RM on both the chest press and squat exercises, according to standard protocol.[27] Additionally, subject's height, weight, and lean body mass were measured, as performed during baseline testing. During follow-up session 2, subjects performed a 1RM on both exercises. Additionally, during follow-up session 2, subjects performed four sets (52.5% 1RM) for both exercises, as performed during baseline testing. The 1RM testing and 52.5% 1RM testing was separated by a 10 minute break, in an effort to offset fatigue.

Dietary Analysis

Subjects were given standard dietary instructions for nutrient intake for the one day prior to blood acquisition. Intake instructions were based on American Heart Association Guidelines (i.e. 50-60% carbohydrate, <30% fat, 10-15% protein).[120] Subjects were asked to complete a three-day dietary record at the onset of the study and one-day dietary records on the day prior to each blood draw (Appendix D). When reporting for blood draws, subjects were asked to refrain from food, drink, alcohol, and caffeine consumption for 12 hours prior to blood collection (i.e. overnight fast). Analysis of total dietary kilocalories and macronutrients consumption was performed using the DietOrganizer 2.2 (MulberrySoft) dietary analysis program.

Sleep Analysis

Subjects were given standard instructions for sleeping on the one day prior to blood acquisition. Instructions were based on the National Sleep Federation recommendations of 7-10 hours per night. Subjects were asked to record their total number of hours slept each night, throughout the study.

Blood Collection

Whole blood was collected by a certified phlebotomist via venipuncture or catheter from an antecubital forearm vein. Blood samples (10mL) were collected immediately before (t=0) and after exercise (t=1, 15, 30, 45, and 60 minutes) into serum tubes with no additives (red top) and plasma tubes with an EDTA additive (pink top). The total volume of blood collected per day was 60 mL. Samples were stored at 4°C until centrifugation. Hematocrit, hemoglobin, and lactate determinations were determined using whole blood and the remaining blood was centrifuged at 3000g for 12 minutes. Serum and plasma samples were separated and stored at -80°C until analyzed. Day-to-day variability in blood parameters was minimized by collecting blood samples during the same time of day (7:00-10:30am) for each subject.

Biochemical Analyses

Hematocrit percent was determined by the microcapillary tube method.[40] Hemoglobin concentration was determined with the Hgb Pro hemoglobin analyzer (ITC, Edison, New Jersey). Whole-blood lactate was measured by the Accusport Lactate Analyzer (Roche Molecular Biochemicals, Mannheim, Germany). Serum aliquots were analyzed for growth hormone (GH), total testosterone, and bioavailable testosterone. Serum growth hormone (GH) was determined by an enzyme-linked immunosorbent assay (ELISA) (Diagnostic Systems Laboratories, Inc., Webster, Texas). Serum total testosterone was determined by enzyme immunoassay (EIA) (Diagnostic Systems Laboratories, Inc., Webster, Texas). Serum bioavailable testosterone was determined by an ammonia sulfate precipitation method.[121] Briefly, a saturated ammonia sulfate/DI water solution was combined with serum (1:1) to induce precipitation of sex-hormone binding globulin. The combined samples were immediately vortexed and stored at room temperature for 10 minutes prior to centrifugation. The supernatant was then analyzed by EIA (Diagnostic Systems Laboratories, Inc., Webster, Texas). All samples were performed in duplicate and in a single run. Serum hormone concentrations were subsequently corrected for plasma volume changes, estimated by hemoconcentration.[40]

Data Analysis

The SPSS 12.0.1 statistical package was used for the statistical analysis. All values are reported as the mean ± SE. Pre- to post-comparisons were performed using a 2 (Groups) x 2 (Time) repeated measures ANOVA. Biochemical markers were compared using 2 (Groups) x 6 (Time) Repeated Measures ANOVAs. When necessary a Tukey's *post hoc* analyses was implemented. Alpha levels for all measurements were set at $p \leq 0.05$.

Sample Size

The hormonal dependent variables in this study are serum growth hormone, total testosterone, and bioavaible testosterone. Of these measures, growth hormone has been reported to be the most responsive to resistance exercise and thus was used for sample size calculations. Standard sample size calculations were used to estimate the number of subjects required[123] and were based on previously reported data (4 sets 12RM squat exercise).[8] The results of the power calculation indicated fourteen subjects (n=7 each group) would provide a power of 80% at an alpha level of 0.05 to detect differences in growth hormone (See Power calculation, Appendix E).

CHAPTER 4
RESULTS

Subjects

Twenty-four previously untrained, college-aged males (21.9 ± 0.8 years), randomized into traditional (n=12) or eccentric-*enhanced* (n=12) groups participated in this study. No significant differences were observed for any demographic measure, between groups (Table 2).

Table 2. Subject characteristics pre and post 5 weeks of resistance training

	TRADITIONAL		ECCENTRIC-*ENHANCED*	
	PRE	POST	PRE	POST
BMI (kg/m^2)	25.9 ± 1.2	25.8 ± 1.1	25.8 ± 1.3	26.2 ± 1.4
Weight (kg)	78.8 ± 2.9	78.5 ± 2.7	81.1 ± 3.0	82.1 ± 3.2
Body Fat %	19.5 ± 2.1	19.9 ± 2.1	19.5 ± 2.5	19.8 ± 2.3

Data are expressed as Mean ± SE.

Biochemical Results

For clarity, the terms untrained and trained will be used to describe the groups at baseline (before) and following the five-week exercise intervention, respectively. At baseline, both groups performed two testing sessions separated by ≥ 48 hours. During session 1 both groups performed a standardized traditional resistance exercise protocol (4 sets x 6 reps; 52.5% 1RM), whereas during session 2, the traditional group performed the standardized traditional protocol and the eccentric-*enhanced* group performed an eccentric-*enhanced* (3 sets x 6 reps; 40% 1RM concentric, 100% 1RM ecccentric) resistance exercise protocol. At the completion of the exercise intervention, subjects again completed a bout of either traditional (4 sets x 6 reps) or eccentric-*enhanced* (3 sets x 6 reps) exercise, utilizing the maximum load completed by the end of the five-week intervention. This study design allowed comparison of the metabolic and neuroendocrine responses between traditional and eccentric-*enhanced* resistance exercise, in both the untrained and trained states. Blood samples were not acquired from two subjects in the traditional group; therefore all biochemical analyses were performed on 22 subjects (n=10 traditional; n=12 eccentric-*enhanced*).

Lactate

Lactate Response to the Standardized Traditional Exercise Protocol in Untrained Men

The (whole-blood) lactate responses after the standardized resistance exercise protocol for both groups prior to the training intervention are presented in Figure 2. Lactate concentrations increased (~250%) immediately after exercise ($p<0.05$) and gradually returned to baseline by 45 minutes post-exercise. No significant differences in lactate concentrations were observed between groups, at any time point.

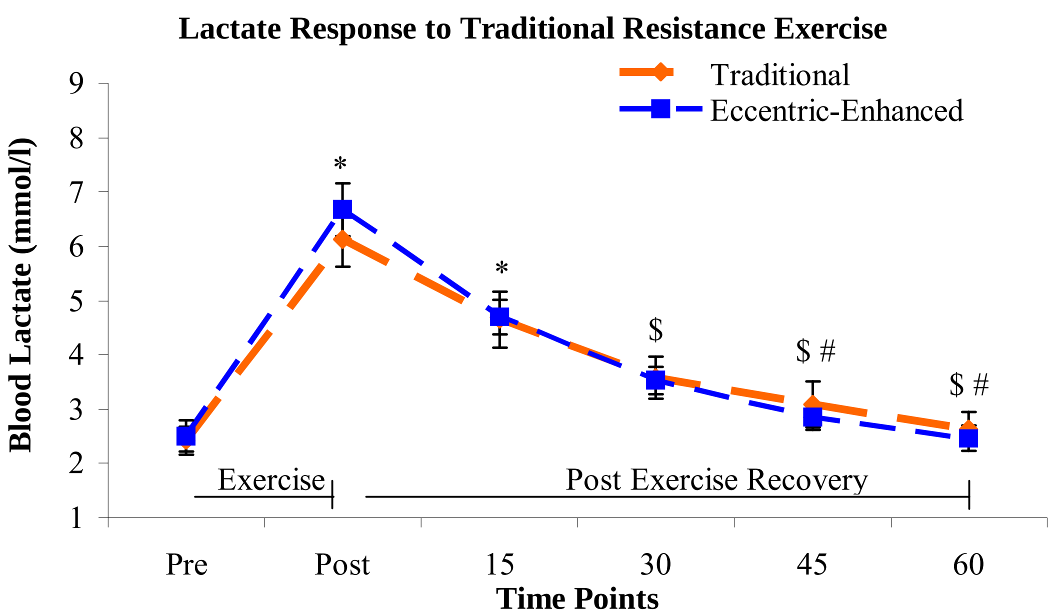

Figure 2. Lactate responses to traditional resistance exercise. * Indicates significantly different than Pre; $ indicates significantly different than Post; # indicates significantly different than 15 min ($p<0.05$). Data are Mean ± SE.

Lactate Responses to Standardized Traditional and Eccentric-*Enhanced* Exercise in the Untrained

Lactate responses following a single bout of traditional and eccentric-*enhanced* resistance exercise protocols performed at baseline are presented in Figure 3. Before exercise, lactate concentrations were similar between groups (~2.5 mmol/l) and increased following exercise, representing 210% and 340% in the traditional and eccentric-*enhanced* groups, respectively ($p<0.05$). During the post-exercise recovery period, lactate gradually returned to baseline within 45 minutes of exercise completion. The immediate post-exercise lactate concentration was greater in the eccentric-*enhanced*, compared to the traditional group (7.8 ±0.4 mmol/l vs. 5.8 ± 0.3 mmol/l, $p<0.05$).

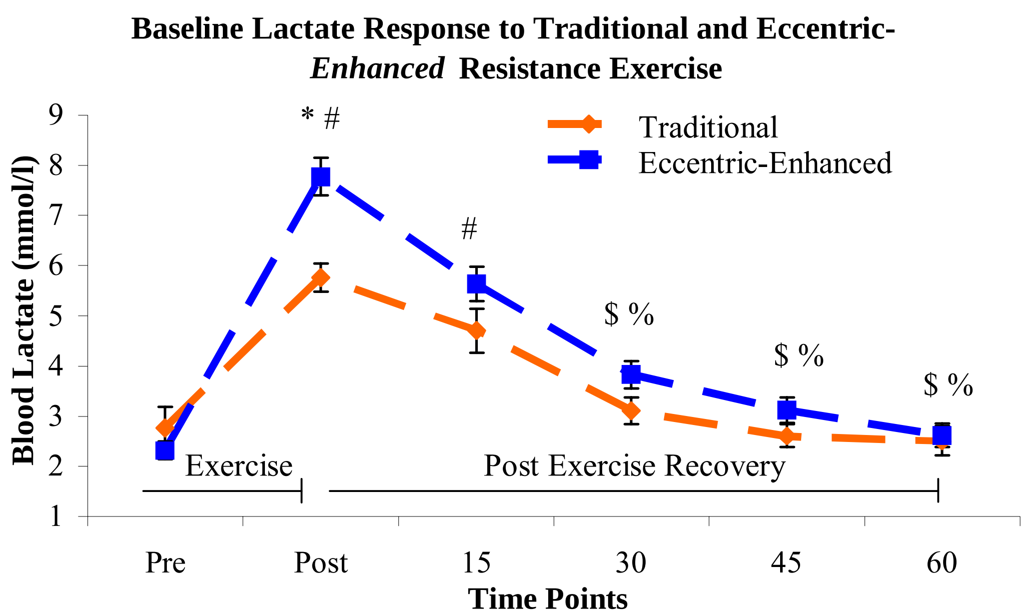

Figure 3. Baseline lactate responses to traditional and eccentric-*enhanced* resistance. * Indicates significant difference between groups; # indicates significant difference from baseline, $ indicates difference from post, % indicates difference from 15 minutes ($p<0.05$). Data are Mean ± SE.

Lactate Response to Standardized Traditional and Eccentric-*Enhanced* Exercise in Trained Men

Following the five-week training intervention, the post-exercise lactate concentrations increased in both the traditional (~420%) and eccentric-*enhanced* (~340%) groups immediately following exercise ($p<0.05$) and gradually returned to baseline within 45 minutes of exercise cessation (Figure 4). No significant differences in lactate concentrations were observed between groups at any time point, including pre- and post-exercise as well as recovery.

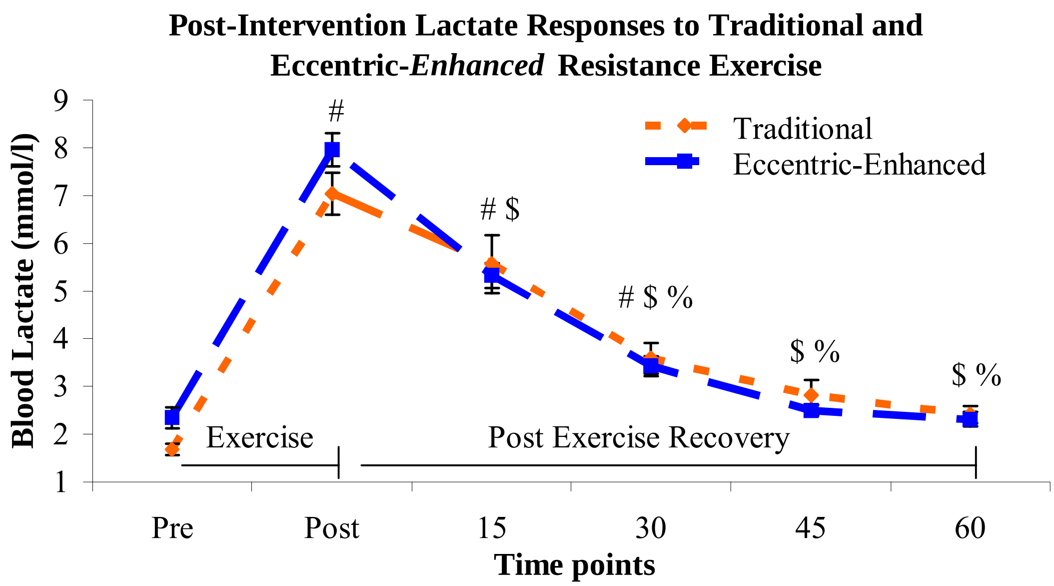

Figure 4. Post-intervention lactate responses to traditional and eccentric-e*nhanced* resistance exercise. # indicates difference from baseline, $ indicates difference from post, % indicates difference from 15 minutes ($p<0.05$). Data are expressed Mean ± SE.

Testosterone

Resting Testosterone

To account for diurnal variation in testosterone secretion, two resting baseline blood samples were acquired 48 hours apart. No significant differences in either total (6.45 ± 0.47 ng/ml session 1 vs. 6.96 ± 0.55 ng/ml session 2) or bioavailable (4.10 ± 0.30

ng/ml session 1 vs. 4.13 ± 0.27 ng/ml) testosterone concentrations were observed on either day; therefore, the average testosterone concentrations were used as the baseline resting value. Resting total serum testosterone concentrations (Figure 5) remained unchanged with training for both groups. However, resting bioavailable testosterone

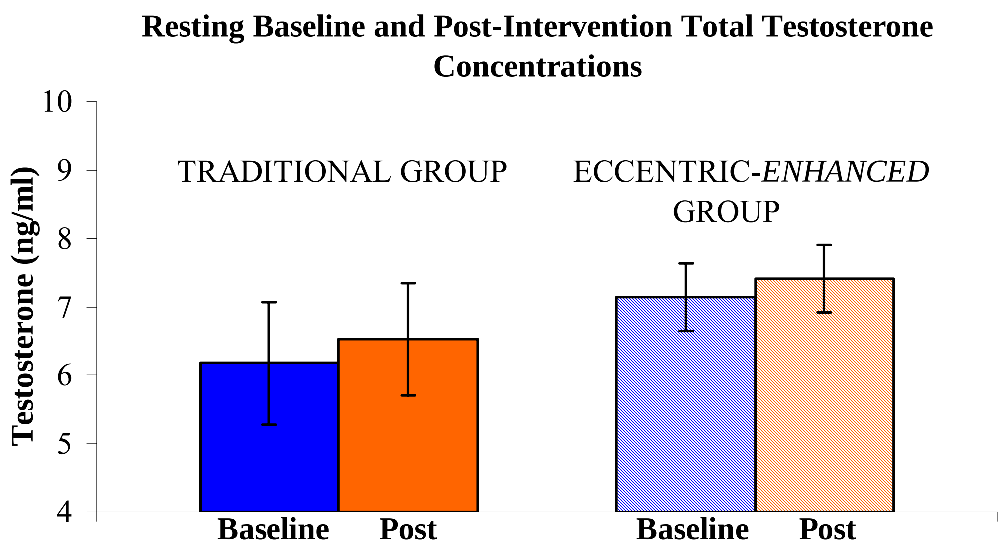

Figure 5. Total serum testosterone before (Baseline) and after (Post) the training intervention. * Indicates a significant difference is present ($p<0.05$). Data are presented as Mean ± SE.

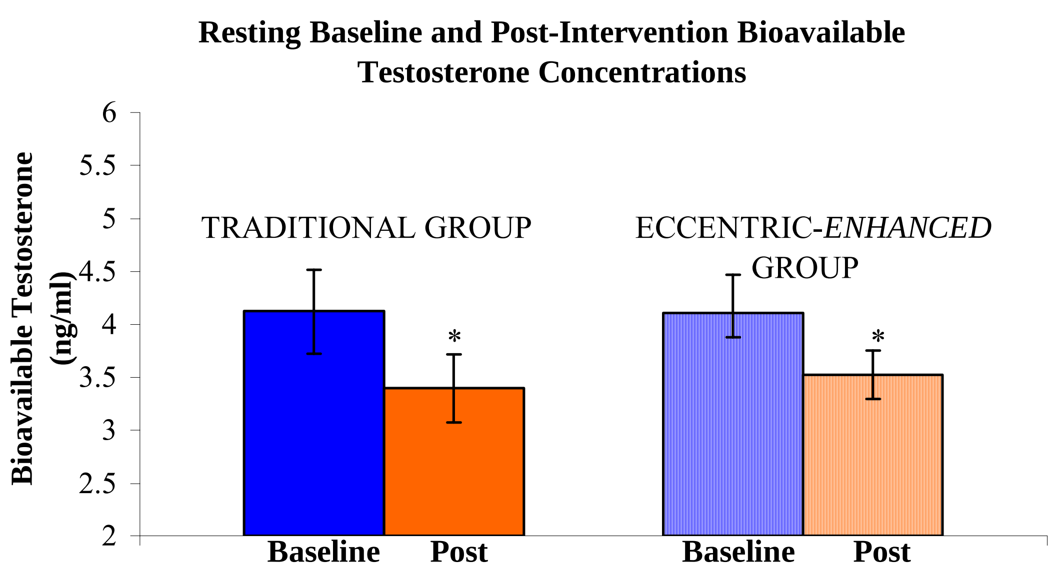

Figure 6. Total bioavailable testosterone before (Baseline) and after (Post) the training intervention. * Indicates a significant difference is present compared with baseline value ($p<0.05$). Data are presented as Mean ± SE.

concentrations (Figure 6) were ~24% lower in both groups following the five-week resistance training intervention ($p<0.05$). Additionally, resting bioavailable testosterone accounted for 61% and 46% of total resting testosterone at baseline and post-intervention in both groups, respectively. No significant differences were observed between groups for either resting total or bioavailable testosterone concentrations, in either the trained or untrained states.

Testosterone Responses to the Standardized Traditional Exercise Protocol in Untrained Men

Following the standardized traditional resistance exercise protocol, the post-exercise total testosterone concentrations (immediately to 30 minutes post) were not significantly different from baseline (Figure 7); however, 45-60 minutes following training the total testosterone concentrations decreased below baseline ($p<0.05$). Similarly, the post-exercise bioavailable testosterone concentrations (immediately to 15 minutes post) were not significantly different from baseline (Figure 8); however 30-60 minutes following training the bioavailable testosterone concentrations decreased below baseline ($p<0.05$). No significant differences in either total or bioavailable testosterone concentrations were observed between groups at any time point.

Testosterone Responses to Standardized Traditional and Eccentric-*Enhanced* Exercise in Untrained Men

Total testosterone responses following a standardized traditional and eccentric-*enhanced* resistance exercise protocol (Figure 9) were not significantly different than baseline (immediate to 45 minutest post); however, total testosterone was lower than both baseline and immediate post concentrations at 60 minutes ($p<0.05$). The bioavailable testosterone concentrations (Figure 10) increased immediately following exercise and decreased to below baseline concentrations within 60 minutes of exercise completion

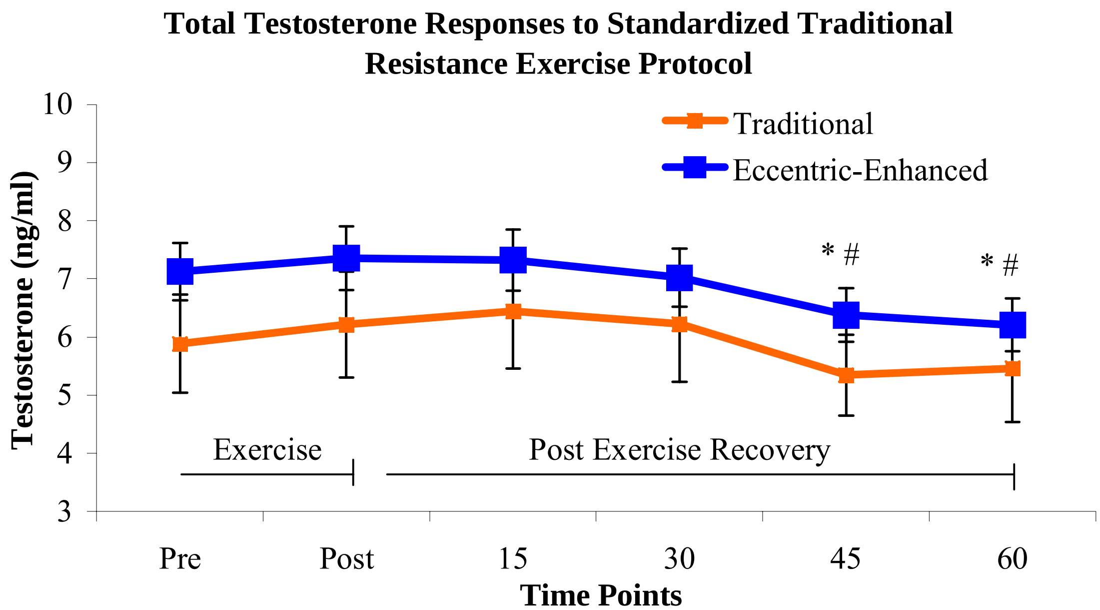

Figure 7. Total testosterone responses to standardized traditional resistance exercise protocol. * Indicates significantly different value than Post; # indicates significantly different value than 15 min ($p<0.05$). Data are expressed as Mean ± SE.

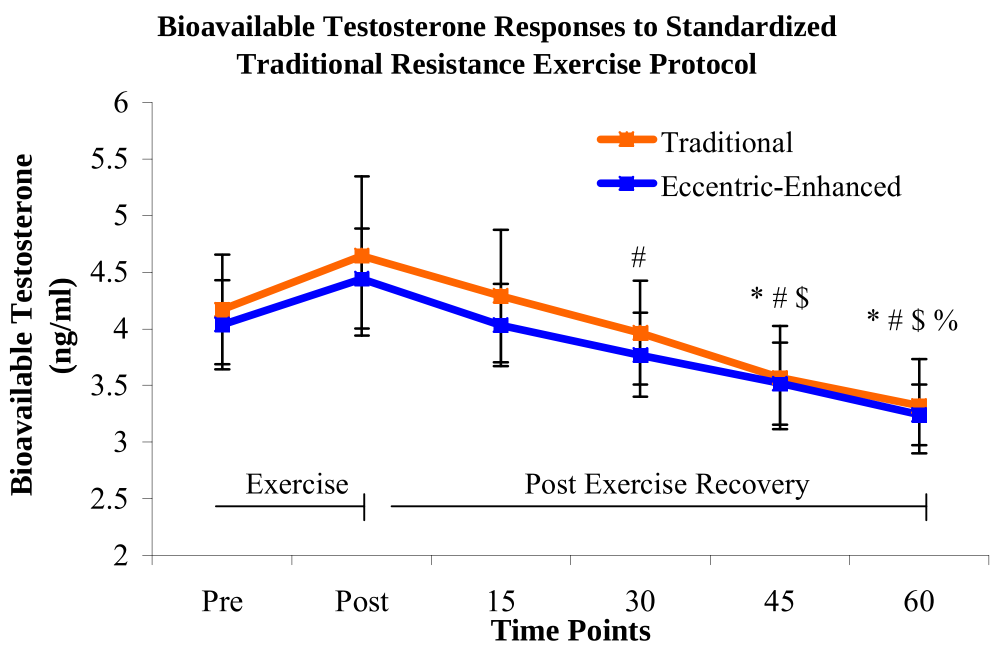

Figure 8. Bioavailable testosterone responses to standardized traditional resistance exercise protocol. * Indicates significantly different value than Pre; # indicates significantly different value than Post; $ indicates significantly different value than 15 min; % indicates significantly different value than 30 min ($p<0.05$).

(p<0.05). No significant differences were observed for either total or bioavailable testosterone concentrations between groups at any time point, including pre- and post-exercise as well as recovery.

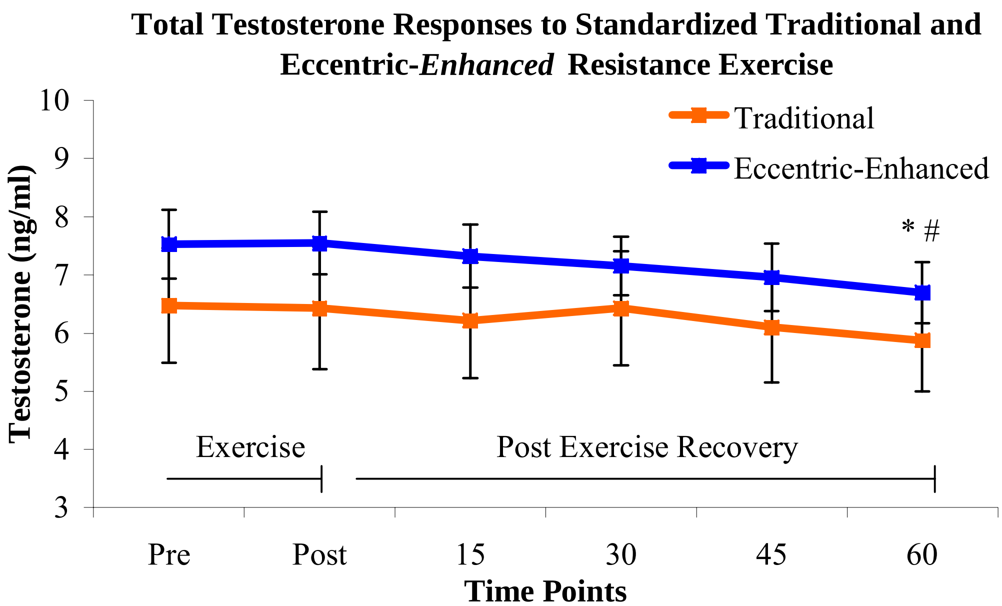

Figure 9. Total testosterone responses to standardized traditional and eccentric-*enhanced* resistance exercise in untrained men. * Indicates difference from baseline; indicates difference from post. Data are expressed Mean ± SE.

Testosterone Responses to Standardized Traditional and Eccentric-*Enhanced* Resistance Exercise in Trained Men

At post-intervention testing, total testosterone concentrations (Figure 11) increased immediately following exercise and decreased to below baseline values within 30 minutes of exercise completion (p<0.05). Bioavailable testosterone concentrations increased immediately following exercise in both groups and remained elevated for 15 minutes (p<0.05), before returning to baseline (Figure 12). No significant differences were observed between groups for either total or bioavailable testosterone concentrations, at any time point.

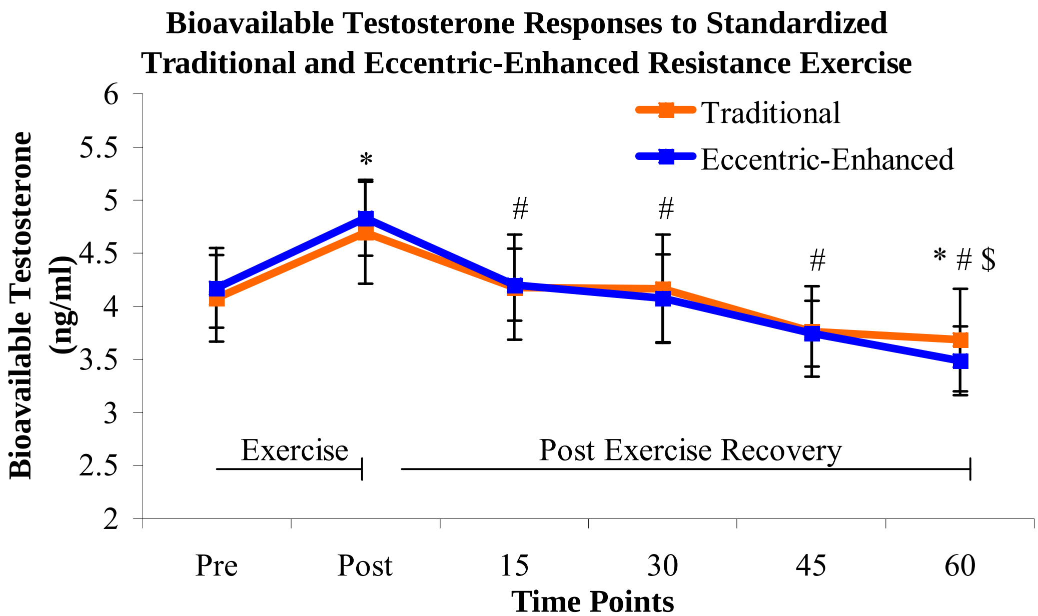

Figure 10. Bioavailable testosterone responses to standardized traditional and eccentric-*enhanced* resistance exercise in untrained men. * Indicates significantly different value than Pre; # indicates significantly different value than Post; $ indicates significantly different value than 15 min (p<0.05). Data are expressed Mean ± SE.

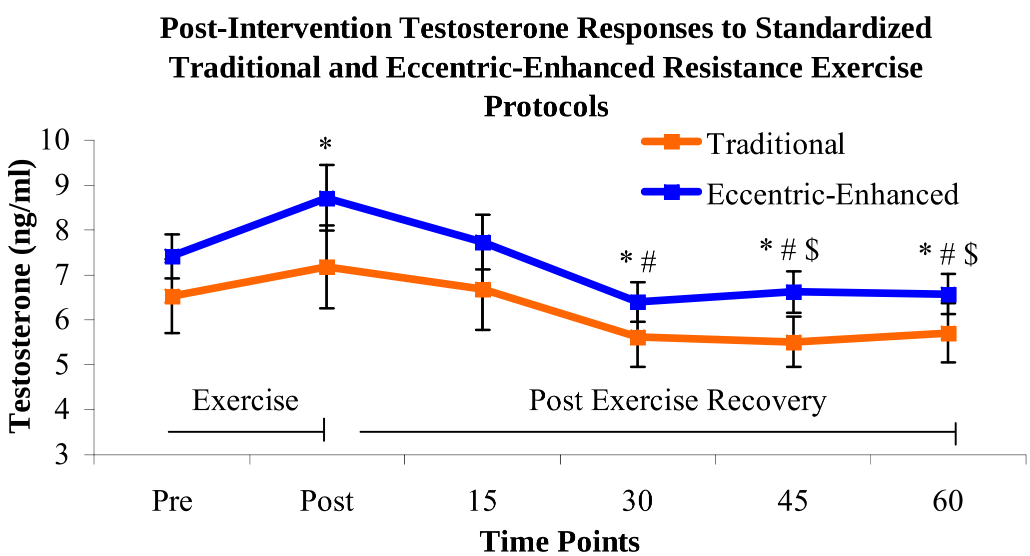

Figure 11. Post-intervention total serum testosterone responses to standardized traditional and eccentric-*enhanced* resistance exercise protocols. * Indicates significantly different value than Pre; # indicates significantly different value than Post; $ indicates significantly different value than 15 min (p<0.05). Data are expressed Mean ± SE.

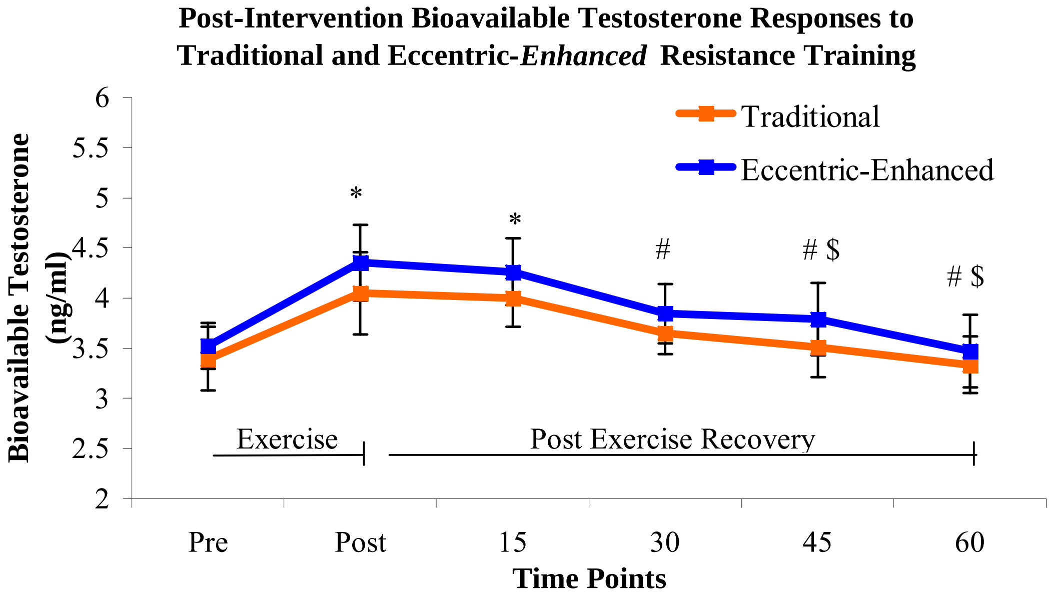

Figure 12. Post-intervention bioavailable serum testosterone responses to standardized traditional and eccentric-enhanced resistance training. * Indicates significantly different than Pre; # indicates significantly different than Post; $ indicates significantly different than 15 min ($p<0.05$). Data are Mean ± SE.

Growth Hormone

Growth Hormone Response to Standardized Traditional Exercise Protocol in Untrained Men

Following the standardized traditional resistance exercise protocol, post-exercise growth hormone (GH) concentrations increased above baseline 15-30 minutes after exercise cessation ($p<0.05$) and subsequently returned to baseline by 45 minutes, in both groups (Figure 13). No significant differences in GH concentrations were noted between groups, before of after the exercise bout.

Growth Hormone Response to Standardized Traditional and Eccentric-*Enhanced* Exercise in Untrained Men

Growth hormone responses following a standardized traditional and eccentric-enhanced exercise protocol increased 15-30 minutes post-exercise ($p<0.05$) and returned to baseline by 45 minutes (Figure 14). No significant differences in GH concentrations were observed between groups, before or following exercise.

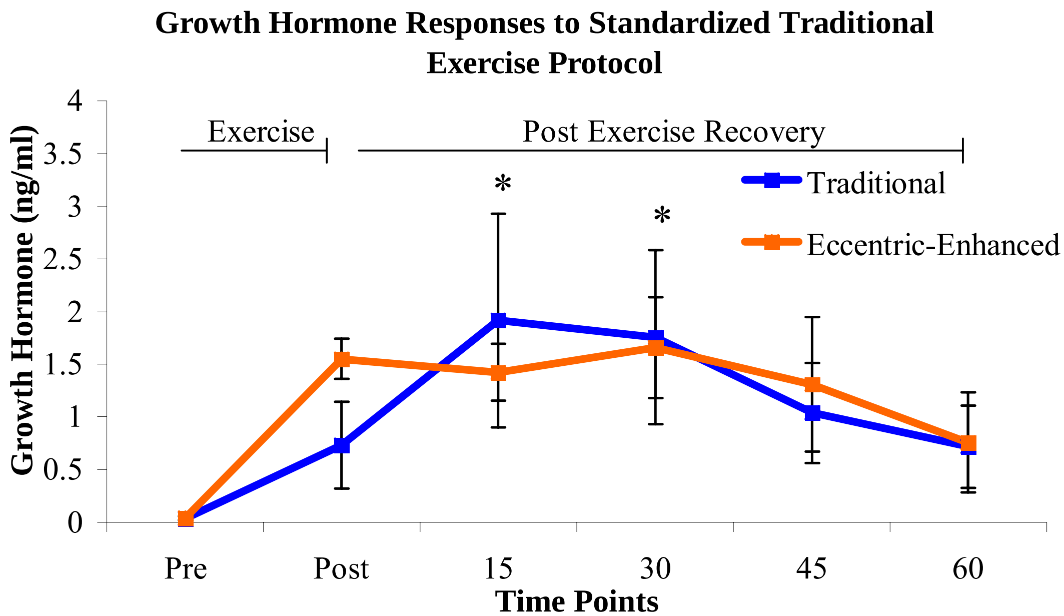

Figure 13. Growth hormone responses to the standardized traditional resistance exercise protocol in untrained men. * Indicates significantly different than Pre ($p<0.05$). Data are presented as Mean ± SE.

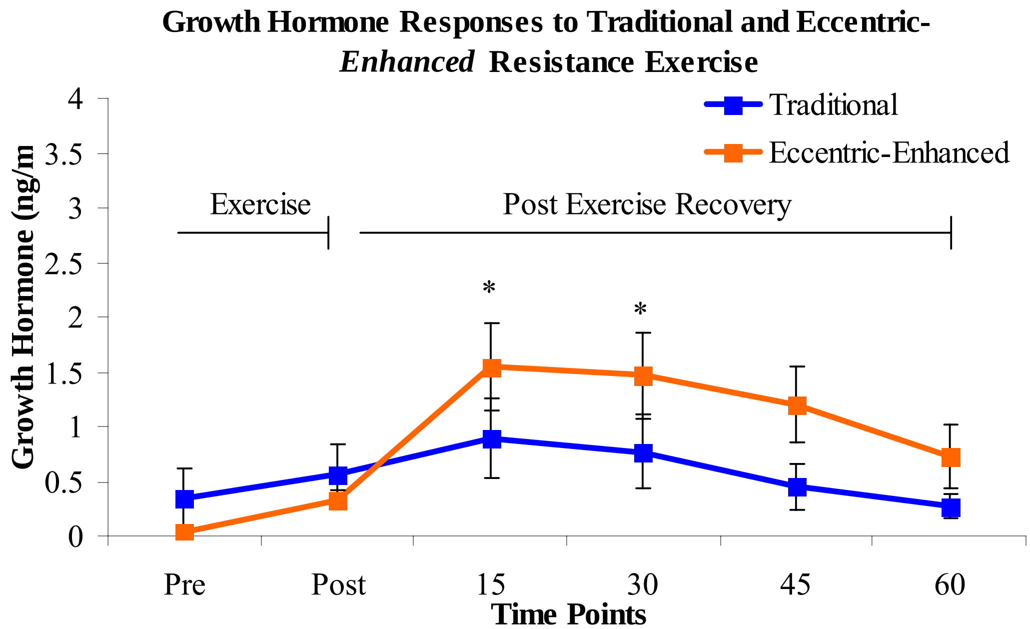

Figure 14. Growth hormone responses to standardized traditional and eccentric-*enhanced* exercise protocols, in untrained men. * indicates significantly different than Pre ($p<0.05$). Data are Mean ± SE.

Growth Hormone Response to Standardized Traditional and Eccentric-*Enhance*d Exercise in Trained Men

Following the five-week training intervention, GH was unchanged from baseline immediately following exercise but increased above baseline 15-45 minutes following exercise ($p<0.05$) and returned to baseline by 60 minutes (Figure 15). No significant differences in GH concentrations were observed between groups, at any time point.

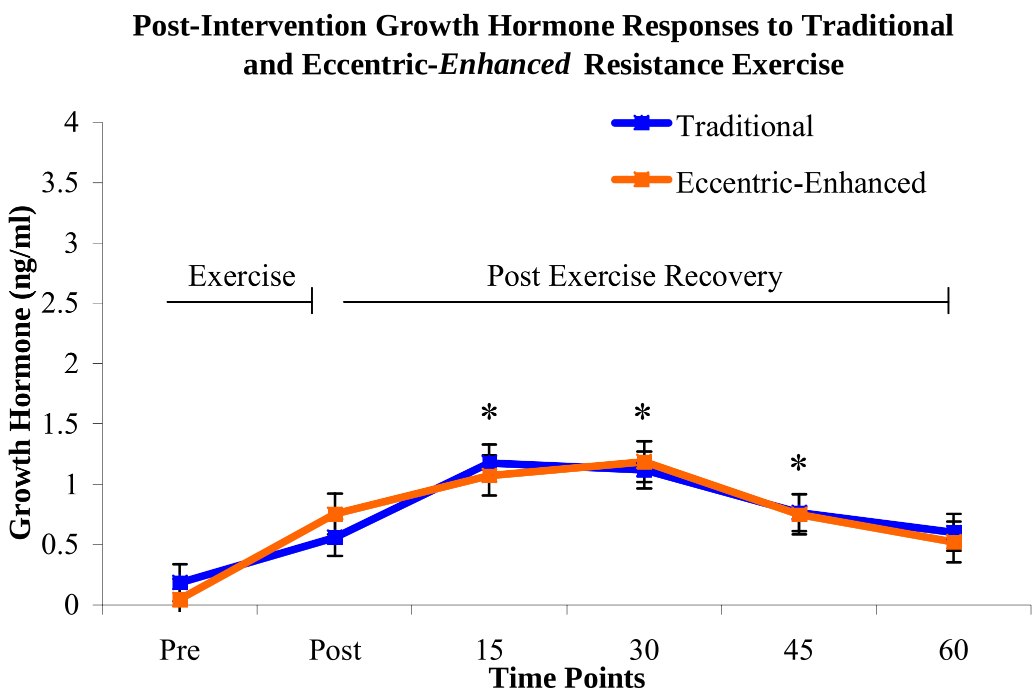

Figure 15. Post-intervention growth hormone responses to standardized traditional and eccentric-*enhanced* resistance exercise. * Indicates significantly different value than Pre ($p<0.05$). Data are presented as Mean ± SE.

Plasma Volume

Pre- and post-exercise plasma volume values for each exercise testing/blood acquisition session are presented in Appendix F. Briefly, plasma volume was reduced immediately post-exercise (5-11%; $p<0.05$) and returned to baseline within 30 minutes of exercise cessation during each testing session. No significant differences in plasma volume were observed between groups, at any time point.

Muscle Function

Muscular strength data is reported as absolute (1RM) and relative (1RM x kg body mass^{-1} and 1RM x kg lean body mass^{-1}) values. Additionally, total work (load lifted x repetitions completed) was used to quantify muscular endurance. Two subjects from the eccentric-*enhanced* group did not complete the training intervention; therefore performance results reflect 22 subjects (n=12 traditional; n=10 eccentric-*enhanced*).

Muscular Strength

No statistical differences in strength were observed between groups at baseline, for the chest (press) or leg (squat) (Table 3). Following the five-week exercise intervention, both groups showed similar increases in absolute (1RM) and relative (1RM x kg body mass^{-1} and 1RM x kg lean body mass^{-1}) chest strength ($p<0.05$). Additionally, both groups showed similar increases in absolute leg strength ($p<0.05$), whereas the traditional group exhibited a greater increase in relative leg strength compared to the eccentric-*enhanced* group ($p<0.05$).

Muscular Endurance

Muscular endurance measures are reported as total work, calculated as:

Total Work (kg) = Load (kg) * Total Number of Repetitions Completed

Chest and leg endurance values were similar between groups at baseline (Table 4). Following the exercise intervention, both groups showed similar increases in chest and leg endurance ($p<0.05$).

Table 3. Muscular strength values at baseline and post-intervention for the traditional and eccentric-*enhanced* groups.

		TRADITIONAL			ECCENTRIC-*ENHANCED*		
		PRE	POST	% Δ	PRE	POST	% Δ
CHEST	1RM (kg)	76.9 ± 4.4	84.7 ± 4.8*	10.1	75.5 ± 4.9	82.3 ± 5.0*	9.0
	kg/mass	0.97 ± 0.04	1.08 ± 0.05*	11.3	0.93 ± 0.06	1.01 ± 0.06*	8.6
	kg/FFM	1.23 ± 0.06	1.35 ± 0.07*	9.8	1.16 ± 0.06	1.25 ± 0.06*	7.8
SQUAT	1RM (kg)	101.5 ± 7.6	127.3 ± 7.0*	25.4	102.7 ± 4.6	121.8 ± 5.8*	18.6
	kg/mass	1.29 ± 0.10	1.62 ± 0.08* #	25.6	1.28 ± 0.06	1.49 ± 0.06* #	16.4
	kg/FFM	1.61 ± 0.09	2.03 ± 0.08* #	26.1	1.59 ± 0.06	1.86 ± 0.07* #	17.0

* Indicates difference from corresponding pre-test value; # indicates difference between groups ($p<0.05$). % Δ reflects the percentage change in muscular strength from baseline to post-intervention testing, mass represents body mass in kg, FFM represents fat-free mass in kg. Data are expressed as Mean ± SE.

Table 4. Muscular endurance (total work) measures at baseline and post-intervention for the traditional and eccentric-*enhanced* groups.

	TRADITIONAL			ECCENTRIC-*ENHANCED*		
	PRE	POST	% Δ	PRE	POST	% Δ
Chest Press	1010 ± 54	1100 ± 63*	8.9%	995 ± 61	1086 ± 65*	9.1%
Squat	1318 ± 97	1604 ± 104*	21.7%	1353 ± 61	1615 ± 78*	19.4%

* Indicates significantly different value than corresponding pre-test value ($p<0.05$). % Δ represents percentage change in muscular endurance from baseline to post-intervention testing. Data are Mean ± SE.

Rating of Perceived Exertion

The ratings of perceived exertion (RPE)[153] acquired during each exercise session throughout the five-week training intervention are presented in Figure 16. The traditional group had a significantly lower RPE during sessions 1-4, compared to the eccentric-*enhanced* group ($p<0.05$). No other significant differences were observed during any exercise training session.

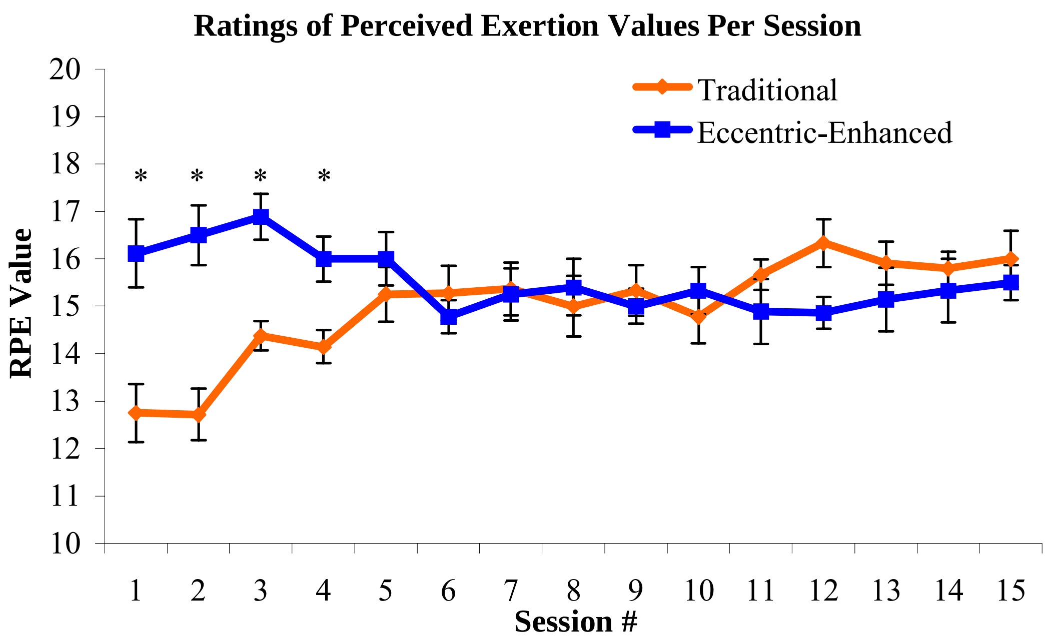

Figure 16. Ratings of perceived exertion (Borg Scale) following each exercise training session. * Indicates significantly different value between groups ($p<0.05$). Data are expressed as Mean ± SE.

Training Volume

Training volume is reported as, 1) training volume per exercise session and 2) total training volume across the five-week training intervention. Training volume per session was determined using the following equation:

VOLUME = [# of CON actions * CON load] + [# of ECC actions * ECC load]

Total training volume during the exercise intervention was determined by summing each *per session* training volume. Further, individual chest press and squat training volumes were quantified to determine the total work performed on each exercise and a combined (chest press volume + squat) training volumes was calculated, as the combined training volume may be indicative of post-exercise hormonal responses.[113]

Training Volume Per Exercise Session

The chest press volume per session (Figure 17) was greater during sessions 2-11, 13, and 15 for the traditional group, compared to the eccentric-*enhanced* group ($p<0.05$). The squat volume per session (Figure 18) was greater during sessions 9, 10, 14, and 15 for the traditional group, compared with the eccentric-*enhanced* group ($p<0.05$). The combined training volume per session (Figure 19) was greater during sessions 7 and 15 for the traditional group, compared to the eccentric-*enhanced* group ($p<0.05$).

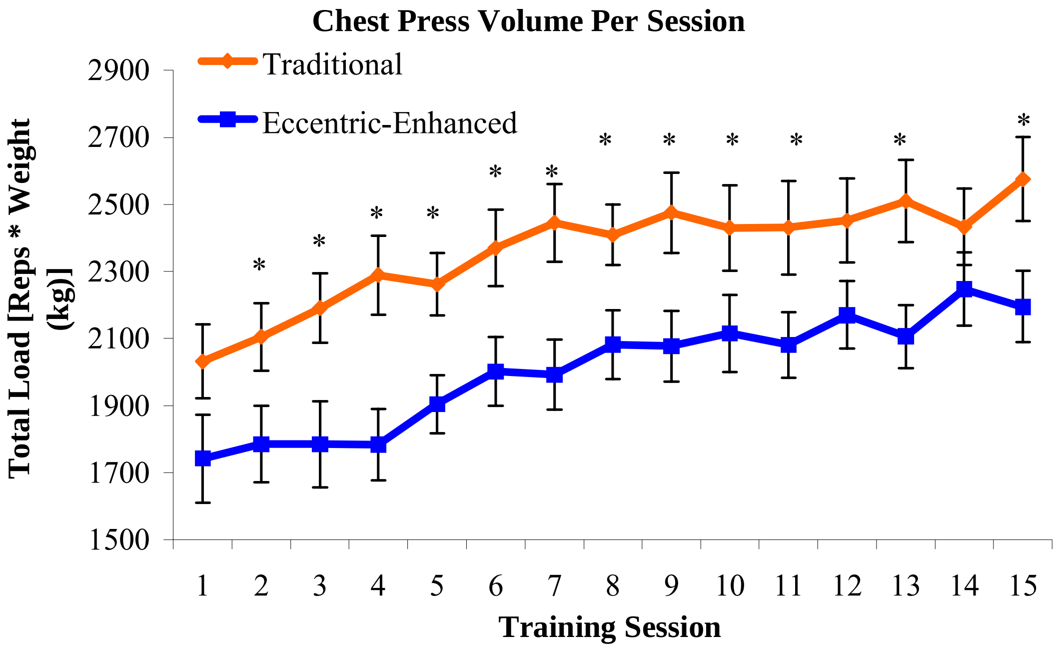

Figure 17. Chest press training volume per session for the traditional group and eccentric-*enhanced* groups. * indicates significantly different value between groups at the designated session ($p<0.05$). Data are Mean ± SE.

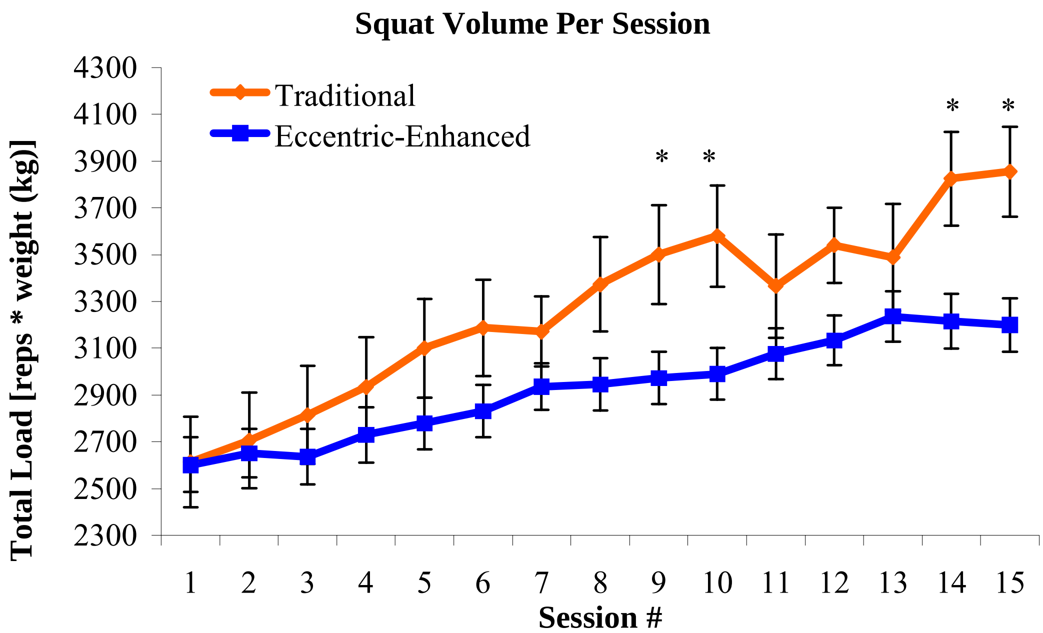

Figure 18. Squat training volume per session for the traditional and eccentric-*enhanced*. * Indicates significantly different value between groups at the designated session ($p<0.05$). Data are Mean ± SE.

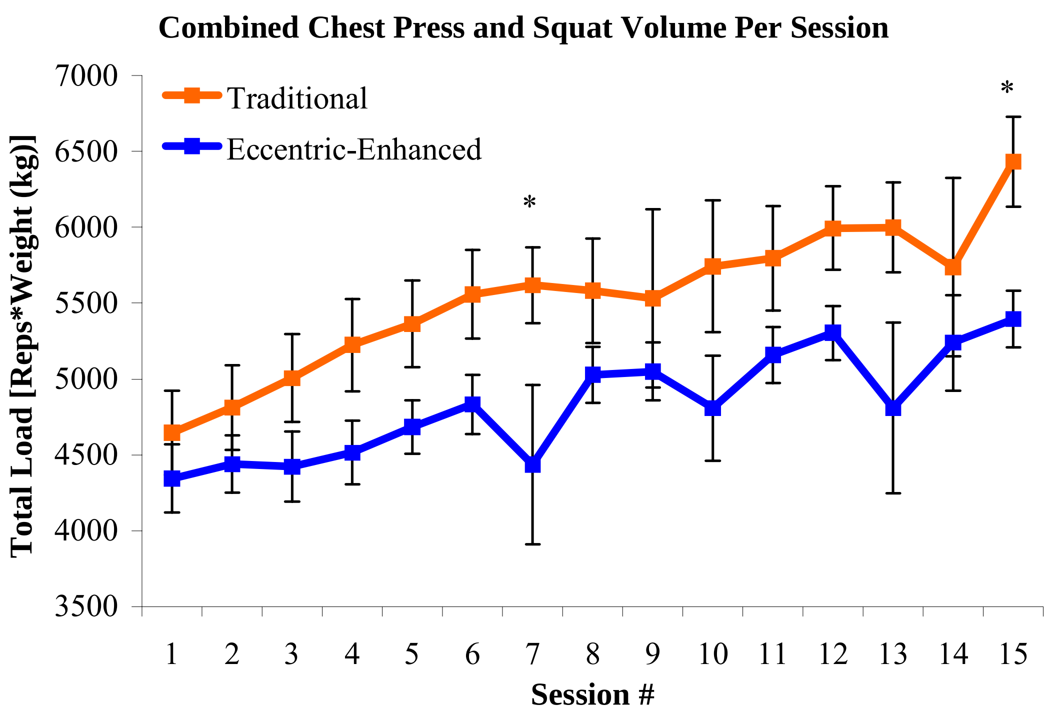

Figure 19. Combined training volume per session (Chest Press + Squat) for the traditional and eccentric-*enhanced* groups. * Indicates significantly different value between groups at the designated session ($p<0.05$). Data are Mean ± SE.

Total Accumulated Training Volume Across Five-Week Intervention

In this section, total training volume refers to the total training volume performed during the entire five-week exercise intervention. The chest press training volume (Figure 20) was greater in the traditional group, compared with the eccentric-*enhanced* group (34,802 ± 1550 kg vs. 29,438 ± 1683 kg, $p<0.05$), while the total squat training volume (Figure 19) was not statistically different between the traditional and eccentric-*enhanced* groups (48151 ± 2764 kg vs. 43020 ± 1838 kg). The total combined training volume (chest press + squat volumes) (Figure 21) tended to be greater for the traditional group, compared with the eccentric-*enhanced* group (83037 ± 4082 kg vs. 72485 ± 3164 kg); however, statistical significance was not achieved ($p=0.061$).

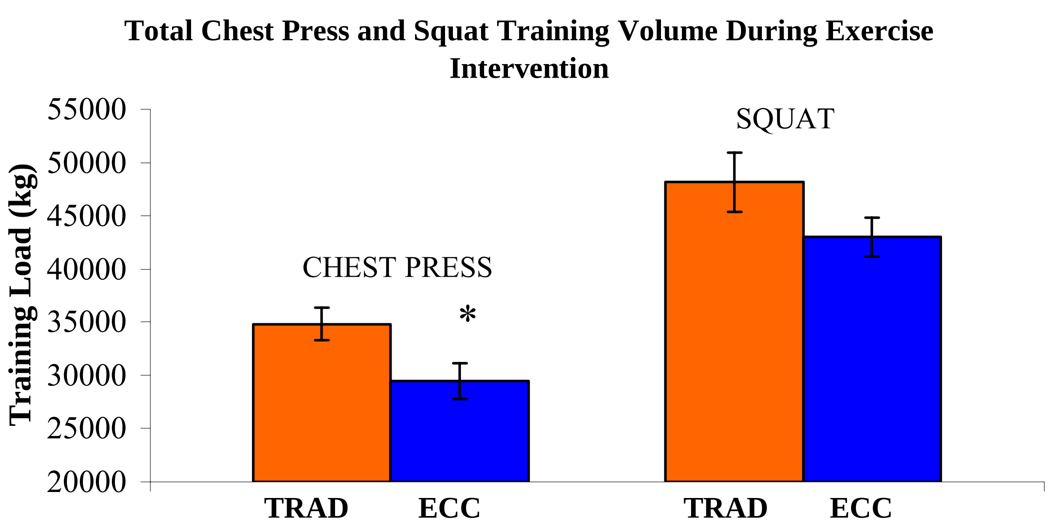

Figure 20. Total chest press and squat training volume during the five week resistance exercise intervention. TRAD represents the traditional group, ECC represents the eccentric-*enhanced* group. * Indicates significantly different value between groups ($p<0.05$). Data are expressed as Mean ± SE.

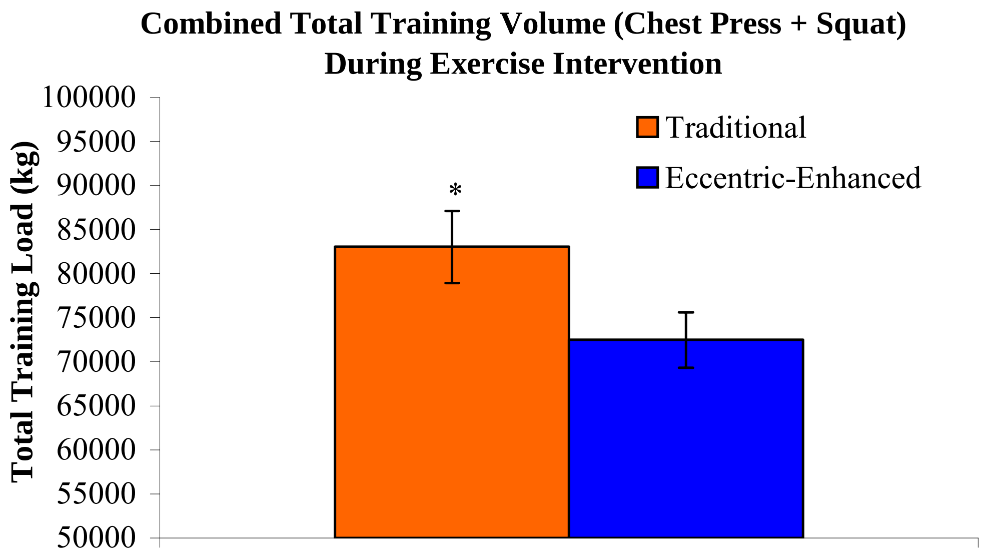

Figure 21. Combined total training volume (Chest Press + Squat) during the five-week exercise intervention. * Indicates a trend towards significantly different values between groups ($p=0.061$). Data are expressed as Mean ± SE.

Dietary Analysis

No significant differences were noted between groups for any dietary measure (total daily kilocalorie, carbohydrate, protein, or fat consumption) throughout the duration of the study (Table 5). On average, subjects consumed ~2238 kcals per session, which was comprised of ~50.3% carbohydrates, ~33.2% fat, and ~16.2% protein (~1.1g x kg body mass^{-1}). Additionally, all subjects completed a 12 hour fast prior to blood acquisitions; as indicated by dietary records and follow-up questions concerning food, drink, alcohol, and caffeine consumption prior to blood acquisition.

Sleep Analysis

The average number of hours slept per night in the traditional (7.2 ± 0.4 hours) and eccentric-*enhanced* (7.8 ± 0.2 hours) groups were not statistically different throughout the exercise intervention. Additionally, 100% of subjects reported 7-10 hours of sleep on the night preceding blood acquisition sessions.

Table 5. Average reported kilocalories, carbohydrates, protein, and fat in the traditional and eccentric-*enhanced* groups.

	TRADITIONAL		ECCENTRIC-*ENHANCED*	
	KCALS	% TOTAL INTAKE	KCALS	% TOTAL INTAKE
Total Kcals	2162 ± 495		2320 ± 853	
Carbohydrates	1135 ± 127	52.5%	1093 ± 117	47.1%
Protein	326 ± 26	15.1%	427 ± 71	18.4%
Fat	689 ± 60	31.9%	771 ± 77	33.2%

Data are presented as Mean ± SE.

CHAPTER 5
DISCUSSION

Skeletal muscle atrophy, reduced strength, and heightened fatigue are associated with aging[175] and degenerative diseases such as multiple sclerosis[155] and muscular dystrophy.[11] Participation in progressive resistance training has been shown to attenuate loss of strength and function, improve functional capacity, and decrease hypokinetic disease risk in both young and elderly populations.[65, 104] Thus, determining and implementing effective resistance exercise protocols may ultimately minimize the deleterious effects of both aging and degenerative diseases on skeletal muscle quality and performance outcomes.

Traditional resistance training consists of identical loading performed during both concentric (shortening) and eccentric (lengthening) muscle actions.[104] Eccentric-*enhanced* resistance exercise is performed with a greater eccentric loading (~180-250% of concentric load) and has been shown to result in similar[17, 25, 59] or superior[25, 51, 86, 87, 95] skeletal muscle strength and mass adaptations compared to traditional resistance training. However, the mechanism(s) underlying the purported superior muscle adaptations following eccentric-*enhanced* resistance training have not been determined. Therefore, the purpose of our study was to test the hypothesis that eccentric-*enhanced* progressive resistance training would result in greater neuroendocrine (total testosterone, bioavailable testosterone, and growth hormone) and muscle performance responses and lower metabolic (lactate) responses than traditional progressive resistance training. The primary findings of our research are that the early-phase (first five-week) neuroendocrine and performance responses are similar between traditional and eccentric-*enhanced* resistance training, in previously untrained college-age men.

Only one published study has attempted to elucidate the mechanism(s) underlying the purported superior muscular adaptations associated with eccentric-*enhanced* resistance training.[51] For comparison, we used investigations with training programs most similar in training volume and intensity to ours; however, we were limited to 1) traditional, 2) concentric-only, and 3) eccentric-only resistance training protocols, as mechanistic studies on eccentric-*enhanced* training were limited. Eccentric-*enhanced* resistance exercise is somewhat unique in that it includes a combination of the previously mentioned program designs; therefore, direct comparison between study findings should be interpreted cautiously.

Metabolic Response to Resistance Exercise

Metabolic acidosis, associated with lactate accumulation, may contribute to skeletal muscle fatigue during high-intensity exercise.[149] Strategies designed to reduce lactate accumulation during exercise may decrease overall fatigue and ultimately result in improved exercise prescriptions for both healthy and at-risk populations. We are the first to compare the blood lactate responses to eccentric-*enhanced* resistance exercise and traditional resistance exercise, in both the trained and untrained states.

Lactate Responses to Standardized Traditional and Eccentric-*Enhanced* Resistance Exercise in Untrained Men

The immediate post-exercise blood lactate concentrations were greater in subjects following a standardized eccentric-*enhanced* resistance exercise protocol compared to a traditional resistance exercise protocol, matched in volume. Our findings may, in part, be due to the greater eccentric-specific exercise intensity in the eccentric-*enhanced* group

(40% 1RM concentric; 100% 1RM eccentric), compared to the traditional group (52.5% 1RM concentric and eccentric). Previous reports demonstrate that both exercise volume[67] and intensity[117] are associated with lactate accumulation. Our results are consistent with Lagally et al.[117] (2002), who reported that higher intensity exercises result in greater lactate accumulation. In our study, the eccentric-specific training intensity was 48.5% greater in the eccentric-*enhanced* group, but volume was matched between groups (4646 kg, traditional vs. 4344 kg, eccentric-*enhanced*; $p>0.05$).

In our study, the higher eccentric-specific intensity in the eccentric-*enhanced* group may reflect a greater recruitment of fast glycolytic (type IIx) and/or fast oxidative glycolytic (type IIa) muscle fibers[51] and associated lactate accumulation.[89] Previous research suggests that eccentric muscle actions recruit all available fast motor units (type IIa and IIx) at lower relative intensities (>60% maximal voluntary contraction) than concentric actions (>80% maximal voluntary contraction);[122] therefore, it is possible that the eccentric-*enhanced* group recruited a larger portion of fast motor units during exercise resulting in greater lactate accumulation.

It is also possible that differences in (load dependent) skeletal muscle blood flow characteristics may have influenced the lactate response between groups. For example, arterial blood flow to contracting skeletal muscle has an inverse relationship with exercise intensity.[150] Additionally, combined venous occlusion and low-intensity resistance exercise result in greater lactate accumulation than low-intensity resistance exercise alone.[98] Although blood flow characteristics were not evaluated in our study, greater venous occlusion and/or reductions in arterial blood flow may have occurred in the eccentric-*enhanced* group (due to the higher eccentric-specific load) thus resulting in greater blood lactate concentrations.

Lactate Response to Resistance Training in Trained Men

The immediate post-exercise lactate response to the traditional resistance exercise protocol was greater following the five-week training program when compared to pre-training, possibly due to the greater exercise intensity (64% 1RM vs. 52.5% 1RM), enhanced recruitment of fast glycolytic muscle fibers, and/or improved storage and utilization of glycogen[12] in the trained state. In contrast, the immediate post-exercise lactate responses to eccentric-*enhanced* exercise were similar in the trained and untrained states, despite a greater post-intervention eccentric-specific exercise intensity (~106% post-intervention 1RM vs. 100% pre-intervention 1RM). Our results contrast the supposition by Kraemer et al.[103] who suggested that the post-exercise lactate concentrations increase as the eccentric-specific exercise intensity increases.

Similar post-exercise blood lactate concentrations were observed in the eccentric-*enhanced* group in both the untrained and trained states, despite the greater exercise intensity performed in the trained state. Friedmann and colleagues[51] (2004) reported that eccentric-*enhanced*, but not traditional, resistance training upregulates lactate dehydrogenase type (LDH) A mRNA following four weeks of training; indicating a possible lactate buffering effect associated with eccentric-*enhanced* exercise. Additionally, improvements in intracellular lactate buffering and/or delayed lactate accumulation due to a repetitive training stimuli above anaerobic threshold have been observed[84, 125, 132] and may help explain our findings.

It is also possible that recruitment of additional type IIx (high lactate generating) muscle fibers may not have occurred in the eccentric-*enhanced* group in the trained state.[122] Recall that complete recruitment of fast motor units has been observed during eccentric-only muscle actions performed at intensities (~60% maximal voluntary contraction)[122] below that used during baseline testing in our study (100% 1RM); suggesting that full recruitment of fast motor units may have occurred during baseline testing. However, Friedmann et al.[51] (2004), reported that both type IIa and IIx myosin heavy chain (MHC) mRNA are increased following eccentric-*enhanced* resistance exercise; suggesting that fast motor units are extensively recruited during eccentric-*enhanced* exercise.

Alternatively, decreased skeletal muscle glycogen content and/or decreased utilization of skeletal muscle glycogen stores may have occurred in the eccentric-*enhanced* group, as a result of heavy eccentric training. Decreased skeletal muscle glucose transporter (GLUT4) protein concentrations,[12, 13] impaired glycogen resynthesis,[13] and decreased post-exercise glycogen accumulation (for up to 72 hours)[178] have been observed following eccentric exercise; suggesting a reduced glycogen availability for subsequent exercise sessions, following heavy eccentric exercise. Although we did not measure glycogen synthesis rates or concentrations, it may be possible that reduced skeletal muscle glycogen content limited lactate accumulation during post-intervention testing.

Testosterone

Testosterone has been shown to enhance muscle hypertrophy by directly increasing protein synthesis,[19, 26, 50, 66, 160, 161, 170] thus it is not surprising that investigators have attempted to identify strategies to enhance endogenous free and total testosterone concentrations and optimize gains in muscle mass with resistance exercise.[7, 8, 32, 47, 68, 70, 71, 78, 106-109, 111, 115, 169, 176] Total testosterone represents the combination of unbound (free) testosterone (~2% of total) and testosterone bound to either sex hormone binding globulin (SHBG) (~50% of total) or albumin (~50% of total).[121] The combination of free and albumin-bound testosterone fractions (bioavailable testosterone) reflect the effective androgen status, as both fractions have been shown to traverse cell membranes, bind with androgen receptors, and consequently stimulate protein translation.[41, 121, 172] To date, there are no published reports on the bioavailable (non-SHBG-bound) testosterone responses to resistance exercise. The majority of studies utilizing resistance training interventions report free testosterone[7, 47, 70, 71, 169] which represents only a small portion (~4%) of bioavailable testosterone; [121] therefore, comparison of our results to previous reports is not possible.

Resting Testosterone

Resting total testosterone concentrations in our subjects were within the normal eugonadal range (300-1000 ng/dl).[126] Resting total testosterone concentrations remained unchanged, while the bioavailable testosterone fraction decreased with training in both groups. Our findings are consistent with previous reports demonstrating that resting total testosterone levels are unaltered following resistance training interventions[10, 71-73, 78, 110, 113, 128] and inconsistent with others showing upward trends.[167]

Considering that total testosterone is comprised of three components (free, albumin-bound, and SHBG-bound), interpretation of our bioavailable testosterone results is speculative as each subfraction may influence the bioavailable fraction. Our results may suggest however, that 1) SHBG-bound testosterone increased, as non-SHBG-bound (bioavailable) testosterone decreased and total testosterone remained unchanged, 2) albumin-bound testosterone decreased, and/or 3) free testosterone decreased. The literature indicates that SHBG is apparently unresponsive to either acute[180] or chronic[73, 114, 128] resistance exercise, in men. Additionally, albumin has been shown to increase following both acute[4] and chronic resistance training interventions;[100] suggesting that albumin-bound testosterone may not diminish following resistance exercise. Further, resting free testosterone has been shown to either increase[110] or remains constant[5] following resistance exercise interventions. Although not measured in our study, alterations in the free:albumin-bound:SHBG-bound testosterone ratio occurred, favoring an increase in SHBG-bound and/or a decline in bioavailable testosterone concentrations at the conclusion of our study.

Alternatively, upregulation of skeletal muscle androgen receptor expression may have occurred in response to training. Support for this idea comes from studies that report increased skeletal muscle androgen receptor expression following resistance training interventions, in both humans[15, 180] and animals.[39, 173] Androgen receptor upregulation with training may help explain the reduction in bioavailable testosterone concentrations observed following the five-week training program.

Previous reports have also suggested that acute sleep deprivation,[1, 62, 135] low dietary total caloric and fat intakes,[154, 174] and/or high dietary protein intake[154] are associated with reduced resting total testosterone concentrations. Our subjects reported normal sleep patterns (7-10 hours)[14] and adequate caloric intakes (~2220 kcals; 50.3% carbohydrates, ~33.2% fat, and ~16.2% protein)[120] on the day prior to each blood acquisition session. Therefore, it does not appear that sleep patterns or dietary intake influenced the resting hormone concentrations in our study.

Testosterone Response to Standardized Traditional Resistance Exercise in Untrained Men

The total and bioavailable testosterone responses to a single bout of standardized traditional resistance exercise were similar between groups before the initiation of training. Overall, total and bioavailable testosterone concentrations remained unchanged acutely following exercise and fell below baseline within 30-45 minutes of recovery. Our results support Kraemer et al.[114] (1998) who reported that total testosterone concentrations remained constant following traditional resistance training, but are inconsistent with others indicating increased testosterone concentrations following resistance exercise in untrained men.[5, 8, 68, 78, 109, 111, 169, 180] Additionally, the reduction in both total and bioavailable testosterone concentrations, below baseline, indicate that testosterone 1) followed normal metabolic pathway biotransformation and/or 2) became bound to androgen receptors and stimulated protein synthesis.[19]

The total and bioavailable testosterone responses observed in our study may be explained in a variety of ways. First, it is possible that the acute testosterone response to resistance exercise is an adaptive physiological response occurring primarily after longer term (>5 week) resistance training protocols.[114] This notion is supported by our data which demonstrate that exercise caused a transient increase in total testosterone, in trained individuals. Second, the exercise volume and/or intensity performed in this study may have been insufficient stimuli to induce a change in testosterone concentrations. High volume[64, 111, 144] and high-intensity[109, 111, 143] resistance exercise protocols have been shown to result in greater post-exercise testosterone concentrations than low volume or low-intensity protocols. The training volume and intensity used in our study were similar to previous studies that reported elevated testosterone following resistance exercise;[64, 116, 156] thus other factors such as the training status of the subjects and/or the exercises performed during the study (chest press and squat) may explain the disparity in findings.

Testosterone Response to Standardized Traditional and Eccentric-*Enhanced* Exercise in Untrained Men

In our study, the post-exercise total testosterone concentrations in untrained subjects, following traditional or eccentric-*enhanced* resistance exercise decreased below baseline concentrations by 60 minutes into recovery; similar to our previously reported findings that indicated total testosterone concentrations decline below baseline concentrations following a standardized traditional resistance exercise protocol. However, we observed an immediate post-exercise increase in bioavailable testosterone concentrations and gradual decline to below baseline within 60 minutes of exercise cessation, in both groups. As no change in total testosterone appeared following exercise, our previously discussed rationale that the 1) testosterone response following resistance exercise is a long-term adaptive response to training and/or 2) training volume and intensity selected for this study were insufficient stimuli to elicit a change in testosterone concentrations, may explain these findings. It is also possible that eccentric muscle actions do not provide an adequate stimulus (metabolic or other) to affect post-exercise total testosterone concentrations, in untrained males.[103] The eccentric-specific exercise intensity in our study (100% 1RM, eccentric-*enhanced* group) was greater than used in previous that reported increased testosterone responses to eccentric-only muscle actions[47] and an unchanged testosterone response to eccentric-only muscle actions.[103]

While total testosterone remained unchanged immediately following a standardized bout of eccentric-*enhanced* and traditional resistance exercise in the untrained state, bioavailable testosterone increased. When analyzed in association with our total testosterone results, it appears that alterations in the free:albumin-bound:SHBG-bound testosterone ratio may occur following a bout of resistance exercise. Recall that changes in both free and albumin-bound testosterone affect the bioavailable testosterone fraction and thus the interpretation of our data. Previous reports have indicated that free testosterone increases acutely following resistance training;[7, 47, 169] although we did not directly measure free testosterone concentrations it is plausible that changes in the free testosterone fraction influenced both our total and bioavailable testosterone results.

Testosterone Responses to Traditional and Eccentric-*Enhanced* Resistance Training in Trained Men

Following the five-week training intervention, both groups exhibited an acute increase in post-exercise total and bioavailable testosterone concentrations, which subsequently fell below baseline 30-45 minutes into recovery. Similar testosterone responses have been observed following resistance exercise interventions in trained men[7, 8, 32, 68, 78, 107-109, 111, 115, 143, 169, 176]. Additionally, our results corroborate previous reports indicating that post-exercise testosterone concentrations increase in trained, but not untrained men.[8, 114]

Total and bioavailable testosterone concentrations were similar between groups at all time points, despite a greater training volume in the traditional group throughout training and post-intervention testing. Briefly, we successfully equated training volume during baseline testing, but were unable to equate training volume during the resistance training intervention because the load and repetition dependent rate of progression accomplished in the traditional resistance training group could not be matched by the eccentric-*enhanced* group. Considering that both exercise volume and intensity are thought to play integral roles in determining the testosterone responses following resistance training;[113] the additional training volume completed by the traditional group may in part, explain the similar testosterone responses between groups. Although no difference in either bioavailable or total testosterone concentrations appeared between groups, our results indicate that 1) eccentric-*enhanced* exercise may result in similar post-exercise testosterone concentrations to traditional resistance exercise, at a lower total volume of work and/or 2) post-exercise testosterone responses may be more responsive to exercise intensity than to total exercise volume.

Growth Hormone

The growth hormone (GH) responses following various resistance exercise protocols have been summarized in several recent reviews.[92, 113, 133, 164] Growth hormone has been shown to directly affect cellular amino acid uptake[9] and protein synthesis,[52-54, 74, 138] thus contributing to skeletal muscle hypertrophy. Our study is the first to compare the GH response between traditional and eccentric-*enhanced* resistance exercise, in both the untrained and trained states.

Growth Hormone Response to Standardized Traditional Resistance Exercise in Untrained Men

Resting GH concentrations were within normal, non-acromegalic, ranges (< 2.0 ng/ml) for all subjects.[162] In our study, GH increased 15-30 minutes following exercise and returned to baseline concentrations within 45 minutes of exercise cessation, similar to previous reports.[8, 37, 73, 110, 114, 128, 152] A variety of factors, including higher training volumes,[64, 82] moderate intensities (8-12 RM),[109, 111, 142, 171] large muscle group exercises,[75, 108] and short rest intervals[109, 111] have been reported to increase the GH response to exercise. A smaller change in GH concentrations (~2 ng/ml) was observed in our study, compared to previous reports (~3.5-10.0 ng/ml).[8, 37, 73, 110, 114, 128, 152] The training volume (4 sets x 6 reps), exercise selection (chest press and squat), and rest periods length (1 minute between sets) we selected were similar to previous reports;[8, 37, 73, 110, 114, 128, 152] however, the exercise intensity in our study (52.5% 1RM) was lower than most,[8, 37, 73, 110, 114, 128, 152] but not all[63] previous reports demonstrating increased post-exercise GH concentrations. Therefore, it appears that the relatively lower exercise intensity used in our study may explain the lower post-exercise GH concentrations, compared to others.

Growth Hormone Response to Standardized Traditional and Eccentric-*Enhanced* Exercise in Untrained Men

During baseline testing, we observed an increase in post-exercise GH concentrations 15-30 minutes following the traditional and eccentric-*enhanced* resistance training protocols. However, a relatively modest change in post-exercise GH concentrations was observed in our study (~1.5 ng/ml) compared with prior reports (~3.5-10 ng/ml),[8, 37, 73, 110, 114, 128, 152] similar to the response we reported following the standardized traditional resistance exercise protocol; therefore, our previously discussed rationale may apply. Additionally, several studies have reported that eccentric muscle actions result in lower post-exercise GH responses than concentric muscle actions, in untrained subjects;[47 103, 105] suggesting that GH may be less responsive to eccentric muscle actions than concentric actions, regardless of load. Overall, the relatively low concentric-specific exercise intensity performed in both groups may explain the post-exercise GH responses.

Growth hormone concentrations have been found to be positively associated with blood lactate[69] and H^+ accumulation.[48] Additionally, Luger et al.[124] (1992) suggested that lactate accumulation partially regulates the exercise induced GH response. During pre-intervention testing, we observed a greater post-exercise lactate response in the eccentric-*enhanced* group, compared with the traditional group, but no differences in post-exercise GH concentrations were observed. Further, we did not observe a relationship between lactate concentrations and either the post-exercise GH concentrations or GH area under the curve. Our results suggest that additional factors, beyond lactate/H^+ accumulation, may regulate the post-exercise GH responses to eccentric exercise in untrained subjects, such as blood flow characteristics, nitric oxide release, and higher brain center/anterior pituitary input.[60]

Growth Hormone Response to Traditional and Eccentric-*Enhanced* Exercise in Trained Men

Similar to previous findings,[6-8, 64, 82, 105, 106, 108, 109, 111, 113, 115, 142, 171] at post-intervention testing both groups exhibited acutely increased post-exercise GH concentrations (15-45 minutes) that returned to baseline by 60 minutes into recovery. Additionally, no differences in GH concentrations were observed between groups at any time point, despite a larger training volume in the traditional group. Our results are consistent with Kraemer and colleagues[105] (2001), who reported that maximal eccentric muscle actions result in greater GH responses than maximal concentric muscle actions, in trained subjects; possibly indicating that the higher exercise intensities stimulate a greater GH response.

Muscular Function and Eccentric-*Enhanced* Resistance Training

A myriad of positive health outcomes are associated with improvements in muscular strength and mass, thus determining effective resistance exercise protocols is important when prescribing weight training programs in both healthy and at-risk populations.[99] While traditional resistance training programs are often prescribed, recent reports demonstrate that eccentric-*enhanced* resistance training may result in greater improvements in skeletal muscle strength and/or mass.[25, 51, 86, 87, 95] We are the first to report muscular strength and endurance responses to eccentric-*enhanced* resistance training, using multiple joint exercises.

Muscular Strength

Similar improvements were observed between groups for both chest (press) and leg (squat) muscular strength (kg), which is consistent with reports suggesting that eccentric-*enhanced* resistance training results in similar strength gains compared with traditional resistance training[17, 59] and in contrast to others indicating greater strength improvements following eccentric-*enhanced* resistance training.[25, 51, 86, 87, 95] In some studies, higher training volumes have been shown to result in larger improvements in muscular strength than lower training volumes, in untrained men;[18, 23, 148] while others report no differences between low and high volume protocols.[34, 147, 166] The relatively lower training volume performed by the eccentric-*enhanced* group may have resulted in compromised strength gains relative to the traditional group. Given that the eccentric-*enhanced* group showed similar improvements in muscular strength compared to the traditional group, despite having a lower training volume, eccentric-*enhanced* resistance exercise could be considered a more efficient mode of training, when total work is considered.

Results from a recent meta-analysis reveal that maximal strength gains are achieved at 60% 1RM, in previously untrained men;[148] however, strength gains have also been observed with exercise intensities below 50% 1RM, in untrained men.[56] In our study, the exercise intensity in the traditional group varied between 52.5-70% 1RM (similar to the suggested intensity), whereas the concentric and eccentric exercise intensities in the eccentric-*enhanced* group were ~40% and 100-120% 1RM throughout the duration of training, respectively. Therefore, it is also possible that optimal exercise intensities were not selected for the eccentric-*enhanced* group.

Additionally, both traditional and eccentric-*enhanced* resistance training may result in similar neural adaptations (e.g. improved motor unit recruitment and/or synchronization) associated with early-phase (<12 weeks) enhancements in muscular strength, as minimal muscle hypertrophy typically appears during this time frame.[29, 44, 55] Early-phase muscular strength adaptations following concentric-*only* resistance training are similar to[93, 158] or greater than[146] the adaptations following eccentric-*only* resistance training in some studies, while others report that eccentric-only resistance training results in greater early-phase muscular strength adaptations.[35, 49, 119, 130] Recall however that type IIa and IIx MHC mRNA have been shown to increase following four weeks of eccentric-*enhanced* resistance training, in untrained males;[51] suggesting that skeletal muscle hypertrophy and associated strength improvements may occur during early-phase resistance training. In our study, significant improvements in muscular strength were observed, without significant concomitant increases in lean mass; suggesting that neural adaptations, including enhanced motor unit recruitment and/or motor unit synchronization may be an important mechanism explaining our strength outcomes. However, alterations in muscle mass and assocoiated hypertrophy-related strength adaptations cannot be excluded as underlying factors in the muscular strength improvements observed in our study.

Muscular Endurance

Both training groups displayed similar improvements in muscular endurance following the five-week exercise intervention, despite dissimilar training volumes.

Friedmann and colleagues[51] (2004), observed improved endurance in traditional, but not eccentric-*enhanced* resistance training. Additionally, Marx et al.[127] (2001), reported that muscular endurance outcomes are related to training volume; which, if true, would indicate that the traditional group should have outperformed the eccentric-*enhanced* group. The lack of agreement between our outcomes and previous reports may be explained by the 1) differences in training volume and/or exercise intensity between groups, 2) presence of similar neural adaptations and resulting strength/endurance improvements between groups, 3) the length of the exercise intervention, and/or 5) the presence of delayed-onset muscle soreness in the eccentric-*enhanced* group.

Training Volume

Total training volume performed during exercise interventions has been shown to affect muscular performance outcomes,[18, 23, 127, 148] as well as hormonal[64, 111, 144] and metabolic responses.[96, 144] In our study, training volume was matched between groups during the standardized baseline testing sessions but was unmatched during the five-week exercise intervention. The disparity in training volumes between groups may be explained by delayed-onset muscle soreness (DOMS) symptoms, including 1) reduced muscular strength, 2) reduced muscle activation, 3) decreased range of motion (ROM), 4) impaired proprioception, and 5) increased muscular and connective tissue inflammation [33, 61, 137], and/or delayed leukocytosis or skeletal muscle myokines, such as interleukin (IL)-6 or IL-8,[80, 140, 141, 179] in the eccentric-*enhanced* group. In our study, cellular markers of inflammation were not measured, though a large percentage (>50%) of subjects in the eccentric-*enhanced* group reported (moderate to extreme) muscle soreness and impaired ROM following the initial eccentric-*enhanced* exercise bout and throughout the first week of exercise training, corresponding to the initial four exercise sessions. In contrast, no reports of muscle soreness occurred in the traditional group. Our findings are similar to previous reports, indicating that DOMS and its associated symptoms last 5-7 days following the initial eccentric exercise bout and may indicate the presence of acute muscular microtrauma and/or inflammation, thus reducing exercise capacity and associate performance improvements.[61]

Further, lactate accumulation has been associated with muscular fatigue during resistance exercise and may limit exercise performance.[149] Blood lactate concentrations have been shown to be greater during an exercise test performed two days after eccentric training;[57, 58] suggesting greater metabolic fatigue occurs following heavy eccentric training. Recall, before the onset of training, we observed a greater post-exercise lactate response in the eccentric-*enhanced* group, compared with the traditional group; therefore it is possible that a greater lactate response also occurred throughout the exercise intervention. Further, a positive relationship between lactate and RPE has been reported;[77, 117, 165] in our study RPE was greater during training sessions 1-4 in the eccentric-*enhanced* group, compared to the traditional group, lending support to the notion that greater lactate accumulation occurred during eccentric-*enhanced* training. These results suggest that the eccentric-*enhanced* group may have experienced greater metabolic fatigue throughout the exercise intervention, thus attenuating progression during resistance exercise compared to the traditional group.

Conclusion

Our study determined the early-phase (single session to five-week) metabolic, neuroendocrine, and performance responses to traditional and eccentric-*enhanced* resistance exercise in previously untrained individuals. We observed that short-term eccentric-*enhanced* resistance training results in similar neuroendocrine and performance responses as traditional resistance training, in college-age males. The lower training volume completed by the eccentric-*enhanced* group suggests that this form of training may be more efficient in eliciting both anabolic stimuli and muscular strength improvements than traditional resistance training, relative to training volume.

Clinical Implications

Determining the neuroendocrine, metabolic, and performance responses to various resistance training protocols may enable clinicians, therapists, and coaches to prescribe safe and effective training programs to both healthy and at-risk individuals. Although the results of our study indicate that traditional and eccentric-*enhanced* resistance training result in similar neuroendocrine and performance responses, each specific form of training may have population specific advantages. Theoretically, athletes who practice and/or compete above their lactate threshold (e.g. boxers, wrestlers, rowers, etc.) might benefit from eccentric-*enhanced* resistance training, as greater intracellular lactate buffering and/or delayed lactate accumulation may occur with this form of training.[84, 125] Additionally, strength trainers who have limited time to participate in resistance exercise may benefit from eccentric-*enhanced* resistance training, evidenced by the similar improvements in muscular strength which occurred at a lower training volume and time commitment (~66% less time to complete the eccentric-*enhanced* protocol) following this form of training.

Eccentric-*enhanced* resistance training may not be as appropriate for clinical populations (e.g. multiple sclerosis, muscular dystrophy, etc) that experience muscular fatigue, pain, and/or weakness associated with their condition. Eccentric-*enhanced* exercise has been show to result in moderate to extreme muscle soreness, thus limitations in mobility and muscular strength may occur at the onset of eccentric-*enhanced* resistance training. Clearly, further research is indicated to determine the specific effects of eccentric-*enhanced* resistance training in various populations.

Future Directions

Examining both the acute and chronic anabolic (e.g. total testosterone, bioavailable testosterone, growth hormone, insulin-like growth factor, mechano growth factor) and catabolic (e.g. adrenocorticotropic hormone, cortisol) hormone responses to eccentric-*enhanced* resistance training would improve current understanding of the neuroendocrine responses to resistance training. Additionally, given the influence of binding proteins on both the biological effects and measurement of testosterone, future studies designed to carefully measure the free, albumin-bound, and SHBG-bound fractions of testosterone are indicated. Further, evaluating androgen receptor expression and androgen affinity following resistance training would advance our understanding of skeletal muscle adaptations to resistance training. Moreover, determining the responses of cellular proteins that regulate skeletal muscle protein synthesis (e.g. mTOR, AKT, etc) and degredation (myostatin, ubiquitin proteasome pathway, etc) may advance current knowledge of the underlying mechanism(s) of muscular hypertrophy and/or atrophy.

Delayed onset muscle soreness (DOMS) is commonly experienced by individuals who perform resistance training and may be indicative of muscle injury. The underlying mechanism(s) of DOMS remain unclear; therefore, evaluating cellular markers of inflammation following heavy eccentric exercise may enhance our understanding of the skeletal muscle injury and repair process. Evaluating both the plasma and muscle tissue specific responses of creatine kinase, myoglobin, neutrophils, and various myokines such as IL-6 or IL-8, among others may provide valuable information for enhancing recovery from muscle injury or loss and/or reducing the muscle soreness associated with resistance training. Since, eccentric exercise induced muscle inflammation is a stimulus for satellite cell proliferation and associated muscle repair,[43, 145] evaluating satellite cell expression following eccentric-*enhanced* exercise may improve the understanding of skeletal muscle repair/regeneration.

Our data suggest that eccentric-*enhanced* exercise results in higher metabolic (lactate) responses and RPE values than traditional resistance exercise, in untrained individuals. Future research comparing metabolic (e.g. lactate, heart rate, VO_2, etc) and RPE responses between traditional and eccentric-*enhanced* resistance protocols would improve our current understanding of fatigue and exertion as they relate to resistance exercise. Additionally, evaluating intracellular lactate buffering mechanisms, motor unit recruitment patterns, and blood flow characteristics during eccentric-*enhanced* resistance exercise may provide insight into the mechanism(s) underlying lactate accumulation.

We reported that eccentric-*enhanced* resistance training provides a means of improving early-phase muscular performance in previously untrained college-age males. Future research designed to directly control intensity and volume between exercise protocols is warranted and would clarify the muscular strength responses to resistance exercise. Additionally, evaluating long-term (>12 weeks) adaptations to eccentric-*enhanced* training may allow the individual neural and hypertrophic dependent mechanisms of muscular strength enhancement to be more clearly understood. Overall, research examining the interrelationship between exercise intensity, volume, and/or training status would contribute to a more complete understanding of the neuroendocrine, metabolic, and muscular performance responses to resistance exercise.

Several studies have evaluated the effects of eccentric-*enhanced* resistance training in healthy college-age males; however, few studies have evaluated the performance responses in other populations. Skeletal muscle atrophy, reduced strength, and increased fatigue are associated with aging and degenerative diseases such as multiple sclerosis and muscular dystrophy, thus determining the effects of eccentric-*enhanced* resistance training in at-risk populations may benefit clinicians and therapists in devising safe and effective exercise protocols to reduce the deleterious effects of disease on muscle. Additionally, both athletes and recreational weight lifters utilize resistance training to improve muscular strength and mass; thus determining the performance responses to eccentric-*enhanced* resistance training in both athletes and previously trained individuals would enhance current knowledge related to the long-term training adaptations to this form of exercise.

APPENDIX A
HEALTH HISTORY QUESTIONNAIRE

SUBJECT # _____________ Date of Birth :_____________

Height _____ Weight ______ Blood Pressure Measurement:______ /______

Do you currently have any of the following conditions or has a medical doctor ever informed you that you have any of the following conditions?

1. Diabetes mellitus Yes / No
2. High blood pressure Yes / No
3. Osteoporosis Yes / No
4. A heart condition Yes / No
5. High cholesterol Yes / No
   If Yes, do you know your cholesterol numbers? ______________________
6. Thyroid problems Yes / No
7. Kidney disease Yes / No
8. Liver disease Yes / No

Please answer the following questions regarding your general health:

1. Do you feel pain or pressure in your chest, neck shoulders, or arms during or after physical activity? Yes / No
2. Do you ever lose your balance because of dizziness Yes / No
3. Do you ever lose consciousness? Yes / No
4. Do you consider yourself to be generally healthy? Yes / No
5. Do you currently smoke? Yes / No

6. Are you a former smoker? Yes / No
   If Yes, how long has it been since you quit smoking? ____________________

7. Have you ever had an adverse reaction during or following a blood donation? Yes / No

8. Do you mind having blood draws? Yes / No
9. Do you currently have an injury to any area in your upper or lower body? Yes / No
   If Yes, please explain the injury: ______________________________________
   ____
   ____

10. Are there any other health related issues we should know about? ___________
   ____
   ____

Are you <u>currently</u> taking any of the following products or have you taken them in the previous 2 months?

1. Anabolic steroids Yes / No

2. Creatine Yes / No

3. Protein powder Yes / No

4. Other Yes / No
   If Yes, please list the specific supplements:____________________________
   ____
   ____

Please list all of the <u>supplements</u> you are currently taking (including vitamins):

Item name Amount taken per day Length on supplement Reason

a.____

b.____

c.____

Please list all of the __prescription medication__ you are currently taking

Medicine Amount taken per day Length on medication Reason

a.____

b.____

c.____

APPENDIX B
PHYSICAL ACTIVITY AND DIETARY QUESTIONNAIRE

PHYSICAL ACTIVITY & DIETARY QUESTIONNAIRE

Subject #:______________________

Please answer the following questions regarding your current exercise participation and dietary habits:

1. Do you currently participate in weight lifting? Yes / No
   If Yes, how often and how much resistance exercise do you perform:
   ____
   ____

2. During the past two years have you participated in either bodybuilding or powerlifting? Yes / No

3. Do you currently perform aerobic exercise? Yes / No

   If Yes:
   How many times per week _____________________________________

   How long do you perform cardio each session _______________________

   What type of exercise (running, biking, etc) _________________________

   How intense (mild, moderate, high) ______________________________

4. Do you currently perform any recreational sports activity or participate in any physical activity? Yes / No

   If Yes:
   How many times per week _____________________________________

   How long do you perform cardio each session _______________________

   What type of exercise (running, biking, etc) _________________________

   How intense (mild, moderate, high) ______________________________

5. Are you currently on a diet, including a low calorie, low fat, high protein, or a low carbohydrate diet? Yes / No
   If Yes, please explain your diet:
   ____
   ____

APPENDIX C
LIST OF EXCLUDED NUTRITIONAL SUPPLEMENTS

Subjects were excluded from this study if they had consumed any of the following nutritional supplements within 1 month from beginning the study:

1. Creatine
2. Ephedra
3. Dehydroepiandrosterone (DHEA)
4. Tribulus Terresteris
5. ZMA™
6. Androstendione
7. GAKIC
8. Any other nutritional supplement/ergogenic aid that is intended to enhance exercise performance
9. Any other nutritional supplement that has been demonstrated to affect hormonal levels

APPENDIX D
DIETARY RECORD

SUBJECT #____________ SESSION #_____________

Please record what you eat and drink for the entire day. Please be as specific as possible for serving size, how food is prepared, and amount of each serving.

Time	**Food/Drink**	**Brand Name/Restaurant**	**Serving Size**

APPENDIX E

POWER CALCULATIONS

Ahtiainen et al.[8] 2004 (N=8)

Pre Exercise Growth hormone concentrations: 0.1 ± 0.2 μg/L
Post Exercise: 15.9 ± 9.9 μg/L

n per group = $2[(Z\alpha - Z\beta)\sigma/(u_1 - u_2)]^2$

$Z\alpha$ = alpha level for two tailed Z
$Z\beta$ = lower one-tailed Z value that is related to β
σ = maximum variance
$u_1 - u_2$ = difference between mean 1 and 2

$n = 2[(1.96 + 0.84)(9.9)/(15.9)]^2$

= 2(3.08) = 6.16 subjects
so, 7 subjects per group or 14 total subjects

Power = 0.80
Significance = 0.05

APPENDIX F
PLASMA VOLUME FLUCTATIONS FOLLOWING EXERCISE

Table 6. Percent plasma volume fluctuations following traditional and eccentric-*enhanced* resistance training.

	PLASMA VOLUME	TRADITIONAL GROUP	ECC-*ENHANCED* GROUP
TRADITIONAL RESISTANCE EXERCISE TESTING	Baseline	100 %	100 %
	Immediately Post Exercise	-7.8% ± 2.3*	-5.3% ± 1.8*
	15 Minutes Post Exercise	-1.9% ± 2.1	-1.2% ± 1.6
	30 Minutes Post Exercise	-0.4% ± 2.6	+2.4% ± 1.2
	45 Minutes Post Exercise	+5.1% ± 3.1	+1.1% ± 1.1
	60 Minutes Post Exercise	+3.5% ± 2.8	+1.3% ± 2.3
BASELINE TRADITIONAL VS. ECC-	Baseline	100%	100%
	Immediately Post Exercise	-6.5% ± 2.9*	-8.1% ± 1.6*
	15 Minutes Post Exercise	+6.2% ± 2.6	+4.3% ± 2.0
	30 Minutes Post Exercise	+2.9% ± 3.1	+4.1% ± 2.1
	45 Minutes Post Exercise	+7.8% ± 2.2*	+4.5% ± 1.9*
	60 Minutes Post Exercise	+2.7% ± 3.1	+4.5% ± 2.2
POST-INTERVENTION TRADITIONAL	Baseline	100%	100%
	Immediately Post Exercise	-11.0% ± 1.1*	-10.6% ± 1.8*
	15 Minutes Post Exercise	-2.5% ± 1.9	-1.9% ± 1.9
	30 Minutes Post Exercise	+2.1% ± 1.3	+1.9% ± 1.8
	45 Minutes Post Exercise	+3.3% ± 1.7	+2.0% ± 2.1
	60 Minutes Post Exercise	+0.9% ± 0.8	+1.0% ± 2.0

* Indicates significant difference from corresponding baseline value ($p<0.05$). Data are presented as Mean Change ± SE.

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BIOGRAPHICAL SKETCH

Joshua F. Yarrow was born in Aurora, Illinois. He moved to Phoenix, Arizona, in 1986 with his family. In 1997, Joshua graduated from Horizon High School, in Scottsdale, Arizona. He started his college career at Paradise Valley Community College in Phoenix, Arizona, in August 1997. One year later, he transferred to Arizona State University where he completed his bachelor's degree in exercise science in May 2000. In May 2002, he received a master's degree in exercise and wellness at Arizona State University. In August 2002, he began his doctoral degree in sports medicine/athletic training with a minor in human nutrition at the University of Florida.